



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 $\leq 50\%$ 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 $>27 \text{ kg/m}^2$ 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 anti-drug 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.

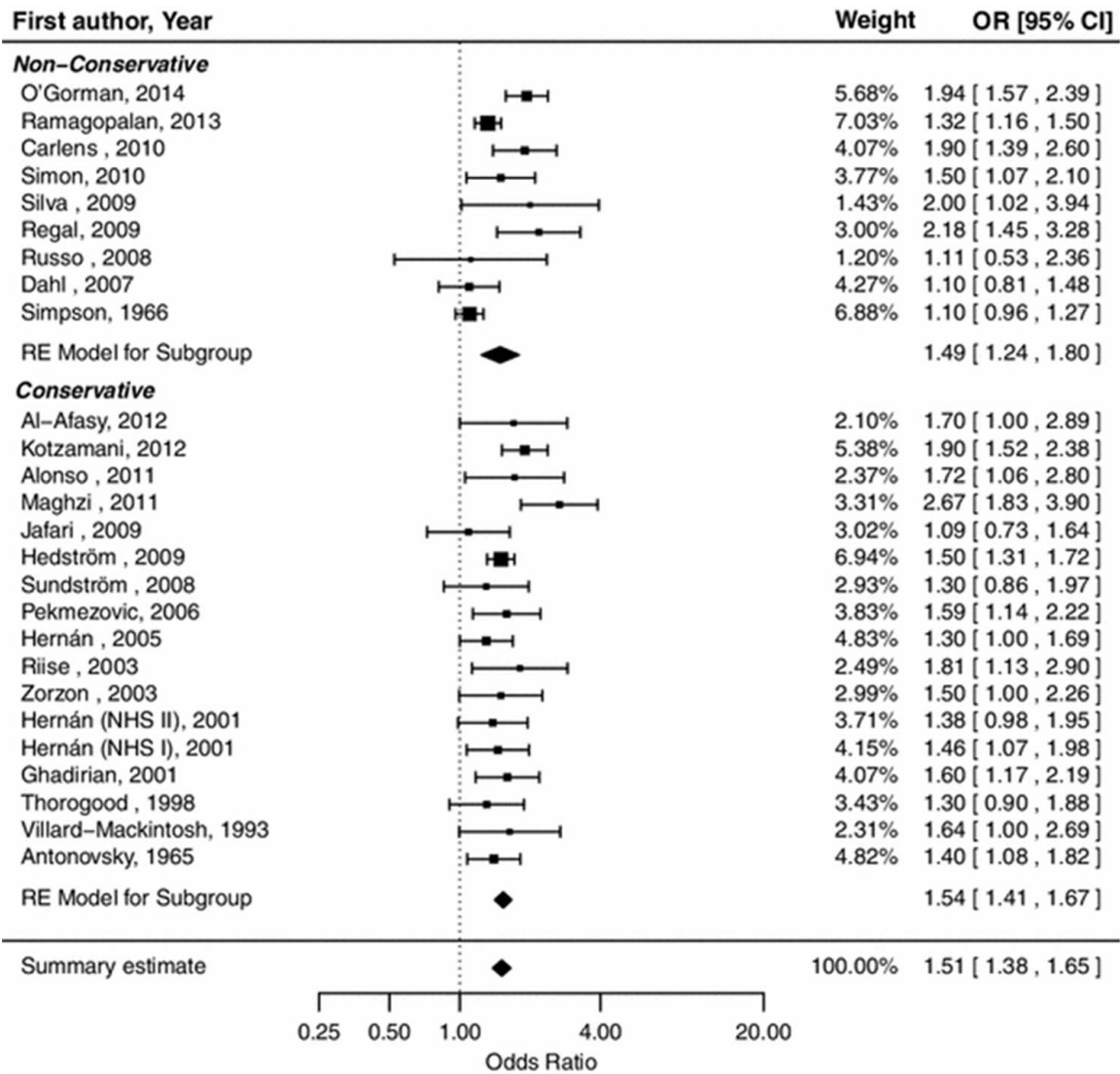
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Boston,
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Figure 1. Meta-analysis of the Association Between Smoking and Multiple Sclerosis



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.

