

Posters

(S01) Cognitive Impairment in Benign Forms of MS

Cognitive impairment (CI) is a known effect of multiple sclerosis (MS). Previous studies have shown its independence from the evolution time and degree of disability (Expanded Disability Status Scale [EDSS]) determined by the disease. On the other hand, CI is considered to have a great impact on patients' life quality. This study focused on early detection of CI in forms considered benign (≤ 2.5 EDSS score and ≥ 5 years of MS). An initial group of 20 outpatients with a definitive MS diagnosis from the Montevideo Neurological Institute MS Department were brought in for study. They were given a neuropsychological battery, which included memory, attention, and executive function tests. Eight of the patients (40%) had a completely normal evaluation. Twelve patients (60%) presented alterations, 6 (30%) with minor alterations: two (10%) in the executive function tests, two (10%) in visual memory and executive function tests, and two (10%) in verbal memory, visual memory, and executive function tests. Six patients (30%) had moderate alterations: three (15%) in verbal memory and visual memory tests, one (5%) in the verbal memory and executive function tests, one (5%) in visual memory and executive function tests, and one (5%) in visual memory, verbal memory, and executive function tests. None of the patients had severe alterations in the tests. Our study showed a high incidence of CI in the benign forms of MS, reaching 60% of the patients, half of them with moderate impairment. The neuropsychological evaluation in the benign forms of MS is proposed for the early detection of CI to establish a more precise outcome and adequate evolutive control and treatment of affected patients.

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(S02) New Formulation of Subcutaneous Interferon Beta-1a: Phase 1 Safety Tolerability and Pharmacokinetic and Pharmacodynamic Results

Treatment adherence is key to obtaining maximal benefits from interferon (IFN)-beta therapy in multiple sclerosis (MS). Injection-site reactions are a frequent treatment-emergent adverse event (TEAE) with subcutaneous (SC) injections, and, although generally mild in patients receiving SC IFN beta-1a three times weekly (tiw) (Rebif; R), they may cause treatment discontinuation in some patients. This phase 1 study (25394) assessed two new formulations of R (RNF1 and RNF2) by comparing the safety and tolerability of single 0.5-mL doses (44 μ g IFN beta-1a SC) with those of R or placebo (normal saline). In this double-blind, placebo-controlled, parallel-group study, 48 healthy volunteers were randomized (1:1:1:1) to receive one of three active treatments or placebo. Evaluations of pain intensity on injection were based on the McGill short-form questionnaire and a 100-mm visual analog scale (VAS > 5 mm = pain). Safety, tolerability, and pharmacokinetic and pharmacodynamic (PK/PD) effects were monitored for 24 hours postdose, and further evaluations were made until 10–14 days after dosing. Although TEAEs occurred in equal numbers of subjects (10) in the

RNF1, RNF2, and R groups, overall incidence was lower with RNF2 (22 events) than RNF1 or R (31 and 33 events, respectively). Worst pain intensity was lower with RNF1 and RNF2 than with R or placebo (mean VAS score [SD] 1.4 [2.61], 1.0 [1.04], 10.7 [17.08], and 3.9 [8.01] mm, respectively). Furthermore, fewer subjects receiving RNF2 experienced injection-site redness than those receiving RNF1 or R (3 vs 7 and 4, respectively), and the RNF2 group also had fewer subjects with local injection pain than the RNF1, R, or placebo group (1 vs 4, 6, and 3, respectively). The PK/PD profile of RNF2 was similar to that of R. These results suggest that RNF2 could offer further improvement in tolerability and, hence, adherence. A phase 3b study (25632) investigating this formulation in patients with MS is ongoing.

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(S03) Reduced Immunogenic Potential of New Formulation of Interferon Beta-1a in Murine Model

The efficacy of interferon (IFN) beta-1a in multiple sclerosis (MS) may be attenuated by the presence of persistent neutralizing antibodies (NAbs) in a few patients. A new formulation of interferon (IFN) beta-1a (Rebif New Formulation; RNF) has been developed to improve tolerability and reduce immunogenicity. An in vivo murine model was used to compare the relative immunogenicity of RNF, Rebif, and Avonex. RNF, Rebif, Avonex, or phosphate-buffered saline (control) was administered to female BALB/c mice subcutaneously three times weekly at 0.1 μ g/mL. Serum samples collected on Days 7, 21, and 35 (study 1) or Days 28, 42, 49, and 60 (study 2) were tested for NAbs to IFN beta-1a using a cytopathic effect assay. NAb titers were calculated using the Kawade method and expressed as the dilution of serum that reduced 10 laboratory units (LU)/mL of IFN to 1 LU/mL (t_{10}). Titers are presented as \log_{10} and represent the mean (standard deviation) of two independent determinations. Twenty-four mice were used per study (RNF, $n = 6$; Rebif, $n = 6$; Avonex, $n = 6$; control, $n = 6$). NAbs were not detected at Day 7, but by Day 21, one mouse receiving RNF had NAbs, compared to three mice receiving Rebif and five receiving Avonex. Throughout the study, NAb titers were lowest in mice receiving RNF and highest in those receiving Avonex. All actively treated mice had NAbs by Day 35, but titers were significantly lower in mice receiving RNF (1.91 t_{10} [0.55]) than those receiving Rebif (2.55 t_{10} [0.35]; $P = .037$), which were also significantly lower than in mice receiving Avonex (3.10 t_{10} [0.38]; $P = .026$). NAbs were not detected in the control group. Mice treated with RNF developed NAbs more slowly and produced lower titers than with identical doses of Rebif or Avonex. On a gram-for-gram basis, RNF appeared to have lower immunogenic potential than other formulations of IFN beta-1a.

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(S04) Effect of Song-Singing Intervention on Speech of MS Patients With Dysarthria

Therapeutic singing can be an effective tool in the treatment of various neurological communication disorders. There is a connection between singing and speech in that they are both forms of communication and share many neural speech mechanisms, respiratory muscles, and articulators. Singing familiar songs provides the rhythmic and melodic patterns for patients to organize their speech production and subsequently improve intelligibility and naturalness. A speech-language pathologist and an occupational therapist worked together to treat multiple sclerosis (MS) patients with dysarthria by making them sing familiar songs that included messages of hope and faith. The participants had the final assignment to make a Christmas-related film to be shown at the Christmas party of the Brazilian MS Society. In this film, patients sang songs with a guitar played by a therapist and shared Christmas messages. **Objective:** Improve speech of MS patients with dysarthria by singing. **Methods:** Twenty-one 1-hour weekly meetings, coordinated by an occupational therapist and a speech therapist in a 6-month period. The speech therapist made the individual speech assessment at the beginning and after 6 months. Verbal diadochokinesia, articulation disorder, speech, speed, quality of voice, prosody, resonance, pitch, and loudness were assessed. **Results:** Five MS patients with dysarthria (2 women, 3 men) with EDSS scores of 7.0–8.5 and ages 39–58 years were included in the study. All patients improved diadochokinesia, 60% speed of speech, 40% resonance, and 20% quality of voice. **Conclusion:** Singing was effective in the treatment of MS patients with dysarthria. The intervention also improved emotional conditions and cognitive performances. This interdisciplinary approach was successful. The film motivated patients to practice singing at home and to get involved in their treatment.

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(S05) Predictors of Assistive Technology Use for Cognitive Aids in MS

Individuals with multiple sclerosis (MS) often experience limitations in participation in important activities. Assistive technology (AT) is one method to address these limitations and may take the form of mobility aids, devices for use in self-care tasks, screen-enlargement software, vehicle modifications, and memory aids such as personal digital assistants. Although most research on AT use in MS has focused on mobility aids, it is critical to examine the use of AT as a cognitive prosthesis. Cognitive problems are common for individuals with MS, and a growing number of tools are available to help individuals compensate. We report on an evaluation of predictors of self-reported use of or need for assisted cognition from a community-dwelling sample of adults with MS. We found that of all types of AT assessed, cognitive aids and memory strategies were most frequently used or needed in our analysis of a 2005 self-administered mail survey ($N = 110$). Multiple logistic regression analysis was completed to determine which factors were significantly associated with memory aid use and need. Variables examined as predictors of current use of memory aids included education, employment status, difficulties thinking, use of mobility aids, pain,

fatigue, and depression. Self-report of severity of problems with thinking was the only variable significantly associated with use of memory aids (Wald test [$df = 1$]: $\chi^2 = 5.66$, $P = .02$). Need for memory aids, defined as needed but not available, was also examined, and regression analysis determined that self-report of high severity of problems thinking was the only significantly associated variable (Wald test [$df = 1$]: $\chi^2 = 4.33$, $P = .04$). Interestingly, this analysis suggested that individuals who perceived the highest decline in their cognitive function were more likely to currently use or want to use memory aids, regardless of other factors. Clinical and policy implication is also discussed.

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(S06) Role of Historical Leisure Activity in Starting Home Exercise Program

Background: Despite the numerous benefits of exercise, only 25% of Americans are physically active. One obstacle to elevating physical activity levels among sedentary individuals is poor adherence to exercise interventions. Exercise participation in the disabled population is even less, because these populations face additional barriers to exercise. The factors that predict exercise adherence and physical activity participation in the multiple sclerosis (MS) and other disabled populations are not well documented. We hypothesized that historical leisure activity (HLA) would influence exercise levels of MS patients after starting a home exercise program. **Design/Methods:** Exercise levels in MS patients starting a home exercise program were collected from a 5-year study, The Effects of Exercise on Preserving Function and Participation in MS. To determine HLA, we administered the HLA questionnaire. We assessed any associations between HLA and change in exercise levels after the start of the exercise program. **Results:** Patients with higher levels of HLA were more likely to report significant exercise change during the exercise program than those with low HLA. **Conclusion:** Greater HLA levels may afford skills to change exercise behavior, but the observation that no subject maintained increased exercise levels demonstrated that exercise behavior was difficult to change.

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(S07) Needle Size and Injection-Site Pain: Results From Subgroup Analysis of BRIGHT Study

Background: Injection-site pain (ISP) can occur with interferon-beta (IFNB) treatment in multiple sclerosis (MS) patients. Its intensity diminishes after injection. With subcutaneous injections, needle size has been postulated as one factor that may influence the frequency and severity of injection-related events. We report results from a subgroup analysis of the BRIGHT (Betaseron versus Rebif Investigating Higher Tolerability) study on the influence of needle size (27- or 30-gauge) on ISP in Betaseron patients using the Betaject Light autoinjector. **Design/Methods:** BRIGHT was a multicenter, international, nonrandomized, prospective, observational study comparing Betaseron with Rebif. Patients had started treatment within 3 months before recruitment and were on full-

dose therapy. A post hoc analysis identified a subgroup of patients using the Betaject Light autoinjector to administer Betaseron, with either a 27- or 30-gauge needle. Patients self-injected IFNB and self-assessed ISP for 15 consecutive injections using a 0- to 100-mm visual analog scale diary immediately, 30 minutes, and 60 minutes postinjection. **Results:** Subgroup data are available for 226 of 445 patients. These patients used the Betaject Light autoinjector: 186 with a 27-gauge needle and 40 with a 30-gauge needle. Baseline characteristics were similar between the groups, although the 30-gauge-needle group had a higher proportion of male patients and slightly more relapses. At 60 minutes postinjection, significantly more patients using the 30-gauge needle were pain free over all 15 injections than those using the 27-gauge needle (75.0% vs 52.2%, $P = .0086$). The mean proportion of pain-free injections was significantly greater at 60 minutes with the 30-gauge needle (95.0% vs 85.0%, $P = .0266$). **Conclusion:** These results show that administering Betaseron using the Betaject Light autoinjector with a 30-gauge needle caused less ISP than with a 27-gauge needle. Therefore, use of a 30-gauge needle may lead to improvement in treatment adherence.

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(S08) Practical Model of Rehabilitation Screening Demonstrated Through Case Study

Physical rehabilitation benefits in multiple sclerosis (MS) are to maintain, improve, or restore functional independence and quality of life. A multidisciplinary and practical model of care done in the MS center by a physical therapist is presented through algorithm and case study. Key to this model is the rehabilitation screening tool. Unique aspects of the tool include subjective specific MS symptom history, timed 25-foot walk, and 9-hole peg test. The tool aids the therapist in recommending the setting of care: outpatient, inpatient, or home care. The need for further assessment of occupational therapy, speech therapy, and/or nutritional therapy is indicated. It also specifies individual physical therapy services and other recommendations as part of the care plan. These recommendations include durable medical equipment, orthotic evaluation, seating and positioning evaluation, and referral to community programs and community resources. Suggested services, programs, referrals, and billing used in the model are described. This practical model demonstrated the ability to use the collaborative effort of a rehabilitation practitioner and an MS center to ensure a comprehensive look at the whole individual with MS within the scope of rehabilitation. It offered appropriate referral and action taken to meet the goals of the individual for fitness, function, and quality of life.

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(S09) Supervised Fitness Class for People With MS Improves Physical Performance and Quality of Life

Background: People with multiple sclerosis (MS) present with diverse neurological impairments. Common to most individuals are fatigue and a significant problem with de-conditioning, which over time lead to compromised physical performance. This limits participation in life-role functions, which

in turn leads to diminished health-related quality of life.

Objective: Improve the physical performance of people with MS in their individual life roles through an exercise program tailored to address each individual's specific impairments. **Methods:** The exercise groups consisted of four to six people with MS. The groups met for 1 hour twice weekly for 24 weeks. A precourse evaluation was conducted by an experienced physical therapist with expertise in neurological assessment and treatment. Initial self-reports included SF-36, Activities Specific Balance Confidence Scale, and Dizziness Handicap Inventory. Strength testing, range of motion, balance, and endurance were objective measures included in this program to determine individual progress. The 1-hour sessions were tailored to each participant's abilities and included stretching, balance, endurance, and strengthening exercises. The self-reports and objective measurements were also completed at the end of the course. **Results:** Eighteen individuals with MS participated in the exercise program, and all the evaluations indicated physical performance improvements. Significant findings in the SF-36 were observed. As a result of the improvements in self-reports and physical assessment findings and the positive program evaluations completed by the participants, the Allegheny District Chapter of the National MS Society has offered to assist with funding of this program and two additional programs for clients in 2007. **Conclusion:** Participation in a long-term, individually designed, supervised exercise program for people with MS improved physical performance in life roles and overall fitness and health.

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(S10) Children With MS Adhere to Disease-Modifying Therapy Poorly Compared With Adults

Background: We have shown that in our population-based clinic, adherence to multiple sclerosis (MS) disease-modifying therapy (DMT) in adults with relapsing-remitting MS decreased from 91% at 1 year to 66% at 5 years. This study reports adherence among children in our clinic. **Methods:** We collected age and DMT utilization data on all our clinic patients. All children with MS and suspected MS from Southern Alberta were followed in our clinic by a pediatric neurologist and an adult MS neurologist. We evaluated the rate of adherence to DMT in all patients who started DMT before age 18 years by reviewing our database. **Results:** Seventeen children started DMT before age 18 years; 65% were girls. The mean age at first drug start date was 15.8 years (standard deviation [SD] 2.0), with median disease duration of 13 months (interquartile range [IQR] 10–24 months). First drug started was glatiramer acetate in 58.8%, interferon beta-1b in 5.9%, interferon beta-1a (intramuscular) in 5.9%, and interferon beta-1a (subcutaneous) in 29.4%. Eight (47%) children discontinued DMT after a median duration of 22.0 months (IQR 4.0–29.5 months). **Conclusions:** Children with MS were much more likely to discontinue DMT than adults. They required additional care to improve their adherence to treatment and health-related outcomes.

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(S11) Assessment of Betaferon Application Systems in Portugal: Patient Feedback

Multiple sclerosis (MS) patient adherence to immunomodulatory treatments is an important factor in therapeutic success. Betaferon (interferon beta-1b 250 µg; Betaseron) has to be injected every other day. Satisfaction with the application system may be one factor that influences treatment adherence. Previous studies have shown that patients who use an autoinjector have fewer and less intense injection-site reactions than those using a manual injection technique. This survey evaluated Betaferon patient satisfaction with the current application system (the Betaject Light autoinjector with the current syringe) and with an advanced system (the new Betaject Lite autoinjector with a modified syringe). The survey was conducted in Portugal and included 249 patients being treated with Betaferon for relapsing-remitting MS. All were using the current application system. Patients rated their previous experience with the current system via a questionnaire, which included questions regarding their overall satisfaction and their perception of the ease or difficulty of each preparation step. Nurses demonstrated the new system and supervised the first injection. Patients used the new application system for an observation period of 15 injections. They assessed the new system after the 1st, 7th, and 15th injection via the same questionnaire. To date, evaluable data are available for all 249 patients for the current system and for the first injection with the new system. Data are also available for 235 patients after the 7th injection with the new system and for 174 after the 15th. The patients' mean age was 41.5 ± 11.3 years, and 67.5% were female. A preliminary reflection on the data in January showed an increase in patients' overall satisfaction level with the advanced application system. The final results from the full data set of the survey are presented and discussed.

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(S12) Intrathecal Baclofen Tolerance: Myth or Reality?

Intrathecal baclofen (ITB) is effective therapy for treatment of spasticity. Effectiveness is typically assessed during an ITB trial when baclofen is injected via lumbar puncture directly into the cerebrospinal fluid (CSF). Candidates with successful ITB trials undergo permanent implantation of ITB pump to enable continuous delivery of medication. Optimal clinical outcome is then obtained by sequential pump rate/dose adjustment. ITB therapy failure after successful trial and implantation is typically caused by inadequate medication delivery. Commonly, this problem is from catheter line blockage or leak. Rarely is failure of therapy caused by rotor failure or medication. The standard approach for analysis of treatment failure includes replacing medication in pump reservoir, assessing reservoir volume, serial dose increments, and, if ineffective, a programmed bolus dose. If clinical improvement is not obtained, then a rotor study and catheter-line dye study under fluoroscopy is performed for definitive analysis. For patients who have had successful ITB trial and implantation, effective spasticity reduction, and subsequent ITB failure, the described diagnostic algorithm is the standard approach to troubleshooting. For patients who undergo this

analysis without identification of a source of therapy failure, ITB tolerance/Insensitivity is diagnosed. ITB tolerance is defined as resistance of clinical effect from continued or increasing dose of medication. There are reports of ITB tolerance/insensitivity dating back to the original series reported by Penn. We report 3 of 175 consecutive ITB patients who, by clinical and diagnostic criteria, have ITB tolerance/insensitivity. Our diagnostic approach included bypassing ITB pump, side port, and catheter by injecting baclofen directly into CSF. This achieved resumption of ITB effectiveness, maintained after replacement of catheter line even when no problem was documented. The concept of ITB intolerance/insensitivity is more myth than reality propagated by a subtle catheter line/placement problem not identified by standard diagnostic algorithms used to assess ITB therapy failure.

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(S13) Brief Cognitive Screening of MS Patients in Medical Setting

Objective: Explore the effectiveness of a brief cognitive screening battery that is simple, quick, and reliable in the detection of cognitive dysfunction in multiple sclerosis (MS) patients. **Background:** It is estimated that 50–70% of MS patients experience MS-related cognitive dysfunction. Because information processing speed and memory function are most commonly impacted in the MS patient population, the Mini-Mental Status Examination (MMSE) appears to be an inadequate screening instrument in this regard. Furthermore, an objective screening battery specifically designed to evaluate MS patients is needed for use in the outpatient medical setting. **Pilot Data:** A brief, modified cognitive screening battery (including measures of memory, information processing speed, and language skills, among others) was administered by a trained technician to 15 MS patients. Mean time to complete the entire battery was <30 minutes. All patients easily completed testing. Initial composite results revealed that the modified cognitive screening battery was more sensitive than MMSE alone (as expected) in the detection of MS-related cognitive dysfunction. **Future Directions:** The test findings support the use of an objective, brief cognitive screening battery for MS patients in the medical setting. Until a computerized screening battery is available for use in the outpatient clinic, it appears that the modified screening battery is more effective than MMSE in the detection of possible cognitive dysfunction in MS patients. Because increased stabilization of cognitive function has been demonstrated to improve quality of life, decrease unemployment rates, and improve mood in MS patients, accurate and early detection appears to be a critical component of comprehensive clinical care. We hope that this screening battery (which can be administered by any trained technician) will provide an objective means to evaluate possible cognitive dysfunction in the medical setting.

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(S14) Natural Killer Cell Cytotoxicity in Treatment-Naive MS Patients

Background: The innate immune response has been the focus of little investigation as it relates to the pathogenesis of multiple sclerosis (MS). Natural killer (NK) cells are one of the cellular mediators of innate defense. Cytotoxicity is one of the mechanisms used by NK cells to scrutinize the nature and scale of adaptive immune response. **Objective:** Our objective was to better characterize the NK cell neuroregulatory function by measuring NK cytotoxicity in MS patients naive to treatment, compared with healthy control subjects. **Methods:** After consent, we collected blood from MS patients and age- and sex-matched control subjects. All blood was drawn in the morning. A 4-hour chromium-51 release assay using a K562 target cell line was performed, with the technician blind to the clinical status of the subject. Three different effector–target cell ratios were studied, and means at each were analyzed with paired *t* test. **Results:** Eleven MS subjects naive to any immunotherapy and 11 healthy laboratory control subjects individually matched by age and sex were studied. The group consisted of seven women and four men. There was a statistically significant reduction in NK cell percent kill in the MS subjects compared with control subjects (25:1 mean [standard deviation] 5.8 [2.8] vs 19.9 [10.9]; 50:1 mean 15.0 [14.5] vs 35.4 [15.4]; 100:1 mean 26.5 [19.4] vs 45.9 [19.7]). This difference was statistically significant at all three effector–target cell ratios (at 25:1, *t* = 3.03, *df* = 10, *P* = .01; at 50:1, *t* = 4.03, *df* = 10, *P* < .01; at 100:1, *t* = 2.80, *df* = 10; *P* = .02). **Conclusion:** MS patients had a significant reduction in NK cell cytotoxic ability. Because there is evidence that their cytotoxic ability may have been one way they orchestrated their neuroregulatory function, these data would implicate them as potential targets for future therapy.

