

Posters

(S01) Religious Beliefs of People With Multiple Sclerosis

Religious beliefs may help in coping with multiple sclerosis (MS). People with MS are looking for answers that cannot be found in science. A questionnaire was given to patients in an occupational therapy program, who returned 54 patient responses. This questionnaire was given 1 week before Easter and Christmas.

Questions and Responses: 1) Do you believe in a higher being? 94.4% yes, 3.8% no, 1.8% don't know. 2) How is your relationship with Him? 22% worship, 11% as father and son, 11% friendship, 7.3% submission, 7.3% strength. 3) What makes you happy? 30% family, 26% friends, 11% God, 11% healthy, 7.3% do things. 4) What gives you peace? 11% family, 11% friends, 11% calm environment. 5) What do you love most in life? 68% family, 20% life, 12% God. 6) What is good? 55% help people, 17.6% God, 15.5% help yourself and others. 7) What is evil? 29% harm others or yourself, 15.6% harm others, 15.6% bad thoughts, 15.6% don't know, 7.8% opposite God. 8) Do you believe in the devil? 41% no, 41% yes, 8% don't know. 9) Do you believe in the Bible? 68% yes, 22% no, 10% do not know. 10) What is sin? 54% do bad things; 30% do things against God, 12% do not know, 4% doesn't exist. 11) What is forgiveness? 30% only God can forgive, 70% wonderful thing to do. 12) Do you believe in life after death? 72% yes, 20% do not know, 8% no. 13) Are you afraid of death? 72% no, 28% yes. 14) Who is Jesus? 36.7% God, 24% son of God, 11.7% the savior, 21.5% nice man. 15) What is the relationship between God and MS? 25% God gave me MS to make me a better person, 17% disappointed with God, 14.5% God is proving my faith, 17% God has nothing to do with MS, 14% sin in other life, 9% God helps, 4% do not know.

Conclusion: Those treating MS should be aware of some of the diverse beliefs of people with this disease.

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(S02) Psychometric Evaluation of PHQ9 Using Item-Response Theory

Background: The nine-item patient health questionnaire (PHQ9) is a scale used to screen for depressive episodes and symptoms in medical patients. Although it has shown promise in other populations, it has not been validated in individuals with multiple sclerosis (MS).

Purpose: The purpose of this study was to apply item-response theory (IRT) methods to explore the psychometric properties of PHQ9 and examine functioning of the scale in individuals with MS.

Sample: Data were collected from 107 people with MS. Participants responded to PHQ9 items as well as demographic, clinical, and other quality-of-life measures.

Analyses: An IRT model appropriate for items with more than one response option (Andrich's rating scale model) was used to calibrate the PHQ9 items. IRT assumptions of unidi-

dimensionality and local item independence were assessed by confirmatory factor analysis. Fit of PHQ9 items to the rating scale model was evaluated. The effective measurement range of the measure was estimated.

Results: The interitem consistency of PHQ9 was extremely low (Cronbach's $\alpha = .30$). The measure had modest fit to a unidimensional model (comparative fit index = 0.928, TLI = 0.944, RSEA = 0.145), and a substantial percentage (44%) of item pairs exhibited higher than optimal residual correlation (>0.10). All but two of the items met traditional fit standards after calibration to the rating-scale model. Least fitting items were "moving/speaking slowly" and "better off dead." The PHQ9 items were most effective at measuring people with higher levels of depression.

Conclusions: Appropriate to its purpose as a screening instrument, the PHQ9 best discriminates among people with higher levels of depression. The results suggest that it would not be a good instrument for discriminating among lower levels of depression. There are several published cut points for the PHQ9. Future research should evaluate the equivalence of these cut points based on an IRT calibration of item responses.

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(S03) CellCept in Multiple Sclerosis Patients: Failing Treatment With Azathioprine

Background: In more than 400 multiple sclerosis (MS) patients on continuous monotherapy with interferon- β (IFN β) or glatiramer acetate, followed over 2 years, relapses or breakthrough symptoms were absent in $<20\%$ of the individuals treated. To optimize disease control in individual MS patients, added-on immunosuppressive medications are necessary. Low serum thiopurine methyltransferase level or idiosyncrasy to azathioprine (AZA) prevents its use.

Objective: Establish safety and efficacy of mycophenolate mofetil (CellCept) in MS patients on continuous combined therapy (CCT) with IFN β (Avonex) and prednisone failing added-on AZA.

Design and Methods: Currently, from the 34 MS patients enrolled, 15 were treated over 1 year with IFN β -1a (Avonex, 30 $\mu\text{g}/\text{week}$), prednisone (8.5 ± 2.9 mg/kg daily), and CellCept (targeted dose 2 g/day). Annualized relapse rate (ARR; transient or persistent increase in the Expanded Disability Status Scale [EDSS] rating by ≥ 1.0 point), EDSS rating, and peripheral blood flow cytometry (FC) were studied. Patients were followed in 10- to 12-week intervals.

Results: AAR was 0.11 for ≥ 1.0 EDSS rating and 0.22 for ≥ 0.5 EDSS rating. The mean EDSS score did not change during the treatment (5.80 ± 0.94 at the beginning and 5.77 ± 1.16 by the end of 12 months; $P = .8760$). Compared with healthy control subjects, FC studies revealed a significant decrease in peripheral blood CD19+ ($76.13 \pm 66.17/\text{cmm}$; $P = .0011$) and CD8+ ($258.93 \pm 182.01/\text{cmm}$; $P = .0049$) cell counts and upregulation in the CD14+ cell count ($478.73 \pm 179.89/\text{cmm}$; $P = .0081$). In one patient, discontinuation of CellCept was necessary because of persistent elevation in liver enzymes. IFN β antibody titer was $<1:16$ in all patients.

Conclusion: In MS patients who require CCT and are unable to use AZA, therapeutic trial with CellCept is indicated.

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(S04) Information Needs of Newly Diagnosed Multiple Sclerosis Patients and Their Significant Others

The London Health Sciences Centre Multiple Sclerosis Clinic conducted a survey of the information needs of people newly diagnosed with MS and of their significant others. The goal of the research was to develop an information package for newly diagnosed patients based on patient needs. Seventy-five people diagnosed with MS within the previous 2 years and 51 significant others completed a survey questionnaire. Respondents were asked to rank in importance the topics of information they received or would have liked to receive at the time of diagnosis. They also indicated their preference in respect to 1) who should receive information at the time of diagnosis (partner, child, employer, etc.), 2) the method through which information is given (written material, group sessions, etc.), and 3) who should provide the information (health care professional, MS Society). There was little difference between the information needs of people diagnosed with MS and their significant others. Information resources relating to psychosocial issues were ranked number one for both groups. Newly diagnosed people and significant others ranked information received from health care professionals and written material high as well. Findings were consistent with a previous study. The results support the current process of information sharing in the MS clinic and will be used to refine the information provided to the newly diagnosed population and their significant others.

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(S05) Factors Associated With Sexual Function in Women With Multiple Sclerosis

Objective: Describe demographic, urinary symptom distress, and disability-level factors associated with sexual function in women with multiple sclerosis (MS).

Methods: Sixty-eight women with a relapsing form of MS were recruited during routine clinic visits, educational programs, or support group meetings. Consented participants completed a demographic and medical history form, the Patient-Determined Disease Steps (PDDS) and performance scales questionnaires, Urge-Urinary Distress Inventory (U-UDI), Female Sexual Function Index (FSFI), and the SF-36. Demographic, urge-urinary distress, and disability ratings were examined for their association with sexual function via regression analysis.

Results: Women were 48.5 ± 10.0 years old, predominately white (94%), with an 11.9 ± 8.3 -year history of MS and a median PDDS score of 3.0 (indicating gait disability). Mean physical function, general health, and mental health SF-36 subscale scores were 39.3 ± 26.6 , 46.6 ± 21.2 , and 62.8 ± 17.2 , respectively. Based on performance scale rat-

ings, they had minimal depression, vision disability, and cognitive disability; mild pain and mild gait; bladder, sensory, and spasticity disability; and moderate fatigue disability. The mean FSFI full-scale score was 17.3 ± 10.6 , lower than reported (19.2 ± 6.6) for a slightly younger (40.5 ± 13.0 years) sample of women with sexual arousal disorder. The mean U-UDI urge score was 1.92 ± 0.92 . Visual disability emerged as an important predictor of arousal, orgasm, lubrication, and satisfaction. Pain disability emerged as an important predictor of arousal and satisfaction, whereas gait disability was an important predictor of orgasm. Age approached statistical significance as an important predictor of lubrication.

Conclusions: Among demographic, disability ratings, and urge-urinary distress variables, sexual dysfunction was most consistently predicted by vision disability in this sample of women with MS.

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(S06) Test Retest Reliability of Urge-Urinary Distress Inventory and Female Sexual Function Index in Women With Multiple Sclerosis

Introduction and Objective: Genitourinary dysfunction is common in women with multiple sclerosis (MS), yet accepted urinary symptom distress and sexual function measures have not been adequately tested in this population. This study aimed to assess the test-retest reliability of the Urge-Urinary Distress Inventory (U-UDI) and the Female Sexual Function Index (FSFI) in women with MS.

Methods: Sixty-five women with a relapsing form of MS were recruited during routine clinic visits, educational programs, or support group meetings. A consent form, demographic and medical history form, the Patient-Determined Disease Steps (PDDS) questionnaire, and initial set of questionnaires (U-UDI, FSFI, and SF-36) were sent by mail to participants. Within 2 weeks of returning the signed consent form and initial questionnaires, participants received a second set of questionnaires. The test and retest subscale and summary scores for U-UDI and FSFI were calculated. Intra-class correlation coefficients were calculated to assess each instrument's test-retest reliability.

Results: Women were 48.5 ± 10.0 years old, predominately white (94%), with a median PDDS score of 3.0 (indicating gait disability). Fifty-seven and 55 completed sets of U-UDI and FSFI, respectively, were returned and suitable for analysis. Mean SF-36 physical function subscale scores were similar at test and retest (39.6 ± 26.1 vs 38.0 ± 24.2 , respectively; $P = .30$). The mean U-UDI urge summary score was 1.87 ± 0.97 at test and 1.76 ± 0.90 at retest. U-UDI subscale intraclass correlation coefficient (ICC) ranged from 0.38 (frequent urination) to 0.87 (leakage with urge). The U-UDI urge summary score showed good reproducibility, ICC = 0.70 (95% confidence interval [CI] 0.54–0.81). The mean FSFI full-scale score was 17.48 ± 10.61 at test and 17.16 ± 10.38 at retest. FSFI subscale ICC ranged from 0.77 (satisfaction) to 0.90 (orgasm). Excellent reproducibility was observed for the FSFI full scale, ICC = 0.90 (95% CI 0.83–0.94).

Conclusions: The U-UDI and FSFI can be used to reliably assess urinary symptom distress and sexual function in women with MS. Further exploration of the instruments' validity in this population is needed.

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(S07) Benign Relapsing Neuromyelitis Optica

Background: The epidemiological study of relapsing neuromyelitis optica (R-NMO) in Cuba showed a prevalence of 0.49 in 105 (95% confidence interval [CI] 0.4–0.6, classic and Bayesian), although a higher prevalence was found in the province of Cienfuegos, with 1.76 in 105 (95% CI 0.5–3.1 classic; 0.8–0.6 Bayesian). Evaluation of patients showed cases with R-NMO of long duration and slight to moderate physical and visual disability.

Objective: The object of this study was to present cases considered benign forms of R-NMO.

Design/Methods: Data were obtained from 26 patients with R-NMO from the prevalence study, with ≥ 5 years of evolution and physical disability according to Kurtzke's Expanded Disability Status Scale (EDSS) score of 4.5 and a degree of impairment of 3 in the visual (or optic) functions according to the neurological assessment Kurtzke Functional Systems (FS). These patients were considered to have a benign form of R-NMO. The demographic, clinical, and laboratory data were compared with patients having the same physical disability (EDSS 4.5) but with a visual FS of 4 or more, and it was considered a clinical form with predominant visual impairment. Demographic, clinical, and laboratory data were compared between groups. Statistical analysis was carried out with the Mann-Whitney nonparametric test and the χ^2 -test.

Results: No significant differences between the benign form (B-RNMO) and that with predominant visual impairment (V-RNMO) were demonstrated according to age at onset (34.1 ± 6.8 vs 29.7 ± 8.9 years, respectively; Mann-Whitney $z = 1.300$, $P = .193$); number of relapses (4.0 ± 2.8 vs 3.4 ± 1.6 ; Mann-Whitney $z = 1.565$, $P = .117$); or duration of disease (9.6 ± 4.3 vs 13.8 ± 7.2 years; Mann-Whitney $z = 1.565$, $P = .117$). Nevertheless, when time between the first and second relapse was analyzed, it was shorter in B-RNMO than in V-RNMO (1.4 ± 1.3 vs 3.8 ± 4.4 years), with a trend toward significance (Mann-Whitney $z = 1.850$, $P = .064$). With respect to the first sentinel event, in B-RNMO, the transverse myelitis (TM) clinical form predominated with nine cases (60%), compared to only two cases in the V-RNMO form (18.2%). However, the opposite occurred regarding optic neuritis (ON) as the initial event, predominating ON in seven (63.5%) of the cases of the V-RNMO form and only four (26.7%) cases of B-RNMO ($\chi^2 = 4.701$, $P = .030$). There were no differences between groups with respect to the simultaneous appearance of TM + ON as the initial neurological symptom.

Conclusions: The possibility of a benign form of R-NMO ≥ 5 years after onset, considering a low physical and visual dis-

ability, is associated with the presence of TM as the initial neurological event and a shorter time for the second relapse.

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(S08) Comprehensive, Personalized, and Intensive Neurorehabilitation Program With a Multidisciplinary Team for People With Multiple Sclerosis: Pilot Study

Introduction: The recent disease-modifying therapies have not eliminated the need for neurorehabilitation strategies in the management of multiple sclerosis (MS). Even if there were drugs that could fully prevent progression of the disease, hundreds of thousands of patients worldwide would still be left with residual neurological damage and the associated impairment and disability.

Objective: Evaluate the efficacy of a comprehensive, personalized, and intensive neurorehabilitation program with a multidisciplinary team for people with MS.

Design/Methods: People with progressive or relapsing-remitting MS were included to receive an integrated, comprehensive, and intensive neurorehabilitation program by a multidisciplinary team. The multidisciplinary team consisted of MS neurologists, physiatrists, psychologists, neuropsychologists, occupational therapists, speech-language therapists, natural and physical medicine specialists, and nurses. The program was an intense neurorehabilitation for 4–8 weeks (2 sessions daily), except on weekends; each patient had a single physiotherapist (one to one). The evaluation was by means of scales on impairment disability by Scripps neurological rating scale (SNRS), Expanded Disability Status Scale (EDSS), and neurological assessment Kurtzke Functional Systems (FS); Fatigue Impact Scale (FIS) was used to evaluate fatigue and quality of life (QOL) by the MSQLI-54 instrument.

Results: Seventeen people with MS (11 progressive, 6 relapsing remitting), 11 (64.7%) women and 6 (35.3%) men, with mean \pm SD 8.76 ± 5.32 years of evolution were included. All the cases completed 4 or 8 weeks of an intensive neurological rehabilitation. The evaluation of impairment/disability was as follows: SNRS: initial, 54.29 ± 19.14 (25; 90); 4 weeks, 74.60 ± 18.94 (36; 95), $P = .0000$; 8 weeks, 69.63 ± 11.30 (51; 86), $P = .003$ student t test. EDSS: initial, 5.40 ± 2.02 (2; 8.5); 4 weeks, 4.55 ± 2.62 (1; 8.5) $P = .01$; 8 weeks, NS student t test. FS demonstrated in pyramidal: initial, 3.71 ± 1.10 (1; 5); 4 weeks, 2.90 ± 1.59 (1; 5), $P = .022$; 8 weeks, 3.00 ± 1.30 (1; 5), $P = .006$ student t test. FS in cerebellar: initial, 0.94 ± 1.14 (1; 5); 4 weeks, 1.000 ± 0.816 (0; 2), $P = .000$; 8 weeks, 2.380 ± 0.916 (1; 4), $P = .002$ student t test. FS in brain stem: initial, 1.880 ± 1.166 (0; 4); 4 weeks, NS; 8 weeks, 1.380 ± 1.302 (0; 4), $P = .007$. FS in sensorial: initial, 1.000 ± 1.118 (0; 3); 4 and 8 weeks, NS. FS in bowel and bladder: initial, 1.410 ± 1.661 (0; 5); 4 weeks, 0.700 ± 1.252 (0; 4), $P = .022$; 8 weeks, NS student t test. FS in cerebral: initial, 0.410 ± 0.712 (0; 2); 4 and 8 weeks, NS. There was reduction of fatigue by FIS 49.33 ± 11.43 (39; 68) initial versus 35.000 ± 6.066 (25; 40) final, $P = .083$. QOL demonstrated an improvement in physical health: 41.0 ± 8.1 (28.4; 54.1) initial and 50.6 ± 12.8 (26.9; 66.7) final, $P =$

.015, whereas an improvement was observed in mental health unless NS.

Conclusions: This pilot study with a multidisciplinary team using a comprehensive, personalized, and intensive neurorehabilitation one to one for 4–8 weeks demonstrated an improvement in impairment, disability, and QOL and decreased fatigue in people with MS. A controlled, randomized, multicenter, clinical trial is needed to confirm the efficacy of this program.

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(S09) Neurorehabilitation in Relapsing-Remitting Multiple Sclerosis

Relapsing-remitting multiple sclerosis (RRMS), the most frequent clinical form, presents with low to moderate degrees of disability. Relapses in RRMS determined a sustained negative impact in the patient's disability that was sustained for a mean of 2 months after the acute episode, suggesting the acute exacerbations of MS have a measurable and sustained effect on accrued impairment and disability. Therefore, consistent with the evidence among the various clinical trials, the immunomodulator and immunosuppressor therapies for RRMS that reduce the frequency of relapses should be beneficial for patients with RRMS. However, other treatment modalities, such as neurorehabilitation could be beneficial for patients with RRMS to reduce the negative impact over impairment and disability of the relapses. The data we present are based on results from controlled clinical trials that have evaluated the efficacy of interventions with neurorehabilitation in RRMS. In this way, the neurologist can have a better idea of how to act in the daily medical practice and obtain a greater benefit with the procedure in RRMS patients. The results of this review confirmed 1) neurorehabilitation produces a significant improvement in all disability scales, motor function, and aspects of quality of life 3 months after the onset of the relapse in patients who received a physical therapy program compared with controls and indicates that combining steroids with planned multidisciplinary team care is superior to administering them in a standard neurology or day ward setting; 2) inpatient rehabilitation is useful in RRMS, particularly in patients with incomplete recovery from relapses who have accumulated moderate to severe disability; and 3) neurorehabilitation is effective in the slight to moderate forms of RRMS between relapses. Neurorehabilitation is a useful tool for the treatment of RRMS.

