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Risk factors for non-adherence to disease-modifying therapy in pediatric multiple sclerosis

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Ethical approval and consent to participate
All patients provided informed consent to participate in this research. Because the MS patients were under the age of 18 years, for those patients who did not have the capacity to consent for themselves, their parent provided consent for both the patient and the parent.

Availability of data and supporting materials
Supporting documentation for the study findings is provided in manuscript data and supplementary tables. Scientists wishing to gain access to the study data may contact the last author (E.A.Y.), who will consider such requests on a case-by-case basis, subject to the scientific rigor of the proposed research question.

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Abstract

Background: Adherence to disease-modifying therapies (DMTs) in pediatric multiple sclerosis (MS) is not well understood. We examined the prevalence and risk factors for poor adherence in pediatric MS.

Methods: This cross-sectional study recruited youth with MS from 12 North American pediatric MS clinics. In addition to pharmacy-refill data, patients and parents completed self-report measures of adherence and quality of life. Additionally, patients completed measures of self-efficacy and well-being. Factor analysis and linear regression methods were used.

Results: A total of 66 youth (mean age, 15.7 years) received MS DMTs (33% oral, 66% injectable). Estimates of poor adherence (i.e. missing >20% of doses) varied by source: pharmacy 7%, parent 14%, and patient 41%. Factor analysis yielded two composites: *adherence summary* and *parental involvement in adherence*. Regressions revealed that patients with better self-reported physical functioning were more adherent. Parents were more likely to be involved in adherence when their child had worse parent-reported PedsQL School Functioning and lower MS Self-Efficacy Control. Oral DMTs were associated with lesser parental involvement in adherence.

Conclusion: Rates of non-adherence varied by information source. Better self-reported physical functioning was the strongest predictor of adherence. Parental involvement in adherence was associated with worse PedsQL School Functioning and lower MS Self-Efficacy-measured confidence in controlling MS.

Keywords

Pediatric multiple sclerosis; adherence; parent; psychosocial; quality of life; protective factors

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Introduction

Pediatric-onset multiple sclerosis (MS) patients are increasingly prescribed disease-modifying therapies (DMTs) at earlier stages of disease.[1] The moderate to high impact of DMT on clinical course reported in clinical trials is mitigated in real life by adherence to medication. In clinic-based adult MS populations, 30%–70% of patients prematurely discontinue DMTs,[2] and 25%–59% are consistently non-adherent with their medications.[3–7] Some studies have indicated high rates of non-adherence in pediatric MS.[1,8] One of these studies (n = 258) revealed that 44% of children do not remain on the first therapy prescribed: one-third discontinue treatment because of poor tolerance or adherence, while the remainder are prescribed an alternative therapy due to breakthrough disease.[1] In a study of 30 adolescents with MS, 37% were non-adherent, primarily due to forgetting to take their medication.[9] The rate of non-adherence in MS youth may increase with disease duration, as evidenced by an increasing rate of non-adherence over a 5-year period of treatment (non-adherence rates of 18%, 25%, 41%, 50%, and 62% at years 1, 2, 3, 4, and 5, respectively).[8] Ultimately, almost half of the patients studied discontinued DMTs altogether.[8]

Evaluating adherence can be challenging methodologically, as all sources of information about adherence have their own limitations. Patient reports underestimate non-adherence as compared to an electronic monitoring device.[10] While parents are the logical source of witnessed adherence reporting, the patient–parent dyad may influence adherence itself. Young children typically receive injections from their parents and are supervised when ingesting oral medications. Adolescents, however, may seek independence and may even resent parental reminders regarding DMT use.

Physicians have been found to miss indicators of poor adherence in patients.[11] This may reflect the topic not being broached in clinical encounters. Furthermore, patients—and youth in particular—are not forthcoming about their non-adherence when speaking to their own doctors, or if doing so in the company of their parents.

Objective measures of adherence, while ostensibly more accurate, are also limited depending on the method used. Electronic devices, such as those that record the number of times a pill bottle is opened or the number of needles disposed of in a safety container, accurately record DMT access but do not necessarily capture the actual ingestion or injection frequency. Patient- or parent-recorded logs, while encouraging documentation, suffer from the same issues as well as requiring adherence to documentation as well as therapy administration.