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(S15) Feasibility of Using American Urological Association Symptom Index Questionnaire in MS Clinic Sample

Objective: Urinary symptoms are reported by at least 60% of people with multiple sclerosis (MS). This study examined the feasibility of using the American Urological Association Symptom Index Questionnaire (AUA) to assess urinary symptoms within the Dalhousie Multiple Sclerosis Research Unit (DMSRU) patient population. **Methods:** Patients receiving care at DMSRU between 1 October 2005 and 31 August 2006 were asked to complete the AUA during routine clinical assessment (Expanded Disability Status Scale [EDSS] score, Functional System Score, and Health Utilities Index). AUA is a self-report Likert scale with seven urinary symptoms and one quality-of-life question. Patient records with diagnosis of MS and an EDSS and AUA score (with no missing data) completed on the same date were included in the analysis. AUA scores were grouped according to mild (<8), moderate (8–19), and severe (>20). **Results:** Four hundred ninety-four patients completed questionnaires at the time of the clinic visit. One hundred sixteen records were deleted from the analysis because of a diagnosis of possible/probable or not MS and/or no EDSS completed at time of visit.

Three hundred seventy-eight records were analyzed: 292 (77.2%) female; 66.5% relapsing-remitting MS, 25.1% secondary progressive MS, and 8.5% primary progressive MS. EDSS score was <4.0 in 72.3%, 4.5–5.5 in 3.8%, and >6.0 in 24%. AUA scores were 34.4% mild, 41.3% moderate, and 18.3% severe. AUA quality of life was rated as mostly satisfied or higher by 55.6%. Average time frame for completing the AUA was 5 minutes. **Conclusions:** Inspection of the face validity of AUA showed that it provided valuable clinical assessment information but neglected to address incontinence and the use of catheters or incontinence supplies. It was not time consuming to complete, and overall number of missing responses was low. With modifications, this questionnaire could be a useful clinical tool for the evaluation of urinary symptoms.

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(S16) Social Anxiety in MS Clinic Population: Relationship With Self-Reported Health Status

Objectives: Depression and anxiety are common in multiple sclerosis (MS), yet little is known about social anxiety (SA) in MS, which is highly prevalent in other disabling neurological diseases. This study identified community-living people with MS at high risk of SA and explored the associations of SA with demographic and clinical features and self-reported health status. **Methods:** Consecutive MS patients attending the Dalhousie MS Research Unit for routine clinical evaluation consented to complete (validated) self-report scales: the Social Phobia Inventory (SPIN) was used to screen for SA, the Hospital Anxiety and Depression Scale (HADS) for generalized anxiety and depression, and the Health Utilities Index (HUI) for self-reported health status. Neurological disability was determined by the Expanded Disability Status Scale (EDSS) and Functional System Score. **Results:** Two hundred sixty-five patients consented to participate: 81.5% were female, mean age was 46 years (range 22–73 years), and 94% completed both SPIN and HUI. A SPIN cut point of >19 was used to identify the proportion of patients at high risk of developing SA (22.9%). Age and EDSS were not significantly different between high and low SPIN groups. Mean total HUI scores for patients with SPIN scores >19 was 0.34 vs 0.63 for those <19 (*P* < .0001). HUI cognition scores and pain scores for patients with SPIN scores >19 was 0.68 and 0.69, respectively, and for SPIN scores <19 was 0.89 and 0.85, respectively (*P* < .0001). SPIN scores were not significantly related to ambulation and emotional HUI mean scores. **Conclusions:** Social anxiety is common in people with MS, contributing to their overall morbidity; however, unlike depression, it appears unrelated to the severity of neurological disability. Patients with higher SA scores generally have lower levels of self-reported health status. Screening for SA is important for comprehensive care of MS patients, and its effective management may improve health status.

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(S17) Comparison of Lithotripsy Rates in Veterans With and Without MS

Objective: Establish the proportion of lithotripsy or other active renal stone treatment in individuals with multiple sclerosis (MS) compared with individuals without MS or spinal cord injury over a 7-year period in one health care setting.

Design/Setting: A cross-sectional analysis of data collected prospectively and analyzed retrospectively from a tertiary veterans hospital. **Participants:** All veterans without a diagnosis of spinal cord injury who were seen at one veterans hospital between 1999 and 2005. **Main Outcome Measures:** Proportion of individuals with MS compared with those without MS requiring active intervention for renal stones, including lithotripsy, cystourethroscopy, or percutaneous nephrostolithotomy. **Results:** There were 148,710 veterans without MS and 551 with MS seen over this period. There was a 1.1% proportion of active intervention in the MS population from 1999 to 2005. This compares to a 0.15% proportion of intervention in the population without MS over the same time frame. The proportion of male veterans with MS (84.0%) was similar to that in the non-MS population (81.5%). Mean age at time of procedure was 58 years (median 56 years) for those with MS and 53 years (median 52 years) for those without MS. **Conclusions:** Our results suggested that in a predominantly male population of individuals using a tertiary veterans hospital, there was an average annual proportion of lithotripsy or other active intervention of 1.1% in those with MS and 0.15% in those without MS. Both groups required a relatively low rate of intervention. The difference in rates was not statistically significant. If these results are confirmed by additional work, they may help with formulation of guidelines for diagnostic screening for renal stones in individuals with MS seeing noneurologic specialists.

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(S18) Medication Nonadherence and Its Impact Among Patients With MS

Objective: Estimate adherence to disease-modifying agents and association of adherence to patient characteristics, disease progression, and quality of life among patients with relapsing-remitting multiple sclerosis (RRMS). **Background:** MS is a demyelinating disease of the central nervous system that may cause severe disability in young adults. In the United States, agents used for RRMS (ie, interferon beta [Avonex, Rebif, and Betaseron] and glatiramer acetate [Copaxone]) have been shown to reduce relapse rate, magnetic resonance imaging lesion burden, and short-term disability. Non-adherence to therapy may reduce the effectiveness of these agents and affect quality of life and progression of disease. **Design/Methods:** The study population consisted of 252 health maintenance organization-insured patients with RRMS over 2 study years (2004–2006). Adherence to injectable medication was measured by the proportion of days the patient had an injectable medication on hand per prescription drug claims data. Other constructions to measure adherence are being explored. To determine relapse rates and

quality of life, medical chart abstraction and patient surveys, respectively, were used. **Results:** Among patients with RRMS (78% female, 40% African American), 62.7% were dispensed a disease-modifying drug. Among those with two or more dispensings, mean adherence was 84% (95% confidence interval [CI] 81, 87%), with 72% adherent (using 80% cut point). Adherence was associated with white race (80% vs 62% adherent; $P < .05$), increased age (46.7 vs 42.9 years; $P < .05$), and higher income. The response rate for patient surveys was 76%. Among survey participants, the proportion of adhere patients was 92%. Data from the medical record and patient survey are being used to estimate the association of adherence/nonadherence and disease progression and quality of life. **Conclusion:** Adherence to disease-modifying agents is high among patients with RRMS, with differences in socioeconomic factors that warrant further investigation.

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(S19) Health Care Utilization Over 2000–2005 Among Insured Patients With MS

Objectives: Published estimates of health care utilization in multiple sclerosis (MS) rely on data that may be more than a decade old. We investigated more recent health care utilization by MS patients that has occurred since the introduction of disease-modifying therapies (DMTs). **Methods:** We identified MS patients in a commercial administrative claims database that spanned May 2000 through July 2005 using ICD-9 codes. It was HIPAA-compliant and contained integrated inpatient, outpatient, and pharmacy records on >12 million covered lives per year from all major US regions. Data for subjects with continuous data for ≥ 1 year were analyzed with descriptive statistics. **Results:** Seventy-eight percent of subjects were female, and 84% were ages 30–60 years (mean 46 years). Significant comorbidity was common. Fifty-five percent of subjects used at least one DMT, with Avonex being most common (32%), followed by Copaxone (13.4%), Betaseron (6.5%), Rebif (5.6%), and Novantrone (1.6%). In a given year, 3.9% of subjects used two DMTs, and 0.2% used three or more. Subjects who took DMTs were more likely to use medications for symptom relief than those who did not: 41% used medication for depression, 42% for spasticity, 22% for fatigue, and 14% for bladder problems. The mean (standard deviation) number of visits per year was 9.1 (7.5); 4.1 (4.9) were MS related. Annual mean hospitalization was 1.6 days; 12.4% of subjects were hospitalized during the study period. For 62% of hospitalizations, MS was the first or second diagnosis coded: 5.7% of patients had emergency department admissions (37% condition related); 2.4% had intensive care unit visits (50% condition related); and 1.9% had skilled nursing facility admissions (63% condition related). **Conclusions:** Despite the introduction of DMTs, many patients with MS still require intensive medical care, including frequent outpatient visits and hospital stays. Novel treatments for MS may reduce this burden in the future.

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(S20) Rapid Cognitive Screening in MS Accomplished by Free Recall and Recognition Test

This study sought to investigate the feasibility of the Free Recall and Recognition Test (FRRT) as a practical screening tool of cognitive impairment in multiple sclerosis (MS). People with MS ($n = 227$) were consecutively recruited and assessed with four cognitive tests; FFRT, Symbol Digit Modalities Test, Paced Auditory Serial Addition Test, and Mini-Mental State Examination. Disease severity was assessed with the Extended Disability Status Scale (EDSS), the Multiple Sclerosis Functional Composite, and the Short and Graphic Assessment Scale. FFRT was repeated after 6 months. FFRT was completed by 99% of the cohort in ~5 minutes per assessment, and it correlated significantly with the other cognitive test and disease severity ratings. Test-retest reliability of FFRT was $r = 0.79$ for recall and $r = 0.55$ for recognition. A cutoff of 4 for the FRRT free recall rendered 90% sensitivity and 25% specificity, and a cutoff of 4.2 for the FRRT recognition resulted in 70% sensitivity and 51% specificity. We conclude that the FFRT proved to be feasible as a practical screening tool of cognitive impairment in MS in a clinical setting.

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(S21) Factors Associated With Adherence to MS Immunomodulatory Therapy

Introduction: Immunomodulatory agents for multiple sclerosis (MS) have been shown to effectively moderate the progression of disease for relapsing-remitting MS; thus, optimal adherence preserves quality of life and reduces health care costs. Identifying factors associated with suboptimal adherence to MS immunomodulatory therapies can alert health care providers to patients who may require additional attention during their course of care. **Methods:** A comparative study of adherent and nonadherent MS patients was done to identify factors associated with adherence. MS patients were identified by a pharmacy claim for Avonex, Betaseron, Copaxone, or Rebif between 1 January and 31 December 2004. Adherence (medication possession ratio, defined as total days patients had medication on hand over a 12-month follow-up period) was calculated during the 12 months after their index prescription. Existing users had a history of treatment with Avonex, Betaseron, Copaxone, or Rebif in the 6 months before the index prescription, whereas new users did not. New users who only had one fill during the 12-month period were excluded. Logistic regression models were constructed to identify factors associated with adherence (<85% vs 85%+) among new and existing users. **Results:** For both new and existing users, optimal adherence was associated with older age (45+ years), an average supply of 90 days, and <\$50 cost share. For existing users only, depression as a comorbidity to MS was associated with suboptimal adherence. For new users, depression was not a statistically significant factor in optimal adherence. However, new users had a higher prevalence of depression than existing users. Patient sex, proximity of residence to an urban/metropolitan area, and the specialty of the treating physician were not significantly associated with adherence. **Discussion:** Awareness

of factors related to poor suboptimal adherence for MS immunomodulatory agents may assist in management of patient care to improve adherence and outcomes for MS patients.

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(S23) Classification and Regression Tree Analysis of Neurocognitive Functioning in Patients With and Without MS

Multiple sclerosis (MS) is a debilitating demyelinating disorder associated with neurofunctional deficits. Although the hallmark of MS symptomology tends to focus on white matter degeneration, many patients with MS experience deficits in higher-order cortical processes such as attention, executive functioning, and working memory. Despite neurocognitive decline often being the first indicator of the disorder, diagnosis is primarily made by neurologists after patients note decrements in sensorimotor functioning. This study examined the results of a hierarchical decision tree that investigated the neurocognitive functioning of a group of 51 patients with MS (mean age [standard deviation] 45.70 [9.17] years) and 51 demographically matched normal control subjects, who completed the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Classification and regression tree (CART) analysis partitions the participants based on the dependent variables (RBANS composites) until the optimal split is achieved. These partitions are carried out in multiple stages until further divisions do not markedly improve the classification accuracy of the heuristic. The primary division of the data was on the delayed memory composite. Further investigation of the construction of these terminal nodes revealed that patients with poor performance on the delayed memory, attention, and immediate memory composites tended to be placed in the MS group. Conversely, individuals who exhibited intact functioning on delayed memory, language, and/or attention were unlikely to have been diagnosed with MS. Interestingly, it seems that relatively intact attention may ameliorate the severity of long-term memory deficits in patients with MS. This hierarchical decision tree can aid in differential diagnosis of MS and provided evidence for the severity of symptoms in this sample. This poster discusses the implications of the results for practitioners and researchers.

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(S24) Corrected Visual Acuity and Measured Attention Deficits in Patients With MS

Attention deficits are common in patients with multiple sclerosis (MS) and have detrimental synergistic impact on other neurofunctional domains, such as long-term memory. Coding tasks are fairly ubiquitous measures on neuropsychological and psychological tests and are thought to represent deficits in visual attention, working memory, vigilance, and mental flexibility. Vision difficulties and visual processing problems

are well documented in patients with MS; yet, most neuropsychological assessment batteries do not examine simple visual acuity. Visual acuity is an essential component of completing many neuropsychological tasks, including coding tests. This study used regression to evaluate the impact of uncorrected visual acuity on a widely used measure of attention, the coding subtest from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Participants were 35 patients with MS (mean age [standard deviation] 44.56 [8.46] years) who completed the RBANS and the visual acuity subtest from the Dean-Woodcock Sensory-Motor Battery (DWSMB) as part of a comprehensive neuropsychological evaluation. Regression results revealed that measures of visual acuity predicted 21.3% of the variance in the coding subtest and explained a significant proportion of the variance ($F = 4.338$, $P = .022$). The fact that a measure of simple uncorrected visual acuity was able to predict >20% of the variance in the coding task is magnified in importance because most neuropsychologists do not assess uncorrected visual acuity before administering measures of visual attention. This poster discusses the implications of these results for practitioners and researchers.

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(S25) Evaluating Neurocognitive Differences in Patients With and Without MS

Although neurocognitive deficits are often reported by patients with multiple sclerosis (MS), the research is surprisingly limited regarding the quantification of these deficits. There is also uncertainty regarding neurocognitive findings because factors such as fatigue, sensorimotor deficits, and medications can all contribute to impaired neurological processing. Empirically assessing the severity of neurocognitive deficits is critical because declines in memory, attention, language, and visuospatial skills have a salient impact on a patient's functional capacity (eg, ability to make medical decisions, work, drive, take medication safely, and manage finances). This study compared the results of 51 patients with MS (mean age [standard deviation] 45.70 [9.17] years) and 51 demographically matched normal control subjects who completed the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). RBANS is a widely used comprehensive measure of neuropsychological functioning that is particularly well suited for patients with MS because it was designed to be used longitudinally. Despite the short administration time (~30 minutes), ease of scoring, repeatability, and sensitivity to deficits, there is a paucity of research regarding the utility of RBANS to assess MS symptomology. Multivariate analysis of variance (MANOVA) revealed that the Wilks' lambda was significant ($P < .001$), which indicated the two groups differed in the population on at least one of the five composites. Descriptive discriminant analysis was used to ascertain which composites most contributed to this significant result. All of the RBANS scales except for visuospatial/construction contributed to the between-group difference identified by MANOVA, with the largest contributors being attention, immediate memory, and delayed memory. The results of this study were consistent with evidence that the

white matter degeneration seen in MS is associated with higher-order cognitive processing deficits. This poster discusses the implications of the results for practitioners and researchers.

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(S26) New Directions in MS Tissue Banking

New research methods, new discoveries, and new research ideas require innovations in multiple sclerosis (MS) tissue banking. The specific aims of the Rocky Mountain MS Center Tissue Bank are to procure, process, preserve, and distribute the highest-quality autopsy material to research laboratories involved in MS investigations. We continue to move forward in numerous ways to keep pace with the evolving world of MS research. Collaborative efforts are becoming increasingly important to provide large quantities of high-quality research tissue with corresponding clinical data. We continue to develop tissue banking methodology with Dr. W. Tourtellotte, Dr. R. Nagra, and others at the Human Brain and Spinal Fluid Resource Center at the West Los Angeles Veterans Administration. Normal neurological control tissues are absolutely essential. A full understanding of MS pathology requires understanding of normal conditions. Recently, we have been working with three other organizations to collect additional control tissue. Dissections designed specifically for MS inquiries are available, including defined cortical regions and hippocampus. New tools provide more precise dissections and reduce local artifact. We are now able to provide histological characterization of each dissected plaque. Investigators can now obtain detailed microscopic descriptions of the cell types, condition of myelin and other structures, and other features found in each plaque provided for research. Marketing is not traditionally thought of as an aspect of tissue banking, but it has become an essential component, both for donor recruitment and investigator awareness. The recent article in the national publication of the National MS Society, *InsideMS*, provided a significant increase in donor inquiries. Animal models of MS are important tools for research. However, they cannot substitute for examination of the actual human disease. Many new research initiatives in MS require the ready availability of human tissue.

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(S27) MS Quality-of-Life Project: Free Case-Management Program in Semirural Area

History: The Multiple Sclerosis Quality-of-Life Project (MSQLP) began its case-management program in August 2004, following the results of a comprehensive needs assessment. For individuals with MS, achieving an optimal quality of life is often a frustrating, exhausting, and overwhelming challenge. MSQLP offers ongoing assistance to people with MS in the tricounty area of Monterey, San Benito, and Santa Cruz, California. With two employees and an active volunteer board, MSQLP has accomplished much on an annual

budget of less than \$150,000. **Current Program:** When the case manager receives referrals, she or he contacts the people with MS and, during house calls, helps them complete an extensive assessment of eight areas: finances, health care, social support, functional abilities, activities of daily living, home environment, community services, and perceived future needs. After evaluating the assessment and analyzing the data, the case manager helps patients identify objectives (in the format of an individualized treatment plan) that, if met, would improve the quality of their lives. The case manager monitors their progress toward achievement of these objectives. In the process, she or he works with physicians, caregivers, landlords, social service organizations, other MS organizations (local, state, national, etc.) to help clients meet their needs. The case manager helps clients navigate through various complex systems/situations (eg, disability, drug plans, equipment procurement, caregiving, social services). **Accomplishments:** Assisted 120 clients and 48 caregivers; made 10,923 telephone calls; identified 2034 objectives with 1613 completed; made 200+ linkages with physicians, agencies, organizations; offers 3 monthly support groups; offered 2 outreach events and 2 educational symposia; offers weekly water aerobics class and quarterly newsletter. **Challenges:** Dealing with a chronic illness spanning decades, case management in a semirural area, complexity of the various systems people with MS have to deal with, mental health issues and MS, crisis management, and clients with little or no support system.

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(S28) Decreased Pulmonary Function in People With MS

Purpose: Compare pulmonary function of people with multiple sclerosis (MS) with mild to moderate disease severity with matched control subjects and predicted normal values. **Subjects:** Thirty-four people with MS (MSP) who were participants of the University of Utah Rehabilitation and Wellness Program and 34 control group (CG) subjects matched by sex, age, and height participated in this study. **Methods:** Subjects underwent measurement of forced vital capacity (FVC), forced expiratory volume in first second (FEV1), and maximal voluntary ventilation (MVV) with standard spirometric methods. Maximal expiratory pressure (MEP) and maximal inspiratory pressure (MIP) were measured with a handheld respiratory pressure meter. A count test was administered as a gross indicator of ventilatory function. **Results:** MEP ($P < .0001$), MIP ($P = .035$), MVV ($P = .0035$), and count test values ($P < .0001$) were significantly lower in people with MS than in CG subjects. There were no significant differences in FVC ($P = .21$), FEV1 ($P = .88$), and FEV1/FVC ($P = .26$) between the two groups. When comparing respiratory muscle strength measurements of MSP with predicted normal values from three commonly cited studies, three of the six comparisons were significantly different. MSP had significantly ($P < .0001$) lower MEP than two of the other studies. MSP had significantly ($P = .028$) lower MIP than one of the studies. **Conclusions:** These findings suggest that pulmonary function may be impaired in MSP with mild to moderate disease severity. Periodic measurement of pulmonary

function may be indicated in MSP. Future studies should examine whether a deterioration of pulmonary function can be avoided or reversed with respiratory resistance training.