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(S10) Fatigue Educational Workshop: Does It Help a Veteran Cohort?

Objective: Assess feasibility and clinical impact of structured multiple sclerosis (MS) fatigue workshop in a US Department of Veterans Affairs (VA) outpatient clinic setting.

Background: Fatigue is a common and often disabling symptom of MS. Medications and physical therapy offer only modest help, so the new Fatigue: Take Control! workshop, developed with support of the National Multiple Sclerosis Society (NMSS), merits a trial in a health care system with at least 16,000 individuals with MS.

Participant Characteristics and Workshop Design:

Eight male veterans enrolled. Six had relapsing-remitting MS, and two had secondary progressive MS. Five had moderate ambulation limits (Expanded Disability Status Scale [EDSS] score 5.5); three had mild limits (EDSS 4.5). One was gainfully employed. Their mean age was 56 years; mean education was 13.4 years. Seven took fatigue medication (4 amantadine, 2 modafinil, and 1 gabapentin); all took antidepressants. We expanded the workshop from 6 to 12 sessions, added a 30-minute socialization opportunity before each class, and expanded the guest lecturer roster to 5 disciplines.

Results: Sixteen veterans were referred for the workshop; 11 started and 8 finished. Those who finished came consistently (mean 9.6 of 12 sessions). Two family caregivers attended all sessions. On the postworkshop NMSS survey, enrollees reported improved planning and coping strategies. After hearing the physical therapy lecturer, 4 requested and were given physical therapy referrals. Two reported that the highlight was the naturopathic physician lecture. Mean MS Fatigue Severity Scale (FSS) results were 5.75 at outset, improved to 4.99 after the class; mean quality-of-life measure (Quality of Life Enjoyment and Satisfaction Questionnaire; Q-LES-Q) was 48.2 at outset, improved to 50.71. Data from a second survey of both measures, conducted 6 months after the class, are being collected and will be presented.

Conclusions: Piloting this workshop proved both easy for VA providers and satisfying for the veteran. The FSS and the Q-LES-Q showed improvement, warranting a larger study.

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(S11) Assessing Patient Satisfaction With Care in Canadian Multiple Sclerosis Center

Background: Patient satisfaction is a useful outcome measure in evaluating health care services. A literature review did not reveal an instrument that would evaluate patient satisfaction with specific services provided in a multiple sclerosis (MS) clinic. The development of such an instrument was undertaken at the Dalhousie MS Research Unit (DMSRU).

Methods: DMSRU is the only referral center for MS patients in Nova Scotia. Using the DMSRU database, all new patients ($n = 130$) seen between January 2004 and July 2005 were identified. A customized questionnaire assessing patient satisfaction was developed and mailed to these 130 patients. Patient satisfaction with physician services, nursing care, wait times, education, and telephone support was evaluated. Respondents were given the opportunity to provide qualitative responses to most questions. Questionnaires were not coded so that patient anonymity was protected. This created a limitation for data analysis. Data analysis was completed using SPSS.

Results: There was a 52% response rate of which 81% were women. Seventy-two percent reported having a diagnosis of relapsing-remitting MS, and 25% were unsure of their type of MS. Respondents were highly satisfied with the care they received from DMSRU. Eighty-one percent rated the quality of care by their neurologist as very good or excellent, and 92.6% perceived their neurologist's knowledge of MS to be very good or excellent. Fifty-seven percent rated the nurse's knowledge of disease-modifying therapies as very good/excellent (35% said this section was not applicable). Fifty-four percent responded that a one-on-one education session with an MS nurse reduced fears and was helpful in making the decision to start on therapy (48%).

Conclusions: Measuring patient satisfaction provides useful feedback on the quality and utility of care programs. A clinic-specific questionnaire may provide valuable outcome measures that may further enhance the care provided. The DMSRU Patient Satisfaction Survey requires further study to determine its reliability and validity.

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(S12) Comparison of Aquatic Exercise and Land-Based Exercise for Women With Multiple Sclerosis

Background: Research has shown that people with multiple sclerosis (MS) experience similar benefits from exercise to those without MS. Although there are some answers regarding the benefits of exercise for people with MS, the research is far from comprehensive and has not explored the numerous options available for exercise programs. An aquatic environment provides many benefits for the participant; many risks associated with exercising on land are minimized in the water. Current research suggests that the training response for aquatic exercise is similar to that demonstrated via land exercise. With the additional advantages of an aquatic environment for people with MS, further research in this area is warranted.

Purpose: Examine whether aquatic and land-based exercise programs could improve physiological and psychological variables in people with MS and whether aquatic or land-based exercise provides a greater benefit.

Methods: Six women with MS were randomly assigned to 16 weeks of land-based exercise, aquatic exercise, or a control group. Participants were evaluated pre- and posttraining for changes in aerobic power, handgrip strength, lower-extremity muscular strength and endurance, 200-meter walk, and the Fatigue Impact Scale.

Results: Aerobic power improvement ranged from 0 to 10.2%, and both exercise groups improved their 200-meter walk time (6.8–19.5%). The aquatic exercise group showed specific improvements in left-leg muscular endurance (10.0–66.7%). Most participants reduced total fatigue and physical fatigue (25.2–41.4%; 21.1–33.3%, respectively).

Conclusions: It is impossible to determine which exercise program provided the most benefits for women with MS. With the potential for positive changes, community-based services should consider developing programs to assist in the prevention of the potential decline in strength, aerobic power,

and increases in fatigue associated with MS. Further investigation of similar exercise programs and their outcomes with a larger sample size is necessary to evaluate the benefits of the prescribed exercise programs.

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(S13) Predictors of Adherence to Exercise Goals in Patients With Multiple Sclerosis

Background: Exercise is important in managing multiple sclerosis (MS) symptoms. However, little is known about factors that contribute to adherence to exercise regimens.

Methods: Sequential MS patients ($N = 119$) who were ambulatory without aid were eligible for inclusion. Participants were randomly assigned to receive motivational exercise counseling and exercise goal setting or to a usual care condition. Baseline characteristics were assessed to determine factors that might potentially influence adherence with exercise goals. Subjects were evaluated for fatigue (modified Fatigue Impact Scale), pain (Brief Pain Inventory), depression (Center for Epidemiologic Studies Depression Scale), disability (MS Functional Composite), and Motivational Readiness to Exercise Scale.

Results: Of 49 evaluable subjects in the exercise condition, 81.2% were women, 98% white, 83.7% had relapsing MS, mean age was 51.5 ± 10.2 years, and mean time since diagnosis was 10.7 ± 6.7 years. Mean timed 25-foot walk was 5.00 ± 1.34 seconds. Mean baseline exercise was 71.5 ± 68.0 min/week. Exercise goals averaged 158.0 ± 96.4 min/week. Actual exercise was 209.3 ± 186.9 at 2 weeks and 301.1 ± 355.2 min/week. At 2 months, exercise goals were met by 2.2%, exceeded by 60.0%, and not met by 37.8%. Actual exercise at 2 months was not statistically correlated with prestudy exercise behavior ($P = .650$, $R = 0.068$), fatigue ($P = .690$, $R = 0.060$), depression ($P = .324$, $R = 0.150$), pain ($P = .518$, $R = 0.125$), 25-foot timed gait ($P = .635$, $R = 0.068$), marital status ($P = .741$, $R = 0.049$), education ($P = .981$, $R = 0.005$), or employment ($P = .162$, $R = 0.207$).

Conclusions: Motivational counseling successfully engages MS patients in exercise programs over a 2-month period. Baseline patient characteristics are not strongly associated with the success of participation in exercise. Patients can successfully exercise despite disability, fatigue, depression, pain, or prior exercise activity.

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(S14) Veterans Health Administration Multiple Sclerosis Center of Excellence Second Annual Descriptive Report

The Veterans Health Administration established the Multiple Sclerosis (MS) Centers of Excellence in 2002 with a mandate to generate annual reports describing the veteran MS population and their health care utilization and costs. Using the extensive administrative and research databases, we identified MS cases by ICD-9 codes for fiscal years (FY) 1998 through 2003. This case-finding effort overestimated the num-

ber of true cases of MS. We developed a statistical algorithm to identify cases that did not have MS based on chart review. Application of the statistical algorithm eliminated 43% of questionable cases, leaving 15,936 cases classified as MS or possible MS that comprise the MS registry cohort. Patients in the MS registry cohort were significantly younger than the non-MS patients (52.8 ± 12.7 vs 57.4 ± 14.3 years; $P < .01$) and had a significantly larger proportion of female patients (13.4 vs 10.6%; $P < .01$). Significant differences were observed on all demographic variables (eg, race, marital status, type of insurance). Outpatient utilization was relatively stable over the 6-year period. However, the number of outpatient diagnoses increased rather steeply over the last 3 years of the study period (FY 2001–2003). The number of inpatient admissions showed a small but steady increase across the study period; however, the mean length of stay per patient decreased from 53 to 41 days across the same time frame. In contrast, the mean length of stay for nursing home and rehabilitation increased from a mean of 5 days in FY 1998 to 11.5 days in FY 2003. Total health care costs increased from \$95 million in FY 1998 to \$158 million in FY 2003. Inpatient care and medications account for the bulk of the increase in total health care expenditures. Resource utilization and thus costs can only be expected to increase substantially over time, as these MS patients age and their disease progresses.

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(S15) Evaluation of Self-Administered Multiple Sclerosis Disease Course Questionnaire

Multiple sclerosis (MS) is a complicated disease with at least four different subtypes. Determining MS subtype is important for both treatment and the patient's ability to understand and modify expectations about disease course. Although MS subtype is important information for researchers to collect, many patients do not know their MS type, limiting the option to use self-report. To address this, a self-report item displaying graphics of various courses of MS was developed that can be used in self-administered mailed surveys. This item has been evaluated by comparing physician-assessed disease subtype with patient response on this self-report item on 99 consecutive patients seen in an MS specialty clinic. A κ -statistic was calculated ($\kappa = 0.62$) indicating that the questionnaire has good reproducibility compared with physician-assessed MS disease subtype. In addition, this questionnaire was administered by mail to approximately 1400 individuals with MS in Washington and Montana. The proportion of individuals with different MS types was consistent with the distribution of MS subtype reported in literature. A low level of missing data (6%) suggested that most participants were able to respond to the item. However, those who had less than a high school education ($P = .009$) and/or were over age 60 years ($P = .002$) were significantly more likely to leave the item blank. It appears that this item may be used to obtain a rough estimate of MS type in research using self-report surveys.

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(S16) Depression and Fatigue in Correlation Between Disability and Quality of Life in Relapsing-Remitting Multiple Sclerosis

Background: Specialty pharmacies have well-established programs for providing multiple sclerosis (MS) medications and monitoring patients' therapy adherence. Our specialty pharmacy initiated a study to include the assessment of health outcomes.

Purpose: Evaluate the relationship between disability, quality of life (QOL), fatigue, and depression among people with relapsing-remitting (RR) MS during the first year after beginning immunomodulatory therapies.

Methods: Consecutive RRMS patients were invited to participate in a prospective open-label survey research project designed to assess QOL (SF-12) and its two composite scores physical (PCS) and mental (MCS) QOL; depression (CES-D); and fatigue (Fatigue Severity Scale and daily Fatigue Impact Scale). Verbal consent was provided for baseline surveys before beginning therapy; mailed written informed consents were returned before initiation of follow-up surveys at months 1, 3, 6, and 12. The consent mailing included Guy's neurological disability scale (GNDS) assessing 12 disability domains commonly affected by MS.

Results: One hundred forty-five patients completed 12 months of follow-up. Mean age was 44.3 years (range 22–65 years); 89.2% were women, and 87.2% were white. Patients' levels of disability at baseline were highly correlated with changes in physical ($r = -0.26$, $P = .001$) and mental ($r = -0.36$; $P < .001$) QOL over the 12 months. However, these relationships were mediated in different ways by changes in patients' levels of fatigue and depression. Changes in the severity of fatigue mediated the impact of disability on changes in physical QOL, whereas changes in severity of depression mediated the impact of disability on changes in mental QOL.

Conclusions: Through our specialty pharmacy assessment of health outcomes, we advised patients and their physicians about problematic fatigue and depression. These results suggest that addressing fatigue and depression may be an effective way to impact MS patients' physical and mental QOL, respectively, and avoiding drugs that worsen fatigue and depression should offer significant QOL benefits.

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(S17) Evaluation of Novel Palliative Care Service for Patients Severely Affected by Multiple Sclerosis

Aim: Evaluate a new clinical service for people severely affected by multiple sclerosis (PwMSs) in southeast London.

Methods: PwMSs were referred to the new service by health and social care providers. Patients consenting to participate in the evaluation were randomized to be seen by the service as soon as possible (fast track, FT) or after 3 months (standard intervention, SI). All study PwMSs underwent baseline interviews (I1), then were interviewed after 4–6 weeks (I2), 12–16 weeks (I3), and 24–26 weeks. SI patients under-

took an additional interview 16–18 weeks postbaseline, after they had received the clinical service. The outcome measures used were UK neurological disability scale, abbreviated mental test score, multiple sclerosis impact scale, palliative care outcome scale (POS), POS-MS-S1, and health and social services questionnaires. The data were entered into SPSS and analyzed using descriptive statistics.

Results: Sixty-nine PwMSs were referred to the service; 52 were randomized to the evaluation study: 26 to FT and 26 to SI. The demographics of the two groups were equally matched. At 12, PwMSs in the FT group had a small but significant improvement in nausea compared with those in the SI group (Mann-Whitney *U* test, $P = .039$). In the FT group, PwMSs were also more likely to have seen a paid carer more recently ($P = .018$) than those in the SI group. By 13, the improvement in nausea among FT PwMSs was maintained but was borderline significant. There was no difference in time since last seeing a paid carer between the groups. However, informal carers in the FT group reported less suffering of health ($P = .018$) and less loss of control over their life ($P = .020$), and more reported that they had learned new skills than in the SI group ($P = .005$).

Conclusion: Involvement with the palliative care service appears to affect nausea and informal carer well-being but not other outcomes. This effect is strongest after the initial contact.

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(S18) Botulinum Toxin for Leg Spasticity in Multiple Sclerosis Instead of Intrathecal Baclofen

Background: Patients with advanced multiple sclerosis (MS) who suffer from significant paraparesis or paraplegia and quadraparesis often have severe bilateral leg spasticity that requires treatment. Intrathecal (IT) baclofen may be offered to such a patient to achieve better control of the person's spasticity without the side effects of oral medication. IT baclofen has significant costs and risks associated with its use and can substantially increase weakness as a side effect. Ten of our MS patients who were offered IT baclofen chose to be treated with botulinum toxin type A (BoNT-A) for their spasticity.

Methods: Ten patients with secondary progressive MS were retrospectively reviewed who had significant lower-extremity spasticity. Each patient was given injections of BoNT-A via electromyograph-guided technique in 25- to 50-U amounts to the appropriate muscles. Total amounts ranged from 200 to 500 U in a single session. Injections were repeated at 3- to 6-month intervals depending on the duration of benefit. Paraspinal muscular injections were included in patients who were having extensor spasms. Adductor magnus muscles were injected for adductor spasms. Quadriceps were injected for leg extensor spasms. Some patients had all of these sites injected, whereas others had more limited injections.

Results: All patients had a significantly beneficial response to treatment within 2 weeks, with reduction of spasticity and associated pain. The duration of benefit was 3–6 months. Side effects were limited to transient discomfort during the

injection. Oral medications were reduced in most patients. No patients required IT baclofen.

Conclusions: BoNT-A may be an alternative treatment for some MS patients with significant lower-limb spasticity who otherwise might be candidates for IT baclofen. A controlled treatment trial is warranted.

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(S19) Botulinum Toxin for Management of Leg Spasticity in Multiple Sclerosis

Background: Spasticity is commonly associated with motor dysfunction in patients with multiple sclerosis (MS). Spasticity also may be associated with significant pain. Botulinum toxin type A (BoNT-A) is used for spasticity in various conditions, including MS. We have been using BoNT-A as a treatment option for spasticity for MS patients who have not responded well to standard treatments.

Methods: This is a retrospective chart review of 20 consecutive MS patients who received BoNT-A for clinically significant spasticity of one or both lower extremities. BoNT-A was administered intramuscularly via an electromyography-guided technique. Muscles included the posterior tibialis and medial gastrocnemius for equinovarus; vastus medialis, vastus lateralis, and rectus femoris for extensor spasms at the knee; and the adductor magnus for adductor spasms of the thighs. The amount of BoNT-A injected in each muscle varied from 25 to 150 U administered in 12.5- to 50-U doses, with a maximum dose of 500 U in a single administration.

Results: Of the 20 patients, 3 were men and 17 were women, with a mean age of 53.6 years. Seventeen patients had secondary progressive MS, one had relapsing-remitting MS, and two had transverse myelitis. All 20 patients had significant improvement of their spasticity within 2 weeks of the injections. Functional benefits with improved gait for ambulatory patients or improved transferring and reduced pain for nonambulatory patients were seen. Benefits lasted from 3 to 6 months. Side effects were limited to transient discomfort during injection.

Conclusions: BoNT-A may offer an alternative treatment for patients with lower-extremity spasticity who have not responded well to standard treatment. A prospective, multicenter, placebo-controlled study is warranted.

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(S20) Weight Training With Protein Loading for Fatigue in Multiple Sclerosis

Background: Fatigue is one of the most common complaints in patients with multiple sclerosis (MS). Medications, rest, and physical therapy are standard treatments. We propose a progressive weight-lifting program to overcome patient fatigue by increasing muscle fiber strength along with a protein-loading dietary program for muscle building.

Methods: Four stable MS patients, three women and one man, mean age 53.5 years, with significant fatigue began a twice-weekly training program under the supervision of an Aerobics and Fitness Association of America-certified person-

al trainer. The program included 20–40 g of protein loading with fluid loading 1–2 hours before and after each workout. The workout session consisted of a 30-minute aerobic exercise period followed by a 30-minute weight-lifting session. The weight training was largely free weights with 20 repetitions individualized to the patient's abilities but with gradually increasing weights over the weeks of training as tolerated and appropriate.

