1. **Depression in multiple sclerosis, prevalence and contributing risk factors**
   Nikseresht A., Sharifian Dorche M., Nomovi M.
   Mult. Scier. 2016 22: (692-693)

   **Abstract**
   Introduction: Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system (CNS) which is affect young adult especially young females. In this study we tried to investigate the prevalence of depression among female patients with MS and the most important contributing risk factors.
   Methods: During a cross-sectional study 1750 female patients with MS from our outpatient's clinic in Shiraz Southern Iran were involved. Depression was assessed using the Beck Depression Inventory-II (BDI-II).
   Descriptive analysis and multiple logistic regressions were performed to examine the association between depression and disability, education, employment, marriage status, course and income.
   Results: Overall, 647 patients (37 %) had moderate to severe depression. The mean age of participants was 38.2 years (SD = 9.57). The results obtained from logistic regression analysis showed that expanded disability status scale (EDSS), Progressive course and unemployment (P < 0.01) were significantly related to the severity of depression. Marriage and higher education had related to lower depression scales.
   Conclusions: These findings suggest that depression in patients with MS has multiple contributing factors and patients with higher social supports and lesser disability have lower rates of depression. Physiotherapy, regular employment and family supports may help to reduce depression.

2. **Development of a conceptual framework for daily life activities in patients with early stage relapsing-remitting multiple sclerosis**
   Chen S.-Y., Pomplius F., Strzok S., Cleanthous S., Cano S., Marquis P., Cohan S., Goldman M.D., Kresa-Reahl K., Petrillo J., Castrillo-Viguera C., Cadavid D.
   Mult. Scier. 2016 22: (690)

   **Abstract**
   Objectives: A disease and its treatment may impact patients' lives in different ways that are only known by the patients. This study sought to identify daily life activities important to patients with early stage relapsing remitting multiple sclerosis (RRMS) that are impacted by the disease. Findings will also inform patient-reported outcomes instrument use and development.
   Methods: Semi-structured interviews were conducted with RRMS patients scoring 0 or 1 (none to mild disability) on the Patient Determined Disease Steps. Interviews were audiorecorded, transcribed and analysed using an inductive and iterative line-by-line coding technique using ATLAS. TI software. A saturation analysis was conducted in order to confirm the appropriate sample size.
   Concepts derived from the patient interviews were inductively categorized into conceptual domains and subdomains. Codes reflecting Impacts of early RRMS were further reviewed and inductively selected for inclusion in a conceptual framework focusing on daily life activities that were identified as relevant and important by early RRMS patients.
   Results: A sample of 88 early RRMS patients were interviewed (mean age = 40 years; 74% female), 97% of whom were diagnosed within the previous two years. A rich pool of 446 unique concept codes was generated. These codes were separated into symptoms, bodily function, and impacts. A saturation analysis yielded only 3% (n=12) of the total concept codes emerging in the final eight interviews, suggesting that saturation was reached.
   The final conceptual framework of daily life activities comprises five sub-domains: Selfcare (e.g. dressing and bathing); Domestic life (e.g. shopping, driving, and cleaning); Social and recreational (e.g. attending social events and hobbies); Sports and exercise (e.g. running), and Work and school (e.g. work attendance and productivity).
   Conclusions: In order to fully understand the impact of early stage RRMS symptoms, it is vital to collect information about the extent, type and kind of issues important to this patient population. In this study, we have provided a comprehensive conceptual framework of relevant daily life activities important to early stage RRMS patients. This framework can be used as a foundation for future patient-reported outcomes instrument development and selection to quantify and capture the impact of new treatments in a clinically meaningful and individualized way.
3. **Is fatigue associated with exercise tolerance among patients suffering from multiple sclerosis?**
Valet M., Stoquart G., Gilbert Y., Hakizimana J.-C., Lejeune T.
Mult. Scler. 2016 22: (824-825)