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(S29) Factors Associated With Independence in Activities of Daily Living and Social/Lifestyle Activities in MS

Purpose: The purpose of this study was to describe and analyze independency in personal and instrumental activities of daily living (ADL) and frequency of social/lifestyle activities in a population-based sample of people with multiple sclerosis (MS) in Stockholm, taking into account motor and cognitive function, sociodemographic factors, and coping capacity. **Participants:** One hundred sixty-six people with MS. **Methods:** Data were collected using measurements and structured interviews in the home environment of the people with MS. Cognitive function was assessed by the Symbol Digit Modalities Test; manual dexterity by the Nine-Hole Peg Test; walking ability by need for aid/support when walking 10 meters, coping capacity by the Sense of Coherence Scale, independency in ADL by the Barthel Index and the Katz Extended ADL Index, and frequency of social/lifestyle activities by the Frenchay Activities Index. **Results:** Significantly more favorable results, with regard to ADL and normal frequency of social/lifestyle activities, were found in the subgroups: people with MS with normal cognitive function, normal manual dexterity, ability to walk without walking aid and support, living in a private household, and working. Ability to walk without aid and support and current employment were associated with independence in ADL and normal frequency of social/lifestyle activities. In addition, living together with a partner was associated with independence in the Barthel Index, normal manual dexterity speed with independence in the Katz Extended ADL Index, and normal coping capacity with normal frequency of social/lifestyle activities. **Conclusions:** The most important factor associated with independency and normal frequency of daily and social activities was the ability to walk. There is a great need for effective rehabilitation interventions focusing on cognitive function, manual dexterity, walking ability, ADL, and social/lifestyle activities for people with MS in Stockholm.

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(S30) Behavioral Approach to Weight Loss in Individuals With MS: 3-Year Follow-Up

Objective: Determine the long-term efficacy of a behavioral lifestyle program in a small cohort of overweight patients with multiple sclerosis (MS). **Background:** A group of mobility-impaired MS patients participated in a behavioral lifestyle program involving self-monitoring of calorie intake and expenditure. The chronic nature of the disease often leads to a sedentary lifestyle contributing to increased body weight and its related side effects. Participation in the 20-week Lifestyle Initiatives, Fitness and Energy (LIFE) program demonstrated that mobility-impaired overweight patients were successful at losing weight. A 3-year follow-up was

completed to examine the long-term efficacy of the behavioral lifestyle treatment. **Method:** Five overweight patients with MS from the LIFE program were followed over a 3-year period during informal bimonthly meetings. Patients included one man and four women with a mean age of 57.8 years. The mean disability score measured by the Kurtzke Expanded Disability Status Scale (EDSS) was 6.0. Behavioral strategies to manage weight while living with the unpredictable nature of MS were shared in a group format. Calorie intake and expenditure were tracked for 1 week per month through self-report. Body weight was recorded at each visit. **Results:** The mean weight loss during treatment was 20.4 pounds, with an additional loss of 5.9 pounds at follow-up. EDSS remained at 6.0. The mean physical activity expenditure increased slightly from 1206.2 to 1256.2 calories/week. Record keeping was relatively constant at 79.6%. **Discussion:** These results indicate that mobility-impaired overweight patients can maintain weight loss long term, suggesting that behavioral skills practiced during the treatment phase became learned behaviors. Intermittent self-monitoring and group support were important components of the program. Patients reported stabilized blood lipids, lower blood pressure, and decreased fatigue.

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(S31) Positive Impact of Resistance Training in MS With Varied Disability Levels

Muscle weakness and fatigue have long been hallmarks of multiple sclerosis (MS). Contrary to historic opinion, muscles weakened by MS appear to improve from strength training. There is indication that exercise may go beyond symptomatic treatment and could significantly impact fatigue and disability. Recent studies reported that MS patients benefit from physical exercise with profound effects on immune and endocrine parameters. Outcome data were evaluated related to strength and endurance before and after completion of a 6-month program of weight-resistance exercise. This unique study, unlike previous studies, evaluated MS patients with all levels of disability for changes despite the degree of original disability. Results demonstrate that all subjects show parallel improvement in both strength and endurance and support the use of exercise, to include weight-resistance programs, for all MS patients. The objective of study was to evaluate effectiveness of weight-resistance exercise in MS patients. This was a retrospective evaluation of specific outcome measures related to strength and endurance before and after completion of a 6-month program of weight-resistance exercise. Specific strength and endurance outcome measures were evaluated for designated muscle groups. The study population consisted of 67 consecutive MS patients completing 6 months of exercise therapy, including a specific regimen of conditioning and strength training. Between-subject analysis demonstrated that individuals with lower Expanded Disability Status Scale scores started at higher training weight and continued throughout the program to perform at proportionally higher levels. Each within-treatment analysis was significant. All exercises showed significant improvement in strength for participants, despite disability level. Increases in muscle strength followed parallel improvement pathways, reflected at all dis-

ability levels. All treatments displayed highly significant ($P < .0001$) improvement over the exercise course.

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(S32) Meeting the Challenges of MS: Educational Program for Caregivers

This poster describes the process of developing a program to meet the needs of caregivers of aging people with multiple sclerosis (MS). Three hundred two caregivers were interviewed as part of a larger study focused on unmet needs of people aging with MS in the Great Lakes region of the United States. During the interviews, caregivers were asked about the challenges they were experiencing in the context of their caregiving role. Qualitative analyses of these data uncovered several themes, including dealing with the physical and emotional aspects of caregiving, accessing formal services, and planning for the future. With these issues in hand, the research team searched for caregiver programs that matched the needs identified by the caregivers. A total of 21 programs were found, but none covered all of the issues raised by the caregivers. In response, the research team developed an education program targeting caregivers of people aging with MS. The resulting program, Meeting the Challenges of MS: Providing Support Through Problem Solving, is a 10-hour education program led by a registered occupational therapist. Participants engage in several learning activities, including lecture, group discussion and peer support, demonstrations, videos, and experiential learning. Participants also complete homework assignments designed to help caregivers apply concepts to their everyday caregiving dilemmas. The program uses a psychoeducational group approach and is based on problem-solving and self-efficacy theories. The program's intended objectives are to improve caregivers' self-efficacy for caregiving, increase their caregiving preparedness, and ultimately promote the health and well-being of caregivers of people with MS. The poster describes the process of developing the educational program, including identification of the challenges of caregivers, the strengths and limitations of existing caregiving programs, and an overview of the newly developed program.

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(S33) Validation of MS Intimacy and Sexuality Questionnaire in Large National Sample

There has been only one self-report instrument found in the literature assessing sexual dysfunction in both men and women with multiple sclerosis (MS). This 19-item Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19) assesses primary (directly stemming from MS symptoms), secondary (indirectly stemming from MS symptoms or symptomatic treatments), and tertiary (stemming from psychosocial and cultural issues) sexual dysfunctions. We aimed to revalidate the MSISQ-19 by surveying 8580 MS patients from the NARCOMS registry, out of which 5976 agreed to complete the questionnaire. Unforced principal component analysis (PCA) via promax rotation with Kaiser normalization assessed the construct validity of the instrument. With a stan-

ward eigenvalue cut-off score of 1.0 (identical to the original validation study), three factors emerged explaining 63% of the total variance. These factors closely mirrored the original three factors measuring primary, secondary, and tertiary sexual dysfunction. PCA was also performed separately for men and women. For the primary sexual dysfunction subscale, there was 100% concordance among the five items in the original study and the items that emerged in the current study. For the secondary sexual dysfunction subscale, five of the original nine items were retained. For the tertiary subscale, the five original items were retained. Thus, the revised MSISQ scale contains 15 items, applying equally well to men and women (with one primary item specific for each sex). The factors were found to be moderately correlated (Pearson r range 0.53–0.65), with the secondary subscale correlating most highly with self-reported disability (r [5776] = 0.45, $P < .001$) and the tertiary subscale correlating most highly with psychological distress (r [5725] = 0.41, $P < .001$). Cronbach α on the total scale ($\alpha = .92$) and subscales ($\alpha = .87$ primary, $.81$ secondary, $.91$ tertiary) demonstrated good reliability. Thus, the revised 15-item MSISQ is a reliable and valid measure of sexual dysfunction in both men and women with MS.

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(S34) Phase 3 Clinical Program to Assess Efficacy and Safety of BG00012 in MS

Objective: Determine the efficacy and safety of BG00012 in patients with relapsing-remitting multiple sclerosis (RRMS).

Background: Data suggest that BG00012, an oral fumarate derivative, is an immunomodulator that has a novel mechanism of action with a combination of cytoprotective and anti-inflammatory properties. In a dose-ranging phase 2b study of 257 patients with RRMS, BG00012 720 mg/day significantly reduced the formation of new gadolinium-enhancing (Gd+) lesions after 24 weeks of treatment compared with placebo ($P < .001$). BG00012 was safe and well tolerated. These findings support further study of the agent for the treatment of RRMS. **Methods:** Two multicenter, randomized, 2-year phase 3 studies of BG00012 in patients 18–55 years of age with a confirmed diagnosis of RRMS, a baseline Expanded Disability Status Scale score between 0.0 and 5.0, and either one relapse within the past year or evidence of Gd+ lesions on magnetic resonance imaging scans within 6 weeks of randomization are planned. In the DEFINE (Determination of the Efficacy and Safety of Oral Fumarate in RRMS) study, patients are being randomized to receive BG00012 480 or 720 mg/day or placebo. The primary endpoint is the proportion of patients relapsing. In the CONFIRM (Comparator and an Oral Fumarate in RRMS) study, patients are being randomized to receive BG00012 480 or 720 mg/day, placebo, or glatiramer acetate. The primary endpoint is annualized relapse rate. Relapses are confirmed by an independent panel of blinded neurologists. In both studies, secondary endpoints include disability progression and the formation of Gd+, T1-hypointense, and T2-hyperintense lesions. Safety will also be assessed. **Results:**

Patient recruitment into the two studies began in early 2007. More than 2000 patients will be enrolled across the studies.

Conclusion: BG00012 is a promising new treatment for RRMS. The phase 3 study results will better define the role of BG00012 in disease management.

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(S35) Reanalysis of CHAMPS Study Based on New Classification Criteria

Background: Clinical trials of interferon beta (IFN β) in patients with clinically isolated syndrome (CIS) found that early treatment was associated with a reduced risk of progression to clinically definite multiple sclerosis (CDMS). The impact of treatment on different CIS presentations remains unclear. **Objective:** Reanalyze the 2-year data from the Controlled High-Risk Subjects Avonex Multiple Sclerosis Prevention Study (CHAMPS) using more recent classification criteria for CIS. **Methods:** CHAMPS data were reanalyzed to determine the effect of treatment on CIS patients. With an algorithm derived from Uitdehaag and colleagues, the CIS population was reclassified as either monofocal or multifocal. The ability of intramuscular IFN β -1a to delay progression to CDMS according to each classification was assessed.

Results: The 2-year adjusted hazard ratio in the overall population was 0.45 (95% confidence interval [CI] 0.29–0.70; $P = .0003$). On reclassification, 30% of the CHAMPS population had evidence of multifocal disease. Over 2 years, the unadjusted hazard ratio for risk of converting to CDMS in patients with a monofocal presentation was 0.45 (95% CI 0.27–0.74; $P = .0013$). In patients with a multifocal presentation, the hazard ratio was 0.64 (95% CI 0.32–1.28; $P = \text{NS}$). No treatment-by-subgroup interactions were observed. Additional subgroup analysis showed a trend toward greater reduction in development of CDMS in patients with >1 gadolinium-enhancing (Gd+) lesion compared with patients with no Gd+ lesions. **Conclusions:** Although the treatment effects of IFN β -1a were more pronounced in monofocal patients and those with Gd+ lesions, no treatment-by-subgroup interactions were detected. These data are similar to a recently reported study that analyzed the effect of IFN β -1b in delaying the conversion to CDMS in patients with monofocal or multifocal presentation of CIS.

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(S36) Immunologic Markers in MS Patients on Combination Therapy

In responders, combination therapy (CT) enhances optimal control of the multiple sclerosis (MS) process. **Material/Methods:** In 160 MS patients on interferon beta (IFN β)-1a subcutaneous (SC) (Rebif 22–44 μg three times per week; R) or intramuscular (IM) (Avonex 30 μg weekly; A) presenting worsening in Expanded Disability Status Scale scores by ≥ 1.0 , CT with prednisone (P) < 0.12 mg/kg daily, azathioprine (AZA) 1.5–3.0 mg/kg daily or mycophenolate mofetil (CellCept [CC]) 2 g/day was initiated. There were 21 patients on RP and 83 on AP. With suboptimal clinical stabi-

lization on RP and AP, 6 patients were placed on RPAZA and 21 on APAZA. In 29 individuals failing CT with AZA, AZA was replaced with CC (APCC). Serum levels of tumor necrosis factor (TNF) α , soluble intercellular adhesion molecule-1, soluble interleukin (IL) 2 receptor, IL-10, and IL-12 were monitored in 3-month intervals. There were 18 healthy control subjects (HC). Peripheral blood (PB) flow cytometry (FC) using CD3, CD4, CD8, CD14, CD16, and CD19 antigens was performed after 6 months of treatment. Twenty untreated MS patients (UP) served as control subjects. A generalized estimating equation population-averaged model was applied for statistical evaluation of serum markers. **Results:** Compared with HC, patients on RP and RPAZA showed downregulated mean serum levels of TNF- α and IL-12 ($P < .0001$). Similar findings were obtained in patients on APCC but not on AP and APAZA. Compared with HC and patients on RP, RPAZA, and APCC, in patients on APAZA, upregulated mean serum levels of IL-10 ($P < .0001$) were recorded. Compared with UP, patients on APCC demonstrated the lowest mean cell count of PB CD8 T and CD19 B cells ($266.6 \pm 171.4/\mu\text{L}$, $P < .0034$; $82 \pm 78.5/\mu\text{L}$, $P < .0001$) with CD19 B cell count as low as $12/\mu\text{L}$. **Conclusions:** Immunological markers provide essential information regarding response to CT that cannot be substituted by routine magnetic resonance imaging. Monitoring of immunological markers enables early detection of suboptimal responders to ongoing treatment.

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(S37) Evidence to Support Need for Family Caregiver Programs

Rationale: Canada is a high-risk area for multiple sclerosis (MS), with ~1000 new cases of MS diagnosed each year. The MS Society of Canada recognizes the gap in services for family caregivers and has made a commitment to respond to the need for additional support and services. According to an article by Benjamin Gottlieb, PhD, there are enormous pressures on families to provide practical care and emotional support on behalf of family members who suffer from chronic illness. The family caregivers' stamina is depleted over time, compromising their physical and psychological health. A caregiver may be a parent, adult child, spouse, friend, or neighbor. The MS Society of Canada, Calgary Chapter has conducted two family caregiver surveys and one focus group over the past 3 years. After offering various programs, the Family Caregiver Retreat continues to be the most successful. **Outcome Measures:** Service providers, governments, other funders, and the public are asking for clearer evidence that the resources they expend actually produce benefits for people. Outcome measurement evaluates whether a program really makes a difference in the lives of people. It offers findings that can be used to support, adapt, or improve services. The Calgary Chapter has used outcome measurement for more than a decade and has a program logic model (PLM) for each of the programs, including the Family Caregiver Retreat. A PLM is a road map that tells you where you are going, how you will get there, and when you have arrived. The evaluation results from the 2006 Family Caregiver Retreat showed that the program goals were met

and that 100% of the respondents rated the retreat overall as excellent or very good. This presentation highlights the Family Caregiver Retreat and the findings that support the need and impact, which include results from the client surveys and outcome measures.

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(S38) BENEFIT Study: Characteristics of Patients With Potentially Benign MS

Background: There is uncertainty regarding how to identify patients with a potentially benign course of multiple sclerosis (MS) after a clinically isolated syndrome (CIS) suggestive of MS. Possibilities include certain baseline disease characteristics or the absence of any clinical or subclinical disease activity in the immediate follow-up period. This analysis aimed to determine factors that may identify patients with possible benign MS. **Design/Methods:** In the BENEFIT (Betaferon/Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment) study, 176 CIS patients with magnetic resonance imaging (MRI) evidence suggestive of MS received placebo for up to 2 years or until they developed clinically definite MS (CDMS). Within this period, patients were monitored by clinical visits at Months 1, 2, 3, 6, 9, 12, 18, and 24 after start of treatment, with cerebral MRI obtained at Months 3, 6, 9, 12, 18, and 24. Baseline characteristics of patients without disease activity (ie, inactive patients without relapse, Expanded Disability Status Scale score progression, new gadolinium-enhancing lesion on T1-weighted MRI, no new or enlarging lesion on T2 weighted MRI) were compared with patients exhibiting any such activity. **Results:** Of the 176 placebo-treated patients, 12 (6.8%) were inactive and 164 (93.2%) were active (of which 142 developed McDonald MS and 77 developed CDMS). At the time of the CIS, inactive patients were significantly older, had a lower T2-lesion number and volume, and had less frequent positive cerebrospinal fluid (CSF) findings. Clinical characteristics (including the presentation of the first event) did not differ between the groups. **Conclusions:** Older patients have a higher chance to not show any further disease activity after a CIS suggestive of MS. MRI and CSF findings at the time of the first event suggestive of MS (CIS) and other molecular parameters may help to identify such patients with possible benign MS. Further data on the disease course of patients based on the 3-year interim analysis of the BENEFIT study are available.

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(S39) Evaluating High-Dose High-Frequency Interferon-Beta Regimens

Clinical trials have demonstrated the benefits of interferon beta (IFN β) treatment in multiple sclerosis (MS). However, the optimal dosing of IFN β is a controversial topic in the MS community. High-dose high-frequency (HDHF) IFN β regimens (IFN β -1b 250 μg subcutaneous [SC] injection every other day; SC IFN β -1a 22 or 44 μg three times weekly) and the

low-dose low-frequency regimen (intramuscular [IM] IFN β -1a 30 μ g once weekly) have demonstrated similar efficacy compared with placebo during phase 3. Post hoc analysis of the IM IFN β -1a study showed a 55% reduction in brain atrophy in IM IFN β -1a-treated patients compared with placebo-treated patients. A similar analysis showed no significant treatment effect for patients treated with SC IFN β -1a three times weekly compared with those treated with placebo. In contrast, patients treated with SC IFN β -1a once weekly had fewer new T2 lesions and a smaller increase in lesion burden compared with placebo. A dose-comparison study showed equal rates of disability progression and no dose-related benefits among patients treated with IM IFN β -1a 30 or 60 μ g once weekly. In addition, abnormal laboratory values such as leukopenia, neutropenia, lymphopenia, and elevated levels of hepatic transaminases are more commonly associated with HDHF IFN β products. These data suggest a possible ceiling effect of therapy. It appears that high-dose high-frequency formulations may cause negative feedback regulation that can lead to dampening of IFN effects. In choosing an optimal dose for the MS patient, the practitioner must consider the regimen that provides maximal clinical benefit with minimal risk. Careful consideration will provide the patient with the greatest long-term efficacy and quality of life.

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(S40) Clutter Management in MS: Integrated Occupational Therapy Approach

Clutter or hoarding is an area commonly overlooked in multiple sclerosis (MS) management. Those who hoard have more difficulty performing activities of daily living (ADLs) because of physical, cognitive, and emotional interferences. Clutter promotes confusion and places patients in potentially harmful situations by increasing the risks of falling, losing medications, or misplacing important documents. Clutter increases a person's sense of helplessness and loss of independence. Using James Prochaska's Stages of Change model, an occupational therapy clutter-reduction protocol has been developed and implemented to two cohorts of six patients for 8 weekly sessions. The group addressed the psychological issues preventing organization and offered strategies for clutter removal and management. Because eliminating clutter too rapidly can create anxiety and prevent long-term progress, a critical component of the intervention is to introduce changes incrementally. For example, by slowly removing the ties to "beloved" inanimate objects, such as a stuffed animal or a broken record player, patients are ultimately able to let go of unnecessary items. Participants gradually integrated the concepts into their daily routines, and, at the completion of the program, 10 of 12 participants maintained a clutter-free area. Six months after the workshop, 7 patients reported the ability to maintain a clutter-free space within their home environment. Clutter management is an important domain of occupational therapy intervention and may significantly impact safety, ADLs, and quality of life.

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(S41) Improving Quality of Life Through Participation in Self-Management Interventions

Impaired quality of life (QOL) is a major manifestation of multiple sclerosis (MS) and is related to physical disability, cognitive impairment, social isolation, loss of independence, and loss of employment. Many MS centers provide physical rehabilitative treatment options, but few centers offer psychosocial interventions addressing broader QOL issues. An effective rehabilitation program should maximize functional independence, enhance cognitive and psychosocial abilities, evaluate and identify functional challenges, and offer appropriate client-centered interventions to increase participation in meaningful occupations. Under the guidance of occupational therapy, the New York University Hospital for Joint Diseases MS Care Center has undertaken an initiative to improve emotional and psychosocial health in MS. To address activities of daily living and enhanced QOL, various group interventions have been implemented. Examples include fall prevention, shopping, clutter management, pet therapy, art therapy, health and wellness, stress reduction, and caregiver support. An intensive cognitive rehabilitation program focuses on remediation of impairments of memory, attention, and speed of processing. Community reintegration groups address psychosocial isolation. For example, patients attend Broadway musicals, theatrical events, and other community-based recreational activities. More than 500 patients have participated in these client-centered programs. Patients reported enhanced QOL and physical, social, and emotional improvement. After being socially isolated for months and then attending group programs, many patients have initiated social activities. Preliminary findings showed that patients who received more comprehensive treatment demonstrated improved coping skills and reported increased participation in meaningful occupations. The role of an occupational therapist designing and executing these programs is presented.

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(S42) Impact of Estrogen Use on Memory and Quality of Life in Postmenopausal Women With MS

Recent studies have shown that some forms of estrogen favorably impact multiple sclerosis (MS) disease course. Some studies have also demonstrated that healthy postmenopausal women on estrogen replacement therapy (ERT) perform better on cognitive tests than women without ERT. We performed a pilot study to investigate the potential benefit of ERT in MS.