Psychosocial and environmental factors may influence medication adherence in children and youth with MS. Cognitive difficulties, socioeconomic status (e.g. lower education),[12] high-risk behaviors (e.g. high levels of alcohol consumption), longer disease duration, and physical disability status are associated with non-adherence in adult MS.[6] Psychological morbidity (e.g. mood or anxiety disorders) has also been associated with poor adherence,[13] while higher levels of self-efficacy, quality of life, and perceived cognitive functioning have been associated with better adherence.[4,14] Whether these or other factors influence adherence in children and youth remains to be determined.

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Given the increasing prescribing and range of therapeutic options, increased efficacy, and sizeable cost of DMTs, it is timely to evaluate injectable and oral medication adherence and reasons for non-adherence in youth with MS and to examine risk factors for poor adherence.

Methods

Sample

This multi-site study recruited English-speaking youth with MS, age at enrollment between 10 and 18 years, from 12 pediatric MS clinics in North America from October 2013 to January 2016. Eligible patients had a diagnosis of MS as per the most recent McDonald and International Pediatric MS Study Group criteria[15,16] and had been taking an oral or injectable DMT for MS for at least 6 months. Pediatric MS patients receiving intravenous DMT (e.g. natalizumab) were not included. For each eligible participant, at least one parent or guardian was required to be fluent in English and willing to complete the parental questionnaires. Written informed consent was obtained from the parent, and assent was obtained from participants as appropriate. The study was reviewed and approved by the institutional review boards at each site.

Procedure

This study reports baseline data from a randomized trial testing an intervention to improve adherence. We collected demographic information and the Patient-Determined Disease Steps (PDDS)[17] to assess perceived MS-specific disability. Recruited and consented participants (patients and parents) were sent an email with a link to a survey using our Health Insurance Portability and Accountability Act (HIPAA)-compliant and secure web-based survey engine (www.surveygizmo.com). The measures included in the web survey are listed below and described in the supplementary text.

Since several of the measures used in this study had been heretofore used primarily with adults, we pre-tested all the measures with 10 youth (age 10–18 years) seen in clinic prior to initiating data collection for this study. These subjects were also asked to complete the study questionnaires and to provide feedback as to whether the questionnaires were understandable. For this study, we retained only those tools that pre-testers were able to complete and endorsed as understandable.

Measures

The supplementary text provides full detail on the measures used in this study. Briefly, *adherence* was measured using pharmacy-refill data (past 12 months) collected by each site's research assistant, the self-and parent-reported Morisky Adherence Measure,[18] and Multiple Sclerosis Treatment Adherence Questionnaire (MSTAQ).[19] Parental involvement in DMT administration was assessed with three items tracking the proportion of time the parent reported (1) reminding the child to take her or his DMT, (2) being present when the child took her or his DMT, and (3) administering the child's DMT.

Psychosocial risk factors were measured using the following self-report measures: the patient and informant versions of the PedsQL 4.0,[20] the patient-reported Multiple Sclerosis

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Self-Efficacy Scale (MSSE),[21] and three subscales from the patient-reported Ryff Scales of Psychological Well-Being.[22] Neurocognitive functioning was assessed using the parent-report version of the Multiple Sclerosis Neuropsychological Screening Assessment Questionnaire (MSNQ).[23]

Statistical analysis

We examined correlations among the continuous measures of adherence. We defined non-adherence for specific analyses as receiving less than 80% of expected doses. Principal component factor analysis was used to create orthogonal composite scores for different aspects of adherence. Due to missing data on several MSTAQ subscales, we included in the factor analyses only those subscales on which we had complete data: the parent-reported proportion missed doses and parent- and patient-reported barrier scores. Given the relatively small sample size of this study, two separate factor analyses (one for each presumed unidimensional construct) were implemented on item sets that were related on the basis of content (i.e. face validity). Unidimensionality was ascertained on the basis of all items loading higher than 0.40 on the first factor, with an eigenvalue greater than 1.0. Factor scores were created by standardizing measures, then multiplying the factor loading of items loading greater than 0.40 on the factor, and summing those weighted item scores. Alpha reliability coefficients were used to assess internal consistency reliability. Linear regression analyses began with univariable analyses to identify relevant predictors for each factor score. Backward stepwise regression was then implemented with a retention rule of $p <= 0.10$.