Results: Over a 6-month period, three of the four patients substantially improved their overall strength and had reduced fatigue. One patient could not continue the program because of increased fatigue. For the three patients who were improving, the weights were gradually and progressively increased over the months. Although each patient experienced considerable fatigue during and for about 15 minutes after each workout, this effect became less evident over time. Each patient became stronger, had much less fatigue, and was able to increase everyday activities significantly from baseline status.

Conclusions: Weight training, aerobic conditioning, and fluid and protein loading in a controlled manner can be a successful part of overcoming fatigue in some patients with MS. The potential benefit of weight training with protein supplementation in MS patients may be underappreciated.

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(S21) Idiopathic Bone Loss in Newly Diagnosed Multiple Sclerosis Patients Naive to Treatment

Preliminary data are presented from a prospective clinical evaluation of the incidence of idiopathic bone loss by dual-energy x-ray absorptiometry in individuals with multiple sclerosis (MS) naive to treatment or those just starting an immunomodulator for the treatment of MS. Expanded Disability Status Scale scores were ≤ 5.0 . Patients identified with less than -1.0 SD bone loss in either Z or T score were included. Of the initial 46 patients evaluated, 52% met clinical criteria for osteopenia or greater bone loss. Of the men evaluated, 57% met clinical criteria. Patients identified with loss of bone density were invited to participate in a yearlong treatment trial for bone loss. In these individuals, serum calcium levels remained within the normal range and vitamin D levels were in the low-normal range, even after supplementation. Testosterone levels were in the low-normal range in all male participants.

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(S22) Falls Among Older Adults With Multiple Sclerosis

Background: Falls are a major public health concern, yet little research addresses falling or fall prevention among older adults with multiple sclerosis (MS). This study examined the prevalence and risk factors for falling among 354 people with MS aged ≥ 55 years, as well as their interest in fall-prevention education.

Methods: A national random sample of 700 older adults with MS was drawn from the North American Research Committee on Multiple Sclerosis (NARCOMS) database for this

study. A total of 354 individuals between ages 55 and 94 years completed a telephone interview collecting information on sociodemographics, MS status, fall experiences, fear of falling, and fall risk factors. Interest in and preferences for an MS-specific fall-prevention program were also addressed. Statistical analyses were conducted with SPSS 12.0.

Results: Of the 354 participants, 91% had experienced a fall: 11% reported falling multiple times a week, one-third reported falling at least once a month, and 51% required medical attention for a fall in the past 6 months. Factors that increased fall frequency included greater MS symptom interference, deteriorating MS status, being male, reporting fear of falling, and using walking aids. Seventy-one percent of respondents were interested in an MS-specific fall-prevention program. They wanted to learn about exercises to reduce risk of falls (96%), ways to reduce risk in new situations (95%), what to do if they did fall (94%), ways to reduce environmental hazards (92%), and behaviors that can increase risk of a fall (74%). Seventy-eight percent of individuals wanted the option of having a family member or friend attend with them.

Conclusions: Falls are common and frequent among older adults with MS, and many factors contribute to these events. The findings of this study point to specific risk factors that need to be addressed in a comprehensive fall-prevention program and suggest direction for program development and organization.

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(S23) Factors That Influence Depression in Multiple Sclerosis: Prospective Study

Clinical depression and depressed affect are frequently associated with multiple sclerosis (MS). The current study sought to investigate the frequency of depression in a hospital outpatient population and evaluate factors that influence change in depression scores prospectively.

Methods: Patients with definite MS were recruited at scheduled appointments. The Beck Depression Inventory-II (BDI-II) was completed by the patient at the clinic visit. Demographic information, results of the neurological exam (Functional Systems Scale scores from the Minimal Record of Disability in MS [MRD]) and the neurologists' ratings of patient disability (Incapacity Status Scale scores from the MRD) were extracted from the chart at the time of the visit. In addition, all psychotropic medicines that patients were taking at the time of the visit were recorded in the database.

Sample: At the time of this writing, 530 patients consented to participate at Time 1, completed the BDI-II, and had the medical data entered into the database. Two hundred thirty patients of the Time 1 cohort consented and participated at Time 2.

Analysis: Frequencies, correlations, and various regression approaches will be used to evaluate correlates of depression and prospective change in depression status. Only preliminary analyses are ready to be reported.

Results: Of the subjects, 26.6% were men. The mean age of participants was 45.6 years (SD 9.5 years). At Time 1, 45.7% were employed full time outside the home for pay

or full-time homemakers without limitations; 9.5% were employed part time, 24.8% received disability insurance, 2% were full-time students, and 18.1% were unemployed without receiving disability. Mean BDI-II score was 14.24 (10.3) at Time 1 and 15.17 (12.3) at Time 2. Of the participants, 43.2% were taking an antidepressant or antimanic agent, with 31.5% taking an anti-anxiety agent at Time 1. Hierarchical multiple regression found that independent predictors of higher depression scores at Time 1 included younger age, greater disability, being male, and not taking antidepressants. Of the sample, 17.5% endorsed suicidal ideation within the past 2 weeks at Time 1, but only 0.4% of this cohort endorsed suicidal intent. Additional analyses will evaluate severity of depression and factors that prospectively moderate depression scores.

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(S24) Psychometric Testing of the Americanized Guy's Neurological Disability Scale

Purpose: Test the reliability, validity, and sensitivity of the Americanized version of Guy's neurological disability scale (GNDS).

Research Questions: 1) Is there convergent validity of the Americanized version of GNDS as evidenced by a significant relationship with the SF-36 and activities of daily living self-care for MS scale? 2) Does the Americanized version of GNDS have the same four-factor structure as reported in the psychometric testing of the original GNDS? 3) Is the Americanized version of GNDS a reliable measure when examined with a 2-week retest? 4) Does the Americanized version of GNDS have internal consistency? 5) Is the Americanized version of GNDS sensitive to changes in neurological disability in multiple sclerosis (MS) over time?

Research Design/Methods: Longitudinal study: Time 1, initial; Time 2, 2-week retest; Time 3, 6-month follow-up. Eligibility criteria included being diagnosed with relapsing-remitting MS, having a history of one or more relapses in the past 2 years, being male or female, age ≥ 18 years, willingness and ability to complete all evaluations related to the study, willingness to provide informed consent, and having an email address. The sample included 253 participants, 87% women ($n = 219$) and 13% men ($n = 32$). They ranged in age from 22 to 77 years (mean 46 years, SD 9 years). The data were entered into SPSS version 11.5 for analysis.

Findings: The Americanized version of GNDS was found to be a reliable, valid, and sensitive multidimensional measure of neurological disability for individuals with MS.

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(S25) Safety and Efficacy of Combined Therapy With Rebif, Prednisone, and Azathioprine

Background: In 167 multiple sclerosis (MS) patients on monotherapy with subcutaneous (sc) interferon β (IFN β) 44 μg three times weekly (Rebif), annualized relapse rate (ARR)

decreased from 0.92 to 0.82, 0.57, and 0.44 for the years 1–4. Expanded Disability Status Scale (EDSS) changes by 1.0 point over 4 years were 0.17 per patient per year, according to the PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) study.

Objectives: To determine incidence of significant adjustment in disease course, ARR and EDSS changes were measured in MS patients on continuous combined therapy (CCT) with Rebif, prednisone, and azathioprine (AZA).

Design and Methods: Fifteen MS patients on Rebif monotherapy, 21 individuals on Rebif and prednisone (7.8 ± 0.9 mg/kg daily) (RP), and 6 patients on Rebif, prednisone, and AZA (138 ± 10 mg/kg daily) (RPAZA) were studied. CCT was initiated in patients on IFN β monotherapy after transient or persistent worsening in EDSS ≥ 1.0 was established. Patients were regularly followed in 10- to 12-week intervals. Peripheral blood (PB) flow cytometry (FC) was performed in 40 individuals.

Results: ARR in patients on CCT with RP and RPAZA treated for a median duration of 2.4 years (range 1.1–3.7 years) was 0.12, without significant differences in EDSS (2.60 ± 1.53 at the beginning and 2.54 ± 1.56 at the end of the study; $P = .43$). Compared with healthy control subjects, PB CD19+ and CD8+ cells showed decreased cell count ($118.17 \pm 135.00/\text{cmm}$, $P = .0354$; $250.11 \pm 293.62/\text{cmm}$, $P = .0296$) in patients on RP and decreased CD16+ cell count ($36.57 \pm 46.40/\text{cmm}$; $P = .0184$) in individuals on RPAZA. Rebif monotherapy did not alter normal PB cell counts.

Conclusions: CCT with RP and RPAZA therapy administered for 12 months resulted in lower ARR than previously reported in patients on Rebif monotherapy. No progression on EDSS rating was established. Significant changes in cell count of PB immunocompetent cells were noticed. No unmanageable comorbidity was established.

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(S26) Efficacy of Up to 8 Years of Subcutaneous Interferon Beta-1a Treatment in Multiple Sclerosis

Background: The Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis (PRISMS) study showed significant efficacy of subcutaneous (sc) interferon (IFN) beta-1a (Rebif) 3 times weekly (tiw) in patients with relapsing-remitting multiple sclerosis. Patients have now been followed for up to 8 years of treatment.

Objectives: Investigate long-term efficacy and safety of sc IFN beta-1a.

Methods: Patients were treated with IFN beta-1a 44 or 22 μg sc or placebo tiw for 2 years. In years 3 and 4 (PRISMS-4), patients continued active therapy or, if originally treated with placebo, were randomized to IFN beta-1a 44 or 22 μg sc (late-treatment group). In years 5 and 6, patients continued blinded treatment, switched to open-label treatment, or withdrew. All patients randomized in PRISMS were eligible for long-term follow-up (LTFU). Prospective clinical, safety, and neutralizing antibody (NAb) evaluations were conducted at LTFU; retrospective chart review was also performed.

Results: Of 560 patients, 382 (68.2%) returned for LTFU. When analyzed with three different scenarios to adjust for patient withdrawal, Expanded Disability Status Scale progression was significantly delayed for the 44- μ g group both when patients who withdrew were assumed to have progressed ($P = .007$) and when they were excluded from the analysis ($P = .012$). Annualized relapse rates were significantly lower for 44 μ g ($P < .001$) and 22 μ g ($P = .014$) versus late-treatment patients. The 44- μ g patients were more likely to be relapse free (15.4%) than the late-treatment group (6.5%). No new safety or adverse events were identified. Fewer patients were NAb positive at LTFU or last assessment (44 μ g, 12.6%) than were anytime positive (44 μ g, 19.2%) during years 1–4. Among patients initially randomized to 44 μ g tiw who were anytime positive, 36.1% seroreverted to NAb-negative status.

Conclusions: Eight years of follow-up data suggest that early treatment with high-dose, high-frequency sc IFN beta-1a is generally well tolerated and has significant, durable benefit on clinical efficacy.

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(S27) Safety, Tolerability, and Adherence to Treatment in BENEFIT Trial

Background: The BENEFIT (Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment) study demonstrated that in patients with a first clinical event suggestive of multiple sclerosis (MS), interferon beta-1b (IFNB-1b) 250 μ g subcutaneously (sc) every other day (eod) reduced progression to clinically definite MS (CDMS) by 50% and progression to McDonald MS by 46% (proportional hazards regression analysis adjusted for standard baseline covariates). The safety and tolerability data are presented here.

Methods: Patients with a first clinical demyelinating event and at least two clinically silent brain magnetic resonance imaging (MRI) lesions were randomized in a 5:3 ratio to IFNB-1b ($n = 292$) or placebo ($n = 176$). A four-step titration scheme was used to ease patients onto their injections. They were then treated until CDMS was diagnosed or they had been followed for 24 months. Thereafter, patients could opt to participate in a follow-up study with open-label IFNB-1b treatment for at least 3 years.

Results: Only 7.2% of IFNB-1b-treated patients prematurely discontinued the study, compared to 5.7% in the placebo group; 15.1 and 10.2%, respectively, discontinued the study drug before the end of the study. In addition, 95% of eligible patients opted for IFNB-1b treatment in the follow-up study. The incidence of adverse events was comparable or lower than observed in other trials of IFNB-1b 250 μ g sc eod in relapsing-remitting or secondary progressive MS. Flulike symptoms (12.7%) and injection-site reactions (30%) occurred less frequently in the second year of this study. Patient-reported outcomes, including quality-of-life measures, did not indicate a negative impact of typical side effects in IFNB-1b-treated patients.

Conclusions: In this study, IFNB-1b 250 μ g eod was safe and well tolerated by patients with a first clinical event suggestive of MS. Use of a special titration scheme, an autoinjec-

tor and concomitant nonsteroidal anti-inflammatory medication, may have contributed to the favorable tolerability and adherence.

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(S28) Prospective Baseline Versus On-Treatment Study Assessing Patient Perceptions of Using Different Needle When Injecting Interferon Beta-1a (Avonex)

Background: Although intramuscular (IM) interferon beta-1a (IFNB-1a; Avonex) offers the convenience of once-weekly dosing, the length of the needle used for IM injections may cause additional discomfort, including anxiety, for patients. Anecdotal evidence suggests that a shorter, thinner needle may improve patient tolerability and satisfaction, but this has not been empirically studied.

Objectives: Assess levels of patient anxiety before and pain after injection with the standard IM IFNB-1a needle (23 gauge, 1.25 inch) compared with a different needle (25 gauge, 1 inch). Patient perception of ease of use, self-injection fear, and injection-site reactions also were assessed.

Methods: This was a prospective, single-arm, single-center study. Relapsing-remitting multiple sclerosis patients on IM IFNB-1a for at least 1 month without interruption who met inclusion/exclusion criteria were enrolled in this study. Patient perception of the needles was assessed using quantitative, 100-mm visual analog scale (VAS), and qualitative patient questionnaire measures. Patients were assessed at baseline while using the standard needle and then over the course of the 4-week study using the different needle.

Results: This is an interim analysis of 10 patients who have completed the study. The median IM IFNB-1a treatment duration was 3.5 years. Patients had a 6.70 ± 25.26 -mm ($P = .4262$) mean decrease in anxiety and a 22.00 ± 29.66 -mm ($P = .0422$) mean decrease in pain from baseline to week 4 using VAS. Results from the questionnaire suggested that there were qualitative decreases in patient anxiety and a decrease in oral analgesic use while using the different needle.

Conclusions: Data from this interim analysis suggest that use of a shorter, thinner needle for injection reduces pain in patients on IM IFNB-1a. Injection anxiety may not have been significantly reduced because patients had been receiving IM IFNB-1a for more than 3 years. No change in the number or severity of injection-site reactions between the two needles was observed.

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(S29) Computerized Tapping Tests of Dexterity in People With Multiple Sclerosis

Purpose: Given society's increased use of computers, development of a reliable, functional test of dexterity using a computer keyboard would be a valuable adjunct to current standardized dexterity tests, which primarily utilize pegboards and functional tasks. The purpose of this study was to deter-

mine test-retest reliability of a computerized tapping test (CTT) of manual dexterity in people with multiple sclerosis (MS) and to determine differences in dexterity performance between people with MS and healthy subjects on the CTT.

Methods: Subjects included 42 individuals with a clinical diagnosis of MS and 69 healthy control subjects who were ≥ 18 years old. Twelve subjects from each group were retested 1 week later to determine test reliability. Testing was conducted with the Simple and Complex Motor Speed Tapping Tests program from Brainmetric. Subjects underwent three tapping tests, including single index finger tapping, alternate index finger tapping, and a complex four-digit sequence test on a computer keyboard. Descriptive statistics, intraclass correlation coefficients (ICCs), and multivariate analysis of variance (MANOVA) were calculated.

Results: In both the MS and healthy control populations, test-retest reliability, measured by ICCs for the mean number of taps per trial, was ≥ 0.85 on all three tests. ICCs for the intertap interval (time between taps) were ≥ 0.81 for all three tests. Healthy control subjects tapped significantly faster than subjects with MS on all three finger-tapping tests. Healthy control subjects made more errors than the subjects with MS.

Conclusion: CTT is a reliable test in evaluating manual dexterity in people with MS. Healthy control subjects tap faster than subjects with MS but make more errors in tapping.

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(S30) Fatigue Is Associated With Depression and Disability in Patients With Relapsing-Remitting Multiple Sclerosis

Background: Fatigue is a common and disabling symptom of multiple sclerosis (MS) that is associated with reduced quality of life. There are no clear associations among fatigue and duration of disease, current level of disability, or magnetic resonance imaging (MRI) measures of disease severity. The role of depression in MS-associated fatigue is also unclear.

Objective: Determine the associations between MS-associated fatigue and demographic, clinical, and biological markers of the disease.

Methods: One hundred forty subjects with relapsing-remitting MS (RRMS) enrolled in the CLIMB study were administered the Modified Fatigue Impact Scale (MFIS) and the Center for Epidemiologic Studies Depression Scale (CES-D). Subjects also underwent a clinical neurological examination and MRI at 1.5 T.

Results: Subjects included 111 women (79%) and 29 men (21%), with a mean age of 37.3 ± 9.0 years (range 19–61 years). Duration of disease was 3.7 ± 5.0 years (range 0–29 years). Mean Expanded Disability Status Scale (EDSS) score was 1.4 ± 1.2 (range 0–6.5). Eighty-nine percent of patients were on disease-modifying therapy. Six percent were being treated for fatigue. Patients were divided into two groups based on their MFIS scores. Patients with scores above the mean comprised the high-fatigue group ($n = 64$), and patients with scores below the mean comprised the low-fatigue group ($n = 76$). A multivariate logistic analysis was used to determine the associations between fatigue and age,

sex, duration of disease, EDSS, CES-D score, brain parenchymal fraction, T2 lesion volume, presence of gadolinium-enhancing lesions, immunomodulatory treatment status, and fatigue medication status. Depression ($P < .0001$) and EDSS ($P < .01$) were the only two variables to be associated with fatigue.

Conclusion: Fatigue in RRMS was strongly associated with depressive symptoms. Even in a cohort of mildly disabled subjects, fatigue was also associated with increasing disability. Screening and treating for fatigue and depressive symptoms in all patients regardless of disability may result in improvement in quality of life.

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(S31) Language Manifestations of Executive Dysfunction in Multiple Sclerosis

Language deficits are not typically considered part of the constellation of declining abilities in multiple sclerosis (MS) patients. However, executive dysfunction is often seen in patterns of performance on neuropsychological assessment. In the current study, the authors hypothesized a positive correlation between executive search and retrieval strategies and confrontational naming in MS patients. The retrospective analysis of neuropsychological performances of 90 MS patients and 151 brain-injured (TBI) patients was conducted. Both groups were significantly impaired in confrontation naming, with greater impairment in the TBI sample. Linear regression revealed strong association between naming performances and performances on measures thought to be mediated by executive activities. This relationship was even stronger in TBI populations with documented dysexecutive syndromes. The discussion addresses the contribution of executive dysfunction to compromise in areas such as language, not typically considered vulnerable to MS impact.