Methods: Eighteen postmenopausal women with MS, nine on ERT and nine not on ERT, completed a battery of cognitive tests and quality of life (QOL) measures. **Results:** The groups did not significantly differ by age (mean 50 years), education level (mean 13.6 years), or disability as measured by the MS Functional Composite (mean z score .08). Group mean scores were similar on the Beck Depression Inventory and QOL measures, but higher levels of depression were associated with lower QOL ratings ($P = .002$). Overall performance on cognitive tests was not significantly different

between groups. Although the groups showed equivalent word-list learning, the women on ERT recalled significantly more words after a delay ($P = .009$). **Conclusions:** Similar to studies of healthy postmenopausal women, this pilot study of women with MS demonstrated a significant benefit of ERT on delayed verbal recall. It remains uncertain whether this statistically significant difference translates into a meaningful clinical benefit that would balance the potential risks of ERT for this population.

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(S44) Comparing Quality-of-Life Measures With Best Method of Collecting Quality-of-Life Data in MS

To evaluate the best methods and tools to assess quality of life (QOL) in multiple sclerosis (MS), this original study compared the SF-36 and its variant, the MSQOL-54 with WHOQOL-100, against a subjective client-rating tool. Analyses and examinations of these instruments showed a clear need for extensive rather than restricted measurement of QOL to best represent what clients/patients considered imperative for QOL. WHOQOL-100 provided the best representation via a wider sampling of life areas, whereas disease-specific and so-called health-related QOL measures represented only two elements of QOL that were of lesser importance in participants' subjective ratings. Discussion of the clinical, service planning, and methodological issues of using QOL measures is provided in this presentation.

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(S45) Reasons for Adopting Trauma Model Approach to Assessment and Therapy for People With MS

A survey of multiple sclerosis (MS) clients in New South Wales (NSW), Australia, revealed that a third of respondents may have posttrauma reactions (thought intrusion, hyperarousal, and avoidance) to their experience of receiving a diagnosis of MS. A more detailed study was performed via phone interview of volunteer clients to psychometrically assess trauma symptoms and to discover which elements of the diagnosis experience were helpful and unhelpful. Information was gathered using psychometric scales and evaluation of interview content. Results reaffirmed that for 10%, the experience of receiving an MS diagnosis resulted in the development of posttraumatic stress disorder (PTSD), and, for an even greater percentage (15%), posttraumatic stress symptoms occurred in regard to the disease itself. More significant, diagnosable partial PTSD was evident in two thirds of the MS sample. These posttrauma reactions affect health behaviors and MS management, and the interview analysis provided guidelines for education of medical practitioners to assist them in ways in which they present patients with an MS diagnosis. It also provided a model for intervention practices with people with MS.

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(S46) Fatigue and Restless Leg Syndrome in MS

Fatigue is a common complaint in patients with multiple sclerosis (MS). Fatigue is commonly attributed to depression, medication, nocturia, pain, spasticity, and MS itself. Treatment of MS fatigue is often reported to be ineffective or less than satisfactory. Restless leg syndrome (RLS) is a clinical disorder characterized by abnormal sensations in legs/limbs at rest that are relieved by movement of affected limbs. This extra movement can result in fatigue, difficulty falling asleep, and impaired sleep efficiency. RLS is commonly associated with Parkinson's disease but can be seen independently. There are few reports associating RLS and MS. Patients with MS who report RLS nocturnal limb movements may be misinterpreted by MS clinicians as reporting symptoms of spasticity or involuntary spasms. Although the age demographics for both RLS and MS overlap, these disorders are not often associated. We identified patients with MS fatigue and RLS. These patients have had symptomatic RLS and were initially presumed to have nocturnal spasticity or spasms. Patients with MS and symptomatic RLS can have target symptoms effectively treated with standard dopamine agonist therapy. Symptomatic fatigue in MS may be caused by many factors, including sleep disorders and RLS. The association of MS, fatigue, and RLS may be more common than appreciated. Appropriate effective treatment of fatigue in MS must start with accurate identification of the cause of fatigue.

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(S47) Severity-Based Classification for MS: Defining Malignant MS

Background: A subgroup of multiple sclerosis (MS) patients experience more aggressive disease (AMS). Lublin and Reingold provided a qualitative definition for malignant MS (MMS) that does not define disability/duration (D/D) parameters. Poser, Wikstrom, and Bauer suggested quantitative descriptors, Expanded Disability Status Scale (EDSS) score of 7 at 5 years disease duration, and recorded 3% prevalence. **Objective:** Rigorously define AMS and MMS. **Method:** Global Multiple Sclerosis Severity (MSSS) score is an algorithm relating EDSS scores to distribution of disability in a reference patient population with comparable disease duration. Patients are ranked on a decile scale; MSSS scores thus represent prevalence of patients with particular D/D coordinates in the reference population. For MS patient subpopulations, single-point MSSS scores based on cross-sectional EDSS measurements after 1 year are representative of overall disease severity over time. To define AMS and MMS, a consensus of 25 MS specialists was obtained, and resulting D/D coordinates were applied to the MSSS algorithm. **Results:** (1) AMS is defined as an EDSS of ≥ 6.0 7 years after onset of symptoms, yielding an MSSS score of ≥ 8.24 . This predicts prevalence of 17.5%, or approximately one sixth, in the reference population. MSSS 8.24 corresponds to the following approximate D/D coordinates: EDSS 3.5/1 year, 5.0/4.5 years, 7.5/18 years. (2) MMS, a subpopulation of AMS, is defined as EDSS ≥ 6.0 2 years after symptom onset, yielding an MSSS score of ≥ 9.9 . This predicts preva-

lence of 4% in the reference population. MSSS 95.9 corresponds to D/D coordinates: EDSS 7.0/5 years (corresponding precisely with the definition of Poser et al.) and 8.0/10 years. **Conclusion:** AMS is defined quantitatively as an MSSS score ≥ 8.24 (prevalence 17.5%). MMS is a subset of AMS and is defined as MSSS score ≥ 9.59 (prevalence 4%).

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(S48) Severity-Based Classification for MS: Description of Six-Tiered System

Background: Multiple sclerosis (MS) is generally categorized according to clinical phenotype, level of disability, or pathological subtype. These classifications are of limited therapeutic utility because they do not accurately reflect disease severity. Identification of subpopulations based on disease severity would enable more homogeneous stratification for purposes of treatment and clinical trial design. **Objective:** Develop a classification system for MS based on disease severity. **Methods:** Global Multiple Sclerosis Severity Scale (MSSS) score is an algorithm relating Expanded Disability Status Scale (EDSS) scores to distribution of disability in a reference patient population with comparable disease duration. Patients are ranked on a decile scale; MSSS scores thus represent prevalence of patients with particular disease disability/duration (D/D) coordinates in the reference population. For patient subpopulations, single-point MSSS scores based on cross-sectional EDSS measurements after 1 year are representative of overall disease severity over time. To define MS subpopulations of varying severity, various D/D coordinates were applied to the MSSS algorithm. **Results:** Six subpopulations were defined: grade 1 (mild MS) is MSSS below 17th percentile (1.7th decile), grade 2 is MSSS between 17th and 50th percentile, grade 3 is MSSS between 50th and 83rd percentile, grade 4 (aggressive MS) is MSSS above the 83rd percentile. Grade 2 was further subdivided into 2A (moderate MS) and 2B (intermediate MS) at 34th percentile and grade 3 into 3A (advanced MS) and 3B (accelerated MS) at 67th percentile, thereby creating six equally distributed subgroups. Percentile boundaries represent D/D coordinates: 17th = EDSS <3.5/30 years; 34th = 3.0/11 years; 50th = 6.0/22–24 years; 67th = 6.0/13 years; 83rd = 6.0/7 years. **Conclusion:** A new MS clinical classification system is described, based on MSSS and disease severity. Six subpopulations are defined, of equal prevalence in the reference MS population. This classification should contribute greatly to the development of MS treatment guidelines and clinical trial design.

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(S49) Effect of Natalizumab on MS Severity Score in Highly Active Patients

Background: The Multiple Sclerosis Severity Scale (MSSS) is a disease severity algorithm that relates disability to disease duration and may be more robust than currently used measures of disease severity. Post hoc analyses from the AFFIRM study showed that the effect of natalizumab monotherapy on several clinical and magnetic resonance imaging (MRI) measures was more pronounced in a sub-

group of highly active (HA) treatment-naive patients. We conducted an analysis to determine change in MSSS scores in this subgroup of study participants. **Methods:** MSSS scores were assigned based on Expanded Disability Status Scale (EDSS) scores and disease duration in two subgroups of patients from AFFIRM: HA (patients with two relapses in the year before study entry and one gadolinium-enhancing lesion at study entry) and non-HA (nHA). Patients were assigned to one of six disease severity subgroups based on MSSS scores at baseline and at trial completion; analyses were conducted with baseline EDSS scores and those confirmed at Week 120. Shifts between MSSS severity groups from baseline to study completion were determined. **Results:** Data from 206 HA patients and 718 nHA patients were included in this analysis. There was a trend toward higher baseline MSSS scores for HA patients compared with nHA patients (4.13 vs 3.54; $P = .0655$). In both groups, median MSSS score was significantly lower in natalizumab patients than placebo patients at study completion (2.65 vs 3.34; $P = .0004$). Also, in both HA and nHA groups, more natalizumab-treated patients shifted to a lower severity group (55% vs 42% and 43% vs 36%) and fewer to a higher severity group (8% vs 23% and 10% vs 19%) compared with placebo during the study ($P = .0056$). **Conclusion:** These results demonstrated that natalizumab treatment effectively reduced disease severity regardless of baseline disease activity.

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(S50) Intravenous Immunoglobulin Adjuvant Therapy and MS Quality of Life: Retrospective Survey

Background: The utility of intravenous immunoglobulin (IVIg) in multiple sclerosis (MS) management is controversial. Studies to date have generally examined use of IVIg as monotherapy and its effect on relapse rate or recovery. However, our clinical experience suggested that major beneficial effect of IVIg may derive from its use as adjuvant therapy and its effect on "insensible" symptoms affecting quality of life, such as fatigue and malaise. **Objective:** Assess perception of quality of life by retrospective survey in MS patients treated with IVIg as adjuvant therapy. **Method:** We surveyed 100 patients with relapsing-remitting or secondary progressive MS and suboptimal disease control who had received adjuvant IVIg 0.7 g/kg monthly for at least 6 months in combination with a primary immunomodulating agent. Patients self-rated their response to treatment in 12 categories reflecting subjective symptoms, quality of life, sense of well-being, self-efficacy, and stability of disease as worse, the same, improved, greatly improved, not sure, or not applicable. **Results:** Male:female distribution was 15:85. Mean duration of IVIg therapy was 22 months (range 6–60 months). Percentage improved or greatly improved by category: overall quality of life, 62%; energy level, 57%; pain, 21%; cognitive function, 27%; sense of health and wellness, 58%; frequency of exacerbation, 58%;

mobility, 40%; stability of MS, 49%; sense of control of MS, 57%; family relationships, 39%; social life, 59%; emotional well-being, 43%. Response to concluding statement, "Since taking IVIG, I am feeling in general less sick and in a better state of health and wellness": 57% strongly agreed, 24% somewhat agreed. **Conclusions:** Most patients with unstable MS perceived beneficial effect from IVIG adjuvant therapy. Major categories of perceived benefit were overall quality of life, energy level, frequency of exacerbation, sense of control, sense of health and wellness, and social life. A blinded, prospective, controlled study is warranted.

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(S51) Effectiveness of Exercise as Treatment for Depression in People With MS

Background: Major depressive disorder (MDD) is a highly prevalent condition in people with multiple sclerosis (MS), with a lifetime risk between 22.8% and 54.0%. Depression is associated with greater disability and suffering. Exercise is an effective treatment for depression in healthy human subjects. Therefore, exercise may have promise as a means of treating depression in people with MS. **Research Aim:** Evaluate the impact of exercise on depression, fatigue, pain, community participation, and health-related quality of life in people with MS. **Methods:** This is a randomized controlled study. Participants meet criteria for MDD and/or dysthymia and are sedentary. The treatment group receives nine sessions of a mostly telephone-based intervention designed to improve motivation to exercise and activity over 16 weeks. The waitlist control group receives treatment after 16 weeks. Outcome measures are PHQ-9 and SCL-20 depression measures and minutes of exercise. **Results:** The study is ongoing; therefore, the main analyses are pending. Here, we present the results of several cases to illustrate reactions to the intervention and changes observed. Case 1 is a 53-year-old woman diagnosed in 2001 with an Expanded Disability Status Scale (EDSS) score of 5. Her exercise activity increased from 0 to 165 minutes/week of gardening. Her SCL depression scores declined from 15 to 8. At Week, 6 she reported, "My mood has improved. I feel like I am accomplishing something." Case 2 is a 57-year-old man diagnosed in 2005. His EDSS score was 6. His activity went from 0 to 300 minutes of rowing, stacking wood, and woodworking. His SCL depression scores fluctuated among 22, 10, and 25. He reported, "I'm doing this (exercise) for the purpose of being able to do the enjoyable activities that I used to be able to do.... I can't do everything like I did before, but I feel like I am getting part of my life back."

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(S52) Campath (Alemtuzumab) Off-Label Use in MS Clinic: Candidate Selection, Education, Administration, and Monitoring

Background: Campath (alemtuzumab, Berlex/Bayer), an anti-CD52 humanized, potent, complement-fixing, cytotoxic monoclonal antibody, has shown outstanding effectiveness in

a randomized phase 2 trial with rater blinding and has about 15 years of study in open-label phase 1 trials in both relapsing and secondary progressive multiple sclerosis (MS) in the United Kingdom. This agent appears more effective when given earlier in the course of relapsing MS. Campath is marketed for treatment-refractory chronic lymphocytic leukemia and available for off-label use. Alternative off-label therapies are needed given the time-limited and unexpected significant infectious, neoplastic, and cardiac toxicities of mitoxantrone chemotherapy. Given the current regulatory environment in North America, alemtuzumab appears to be years away from formal labeling for MS, but efficacy data warrant consideration for use in suboptimal treatment responders or those with risk factors for poor prognosis. However, significant toxicities of alemtuzumab (thyroid, thrombocytopenia) have been noted that require monitoring. **Hypothesis:** Alemtuzumab can be safely, ethically, relatively inexpensively, and effectively administered to people with MS with appropriate screening, informed consent, and monitoring. **Method:** Prior publications regarding efficacy and toxicity of alemtuzumab in relapsing and secondary progressive MS were reviewed. We implemented selection criteria using treatment failure, traditional risk criteria (relapse, progression, magnetic resonance imaging), and MS Severity Scale (MSSS) to predict prognosis. Individuals with higher Herbert classifications (3-4) or MSSS (>5.0), suboptimal treatment responders, intolerant of therapies, and unremitting mild disabilities were considered. An informed consent document and information regarding treatment alternatives were presented to each patient. Baseline laboratory including immunoglobulin levels, CD4/CD8 counts, thyroid function, and hemogram were obtained. A single 60-mg course of Campath was administered over 3-5 days in conjunction with 3 days of high-dose intravenous Solu-Medrol for first-year therapy after withdrawal of other immunotherapy. Pneumocystis and herpetic prophylaxis drugs were used during periods of low CD4 counts. Monthly hemograms, semiannual thyroid functions, and CD4 counts were obtained. Our institute used a monitoring program to ensure regular monthly follow-up of hemograms and patient and primary care physician education to obtain immediate care in the event of fever, bruising, or bleeding complications. **Results:** Patient satisfaction and enthusiasm for the treatment was favorable. Minor adverse events of headache, malaise, pruritis, and rash were self-limited and easily treated with prescription and over-the-counter antihistamines and analgesics. Laboratory test results demonstrated prolonged lymphopenia after treatment. Significant neurological improvements were noted at follow-up. **Conclusions:** Alemtuzumab can be implemented in off-label use as a safe, cost-effective, practical, and neurologically effective therapy for treatment-refractory or poor-prognosis MS in the most common variants of relapsing and secondary progressive MS. Substantial care is required in informed consent, patient education, and treatment monitoring to avoid serious adverse effects.

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(S53) Enhancing Quality and Value of Magnetic Resonance Imaging for MS

Background: Magnetic resonance imaging (MRI)-based techniques remain the gold standard of visualizing cerebral disease in multiple sclerosis (MS). Straightforward measures are needed to ensure the usefulness of this expensive and difficult-to-obtain study and enhance its long-term value. **Thesis:** A discrete set of measures obviously enhance the quality and value of MRI studies for management of MS. These include provider and personnel training, guidelines for timing and technique of studies, newer MRI software, imaging review software, appropriate workstations, electronic and digital media storage of images for comparison, and reporting formats suitable for MS management. **Method:** Physician continuing medical education credit for MRI was obtained. Policies regarding timing of imaging and the scope of neuraxis imaging were developed. Imaging center technicians were trained in CMSC techniques. Clinic personnel were trained in completion of an imaging referral to obtain the desired study with a standardized set of orders. Additional advanced imaging techniques were used where possible. Simple linear measurements for brain volume morphometry were instituted. Clinic viewing workstations were obtained with professional viewing software, and physicians and practitioners were trained in software use for review of images and patient education. A filing system for studies, including an electronic archive, was inexpensively procured. Standardized reporting formats for described disease burden, severity, and activity were put into use. **Results:** The specified measures greatly enhanced utility of the information derived from MRI in our clinic. **Conclusion:** A great amount of additional value can be obtained in the use of MRI with appropriate personnel training, a standardized policy regarding imaging timing and technique, improved hardware and software platform for image viewing, and standardized reporting format.

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(S54) Treatment of Neuropathic Pain in MS: Willingness-to-Pay Study

Objectives: Multiple sclerosis (MS) is a chronic disease affecting the central nervous system. Its prevalence in Canada is ~0.24%, and the prevalence of pain among these patients is ~71%. Sativex is a new cannabis-based drug approved in Canada for adjunctive treatment for symptomatic relief of neuropathic pain in adult MS patients. A study was conducted to determine how much people from the general public are willing to pay for Sativex. **Methods:** A willingness-to-pay (WTP) approach was used. It measures patients' preferences for treatments by elucidating which treatment they prefer and how much they would be willing to pay in additional insurance premiums to have access to the treatment should they ever need it. The WTP instrument included a modified decision board (DB) and a bidding game. A DB is a visual aid developed to help physicians present treatment options to patients in a standardized manner. Two treatment options were presented: a cocktail of three medications (gabapentin, amitriptyline, and acetamin-

open [pills]) and the same cocktail plus Sativex (pills and oral spray). Information about safety and efficacy for each option was derived using published literature and input from clinical experts. The WTP instrument was administered to 500 Canadians, and descriptive statistics were calculated.

Results: The study sample had a mean age of 39 ± 13 years, and 56% were women. Of the 500 interviews conducted, 85% were in English and 15% in French; 253 respondents chose pills and oral spray. For these subjects, the mean WTP in additional monthly insurance premiums was CAD \$8 (range \$0–200, median \$4). **Discussion:** Assuming that 51% of the general population is willing to pay for the pills and spray as reported in this study, the premiums collected would cover the cost of Sativex for all Canadian MS patients suffering from pain who want this treatment, with a surplus.

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(S55) MS and Other Autoimmune Diseases

Introduction: Multiple sclerosis (MS) is a demyelinating disease affecting the central nervous system, with an unknown origin. The immune system plays a crucial role in its pathogenesis. Various previous studies have supported the concurrence of autoimmune diseases in genetically susceptible populations. Coexistence of other autoimmune disorders with MS supports the autoimmune hypothesis. **Objectives:** Look for cooccurrence of autoimmune diseases including thyroid disease, diabetes, lupus, Sjögren's syndrome, and rheumatoid arthritis in our patient population with MS. **Methods:** We selected 400 patients with MS by a retrospective chart analysis. Patients previously tested for serum glucose, thyroid function, antinuclear antibody (ANA), anti-DNA, SSA, SSB, erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), granular and perinuclear anti-neutrophil cytoplasmic antibody (cANCA and pANCA) were included. Patients with myasthenia gravis, steroid-induced diabetes, or hypothyroidism due to interferons were excluded from the study. **Results:** Eighty-four percent of patients were female. In the sample, 82.8% had relapsing-remitting MS, 16.3% had secondary progressive MS, 0.8% had primary progressive MS, and 0.3% had primary relapsing MS. Serum glucose was abnormal in 19.8%, ANA elevated over 1:80 in 19.7%, ESR abnormal in 18.5%, anti-DNA in 13.8%, hypothyroidism in 13.7%, hyperthyroidism in 4.8%, RF positive in 4.3%, and SSA positive in 2.7% that were screened for the conditions. **Conclusion:** Association of autoimmune responses appeared to be present in some MS patients. Whether this represents an asymptomatic epiphenomenon deserves further study.

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(S56) Exploring Intervention for Management of Injection-Site Reactions With Glatiramer Acetate

Background: A common reason for discontinuing therapy early in the course of treatment for multiple sclerosis (MS) is

the development of local injection-site reactions (LISRs). Research directed toward reduction of LISRs can aid nurses who provide training and advice to patients regarding regular self-injection. **Objective:** Three studies were implemented to explore interventions for reducing LISRs before daily injections of glatiramer acetate (GA): elimination of alcohol wipes, use of warm compresses, and use of oral antihistamines. **Design/Methods:** Single crossover designs with 50 patients were used to investigate the effect of (1) removing alcohol wipes from the injection-site preparation and (2) using warm compresses on the injection site for 5 minutes before self-injection of GA. A randomized placebo-controlled group design with 80 patients was used to investigate the effect of using an oral antihistamine 30 minutes before self-injection of GA. Patients used standardized daily diaries to record LISRs and were required to pass concordance testing before participating in the studies. The primary endpoint was total number of LISRs recorded at 5 minutes postinjection.