Our study has a sample size that has 80% power to detect medium to large effect sizes,[24] depending on the analysis and subgrouping. We report effect sizes when relevant rather than *p*-values. This approach enables one to interpret the magnitude of the detected effects and use it for planning future studies. We report results using Cohen's criteria for delineating small, medium, and large effects,[24] so that future researchers can plan studies to have the power to show *statistical* significance (Type I error rate (alpha) of 0.05, power (beta) of 80%) given the same detected effect sizes. All analyses were done using Stata 14.[25]

Results

Sample characteristics

Table 1 shows the demographic characteristics of the sample ($n = 66$ youth with MS and 66 parents). Table 2 shows the descriptive statistics for the patient- and parent-reported outcomes. On the basis of these data, the sample has a low level of MS-related disability (mean PDDS = 0.50 out of 8). Compared to published norms from healthy youth,[20] the sample's PedsQL scores were in the normal range for all subscales for both parent and patient reports with the exception of parent-reported school functioning, on which they were lower than healthy norms. Compared to published norms for adults on the MS Self-Efficacy scale,[21] the sample had similar mean scores. Compared to published values for adolescents using the Ryff Psychological Well-Being measure,[26] the sample showed lower values on all subscales.

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Estimates of adherence

Table 3 shows the adherence-related scores for the sample, and Figure 1 illustrates differences in esti-mates of non-adherence as a function of source of information. Based on pharmacy records for 12 months prior to study start, the sample received slightly fewer than the expected number of refills (mean of 0.95 out of 1.0), and 7% of the sample ($n = 4$) were non-adherent (i.e. received less than 80% of expected refills). On the basis of the parent report, the sample missed an average of 10% of DMT doses over the past 28 days, and 14% ($n = 8$ patients) were non-adherent. Parents reported reminding their child a median of half the time, being present for the DMT doses a median of 75% of the time, and administering the medication a median of 25% of the time (Table 3). Parents reported an average Morisky score reflecting medium adherence (score of 6 or 7 out of 8), with 28% of the sample scoring in the low-adherence range. In contrast, youth reported an average Morisky score reflecting low adherence, with 41% of the sample scoring in the low-adherence range, suggesting either that parents are not aware of their child's non-adherence and/or over-report compliance. The mean patient rating of the Barriers subscale was also slightly lower than the parents' rating of Barriers on the MSTAQ.

Relationships among adherence variables

Table 4 shows the inter-correlations among the adherence measures, with conditional formatting to show small, medium, and large effects using Cohen's criteria.[24] The largest correlations were between the parent being present and administering the child's DMT, and being present and parent-reported behavioral coping of the child. There was also a large correlation between parent- and patient-reported Morisky adherence scores. There were medium effect-size correlations among pharmacy refills and parent-reported missed doses, and with both sources of Morisky scores (i.e. parent- or patient-reported). Parent-reported missed doses and Morisky scores were moderately correlated, as were parent-reported behavioral coping and side effects. There were small effect-size correlations among the majority of the adherence measures (see Table 4).

Supplemental Table 1 shows the results of the factor analysis of the adherence variables, which was done for the purpose of data reduction. The first factor score—*adherence summary*—comprised pharmacy refills, proportion missed doses, and parent- and patient-reported Morisky adherence scores. The second factor score—*parental involvement in adherence*—comprised the parent reminding, being present, administering the DMT, and parent- and patient-reported barriers. These factors were orthogonal and thus not correlated with each other and had internal consistency reliability of 0.56 and 0.63, respectively, which is on the low end of accepted standards of 0.50–0.70.[27]

Predictors of adherence

Univariate models predicting adherence summary revealed that higher levels of patient-reported PedsQL Physical Functioning were significantly associated with better adherence; and there were trends suggesting that worse parent-reported cognitive functioning on the MSNQ and better patient-reported PedsQL Emotional Functioning were associated with better adherence (Supplemental Table 2). Univariate models predicting parental involvement in adherence revealed that worse parent-reported PedsQL School Functioning and

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Psychosocial Health Summary and worse patient-reported Self-Efficacy Function and Control were associated with more parental involvement in adherence, and there were trends suggesting that worse parent-related PedsQL Social Functioning and patient-reported PedsQL School Functioning were associated with more parental involvement in adherence (Supplemental Table 2).