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(S32) Cost-Effectiveness Model of Disease-Modifying Drugs Used to Treat Multiple Sclerosis

Disease-modifying drugs (DMDs) currently indicated for the management of relapsing forms of multiple sclerosis (MS) have been shown to exhibit varying degrees of benefit on relapse rates and disability progression. Payers and clinicians make formulary recommendations based on the clinical and economic value of the different drugs approved by the US Food and Drug Administration (FDA); therefore, it is the objective of this model to be used as a tool to compare the relative cost-effectiveness of these drugs from a payer perspective. An interactive Excel-based model was developed to compare the relative cost components of relapses, disability progression, and DMDs in the treatment of MS. Relapse rates and disability progression were the key outcomes used to determine the medical savings offsetting drug expenditures. Drug effectiveness with respect to reduction in relapses and the slowing of disability progression was based on the published level I clinical trials for the four DMDs approved by

FDA. Data derived from research by O'Brien and colleagues and Weinshenker and colleagues were used to model the cost of relapses and disability progression, respectively. Drug costs were based on annual therapeutic price based on wholesale acquisition cost, with consideration for contractual discounts and patient copayment. The primary economic endpoint was cost per relapse avoided over a 4-year period of treatment. Results showed significant difference in the cost-effectiveness ratio among the DMDs, with interferon beta-1a subcutaneous injection (Rebif) having the most favorable cost-effectiveness ratio (\$47,958/relapse avoided) and interferon beta-1a intramuscular injection (Avonex) having the least favorable cost-effectiveness ratio (\$121,147/relapse avoided). The difference in the cost-effectiveness results among the four DMDs was significant.

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(S33) Principal Components Analysis of Multidimensional Affect and Pain Survey (MAPS 189) in Patients With Multiple Sclerosis-Related Pain Demonstrates Four Factors Related to Both Physical and Emotional Aspects of Pain

Pain is regarded as one of the most significant symptoms of chronic disease; however, the way in which pain is measured is often a subject of debate. Pain measurements vary in their presentation, with the most simple being a rating on a scale of 1–10 to the most complex offering words to attempt to describe the pain. Pain is not only experienced physically but is often multidimensional in its emotional experience as well. The Multidimensional Affect and Pain Survey (MAPS 189) is a 189-item pain instrument that presents a multitude of physical and emotional descriptors to patients, asking them to rate the degree to which they experience each descriptor. In an effort to study MS-related pain, 65 patients with a diagnosis of MS and experiencing MS-related pain completed a series of questionnaires, including MAPS 189. Principal components analysis was completed to determine whether the 189 descriptors on MAPS would in fact group into factors. Results demonstrated that 24 of the 30 subclusters loaded on four factors, accounting for 73% of the variance. Eleven of the somatosensory subclusters loaded on severe pain and accounted for 41% of the variance, whereas 4 of the well-being subclusters loaded negatively on the second factor, general health, accounting for 11% of the variance. The third and fourth factors, negative emotions and mild pain, were loaded on by both the emotional pain subcluster and the somatosensory subcluster and accounted for 7% and 6% of the variance, respectively. These results were similar to those found in a study of MAPS 101 in patients with cancer pain. The current study suggests that pain may be better treated when measured more qualitatively through a measure like MAPS 189, which not only addresses physical pain but also examines emotional experiences.

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(S34) Physical Activity Among People With Multiple Sclerosis

Background: Most studies reported in the literature regarding physical activity among people with multiple sclerosis (MS) focus on structured physical activity interventions. However, physical activity can be gained through many nonstructured physical activities. Little is known about the type and extent of physical activity engaged in by people with MS through activities of daily living (ADL), home responsibilities, and recreation that may contribute to the Centers for Disease Control and Prevention (CDC) recommendation for a minimum of 30 minutes of physical activity on most, if not all, days of the week.

Objectives: Survey people with MS about the type and time spent during a typical week performing specific physical activities and identify their sources of physical activity information.

Methods: A descriptive and comparative design was used in analyzing self-reported data obtained from 123 MS patients' self-reported responses to the Yale Physical Activity Survey and sources of physical activity information according to disability status (mild, moderate, cane users, scooter/wheelchair) as determined by the Patient-Determined Disease Steps.

Results: Mild, moderate, and cane-using groups spent considerable physical activity engaging in housework. Engaging in sedentary recreation increased with increasing disability. Participation in ≥ 3 hours of total physical activity (including housework and yardwork, caretaking, walking, recreation) per week was 100% for the mildly disabled, 96% for moderately disabled, 93% for cane users, and 62% for wheelchair/scooter participants. Books and newspapers were the largest source of physical activity information for mildly disabled people, the National Multiple Sclerosis Society and physicians were used most by moderately disabled people, health clubs by those requiring a cane or crutches, and physical therapists and nurses for those requiring wheelchair/scooter assistance.

Conclusion: Physical activity obtained through housework, yardwork, caretaking, walking, and recreation can contribute significantly to CDC's recommendation for a minimum of 30 minutes of physical activity on most, if not all, days of the week.

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(S35) Patients' Perceptions of Self-Efficacy After Specialized Rehabilitation

Multiple sclerosis (MS) commonly causes limitations in functional abilities and can negatively affect an individual's self-image. Disease course variability may also lead to feelings of uncertainty and hopelessness and reduced ability to cope. Rehabilitation focuses on maximizing a person's functional abilities and improving self-image, psychological well-being, coping, and adjustment to MS. A specific goal of our interdisciplinary outpatient rehabilitation program, OPTIMUS, is to improve patients' sense of control and ability to manage their MS symptoms, an important component of successful adjustment. The Multiple Sclerosis Self-Efficacy Scale (MSSE), a self-

report measure comprised of two subscales, has been used to evaluate this outcome in our program in recent years. One subscale assesses “sense of confidence to perform behaviors that allow them to engage in daily living activities” (SE function), and the second subscale measures “confidence in one’s ability to manage disease symptoms, reactions to disease-related limitations, and the impact of the disease on life activities” (SE control). Evaluation of 96 consecutive OPTIMUS patients with Expanded Disability Status Scale scores ranging from 1.0 to 8.0 revealed no significant change in SE function scores from admission to discharge but substantial improvement in SE control ($P = .0004$). Thus, preliminary analysis suggests that a rehabilitation program specialized for the treatment of MS substantially improved patients’ perceptions of self-efficacy regarding the ability to manage symptoms, reactions to disease-related limitations, and the impact of MS on life activities. This poster presentation focuses on results of MSSE data collected from a larger patient sample over 3 years, with particular attention to item responses in the SE control subscale. This analysis will help determine which aspects of perceived self-efficacy change with participation in the OPTIMUS program. Relevance of the findings for program planning and quality improvement are discussed.

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(S36) Central Auditory Function in People With Multiple Sclerosis

Introduction: The prevalence of peripheral hearing loss in individuals with multiple sclerosis (MS) is estimated at <10%. However, 40–60% of people with MS report difficulty understanding speech in background noise. Research suggests that, although most MS patients have normal pure-tone sensitivity in regard to traditional measurements of hearing, this population may have auditory deficits that reside within the central auditory nervous system.

Objective: The purpose of this investigation was to evaluate dichotic listening and speech perception in noise for people with MS.

Methods: Subjects were 50 individuals with MS and 50 without MS. A comprehensive battery of auditory tests designed to characterize both the periphery and structures within the central auditory system was administered to both groups. There were no significant differences between groups with respect to age, sex, and pure-tone hearing sensitivity. Two tests of central auditory processing, the staggered-spondaic word (SSW) test and a test of speech intelligibility in noise, are described in this investigation.

Results: Statistical analyses revealed significant differences between groups on both auditory test measures. This finding was prevalent despite normal sensitivity for pure-tone and speech perception in quiet. Moreover, MS subjects with the greatest number of errors on the SSW test also scored more poorly on the speech-in-noise test.

Discussion: Findings to date suggest that people with MS have more difficulty with dichotic listening tasks and with speech perception in noise than healthy individuals. For the SSW test, this finding presents in both ears, although the

deficit appears more pronounced in left-ear conditions. This knowledge may help health care professionals better understand and manage people with MS. Future investigations will explore rehabilitative interventions that may improve the auditory processing abilities of individuals with MS in hopes to enhance their communicative quality of life.

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(S37) Prevalence and Cost of Pain Due to Multiple Sclerosis in Canada

Objectives: Multiple sclerosis (MS) is a chronic disease affecting 100–240 per 100,000 people in Canada. It is often associated with severe pain, the prevalence of which ranges from 10 to 80% (average ~50%). Pain impacts negatively on patient well-being, as well as costs to patients and the health care system. We determined the prevalence and societal burden of pain due to MS in Canadian patients.

Methods: After approval from an independent ethics review board, patients were recruited through the MS society and from individual participating hospitals. Epidemiological and costing data over the previous 6 months were collected from 297 patients by telephone interviews. Mean total cost per patient was calculated. The burden was extrapolated to the Canadian population with national demographics and prevalence rates. Trends were analyzed, using Spearman’s rho, for relationships among cost, Expanded Disability Status Scale (EDSS) levels, and pain severity.

Results: The average age was 49 ± 11 years, with 77% women; average age at diagnosis of MS was 37 ± 10 years. The prevalence of pain due to MS was 71% (211/297). The mean severity level was 6.8 as measured by the BS-11 scale, with a median of 4.5. Although no relationship was observed between either the clinical form of MS or EDSS level with the number of patients reporting pain, a significant positive trend was observed between total cost and EDSS ($p = 0.170$, $P = .014$) and pain severity measured by the BS-11 scale ($p = 0.291$, $P = .0001$). The mean estimated total (direct and indirect) cost per patient experiencing pain was $\$3198 \pm 5965$ over the 6-month period. The projected 6-month burden for Canada was $\$65,034,679$.

Conclusions: The burden of pain due to MS in Canada is high for both patients and society. Cost increases with EDSS level and pain severity.

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(S38) CD4+CD25+ Regulatory T Cells Contribute to Therapeutic Effects of Glatiramer Acetate in Experimental Autoimmune Encephalomyelitis

CD4+CD25+ regulatory T cells (T_{reg}) are potent immunosuppressive cells that are pivotal in the maintenance of self-tolerance. Involvement of T_{reg} cells in immune therapies in various immune-mediated diseases has been proposed, but the direct supporting evidence is still lacking. In the investigation of

mechanisms underlying the clinical benefits of glatiramer acetate (GA) in an animal model of multiple sclerosis (MS), experimental autoimmune encephalomyelitis (EAE) in C57BL/6 mice, we recently demonstrated that GA can confer protection of interleukin (IL)-4, IL-10, and IL-4/IL-10-deficient mice against EAE, suggesting that mechanisms other than Th2 cells may be responsible for therapeutic effects of GA. Here we demonstrate that GA treatment boosts expression of Foxp3 on T_{reg} cells during EAE. Depletion of CD25+ cells completely abrogated the therapeutic effects of GA in EAE. Furthermore, adoptive transfer of purified T_{reg} cells from GA-treated EAE mice is much more effective in preventing EAE development. Thus, our current data provide compelling evidence that T_{reg} cells may be the major contributor to the therapeutic effects of GA in EAE and, possibly, MS. Further mechanistic studies to reveal the molecular events linking GA with T_{reg} cells may enable optimization of GA treatment and may guide the development of new therapeutic strategies using this mechanism of action but with higher levels of therapeutic efficacy.

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(S39) Prevalence of Overweight and Obesity in Veterans With Multiple Sclerosis

Background: The objective of this study was to estimate the prevalence of overweight and obesity in veterans with multiple sclerosis (MS) compared with sex-specific published rates for the US population, outpatients at US Department of Veterans Affairs (VA) medical facilities, and male veterans with spinal cord injury (SCI).

Setting: A retrospective study of 9688 veterans with MS enrolled in the Veterans Health Administration (VHA), identified by linking the VA MS Centers of Excellence Data Repository to the VA Office of Quality and Performance 1999 Large Health Survey and the Survey of Healthcare Experiences of Patients (2002–2004).

Methods: Body mass Index (BMI [kg/m²]) was calculated from self-reported weights and heights. Subjects were classified into four weight categories using Centers for Disease Control and Prevention guidelines: underweight (BMI <18.5), normal weight (BMI 18.5–24), overweight (BMI 25–29), and obese (BMI ≥30).

Findings: The proportion of men with MS ($n = 8536$) and 95% confidence intervals in the four weight classifications is 2.9% [2.55–3.27] underweight, 32.3% [31.29–33.29] normal weight, 42.1% [41.02–43.12] overweight, and 22.7% [21.84–23.64] obese. The proportion of women with MS ($n = 1137$) in each weight class is 4.1% [2.86–5.24] underweight, 39.2% [36.35–42.11] normal weight, 27.8% [25.14–30.44] overweight, and 28.9% [26.26–31.62] obese. In comparison, the proportion of men who are overweight and obese is 39.7% and 27.5%, respectively, for the US population, 40.1 and 32.9% for veterans, and 38.7% and 27.2% for SCI. The proportion of women who are overweight and obese is 28.5% and 33.4% for the US population and 31.0% and 37.4% for veterans.

Conclusions: Overall, individuals with MS treated in VHA have rates of overweight similar to other populations and slightly decreased rates of obesity compared with the veteran and US populations.

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(S40) Cognitive Dysfunction in Multiple Sclerosis: Interferon Beta-1b 16-Year Long-Term Follow-Up Study

Background: Cognitive dysfunction is estimated to affect around 40–65% of patients with multiple sclerosis (MS) and has a major impact on many aspects of patient's lives, including safety, physical independence, and quality of life. These negative effects occur over and above the handicaps imposed by physical impairment. Affected patients usually experience deficits in the cognitive function domains of memory, learning, attention, and information processing.

Methods: The 16-year long-term follow-up study is a multi-center, open-label, observational study that generates cross-sectional data from patients who participated in the pivotal North American interferon beta-1b (IFNB-1b, Betaseron) trial in relapsing-remitting MS. From the end of the pivotal trial until today, most patients have been under regular medical care, making it an ideal cohort to investigate the evolution of the disease over time. A battery of tests was selected to evaluate cognitive function (verbal fluency, memory, selective attention, executive function, and sustained attention).

Results: All 11 North American centers that were involved in the original trial contributed to this study. Recruitment into the current trial started in January 2005 and was completed in December 2005, with an identification rate of almost 90% of the original pivotal trial population ($n = 372$). The cognitive profile of this cohort is presented and compared with quality of life, clinical, and magnetic resonance imaging parameters.

Conclusion: This study represents the longest follow-up of patients treated with an IFNB therapy. The high identification rate of the pivotal trial patients, together with the broad range of assessments, will provide more insights into the long-term cognitive status of MS patients. The participants are a unique cohort in the middle and later stages of MS. A precise description of their cognitive function is of scientific interest and will help in planning further studies.

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(S41) Barriers to Increased Physical Activity in Ambulatory Multiple Sclerosis Sample

Background and Significance: Physical exercise has been shown to improve gait and reduce weakness and fatigue in people with multiple sclerosis (MS). Perceived barriers that result in decreased exercise may contribute to lower quality of life and decreased participation and function. This study sought to examine the perceived barriers to exercise observed in a sample of people with MS.

Methods: Fifty-one people with MS were recruited from a large university-based clinic. Participants received five counseling sessions, in person and over the phone, during a 6-month period, using motivational interviewing to create and maintain an exercise program. During these sessions, a counselor elicited perceived physical and nonphysical barriers to exercise.

Findings: Thirty-four percent of the total barriers reported by participants were MS symptom related; of those, participants reported fatigue (10.6%), exacerbation (10.6%), heat sensitivity (6.9%), and cognitive problems (3.5%) most often. Other barriers included scheduling difficulties (12.8%), non-MS-related illness or injury (11.2%), pain (7.1%), weather-related difficulties (6.5%), and work/family issues (6.3%).

Conclusions: Although some symptoms of MS can be ameliorated by exercise, those symptoms themselves may act as barriers to exercise. Intervention on the symptom level may help patients with MS gain the benefits associated with increased exercise.

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(S42) Predictors of Setting Exercise Goals in Patients With Multiple Sclerosis

Background: Exercise is important in managing multiple sclerosis (MS) symptoms. However, little is known about factors that contribute to patients' decisions to set exercise goals.

Methods: Sequential MS patients ($N = 119$) who were ambulatory without aid were eligible for inclusion. Participants were randomly assigned to receive motivational exercise counseling and exercise goal setting or to a usual-care condition. Baseline characteristics were assessed to determine factors that might potentially influence the setting of exercise goals. Subjects were evaluated for fatigue (Modified Fatigue Impact Scale), pain (Brief Pain Inventory), depression (Center for Epidemiologic Studies Depression Scale), disability (MS Functional Composite), and Motivational Readiness to Exercise Scale.

Results: Of 49 evaluable subjects in the exercise condition, 81.2% were women, 98% were white, 83.7% had relapsing MS, mean age was 51.5 ± 10.2 years, and mean time since diagnosis was 10.7 ± 6.7 years. Mean 25-foot timed walk was 5.00 ± 1.34 seconds. Mean baseline exercise was 71.5 ± 68.0 min/week. Exercise goals averaged 158.0 ± 96.4 min/week. The amount of exercise set as a goal was not statistically correlated with prestudy exercise behavior ($P = .168$, $R = 0.207$), fatigue ($P = .373$, $R = 0.135$), depression ($P = .872$, $R = 0.025$), pain ($P = .195$, $R = 0.253$), 25-foot timed gait ($P = .201$, $R = 0.192$), marital status ($P = .470$, $R = 0.109$), education ($P = .157$, $R = 0.212$), employment ($P = .442$, $R = 0.158$), or readiness to exercise ($P = .535$, $R = 0.096$)

Conclusions: Baseline patient characteristics are not strongly associated with the ability to set exercise targets in ambulatory adults with MS. Patients can successfully set exercise

goals despite disability, fatigue, depression, pain, or prior exercise activity.

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(S43) How Often Do Multiple Sclerosis Patients Miss Injections of Disease-Modifying Therapy?

Background: The Calgary Multiple Sclerosis (MS) Treatment Outcomes Study determined long-term safety and outcomes in a population-based cohort exposed to disease-modifying therapy (DMT). Adherence is an important determinant of efficacy that may be improved with better understanding of why patients miss doses. In this dynamic cohort study, participants completed questionnaires at 3, 6, and 12 months, then annually.