Results: There was no statistically significant difference in LISRs when alcohol wipes were used in the injection preparation for 30 days. However, patients recorded a significantly lower number of LISRs when warm compresses were applied to GA injection sites over 14 days compared with the usual site preparation ($P = .002$). Compared with using placebo, patients who took an oral antihistamine before each self-injection of GA for 14 days did not record a statistically significant difference on the primary endpoints, but some post hoc exploratory analyses did reveal some statistically significant differences between the treatment groups. **Conclusion:** At this time, only warm compresses can be recommended for the management of LISRs associated with self-injection of GA.

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(S57) Partnership Between Shared Solutions and MS Office Nurses: Adherence Enhancement Program

Objective: Examine the effectiveness of the Partnership Program, a 90-day adherence enhancement program for multiple sclerosis (MS) patients undergoing therapy with glatiramer acetate who are at high risk of early nonadherence. Patients in this program received support from Shared Solutions (SS) combined with regularly scheduled contacts from MS office nurses (PS condition). The combined program was compared with the SS program alone (SS condition). **Background:** MS patients beginning therapy with disease-modifying therapies sometimes find it challenging to remain on therapy during the first 90 days. SS has developed a program to identify patients who are at high risk of early nonadherence and then tailor communication and support to the needs of each patient. This study was designed to evaluate the efficacy of supplementing the SS program with contacts by MS office nurses in terms of increasing adherence beyond that achieved by the SS program alone. **Design/Methods:** This study conformed to an open-label, prospective, parallel cohort design with participants assigned to either the PS condition ($n = 87$) or the SS condition ($n = 220$). Both conditions afforded unlimited telephone interactions between the patient and SS nurses. The PS condition included four additional

office visits and one scheduled telephone contact conducted by MS office nurses over the course of the 90-day study. The primary outcome measure was the 90-day adherence to glatiramer acetate therapy. **Results:** Preliminary data on 97% of 307 participants that completed 90 days of therapy revealed that 94% were adherent in the PS condition compared to 88% adherence in the SS condition. **Conclusion:** Preliminary results indicate that the adherence enhancement program partnering the MS office nurses with SS may improve 90-day adherence to glatiramer acetate.

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(S58) Fatigue and Depression: Relationship to Disease-Modifying Therapy

Fatigue is the most common symptom for multiple sclerosis (MS) patients, and >40% describe it as their worst symptom. At the University of Louisville MS Care Center Program site at Baptist Hospital East, patients are evaluated for fatigue using the Modified Fatigue Impact Scale (MFIS) at each visit in addition to assessments for changes in response to their disease-modifying therapy (DMT). These assessments include the Expanded Disability Status Scale (EDSS), timed 25-foot walk, box and blocks, 9-hole peg test, Beck inventory (BI), and CogniStat to assess cognitive impairment. A retrospective analysis in 2003 suggested improvement in MS fatigue in patients treated with glatiramer acetate (GA). The current study conducted a more comprehensive analysis to determine the relationship, if any, between DMT and fatigue and depressive symptoms. The analysis included 142 MS patients who had been on either GA or interferon beta exclusively. The assessments were obtained at baseline within 6 weeks of initiating a DMT. A mean difference between the baseline MFIS score and the BI score and the last assessment was used. This eliminated the difference in baseline scores between the two treatment groups. Patients on GA showed a greater improvement in MFIS scores than interferon-treated patients. This was statistically significant at 4 years in patients receiving GA who were not on treatment for fatigue. There was no difference in the change in BI scores between the two groups whether treated or not treated with antidepressants. No statistically significant difference was found, although the interferon-beta group showed a decrease over time compared with the GA group.

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(S59) Evaluation of Topical Interventions in Reduction of Injection-Site Reactions After Interferon Treatment for MS: Final Results

Background: Injection-site reactions (ISRs) are common with injected multiple sclerosis (MS) treatments. Over-the-counter (OTC) topical anti-inflammatory agents are often recommended to treat ISRs, but their efficacy has not been studied in well-controlled clinical trials. **Objective:** Evaluate the ability of three OTC topical agents to reduce ISRs in patients with relapsing-remitting MS (RRMS) treated with subcuta-

neous interferon beta-1a. **Methods:** This analysis included two independent, 9-week, multicenter, open-label, crossover studies to assess the effect of hydrocortisone, witch hazel, or moisturizing lotion in patients with ISRs. Patients with ISRs (defined as redness at least 20 mm in diameter 48–72 hours postinjection) were randomly assigned to either study to apply an anti-inflammatory or moisturizing lotion immediately postinjection for 2 weeks. Participants then switched from moisturizing lotion to an anti-inflammatory or vice versa for the final 2 weeks. ISRs were measured at 48–72 hours and 1 week postinjection. The primary outcome measure was the difference in the mean diameter of redness 48–72 hours postinjection. Planned enrollment was 150 subjects in each crossover study. **Results:** Subjects were typically female (>80%) and white (>90%), with a mean age of 41 years. The average baseline diameter of injection-site redness before topical intervention in the hydrocortisone/moisturizing lotion crossover study was 35.9 mm ($n = 49$), and mean redness diameter at 48–72 hours postinjection (\pm SE) was 32.5 mm (\pm 1.8) with hydrocortisone and 29.6 mm (\pm 1.8) with moisturizing lotion ($P = .042$). After 1 week, the respective diameters were 28.2 mm (\pm 2.0) and 26.3 mm (\pm 2.0; $P = .208$). Similar results were found in the witch hazel/moisturizing lotion study at interim. **Conclusions:** Hydrocortisone and moisturizing lotion appear to reduce redness in patients with severe ISRs but may be useful when redness is not as severe. The final results of this study are presented.

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(S60) Behavior of MS During Pregnancy and After Delivery

Introduction: Multiple sclerosis (MS) most commonly affects women during childbearing years. Therefore, it is important for health care providers to know more about the behavior of MS during pregnancy to provide appropriate counseling. Recent studies have shown significant decreases in the relapse rate during the third trimester of pregnancy and an increased risk of exacerbations after delivery. During the postpartum period, various regimens have been studied to decrease the relapse rate, including the use of intravenous (IV) steroids right after delivery. **Objective:** Assess frequency of relapses during pregnancy and the first year after delivery and the relationship between relapses and treatment in a large academic MS clinic. **Methodology:** Prospective and retrospective study in progress. Up to 50 women with MS who are or were pregnant and were seen at the MS clinic between January 2000 and December 2006 are included. Their medical records are being reviewed for frequency, quantity, and treatment of relapses during pregnancy and first postpartum year. Information is also being collected regarding the pre- and postpregnancy immunomodulatory therapy used. **Results:** Sixteen patients have been screened so far. Nineteen pregnancies occurred after MS was diagnosed. Five patients are currently pregnant. Two patients had a relapse while pregnant. Fourteen patients were treated with prophylactic IV steroids after delivery. Four patients had a relapse within the first postpartum year, one of whom had

not received steroid prophylaxis. Ten patients were on interferon beta before pregnancy, three on glatiramer acetate, and one on monthly IV steroids. Two patients were not on MS therapy. **Conclusions:** Understanding the relationship between MS and pregnancy will help provide better care and management for patients during and after pregnancy. Greater knowledge in this area will lead to more effective standardized management, helping to decrease the relapse rate among postpartum MS patients.

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(S61) Combination Therapy With Mycophenolate Mofetil in MS

Objective: Establish safety, clinical, and immunological findings in multiple sclerosis (MS) patients on combination therapy (CT) with mycophenolate mofetil (CellCept; CC).

Design/Methods: In 35 MS patients with progressive neurological symptomatology on CT with interferon beta (INFB)-1a (Avonex), prednisone, average dose <0.12 mg/kg daily, and azathioprine (AZA), 1.5–3 mg/kg daily, AZA was replaced by CC 2 g/day and continuously administered for 12 months. There were six (17%) dropouts: one with increased aspartate aminotransferase and alanine aminotransferase for >3 months, two for treatment-unrelated medical problems, and three because of nonadherence. Flow cytometry (FC) using CD3, CD4, CD8, CD14, CD16, and CD19 antigens after 6 months of treatment including 20 untreated MS patients (UMS) was performed. Serum tumor necrosis factor (TNF) α , soluble interleukin (IL) 2 receptor (sIL2R), soluble intercellular adhesion molecule, IL-10, IL-12, and soluble CD95 were monitored in 3-month intervals, including 18 healthy individuals (HC). **Results:** No serious adverse effects of CT with CC were established. Expanded Disability Status Scale rating remained unchanged (from 4.70 ± 1.78 to 4.80 ± 1.98 in 1 year, $P = .7689$). Annualized relapse rate was 0.31. No opportunistic infections were reported. Compared with UMS depletion of CD3+ cells ($944.07 \pm 628.08/\mu\text{L}$; $P = .0019$), CD8+ T cells ($266.58 \pm 171.41/\mu\text{L}$; $P = .0157$), CD16+ cells ($90.24 \pm 50.50/\mu\text{L}$; $P = .0007$), and CD19+ B cells ($81.96 \pm 78.49/\mu\text{L}$; $P = .0003$), with cell count low as $12/\mu\text{L}$ and increase in CD14+ cells ($410.58 \pm 162.53/\mu\text{L}$; $P = .0003$) was established. Compared with HC, downregulation of serum TNF- α ($P = .0099$) and IL-12 ($P = .0129$) levels was recorded. There was no correlation between serum immunologic markers and subpopulations of immunocompetent cells. **Conclusions:** Therapeutic trial with CT using CC is indicated in individual MS patients presenting breakthrough symptoms on monotherapy with INFB. Absent depletion of CD8+ T cells and/or CD19+ B cells or downregulation of serum TNF- α and IL-12 levels suggested suboptimal response to CT with CC not correlated with routine magnetic resonance imaging studies.

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(S62) Is Percutaneous Tibial Nerve Stimulation Useful for Detrusor Hyperactivity in MS Population?

Detrusor hyperactivity is one of the most frequent urinary features. In fact, 34–99% of multiple sclerosis (MS) patients have this problem during the disease course. High frequency is one of most disabling urinary symptoms, because it affects patients in different settings, affecting quality of life (QOL) because patients often change their social behavior. This study evaluated the effectiveness of a rehabilitation program with percutaneous tibial nerve stimulation (PTNS) in MS patients with detrusor hyperactivity without obstructive feature being followed in a specialized rehabilitation center and the impact of this problem on their QOL. Fifty MS patients with detrusor hyperactivity symptoms (frequency, urgency, urge incontinence, nocturia) were enrolled in the study. Data collected at Time 0 (pretreatment) included age, Expanded Disability Status Scale, course and duration of disease, current pharmacological therapies, mobility status with Hauser ambulation index, symptoms (urgency, retention, hesitation, urge incontinence, frequency), postvoid residual (PVR) with bladder ultrasound, Wagner test, visual analog scale (VAS), urodynamic investigation (if PVR 80 ml or if patient presents retention symptoms). Patients also completed a 5-day bladder diary. The rehabilitation program consisted of 12 sessions, twice a week, of PTNS with superficial electrodes. During the rehabilitation treatment period, pharmacological therapies were not modified. At the end of the rehabilitation program, we recorded all patient symptoms, PVR, Wagner test, VAS, and 5-day diary. Primary outcomes included mean number of episodes of urinary frequency in 5 days (bladder diary) and mean number of episodes of leakage (bladder diary). Secondary outcomes included change in Wagner test and VAS. They also submitted PVR to exclude retention as complication of the treatment.

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(S63) Effectiveness of Education in Addressing Issues of Abuse and Neglect in People With MS

Background: Reports from health care professionals have identified the need for information about abuse and neglect. Reports from 10% of women with multiple sclerosis (MS) who participated in a home-based gynecological care program indicated that they were victims of domestic violence.

Objectives: Provide health care professionals, people with MS, and care partners with tools to identify people at risk of abuse and neglect and offer subsequent safety options and referrals to National MS Society (NMSS) Chapters and other community resources. **Methods:** A part-time medical advocate provided education to grand rounds physicians, interns, residents, and nurses; interdisciplinary team members at both MS centers; judiciary, attorneys, and law enforcement; other health care professionals, including occupational and physical therapists and medical office staff; and community organizations. On state and national levels, the medical advocate provided education to members of Pennsylvania Home Health Care Nurses, NMSS staff, people with MS and their care partners, Pennsylvania State Legislature, and members of the US House and Senate. Seminars, testimony, teleconferences, webcasts, support groups, and newsletters were the

modalities used to present information about definition and types of abuse, assessing and identifying signs of abuse and neglect, safety planning, and options and community referrals. **Results:** Collectively since the project's inception, >7000 people with MS, health care professionals, and others have received prevention/education and community resource information. Referrals from people with MS and health care professionals increased weekly by 200% to NMSS Chapter. **Conclusions:** Health care professionals were more prepared to provide a comprehensive system of care, with focus on increased patient safety. People with MS who were experiencing abuse or neglect were more likely to disclose to a trained professional equipped with information and immediate access to referrals for protective services.

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(S64) Bladder Care for Veterans With MS Differs by Treatment Location

Background: More than 25,000 veterans with multiple sclerosis (MS) receive care through the Veterans Health Administration (VHA). Previous work suggested that veterans with MS treated through VHA had greater access to multidisciplinary care than veterans treated elsewhere. It is unknown whether other VHA-related differences in processes of MS care exist. **Objective:** The North American Research Committee on Multiple Sclerosis (NARCOMS) registry is a self-report registry for MS patients, including veterans who receive care through VHA (VHA veterans) and veterans who do not (non-VHA veterans). We aimed to compare bladder management reported by the two groups. **Methods:** Registry participants self-report demographics and clinical information regarding their MS at enrollment and semiannually thereafter. In the fall 2005 update questionnaire, we collected the Urogenital Distress Inventory-6 (UDI-6), urological investigations, and treatments. We compared VHA and non-VHA veterans using χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables. Using multivariate logistic regression, we assessed the independent association of VHA care with investigations or treatments, after adjustment for confounders. **Results:** One thousand two hundred forty-seven veterans responded to the questionnaire, of whom 1230 (98.6%) reported where they received their health care. Of these, 583 (47.4%) received some or all of their care through VHA. Most participants were men (82%), white (91%), and had a mean age of 52.5 (standard deviation 10.6) years. VHA veterans were older, more likely to be nonwhite, less likely to have a bachelor's or postgraduate degree, and had lower annual income than non-VHA veterans. VHA veterans were younger at symptom onset and diagnosis and reported higher levels of disability in all domains. VHA veterans more frequently reported undergoing urological investigations than non-VHA veterans (adjusted odds ratio 2.02, range 1.55–2.61). VHA veterans more frequently reported using pharmacologic and nonpharmacologic interventions. **Conclusion:** There are differences in the processes of MS bladder care between VHA and elsewhere; this type of variation suggests there are opportunities to optimize such care.

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(S65) Comorbid Conditions Are Common in MS

Background: Multiple sclerosis (MS) is associated with substantial morbidity and mortality. The impact of comorbidity on MS-related outcomes is unknown. Comorbidity is common in the general population, increases with age, and is associated with a broad range of adverse health outcomes. The potential benefits of studying comorbidity in MS include improved prognostication, insights into the etiology and pathogenesis of MS, and the treatment of comorbidities as an avenue for improving outcomes. **Objective:** Describe the comorbid health conditions of participants in the North American Research Committee on Multiple Sclerosis (NARCOMS) registry. **Methods:** Registry participants self-report demographic and clinical information regarding their MS at enrollment and semiannually thereafter. In the fall 2006 update questionnaire, we queried participants regarding physical and mental comorbid conditions. Inclusion criteria were residence in the United States, age at symptom onset between 16 and 60 years, and date of birth reported at enrollment. Results are age standardized to the US 2000 Census population. **Results:** Of the 17,961 registry participants eligible for this survey, 16,189 met the inclusion criteria. Of these, 8983 (55.5%) responded to date. Most participants were women (75.8%), white (94.3%), and had a mean age of 52.7 (standard deviation 10.4) years. Comorbidity was common; 6887 (76.7%) participants had ≥ 1 physical comorbidity, of whom 2098 (30.4%) participants had 1 comorbidity, 1760 (25.6%) had 2, and 3025 (44.0%) had ≥ 3 . The most frequently reported comorbidities (age adjusted) were hypercholesterolemia (28.4%, 24.4–32.4%), hypertension (22.0%, 21.1–22.9%), arthritis (10.9%, 10.2–11.6%), irritable bowel syndrome (10.9%, 10.0–11.7%), and lung disease (12.8%, 12.0–13.6%). Compared with the general population, hypertension (popn 25.3%, 23.3–27.3%) and irritable bowel syndrome (popn 3.3%) are more common in MS. More than 15% of the general population has hypercholesterolemia, and 9.3% use lipid-lowering agents, suggesting this is also more common in MS. **Conclusion:** Comorbid health conditions are common in MS and deserve further investigation.

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(S66) New Scale for Measuring Fatigue in MS: Linear Fatigue Index (LFI-10)

Background: The objective was to design a new scale that would measure the symptom of fatigue in multiple sclerosis (MS) by generating data that would fit the Rasch measurement model. The Rasch model satisfies the axioms of fundamental measurement and is the only way to convert ordinal scale scores into interval level data suitable for parametric analysis. Fatigue was defined as reversible motor and cognitive impairment with reduced motivation and desire to rest, either appearing spontaneously or brought on by mental or physical activity, humidity, acute infection, and food ingestion. It was relieved by daytime sleep or rest without sleep and occurred at any time but was usually worse in the afternoon. This was the underlying construct of the scale. **Method:** Scale items were based on themes and phrases

derived from 40 semistructured interviews on fatigue in MS and appraised by an expert panel of neurologists, rheumatologists, sleep physicians, and therapists. A 52-item scale with a 4-point Likert response option was put to 15 patients, in the MS clinic, who were asked to provide a running commentary during completion; this enabled identification and remedy of any gross problems with wording. It was then mailed to patients with clinically definite MS of any age, sex, disability, and disease type attending two centers in the United Kingdom. **Results:** Data from 635 respondents (52% response) were analyzed. Misfitting items, including those displaying differential item functioning for any of a wide range of person factors, were discarded. A final 10-item scale was produced. External comparison was made to some commonly used, existing fatigue scales. **Conclusion:** The resultant scale was shown to fit the Rasch model; the scale can therefore be assumed to both measure a unidimensional construct of fatigue and generate interval level data. Concepts underlying the scale are discussed.

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(S67) Physical Activity, Neurological Impairment, and Disability in Individuals With MS

Background: Multiple sclerosis (MS) is a chronic neurological disease that involves demyelination and transection of axons with the disease process resulting in neurological impairment and disability. **Objective:** This study examined the association of physical activity with neurological impairment and disability in people with MS. **Methods:** Eighty individuals with MS wore an accelerometer for a 7-day period as a measure of physical activity and completed the Symptom Inventory and Performance Scales. **Results:** There was a large correlation between scores from the accelerometer and Symptom Inventory ($r = -0.56, P < .0001$; $\rho = -0.58, P < .0001$) and a moderate correlation between scores from the accelerometer and Performance Scales ($r = -0.39, P < .0001$; $\rho = -.48, P < .0001$). Regarding the subscales of the Performance Scales, there was a large correlation between scores from the accelerometer and the mobility subscale ($r = -0.60, P < .0001$; $\rho = -.64, P < .0001$). **Conclusions:** Our findings indicated that physical activity was associated with reduced neurological impairment and disability in individuals with MS and provided a basis for using an accelerometer and the Symptom Inventory and Performance Scales as outcome measures in large-scale prospective and experimental examinations of the effect of physical activity behavior on disability and dependence in MS.

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(S68) Lived Experience of MS: Family Perspective

Goal: The goal of this study was to increase understanding of how parents and children cope with parental multiple sclerosis (MS). **Background:** MS is a common neurological illness affecting individuals in the most productive time of their lives. It can be diagnosed at any age; however, it is usually diagnosed during the early adult years, when parenting is most important. Individuals are not only affected by the physical symptoms such as vision problems and debilitating

fatigue, they also face emotional problems such as depression and anxiety. The ability to cope effectively with the physical and emotional symptoms of MS directly affects the person's ability to maintain a high quality of life. The inability to adjust will not only negatively influence individuals with the illness but the entire family, including their children. Consequently, it is important that family therapy interventions are developed to assist the families that are facing chronic illnesses, specifically MS. **Methods:** A qualitative approach, the phenomenological method, was used for this study because it allowed the researcher to understand the essence of living with or having a parent with MS. Participants included five male and female parents age >18 years and children ages 11–16 years who volunteered after being recruited through self-help groups. They responded to short questionnaires concerning their level of disability, symptoms, ability to cope, and family relationships. They participated in separate open-ended interviews answering 10 questions about the experience of having MS or a parent with MS. **Results:** This poster identifies the emotional responses of children who have a parent with MS, how a parent's coping style affects the children's adjustment, and how having MS affects parenting abilities. One significant theme that emerged in this study was the value of being involved in peer support groups. The groups not only helped the parents cope with MS but also their children. **Conclusion:** This information will assist family therapists who provide intervention to families living with MS to achieve a deeper understanding of how MS affects families. The insights gained from this study will help family therapists with planning treatment goals.

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(S69) Assessing Functional Status of Cohort of Patients With MS Using LIFEware System

Through our studies of functional status, we have developed a measure of disability and associated limitations as experienced and self-reported by patients with multiple sclerosis (MS) called the MSPPhysical, which is a component of the LIFEware System. Specifically, the MSPPhysical is a composite of self-report measures (patient-reported outcomes) of disability and associated limitations. This study used the MSPPhysical measure to assess MS patients from the Jacobs Neurological Institute (JNI) in Buffalo, New York; JNI is the largest site within the New York State MS Consortium. There were 788 patients in the cohort. Patients were assessed at enrollment and 5-year follow-up. The study objectives were twofold: to assess changes in health and functional status in patients over time and to determine relationships between self-reported daily functioning and other quality-of-daily-living indicators. Longitudinal analyses demonstrated consistent ratings (no change) from enrollment to 5-year follow-up in the number of patients reporting limitations in bowel and bladder function, pain, or fatigue. The percentage of patients reporting good mood increased ($P < .05$) over the 5-year period. There was a significant correlation between reported overall satisfaction with life and disease severity. The MSPPhysical correlated highly with the Expanded Disability Status Scale (EDSS) ($r = -0.79$), although the MSPPhysical ratings were better distributed across the sample than were EDSS scores.

