

Overcoming MS

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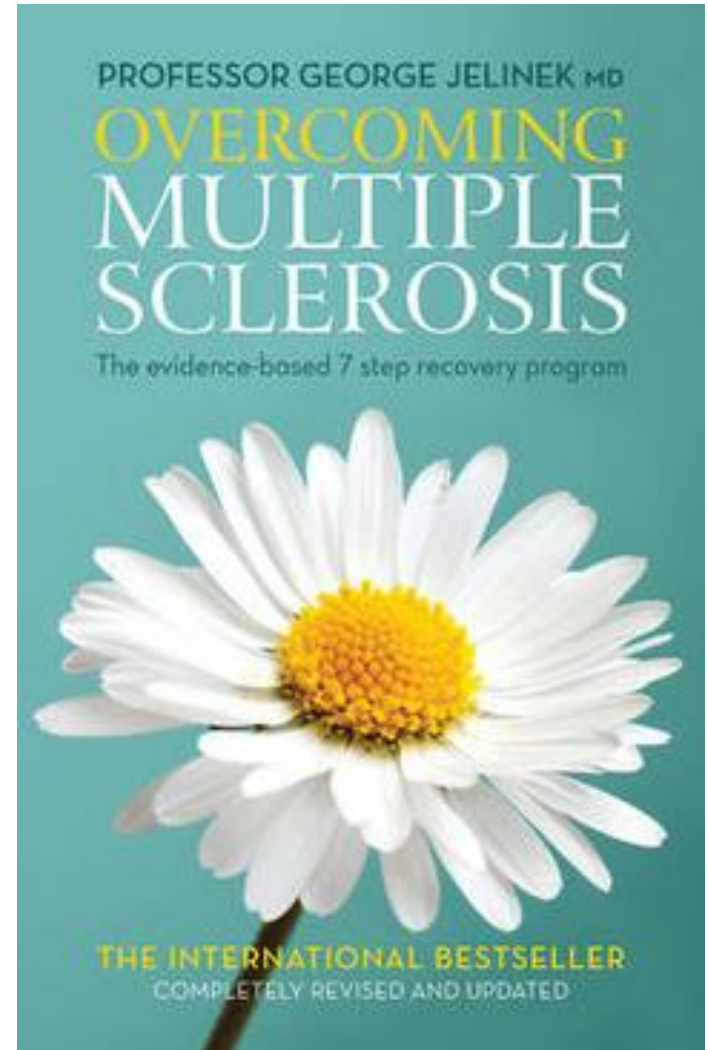
“Overcoming MS”

- Prof George Jelinek
- Lifestyle and self-help therapies for MS
 - Jelinek G, Hassed CS. Managing multiple sclerosis in primary care: are we forgetting something ? Qual Prim Care 2009;17(1):55-61.



Overcoming MS

- “This is a book that all patients with multiple sclerosis should read and use as a platform for discussion with their neurologist.”
 - Professor Peter Silbert MBBS
FRACP: State Director of Neurology
in W.A., Head of Dept. of Neurology,
Royal Perth Hospital



Seven step program

1. Diet
2. Sunlight / vitamin D
3. Exercise
4. Meditation
5. Medication
6. Prevention in family members
7. Change your life, for life
 - <https://overcomingms.org>

Lifestyle and MS

- Study on 5-day residential retreat for people with MS (based on Prof Jelinek's Overcoming MS program) promotes lifestyle modification within a patient-centred model of care
- Analysis of the health-related quality of life (HRQOL) of the retreat participants was undertaken using the MSQOL-54, prior to attendance, 1 and 5 years after the retreat
- 274 retreat participants (71%) completed baseline questionnaires
 - Hadgkiss EJ, Jelinek GA, Weiland TJ, et al. Health-related quality of life outcomes at 1 and 5 years after a residential retreat promoting lifestyle modification for people with multiple sclerosis. *Neurol Sci* DOI 10.1007/s10072-012-0982-4

Lifestyle and MS

- Participants demonstrated clinically and statistically significant improvements in HRQOL
- At 1 year median improvements of 11.3% in overall QoL
 - 18.6% in the physical health
 - 11.8% in the mental health
- At 5 years there was a 19.5% median improvement in overall QoL compared to baseline
 - 17.8% in the physical health
 - 22.8% in the mental health
- “Non-drug therapies should be considered as part of any comprehensive treatment plan for people with MS.”
 - Hadgkiss EJ, Jelinek GA, Weiland TJ, et al. Health-related quality of life outcomes at 1 and 5 years after a residential retreat promoting lifestyle modification for people with multiple sclerosis. *Neurol Sci* DOI 10.1007/s10072-012-0982-4

Lifestyle and QoL

- Health-related quality of life (QOL) is a key outcome for people with multiple sclerosis (MS)
 - Patient-reported data from 2312 people with MS explored associations of socio-demographic, therapeutic and lifestyle factors with QOL, using the Multiple Sclerosis Quality of Life-54 (MSQOL-54)
 - Controlling for socio-demographic factors and disability, factors associated with better physical health composite (PHC) (on a 100 point scale) were:
 - moderate and high physical activity compared to low (5.9 and 9.9 pts higher score)
 - non-smoking compared to current smoking (4.6 pts)
 - better diet (/10 pts on the 100 pt Diet Habits Questionnaire scale (DHQ) 1.6 pts)
 - normal body mass index (BMI) versus overweight or obese (2.1 points and 2.4 pts)
 - fewer comorbidities (4.4 pts)
 - not taking a disease-modifying drug (DMD) (2.1 pts)
- Jelinek GA, De Livera AM, Marck CH, Brown CR, Neate SL, Taylor KL, Weiland TJ. Lifestyle, medication and socio-demographic determinants of mental and physical health-related quality of life in people with multiple sclerosis. BMC Neurol. 2016 Nov 22;16(1):235.

Lifestyle and QoL

- Better mental health composite (MHC) determinants were:
 - moderate and high physical activity compared to low (4.0 points and 5.7 points)
 - non-smoking compared to current (6.7 points)
 - better diet (2.8 points)
 - normal BMI versus overweight or obese (3.1 points and 3.5 points)
 - meditating regularly (2.2 points)
 - no DMD use (2.9 points)
- While causality cannot be concluded from cross-sectional data, the associations between modifiable lifestyle factors and QOL suggest significant potential for secondary prevention of the known deterioration of QOL for people with MS through lifestyle risk factor modification.
 - Jelinek GA, De Livera AM, Marck CH, Brown CR, Neate SL, Taylor KL, Weiland TJ. Lifestyle, medication and socio-demographic determinants of mental and physical health-related quality of life in people with multiple sclerosis. *BMC Neurol.* 2016 Nov 22;16(1):235.