Methods: Questionnaires returned before May 2005 were analyzed in aggregate, by drug, and by follow-up period. The number of missed injections during each interval and contributing reasons were tabulated. Incidence rates of non-adherence (by drug and interval) are compared. Patients will be categorized by degree of adherence.

Results: This analysis is based on data from 963 patients who completed 3177 questionnaires over 7 years. The average return rate was 73.2%. Participants included 78% women and 22% men. Mean age was 39.8 years. Mean disease duration was 7.9 years. During 50.9% of treatment intervals, patients reported missing one or more injections. Mean annualized number of missed injections was 3.2 during the first 3 months, then averaged 5.4 from month 3 to month 60. Forgetting was the most frequent reason for missing injections. The proportion reporting forgotten injections increased from 16% at 3 months to 36% (mean) over years 2–5. The proportion of respondents that reported missed injections at 2 years for other reasons were: travel, 17%; drug holiday, 10.9%; non-MS medical, 7.1%; busy or tired, 4.6%; lack of drug, 3.6%; and MS-related medical, 2%. Missed injections due to travel or drug holiday increased in frequency over the first 2 years of therapy. Ongoing analysis will compare the proportion of missed injections by interval for each drug and categorize patient adherence.

Conclusions: Better understanding of adherence issues for each drug and during each time interval will guide strategies to improve adherence.

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(S44) Experience With Interferon Beta-1b Treatment Over 16 Years: Nurse Perspective

Background: Patient registries and follow-up studies are common tools in chronic illness to determine long-term outcomes. In recent years, attention to long-term outcomes has increased because of higher standards in the assurance of safety of marketed products. Betaseron was the first drug approved for the treatment of multiple sclerosis (MS) in 1993. The Betaseron 16-year long-term follow-up study followed patients who participated in the pivotal trial and is the

longest follow-up of MS patients treated with an interferon-beta therapy.

Design/Methods: The current trial was designed to assess long-term safety, tolerability, and efficacy in patients using interferon beta (IFN β)-1b for up to 16 years. Recruitment started in January 2005 and ended in December 2005. Patients underwent clinical, laboratory, and magnetic resonance imaging examinations and were asked to complete questionnaires assessing patient-reported outcomes within 21 days after signing the consent.

Results: Approximately 90% of the original 372 patients were identified. All 11 North American sites from the pivotal study participated. Thirty-five identified patients had died, of which most were treated in the placebo group during the randomized, double-blind pivotal trial.

Conclusions/Relevance: After 16 years, approximately 90% of the patients from the original IFN β -1b pivotal trial have been located. The final results from the Betaseron 16-year long-term follow-up study will enable caregivers and patients to assess the safety and tolerability of long-term IFN β -1b administration and its effects on clinical and paraclinical outcomes.

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(S45) Flow Cytometry in Multiple Sclerosis Patients on Continuous Combined Therapy

Background: Continuous combined therapy (CCT) in multiple sclerosis (MS) patients on interferon β (IFN β) experiencing breakthrough symptoms improves disease control. Peripheral blood (PB) flow cytometry (FC) may be helpful in managing ongoing treatment.

Objective: Establish effect of CCT on PB cell count of immunocompetent cells.

Methods and Design: PB FC using CD3, CD4, CD8, CD14, CD16, and CD19 antigens was performed in 18 healthy control subjects and 124 MS patients: 16 on Avonex monotherapy; 37 on Avonex and prednisone (<0.12 mg/kg daily) (AP); 16 on Avonex, prednisone, and AZA (1.5–3.0 mg/kg daily) (APAZA); 15 on Avonex, prednisone, and Cell-Sept (target dose 2 g/day) (APC); 15 on Rebif monotherapy; 18 on Rebif and prednisone (RP); and 7 on Rebif, prednisone, and AZA (RPAZA).

Results: CD4+ (<400/cmm) and/or CD8+ (<200/cmm) lymphocytopenia was established in 10.8% and 13.5% patients on CCT using Avonex and in 22.2% and 44.4% treated with Rebif in absence of opportunistic infections. Compared with control subjects, PB CD19+ cell count was lowest in individuals on APC (76.13 \pm 66.16/cmm; P = .0011), with lowest CD8+ cell count in patients on RP (250.11 \pm 293.62/cmm; P = .0246). CD14+ cell count was highest in patients on APC (478.73 \pm 179.89/cmm; P = .0081). PB CD16+ cell count was significantly decreased in patients on APAZA (36.57 \pm 46.40/cmm; P = .0184). IFN β monotherapy did not alter PB cell counts significantly. Beneficial effect of CCT in the MS patients treated will be reported elsewhere.

Discussion: Absent suppression of PB CD19+ and/or CD8+ cell counts in some MS patients on CCT probably reflects immunogenetic and/or pharmacogenomics phenotypes requiring more intensive immunosuppression. On the other hand, therapeutic plasma exchange in MS on CCT patients with low CD19+ cell count is probably not indicated.

Conclusion: In management of MS, PB FC is underutilized and may be useful in optimizing therapy in individual patients.

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(S46) Validation of NARCOMS Registry: Bladder Assessment

Background: Participants enrolled in the North American Research Committee on Multiple Sclerosis (NARCOMS) registry report disability status via two self-report measures, performance scales (PSs) and Patient-Determined Disease Steps (PDDS). The bladder/bowel subscale of PS (PSB) has not been validated.

Objective: We aimed to validate the PSB question using the bowel control scale (BWCS) and Urogenital Distress Survey (UDI-6) as our criterion measures.

Methods: In the fall 2005 semiannual update questionnaire, we collected the BWCS and UDI-6. Spearman correlations between the bladder (PSB, UDI-6) and BWCS scales were used to assess criterion validity. Spearman correlations between PSB and various PS subscales and PDDS were used to assess construct validity.

Results: We report interim results reflecting the initial 4927 responses to date (of 17,142 surveys distributed). Respondents were predominantly women (74.1%) and white (93.8%), with a mean (SD) age at onset of 30.2 (9.5) years. Only 8 (0.19%) participants did not answer the PSB question. Among participants without suprapubic or Foley catheters or previous bladder diversion surgery, urinary symptoms were common: urinary frequency, 75.6%; urgency, 72.3%; urge incontinence, 60.9%; stress incontinence, 56.3%; nocturia, 78.9%; and hesitancy, 60.0%. Nine hundred four (18.4%) participants reported no disability, whereas 2796 (56.8%) reported minimal/mild, 696 (14.1%) reported moderate, and 532 (10.6%) reported severe/total disability related to bladder/bowel symptoms. For UDI-6, the median (Q25–Q75) score was 5 (2–9), for BWCS 3 (1–6), and for PSB 1 (1–2). The correlation between PSB and UDI-6 was r = 0.67 and between PSB and BWCS was r = 0.53 (both P < .0001). Correlations between PSB and vision, cognition subscales were low, indicating expected divergent validity. Correlations between the PSB and the spasticity subscale and PDDS were moderate, indicating convergent validity.

Conclusion: The PSB question has adequate criterion and construct validity in MS.

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(S47) Comparison of Multiple Sclerosis Family Caregiver Needs and Characteristics in Two Clinical Settings

Background: Multiple sclerosis (MS) family caregivers spend a lot of time caring for afflicted family members and report an overall decrease in their quality of life. Caregivers require support services to manage their emotional, physical, and financial burden as they coordinate and provide care. The literature calls for consistent evidence-based practices that will enable health care practitioners to educate and support MS caregivers so that those caregivers may 1) continue their caregiving role and 2) maintain their own physical and emotional health and quality of life.

Purpose: To identify and compare family caregiver needs and characteristics between two samples, our descriptive pilot study included a voluntary self-reported survey conducted among a convenience population of caregivers at two Baltimore, Maryland, clinics in close proximity: University of Maryland MS Center (UM) and Baltimore VA Medical Center MS Center of Excellence (VA).

Methods: We defined MS family caregivers as a spouse, relative, or significant other living in the home. The survey included 1) questions to help improve communication between the health care provider and family caregiver and 2) a self-assessment section designed to measure indices of emotional and physical distress. We assessed caregiver knowledge about MS, caregiver education level, resources utilized (eg, assistive devices, use of veteran caregiver resources, home health aides), and MS patient symptoms. The survey also inquired about the caregiver's health and the family burden.

Results: There were no significant differences between the caregiver populations. Both populations of caregivers were predominantly white female spouses over age 45 years with at least a high school education. Seventy-five percent were spousal caregivers, and 88% (UM) or 96% (VA) have provided care for >1 year. More than half of our caregivers worked outside the home; 26% of VA and 40% of UM caregivers worked full time. From 40 to 50% of households used additional, paid caregiver support, with most requiring extra help ≥ 16 hours/week. More than half of both populations expressed the need for more emotional and peer support, more physical support, more knowledge about caregiver support services, and more educational opportunities about MS care and community resources.

Conclusions: More than 50% of caregivers reported that their care recipients were wheelchair dependent, indicating more advanced disease in their care recipients and, thus, more hours of caregiving. We will use the data from this study to design and implement needs-based caregiving programs in both centers that will be generalizable to the family caregiver population, be it veteran or civilian.

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(S49) Assessment of Interventions to Decrease Injection-Site Reactions With Subcutaneous Interferon Beta-1a Treatment

Background: Injection-site reactions (ISRs) are a common adverse effect of all injectable therapies and may result in treatment interruption. Anecdotal evidence suggests that over-the-counter (OTC) topical anti-inflammatory agents, including steroids and products containing witch hazel, are useful for treating ISRs, but no well-controlled clinical trials have evaluated such agents.

Objective: Compare the ability of two topical medications to reduce the severity of ISR in patients with relapsing-remitting multiple sclerosis (RRMS) receiving Rebif (interferon beta-1a) therapy.

Design: ASSIST is an ongoing open-label, 9-week crossover trial consisting of two independent studies, each of which will directly compare a topical anti-inflammatory agent (Cortizone-10 cream [hydrocortisone] or Tucks pads [witch hazel]) to Lubriderm lotion (control). Patients on Rebif with ISRs at least 20 mm in diameter 48–72 h postinjection will be randomized to apply one of the test agents or Lubriderm topically after each injection for 3 weeks. After a 1-week break, participants who used the control will apply the test agent, and those who used the test agent will apply the control, for the final 3 weeks. ISRs will be measured 48–72 h after each injection and at day 7. The primary study endpoint is the difference in mean maximum diameter of redness at injection site 48–72 h postinjection.

Results: This study is actively recruiting 100 participants (50 per substudy). Twenty-eight patients have been randomized to date. Baseline demographic data reveal that 11% are men and 89% women, with a mean age of 43 years. An interim data analysis will be presented.

Conclusion: This clinical study provides a unique opportunity to prospectively evaluate the ability of two over-the-counter topical anti-inflammatory agents (hydrocortisone and witch hazel) to decrease ISRs in RRMS patients taking Rebif.

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(S50) Weekend Retreat for Teens With Multiple Sclerosis

Goal: Demonstrate improved quality of life (QOL) from a weekend retreat for teens with multiple sclerosis (MS).

Background: MS, an autoimmune disorder targeting the central nervous system, most frequently affects young adults 20–40 years of age. However, 3–5% of patients are diagnosed before age 18 years, with an estimated 15,000 youngsters in the United States representing an underserved MS subpopulation. Faced with the diagnosis of MS, children and families report feeling lost. Resources are few, and when speaking with their own support network, they often hear “MS doesn't happen in kids.” Rarely do they have the opportunity to meet another affected family. A special 4-day recreational retreat was developed to bring the teens together to build relationships and improve QOL.

Methods: Twenty-eight teens with MS (10 male), ages 12–19 years, participated in this therapeutic program during the summers of 2004 and 2005. The program drew participants from throughout the United States, including Hawaii and Alaska, as well as Canada. Activities were designed and implemented by Access-2-Adventure, a nonprofit organization that provides recreational activities for children, adolescents, and adults with physical disabilities. Activities included kayaking, sailing, ropes course, a drumming circle, swimming, team-building group activities, drama workshop, and closing ceremony.

Results: The teen retreat was a tremendous success. Improvement in QOL was determined by structured interview and self-report questionnaires. Enhancement of well-being, a feeling of cohesion, and a sense of “not being defined by MS” were described by participants. Postcamp, communication continues among the attendees. Medication compliance, by self-report, has improved since the camp program. One attendee who had discontinued her therapy returned home and restarted her treatment.

Conclusion: Recreational interventions such as the teen weekend retreat are valuable in fostering a sense of belonging for affected individuals and families, enriching QOL, and improving medication compliance.

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(S51) Combination Therapy With Intramuscular Interferon Beta-1a and Oral Doxycycline in Patients With Multiple Sclerosis: Open-Label Trial

Background: Doxycycline, a potent matrix metalloproteinase (MMP) inhibitor, can potentially suppress destruction of extracellular matrix and therefore limit transendothelial migration of activated leukocytes in multiple sclerosis (MS). Additionally, because MMP-9 is capable of cleaving interferon beta (IFNB), thereby potentially contributing to relapses during therapy, doxycycline may be expected to reduce the frequency of relapses. Despite effective treatment with intramuscular (IM) IFNB-1a, some patients may progress and require combination therapy.

Objective: Determine the safety, tolerability, and efficacy of doxycycline combined with IM IFNB-1a in MS patients experiencing breakthrough disease.

Methods: This was an open-label, single-center, single-arm, crossover study. Patients aged 18–55 years with relapsing MS, an Expanded Disability Status Scale (EDSS) score of 1.5–4.5, one or more gadolinium-enhancing (Gd+) lesions on magnetic resonance imaging (MRI), continuous treatment with IM IFNB-1a for at least 6 months, and a relapse within 60 days of their baseline visit (month –3) were eligible. Patients underwent MRI at months –3, –2, –1, 0, +1, +2, +3. Daily oral doxycycline 100 mg combined with weekly IM IFNB-1a 30 µg, began at month 0.

Results: To date, 15 patients have been enrolled, and 11 have completed the study. An interim analysis included 11 patients with >1 pretreatment and 1 on-treatment MRI and neurological examination. The patients had a mean age of

42.0 ± 13.3 years, and 9 were women. During pretreatment (months –3, –2, –1, and 0), the mean number of Gd+ lesions was 10.3 ± 6.6, decreasing to 6.2 ± 5.4 during combination therapy ($P = .001$). Mean pretreatment EDSS was 3.9 ± 0.4, decreasing to 1.4 ± 0.5 during treatment ($P = .001$). One patient had transiently elevated hepatic enzymes on combination therapy; none have withdrawn. Final results of MRI and clinical measures are presented.

Conclusions: Combination therapy with doxycycline 100 mg daily and IM IFNB-1a 30 µg weekly appears to be safe and effective in patients with relapsing MS.

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(S52) Analysis of Relapse Measures in Patients Undergoing Monthly Magnetic Resonance Imaging in BECOME Study

Objective: Clinical relapses are the main outcome measure in most multiple sclerosis (MS) clinical trials; however, measuring disease activity is difficult. We compared a composite disease activity score at the time of regular scheduled visits with unscheduled relapse visits in patients undergoing monthly magnetic resonance imaging (MRI) in the BECOME study.

Background: All relapse measures routinely used in MS clinical trials have problems of sensitivity or specificity. We took advantage of an ongoing randomized, prospective, clinical trial in which patients are undergoing monthly MRI to compare multiple clinical and radiological measurements of MS disease activity into a composite score.

Design/Methods: Patients with relapsing forms of MS who were enrolled in the BECOME study at the MS clinic at University of Medicine and Dentistry of New Jersey, New Jersey Medical School, undergoing monthly 3-T MRI with triple-dose gadolinium were evaluated at scheduled visits every 3 months or unscheduled relapse visits by a treating neurologist (Schumacher's), blinded neurologist (Expanded Disability Status Scale [EDSS]), and blinded nurse (Multiple Sclerosis Functional Composite scale [MSFC]). The activity scores for Schumacher's, EDSS, MSFC, and brain MRI were classified as none (0 points), mild (1 point), or moderate-severe (2 points). The sum of points for each visit determined the composite score.

Results: The first 12 patients with relapse visits were included in this pilot study. There were three men and nine women. There were 20 relapse visits. Among these 20 visits, 18 (90%) occurred at the peak of the composite score. Only 2 (10%) occurred at times of low composite scores. The mean composite score was significantly higher for unscheduled relapse visits than scheduled visits (3.9 ± 2.3 vs 1.0 ± 1.2 ; $P < .05$).

Conclusions/Relevance: The frequency of MS relapses varies greatly depending on the individual measurement used. We propose that a composite score of disease activity based on objective clinical and radiological measures is a better measure of true relapses in MS.

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(S53) Needs Assessment Survey of Multiple Sclerosis Patients and Care Partners

Little is known about the changing needs of multiple sclerosis (MS) patients and their care partners. Using the Multiple Sclerosis Association of America (MSAA) client database, a survey was developed covering informational, educational, programmatic, and service needs and sent by mail to 2058 MS patients and care partners, of whom 762 completed and returned the survey (37% response rate). The respondents were highly symptomatic, with more than 50% being at least moderately affected in the past week in 13 of 16 symptom categories. Participants were asked how often they needed information and education over the past year in 16 areas. Information on new medications, treatment, and research was the greatest perceived need (84%). Other areas of informational and educational needs included information about exercise (77%), fatigue management/conservation (74%), better problem solving and coping (74%), and complementary or alternative therapies (72%). From a list of 13 program areas currently provided by MSAA, respondents were asked to identify the 3 most important programs and services. Publications and brochures were rated first, with educational awareness events following. Programs that combine social activities with therapeutic benefits, such as water exercise and Tai Chi classes, were rated third most important. Respondents were asked to choose among 6 potential programs and services using a forced-choice technique. Rehabilitation services (ie, occupational or physical therapy, nutrition assistance, and psychotherapy) were needed most compared with any of the other 5 potential program offerings. Services that provide skills, encouragement, and support to help one manage one's life were identified as needed most compared with all other potential programs except rehabilitation services. The need for both of these programs surpassed the need for assistance in meeting essential financial obligations. Overall, the research suggests that medical information, rehabilitation, and therapeutic services, as well as attaining life skills, are important but unmet needs for MS patients. Implications of the research and recommendations for future needs assessment research in MS are presented.

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(S54) Cost-Effectiveness Analysis of Available Therapies for Multiple Sclerosis

Objective: Determine the cost-effectiveness, and the impact of neutralizing antibodies (NAbs) on the cost-effectiveness, of the currently available multiple sclerosis (MS) disease-modifying agents (DMAs).