The MSPPhysical measure appeared to be a valid measure of functional status with the additional benefit of capturing the patients' perspective.

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(S70) Is There Risk of MS Relapse With Concomitant Use of Glatiramer Acetate and Antihistamines?

Background: Antihistamines (AHs) are used in multiple sclerosis (MS) to control allergic symptoms and for relief from injection-site reactions. The potential for these drugs to interact with immune-modulating therapy is currently unknown. This study was conducted to explore whether concomitant use of glatiramer acetate (GA) and AH therapy affected the rate of MS relapse. **Objective:** Examine the risk of relapse among patients with MS who were simultaneously prescribed GA and AH therapy. **Design/Methods:** Medical and pharmacy claims data were culled from the PharMetrics Patient-Centric Database from January 1997 to March 2004. GA users were identified and followed until discontinuation or disenrollment. Patients receiving concomitant prescription AH therapy were identified; because over-the-counter (OTC) AH use was not detectable but represented a potential exposure of interest, the presence of allergy-related medical encounters was used as a proxy. The outcome of interest was the rate of MS relapse (ie, hospitalization for MS or an outpatient encounter followed by steroid taper). A recurrent-event adaptation of Cox proportional hazards regression was used to generate adjusted relapse risk estimates. **Results:** Four thousand three hundred thirty-four patients receiving GA therapy were identified and followed for 10 months on average; 537 (12.9%) had concomitant AH use, and 1015 (23.4%) were potential OTC AH recipients. The mean (standard deviation) age of the sample was 42.9 (9.6) years; 78% were women. The overall incidence of relapse was 169.1 events per 1000 person-years. Concomitant AH use did not significantly affect relapse risk in recurrent-event modeling controlling for age, sex, OTC AH use, and prior relapse (hazards ratio [HR] 0.816; 95% confidence interval [CI] 0.638–1.043). A second model was specified excluding potential OTC AH users; findings for AH were similar (HR 0.962, 95% CI 0.675–1.373). **Conclusions:** No signal for increased relapse frequency was seen in patients using prescription AH concomitantly with GA.

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(S71) Optimal Interferon Therapy in RRMS: Systematic Review of Head-to-Head Trials

Background: Interferon-beta (IFN β) treatments have been shown to limit disability progression, relapse rate, and magnetic resonance imaging (MRI) progression in relapsing-remitting muscular sclerosis (RRMS). However, it remains unclear which IFN β agent or dose is optimal. We compared the efficacy of the three IFN β treatments in head-to-head trials in adults with RRMS. **Methods:** We searched the OVID Med-

line and Cochrane Library databases using keywords *multiple sclerosis*, *interferon beta-1a*, and *interferon beta-1b* and limited our search to 1966 to present, English language, RRMS, and clinical trials. A bibliographic search for additional sources was also performed. Selected studies had to be head-to-head trials involving at least two of the three IFN β agents and measure at least one primary endpoint, including MRI progression, relapse rate, or disability progression. Three independent reviewers abstracted data using a standard form. Data were pooled qualitatively by MRI progression, relapse rate, and disability progression endpoints. A meta-analysis of the findings is presented. **Results:** Seven trials met inclusion criteria. All three studies measuring relapse rate found better reductions for high-dose IFN β -1a (HD1a) or high-dose IFN β -1b (HD1b) compared with low-dose IFN β -1a (LD1a). Both trials measuring MRI progression clearly favored high-dose IFN β . Two of three studies measuring disability progression favored HD1a or HD1b over LD1a, with the other trial finding no difference. There were no major differences between HD1a and HD1b on any of the primary endpoints. **Conclusions:** HD1a or HD1b was favored over LD1a for reducing relapse rate and MRI progression. There may be marginal advantage to HD1a or HD1b for reducing disability progression. Most studies had methodological flaws, and there was variability in measurement of primary endpoints across studies. Standardization of definitions and measurement of primary outcomes, improved study design, and more detailed adverse event investigation is recommended for future MS immunotherapy trials.

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(S72) Impact of Neutralizing Antibodies to Interferon Beta on Biomarker Response: Results From INSIGHT Study

Binding to the interferon (IFN) receptor, IFNAR, is essential for the pharmacologic effect of IFN β . This study examines the impact of neutralizing antibodies (NABs) against IFN β on the in vivo response of three biomarkers, including the two most sensitive, that increase after IFNAR receptor binding. NAB development to IFN β and its negative impact on clinical outcomes is well established in cross-sectional studies. However, several variables confound the detection of a clear impact of NABs in individual MS patients. Hence, there is a need to assess the effect of NABs on the biological response in individuals. This is a multicenter, open-label, serologic study comparing IFN β -induced biomarker response in NAB+ vs NAB- patients continuously treated with any currently approved IFN β . Blood was collected for enzyme-linked immunosorbent assay, viral cytopathic effect, and biomarker analysis 9–12 hours after the patients' last dose of IFN. Patients were assigned to one of three groups based on screening BAb and NAb titers (group 1, BAb+/NAB+ [$\geq 8/\geq 20$ NU/mL], $n = 84$; group 2, BAb-/NAB- [$< 8/< 20$ NU/mL], $n = 10$; and group 3, BAb+/NAB- [$\geq 8/< 20$ NU/mL], $n = 9$). Final data from all patients are presented. Current data available from 555 screened and 103 enrolled patients were examined. The incidence of NAB positivity was 22%, 22%, 26%, and <1% for Rebif 22 μ g, Rebif 44 μ g, Betaseron, and

Avonex, respectively. Human myxovirus protein (MxA) mRNA response in NAB+ vs NAB- patients demonstrated that NAB+ patients had a significantly reduced response to IFN β (NAB+ median 2.7, NAB- median 19.3, $P < .0001$). Similar results were seen for viperin and IFIT-1. Significant negative correlations were observed between NAB titer levels and biomarker response (Spearman $r = -0.763, -0.732, -0.709$ for MxA, viperin, and IFIT-1, respectively, all $P < .0001$). These data confirm the wide variability in incidence of NABs among the IFN products and provide evidence that even modest titers of NABs can abolish the pharmacologic response to IFN.

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(S73) Vinpocetine and Rivastigmine in Amelioration of Cognitive Impairment in MS

Introduction: Cognitive impairment represents one of the prominent clinical modalities in multiple sclerosis (MS) patients. Treatment of this disorder is difficult because of progressive organic brain damage. No superior drug or other treatment mode was established so far. We present our experience with two drugs, the nootropic agent vinpocetine and the cholinergic drug rivastigmine. **Methods:** Twenty-five whites, 17 women, with mean age 44 ± 4 years were treated for 12 weeks with vinpocetine 15 mg/day and rivastigmine 3 mg twice daily. Treatment effect was assessed using the Brief Cognitive Rating Scale (BCRS) at baseline, 6 weeks, and 12 weeks. **Results:** At the start of the treatment, the mean BCRS scores for concentration, recent memory, past memory, orientation, and functioning/self-care were $4.3 \pm 0.5, 3.3 \pm 1.0, 3.5 \pm 0.9, 2.2 \pm 0.4,$ and 3.1 ± 0.8 , respectively. After 6 weeks, BCRS scores were $3.1 \pm 0.7, 3.6 \pm 0.8, 3.6 \pm 1.0, 1.1 \pm 0.3,$ and 2.1 ± 0.9 , respectively. At the study end, BCRS scores were $2.1 \pm 0.9, 2.5 \pm 1.2, 3.3 \pm 1.4, 1.9 \pm 0.7,$ and 2.4 ± 1.4 , respectively. **Discussion:** Our results showed that vinpocetine and rivastigmine, in combination, were clinically effective in ameliorating cognitive impairment in MS.

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(S74) Impact of Oral Antihistamine on Local Injection-Site Reactions With Glatiramer Acetate

Background: Although generally not serious in nature, local injection-site reactions (LISRs) can be troublesome to patients beginning injectable multiple sclerosis (MS) therapies and can lead to treatment discontinuation. This was one of several studies designed to explore the effect of a short-term intervention on the frequency and type of LISRs encountered by patients using glatiramer acetate (GA). **Objective:** Compare LISRs between patients receiving an oral antihistamine or a placebo 30 minutes before daily injections of GA. **Design/Methods:** This double-blind, randomized, placebo-controlled study enrolled patients who had started GA therapy within the past 3 months. Patient diaries were used to determine the number of LISRs occurring across a 14-day baseline period followed by a 14-day treatment period, expressed as LISR scores. The outcome measures were the

LISR scores reported immediately, 2 minutes, and 5 minutes postinjection for 2 weeks during both baseline and treatment periods. Mean LISR scores during the baseline period were compared with those during the treatment period using paired-sample *t* tests. **Results:** Eighty-five patients were randomized; 83 completed a 14-day baseline period followed by a 14-day treatment period. A decline in the LISR scores at each postinjection time interval in the antihistamine arm, but not in the placebo arm, was observed. However, the comparison between arms was not statistically significant (primary endpoint). Post hoc exploratory analyses did reveal some statistically significant differences between the treatment and placebo arms. **Conclusions:** Although modest effects were seen in the active treatment group when LISRs were compared before starting the antihistamine and during antihistamine therapy, there were no statistically significant differences between the treatment group and the placebo group on the primary endpoint. Antihistamine use as a strategy to reduce LISRs in patients on GA therapy cannot be recommended at this time.

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(S75) Care Plan to Improve Adherence to Glatiramer Acetate Among Patients at Risk of Nonadherence

Background: Published studies have shown that all four of the multiple sclerosis (MS) injectable therapies have poor adherence during the first 6 months of therapy. Shared Solutions (SS), a company-sponsored MS patient support program, maintains data that further indicate 72% of the patients who stop glatiramer acetate (GA) therapy within the first 6 months of initiating therapy actually do so within the first 90 days. **Objective:** Determine whether patients who are likely to stop GA therapy in the first 3 months can be identified using a predictive model and whether patients at high risk of nonadherence will maintain their therapy when additional SS support is provided. **Design/Methods:** Drawing from published literature and the experiences of the SS nurses who counsel patients beginning therapy with GA, characteristics for a predictive model of early nonadherence were identified. Questions assessing these characteristics and a statistical framework for the responses, as well as patient-specific care plans, were implemented. Ninety-day adherence to GA therapy was compared to adherence in a sample of 5433 patients who initiated therapy before the advent of the model. **Results:** Among 10,814 patients, the predictive model successfully identified 70% who were at high risk for stopping therapy in the first 90 days. Of patients placed in the extensive care plan, ~30% who would have stopped remained on GA therapy through the first 90 days of use. SS's 90-day discontinuance rate has been reduced from 11% to 8.9%, a 19.1% improvement. Additionally, beyond 90 days, these patients demonstrated normal adherence patterns. Approximately 420 patients per year now maintain their GA therapy rather than stopping early. **Conclusions:** The predictive model does identify patients who are likely to stop GA in the first 90 days of therapy, and additional SS support is successful in helping more patients to be adherent through 90 days.

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(S76) Assessing Patient Satisfaction With Autoinjector for IM IFN β -1a (Avonex)

Background: Patients with multiple sclerosis (MS) may experience difficulty administering disease-modifying therapies (DMTs) because of disability or fear of self-injection. Autoinjectors may make DMTs easier to administer. **Objective:** Evaluate patient satisfaction with a single-use autoinjector for intramuscular (IM) interferon beta-1a (IFN β -1a, Avonex; Biogen Idec, Inc.). **Design/Methods:** Patients with MS were included in this multicenter, open-label, crossover comparator study if they were 18–65 years of age (inclusive) and had used IM IFN β -1a for ≥ 12 weeks. Patients injected IM IFN β -1a 30 μ g once weekly for 4 weeks. During Week 1, patients injected the IM IFN β -1a manually, and during Weeks 2–4, patients injected IM IFN β -1a using the autoinjector. Patient satisfaction was assessed with a Subject Satisfaction Questionnaire, Ease of Use Grading Scale, and subject assessment of injection-site pain. Clinicians monitored patients for adverse events (AEs). **Results:** A total of 74 patients were enrolled in the study. Two patients withdrew from the study: one withdrew consent and one withdrew because of device malfunction. Most patients (84%) were satisfied with the autoinjector, and 86% of patients would use it again. Compared with manual injection, most patients reported the autoinjector was easier to inject (76%), easier to prepare (64%), and reduced injection anxiety (64%). Pain ratings were low with both injection methods; however, pain ratings were slightly lower with the autoinjector. The most common adverse events (AEs) were injection-site bruising (14%), injection-site pain (4%), flulike illness (3%), and myalgia (3%). All AEs were mild or moderate, and no serious AEs were reported. **Conclusions:** Overall, patients (84%) were satisfied with the autoinjector and found it more convenient than manual injection. These results suggested that use of an autoinjector may increase adherence to therapy.

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(S77) Prevalence of and Associations With Chronic Pain Treatment in Veterans With MS

Objective: Estimate the prevalence of self-reported treatment for chronic pain in veterans with multiple sclerosis (MS), and explore the associations between demographics, utilization, and provider satisfaction and report of chronic pain treatment. **Design:** Cross-sectional study. **Results:** Of veterans with MS who responded to a mail survey between 2002 and 2004, 44.7% [95% confidence interval (CI) 41.7–47.7%] reported being treated by a Veterans Health Administration (VHA) provider for chronic pain in the past 12 months. Report of treatment for chronic pain was associated with being female ($\chi^2 = 6.33$, $P = .011$), increasing body mass index (Cochran-Armitage $Z = 2.76$, $P = .0058$), increasing number of days the veteran sought care at VHA in the 2 months preceding the outpatient visit (Cochran-Armitage $Z = 7.96$, $P = .0001$), and help or need for help at home ($\chi^2 = 21.23$, $P = .0001$). Veterans reporting definite trust in their VHA health care provider were less likely to report treatment for chronic pain (relative risk [RR] 0.79, 95% CI 0.65–0.96) than those who did not trust their

provider. Of those reporting treatment for chronic pain in the past year, 38.9% of veterans had two or more refills for medications commonly used to treat chronic pain in the 12 months preceding the outpatient visit, compared to 13.8% of veterans who reported not being treated for chronic pain (RR 1.91, 95% CI 1.76–2.07). **Conclusions:** This work suggested that chronic pain was a prevalent problem for veterans with MS, with nearly one-half reporting treatment in the past 12 months. Self-report underestimates the proportion receiving treatment given the frequency of pain medication used by the survey nonresponders. The data also suggested that nonpharmaceutical treatments played a role in the management of chronic pain for a significant proportion of individuals.

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(S78) Intrathecal Bupivacaine for Treatment of Neuropathic Pain in Patients With Intrathecal Baclofen Pump

Muscle spasticity may adversely affect outcomes of rehabilitation in spinal cord injury and multiple sclerosis (MS) patients. Spasticity is often seen in conjunction with neuropathic pain; often, these two problems coincide, frequently exacerbating one another, and the management of the two simultaneously becomes difficult. We review the pathophysiology, evaluation, and management of spasticity and neuropathic pain. This is aimed at formulating a new treatment approach for refractory cases of spasticity in conjunction with neuropathic pain. The patients in this multicase study had already failed oral therapy with baclofen and various other spasticity medications (eg, tizanidine, clonidine, valium, gabapentin) and were currently on intrathecal baclofen therapy. Bupivacaine was added to the intrathecal therapy for management of neuropathic pain. With the addition of bupivacaine, not only was the neuropathic pain relieved or lessened but the spasticity was also helped to a degree with a decrease in the dose of intrathecal baclofen therapy. Whether there were synergistic effects of the two medications was unclear; however, there was proven benefit seen in these patients in terms of the resolution or lessening in severity of symptoms of neuropathic pain and spasticity. The current combination intrathecal regimen not only decreased the symptoms but also facilitated better outcomes in patient rehabilitation and daily function. At this time, it has become a delicate balancing act in these patients to determine how much the dose of baclofen can be reduced as the bupivacaine dose is increased to optimally control their spasticity and neuropathic pain.

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(S79) False-Negative Oligoclonal Bands Provoked Change in Laboratory Protocol

Objective: Report the experience of changing the protocol for cerebrospinal fluid (CSF) analysis in a university hospital.

Background: Recommendations for CSF analysis were published in a consensus statement in June 2005 by a study group commissioned by the Consortium of Multiple Sclerosis

(MS) Centers. The report contains 12 criteria to establish the minimal acceptable standard of CSF analysis in the diagnosis of MS. The study group sought to inform neurologists and laboratory specialists of the variation in sensitivity and specificity among methodologies and ensure use of isoelectric focusing (IEF) with immunodetection (ID), defining it as the gold standard. **Method:** This is a case report describing CSF analysis performed on the same specimen obtained from a patient with relapsing neurological symptoms using two different techniques. Agarose gel protein electrophoresis was done at St. Louis University, followed by IEF with ID at a national reference laboratory. Subsequently, we informally asked other university and reference laboratories about their methods of CSF analysis. **Results:** Our laboratory system of CSF agarose gel electrophoresis, despite careful analysis by two pathologists, failed to identify oligoclonal bands. ID/IEF detected five oligoclonal bands. Quantitative IgG analysis was within normal limits at both laboratories. As a result, we switched from agarose gel electrophoresis to ID/IEF. Some university laboratories still use agarose gel electrophoresis; other responders use in-house IEF or send specimens to reference laboratories that use various techniques. **Conclusions:** Based on our experience, condition-specific published standards may not filter down to the testing laboratory. Consequently, we strongly advocate that clinicians establish communication with their pathologists when new or revised standards are made available to enable prompt investigation and implementation of laboratory techniques. This concept applies to MS and other disciplines and diagnostic methodologies.

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(S80) Implications of Nonalcoholic Fatty Liver Disease in MS

Objective: Examine the implications of elevated hepatic enzymes in a patient with multiple sclerosis (MS) and non-alcoholic fatty liver disease (NAFLD). **Background:** Liver enzyme elevations in individuals receiving interferon (IFN) beta are usually transient, although fulminant hepatic failure and autoimmune hepatitis have occurred. The literature reports that NAFLD is associated with obesity, insulin resistance, and hypertriglyceridemia and is the most common cause of chronic liver disease in the United States. Up to 30% of NAFLD cases may progress to more serious hepatic disease. **Method:** Case report of a 39-year-old woman with MS and normal baseline hepatic enzymes who developed alanine aminotransferase 3.4 times the upper normal limits (ULN) and aspartate aminotransferase 1.8 times ULN within 4 months of starting IFN treatment preceded by 3 days of solumedrol. **Results:** Reduction then discontinuation of IFN improved her hepatic enzymes to near ULN over 5 months. Her chronic use of diet pills and ephedra was stopped at the onset of her neurological symptoms; however, her body mass index rose from 30.9 to 34.5 kg/m². Labs showed triglycerides 314 and negative antinuclear, mitochondrial, and actin antibodies. Ceruloplasmin and viral hepatitis serologies were negative. Abdominal imaging showed a fatty liver. Her obesity, hypertriglyceridemia, and fatty liver (insulin resistance) place her at high-risk for continued NAFLD. **Implica-**

tions: Early recognition of NAFLD in patients treated with IFN enables appropriate diagnostic evaluation and intervention. Our concern regarding effects of underlying NAFLD on clinical trial data and recruitment are additive to other authors. We raise the question whether using IFN and/or corticosteroids in MS with NAFLD increases susceptibility to a two-hit theory of injury. In summary, modification of risk factors of NAFLD should be considered in patients with MS to improve their health. Future studies should examine the prevalence of risk factors for NAFLD in patients with MS.

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(S81) Efficacy of Three Antidepressants in Treating Depression in MS

Introduction: Depression often appears in multiple sclerosis (MS) because of organic brain substrate damage. The most common type of depression is a major depressive episode with organic modalities. We present our experience in using various antidepressant medications and their efficacy to ameliorate depressive mood in heterogeneous types of MS patients. **Methods:** During the past 5 years, we treated 34 patients of both sexes (21 women, 13 men), mean age 42.5 years, with antidepressant drugs: venlafaxine (VE; 8 subjects), paroxetine (PA; 15), clomipramine (CL; 11). The mean daily doses were VE 75 ± 32 mg, PA 20 ± 4 mg, and CL 50 ± 9 mg. Diagnosis of major depression was established using DSM-IV criteria, and severity of mood disturbances was assessed using HAM-D scale, at baseline and after 3 and 6 weeks of treatment. **Results:** The most efficacious drug was PA, then VE and CL equally. The baseline HAM-D scores were 27 ± 3 , 26 ± 4 , and 27 ± 5 for PA, VE, and CL groups, respectively. After 3 weeks, there were no significant differences between groups in HAM-D scores. However, at the end of the study, the lowest HAM-D scores were in the PA group (11 ± 2) compared to VE (13 ± 3) and CL (14 ± 5), although the differences were not statistically significant. No unexpected adverse treatment events were noted. **Conclusion:** PA was clinically the most useful antidepressant in organic damage of brain, but many patients treated with VE and CL still had benefit.