Significant/trend variables from the univariate regression were then entered into the backward step-wise regression models. These models kept only patient-reported PedsQL Physical Functioning in the model predicting adherence summary, suggesting that the patients with better self-reported physical functioning were more adherent, and explaining about 6% of the variance (Table 5). Backward step-wise models predicting parental involvement in adherence kept only parent-reported School Functioning and patient-reported Self-Efficacy Control, suggesting that parents were more likely to be involved in medication administration when their child had worse school functioning and a worse sense of control over their MS ($R^2 = 0.31$; Table 5).

We examined initial differences in adherence between injectable and oral DMTs. Figure 2 shows the mean scores on adherence summary and parental involvement in adherence as a function of type of DMT used. While there was no difference between injectable and oral DMTs on adherence summary (Effect Size = −0.06), oral DMTs were associated with lower levels of parental involvement in DMT administration (Effect Size = 0.29). Of note, only 2 of the 20 oral DMT patients were concurrently enrolled in a clinical trial.

Discussion

Our study provides an estimate of medication adherence in youth with MS after oral DMTs were introduced to the MS treatment landscape. We found higher levels of medication adherence overall than past research on both youth and adults with MS. We did not find a difference in adherence between oral and injectable DMTs. Worse patient-reported physical functioning was the strongest predictor of lower medication adherence in our study. In contrast to past research on medication adherence which suggests that children over-estimate their levels of adherence,[9] our “objective data” (pharmacy-refill data) suggested higher rates of medication adherence than patient self-report.

Other studies have suggested that pharmacy-refill data may comprise a good surrogate measure of medication adherence in some adult populations, but its accuracy in children is unknown. For example, pharmacy-refill data were found to be superior to pill counting in predicting viral load in adult HIV-positive patients on therapy.[28] This was not found to be true in pediatric HIV patients; viral load could not be predicted using any single measure (caregiver report, pharmacy refill and appointment maintenance data), but rather use of all three above-mentioned data points were necessary to predict viral load, and, by inference, true medication adherence levels.[29] It is possible that multiple measures must be used in our population to establish true medication adherence levels.

Youth with MS reported lower levels of medication adherence than parent reports of their behavior. Further exploration of the discrepancy between parent, child, and pharmacy

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finding is necessary and will be corroborated in future studies exploring the use of an objective electronic monitoring device in this population. The discrepant reports may be in line with other studies that have found significant discrepancies between parent and child report of other MS symptoms.

We found a relationship between parental involvement in their child's DMT administration and the child's DMT adherence. Although there were no differences in adherence as a function of type of DMT, we did find mode-of-administration differences in how much parents were involved in their child's DMT administration, with less parental involvement with oral than injectable medications. Higher levels of parental involvement in medication adherence were associated with worse reported PedsQL School Functioning and a lower sense of control with regard to MS. These findings suggest that cognitive factors matter in pediatric MS adherence. In this study, the cognitive factors that were found to be important were parent-reported school functioning (i.e. paying attention, forgetting, keeping up with school work, missing school) and cognitive appraisal with regard to self-management (i.e. sense of confidence or self-efficacy in controlling the impact of their MS symptoms on their daily activities). In diabetes, another chronic disease population of adolescents who must also use injectable therapies, self-control in both parents and children has been shown to be associated with higher medication adherence in the adolescents.[30] Future research should evaluate the reasons for decreases in quality of life with increasing parental involvement in youth with MS. Based on the aforementioned work, it may relate to adolescent perceptions of self-control. Interventions might focus on these functional and psychosocial aspects of cognition to improve patient self-management and independence in managing their MS treatments.