Methods: A cost-effectiveness model was developed with relapse rate and disability progression endpoints from pivotal phase III trials of currently approved DMAs for MS: intramuscular (IM) interferon beta (IFNB)-1a (Avonex), subcutaneous (SC) IFNB-1a (Rebif), IFNB-1b (Betaseron), and glatiramer acetate (GA; Copaxone). The model was created from a managed-care perspective, with time horizons of 24 and 48 months. Cost-effectiveness was calculated as the ratio of total utilization costs per percent relative risk reduction for relapses

and disability progression; daily cost-effectiveness is expressed as per percentage point reduction. The incidence of NAbs and their effect on efficacy was obtained from prescribing information, open-label extension studies of IFNB products, and a large population study. Costs for each DMA were based on wholesale acquisition cost published as of 6 January 2006. The model includes the following assumptions: comparison of similar endpoints across different clinical trials, constant adverse event rates among products, constant burden of relapse over time, constant persistence/compliance rates among products, similar laboratory testing/frequency among IFNB products. A sensitivity analysis was conducted to test the robustness of the model to changes in NAb incidence.

Results: At 24 months, the cost-effectiveness for disability progression was \$897 (\$1.23/day) for IM IFNB-1a, \$1222 (\$1.67/day) for SC IFNB-1a, \$1150 (\$1.57/day) for IFNB-1b, and \$2789 (\$3.82/day) for GA. Projections of cost-effectiveness over 48 months, after the development of NAbs, were \$1808 (\$1.24/day) for IM IFNB-1a, \$2536 (\$1.74/day) for SC IFNB-1a, \$2622 (\$1.80/day) for IFNB-1b, and \$5577 (\$3.82/day) for GA. Results were similar for relapse rate.

Conclusions: DMAs are cost-effective; per percentage point reductions in disability progression and relapses can be obtained with IFNB products for less than \$2.00/day. Over time, NAbs reduce the cost-effectiveness of IFNB products that have high immunogenicity.

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(S55) Incidence and Effects of Neutralizing Antibodies in Patients With Multiple Sclerosis Treated With Avonex or Rebif in the PROOF Study

Background: Sustained benefits from interferon-beta (IFNB) products used to treat relapsing multiple sclerosis (RMS) require adherence (affected by tolerability and convenience) and clinical efficacy, which can be reduced when neutralizing antibodies (NAbs) are present.

Objective: PROOF, a phase IV retrospective and prospective open-label study, was conducted to evaluate the efficacy and tolerability of intramuscular (IM) IFNB-1a 30 µg once weekly compared with subcutaneous (SC) IFNB-1a 44 µg three times weekly in RMS patients. The goal of this prespecified subanalysis was to determine the incidence of NAb formation and its effects on clinical and MRI endpoints.

Methods: Before enrollment, subjects received IM or SC IFNB-1a for 12–24 months without switch or interruption and had an Expanded Disability Status Scale (EDSS) score of 0.0–5.5. NAbs were evaluated at study enrollment and month 6.

Results: One hundred twenty-three patients (59 IM, 64 SC) were evaluated for NAbs. At study enrollment, 0 and 21% of patients treated with IM IFNB-1a and SC IFNB-1a were NAb+. Persistent NAbs (positive at months 0 and 6) were present in 19% of patients, all treated with SC IFNB-1a. Compared with NAb- patients, NAb+ patients had significantly more new or enlarging T2 lesions (36.4 vs 59.3% with 0

lesions; $P = .003$) and total number of Gd+ lesions (54.5 vs 75.6% with 0 lesions; $P = .04$) and trended toward a higher Gd+ lesion volume (0.31 vs 0.05, $P = .02$, at month 0; 0.21 vs 0.04, $P = .06$, at month 6). Disease progression (EDSS) from study enrollment to month 6 increased significantly more in NAb+ patients than NAb- patients ($P = .02$).

Conclusions: Compared with patients treated with IM IFNB-1a, patients treated with SC IFNB-1a were more likely to have persistent NAb+ titers. NAb+ patients had significantly more signs of disease, as shown by new or enlarging T2 lesions, total Gd+ lesions, and increased EDSS, after 18–30 months on therapy.

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(S56) Interferon Beta-1b: Incidence of Neutralizing Antibodies Over Time

Background: Neutralizing antibodies (NAbs) develop with all current immunomodulatory treatments for multiple sclerosis (MS), including interferon beta (IFNB) and glatiramer acetate. However, controversy exists over the clinical relevance of NAbs. To better understand their relevance, it is important to examine their evolution over time.

Methods: Serum samples were collected regularly from patients with relapsing-remitting (RR) MS during the 3-year pivotal North American IFNB-1b (Betaseron) trial. Samples were tested with the myxovirus protein A assay, and titers ≥ 20 were considered positive.

Results: The evolution of NAbs was analyzed in all patients who were NAb+ at any point during the study ($n = 52/124$ patients studied). The proportion of patients with a positive NAb titer gradually increased from day 1 (2/46, 4.3%) to day 540 (~18 months; 41/49, 83.7%), when the highest median titer of 48 (range 0–2247) was observed. After day 540, the median NAb titer decreased while the proportion of patients with a positive titer also decreased. By day 1170, only 45.9% of this subgroup of patients who eventually became NAb+ remained positive. High NAb titers (≥ 400) were not observed until after 6 months of treatment, and the proportion of patients with a high titer remained low throughout the study (range 1.9–14.6% of patients who eventually became NAb+).

Conclusion: This subgroup analysis of NAb data from the pivotal North American IFNB-1b RRMS trial demonstrated that the incidence of NAb positivity had peaked by 18 months, before declining over the second half of the study; similarly, the median NAb titer peaked at around 18 months. These findings support previous observations that a considerable proportion of patients treated with IFNB-1b revert to NAb negativity within 3 years of starting therapy. The incidence of high NAb titers remained at low levels, similar to those observed in other IFNB-1b trials.

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(S57) Seasonal Variation of Gadolinium-Enhancing Lesions in Multiple Sclerosis

Several studies have claimed there is a seasonal variation in the number of patients with multiple sclerosis (MS) who have exacerbations. Various reasons have been given (eg, vitamin D exposure, incidence of viruses, interferon-gamma production). One study suggests that more patients have gadolinium-enhancing lesions in the first half of the year than in other months. Other studies show no seasonal trend in exacerbations, gadolinium-enhancing lesions, or other magnetic resonance imaging (MRI) abnormalities. Because gadolinium-enhancing lesions are thought to represent an excellent marker of acute disease activity, we retrospectively reviewed monthly MRI scans from relapsing-remitting ($n = 67$) and secondary progressive ($n = 11$) MS patients. Patients were evaluated at the National Institutes of Health between 1989 and 2004 and had monthly MRI scans for 1 year. MRI scans were analyzed based on those treated with interferon beta-1 β for at least 30 days at the time of the first MRI ($n = 38$) and those without disease-modifying therapy ($n = 40$). We counted the number of new enhancing lesions per season: winter (December–February), spring (March–May), summer (June–August), and autumn (September–November). The mean numbers of new enhancing lesions (SD) were 7.37 (8.26), 6.98 (7.80), 6.60 (7.03), and 7.00 (6.12) in the untreated cohort and 2.00 (3.65), 2.34 (4.49), 2.34 (3.59), and 2.05 (3.31) in the treated cohort for winter, spring, summer, and autumn, respectively. The number of new enhancing lesions between the treated and untreated cohorts was found to be statistically significant ($P = .000$). In conclusion, we found no significant seasonal variation in the mean number of enhancing lesions in the treated and untreated cohorts. An alternative analysis looking at best and worst seasons for each patient also failed to show a seasonal variation. Of interest, patients treated with interferon beta-1 β had significantly fewer lesions than the untreated cohort during the 1-year period.

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(S58) Change in Voiding Patterns After Injection of Botulinum Toxin Into Bladder, Urethral Sphincter, or Bladder and Urethral Sphincter

Background: Current medical therapies for voiding dysfunction are not always effective for patients with multiple sclerosis (MS). Catheters and surgical options for urinary symptom management may be presented as the only option. Use of botulinum toxin injections is a nonsurgical method that can manage symptoms and prevent complications of refractive bladder and sphincter dysfunction. In this study, we assess effectiveness of treatments.

Methods: In this observational study, 58 patients with a diagnosis of neurogenic detrusor overactivity (NDO) or detrusor sphincter dyssynergia (DSD) previously refractive to standard therapy received injections of botulinum toxin in total doses ranging from 100 to 300 U. Sites of injections included the bladder, the urethral sphincter, or both.

Results: The 58 patients ranged in age from 24 to 74 years, mean 46 years. Overall, 43% admitted to improvement in some symptoms. Of these, visual analog scale (VAS) scores decreased from 7.2 to 4.7, and diaries demonstrated decreases in frequency, incontinence, and nocturia compared with baseline. Patients demonstrated improvements in nocturic episodes and admitted to improved sleep quality with a decrease in overall fatigue level. Others admitted to using fewer or no pads to manage incontinence. Urinary infection rate decreased in three patients reporting recurrent infections. Effects ranged from 2 to 14 months. Twenty-three patients received repeat injections.

n	Location of injection	Dose range (U)
35	Urethral sphincter	100–200
15	Bladder	100–200
8	Bladder and sphincter	200–300

Conclusion: Many patients receiving injections experienced improvement in symptoms of urgency frequency, incontinence, and nocturia. Although not US Food and Drug Administration approved at this time, Allergan will soon begin a clinical trial for subjects experiencing NDO. Many commercial insurance companies and several medicare insurance programs are covering costs of procedures because effectiveness has been demonstrated with clinical use and in published European studies.

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(S59) Factors Related to Discontinuation or Absence of Disease-Modifying Therapy in Multiple Sclerosis Center

Objective: Data collection on the demographics of untreated multiple sclerosis (MS) patients and causes for treatment suspension.

Background: Current National MS Society (NMSS) guidelines recommend early disease-modifying therapy (DMT) in MS. Patients who do not receive therapy have become an area of interest because there is a lack of pertinent studies.

Methods: Untreated patients were identified from a database of 657 patients at the Maxine Mesinger MS Clinic in Houston, Texas. Retrospective review of medical records was conducted. Variables included age, sex, diagnostic subtype, date of diagnosis, date of last clinic visit, specific treatments, and reason for discontinuation of treatment.

Results: Thirty-six (5.5%) patients were confirmed as not on DMT. Women represented 83.3% of untreated subjects. The mean age was 56.11 ± 12.22 years. The initial diagnostic subtype included 91.7% of patients categorized as relapsing-remitting MS (RRMS) and 8.3% as primary progressive disease (PPMS). Current diagnostic subtypes included 47.2% RRMS, 36.2% secondary progressive MS, 8.3% PPMS, and 8.3% benign MS. Patients who never received treatment of any type represented 27% of the total sample. Seventy-three had received one to six different DMTs. The average number of DMTs used by that group was 1.74 ± 1.02. Discontinuation of therapy was mainly related to progression (26.67%), compliance (22.22%), and adverse effects (22.22%). Lack of insurance or cost issues represented 8.89% of the causes for

discontinuing any therapy. Causes for never initiating therapy were mainly attributed to patient preference (44.4%) and stability of disease (33.3%).

Conclusions: Relatively few MS patients without treatment were extracted from our database. One-third never received therapy, the main cause being patient preference. Progression of disease, compliance, and adverse effects were the most important factors in patients discontinuing therapy.

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(S60) Impact of Warm Compresses on Local Injection-Site Reactions With Self-Administered Copaxone

Introduction: 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 designed to evaluate the effect of warm compresses on the presentation of LISRs among patients who self-inject Copaxone subcutaneously daily.

Objective: Compare LISRs when subjects apply warm compresses to injection sites for 5 minutes before daily injections of Copaxone using the Autoject 2 for glass syringe versus when subjects use their usual injection-site preparation method.

Methods: This study conformed to an open-label, randomized, single crossover design. Fifty subjects used each injection-site preparation method during two consecutive 14-day periods, with the order randomized and counterbalanced across the subjects. Kwik-Heat Instant Hot Packs were used as warm compresses to standardize the temperature. Patient diaries were used to determine the number of LISRs occurring across each 14-day period. Nurses and patients also independently assessed LISRs in the clinic on days 14 and 28.

Results: In terms of the primary outcome measure (ie, the number of LISRs recorded at 5 minutes postinjection), patients had significantly lower mean LISRs during the 14-day period when warm compresses were used than during the period when usual site preparation was used (mean 31.52 vs 36.08; $P = .003$). Similarly, patients recorded fewer LISRs at 2 minutes postinjection during the warm-compress condition than during the usual-preparation condition (mean 31.75 vs 35.22; $P = .011$) and rated the injection-site reactions as less “bothersome.”

Conclusions: Using warm compresses before injection of Copaxone reduces the frequency of LISRs and lessens how bothersome they are perceived.

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(S61) Effects of Natalizumab on Clinical Measures of Efficacy in Multiple Sclerosis

Objective: Present data on the effects of natalizumab (Tysabri) on clinically relevant measures of efficacy in relapsing multiple sclerosis (MS).

Background: The AFFIRM study assessed the efficacy and safety of natalizumab as monotherapy in patients with relapsing MS. At 2 years, natalizumab was shown to reduce annualized relapse rate by 68% compared with placebo ($P < .001$).

Study Design/Methods: AFFIRM was a randomized, double-blind, placebo-controlled phase 3 clinical trial. Pre-specified endpoints at 2 years included disability progression as measured by the Multiple Sclerosis Functional Composite (MSFC), annualized rate of relapses requiring corticosteroid use, annualized rate of hospitalizations due to MS, and change in visual function as assessed by high- and low-contrast (2.5 and 1.25%) Sloan letter charts. MSFC is a composite of three measures: timed 25-foot walk (T25FW), nine-hole peg test (9HPT), and paced auditory serial addition test (PASAT), which assess ambulation, arm/hand function, and cognition, respectively.

Results: Over 2 years of treatment, natalizumab significantly reduced deterioration in ambulation (T25FW, $P < .001$), arm/hand function (9HPT, $P < .001$), cognitive function (PASAT, $P < .005$), and visual function (2.5%, $P < .005$; 1.25%, $P < .019$) compared with placebo. In addition, natalizumab reduced the annualized rate of relapses requiring steroid use (0.13 natalizumab vs 0.43 placebo, $P < .001$) and the annualized rate of MS-related hospitalizations (0.03 natalizumab vs 0.10 placebo, $P < .001$). Natalizumab treatment was generally well tolerated. However, progressive multifocal leukoencephalopathy (PML) was identified in two patients who received natalizumab in combination with interferon beta-1a. Later, an additional case of PML was identified in a natalizumab-treated patient with Crohn's disease.

Conclusions: Natalizumab had significant effects on measures of ambulation, arm/hand function, cognition, visual function, steroid use, and hospitalizations due to MS. Despite the identification of PML as a risk of natalizumab treatment, natalizumab remains a promising new treatment for MS.

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(S62) Impact of Multiple Sclerosis Care Partner Stress in Workplace

The National Alliance on Caregiving estimates that 80% of community care is provided by family caregivers, at an approximate economic value of \$200 billion annually. Studies on the economic impact of Alzheimer's disease (AD), for example, have found that the average caregiver with a full-time job misses more than 3 weeks of work a year and that one-fifth will quit their jobs altogether to provide full-time care. Results from an electronic survey administered to 1461 multiple sclerosis (MS) care partners through the North American Research Committee on Multiple Sclerosis (NARCOMS) registry included questions about the potential impact of MS care partner stress in the workplace. Unlike AD, MS tends to impact individuals earlier in their careers. Survey findings

revealed that 45% of MS care partners had "missed work this year due to caregiving responsibilities." Overall, the MS care partners surveyed missed an average of 7.3 days of work in the past year because of caregiving responsibilities. Seven percent of MS care partners reported having changed their employment altogether because of their role as a caregiver. Indeed, care partners of patients with either primary progressive ($n = 219$) or secondary progressive ($n = 399$) MS were twice as likely to report a change in employment as care partners of patients with relapsing-remitting MS ($n = 516$). The current survey findings suggest that the potential impact of MS care partner stress in the workplace should be further addressed. The literature often addresses the caregiver as "the hidden patient." It is hoped that these data shed light on the situation and help to inform early-intervention programs targeting increased care partner stress management. Effective behavioral-medical interventions for impacted MS care partners may have a positive medicoeconomic benefit, including both decreased absenteeism rates in the workplace and increased productivity on the job.

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(S63) Randomized, Double-Blind, Placebo-Controlled, 32-Week Study to Evaluate Efficacy and Safety of Fluoxetine (Prozac) and Interferon Beta-1a (Avonex) in Treatment of Multiple Sclerosis

Objective: Evaluate the efficacy of Prozac to reduce flulike side effects that are associated with Avonex used in the treatment of multiple sclerosis (MS) and to measure the subjective changes in vitality and quality of life of patients treated.

Design/Methods: Participants ($n = 20$) with relapsing-remitting MS were randomized (1:1) to placebo ($n = 10$) or to Prozac ($n = 10$). Participants were titrated onto the Prozac/placebo over a 1-week period, with the targeted dose being 20 mg/day. At week 4 (visit 2), participants began the Avonex treatment. Participants recorded flulike symptoms and energy levels each week. At visits 1, 2, 3, 4, and 7, participants completed an SF-36 quality of life, clinical global impression change scale (CGIC), patient global impression of change scale (PGIC), and Beck's Depression Inventory-II (BDI-II). At each visit, participants were asked to complete the Modified Fatigue Impact Scale (MFIS). Mixed-effect modeling was used to examine the treatment effect of Prozac over time.

Results: A positive trend was found for the treatment effect on energy level over 6 months, with Prozac plus Avonex showing higher energy levels over time than Avonex ($P = .1591$). Changes in MFIS scores over time were also improved for the Prozac group compared with Avonex alone ($P = .0814$). Although not statistically significant, on the CGIC, 5 of 8 (63%) patients from the Prozac group and 1 of 7 (14%) patients from the placebo group fell into the improved category. On PGIC, 5 of 8 (63%) patients from the Prozac group and 1 of 7 (14%) patients from the placebo group fell into the improved category.

Conclusions: Results show strong trends that taking Avonex in conjunction with Prozac in the treatment of MS has the potential to positively affect fatigue and energy levels in patients. Further studies are warranted.

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(S64) Reliability of Computerized Assessment (Anam) of Multiple Sclerosis Patients Over Time

Background: Traditional neuropsychological evaluation of multiple sclerosis (MS)-related cognitive dysfunction can be costly and time intensive. Therefore, alternatives to traditional paper-and-pencil batteries have been sought. Recent research (2003) indicated that a short, automated, computerized test battery (ANAM) predicts overall performance on a larger traditional battery for MS patients. Whereas the 2003 study was conducted at one time point, the current study is an analysis of data from the same subjects across 2 years to determine whether the predictive validity of the computerized battery for MS patients remains stable.