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(S82) Impact of Alcohol Wipes on Local Injection-Site Reactions With Glatiramer Acetate

Background: Although generally not serious in nature, local injection-site reactions (LISRs) can be troublesome to patients on injectable multiple sclerosis (MS) therapies and can lead to treatment discontinuation. This study was one of several designed to evaluate the effect of an intervention on the presentation (frequency and type) of LISRs among patients who self-inject glatiramer acetate (GA) daily. **Objective:** Compare LISRs when patients use alcohol wipes before daily subcutaneous injection of GA versus when patients do not use alcohol wipes. **Design/Methods:** This study used an open-label, randomized, single crossover design. Forty-six patients used each injection-site preparation method during two consecutive 28-day periods, with the

order randomized and counterbalanced across the patients. The patient used diaries to record the number and type of LISRs that occurred and to rate how bothersome the injection was (scale 1–10) each day in both periods. To evaluate interrater reliability, nurses and patients independently assessed LISRs in the clinic on Days 28 and 56. **Results:** The primary outcome showed that the total number of LISRs recorded at 5 minutes postinjection over 28 days was not statistically different when alcohol wipes were used (mean 61.27 vs 59.62; $P = .45$). Similarly, no differences were found between the alcohol-wipe condition and no-alcohol-wipe condition in terms of the number of LISRs recorded at 2 minutes postinjection (mean 58.40 and 57.86, respectively) nor immediately after the injection (mean 26.31 and 28.18, respectively). The average bothersome rating assigned to the two conditions also did not reach statistical significance (mean 3.00 vs 2.65). **Conclusions:** There was no significant difference in the mean number of recorded LISRs with or without alcohol wipes. The routine use of alcohol wipes before subcutaneous injection of GA did not appear to minimize or increase LISRs.

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(S83) Social Support and Medication Adherence in MS

Background: Disease-modifying therapy (DMT) can slow multiple sclerosis (MS) disease progression. However, adherence to DMT can be complicated by its administration route and side effects. Social support has been associated with better adherence to medications in both MS and non-MS populations. **Objective:** Better understand this association, we investigated the prospective relationships between two different types of social support and DMT adherence in a sample of 53 MS patients. **Methods:** The first type of social support was DMT specific, which assessed support surrounding issues related to medication use. The second type was caregiver support, measured with the Quality of Relationships Inventory–Short Form (QRI-SF), which assessed the general support qualities of the caregiver relationship. Demographic, medical, and social support variables were collected at baseline. Medication adherence was assessed by self-report at a 3-month follow-up and was dichotomized into adherence and nonadherence at the 80% adherence cutoff point. Data were analyzed with logistic regression, adjusting for type of DMT, time on DMT, and disease severity. **Results:** Poor caregiver support, but not DMT-specific support, predicted DMT nonadherence at 3-month follow-up (odds ratio 0.57, 95% confidence interval 0.34–0.98, $P = .03$). **Conclusion:** These findings suggest that general caregiver relationship qualities may be important in DMT adherence for reasons other than support specific to medication adherence.

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(S84) New Formulation of Interferon Beta-1a: 1-Year Results of Phase 3b Study

An extensive research program to improve the current formulation of interferon (IFN) beta-1a (Rebif) by enhancing injection tolerability, removing human serum albumin, and reduc-

ing immunogenicity has led to the development of Rebif New Formulation (RNF). This ongoing 96-week, phase 3b, multicenter, single-arm, open-label study compares the safety and immunogenicity of RNF with a historical cohort given subcutaneous (SC) IFN beta-1a 44 µg three times weekly (tiw) in the EVIDENCE study. The results of the 48-week analysis are presented. Patients ages 18–60 years with relapsing multiple sclerosis (MS) and an Expanded Disability Status Scale (EDSS) score of <6.0 self-injected RNF 44 µg/0.5 mL SC tiw. Safety analyses included eight prespecified adverse event (AE) groups of interest. Patients with neutralizing antibody (NAb) titers ≥20 NU/mL at Week 48 (last observation carried forward) were considered NAb+, and persistent NAb was classified as NAb+ at 24 and 48 weeks. Of the 260 patients enrolled, 227 (87.3%) remained on treatment at Week 48. In this study, seven of eight prespecified AEs occurred in smaller or similar proportions of patients compared with the historical cohort: injection-site reactions, 30% vs 84%, representing nearly a threefold reduction; cytopenia, 10% vs 12%; depression and suicidal ideation, 6% vs 20%; hepatic disorders, 13% vs 17%; skin rashes, 5% vs 12%; thyroid disorders, 2% vs 5%; and hypersensitivity reactions, 5% vs 3%. Flulike symptoms were higher with RNF (71% vs 48%); however, most were mild. A markedly smaller proportion of RNF-treated patients had persistent NAb or NAb at Week 48 than the historical cohort [2.5% [95% confidence interval (CI) 1.0–5.4] vs 14.3% [95% CI 10.7–18.6], and 13.9% [95% CI 9.9–18.7] vs 24.4% [95% CI 19.9–29.4], respectively]. A smaller proportion of patients had high NAb titers (>1000 NU/mL) in the RNF study (11%) than in the EVIDENCE study (20%). These promising results indicate that RNF has an improved overall safety profile and lower immunogenicity than the current formulation of IFN beta-1a.

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(S85) Spasticity Management in Progressive MS: Multidisciplinary Approach

It has been reported by Costello that ~60% of multiple sclerosis (MS) patients have corticospinal involvement with some degree of spasticity. Many patients require spasticity management to facilitate other functions, eg, seating, bed positioning, and mobility. Oral antispasticity medications are often not effective in this group of patients. A 47-year-old woman (LC) was diagnosed with MS 15 years ago. LC is now at the end stage of chronic progressive MS (CPMS). After a multidisciplinary assessment, the following problems were identified: (1) severe cognitive impairment, nonverbal with severe perceptual deficits; (2) painful spasms; (3) nutritional problems, gastrostomy tube in place, recent weight gain; (4) recurrent respiratory infections, tracheostomy in place, profuse drooling requiring frequent suctioning round the clock; (5) impending decubiti, grade 1 pressure sore at the heels, skin excoriation in groin and palms; (6) recurrent urinary tract infections, diapered; (7) seating and mobility problems, severe painful hip adduction/flexion and knee flexion hypertonia; (8) dressing and personal care issues; and (9) social and relationship issues. A combined approach

of oral baclofen, tizanidine, and botulinum toxin A injections was used with good results, avoiding the more expansive and serious procedure of baclofen pump. Education of caregiver in positioning, stretching, and seating was most helpful. Control of drooling with botulinum toxin A injection of salivary glands was helpful in reducing respiratory infections and repositioning of head while seated. Skin condition of groin and personal hygiene improved, not requiring indwelling catheter. Seating improved with reduced risk of decubiti. The care burden decreased, and there was less pain. **Conclusion:** An optimal control of spasticity via multidisciplinary approach alone may be effective in managing and preventing serious complications in CPMS.

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(S86) Symptoms and Physical Activity Behavior in Individuals With MS

Background: Multiple sclerosis (MS) is characterized by unpredictable episodes of demyelination and transection of nerve fibers in the central nervous system. The axonal damage is associated with visual, motor, psychological, sensory, and bladder symptoms. Both overall and specific symptoms of MS have been associated with reductions in a broad spectrum of activities of daily living including work, personal care, and social interaction. The implications are that both overall and specific symptoms might be inversely associated with physical activity behavior. **Purpose:** The current study examined overall and specific symptoms as correlates of physical activity in people with MS. We expected that overall symptoms and motor and sensory symptoms would be the strongest correlates of physical activity behavior. **Methods:** The sample consisted of 80 individuals with a definite diagnosis of MS from the Midwest region of the United States. Participants completed the Multiple Sclerosis Symptom Checklist (MSSCL) and then wore an accelerometer for a 7-day period. MSSCL provides an overall measure of symptom frequency and subscale measures of the frequency of motor, brainstem, sensory, mental/emotional, and elimination symptoms. **Results:** There was a moderate-to-strong inverse correlation between the overall MSSCL score and physical activity ($r = -0.47, P = .0001$). Scores from all five subscales of the MSSCL were significantly correlated with physical activity, and there was a moderate-to-strong inverse correlation for the motor subscale ($r = -0.49, P = .0001$) and moderate-to-weak inverse correlations for the sensory subscale ($r = -0.36, P = .0001$), elimination subscale ($r = -0.28, P = .01$), brainstem subscale ($r = -0.25, P = .03$), and mental/emotion subscale ($r = -0.23, P = .04$). **Conclusions:** The frequency of overall and motor symptoms was most strongly associated with reduced physical activity in this sample of people with MS. The management of MS-related symptoms might be an important aspect of promoting the adoption and maintenance of physical activity behavior in individuals with MS.

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(S87) Psychiatric Symptoms as Presenting Symptoms in MS: Is It More Common Than We Thought?

Background: There is little information published about patients who present with existing psychiatric diagnoses at the time of a multiple sclerosis (MS) diagnosis. Cognitive and emotional MS symptoms can mimic psychiatric symptoms and possibly delay a timely diagnosis of MS while only the psychiatric diagnosis is treated. **Method:** A retrospective chart review of patients ($n = 11$) with major psychiatric diagnosis confirmed by a psychiatrist before a diagnosis of MS was included in the study. **Results:** The diagnosis of psychiatric illness was bimodal in distribution. Diagnosis of MS was delayed in patients <25 years old ($n = 7$) by a mean 18.2 years compared with patients >40 years old ($n = 4$, 8.8 years). There was no difference in Expanded Disability Status Scale at time of MS diagnosis of the young group (3.5) compared with the older group (4.5). Both groups presented with cognitive symptoms, depression, and fatigue. Two MS patients presented with sudden onset of depression, difficult to manage with multiple therapies and resulting in electroconvulsive therapy at ages 17 and 18 years. Access to further investigations after initial psychiatric diagnosis and treatment was difficult for all. **Discussion:** MS is often not considered as a differential diagnosis for patients presenting with psychiatric symptoms. Sudden onset of refractory depression, especially in young patients, may be a red flag for MS. On MS diagnosis, patients with preexisting psychiatric disorders require unique care plans and collaboration with psychiatry for both adherence to treatment protocols and patient safety. A multidisciplinary approach in an enhanced community-based MS clinic can greatly increase the chances for successful management of these MS patients.

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(S88) MS Psychological Consultation: Addressing Mental Health Needs of Individuals With MS

The goal of this study was to examine how patients and families make use of multiple sclerosis (MS) psychology consultation services using retrospective consultation data from a 2-year period. The diagnosis and subsequent progression of MS can have a profound effect on the lives of patients and their families, including physical, mental, emotional, interpersonal, and financial challenges. Consequently, MS patients surpass most other chronically ill populations in their rates of depression and anxiety. Despite effective interventions for mental health concerns, problems often go untreated or undertreated because of patient fatigue, mobility limitations, cognitive problems, and financial strain, as well as mental health stigma and lack of mental health providers with MS expertise. Because untreated psychological difficulties can interfere with MS treatment adherence, a collaborative partnership between medical and mental health providers is crucial. In fall 2003, the Medical College of Georgia's Augusta MS Center initiated the MS psychological consultation service. The goal of this service is to remove barriers to the emotional well-being of individuals with MS through convenient,

compassionate, and coordinated psychological services during routine MS medical appointments. As such, all psychology services are provided onsite at the center and occur alongside patients' MS medical appointments, reducing and often eliminating the need to schedule, attend, and pay for separate mental health services. To better understand how these services have been used thus far, MS psychology consultation documentation from July 2004 through June 2006 are reviewed. In particular, summary data on demographics, presenting problems, and resultant treatment plans are presented as a means to examine the potential of psychological consultation to be an effective delivery method of mental health services to the MS population.

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(S89) Problem-Solving Therapy for Depression: Pilot Intervention for MS Care Settings

Depression is consistently cited as a common psychological problem for individuals living with multiple sclerosis (MS), with lifetime prevalence in some samples of >40%. The primary goal of this pilot research is to evaluate the unique potential of problem-solving therapy for primary care (PST-PC) to treat depression as part of routine MS medical care. PST-PC assists individuals in increasing problem-solving capabilities and confidence by teaching a seven-step model that has been adapted to the needs and pace of a medical clinic and uses real-life problems as learning examples in session. This intervention was specifically chosen because of its brevity, simplicity, and past success in decreasing depression symptoms in other medical populations. This pilot study assesses the efficacy of a problem-solving therapy for depression in the MS clinic setting and evaluates the extent to which it reduces depressive symptoms and increases quality of life and medical appointment adherence. Patients diagnosed with major depression through screening and structured clinical interview are offered the opportunity to participate in this study. Patients are randomized into two groups. The treatment group receives five sessions of PST-PC by a skilled mental health professional as an adjunct to their current care, and control subjects receive treatment as usual by MS physicians and the psychology consult service. At baseline, all patients are screened for depression and quality of life. Treatment outcomes will be assessed at treatment completion and at 6 months post-treatment, including measures of client satisfaction and MS appointment adherence. We have enrolled 40 patients to date, and preliminary data are presented. Given the in-progress status of the study, the primary emphasis is on the facilitation of dialogue.

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(S90) Survey of Issues Related to Prayer and Spirituality Among Large Group of People With MS

Objective: Collect data regarding beliefs about prayer and spirituality among a group of people with multiple sclerosis (MS). **Background:** Prayer and spirituality are widely used forms of complementary and alternative medicine, yet the interaction among MS and belief in God, prayer, and spiritu-

ality has not been closely examined. **Design/Methods:** Using email, a registry (www.ms-cam.org), and a Web-based survey, we collected self-reported data related to prayer and spirituality from 1082 people with MS. **Results:** Of the 1082 respondents, 91% reported that they believe in God (or a higher power); 3% reported that they do not. Among believers in God ($n = 985$), more people (48%) believed that God did not play a role in their having MS than that God did have a role (32%). Among those who believe that God did play a role in their having MS ($n = 310$), only 3% perceived MS as a punishment from God, whereas 94% perceived MS has an opportunity from God. Among nonbelievers ($n = 33$), no one identified that having MS was a reason for not believing. Of all respondents, 83% described themselves as spiritual, 59% reported that having MS has made them more spiritual, 27% reported that MS has not affected their spirituality, and 89% reported that they pray. Among people who pray ($n = 947$), 50% reported that they now pray more than they did before their diagnosis; 2% reported praying less. Among people who reported that praying helped to control their MS or its symptoms ($n = 478$), the most frequently reported health benefits were improved anxiety, depression, and ability to deal with the uncertainties of MS. **Conclusions:** Among our respondents, having MS did not seem to have had a negative effect on belief in God, spirituality, or prayer. The most commonly perceived health benefits related to prayer were decreased anxiety and depression.

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(S91) Long-Term Follow-Up of Ambulatory MS Patients Treated With Botulinum Toxin for Lower-Extremity Spasticity

Objective: Describe baseline characteristics and long-term outcomes in ambulatory multiple sclerosis (MS) patients treated with botulinum toxin (BT) injections in the lower extremities. **Design:** Retrospective analysis of data collected from electronic medical records of ambulatory MS patients with lower-extremity spasticity treated with BT injections in a spasticity clinic within an outpatient MS center. **Main Outcome Measures:** Modified Ashworth Scale (MAS) averaged on eight muscle groups, Spasm Frequency Scale (SFS), pain visual analog scale, timed 25-foot walk (T25FW), Expanded Disability Status Scale (EDSS), Ambulation Index (AI). **Results:** Thirty-nine patients were analyzed: age 50 ± 11 years, 64% women, disease duration 16 ± 9 years, disease course 85% progressive, and 77% used an assistive device. Scores at baseline were (mean SD): MAS 1.4 ± 0.8 , SFS 1.5 ± 1.0 , pain 3 ± 3 , EDSS 6 ± 1 , AI 5 ± 2 , T25FW 23.2 ± 30.9 seconds. Follow-up duration was 21 ± 14 months, with a 46% discontinuation rate. No significant complications were reported. There was a statistically significant worsening of EDSS scores between baseline and last treatment visit but no significant change in other outcomes. Subgroup analysis showed that T25FW improved by >20% in 13% of patients and worsened by >20% in 41%. Two patients (5%) became nonambulatory. No significant differences in baseline characteristics were observed between patients who continued on

therapy and patients who discontinued. EDSS and AI change scores were significantly poorer in patients who discontinued therapy. **Conclusions:** BT therapy was well tolerated in our patients. Worsening of neurologic disability as measured by EDSS most likely represented disease progression. Improvement of gait speed was observed in a small subgroup of patients. No clinical predictors of therapy discontinuation were identified. Discontinuation was associated with worsening of disability.

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(S92) Frequency and Severity of Restless Legs Syndrome in MS Patients From Southeast Texas

Introduction: Restless legs syndrome (RLS) is a sensorimotor disease of uncertain etiology, with 5–15% prevalence in the general population. Currently, there is no test for RLS diagnosis. The main diagnostic criteria are (1) a desire to move the extremities, often associated with unpleasant sensation in the legs; (2) symptoms are worse or present only during rest and partially relieved by activity; (3) motor restlessness; and (4) nocturnal worsening. Associated with the diagnostic criteria, there is a validated scale that can measure the severity of symptoms in patients with RLS. We only found two studies in the literature addressing this topic reporting frequency of RLS in multiple sclerosis (MS) patients between 32.0% and 37.5%. We did not find a study related to severity of the symptoms in these patients. **Materials/Methods:** Prospective study of the first 206 patients that came seeking treatment at the Maxine Mesinger MS Clinic and had MS diagnosis according to the updated McDonald criteria. The patients answered four questions related to the diagnostic criteria of RLS. If the questions were answered affirmatively and the RLS was confirmed, symptom severity was measured using the RLS severity scale. **Results:** Two hundred six subjects participated in the study. From this population (75% women, 25% men), 68 (33%) met criteria for RLS. Of the women, 39% had criteria for RLS compared to 27% of men; 80% of the RLS patients had relapsing-remitting MS, and 20% had documented anemia. Regarding severity of the disease, 17% had very severe, 42% severe, 37% moderate, and only 4% mild symptoms. **Conclusions:** We found a relatively high proportion of MS patients who have RLS compared with the general population and a significant degree of severity of symptoms. Awareness of the association of RLS in the MS population is imperative to proceed with the appropriate management, if needed.

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(S93) MS in African Americans: Cohort From Southeast Texas

Introduction: Multiple sclerosis (MS) affects mainly white individuals from northern latitudes and high socioeconomic status. The proportion of African Americans (AAs) with MS is small compared with white Americans. AA MS patients generally have onset of symptoms at a later age and have a more severe form of the disease. Additional observations

addressing these issues in AA are needed. **Objective:** Assess age at onset, time between onset of symptoms and initiation of treatment, severity of initial symptoms, and progression of the disease in AAs. **Materials/Methods:** We retrospectively identified AA subjects from the database of the Maxine Mesinger MS Clinic in Houston, Texas. **Results:** From 108 AAs, we found that 89% of our study group was female (female:male ratio 7:1). The initial presentation of the disease was relapsing-remitting MS (RRMS) in 96%, primary progressive (PPMS) in 1%, and neuromyelitis optica or clinically isolated syndrome in 3%. Of the RRMS patients, 18% currently had a secondary progressive form of the disease. Most of our patients had disease onset during the third (32%) and fourth (33%) decades of life. The most frequent symptoms at onset were sensory (24%), spinal (24%), and optic neuritis (20%). Sixty percent of our subjects began treatment within the first year after symptom onset, and 85% were currently receiving therapy approved for MS. Of the subjects receiving therapy, 76% were receiving either interferons, copaxone, or tysabri. **Conclusions:** We found a different behavior in our AA patients than in previous studies, including a higher ratio of affected women, a lower frequency of PPMS, a shorter time to diagnosis and start of treatment, and a higher frequency of access to treatment.

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(S94) Balance Analysis in MS Patients by Berg Balance Scale

Multiple sclerosis (MS) is a chronic neurological inflammatory disease, with demyelination of the central nervous system of unknown cause, disseminated, and with multiple symptoms that primarily affects young adults. The balance disorder is the focus of this presentation, and the goal was to analyze the balance deficit on MS patients. Thirty-two MS patients in the study group were given the specific balance test Berg Balance Scale (BBS). BBS is the best test to verify balance and predict the risk of falls in older people. The maximum score is 56 of 14 tasks that are scored 0 when the person is unable to do the task and 4 when the person can execute the task normally. The initial level is seating and the final is supported by just one leg. A score of 45 predicts a risk of falls in older people. In this study, MS patients were divided by sex (53% female, 47% male), age (21–61 years old), diagnostic time (1.5–23.0 years), and type of disease (62.51% relapsing-remitting MS, 28.13% secondary progressive MS, 6.29% primary progressive MS). The results showed that the median score was 44.8. In conclusion, MS patients have a poor balance and a great risk of falls; therefore, balance is a significant symptom to consider. Men had the worst results on BBS: 60% ($n = 9$) had a score <45 points, whereas only three women (17.65%) had this score. Most of them (82.35%) scored >45 points. Also, patient age, time of diagnosis, and level of disease did not have a negative effect on balance test results.