MS, lifestyle and depression

- Depression is the most common co-morbidity and greatest impact on quality of life for people with Multiple Sclerosis (MS)
- Study of 2,459 people with MS on association b/w lifestyle risk factors, medication and depression risk
- Approximately one fifth (19.3%) screened positive for depression
- Analyses showed that poor diet, low levels of exercise, obesity, smoking, marked social isolation and taking interferon were associated with greater depression risk
- Participants who supplemented with omega 3s, particularly flaxseed oil, had frequent fish consumption, supplemented with vitamin D, meditated, and had moderate alcohol consumption had significantly reduced depression risk
 - Taylor KL, Hadgkiss EJ, Jelinek GA, Weiland TJ, Pereira NG, Marck CH, and van der Meer DM. Lifestyle factors, demographics and medications associated with depression risk in an international sample of people with multiple sclerosis. BMC Psychiatry 2014, 14:327 doi:10.1186/s12888-014-0327-3

Fatigue and MS

- Study on international sample of 2469 people with MS
- Increased odds of fatigue associated with:
 - Obesity
 - DMD use
 - Poor diet
- Reduced odds of fatigue with:
 - Exercise
 - Fish consumption
 - Moderate alcohol use
 - Supplementation with vit. D and flaxseed oil
 - Weiland TJ, Jelinek GA, Marck CH, et al. Clinically significant fatigue: prevalence and associated factors in an international sample of adults with multiple sclerosis recruited via the internet. PLoS One. 2015 Feb 18;10(2):e0115541. doi: 10.1371/journal.pone.0115541.

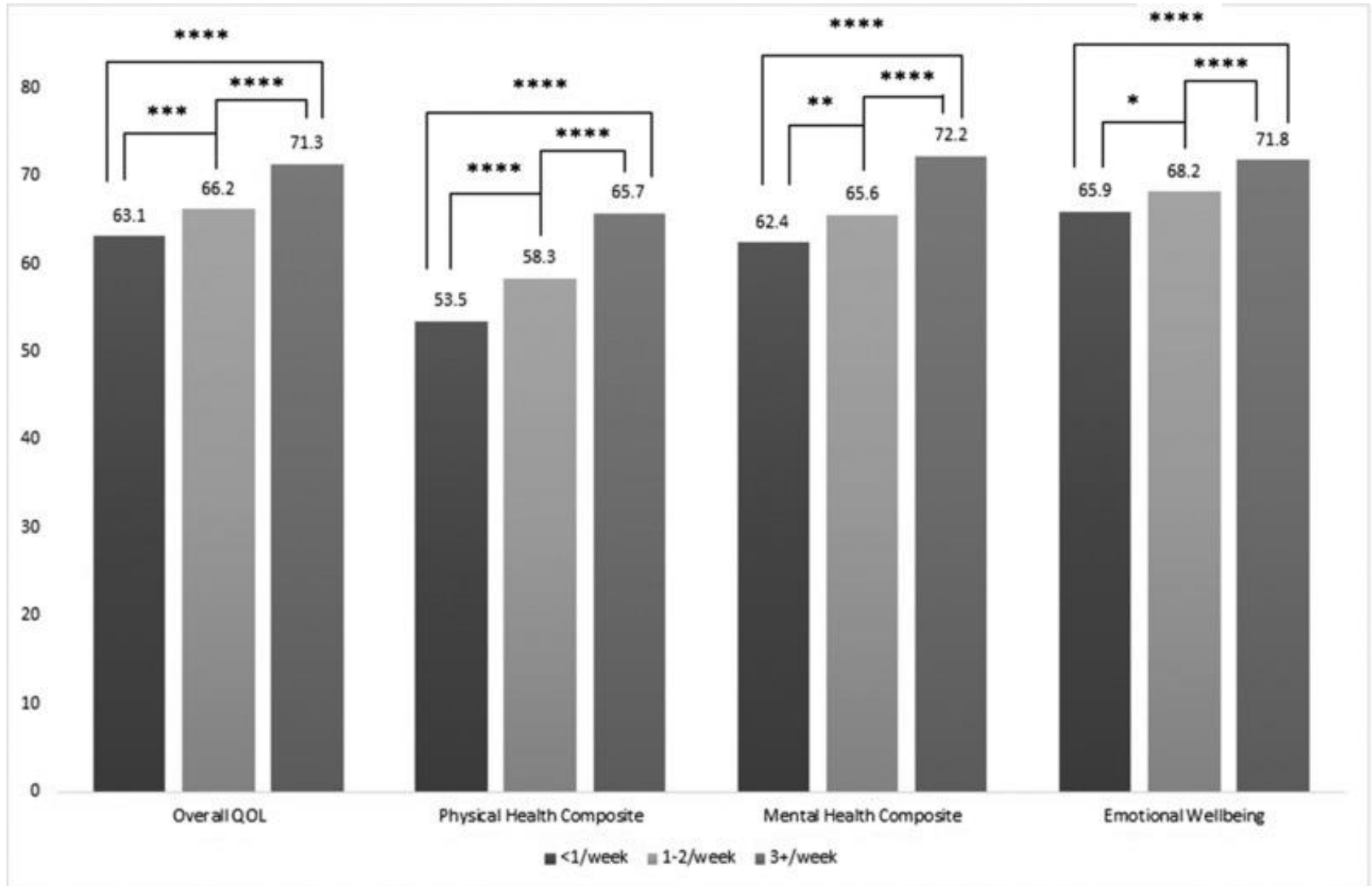
Nutrition and MS

- Prospective study on dietary intervention for MS
- Over 34-year f/up, when other causes of death were excluded, only 31% of MS patients put on a low fat diet (less than 20g/day) had died compared to 80% of MS patients on a higher fat diet
- Rates of disability and progression of the disease were vastly different in the two groups.
 - Swank R. Lancet. 1990;336(8706):37-9.
 - Swank R. Nutrition. 1991;7(5):368-76.