Methods: The 2003 study looked at the predictive validity of ANAM relapsing-remitting (RR) subjects at the initiation of intramuscular (IM) interferon β -1a (Avonex) treatment. The same patients were evaluated again at 6-month intervals over 2 years. The current study uses logistic and multiple regression over the remaining four time points. For the regressions, the traditional measure impairment index included those tests in the battery most sensitive to organicity. ANAM measures included in the regression were those with the highest correlations with traditional measures.

Results: Across all four time points, ANAM predicted performance on the traditional battery with a high degree of accuracy (6 months, 86.5% accuracy; 1 year, 93.1%; 18 months, 94.7%; 2 years, 76.9%). Furthermore, multiple regression analysis revealed that at all time points, three of the ANAM tests accounted for a high percentage of the variance in traditional battery impairment ratings ($r^2 = 58.5\text{--}84.1\%$).

Conclusions: Current findings offer confirmatory data for the use of computerized measures in the screening of cognitive functioning in MS patients. The reliability of ANAM remained high over a long period (2 years). In the future, computerized measures will increase the availability of neuropsychological evaluation to MS patients and improve sensitivity and test-retest capability in clinical trials.

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(S65) High-Dose Methotrexate in Worsening Multiple Sclerosis Patients: Long-Term Follow-Up and Mechanism

Multiple sclerosis (MS) is a central nervous system (CNS) disease, yet no currently approved therapy for MS has been proven to cross the blood-brain barrier (BBB) in significant concentrations. Methotrexate (MTX) is a powerful S-phase chemotherapeutic antimetabolite and anti-inflammatory agent

that can be given at high enough doses to cross the BBB in lymphocidal concentrations while the periphery is protected by leucovorin, an inhibitor of MTX. We have been using high-dose intravenous (HDIV) MTX therapy on MS patients with worsening disease for >7 years, with 150 patients having been treated. These patients include several cohorts who were in pilot clinical studies, including 1 of 15 patients worsening on weekly interferon beta who were treated bimonthly for 1 year. In the 1-year combination study, the Multiple Sclerosis Functional Composite (MSFC) mean showed an improvement of 0.327 ($P = .0002$) over baseline. These patients were followed with MSFC for up to 29 months (average 14 months) after the last treatment. It was found that most of the patients remained stable for an extended period, whereas two patients continued to improve after the treatment period. Similar long-term stability or improvement was found in the patients treated off label for periods extending up to ≥ 5 years. The mechanism of action of MTX within the CNS was investigated by using a coculture system of microglia and activated T cells to study the effects of MTX on contact-dependent cytokine secretion, based on the known upregulation of various inflammatory cytokines by interactions of activated T cells and microglia in the CNS. It was found that MTX downregulated secretion of proinflammatory cytokines and upregulated secretion of anti-inflammatory cytokines, suggesting that switching of the cytokine profile in the CNS may play a role in the sustained clinical effects of HDIV MTX therapy.

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(S66) High Prevalence of Sleep Disorders in Multiple Sclerosis: Effect of Treatment on Cognitive Function

Fatigue is a frequent and debilitating symptom of multiple sclerosis (MS). We routinely screen all of our patients for sleep disorders with a simple questionnaire and follow with polysomnography (PSG), if appropriate. We recently reported a chart review of a series of 102 consecutive patients with clinically definite MS in which we found that 49% had sleep disorders diagnosed by PSG. In that study, the sleep diagnoses found were as follows: 32 with obstructive sleep apnea (OSA), 3 with upper-airway resistance syndrome (UARS), 15 with periodic limb movement disorder (PLMD), 1 with idiopathic hypersomnia, and 5 with an abnormal PSG with elevated arousal indexes of unknown etiology. Several of the patients had two diagnoses (9 with OSA and PLMD, 2 with UARS and PLMD). In the current study, the charts of a series of MS patients who had had a sleep disorder diagnosed by PSG and who had been followed by the Multiple Sclerosis Functional Composite (MSFC) were examined to determine whether there were significant changes in MSFC as a result of treatment of their sleep disorder. Fifty-three patients had MS, a sleep disorder diagnosed with PSG, and MSFC data before and after treatment for the sleep disorder. There was significant improvement in MSFC, particularly the paced auditory serial addition test 3 subset, for patients who had obstructive sleep apnea treated by continuous positive

airway pressure or bilevel positive airway pressure. The high prevalence of treatable sleep disorders in MS patients, and the finding that treatment of the sleep disorders improves patients clinically, suggests that screening for sleep disorders should be a routine part of the management of MS patients. This is especially important for the large majority of MS patients who report fatigue as a major symptom.

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(S67) Comparison of Remote and Traditional Practices of In-Home Rehabilitation for People With Multiple Sclerosis

Teletechnologies offer great promise for providing in-home rehabilitation services to people with multiple sclerosis (MS), particularly those who live in remote areas or have difficulty traveling to a specialty clinic. A randomized clinical trial was undertaken to compare the effectiveness of in-home rehabilitation delivered by interactive teleconference and in-home visit to new users of walkers or wheelchairs. The two intervention groups (tele- and in-person care) received a four-visit rehabilitation intervention aimed at six transfer and mobility tasks. A usual-care group received no intervention. The intervention, developed by an interdisciplinary team, included in-home assessment of mobility and transfer skills, treatment recommendations for home exercises, and adaptive strategies (ie, skill training, provision of assistive technology, and recommendations for environmental modifications). The intervention was delivered by a physical/occupational therapist via teleconference from the clinic or in the home. Primary study outcomes were the number of performance deficit problems and recommendations for adaptive strategies (baseline to 6 weeks) and changes in the Falls Efficacy Scale (FES) and activities of daily living performance. A total of 65 of 82 subjects who were enrolled completed the 6-week protocol. Intervention delivery by telecare versus in-person visits showed a trend for more problems to be identified ($P = .13$) and more recommendations made ($P = .20$) in person. However, this appeared to be predominantly due to differences in the mobility tasks where the telecare group had significantly fewer problems ($P = .003$) and recommendations ($P = .005$). In contrast, there were no significant differences in the transfer tasks for either the mean number of problems per patient ($P = .68$) or recommendations per patient ($P = .68$). Moreover, when compared with the usual-care group, the combined-intervention (via televisits or in-person) group had significantly improved FES scores ($P = .05$). These data suggest that interactive teleconferencing technology may be an effective means of providing rehabilitation services to people with MS, particularly those with transfer difficulty.

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(S68) Comparison of Remote and Traditional Practices to Provide In-Home Assessment for Home Modifications

The need for home-modification services for people with multiple sclerosis (MS) far exceeds the availability of specialists

who provide them. Although remote home assessment would eliminate the need for a specialist to travel to an individual's home, this strategy is dependent on obtaining the same information about the person and his or her environment as would be obtained from a traditional in-home assessment. Two new remote assessments, a "zero-tech" paper-and-pencil protocol (CASPAR) and a high-tech real-time teleconferencing protocol (televideo), were compared to traditional in-home assessments to determine the equivalence of the two strategies. Data collection using CASPAR was conducted by a therapist inexperienced in home modifications. A technician, inexperienced in home modification, collected the televideo data under the guidance of home-modification specialists. In both cases, a specialist analyzed the remote assessment data to determine performance-deficit problems and home-modification needs. Sensitivity (true positive) and specificity (true negative) rates were determined to compare the number and types of problems identified by the remote assessments to the gold standard of a traditional in-home assessment. All sensitivity and specificity rates were significant ($P = .000$). CASPAR had a sensitivity of 79.3% (96 of 121 problems correctly identified) and a specificity of 97.8% (rejection of 1525 of 1559 problems). In contrast, the televideo assessment had a sensitivity of 86.4% (51 of 59 problems correctly identified) and a specificity of 88.2% (rejection of 30 of 34 problems). These findings suggest that both zero- and high-tech methods of remote assessment can potentially be used to identify accessibility problems and home-modification needs. As a result, remote home assessment, which can reach a much broader audience than traditional in-home assessment, has the potential to enable people with MS to live more independently in their own homes.

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(S69) Body-Weight Support Treadmill Training in Patients with Multiple Sclerosis

Purpose: Determine whether body-weight support treadmill training (BWSTT) improves gait velocity and dynamic balance in people with multiple sclerosis (MS).

Design: Single-subject A1B1A2B2 time-series research design study with 4 weeks for each phase.

Methods: Subject 1 was a 62-year-old woman with relapsing-remitting MS since 1992 and an Expanded Disability Status Scale (EDSS) score of 4.0. Subject 2 was a 59-year-old woman with relapsing-remitting MS since 1980 and EDSS 4.0. *Instrumentation/tests:* Subjects completed demographic health forms on intake. Questionnaires completed once in each phase included 1) Modified Fatigue Impact Scale (MFIS), 2) Health-Related Quality of Life Short Form-36 (HRQOL SF-36), and 3) Activities-Specific Balance Confidence (ABC) Scale. Timed functional tests performed once in each phase were a 6-minute walk test (6MWT) to measure endurance and a sit-to-stand test (STS) to measure functional lower-extremity strength. Gait velocity measured by the GAITRite System and dynamic balance measured by the timed pick-up test were performed each session. Subjects reported rating of perceived exertion (RPE) each training session.

Statistical Analysis: Serial dependency determined by one and two lag autocorrelations of phase A1 and A2 data were not statistically significant at $P = .05$. The 2-standard-deviation bandwidth method was performed for primary analysis of gait velocity and dynamic balance. Secondary analysis of strength (STS), endurance (6MWT), fatigue (MFIS), HRQOL (SF-36), and balance confidence (ABC) included descriptive statistics and graphic analysis.

Results: Gait velocity improved significantly in both subjects during both intervention phases. Dynamic balance improved significantly during the first intervention phase for subject 1. Dynamic balance for subject 2 did not show statistical significance.

Discussion/Conclusion: BWSTT is an effective treatment to improve gait velocity in patients with MS. The timed pick-up test may not be sensitive enough to detect meaningful improvement in dynamic balance.

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(S70) Natural Course of Multiple Sclerosis in Novosibirsk, Russia

We observed a group of multiple sclerosis (MS) patients who were treated with corticosteroids only during exacerbation and had received metabolic and symptomatic therapy. The aim of our research was to study the natural course of MS. We examined 93 MS patients with MS course ≥ 5 years on the last visit. The average duration of observation was 11.9 years. Ninety of these patients had remitting MS, 2 had primary progressive MS, and 1 had relapsing-remitting MS. The average age at onset was 23.45 ± 6.99 years. The average duration of disease was 18.21 ± 8.78 years.

Results: At the time of observation, 62 MS patients (66.7%) had reached progression in 11.42 ± 7.47 years. The average time for achievement of progression in women was 11.92 ± 7.73 years and in men 8.44 ± 4.21 years. Patients in the group with early onset (67.7%) reached 3 Expanded Disability Status Scale (EDSS) through 13.81 ± 9.42 years and 48 (78.7%) in the group with typical onset through 10.56 ± 6.31 years. The patients with brainstem symptom onset had severe disability through 13.81 ± 9.42 years and the patients with polysymptom onset through 15.13 ± 8.87 years. Fourteen of 25 MS patients (56%) with the first remission (within 12 months) reached progression through 8.00 ± 4.04 years and among 38 with remission for >3 years through 15.26 ± 6.85 years.

Conclusions: Progression starts after achievement of stable moderate disability. Men reach 3 EDSS and progress more quickly than women. MS patients with brainstem symptom onset have the most benign development of disease. The greater the interval between the first and second exacerbations, the later the disease gains progression and severe disability.

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(S71) Burn Injury: Risk for Patients With Multiple Sclerosis

Objectives: Describe burn injuries and their circumstances in patients with multiple sclerosis (MS) and identify the vulnerabilities of MS patients that put them at risk for burns.

Design/Methods: We identified eight patients seen at our MS clinic who had experienced significant burn injuries. Patients either identified themselves as having had a burn or a burn was identified at the time of their examination.

Results: Four patients acquired burns associated with drinking hot liquids or preparing hot foods. One patient each had burns from a cigarette, a car radiator, a hot clothes iron, and soldering metal. The patients' neurological deficits included paraparesis, cerebellar tremor, numbness of the dominant hand, and significant visual impairment. Only one patient had significant cognitive deficits. Two patients did not initially realize the severity of their burns. In one, medical care was delayed for days. One patient required skin grafting.

Conclusions: MS patients may be particularly vulnerable to burn injury because of primary, secondary, and tertiary factors. Primary factors include sensory loss; motor weakness, incoordination, or tremor; and visual and cognitive impairment. Secondary factors include fatigue, impaired reaction time, and lack of focus/multitasking ability. Tertiary factors include maladaptive approaches to task performance. Factors may overlap. Patients may not recognize the severity of their burn injury, potentially leading to delay in treatment. Increasing patient awareness of potential for burn injury and reviewing individual risk may prevent serious injury.

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(S72) Older Veterans With Multiple Sclerosis: Similarities, Differences, and Policy Implications

Research on older men has been neglected in multiple sclerosis (MS) literature. The predominant focus of the literature is the younger MS patient because MS usually presents in younger adults. Besides, three-quarters of MS patients are women. Available literature shows key differences between younger and older MS populations regarding comorbidity and service utilization and differences between male and female MS patients. Understanding of consumption of health care services in a heterogeneous population is often confounded by sex, age, employment-based insurance, access to health care, and health insurance limitations. The primary aim of this study was to examine similarities and differences between younger and older male veterans with MS and to compare findings with published literature on characteristics and health care consumption. This study uses Veterans Health Administration (VHA) administrative data from 1998 to 2003. The proportion of men <65 years old (77%, $n = 11,599$) to >65 years old (23%, $n = 3497$) with confirmed MS remained unchanged over the study period. Pooled estimates for the 6 years showed that older MS veterans incurred on average \$13,315 in total health care costs per patient per year, compared to \$11,292 for those <65 years old. Among older veterans, about 25% had an average of 2 inpatient admissions per year at a cost of \$33,219 (1.9 and \$26,461 for age <65 years). Outpatient utilization and costs

were similar for both groups (17 visits with 27 encounters at \$3384 for age >65 years, 17 visits with 26 encounters at \$3105 for age <65 years). Younger veterans had higher annual pharmacy costs (\$2407 vs \$1553). Within the older MS group, unadjusted costs increased with age. The study presents adjusted estimates controlling for age, sex, and comorbidities using multivariate analysis. The observed differences have implications for health care policy for veterans with MS.

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(S73) Glatiramer Acetate Therapy Adherence: Impact of Injection Competence

Background: Adherence to therapy for multiple sclerosis (MS) is important for positive long-term patient outcomes. A multicenter, open-label, two-arm prospective study (the READY trial) was conducted to evaluate adherence to therapy with glatiramer acetate over the first year.

Objectives: Evaluate the role of self-injection competence on adherence to glatiramer acetate.

Methods: Thirty-two study sites enrolled 233 MS patients new to treatment with glatiramer acetate, including 145 with no prior immunomodulatory therapy experience (tx-naive) and 88 who previously used interferon-beta therapy (tx-experienced). Nurse assessments of self-injection competence were conducted at three study visits during the first 90 days of the therapy: days 1, 30, and 90. Thereafter, patients were followed by the Shared Solutions patient support program. Logistical regression analysis was used to determine the impact of variables including self-injection competence on adherence to glatiramer acetate.

Results: At baseline, there was no significant difference in nurse-assessed self-injection competence between the tx-naive and tx-experienced groups. However, the tx-naive group adherent at 90 days was rated with significantly greater competency on first self-injection than those who were nonadherent ($P < .001$). Among the tx-experienced group, there were no differences in first self-injection competency between those who were adherent and nonadherent at 90 days. Therapy adherence at 90 days was 86% for both tx-naive and tx-experienced patients, and at 12 months, it was 83.5%. The most significant predictors of adherence included 1) higher self-injection competency rating at day 1 (OR = 1.23, $P = .007$) and 2) greater improvement in self-injection competency in the first 30 days (OR = 1.71, $P = .001$).

Conclusions: Among tx-naive patients, nurse assessments of self-injection competency at day 1 and greater improvement in self-injection competency in the first 30 days of therapy were significant predictors of adherence to glatiramer acetate at 90 days and 1 year.

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(S74) Survey of Issues Related to Cognitive Dysfunction Among Large Group of People With Multiple Sclerosis

Objective: Collect data regarding cognitive dysfunction among a group of people with multiple sclerosis (MS).

Background: Cognitive dysfunction is among the most common and debilitating symptoms affecting people with MS, yet there are relatively few data regarding perceived prevalence, perceived efficacy of various treatment strategies (especially unconventional therapies), frequency of potential confounders, and perceived impact.

Design/Methods: Using email, a registry (www.mscom.org), and a Web-based survey, we collected self-reported data related to cognitive dysfunction from 1466 people with MS.

Results: Of the respondents, 74% reported that they currently experienced cognitive problems. Of the five domains surveyed, the most frequently perceived to be affected were, in order of frequency, memory (90%), speed of information processing (86%), problem-solving ability (79%), communication (77%), and comprehension (69%). Other than MS, the following factors were most frequently identified as contributing to cognitive difficulties: fatigue (89%), anxiety (56%), sleep problems (54%), age (50%), depression (50%), pain (35%), and medication side effects (32%). Of the 54 interventions surveyed, the following 10 were most often perceived to be helpful for cognitive dysfunction: music therapy (75%, $n = 51$), modafinil (Provigil) (71%, $n = 113$), passive cooling garments (70%, $n = 115$), donepezil (Aricept) (68%, $n = 25$), passive cooling techniques (67%, $n = 343$), yoga (63%, $n = 239$), pemoline (Cylert) (59%, $n = 44$), aerobic exercise (58%, $n = 352$), cognitive rehabilitation therapy (57%, $n = 81$), and coffee/caffeine (57%, $n = 497$). Of those who perceived cognitive dysfunction, 48% reported that cognitive difficulties interfered with their ability to earn a living, 42% reported that cognitive difficulties interfered with relationships, and 24% reported that cognitive difficulties interfered with driving. Of those who reported driving difficulties, 8% had had a driving evaluation.

Conclusion: Among our respondents, cognitive dysfunction was reported by 74%. Interventions perceived to be helpful included both pharmacological interventions, especially modafinil (Provigil) and donepezil (Aricept), and nonpharmacological interventions, especially music therapy and passive cooling garments.

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(S75) Paroxysmal Syndromes: First Symptoms of Multiple Sclerosis

Introduction: Paroxysmal syndromes are often frequent and repeated stereotypical symptoms that are generally triggered by movement or sensory stimuli and can be the first symptoms of multiple sclerosis (MS).