**Abstract**
Objective: Fatigue is the most common and disabling symptom among patients suffering from Multiple Sclerosis (MS). Its underlying mechanisms are poorly understood. From the initial stages of the disease, a physical deconditioning is also observed among these patients. The aim of this study is to assess the cardiorespiratory endurance (i.e. exercise tolerance) and self-reported fatigue, as well as their associations with other functional parameters, among patients suffering from MS with mild disability (Expanded Disability Status Scale ≤ 4). Material and methods: Twenty one patients with MS (15 women; age: 26-64 years, median 46 years; duration of disease: 0.33-48 years, median 7.25 years; EDSS 0-4, median 2.5; clinical forms: Relapsing -Remitting: 16, Primary Progressive: 4, Secondary Progressive: 1) were evaluated. Cardiorespiratory endurance was assessed by a maximal exercise test on a cycle ergometer, from which different indices were extracted: VO$_{2\text{-max}}$, Oxygen Uptake Efficiency Slope (OUES) at different points and Physical Working Capacity at 75% of maximal heart rate (PWC75%). The Timed Up-and-Go (TUG) test was performed to assess functional mobility. Perceived fatigue, anxiety and depression and quality of life were respectively assessed by the following questionnaires: Modified Fatigue Impact Scale (MFIS), Fatigue Severity Scale (FSS), Hospital Anxiety and Depression Scale (HADS) and Short Form Health Survey (SF-36v2). Results: The majority of the patients (n = 13, 62%) presented a pathological level of perceived fatigue, based on the FSS criterion (FSS>5). The cardiorespiratory endurance indices are decreased among the patients, compared with the normative values from the general population. Low-to-moderate negative correlations (p < 0.05) are observed between perceived fatigue and VO$_{2\text{-max}}$ (FSS: r = -0.59; MFIS: r = -0.43). The OUES is weakly correlated with the MFIS (r = -0.40). Functional mobility (TUG) is moderately correlated to exercise tolerance (VO$_{2\text{-max}}$: r = -0.56) and fatigue (MFIS: r = 0.64). Discussion: Our data show that our patients are deconditioned and most have pathological level of fatigue. This fatigue, as well as functional mobility, are correlated to physical deconditioning. Our findings suggest that improving exercise tolerance functions could help reducing fatigue and improving functional mobility among patients suffering from MS with mild neurological disability.

4. **Healthcare resource utilisation and costs in patients with active relapsing-remitting multiple sclerosis treated with alemtuzumab vs. SC IFNB-1a (CARE-MS II)**
Smith A., Hashemi L.

**Abstract**
Background: CARE-MS II (NCT00548405) was a 2-year, phase 3, head-to-head trial of alemtuzumab versus subcutaneous interferon beta-1a (SC IFNB-1a) in patients with active relapsing-remitting multiple sclerosis (RRMS) and an inadequate response (≥1 relapse) to prior therapy at baseline.1 Compared with SC IFNB-1a, alemtuzumab demonstrated greater improvements in clinical and MRI outcomes, and significantly more alemtuzumab-treated patients achieved no evidence of disease activity. Goal: To evaluate healthcare resource utilisation and direct costs (US dollars) over the 2-year trial period for RRMS patients randomised to either alemtuzumab or SC IFNB-1a. Methods: Healthcare resource utilisation was a tertiary endpoint of the CARE-MS II trial. Patients’ use of healthcare resources was assessed at scheduled study visits (every 3 months) utilising the Health Resource Utilisation Questionnaire (HRUQ), a patient self-report tool designed to evaluate the economic impact of MS. Healthcare resource utilisation was collected in the following areas: admissions and stays in the hospital, rehabilitation centres, nursing homes, consultations with specialists, general practitioners, or other healthcare professionals. Direct costs in US dollars (adjusted to US 2016 medical inflation) are reported for the alemtuzumab and SC IFNB-1a treatment arms. Results: At baseline, resource utilisation and costs were similar in the alemtuzumab and SC IFNB-1a treatment arms. At 2-years, a statistically significant difference in resource use was observed in favour of alemtuzumab, with the SC IFNB-1a arm having a higher mean number of hospital stays and days in hospital, rehabilitation centre stays and outpatient visits, and nursing home stays and outpatient visits. Higher total direct healthcare costs were observed
for SC IFNB-1a versus alemtuzumab 12 mg ($18,995 vs $10,963 respectively, P=0.0256). No differences were seen with regard to visits with specialists and other healthcare professionals. Conclusion: Direct healthcare resource utilisation and costs as measured by HRUQ in the CARE-MS II trial were decreased with alemtuzumab treatment versus SC IFNB-1a.