Cow's milk and MS

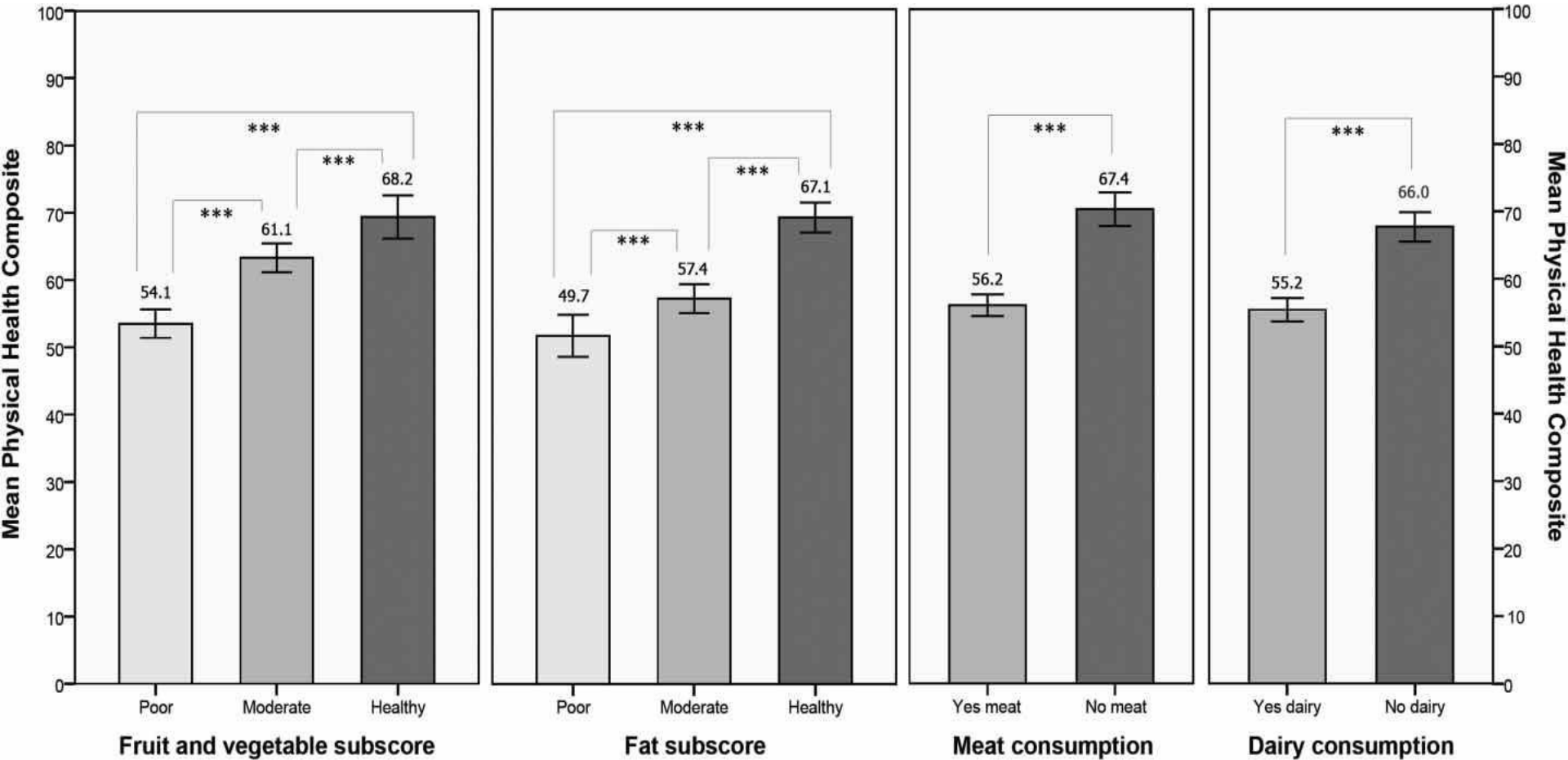
- Long known association of MS with cow's milk consumption
- A number of cow's milk proteins are targeted by the immune cells of people with MS
- Antigens on myelin sheath resemble certain segments of cow's milk protein
- Cow's milk proteins have been associated with other autoimmune diseases e.g. type 1 diabetes
 - Malosse D, Perron H, Sasco A, Seigneurin JM. Neuroepidemiology 1992; 11:304-12.
 - Winer S, Astsaturon I, Cheung RK, et al. J Immunol 2001;166(7):4751-6.
 - Stefferl A, Schubart A, Storch M, et al. J Immunol 2000; 165:2859-65.

Omega-3 f.a. and MS



Diet and MS

- Hadgkiss EJ, Jelinek GA, Weiland TJ, et al. The association of diet with quality of life, disability, and relapse rate in an international sample of people with multiple sclerosis. *Nutritional Neuroscience* 2014, in press.