Objective: The authors describe the uncommon cases of beginning symptoms of MS. Paroxysmal vertigo, Lhermitz's sign, and epileptic seizures were the onset symptoms of MS.

Results: Three case reports are illustrated as rare forms of onset of MS, with supportive MS abnormalities of magnetic resonance imaging, cerebrospinal fluid, and visual evoked potential.

Conclusion: Three cases of uncommon onset of MS were clinical presentations of a symptom complex that was related to a single site in the nervous system (clinically isolated) with no clinical evidence of multiple lesions in space and time.

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(S76) Long-Term Effects of Subcutaneous Interferon Beta-1a on Magnetic Resonance Imaging Activity on Multiple Sclerosis

Background: Subcutaneous (sc) interferon (IFN) beta-1a (Rebif) produced significant reductions in magnetic resonance imaging (MRI) activity and T2 burden of disease (BOD) in patients with relapsing-remitting multiple sclerosis (MS) who participated in the Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis (PRISMS) study. Patients have now been followed for up to 8 years of treatment.

Objective: Investigate long-term effects of sc IFN beta-1a on MRI measures of efficacy.

Methods: In PRISMS, patients were randomized to IFN beta-1a 44 or 22 µg sc or placebo 3 times weekly for 2 years. Patients continued active therapy or, if originally treated with placebo, were randomized to IFN beta-1a 44 or 22 µg sc (late-treatment group) for years 3–4. During years 5–6, patients continued blinded treatment, switched to open-label treatment, or withdrew. At long-term follow-up (LTFU), a cranial proton-density (PD)/T2-weighted MRI scan was performed. BOD was defined as the summed cross-sectional area of lesions in T2 scans. Brain parenchymal volume (BPV) was derived by subtracting each patient's cerebrospinal fluid volume from the intradural volume and normalizing to the whole brain ratio.

Results: Of 560 patients originally in PRISMS, 349 had MRI scans at both baseline and LTFU. T2 BOD median increase was significantly lower in patients originally treated with 44 µg than the late-treatment group (5.0 vs 24.5; $P = .002$). The 44-µg group had greater BPV reduction during the first 24 months than the 22-µg or placebo group. BPV reduction did not differ among treatment groups from baseline to LTFU.

Conclusions: Despite limitations inherent in any long-term study, these data suggest that early treatment with high-dose, high-frequency sc IFN beta-1a had significant, durable benefit on T2 BOD up to 8 years. Differences in BPV reduction between the first 24 months and LTFU may arise from anti-inflammatory effects of IFN treatment resulting in pseudoatrophy.

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(S77) Prevalence and Correlates of Tobacco and Hazardous Alcohol Use Among Veterans With Multiple Sclerosis

Objectives: The Veterans Health Administration provides care to more than 20,000 veterans with multiple sclerosis (MS). Little is known about health behaviors such as tobacco and alcohol use that may contribute to overall physical and mental functioning. The purpose of this study is to describe tobacco and alcohol use patterns and self-report of unmet treatment needs among veterans with MS.

Methods: Linkage of two existing US Department of Veterans Affairs (VA) national databases: Data obtained from the Office of Quality and Performance 1999 Large Health Survey and the newly formed VA MS Centers of Excellence Data Repository, which includes veterans with diagnosed MS (ICD 340) through fiscal year 2004. Linkage produced a sample of individuals with MS who returned surveys ($n = 3540$), including a 20% random subsample ($n = 677$) who completed a more extensive assessment of tobacco and alcohol use. Multivariate logistic regression identified factors associated with tobacco and hazardous alcohol use.

Results: Among survey respondents with MS, 28.2% endorsed current smoking, and 17% reported drinking 5 or more drinks per occasion at least once in the past month (hazardous drinking). Of those responding to the extended survey, 18.5% reported smoking 10 or more cigarettes per day, and 5.7% endorsed 14 or more drinks per week. Many respondents completing the extended survey reported not getting needed services for smoking (57.6% of current smokers) or alcohol (40% of hazardous drinkers) in the past year. Tobacco use was associated with younger age, being unmarried, living alone, higher levels of physical pain, and higher levels of depression. Hazardous alcohol use was associated with younger age, being male, being nonwhite, and living alone.

Implications: Rates based on the 1999 survey response show considerable tobacco and hazardous alcohol use among individuals with MS and correspond with those found in larger veteran samples. Participants reported substantial unmet need for services. This study represents the first effort toward a national assessment of tobacco and alcohol misuse prevalence among veterans with MS. Future research is needed to identify and address these health behaviors that are often overshadowed in a population with considerable health care needs.

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(S78) Understanding Pain and Pain Interference in Veterans With Multiple Sclerosis

Objectives: Only within the past decade have pain syndromes been recognized as important and disabling symptoms of multiple sclerosis (MS). The purpose of this study is to describe pain, pain interference with daily activity, and associated risk factors among a large sample of veterans with MS receiving services in the US Department of Veterans Affairs (VA) health care system.

Methods: Linkage of two existing VA national databases: Data obtained from the Office of Quality and Performance

1999 Large Health Survey (LHS) and the VA MS Centers of Excellence Data Repository, which includes veterans with diagnosed MS (ICD 340) through fiscal year 2004. Linkage produced a sample of individuals seeking services for MS who completed surveys ($n = 3450$). Pain intensity and pain interference with normal activity were assessed over the past 4 weeks with the two body pain scale items from the SF-36 (veteran version) included on the LHS. Hierarchical multiple regression was used to identify factors uniquely associated with pain interference.

Results: Body pain was rated as severe or very severe by 34% of survey respondents with MS (mean [SD] = 3.91 [1.33]), with almost half (49.4%) stating that pain interfered quite a bit or extremely with normal activities (3.27 [1.31]). After controlling for sex, race, age, and education level, pain interference was unrelated to living alone but was positively associated with pain intensity, higher levels of depression, and lack of exercise. Living alone, exercise, and depression failed to moderate the relationship between pain intensity and pain interference (all interactions were nonsignificant). Of veterans with MS and pain, 80% stated they intended to use the VA as a primary source of health care in the future.

Implications: Pain is a common secondary disability among veterans with MS. Pain interference with life functioning is a complex phenomenon associated with psychosocial factors such as physical activity and depression above and beyond pain intensity alone. Most veterans with MS and pain look to the VA as their primary health care resource to address these issues. Correlates of pain such as physical activity and depression may help target interventions to reduce both pain and pain-related disability.

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(S79) Experiencing Chronic Pain: Those in Continuing Care Who May Be at Risk

Background: At least two-thirds of people with multiple sclerosis (MS) may experience pain. Although scientific literature is emerging, little exists regarding the experience of chronic pain for those who reside in continuing care.

Objective: The purpose of this study was to determine factors associated with experiencing chronic pain for MS patients living in continuing care.

Methods: Forty-one MS patients living in seven facilities in a metropolitan area were interviewed about chronic pain, demographic/socioeconomic status, symptoms, activities of daily living, disability level (Expanded Disability Status Scale), and psychological/social factors. Logistic regression models were used to identify the factors associated with ever having experienced chronic pain and currently experiencing chronic pain.

Results: As anticipated, the disability level of the participants was severe ($\mu = 8.0$). The average age of the participants was 60 years (range 38–89 years), and most were women (61%). Fifty-six percent of the sample had experienced chronic pain at some time, and of those, 42% were currently in pain. Greater fatigue ($P = .034$) and urinary infections ($P = .049$) were associated with ever having experienced chronic pain, as well as having fewer family mem-

bers visit ($P = .037$). Participants experiencing these three factors were 32% more likely to have experienced chronic pain ($P = .007$). Participants currently experiencing chronic pain were more likely to be unmarried ($P = .044$) and rated their health to be poorer than 1 year ago ($P = .058$). Participants experiencing these two factors were 47% more likely to be currently experiencing pain ($P = .016$). Muscle spasms and burning/pins/needles sensations were also associated with the dependent variables, perhaps representing the type of pain being experienced.

Conclusions: These results highlight the importance of familial/social support and diligent attention to MS-related symptoms. These findings may assist health care providers in identifying continuing-care patients who may be at risk for experiencing chronic pain, permitting appropriate and timely interventions.

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(S80) Assessment for Ability to Self-Inject of Patients With Relapsing-Remitting Multiple Sclerosis Treated With Avonex

Background: Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system. Adherence to immunomodulatory therapy for MS is important for positive long-term patient outcomes. This single-center study was performed in patients with MS on treatment with intramuscular interferon beta-1a (Avonex). The study's objective was to assess the rate and reasons of patients as able or not able to self-inject the medication.

Method: We retrospectively analyzed patients with MS on treatment with Avonex. Patients were between 18 and 75 years old, had relapsing-remitting MS, and started treatment with Avonex according to manufacturer's recommendations. All patients were from the regional center for MS in the Czech Republic. Evaluated parameters included age, sex, and reasons for patient's inability to self-administer the medication. Disease severity was measured using the Expanded Disability Status Scale (EDSS). Patients were considered by self-report as able or not able to autoinject.

Result: A total of 33 patients (21 women, 12 men) were evaluated. The average age was 38.2 years, and the mean EDSS score was 3.2. Fifty-eight percent were identified as able. These patients had a mean EDSS of 2.5, which was significantly lower than the 42% of patients not able to autoinject (mean EDSS 3.5). The main reasons for inability to self-administer the medication were anxiety about the injection itself (43%), technical factors related to disability (36%), and pain during the injection (21%).

Conclusion: This study demonstrated a significant interaction of neurological disability on the ability to self-inject Avonex. Awareness of these data may improve adherence with long-term therapy.

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(S81) Treatment Adherence in Canadian Patients With Relapsing Multiple Sclerosis

Background: Disease-modifying agents (DMAs) are important in the treatment of patients with multiple sclerosis (MS). To have a clinical effect, patients must receive the DMA. The purpose of this observational study was to assess treatment adherence in MS patients who were treated with the same DMA for at least 3 months.

Methods: Patients with MS and an Expanded Disability Status Scale score of <6 receiving interferon beta-1a (IFN β -1a) by subcutaneous (SC) or intramuscular (IM) injection, IFN β -1b, or glatiramer acetate (GA) for >3 months were sent a letter of explanation and a consent form by mail. Patients who returned the form were called by an MS nurse and answered a questionnaire via telephone.

Results: Of 97 patients, 25 (26%) received IM IFN β -1a, 29 (30%) SC IFN β -1a, 35 (36%) GA, and 8 (8%) IFN β -1b. Because so few patients receiving IFN β -1b were recruited, they were excluded from further analyses. Demographic characteristics were similar among the groups. A high percentage of patients (96% IM IFN β -1a, 97% GA, 91% SC IFN β -1a) reported taking their medication as prescribed; however, 16, 31, and 37% of patients reported that they sometimes forgot an injection. Approximately half of patients indicated that injections were not easy for them, with fear of needles (23% IM IFN β -1a, 44% GA, 25% SC IFN β -1a) and injection pain (39% IM IFN β -1a, 67% GA, 75% SC IFN β -1a) cited most commonly. Approximately two-thirds of patients in each group reported feeling better since starting therapy. There were no statistical differences for any endpoint among the groups due to small sample size.

Conclusions: Patients in this study reported high levels of adherence with prescribed therapy. However, there were barriers to adherence including forgetting to administer an injection, fear of needles, and injection pain. To maximize clinical effects of DMAs, it is worthwhile for health care providers to discuss adherence in general and these issues specifically with their patients on injectable DMAs.

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(S82) NK Cell Degeneration in Multiple Sclerosis and Experimental Autoimmune Encephalomyelitis

Emerging evidence indicates that natural killer (NK) cells play an important and complex role in autoimmune diseases. Humans with autoimmune diseases such as multiple sclerosis (MS) often have reduced NK cell numbers and compromised NK cell functions. Mechanisms underlying this NK cell degeneration and its biological significance are not known. We demonstrated that patients with the relapsing-remitting form of MS have selective reduction in CD56⁺ NK cell subset with unique patterns of activation receptor expression, proliferation, and cytokine release. Removal of CD56⁺ NK cells did not promote T-cell proliferation to myelin antigens. Using two experimental MS models in C57BL/6 and SJL mice with distinct disease course, we have identified that the compartment size and function of NK cells were strikingly different in these

two models during the course of encephalomyelitis (EAE). In the first model, we showed that NK cells undergo expansion during the initiation of autoimmunity to a myelin antigen myelin-oligodendrocyte glycoprotein peptide, followed by significant degeneration concomitant with the establishment of the autoreactive T-cell response. Furthermore, NK cell degeneration was mediated by interleukin 21 derived from autoreactive CD4⁺ T cells, and MOG peptide-immunized interleukin 21 receptor-deficient mice with competent NK cells developed increased neurological disability. Collectively, our current results suggest that 1) NK cells do not inhibit autoreactive T-cell response in MS patients, 2) NK cells may contribute to distinct EAE phenotype in C57BL/6 and SJL mice, and 3) NK cell degeneration may signify the transition from innate immune triggering to emergence of autoreactive T cells, serving as a means evolved by the immune system to control excessive autoimmunity.

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(S83) Persistence of Side Effects From Multiple Sclerosis Disease-Modifying Therapy Over 5 Years

Background: Common side effects of multiple sclerosis (MS) disease-modifying therapies (DMTs) are well known, but their frequencies and persistence in clinical populations are poorly understood. The Calgary MS Treatment Outcomes Study described long-term safety and outcomes in a population-based cohort treated with DMT. In this study, participants completed questionnaires at 3, 6, and 12 months, and then annually.

Methods: Patient-reported side effects from questionnaires returned before May 2005 were tabulated at each follow-up period by treatment group: glatiramer acetate (GA) or interferon (IFN).

Results: This analysis was based on data from 963 patients who completed 3177 questionnaires over 7 years (1812 on GA, 1365 on IFN). The average return rate was 73.2%. Participants included 78% women and 22% men. Mean age was 39.8 years. Mean disease duration was 7.9 years. Three-month side effect rates by group (GA vs IFN) were injection pain (41.7 vs 53.3%), flulike symptoms (15.4 vs 80.7%), headache (14.6 vs 55.2%), injection-site reactions (12.3 vs 18.1%), and postinjection reactions (14.9%, GA only). Side effect rates in the GA group remained similar between 6 and 60 months except for injection-site reactions, which decreased to an average of 6.8%, and postinjection reactions, which increased to an average of 25.2%. Rates of injection pain and injection-site reactions changed little over 5 years in IFN patients, but flulike symptom rates decreased to 54.3% at 6 months and then averaged 44.76% at later intervals, and headache rates decreased to 44.1% at 6 months and then averaged 29.1%.

Conclusions: Although side effects continued at a substantial rate, discontinuation due to side effects ranged from 15 to 20% over 5 years, suggesting that side effects are usually tolerable. These data should help patients better understand

expected side effect rates and persistence for each treatment type and help caregivers target side-effect management.

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(S84) Effect of Combination Modafinil (Provigil) Plus Interferon β -1a (Avonex) Treatment on Quality of Life: Final Study Results

Objective: Demonstrate that combination therapy with modafinil and intramuscular (IM) interferon β -1a (IFN β -1a) in patients with multiple sclerosis (MS) is safe and improves quality of life (QOL).

Background: IFN β -1a treatment of MS slows progression of cognitive dysfunction, but patients may continue to progress. Studies have demonstrated the benefits of using modafinil as adjunctive therapy for MS-related fatigue, but no data exist on whether it improves cognition and QOL. Cognitive findings from this study (published elsewhere) indicated that the addition of modafinil to IFN β -1a had a beneficial effect on cognition in relapsing-remitting MS patients. The final analysis of QOL data are presented.

Design/Methods: This was a multicenter, randomized, parallel-group study. MS patients taking IM IFN β -1a completed an attention-screening battery. Those with significant attention problems continued receiving IFN β -1a and were randomized to receive either modafinil (200 mg/day) or no additional treatment. Subjects underwent a neuropsychological battery at baseline, 2 months, and 4 months. Specific measures of QOL included the SF-36, Multiple Sclerosis Quality of Life Inventory, and Epworth sleepiness scale. Multiple analyses of variance determined between-group differences in safety and QOL at 2 and 4 months.

Results: Fifty-nine patients were enrolled (combination, 29; IFN β -1a alone, 30); 48 patients completed the 4-month evaluation. Dropouts were balanced between the two groups and most often due to patient unwillingness to complete three full neuropsychological evaluations in a short period. There were no significant differences in demographics between groups. Side effects of combination therapy were mild and no different from those described in the package inserts. Compared with the IFN β -1a-alone group, patients in the combination-therapy group reported significant improvements in mood and QOL at 2 and 4 months.

Conclusions: In this study, treatment of cognitive symptoms with modafinil and IFN β -1a was safe and improved QOL.

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(S85) Reduction in Pain Intensity in Multiple Sclerosis Patients With Involuntary Emotional Expression Disorder Treated With AVP-923

Objective: Evaluate pain intensity levels in multiple sclerosis (MS) patients with involuntary emotional expression disorder (IEED) treated with AVP-923 (capsules containing dextromethorphan [30 mg] and quinidine [30 mg]).

Background: IEED is a condition characterized by the disinhibition of emotional expression secondary to neurological disease or injury. Episodes typically involve involuntary emotional expressions such as laughing, crying, or related facial features that are incongruent or exaggerated in relation to underlying mood. IEED is associated with neurological diseases such as MS, amyotrophic lateral sclerosis, Parkinson's disease, dementias, and neurological injuries such as stroke and traumatic brain injury. IEED is also commonly known as emotional lability, pathological laughing and crying, and pseudobulbar affect.

Methods: MS patients with IEED ($n = 150$) from a phase III study of AVP-923 were included in the analysis. Patients were randomized to receive AVP-923 ($n = 76$) or placebo ($n = 74$) at study onset. Pain intensity scores were obtained by all patients at initiation of study. Patients reported amount of pain experienced within the previous 24 hours using a 5-point Likert pain intensity rating scale (none = 0, mild = 1, moderate = 2, severe = 3, extreme = 4) at days 1, 15, 29, 57, and 85 of study. MS patients taking AVP-923 were then stratified into two groups for this analysis: those with baseline pain intensity scores <2 ($n = 36$) and those with baseline scores >2 ($n = 35$).

Results: MS patients taking AVP-923 reported significantly greater reductions in pain intensity than MS patients on placebo (-0.4 vs -0.2 , $P = .0271$). Patients on AVP-923 with moderate to extreme pain (scores >2) had significantly greater improvements in pain intensity at all time points than patients with mild to moderate pain (scores <2).

Conclusion: MS patients with IEED reported significant improvements in pain intensity on treatment with investigational therapy AVP-923.

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