5. **Prevalence of multiple sclerosis in the L'Aquila district, central Italy. A reappraisal after two decades**

Totaro R., Di Carmine C., Carrocci C., Sciamanna S., Raparelli C., Marini C., Carolei A. Mult. Scler. 2016 22: (717)

**Abstract**

Background and objectives: Multiple sclerosis (MS) prevalence in Italy increased over the past years and varied between different regions. In 1996, in the L'Aquila district MS prevalence rate was 53.0/100.000. Continue accurate estimates of MS prevalence provide important insights into possible risk factors and socio-economic burden of disease. The aim of this study was to estimate a reappraisal of MS prevalence rate in the L'Aquila district on December 31, 2014. Methods: Complete case ascertainment was ensured by multiple overlapping sources: clinical records of the departments of neurology within the district and those from neighbouring, files of the neuroradiology services, records of the rehabilitation units, records of the National Health Service, and general practitioners. All patients diagnosed with MS according to Poser and then McDonald criteria, living in the L'Aquila district on the prevalence day, were included. Results: The overall crude prevalence rate was 197.1/100.000 (95% CI 181.4-212.9), 274.9/100.000 (95% CI 249.0-300.8) in women and 114.4/100.000 (95% CI 92.2-131.6) in men. A total of 601 cases (432 women, 169 men, women/men ratio 2.5:1) were alive and resident in the study area by prevalence date. Mean age was 44.8±12.1 years, 45.0±12.2 in women and 44.8±12.3 in men. Conclusions: Findings from our survey indicate that the L'Aquila district is a geographical area at very high risk for MS with a more 3-fold increase in prevalence rates over the last two decades.

6. **Challenges for multiple sclerosis care and research in the Middle East**

Yamout B.I. Mult. Scler. 2016 22: (7)

**Abstract**

Multiple sclerosis (MS) care and research face multiple challenges in the Middle East region. The rapidly rising prevalence of the disease in this region, is putting a strain on medical and financial resources. Lack of awareness in the medical community leading to delayed or wrong diagnosis, is still a major drawback. There is an urgent need to improve such awareness by local educational symposia as well as educational grants to train MS specialists in major European and North American medical centers. MS therapies are quite expensive and are nearly always reimbursed by governmental agencies in Middle Eastern countries. Unfortunately, with the recent political and economic instability in the region, the governments have been less inclined to cover such expensive medications especially the most recent ones. The worsening economic and security situation in many Middle Eastern countries, is also affecting the overall healthcare quality provided to MS patients including availability of MS specialists, radiological facilities, physical therapy centers and other supporting services. Legislations regarding handicapped persons including public facilities, jobs, and discrimination are still lagging behind in our region as compared to the West. Public awareness of the disease, although significantly improved over the last decade, is still a major challenge in our region, leading to delayed medical referral, use of unproven or unconventional therapies, and poor adherence to treatment. Research in the field of MS is one of the major challenges we are currently facing in the Middle East. Short of few exceptions, well structured large patient registries, which are the basis of good clinical research, are lacking in the Middle East. MENACTRIMS launched earlier this year the MENACTRIMS Registry Project which aims at establishing and unifying registries all over the Middle East and North Africa region. This project will for the first time provide a large data base from the region and will help define the clinical and epidemiological characteristics of MS in the region. The research infrastructure, including human resources, laboratories, equipment and funding is also lacking in the Middle East, and is another major challenge that need to be addressed in the near future.
7. **The impact of patient out-of-pocket costs and satisfaction with therapy on adherence to disease-modifying drugs in patients with multiple sclerosis**
Mayer L., Smrtka J., Gupta S., Phillips A.L.
Mult. Scler. 2016 22: (463)
Embase