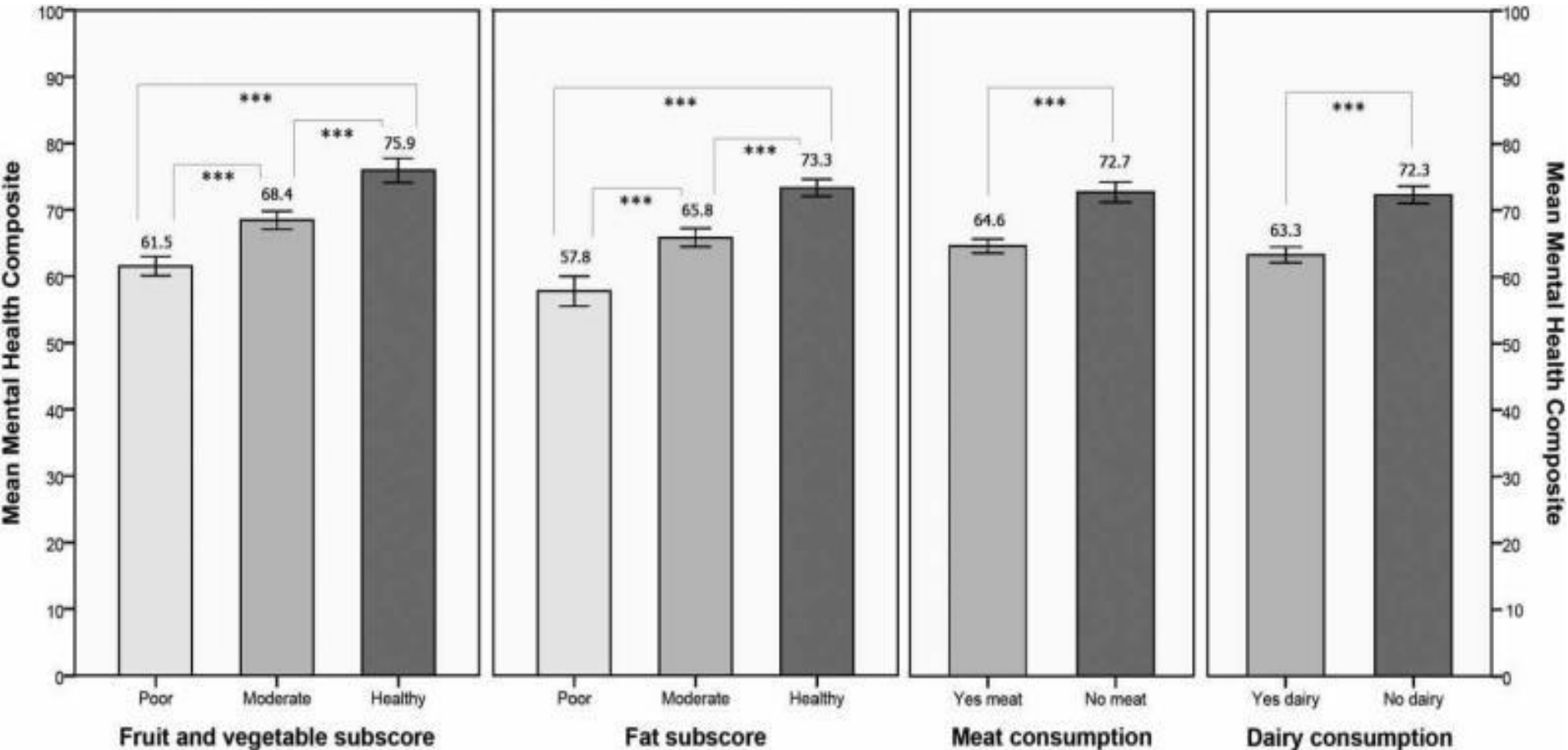
95% Confidence Interval

ANOVA Groupwise comparisons: all $p < 0.001$

*** $p < 0.001$

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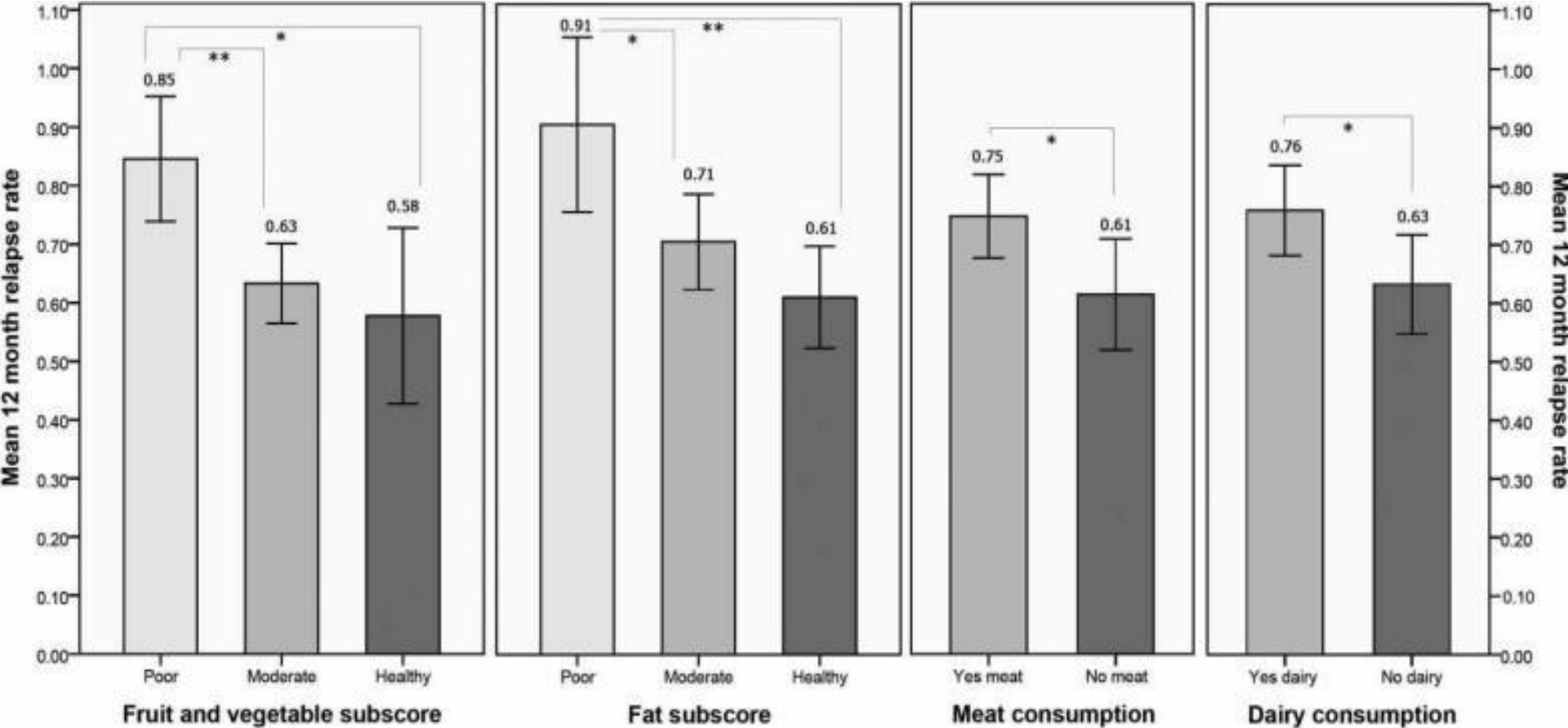
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Diet and MS

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95% Confidence Interval
ANOVA Groupwise comparisons, $p \leq 0.002$
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Environment

- Countries with less sunshine have significantly higher incidence of MS
 - Hayes C. Proc Nutrition Society. 2000;59(4):531-5.
- Benefits may be due to direct effects of sunlight on immune function, melatonin and vitamin D
 - Hutter C. Medical Hypotheses 1996;46(2):67-74.
 - Green M et al. J Epidemiology. 1999;9(6 Suppl):S48-57.
- Death from MS halved for those with higher residential sun exposure and one quarter for those with high residential and occupational exposure
 - Freedman D et al. Occ Environ Med 2000;57(6):418-21.