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(S96) Reduced T2 MRI Burden of Disease: 48-Week Data From EVIDENCE Study

The EVIDENCE (Evidence of Interferon Dose-Response: European North American Comparative Efficacy) study demonstrated the superior efficacy of subcutaneous (SC) interferon (IFN) beta-1a 44 μg three times weekly (tiw) over intramuscular (IM) IFN beta-1a 30 μg once weekly (qw) in patients with relapsing-remitting multiple sclerosis (MS) for relapse measures, number of T2-active lesions, and proportion of patients with no T2 activity. This 48-week analysis compared reduction in T2 burden of disease (BOD) in patients treated with IFN beta-1a 44 μg SC tiw or 30 μg IM qw over 48 weeks. Details of the study design were published previously. Retrospective analyses of data included all patients with evaluable T2 magnetic resonance imaging (MRI) scans before the start of dosing and at Week 48. The primary endpoint was percentage change in BOD (in mm^3) from baseline to Week 48, a measure of total brain MS lesion load. Combined unique lesion activity (CUA) was also assessed. Patient demographics and baseline characteristics were well matched between treatment groups. Median percentage reduction in BOD from baseline to Week 48 was greater in the 44- μg SC group ($n = 279$; -6.7% ; range $-65, 431$) than the 30- μg IM group ($n = 274$; -0.6% ; range $-61, 197$); adjusted mean treatment difference (AMTD) was -4.6% (2SE 2.6; $P = .002$). This change from baseline in BOD at Week 48 significantly correlated with the change from baseline to Week 24 in CUA in the 44- μg SC group ($r = 0.385$; $P = .0001$) and the 30- μg IM group ($r = 0.179$; $P = .01$). Treatment effects for neutralizing antibody-positive patients were similar between groups: AMTD was 0.5% (SE 3.9; $P = .583$). A significantly greater reduction in T2 BOD was demonstrated with IFN beta-1a 44- μg SC than 30- μg IM over 48 weeks. This was consistent with other clinical and MRI findings from the EVIDENCE study.

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(S97) Decline in Quality of Life: Are Possible Warning Signs Indeed Triggers?

Background: Knowledge of factors that may predict poorer health-related quality of life (HRQL) is needed to recognize those at greatest risk for a deteriorating HRQL. **Objective:** The purpose of this study was to ascertain whether the factors associated with HRQL of Saskatchewan adults with relapsing-remitting multiple sclerosis (MS) changed over time. **Methods:** We used data from a population-based follow-up study examining HRQL of MS patients just beginning disease-modifying therapy (DMT). Subjects completed a self-report questionnaire when beginning DMT and again 3 years later. Questions included items on demographics, fatigue, comorbid conditions, disability (Expanded Disability Status Scale), attacks, illness intrusiveness (Illness Intrusiveness Ratings Scale), depression (Beck Depression Inventory), and HRQL (SF-36). Multiple linear regression models identified the factors associated with the physical and mental health summary scores of the SF-36 at baseline and Year 3. **Results:** At both time points, we found poorer physical HRQL in women and those who were older; had muscle,

joint, or bone problems; had greater fatigue; and had higher disability scores. At baseline, poorer mental HRQL was found in those with high illness intrusiveness, along with an interaction between sex and age in which older men had worse mental health whereas older women had better mental health. Three years later, both men and women had improved mental health, with women having a slightly larger gain. Age interacted with illness intrusiveness, meaning those reporting consistently high levels of illness intrusiveness had worsening mental HRQL with time, whereas those reporting consistently low levels of illness intrusiveness had improving mental HRQL, suggestive of a good psychological adjustment for those in whom the disease intruded little on their daily life. **Conclusions:** This study provided insight into the possible triggers of deteriorating HRQL in relapsing-remitting patients on DMT, which may assist health care providers in identifying those at risk for declining HRQL, permitting appropriate and timely interventions.

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(S98) Retrospective Chart Review and Analysis of NAb in Patients Treated With Interferon Beta

The role of neutralizing antibodies (NAbs) in interferon-beta therapy remains unclear and controversial. A retrospective chart review was performed on a population of patients seen in the Medical University of South Carolina Multiple Sclerosis (MS) Center by a single MS specialist over the past 12 years (1994–2006). Inclusion required that patients were diagnosed with definite MS and had been maintained on an interferon-beta preparation for at least 1 year. Data collected included age, sex, MS type, type of interferon beta used, NAb testing, and titer. Reasons for NAb testing generally conformed to the guidelines for possible treatment failure published by the National MS Society (NMSS) in 2004 (ie, “unexpected” number of relapses, increasing disability, and increasing magnetic resonance imaging activity). Of the 132 patients identified to be on interferon beta, 79% were female, and the median age was 48 years. Relapsing-remitting patients constituted 71%, secondary progressive 24%, primary progressive 5%, and one patient had progressive relapsing MS. The initial interferon-beta product used was Betaseron in 57 (43%) patients, Avonex in 58 (44%), and Rebif in 17 (13%). Twelve (9%) of all the interferon-beta-treated MS patients were tested. All but two tests for NAb were Athena (available since 1997); the other two were Specialty Laboratories. Eight of these treatment failures were on Avonex, four on Betaseron, and one on Rebif. One patient with secondary progressive MS on Betaseron was found to be NAb positive on repeat testing (>640); the other positive patient with relapsing-remitting MS (also on Betaseron) was found to be negative on repeat testing 3 months after the first test. Our findings suggested that increasing relapses, disability, and/or magnetic resonance imaging abnormalities in MS patients treated with interferon beta generally were not related to NAb. Treatment failures probably have more to do with the failure of specific patients to respond to interferon beta.

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(S99) Leisure-Time Physical Activity Levels in NARCOMS MS Population

Background: Inactivity is a key cardiovascular risk factor and a major contributing factor in obesity, osteoporosis, and many other health problems. The Centers for Disease Control and Prevention and American College of Sports Medicine recommend 30 minutes of moderate physical activity most days of the week for the general population. Furthermore, in chronic disease populations, exercise assists in maintaining and improving functional independence. **Objective:** Identify and characterize the groups most in need of physical activity interventions and education to guide development of MS patient education programs. **Methods:** NARCOMS multiple sclerosis (MS) patient registry contains self-reported demographic and health-related data collected at enrollment and semiannually thereafter. We analyzed 12-month leisure-time physical activity (LTPA) levels reported by 9699 US responders in spring 2006. Only 182 participants (2%), two thirds of whom had advanced disability, considered the question not applicable. A total of 2981 (30%) reported being inactive, and 4236 (43%) engaged in only light LTPA. Of the responders, 1984 (20%) reported moderate and 316 (3%) heavy LTPA. We analyzed demographic and disease characteristics of the 7217 responders (74%) reporting inactivity or only light LTPA. **Results:** As typical with MS, responders were mostly female (75%), white (93%), and educated beyond high school (66%) and had household income >\$30,000 (68%). Mean age was 54 ± 10 years and mean disease duration 14 years. Eighty-eight percent reported relapsing-remitting MS. Sixty-seven percent had early-onset disability level or higher, and 38% experienced severe or total fatigue. Although the proportion of inactive and light LTPA individuals was comparable (74% vs 78%), the MS group analyzed had a higher socioeconomic status than reported for nonexercisers in the general population. Gait and fatigue disability were higher than in the rest of the NARCOMS population. **Conclusion:** For maximum impact, LTPA interventions, exercise guidelines, and educational material should emphasize LTPA choices applicable to individuals with gait limitations. The relationship between fatigue and LTPA level warrants further investigation.

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(S100) Seven-Year Trends in Relapse Rates in NARCOMS MS Population

Background: Relapse rate is a typical outcome measure in clinical trials. Relapse-rate data collected in earlier studies are often used as guidelines, although it is unknown whether those data remain accurate. **Objective:** Analyze trends over time in the average number of relapses and steroid-treated relapses reported by NARCOMS relapsing-remitting multiple sclerosis (RRMS) participants for 6-month periods in 2000–2006. **Methods:** NARCOMS registry contains self-reported data voluntarily submitted by >31,000 MS patients

at enrollment and semiannually thereafter. We analyzed data from the annual fall update surveys from 2000 to 2006 to identify cross-sectional cohorts of RRMS patients residing in the United States, including only those who had been diagnosed within 15 years at the time of the survey and who were 18–55 years old at diagnosis. The size of each cross-sectional cohort ranged from 1108 to 4265. **Results:** The average age for each of the cohorts ranged between 43 and 45 years. The average disability level as measured by the Patient-Determined Disease Steps scale was between 3.0 and 2.7 (level 3, gait disability, is comparable to Expanded Disability Status Scale level 4). The proportion of patients reporting current use of disease-modifying agents or immunosuppressive drugs increased over time from 66% to 81%. From 2001 to 2006, the average number of relapses in the past 6 months decreased from 0.65 to 0.59, and the average number of steroid-treated relapses in the past 6 months decreased significantly from 0.23 to 0.12. **Conclusion:** Changes in relapse rates and relapse severity over time should be analyzed in further detail and taken into account in clinical trial designs.

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(S101) Effect of Donepezil on Cognitive Dysfunction and Quality of Life in MS Patients

Aims: Up to 70% of all multiple sclerosis (MS) patients experience cognitive dysfunction, which has a serious impact on their quality of life (QOL). So far, there is no effective treatment for the symptoms of their neuropsychological impairments. Evidence indicates, however, a positive effect of donepezil on memory and cognitive functioning in MS. In this research study, we measured the effect of donepezil on cognition and QOL in MS patients. **Design:** Double-blind, randomized, placebo-controlled study. **Method:** During this study, we randomly assigned 17 MS patients with cognitive impairment to receive an 8-week treatment with either donepezil or placebo. At baseline and after 8 weeks, all patients underwent a neuropsychological assessment and filled out a quality-of-life questionnaire. Our primary hypothesis was improvement on the delayed score of the Selective Reminding Test (SRT), a verbal memory test. Furthermore, we expected improvement on the other tests of cognitive function and an interaction effect between cognition and QOL.

Results: We were unable to demonstrate the effect of donepezil on the delayed-recall score of the SRT. However, subjects treated with donepezil significantly improved on several cognitive domains including attention, concentration, and verbal fluency compared with placebo. There was also a significant correlation between these cognitive improvements and mental QOL. **Conclusion:** Donepezil had a positive effect on cognition in MS patients and improved attention, concentration, and verbal fluency. This improvement correlated with improvement in QOL. This study emphasized the importance of investigational studies to find a treatment for cognitive dysfunction in MS patients.

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(S102) VA Longitudinal MS Study: Objectives and Overview of Population-Based Study

Objectives: The primary objective of the VA Longitudinal Multiple Sclerosis (MS) Study (VALOMS) is to determine predictors of long-term morbidity and effectiveness of treatment in veterans with MS. A secondary objective is to determine health care utilization, cost, and quality of life. Because of the unique features of the veteran population, this study focuses on the experience of men and all African Americans with MS. **Methods:** VALOMS is based at the VA MS Center of Excellence—East in Baltimore, Maryland, and currently includes five collaborating VA Medical Centers (VAMCs). The study cohort currently includes 69 veterans, with an overall recruitment goal of 200 veterans with MS. Subjects are randomly drawn at each participating VAMC from a list of all veterans having a diagnosis of MS. Study visits are conducted annually and include morbidity scales, quality-of-life surveys, brain magnetic resonance imaging, a cognitive battery, and a blood collection for banking. Patients are evaluated and MS morbidity scales assessed during relapses. Subjects will be followed for a minimum of 5 years. **Results:** The male-to-female ratio is 3.3:1.0, and 54% of the cohort is African American, the remainder being white. More men had primary progressive and progressive relapsing disease than women ($P = .06$). There was no sex difference in type of onset symptom, age at first symptom onset, or time from symptom onset to diagnosis. Time to initiation of disease-modifying therapy and current or past use of disease-modifying therapies were similar between men and women. **Conclusions:** VALOMS is a unique data resource that focuses on the experience of men and all African Americans with MS. New insights on risk factors for MS, disease course, treatment outcomes, and health care utilization are major byproducts from this study.

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(S103) Managing MS-Related Fatigue From Nursing Perspective

Fatigue in multiple sclerosis (MS) was not readily recognized or discussed before the early 1980s. During the course of the disease, 78–86% of patients complain of fatigue, with 40–60% reporting fatigue as their worst problem. MS fatigue has not been found to correlate closely with demographic characteristics, clinical forms of MS, or disability. The aim of this small study was to determine the role the MS specialist nurse can play in assessing and managing fatigue, particularly where access to the multidisciplinary team is delayed or not always feasible. To evaluate fatigue management principles, 10 patients were studied. Their age range was 28–39 years, and all were female. The clinical course of MS was relapsing remitting and had a mean duration of 5 years for the disease. The prevalence of fatigue according to the Modified Fatigue Impact Scale was high, and all of the patients had complained of fatigue. A fatigue questionnaire and sleep questionnaire were also completed. The presentation includes an overview of the assessment process, along with evidence-based principles for fatigue management. There

appeared to be a correlation between fatigue and mood, and lifestyle modifications were necessary to overcome the problem. It appears that fatigue is underestimated and can appear early in the disease process. MS specialist nurses should be alert about this fact and consider early appropriate management strategies to improve the function and quality of the patient's life.

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(S104) Factors Associated With Outcomes in MS Patients Treated With Intrathecal Baclofen

Rationale: Spasticity is a common symptom of multiple sclerosis (MS), causing pain and discomfort, as well as interfering with mobility and functioning. The intrathecal baclofen (ITB) pump has been shown to control spasticity but requires surgery and long-term monitoring. Currently, predictors of outcomes with ITB therapy in MS have not been identified.

Methods: Nineteen ambulatory MS patients ages 31–77 years (78% female, 95% white, 58% married, and 44% employed), referred to the Mellen Center Spasticity Clinic with severe spasticity poorly controlled with oral medications, underwent implantation of a ITB pump. At baseline and 6 months, evaluations included muscle tone (Modified Ashworth Scale) and gait speed (timed 25-foot walk), along with self-administered questionnaires assessing coping and mental and physical health. Patient satisfaction was assessed at 6 months. **Results:** At follow-up, patients reported a positive change in symptoms (79%) and function (68%) and satisfaction with controlling spasticity symptoms and quality of sleep (79%), with function (63%), and with quality of life (74%). Seventy-two percent experienced an objective decrease in muscle tone and 41% an increase in gait speed. Ninety-five percent experienced no complications, and 63% indicated they would repeat the procedure. Baseline characteristics related to patient-reported positive outcomes included lower muscle tone, slower gait speed, greater use of instrumental and distraction coping, and lower ratings of mental and physical health. Decreased muscle tone and increased gait speed at 6 months were related to both slower gait speed and higher ratings of mental health at baseline. Satisfaction was more related to change in function than change in symptoms. **Conclusions:** Patients less likely to experience positive outcomes could be identified before ITB therapy. Differences in characteristics related to patient-reported versus clinical outcomes suggested differences in how clinicians and patients measured success. Results indicated the need for individualized assessment of expectations at baseline.

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(S105) Clinical Predictors of Falls and Ambulatory Activity in MS: 6-Month Prospective Study

Background: Falling is a frequent cause of morbidity in multiple sclerosis (MS), and health care providers need simple clinical methods that identify patients at risk for falls. This is a preliminary report of a 6-month prospective study of ambulatory MS patients to evaluate the association of four

clinical tests and two questionnaires with ambulatory activity and falls in the MS community performed at the MS Center Evergreen. **Methods:** Forty subjects with definite MS, ages 18–70 years, Expanded Disability Status Scale (EDSS) scores of 0–6.5, and stable disease are being enrolled. Participants are assessed three times in clinic with EDSS, Hauser Ambulation Index, Berg Balance Test, Lower-Extremity Motor Coordination Test, self-report questionnaires, the MS Walking Scale, and Modified Fatigue Impact Scale. Ambulatory activity is recorded by ankle-worn accelerometers (StepWatch3) for 1 week during Months 1 and 6. Falls and near-falls are recorded during the study by diaries and monthly phone monitoring. **Results:** Twenty-three MS patients have completed the study to date, with a mean EDSS score of 5.0, range 3.0–6.5. Falls were reported by 19 participants during the observation period, with a median fall rate of three during 6 months. Average daily steps per subject ranged from 657 to 12,474 (mean 6656). There was only a weak correlation between falls and ambulatory activity as measured by steps/day. There was a negative correlation between average steps/day and EDSS. Based on preliminary analysis, some correlation between the clinical tests and falls was found, but no single clinical measure or questionnaire appeared strongly correlated with falls. **Conclusions:** Most MS patients with some disability will fall during a 6-month period. The level of activity may not correlate with the frequency of falls. Our study is exploring the predictive value of validated clinical tests of gait, balance and coordination, and self-assessment questionnaires for falls and ambulatory activity.

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(S106) Efficacy in Clinical Practice of Mitoxantrone for Worsening MS

Background: Mitoxantrone has been approved by the US Food and Drug Administration for worsening multiple sclerosis (MS), and its efficacy has been demonstrated in clinical trials. In clinical practice, however, patients may receive less than the full dose because of patients' ambivalence, history of noncompliance, or intolerance of the drug. We studied efficacy of mitoxantrone for worsening disease in a clinical setting in an academic multidisciplinary MS center. **Methods:** One hundred three MS patients from the Western MS Center at the University of Washington who were prescribed mitoxantrone for worsening disease between September 1999 and February 2005 were studied retrospectively by medical chart review. Data collection included information on disease, such as type of MS, relapse history, and Expanded Disability Status Scale (EDSS), in relation to mitoxantrone treatment history. **Results:** To date, data from 62 patients have been analyzed. Most of these patients had either secondary progressive MS ($n = 30$) or relapsing-remitting MS ($n = 23$). Twenty-one had completed at least 2 years of mitoxantrone administration, whereas 41 discontinued infusions prematurely. Patients received a mean of 5.6 infusions (median 5). The mean EDSS score at initiation of mitoxantrone was 6.36. At discontinuation, patients had worsened by an average of 0.24 points on EDSS ($P = .04$). Twen-

ty percent of patients showed improvement, 45% remained stable, and 34% declined based on EDSS. The number of relapses decreased during (-0.66 , $P = .005$) and after (-0.85 , $P = .0003$) treatment compared with the relapses reported within the 2 years before initiation of mitoxantrone. Two patients converted from relapsing-remitting MS to secondary progressive MS during mitoxantrone treatment; both received only a few infusions with some delays. **Conclusions:** Our data suggested that mitoxantrone stabilized disease activity in patients with worsening MS treated in a clinical setting. Despite frequent suboptimal conditions and incomplete treatment schedules, patients showed relatively stable neurological functioning and a fewer relapses.

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(S107) Mitoxantrone for Worsening MS: Compliance Problems in Clinical Practice

Background: Management of worsening multiple sclerosis (MS) continues to pose a major therapeutic challenge because of limited treatment options. Available treatments are associated with significant risks. We review our experience with mitoxantrone for worsening MS, including compliance and tolerability for patients treated at an academic multidisciplinary MS center. **Methods:** One hundred three MS patients from the Western MS Center at University of Washington who were prescribed mitoxantrone for worsening disease between September 1999 and February 2005 were studied retrospectively by medical chart review. In addition to demographics and clinical efficacy, data on mitoxantrone treatment history and side effects, including hematological and cardiac toxicity, were collected. **Results:** To date, data from 63 patients have been analyzed. Most of these patients had either secondary progressive MS ($n = 30$) or relapsing-remitting MS ($n = 24$). Twenty-two had completed at least 2 years of administration or received the US Food and Drug Administration's recommended maximal allowable dose of 140 mg/m². Forty-one patients discontinued infusions prematurely, predominantly at their own request ($n = 13$) or because of intolerable side effects ($n = 8$). Among patients analyzed, there were four with decrease of left ventricular ejection fraction to <50% and one case of discontinuation because of thrombocytopenia. In 10 patients, the dosage was reduced to <12 mg/m² at least once because of poor tolerability ($n = 7$), preinfusion leukopenia ($n = 2$), or unknown reason ($n = 1$). Two patients were treated throughout on a reduced dose schedule because of preexisting thrombocytopenia ($n = 1$) or add-on therapy to interferon ($n = 1$). **Conclusions:** This experience identified that as many as two thirds of patients enrolled on mitoxantrone did not receive the intended cumulative dose; they stopped prematurely because of disillusionment or adverse events. However, only a few patients had to discontinue treatment for objective safety reasons. Our data offer relevant insights into challenges of tolerability and compliance in the use of mitoxantrone in clinical practice.

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(S108) Qualitative Study on Compliance With Disease-Modifying Therapy in Relapsing-Remitting MS

The factors influencing compliance have been of particular interest in multiple sclerosis (MS) and parenteral disease-modifying therapies (DMTs). Previous published studies showed that many patients stop or switch in the first 6–18 months of treatment, the most common reason being lack of efficacy or no reason found. It is difficult to realistically assess the efficacy of a DMT in the initial months of treatment, which raises the possibility that DMTs are stopped prematurely in significantly few patients. We conducted qualitative analyses of interviews with patients who had been prescribed DMTs within the past 18 months, including subjects who adhered to treatment and who discontinued for nonclinical reasons. The interviews were conducted in two UK centers by a psychologist who was independent of the patient's care. Anonymized transcripts were read by a psychologist, an MS nurse, and a neurologist to independently identify themes. **Results:** Twelve patients, five men. Nine were on treatment (Avonex Betaseron 4, glatiramer 3, Rebif 2), and three had discontinued (Avonex 1, Betaferon [Betaseron] 1, glatiramer 1). There appeared to be four key areas: attitudes toward medicines and medicine taking, specifically previous good experiences of medication and realistic expectations for treatment; self-efficacy and locus of control, the need to take action and

attempt disease modification as opposed to fatalism about future MS course; attitudes and beliefs about health and illness, including uncertainty whether unpleasant symptoms were the result of MS, taking DMTs, or discontinuing DMTs; and social and professional support. Some of the preliminary analysis was in keeping with previous work on the importance of self-efficacy and patient perception of support. However, knowledge and understanding of the relationship between the treatments and ongoing MS symptoms was novel, underlining the importance of ongoing access to MS specialist nurse support.

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(S109) Self-Efficacy and Physical, Cognitive, and Emotional Functioning in MS

Although the impact of multiple sclerosis (MS) can be heterogeneous, research has shown that the disease is associated with impairment in physical, cognitive, emotional, and social functioning. Disease-related factors alone do not completely explain the variability in functional outcomes seen in MS. Research is increasingly focused on the effect of psychosocial factors on outcomes in individuals with MS such as self-efficacy (the belief of an individual in his or her ability to effectively cope with challenging situations). Self-efficacy has been previously associated with psychosocial adjustment and