Despite its strengths of collecting useful and pertinent data on a relatively rare patient population, the study's limitations should be acknowledged. First, the sample size is limited, which limits the types of analyses that can be done, the statistical power to detect clinically meaningful differences, and the generalizability of the findings. Also, as is typical in pediatric MS populations, patients had very little physical disability and report quality-of-life scores in the same range as healthy youth—challenging our ability to determine clinically meaningful outcomes early in the course of pediatric MS. The cross-sectional design precludes causal inference. Furthermore, the adherence estimates are much higher than documented in previous studies, which may reflect selection biases, changes in the MS population, or advantages of the evolving treatment options for MS. The sample may suffer from selection biases, in part, related to the recruitment sites being pediatric MS centers which may have structures in place that improve adherence and, in part, related to more adherent patients being more interested in a study of adherence or participation in studies in general. Another issue is that pharmacy-refill data are a retrospective review of 12 months of pharmacy-refill data and only provide an estimate of use rather than actual medication administration. Furthermore, our study involved only one of the two possible parents, so we were unable to address the differential effects of the child's caregivers on patient adherence. Future research might focus on inclusion of both parents in a behavioral intervention study and examine whether parents are influencing the adherence in different ways, and whether the type of parental involvement is associated with differences in a patient's self-efficacy.

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In summary, in our study of 66 youth with MS and their parents, rates of non-adherence were relatively low with discrepancies between sources. Estimates based on pharmacy-refill data would suggest that our sample is remarkably adherent, whereas estimates based on the patients themselves are closer to published adult estimates. This contrast is worth exploring, as it may reflect selection biases or methodological issues in measuring adherence that are important to address. Parental involvement in adherence may be a strong protective factor in pediatric MS, particularly among adolescents struggling in school and with confidence in controlling their MS. These findings have possible implications for intervention research and emphasize the need for focus on parental involvement in future studies. Future longitudinal research will need to confirm our estimates and findings, as well as compare estimates of adherence from pharmacy-refill data as compared to MEMS cap data which capture actual efforts to open medication receptacles (e.g. pill bottles). This will be addressed with prospective exploration of differences between refill data and MEMS cap data. Ongoing efforts by our group will investigate the juxtaposition of parent and patient reports using qualitative interview data.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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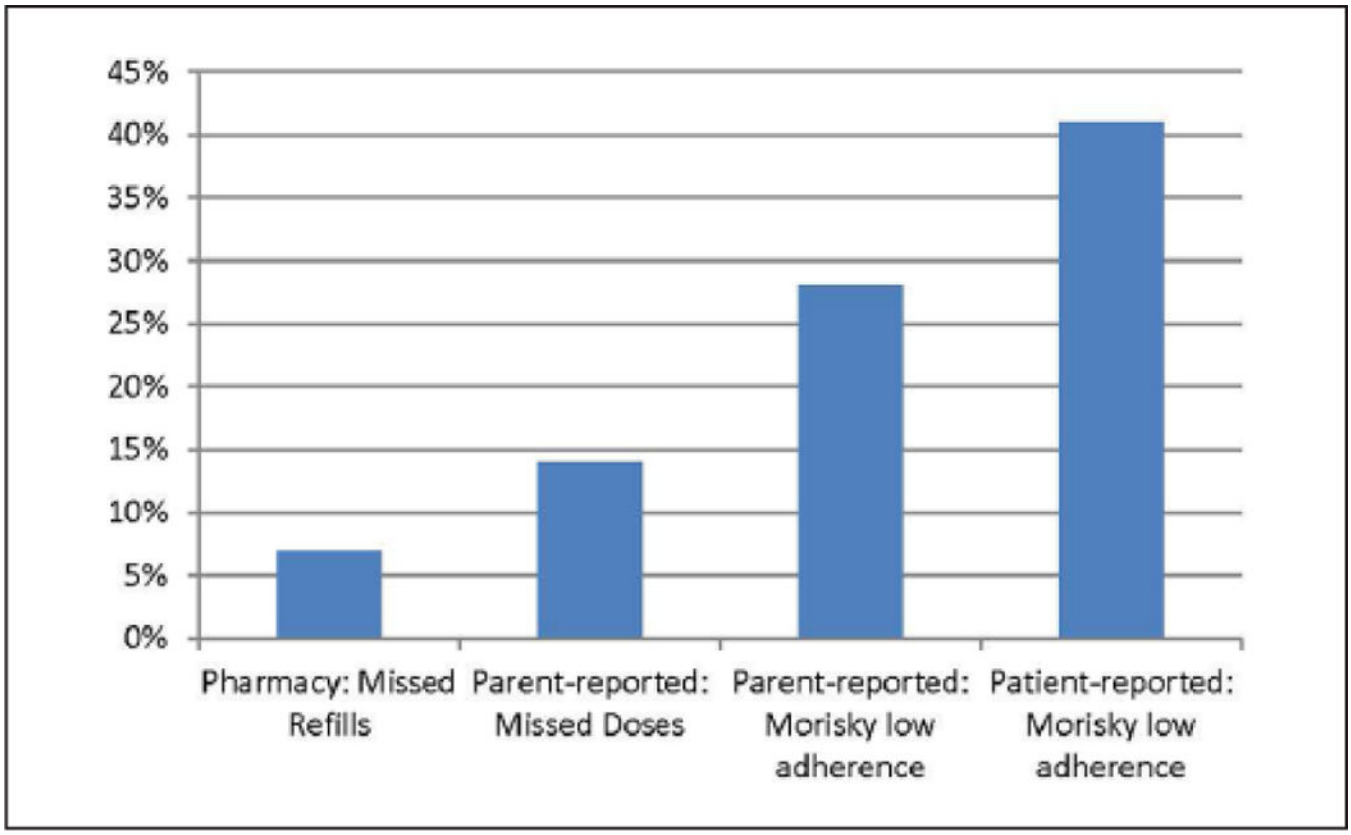