Vitamin D and MS

- “There is compelling evidence that vitamin D is not only a risk factor for central nervous system (CNS) demyelinating disease (namely MS) but also seems to modify both the inflammatory and neurodegenerative elements of the disease, with large-scale treatment trials underway.”
 - Burton JM, Costello FE. Vitamin d in multiple sclerosis and central nervous system demyelinating disease-a review. *J Neuroophthalmol*. 2015 Jun;35(2):194-200. doi: 10.1097/WNO.0000000000000256.

Sunlight and vitamin D

- UV rays falling on the skin required to convert vitamin D to the active form
- Roughly 10-15 minutes of sunlight to most of the body on a day with UV index 7 (moderate) produces 10 000IU of Vitamin D, and optimal immune system modulation
- Sunscreens and glass filter out useful UV rays
- Message
 - Avoid sunburn, strong sun and sun-baking – Slip, Slop, Slap
 - Have regular moderate sun exposure

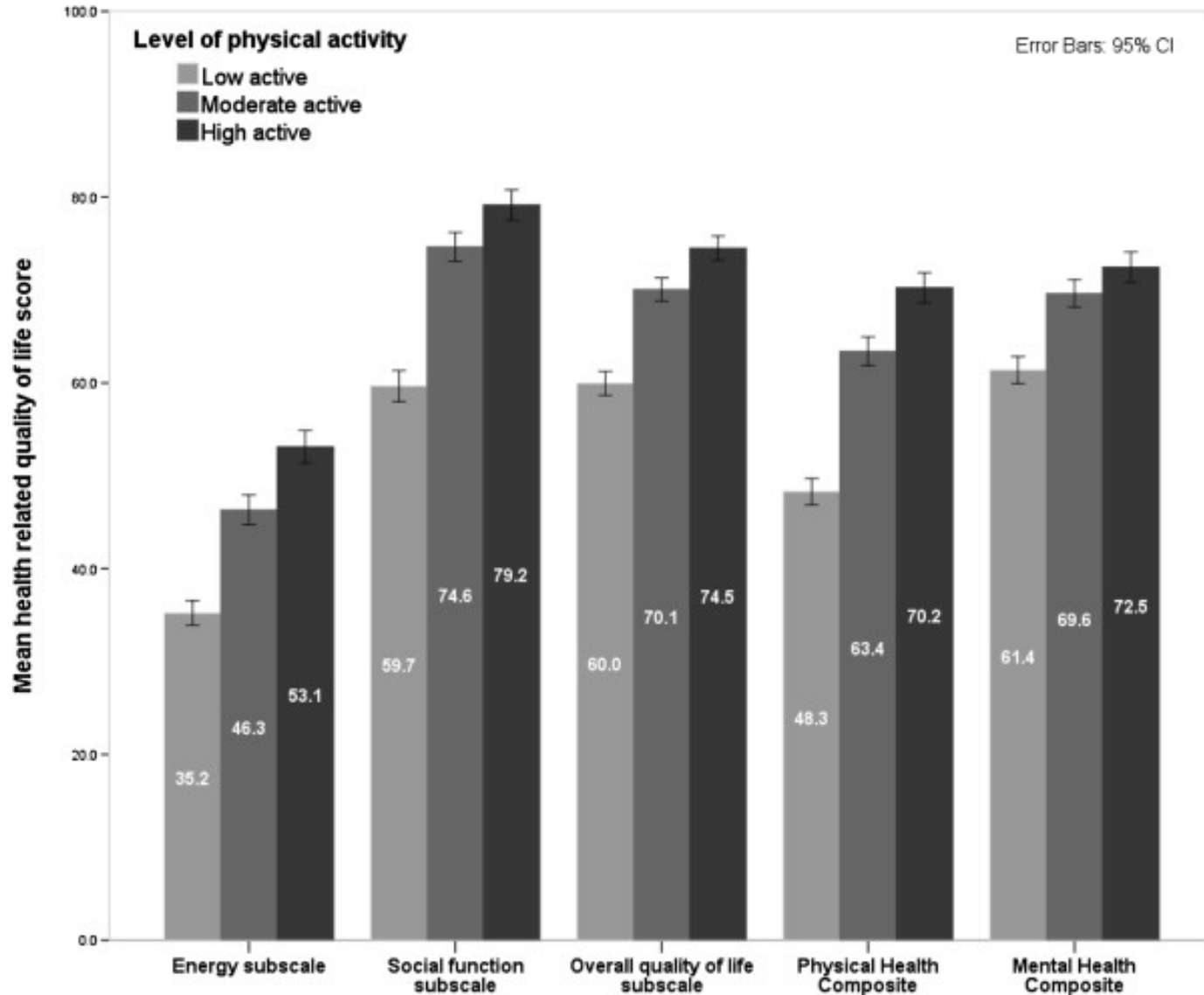
Exercise

- Improvement in fatigue
 - Oken B. Neurology. 2004;62(11):2058-64.
- Increased general fitness and strength
- Reduced disability
 - Patti F. et al. J Neurology 2003;250(7):861-6.
- Better mood and coping
- Better balance, less falls and fractures
- Social interaction
- Outdoor activities
- Improved immune function
- Anti-inflammatory effect

MS and exercise

- US study of MS patients showed that exercise slowed the progression of disability as well as improving quality of life
- Getting into a cycle of disability leading to inactivity leading to greater immobility exacerbates the problem
 - Stuifbergen AK, Blozis SA, Harrison TC, et al. Exercise, functional limitations, and quality of life: A longitudinal study of persons with multiple sclerosis. Arch Phys Med Rehabil 2006; 87:935-943.

