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Patient Preferences in the Choice of Disease-Modifying Drugs for Multiple Sclerosis

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory autoimmune disease associated with neurodegenerative processes in the central nervous system.[1,2] In young adults, it is the most common chronic neurologic disease, often leading to permanent disability.[3]

Relapsing-remitting MS (RRMS) is the most common form of MS.

There are a variety of treatment options available for RRMS associated with different characteristics in key attributes, including route of administration, side effects, and dosing frequency. New therapies offer attributes like new routes of administration (ie, oral).

A quantitative assessment of the importance of different therapy features from the perspective of the patient, especially with regard to different routes of administration, is needed.

The objective of this study was to assess the relative importance of treatment characteristics for patients with MS in choosing their treatment.

METHODS

Study design

- Using a questionnaire-based discrete choice experiment (DCE), patients with MS were asked to choose the most and least preferred treatment type (best-worst scaling) among hypothetical multiattribute alternatives. These were based on typical characteristics of first-line disease-modifying drugs (DMDs).
- Multiattribute alternatives included varying levels of the following key attributes of typical first-line DMDs:
  - Route of administration, frequency of administration, required monitoring of the patient, local and systemic side effects.
  - Previous studies have established efficacy as being of primary importance to patients with MS.[4] Thus, this attribute was not included in the present design as it would have reduced the likelihood of significant trade-offs between other DMD attributes and route of administration.
  - The specific characteristics of escalation treatments for MS were not considered in this evaluation.
- Choices were repeated in a fractional factorial design consisting of orthogonally composed alternatives (ie, multiple scenarios were presented with different hypothetical products with varying levels of the key attributes).
- The impact of each attribute and level on the choices made by participants was estimated by means of statistical analyses, allowing inferences on patients' latent preference structure.
- The specific design (Case 3, multiprofile case) simulates a real choice situation between hypothetical multiattribute treatment alternatives (Figure 1).

Study population

- 1628 patients with RRMS were recruited from 38 neurological practices in Germany, irrespective of their current treatment status (ie, basic, escalation, or no DMD).

Assessments

- Age, age at diagnosis, sex, date of last relapse, current and previous treatment with DMDs, and self-reported health status (measured by the EuroQol 5-Dimension instrument [EQ-5D]).

Figure 1: Example of a DCE scenario as used in the questionnaire

		Treatment 1	Treatment 2	Treatment 3
	Mode of administration	Self-injection into muscle	Self-injection into skin	Taking a pill
	Frequency of administration	3–4x weekly	2–3x daily	1x daily
	Monitoring	Regular blood test	Regular blood test	None
	Local side effects	None	Rash, itching, swelling	None
	Systemic side effects (occur in ≥10% of applications)	When starting therapy flush and gastro-intestinal problems for ~1 month	Flu-like symptoms for ~1 day after medication	Flush, chest tightness, anxiety, rapid heart beat, or breathing difficulty
Please mark the 1 best option...	Treatment I like best:			X
and the 1 worst option...	Treatment I find worst:		X	

DCE, discrete choice experiment.

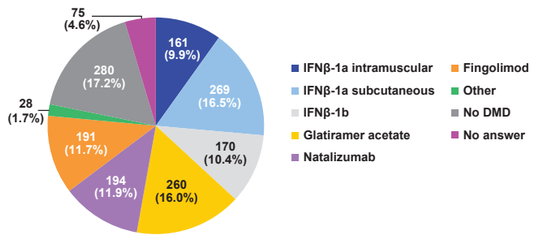
- Continuous population variables (eg, age) were tested with analysis of variance (ANOVA); categorical variables were assessed (eg, sex) with chi-square tests.
- Each questionnaire included 8 orthogonally varied choice situations.

RESULTS

Study population

- On average, patients were aged 42.4 years with 9.9 years of disease duration at the time they answered the questionnaire.
- 74.6% of the patients were females who were significantly younger at time of diagnosis than males (mean, 32.2 vs 33.5 years, respectively; ANOVA, $P<0.05$).
- The majority (53.4%) of patients were currently receiving DMDs approved for baseline therapy in the European Union (EU; mainly interferon beta and glatiramer acetate; Figure 2).
- 24% of patients were receiving DMDs indicated for escalation therapy in the EU at the time of the study (mainly fingolimod and natalizumab; Figure 2).
- 17.2% of patients were not receiving DMDs during this study, of which 3.6% (n=10) were treatment naïve.
- 87.8% of patients reported current or prior experience with injectable DMDs.
- Patients not currently receiving treatment reported more recent relapses (Table 1; chi-square test, $P<0.001$) and rated their health status significantly lower than patients on DMDs, as measured with EQ-5D (mean, 0.81 vs 0.86; ANOVA controlled for age and disease duration, $P<0.001$).