Figure 1.
Proportion non-adherent by data source.

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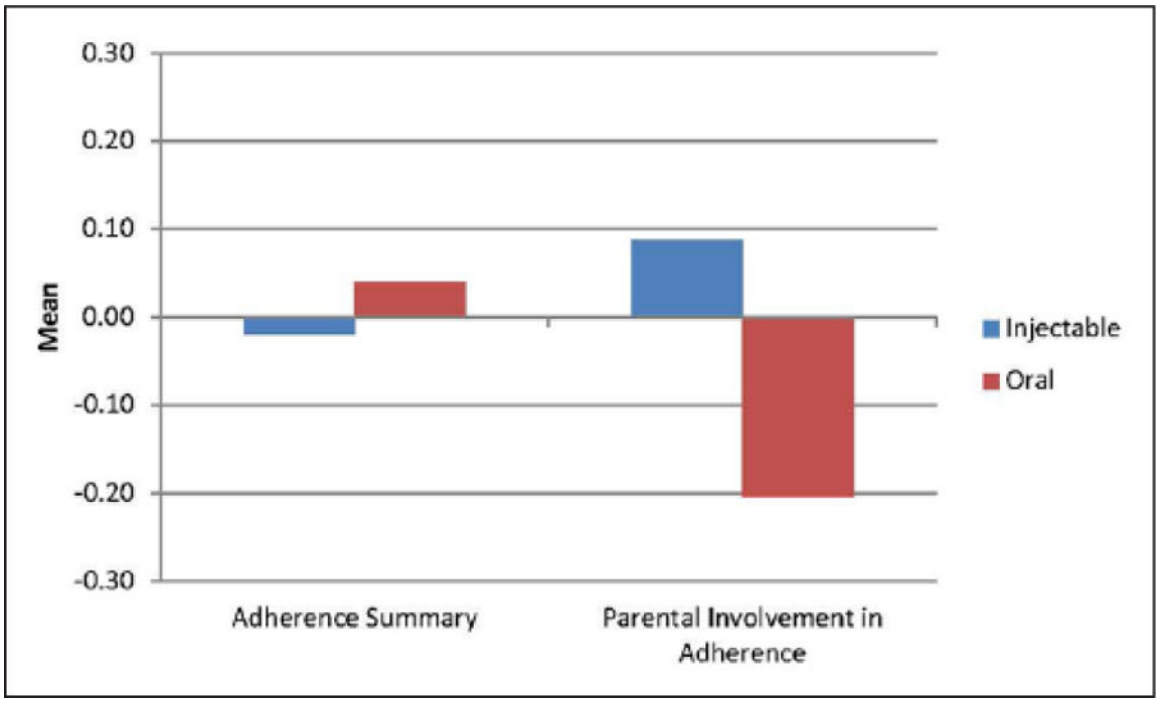

Figure 2.
Comparison of injectable versus oral DMT on adherence outcomes.