Physical activity and MS



Stress, immunity and MS

- PNI mechanisms explain relationships between psychological states, immunity and autoimmune conditions
- Those who have higher (SNS) reactivity to stress (increased blood pressure, heart rate, catechol hormones related to adrenaline) also have the greatest disturbance to immunity
- During high stress periods there is a shift towards the type-2 response (immune 'dysregulation')
 - Explains the increased incidence of infections, latent viral expression, allergic conditions and, importantly, autoimmune conditions
 - O'Leary A. Psychological Bulletin 1990;108(3):363-82.
 - Marsland AL. Bachen EA. Cohen S. et al. Physiology & Behavior. 2002;77(4-5):711-6.
 - Marshall GD Jr. Agarwal SK. Lloyd C. et al. Brain, Behavior, & Immunity. 1998;12(4):297-307.

PNI and MS

- Patients who have major depressive disorder show increases in pro-inflammatory cytokine activity and inflammation
- Inflammation of the central nervous system is a pathologic hallmark of multiple sclerosis (MS)
- Patients affected by MS also show a high incidence of depression and some aspects of depression and fatigue in MS may be linked to inflammatory markers
- Sickness behavior model may be applied to investigate depressive symptoms in inflammatory neurologic diseases like MS
 - Gold SM, Irwin MR. Depression and immunity: inflammation and depressive symptoms in multiple sclerosis. *Immunol Allergy Clin North Am.* 2009 May;29(2):309-20. doi: 10.1016/j.iac.2009.02.008.

Stress Management

- Cardiovascular reactivity of MS patients determined
 - 42% of life events assoc. with exacerbations in 6/52
 - Exacerbations more likely following life events
 - Independent of threat level and type of stressor
 - Autonomic tone and stress reactivity predictive
 - Higher CV reactivity predicted greater number of exacerbations and proportion of weeks ill
 - Ackerman et al. Brain Behav Immun. 2003;17(3):141-51.
- Chronic stress assoc. with significant increase in the number and severity of MS exacerbations
 - Mohr DC et al. BMJ. 2004;328(7442):731.

Stress and MS lesions

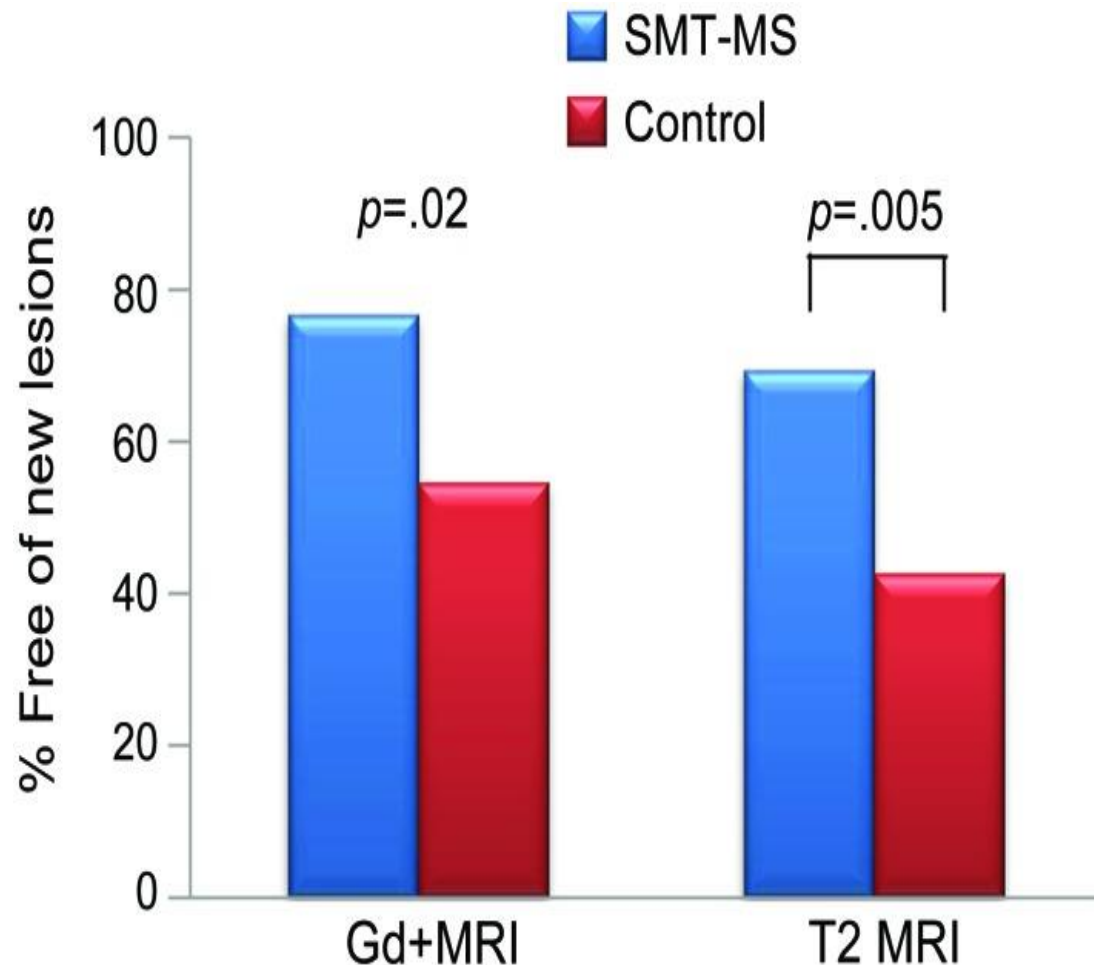
- Study on whether different types of stressful events and perceived stress predict the development of MS brain lesions
- Patients with MS followed for 48 weeks during a RCT comparing stress management therapy for MS (SMT-MS) to a waitlist control (WLC)
- MRI scans every 8 weeks to measure brain lesions
- Monthly interviews measured stressful life events and self-report measures of perceived stress, anxiety and depression
- Participants classified stressful events as positive or negative
 - Burns MN, Nawacki E, Kwasny MJ, Pelletier D, Mohr DC. Do positive or negative stressful events predict the development of new brain lesions in people with multiple sclerosis? Psychol Med. 2013 May 17:1-11.