Figure 2: Current DMD status



DMD, disease-modifying drug; IFNβ, interferon beta.

Table 1: Disease activity by treatment status (N=1522)

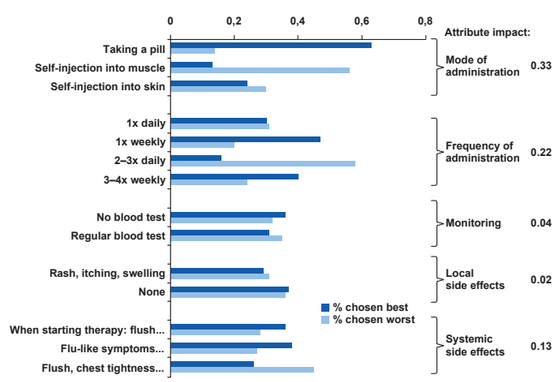
Last relapse	Baseline (%) n=855	Escalation (%) n=387	Other (%) n=13	No DMDs (%) n=267
Within last 6 months	171 (20.0)	83 (21.4)	3 (23.1)	90 (33.7)
Within last 6–12 months	128 (15.0)	76 (19.6)	1 (7.7)	37 (13.9)
Within last 12–24 months	203 (23.7)	90 (23.3)	3 (23.1)	46 (17.2)
>24 months	353 (41.3)	138 (35.7)	6 (46.2)	94 (35.2)

DMDs, disease-modifying drugs.

DCE analysis

- 1311 (80.5%) patients completed the DCE; those not completing the DCE were older, had longer disease duration, lower health status, and were more likely to be without current DMD.
  - Count analysis[6] is based on the percentages of how often a level is picked as best and worst across its total times of presentation. The difference between best and worst choice percentages reflects a level's influence on patients' choices, with larger differences indicating stronger influences. Attribute impact is calculated as the average of the attribute's levels' best and worst choice percentage differences, ie, = (Σ|(% chosen best – % chosen worst)|/number of levels).

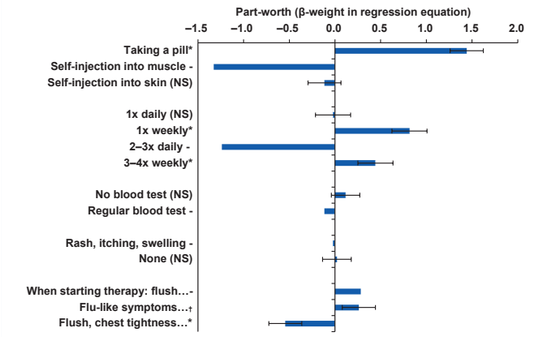
Figure 3: DCE results count analysis



DCE, discrete choice experiment.

- The regression analysis predicts the counts of levels simultaneously chosen as best and worst across DCE scenarios to estimate the levels' influences on patients' choices; β-weights from the regression equation are interpreted as levels' part-worths (utilities).[7] Unlike count analysis, regression analysis allows inferring statistical significance of the levels' influences.
- Negative β-weights indicate a level predominantly picked as worst, thus considered unfavorable (negative utility); positive β-weights indicate a level predominantly picked as best, thus considered favorable (positive utility).

Figure 4: DCE results for part-worths (regression analysis, paired method)



DCE, discrete choice experiment; NS, not significant.
- = reference level in effect coding; *$P<0.001$; †$P<0.01$.

CONCLUSIONS

- In a representative RRMS sample[3,5] in which a majority of patients had prior experience with injectable DMDs, count and regression analyses yielded that, among attributes included in the study, route of administration was most important in guiding patients' preferences, with oral application being most desirable (selected as best in 63% of cases).
- The second most important attribute in guiding patients' preferences was frequency of administration, with administration once a week being the preferred attribute level (in 47% of cases).
- The present study aimed to determine the relative importance of key DMD characteristics for preferences of patients with MS, especially of route of administration. Since the new oral route of administration differs from established injectables, the relative importance of key attributes of DMDs might change from the perspective of the patient. To encourage significant trade-offs between other DMD attributes and route of administration, efficacy was not included across scenarios in the DCE.
- Notably, the studied systemic side effects, such as flu-like symptoms or gastrointestinal disorders, were only about half as important as mode of administration for patients' choices based on the attribute impact in count analysis.

DISCLOSURES

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