**Abstract**
Introduction: Several studies of varying design and methodology have evaluated factors associated with disease-modifying drug (DMD) adherence in multiple sclerosis (MS); however, literature evaluating the influence of patient-centred outcomes on adherence to DMDs is scarce. This study aimed to evaluate the impact of patient out-of-pocket (OOP) costs and satisfaction with therapy on adherence to DMDs in patients with MS. Methods: Patients with MS (n=1112) and currently being treated with a self-injectable or oral DMD from the US National Health and Wellness Survey or Lightspeed Research panel and its affiliates completed an internet survey between April and October 2015. The survey included questions about demographics, disease severity and symptoms, treatments, health behaviours, and comorbidities. MS-related OOP costs for doctor visits, medication, and other costs were reported as monthly estimates. DMD adherence was evaluated using the 4-item Morisky Medication Adherence Scale (MMAS-4). The Treatment Satisfaction Questionnaire for Medication (TSQM) assessed satisfaction (i.e. effectiveness, convenience, and satisfaction) with current DMD. Results: Of 805 survey respondents meeting study criteria, 429 reported high adherence (MMAS-4=0) and 376 reported low adherence (MMAS-4=1-4). Bivariate analyses showed no statistically significant differences in OOP costs between high and low adherers. TSQM scores for effectiveness, convenience, and satisfaction were significantly higher in high adherers compared with low adherers (all p< 0.05). The data were further delineated to elucidate if relationships could be uncovered with different adherence categories. Patients previously categorised as low adherers were re-categorised as either moderate (MMAS-4=1-2) or low (MMAS-4=3-4) adherers. New patterns did emerge with the increased granularity. Compared with high adherers, (newly defined) low adherers had higher monthly MS-related OOP doctor visit costs ($42.60 vs $23.75 for moderate adherers and $24.07 for high adherers; p< 0.05) and other OOP costs ($71.37 vs $42.34 for moderate adherers and $35.57 for high adherers; p< 0.05). Compared with high adherers, (newly defined) low adherers had lower satisfaction TSQM scores (44.53 vs 56.51 for moderate adherers and 57.26 for high adherers; p< 0.05). Conclusions: In this real-world population, lower OOP costs and greater treatment satisfaction were associated with higher levels of adherence to DMD treatment.

8. **Multiple sclerosis, EDSS, and objective cognitive function: A walking scale with no apparent brains and limited thought**
Mult. Scler. 2016 22: (144-145)
Embase

**Abstract**
Background: Multiple Sclerosis (MS) is measured by MRI, relapse rates and EDSS. EDSS scale primarily driven by motorwalking impairment. Cognitive impairment, independent of EDSS, in people with MS (PwMS) impacts: employment, driving, fall risk, Quality of Life (QoL). EDSS is universally accepted to measure treatment efficacy but cognitive function does not impact EDSS. Cognitive function varies independently of walking ability and is an important aspect of PwMS disease impact. Objective: Investigate the sensitivity of EDSS impairment reflecting PwMS cognitive ability. Methods: PwMS completed a computerized cognitive assessment battery (NeuroTrax) with analysis of 7 cognitive domains (CD) and a global cognitive score (GCS) reflecting an average of these domain scores. The number of CD impaired (greater than one standard deviation from age- and education-matched norms) were also explored for each CD. EDSS-groups were defined: low- EDSS (0-2.5), moderate-EDSS (3-4.5), high-EDSS (5-6.5) and severe-EDSS (>7). Percent overlap of NeuroTrax cognitive scores across both adjacent EDSS-groups and extreme EDSS groups (low & severe) were calculated. Results: 258 PwMS (72.5% female, average age = 46.2±10.2). PwMS-GCS had an average overlap: 65.0% across adjacent EDSS-groups, and 42.4% across extreme EDSS-groups. The overlap of the adjacent and extreme cognitive domain scores were respectively: memory (65.3% and 65.3%), executive function (65.1 % and 35.1%), attention (60.3% and 38.1%), information processing speed (58.0% and 42.5%), visual spatial (65.6% and 63.2%),
verbal function (70.1% and 66.4%), and motor skills (55.2% and 32.3%). The overlap of the number of CD scores impaired >1SD was: 72.2% across adjacent groups, and 38.1% across extreme EDSS-groups. Conclusions: EDSS is insensitive to assess individual PwMS cognitive ability and does not predict accumulated cognitive disability. Cognitive impairment in PwMS, independently of EDSS, correlates with many important milestones. EDSS use as a solitary gold standard in measuring unique accumulated PwMS disability should be reconsidered.