Stress and MS lesions

- Positive stressful events predicted halved risk for lesions in the control group (OR 0.53 for each additional positive stressful event) and less risk for new or enlarging lesions regardless of group assignment (OR 0.74)
- Major negative stressful events predicted lesions (OR 1.77) and new or enlarging lesions (OR 1.57) whereas moderate negative stressful events, perceived stress, anxiety and depressive symptoms did not
 - Burns MN, Nawacki E, Kwasny MJ, Pelletier D, Mohr DC. Do positive or negative stressful events predict the development of new brain lesions in people with multiple sclerosis? Psychol Med. 2013 May 17:1-11.

Stress management and new MS lesions

- Percent of participants free of gadolinium-enhancing (Gd+) and T2 lesions by treatment group during 24-week treatment period
- SMT-MS = stress management therapy for multiple sclerosis.
 - Mohr DC, Lovera J, Brown T, et al. A randomized trial of stress management for the prevention of new brain lesions in MS. *Neurology*. 2012 July 31;79(5):412-419.



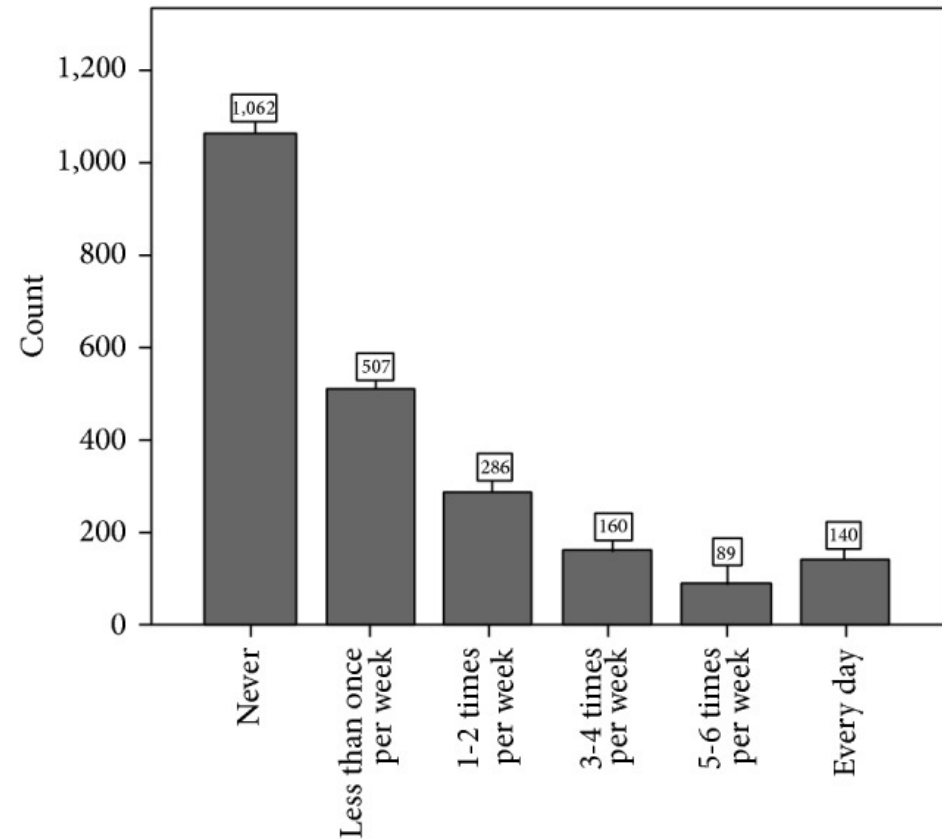
Stress management and MS

- RCT of relapsing-remitting MS patients randomly assigned to undergo either an 8-week stress management program (relaxation breathing and progressive muscle relaxation, twice a day) or not
- Outcomes measured: perceived stress, health locus of control, anxiety, and depression
- Perceived stress and symptoms of depression significantly decreased after 8 weeks of relaxation
- Reduced number of weekly symptoms and the mean intensity per symptom
 - Artemiadis AK, Vervainioti AA, Alexopoulos EC, et al. Stress management and multiple sclerosis: a randomized controlled trial. Arch Clin Neuropsychol. 2012 Jun;27(4):406-16. doi: 10.1093/arclin/acs039.

- “The faculty of voluntarily bringing back a wandering attention over and over again, is the very root of judgment, character, and will. No one is *compos sui* if he have it not. An education which should improve this faculty would be the education par excellence.”
 - William James, *Principles of Psychology*, 1890

Meditation and MS

- Better mental health composite (MHC) scores, cognitive function scale, and health perception scale among those who meditated regularly
- Physical health composite (PHC) scores were higher in those that meditated (clinically significant?)
 - Levin AB, Hadgkiss EJ, Weiland TJ, et al. Can meditation influence quality of life, depression, and disease outcome in multiple sclerosis? Findings from a large international web-based study. Behav Neurol. 2014;2014:916519. doi: 10.1155/2014/916519.



On average in the last 12 months, how often have you meditated?

Mindfulness and MS

- RCT evaluated effectiveness of a group-based mindfulness intervention compared to psycho-educational
- Measured depression, anxiety, perceived stress, illness perception, fatigue and quality of life at the end of the interventions (T1) and after 6 months f-up (T2)
- Of 90 MS patients with depressive symptoms who were randomized, 71 completed the intervention
- Mindfulness intervention producing a greater reduction in score than the psycho-educational intervention, both at T1 and at T2
- Mindfulness intervention improved patients' quality of life and illness perception at T1 relative to the baseline and these improvements were maintained at T2
- Both interventions similarly effective in reducing anxiety and perceived stress; these reductions were maintained at T2
 - Carletto S, Tesio V, Borghi M, Francone D, Scavelli F, Bertino G, Malucchi S, Bertolotto A, Oliva F, Torta R and Ostacoli L (2017) The Effectiveness of a Body-Affective Mindfulness Intervention for Multiple Sclerosis Patients with Depressive Symptoms: A Randomized Controlled Clinical Trial. *Front. Psychol.* 8:2083. doi: 10.3389/fpsyg.2017.02083

Meditation and inflammation

- Novice meditators' inflammatory markers (serum interleukin IL-6 levels) 41% higher than those of expert meditators
- The odds of a novice having detectable C-reactive protein (CRP – a marker of inflammation) 4.75 times as high as that of an expert
- Differences in stress responses between experts and novices provided one plausible mechanism for their divergent inflammatory response to stress
 - Kiecolt-Glaser JK, Christian L, Preston H, et al. Stress, inflammation, and yoga practice. *Psychosom Med*. 2010 Feb;72(2):113-21. doi: 10.1097/PSY.0b013e3181cb9377.