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Table 1.

Sample characteristics ($n = 66$).

		n
Age (years), mean (SD)	15.74 (2.02)	66
Age at diagnosis (years), mean (SD)	13.20 (3.91)	60
Disease duration (years), mean (SD)	2.27 (2.25	60
Age at menarche (years), mean (SD)	11.61 (1.13)	38
Gender		
Male (%)	33	22
Female (%)	67	44
Race/ethnicity[a]		
Hispanic or Latino (%)	6	4
Middle Eastern (%)	6	4
South Asian (%)	5	3
Other Asian (%)	5	3
Black or African American (%)	9	6
White (%)	53	35
Don’t know (%)	2	1
Missing (%)	3	2
Mother’s education		
Less than 12 years of education (%)	9	6
High school diploma/GED (%)	26	17
Associate’s degree (%)	15	10
Technical degree (%)	8	5
Bachelor’s degree (%)	18	12
Post graduate education (masters, doctorate; %)	20	13
Missing (%)	5	3
Father’s education		
Less than 12 years of education (%)	11	7
High school diploma/GED (%)	35	23
Associate’s degree (%)	8	5
Technical degree (%)	9	6
Bachelor’s degree (%)	17	11

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Post graduate education (masters, doctorate; %)	17	11
Missing (%)	5	3
Medication type		
Injectable	68%	45
Avonex or Avonex pre-filled syringe (interferon beta1a—intramuscular)		11
Copaxone glatiramer acetate)		24
Plegridy (peginterferon beta-1a)		3
Rebif (interferon beta1b—subcutaneous)		7
Oral	30%	20
Gilenya (fingolimod)		4
Tecfidera (BG-12 or dimethyl fumarate)		14
Terifluonomide		2
Missing	2%	1
Time on DMT (years)		
Mean (SD)	1.97 (1.86)	61
Range	0.35–9.46	
No. of DMTs in past 12 months		
1	66%	40
2	28%	17
3	5%	3
4	2%	1
Site		
Toronto—The Hospital for Sick Children	33%	22
Children's Hospital of Philadelphia	5%	3
Children's Hospital of Pittsburgh	9%	6
Boston Children's Hospital	11%	7
St Louis Children's Hospital	2%	1
University of Alabama at Birmingham	11%	7
Mayo Clinic	2%	1
University of Colorado Denver	6%	4
University of California at San Francisco	8%	5
Texas Children's Hospital	9%	6
Cleveland Clinic	3%	2

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Alberta Children's Hospital	3%	2
Method of survey administration		
Using paper and pencil	21%	14
Using a computer	67%	44
Missing	12%	8
Help with questionnaire		
No help	76%	50
Help from a parent	15%	10
Help from study personnel	9%	6

SD: standard deviation; DMT: disease-modifying therapy.

[a]Participants could indicate more than one race/ethnicity or not indicate any. We had data on 58 of the 66 respondents, of whom 2 were coded as "missing."

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Table 2.

Descriptive statistics of person-reported outcomes (n = 66).

	Mean (SD)	*n*
Parent-reported measures		
PDDS	0.50(0.90)	61
PedsQL Physical Functioning	79.20(21.31)	63
PedsQL Emotional Functioning	72.22(20.84)	63
PedsQL Social Functioning	81.59(19.13)	63
PedsQL School Functioning	66.90(18.87)	63
PedsQL Psychosocial Health Summary Score	73.57(15.89)	63
MSNQ	18.69(13.41)	61
Patient-reported measures		
PedsQL Physical Functioning	80.17(18.50)	66
PedsQL Emotional Functioning	68.03(23.05)	66
PedsQL Social Functioning	83.18(17.22)	66
PedsQL School Functioning	63.56(18.50)	66
PedsQL Psychosocial Health Summary Score	71.59(16.06)	66
Ryff Autonomy	27.86(5.52)	66
Ryff Self Acceptance	27.08(3.83)	65
Ryff Environmental Mastery	24.47(4.25)	66
MSSE Control	690.15 (208.03)	66
MSSE Function	811.36 (167.35)	66

SD: standard deviation; PDDS: Patient-Determined Disease Steps; MSNQ: Multiple Sclerosis Neuropsychological Screening Assessment Questionnaire; MSSE: Multiple Sclerosis Self-Efficacy Scale.