9. **Multiple sclerosis and disease modifying therapies: If you prescribe it, will they take it? - a population analysis of predicted self-administration of medication adherence behavior**


Mult. Scler. 2016 22: (460)

Abstract

Background: People with Multiple Sclerosis (PwMS) and prescribers have multiple treatment choices. Disease modifying therapy (DMT) non-adherence and delaying DMT initiation impact outcomes. PwMS DMT non-adherence might increase long-term economic costs. Adherence can be measured by direct observation, patient report, prescription refills and other measures. With varied DMT route and frequency, “predicted PwMS adherence behavior” for self-administered treatments needs investigation to evaluate how this might impact prescribing practice and MS care. The Morisky Medication Adherence Score (MMAS-8), a validated 8 point questionnaire, is predictive of medication adherence, pharmacy fill data, relevant for treatments of varied routes/ frequency, and correlates with efficacy and economic outcomes. DMT choice reflects many factors but adherence directly impacts therapy efficacy and perhaps safety. The long term MS economic impact demands treatment safety, efficacy, and adherence. Objective: Explore PwMS predicted adherence behavior to medication if self-administered. Methods: Single site cross sectional analysis of PwMS who completed Morisky Medication Adherence questionnaire (MMAS-8) during routine care. Results: 788 PwMS, 73% female, average age 48. Predicted self-administered adherence behaviors for treatments were: 38% high, 34% medium, and 28% low adherence. The difference in predicted adherence behavior was significant (p< 0.01). Gender and age by themselves had no significant impact on predicted adherence profile. Prescribed DMT route did not appear to impact overall predicted PwMS self-administered adherence profile. Conclusions: Patient adherence is a significant problem in MS care. Reduced DMT efficacy might reflect sub-optimal adherence for those self-administered treatments. High potency DMT, requiring safety monitoring, might have sub-optimal patient adherence. High frequency prescribed self-administered DMT prescribed to PwMS who are likely low adherent might reflect a poor choice of available DMT options. Treatment required for chronic disease requires ongoing efficacy, tolerability and high adherence. Analysis of individual adherence behavior might impact treatment decisions and alter DMT choices. Factors improving adherence or DMT choice might improve efficacy/outcome and reduce long term care costs.

10. **Examining the factor structure of the Multiple Sclerosis Impact Scale**

Fitzgerald S.M., Li J., Rumrill P.D., Merchant W., Bishop M.

Work 2014 49:3 (523-538)

Abstract

The purpose of this study was to investigate the factor structure of the Multiple Sclerosis Impact Scale (MSIS-29) to assess its suitability for modeling the impact of MS on a nationwide sample of individuals from the United States. Investigators completed a Confirmatory Factor Analysis (CFA) to examine the two-factor structure proposed by Hobart et al. [17]. Although the original MSIS-29 factor structure did not fit the data exactly, the hypothesized two-factor model was partially supported in the current data. Implications for future instrument development and rehabilitation practice are discussed.

11. **Multiple sclerosis state of the art (SMART): A qualitative and quantitative analysis of therapy’s adherence, hospital reliability’s perception, and services provided quality**
Abstract

The purpose of this study was to assess the adherence to therapy in patients with relapsing remitting multiple sclerosis (RR-MS) and to analyze the possible influence of factors such as hospital care and patients socioeconomic status. Two hundred eighty-five patients with RR-MS according to McDonald's criteria and naïve disease-modifying drugs (DMDs) naïve were enrolled. Two self-administered questionnaires addressing the management of patients at therapy prescription and the personal perception of the daily life changes caused by DMDs were administered at months 3 and 12. Full adherence, considered as correct use of the therapy prescribed, was observed in a very high percentage of subjects (97.3% and 93.9% at 3 and 12 months). The main cause for reduced adherence was single dose forgetfulness, followed by anxiety, pain at the injection site, and tiredness of “doing all injections.” Nurses and neurologists of MS Center were identified as the major resource in coping with the disease at 3 and 12 months by patients. The neurologist was the health professional involved in MS management in 95% of cases and the nurse appeared to play a central role in patient training and drug administration management (50.3%).