Meditation, genes and immunity

- Study on effect of meditation on genetic expression
- 68 genes found to be differentially expressed (19 up-regulated, 49 down-regulated) after adjusting for potentially confounded differences in sex, illness burden, and BMI
- Up-regulated genes included immunoglobulin-related genes (better defences)
- Down-regulated genes included pro-inflammatory cytokines (less inflammation)
 - Black DS, Cole SW, Irwin MR, et al. Yogic meditation reverses NF- κ B and IRF-related transcriptome dynamics in leukocytes of family dementia caregivers in a randomized controlled trial. *Psychoneuroendocrinology*. 2013 Mar;38(3):348-55. doi: 10.1016/j.psyneuen.2012.06.011.

Mindfulness, MS and QoL

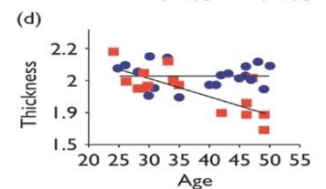
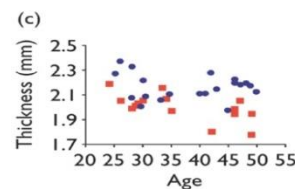
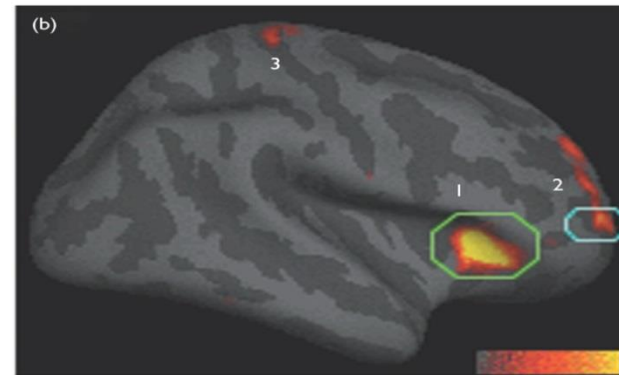
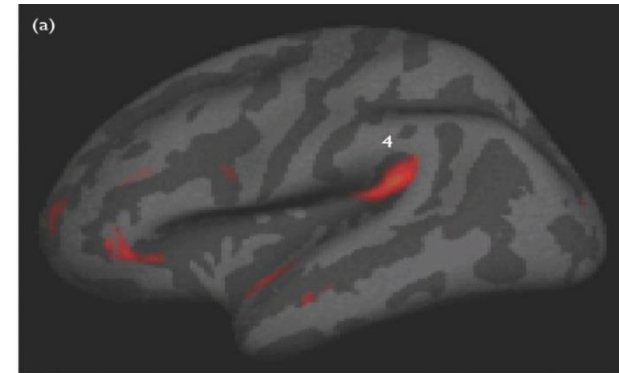
- Health-related quality of life (HRQOL) often reduced and depression, anxiety and fatigue high among people with MS
- 150 patients with MS randomly assigned to 8 week mindfulness course vs. Usual care
- Mindfulness improved outcomes (less depression, anxiety and fatigue and greater HRQOL) at post-intervention and 6 months follow-up
- Effect sizes were largest among those clinically relevant levels of pre-intervention depression, fatigue, or anxiety
 - Grossman P., Kappos L., Gensicke H., et al. MS quality of life, depression, and fatigue improve after mindfulness training. A randomized trial. *Neurology* 2010;75:1141–1149.

Mindfulness for people with MS

- Distress scores lower in the mindfulness group compared with the control group at post-intervention and follow-up
- Pain, fatigue, anxiety, depression and impact of MS were reduced for the mindfulness group compared with control group at post-therapy and follow-up
- 87.4% probability that the intervention saves on service costs and improves outcome
 - Bogosian A, Chadwick P, Windgassen S, Distress improves after mindfulness training for progressive MS: A pilot randomised trial. *Mult Scler.* 2015 Mar 12. pii: 1352458515576261.

Mindfulness and the brain

- Mindfulness training improves functioning in areas related to executive functioning, attentional control, self-regulation, sensory processing, memory and regulation of the stress response
 - Thickening of cortex in regions associated with attention, self-awareness and sensory processing thicker in meditators
 - “The regular practice of meditation may have neuroprotective effects and reduce the cognitive decline associated with normal aging.”
 - Hölzel BK, Carmody J, Evans KC, et al. Stress reduction correlates with structural changes in the amygdala. *Soc Cogn Affect Neurosci*. 2010 Mar;5(1):11-7.
 - Hölzel BK, Carmody J, Vangel M, et al. Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry Res*. 2011 Jan 30;191(1):36-43.
 - Kilpatrick LA, Suyenobu BY, Smith SR, et al. Impact of Mindfulness-Based Stress Reduction training on intrinsic brain connectivity. *Neuroimage*. 2011 May 1;56(1):290-8.
 - Lazar SW, Kerr CE, Wasserman RH, et al. *Neuroreport*. 2005;16(17):1893-1897.
 - Pagnoni G, Cekic M. *Neurobiology of Aging*. 2007;28(10):1623-7.



Social support

- High social support associated with:
 - Better mental health
 - Less heart disease
 - Greater longevity
 - Less substance abuse
 - Better immunity
 - Less dementia
- Quantity and quality both important

Connectedness and MS

- Chronic psychosocial stressors (interpersonal conflicts, loss and bereavement, low perceived social support, anxiety and depressive episodes) increase MS exacerbations
 - Strenge H. Psychother Psychosom Med Psychol. 2001;51(3-4):166-75.
- Unsupportive social environments associated with onset and exacerbation of autoimmune diseases
 - Homo-Delarche F N et al. Steroid Biochem Molec Biol 1991;40:619-37.

Connectedness and MS

- Social support buffers the effects of change in depression on IFN-gamma production.
 - Mohr D. J Psychosom Res. 2004 Aug;57(2):155-8.
- Social factors effect coping, mental health, quality of life, activities of daily living, access to services