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- 50th American Society of Clinical Oncology 2014 Annual Meeting Science & Society**
May 30–June 3 • Chicago, Illinois, USA
- American Academy of Neurology**
April 28–May 3 • Philadelphia, Pennsylvania, USA
- American Academy of Ophthalmology 2014**
May 18–21 • Chicago, Illinois, USA
- American Academy of Orthopaedic Surgeons**
March 11–15 • New Orleans, Louisiana, USA
- American Academy of Otolaryngology-Head and Neck Surgery Foundation Annual Meeting & OTO EXPO**
September 21–24 • Orlando, Florida, USA
- American Association for the Study of Liver Disease**
November 4–7 • Boston, Massachusetts, USA
- American Association of Diabetes Educators**
August 6–9 • Orlando, Florida, USA
- American College of Cardiology 63rd Annual Scientific Session & Expo***
March 29–31 • Washington, DC, USA
- American College of Chest Doctors**
October 25–30 • Austin, Texas, USA
- American College of Emergency Physicians (ACEP14)**
October 27–30 • Chicago, Illinois, USA
- American College of Rheumatology 78th Annual Scientific Meeting**
November 13–18 • Boston, Massachusetts, USA
- American Congress of Obstetricians and Gynecologists 2014 Annual Clinical Meeting**
April 26–30 • Chicago, Illinois, USA
- American Diabetes Association 74th Scientific Sessions***
June 13–17 • San Francisco, California, USA
- American Heart Association Scientific Sessions 2014***
November 15–19 • Chicago, Illinois, USA
- American Orthopaedic Society for Sports Medicine***
July 10–13 • Seattle, Washington, USA
- American Psychiatric Association 2014 Annual Meeting**
May 3–7 • New York, New York, USA
- American Psychiatric Nurses Association**
October 22–25 • Indianapolis, Indiana, USA
- American Society for Microbiology—54th Interscience Conference on Antimicrobial Agents and Chemotherapy***
September 5–19 • Washington, DC, USA
- American Society for Radiation Oncology**
September 14–17 • San Francisco, California, USA
- American Society for Surgery of the Hand**
September 18–20 • Boston, Massachusetts, USA
- The American Society of Hematology**
December 6–9 • San Francisco, California, USA
- American Society of Nutrition Scientific Sessions & Annual Meeting at Experimental Biology 2014**
April 26–30 • San Diego, California, USA
- American Society of Plastic Surgeons Plastic Surgery The Meeting 2014**
October 10–14 • Chicago, Illinois, USA
- American Stroke Association 2014 International Stroke Conference***
February 11–14 • San Diego, California, USA
- American Thoracic Society 2014 Annual Meeting***
May 16–21 • San Diego, California, USA
- American Veterinary Medical Association**
July 25–29 • Denver, Colorado, USA
- Cardio Alex 2014**
June 10–13 • Alexandria, Egypt
- Care for Acute Cardiovascular Conditions**
October 18–20 • Geneva, Switzerland
- Caribbean Cardiac Society 29th Caribbean Cardiology Conference 2014**
July 23–July 26 • Atlantis, Paradise Island, The Bahamas
- Cardiostim EHRA Europace 2014***
June 23–26 • Nice, France
- The Endocrine Society—ICE/ENDO 2014**
June 21–24 • Chicago, Illinois, USA
- ESMO World Congress on Gastrointestinal Cancer**
June 25–28 • Barcelona, Spain
- European Association for the Study of Diabetes 49th Annual Meeting***
September 15–19 • Vienna, Austria
- European Committee for Treatment and Research in Multiple Sclerosis**
September 10–13 • Boston, Massachusetts, USA
- European League Against Rheumatism 2014 Annual Congress**
June 11–14 • Paris, France
- European Lung Cancer Conference**
March 26–29 • Geneva, Switzerland
- European Society of Cardiology ESC Congress 2014***
August 30–September 4 • Barcelona, Spain
- European Society of Cardiology EuroEcho 2014**
December 3–6 • Vienna, Austria
- European Society of Hypertension 2014 Annual Scientific Meeting***
June 13–16 • Athens, Greece
- European Society of Medical Oncology**
September 26–30 • Madrid, Spain
- European Society Traumatology, Knee Surgery, and Arthroscopy**
May 14–17 • Amsterdam, The Netherlands
- Heart Failure 34th Annual Scientific Sessions**
May 17–20 • Athens, Greece
- Heart Rhythm Society 34th Annual Scientific Sessions***
May 7–10 • San Francisco, CA, USA
- International Federation of Foot and Ankle Surgery/American Orthopaedic Foot & Ankle Society***
September 19–23 • Chicago, Illinois, USA
- Kidney Week**
November 5–10 • Atlanta, Georgia, USA
- Movement Disorder Society**
June 9–12 Stockholm, Sweden
- North American Spine Society**
November 12–15 • San Francisco, California, USA
- Obesity Week**
November 2–7 • Boston, Massachusetts, USA
- Orthopaedic Trauma Association**
October 15–18 • Tampa, Florida, USA
- Radiological Society of North America**
November 30–December 5 • Chicago, Illinois, USA
- The Society for Cardiovascular Angiography & Interventions (SCAI)**
May 28–31 • Las Vegas, NV, USA
- Transcatheter Cardiovascular Therapeutics 2014 Interventional Conference**
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