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Table 3.

Adherence-related variables.

Measure of adherence	Time frame	*n*	%	Mean	SD
Pharmacy records					
Proportion refills received/expected refills	Past 12 days	56		0.95	0.12
Proportion non-adherent (i.e. <80% received vs expected refills)		4	7	-	-
Parent-reported					
Proportion missed doses[a]	Past 28 days	58		0.1	0.3
Proportion non-adherent (i.e. <80% received vs expected refills)		8	14	-	-
Parental involvement in DMT use	Past 2 weeks				
Remind					
0%		18	27		
25%		13	20		
50%		7	11		
75%		11	17		
100%		14	21		
Missing		3	5		
Present					
0%		9	14		
25%		8	12		
50%		7	11		
75%		15	23		
100%		24	36		
Missing		3	5		
Administer					
0%		31	47		
25%		8	12		
50%		4	6		
75%		7	11		
100%		13	20		

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Measure of adherence	Time frame	*n*	%	Mean	SD
Missing		3	5		
Reported adherence	No time frame	60		6.3	1.4
Proportion low adherence		18	28	-	-
Contextual factors					
Behavioral coping strategies[a]	Past 4 weeks	41		51.5	11.3
Side effects[a]	Past 4 weeks	43		51.3	9.9
Barriers[a]	No time frame	57		51.3	11.0
Patient-reported					
Reported adherence[b]	No time frame	66		5.8	1.8
Proportion low adherence[b]		27	41	-	-
Contextual factors					
Barriers[a]	No time frame	58		49.6	9.2
Factor scores (standardized)					
Adherence summary		49		0.0	1.0
Parent involvement in adherence		57		0.0	1.0

SD: standard deviation; DMT: disease-modifying therapy.

[a]Multiple Sclerosis Treatment Adherence Questionnaire.

[b]Morisky Adherence Measure.

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Table 4.

Correlation matrix of adherence measures

	Pharmacy proportion refills received/ expected refills	Proportion missed doses (parent report)	Parent remind	Parent present	Parent administer	Morisky adherence (parent)	Behavioral coping (MSTAQ parent)	Side effects (MSTAQ parent)	Barriers (MSTAQ parent)	Morisky adherence (patient)
Pharmacy proportion refills received/expected refills										
Proportion missed doses (parent report)	−0.45									
Parent remind	−0.29	0.27								
Parent present	0.04	0.07	0.35							
Parent administer	0.19	0.17	0.29	0.60						
Morisky adherence (parent)	0.37	−0.46	−0.23	−0.14	−0.19					
Behavioral coping (MSTAQ parent)	0.03	−0.01	0.11	0.58	0.37	0.02				
Side effects (MSTAQ parent)	0.05	0.12	0.03	0.16	0.23	−0.14	0.43			
Barriers (MSTAQ parent)	−0.17	0.06	0.21	0.20	0.13	−0.16	0.12	0.21		
Morisky adherence (patient)	0.34	−0.30	−0.12	0.00	−0.02	0.59	0.01	0.18	−0.07	
Barriers (MSTAQ patient)	−0.31	−0.04	0.12	0.19	0.29	−0.25	0.34	0.09	0.31	−0.14

MSTAQ: Multiple Sclerosis Treatment Adherence Questionnaire.

Small correlation.

Medium correlation.

Large correlation.

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Table 5.

Results of backward stepwise regression models predicting adherence-related factors.

	Coefficient	Standard error	*t*	*p* > *t*	95% CI		
Adherence summary (*n* = 48)							
PedsQL Physical Function (patient)	0.01	0.01	2.01	0.05	0.00	0.03	
Adjusted R^2							0.06
Parental involvement in adherence (*n* = 49)							
PedsQL School Function (parent)	−0.01	0.01	−1.84	0.072	−0.02	0.00	
MSSE control	0.00	0.00	−4.15	0	0.00	0.00	
Adjusted R^2							0.31

CI: confidence interval; MSSE: Multiple Sclerosis Self-Efficacy Scale.

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