PRM118

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] affecting 120,000-140,000 patients in Germany[2].
- MS typically manifests between 20 and 40 years of age and is the most common cause of disability in early adulthood[3].
- Relapsing–remitting MS (RRMS) is the most common form of MS, accounting for 85–90% of patients diagnosed[3].
- There is a variety of disease modifying drugs (DMDs) available for the treatment of RRMS. These drugs are associated with different characteristics in key attributes such as side effects, mode of administration etc.
- The current study was carried out to assess the importance of treatment characteristics for patients' preferences in an ecologically valid design.

METHODS

Study Design

- In a discrete choice experiment (DCE), MS patients were asked to choose the most and the least preferred drug (best-worst-scaling) among hypothetical multi-attribute alternatives – all assumed to be equally effective.
- Multi-attribute alternatives included varying levels of the following key attributes:
  - mode of administration, frequency of administration, required monitoring of the patient, local and systemic side effects.
- Effectiveness was not included in the DCE since this is supposedly the most important attribute for patients anyway.
- Choices were repeated with orthogonally composed alternatives, i.e. each scenario involved different products with varying levels of the same attributes.
- Through statistic modeling the impact of each attribute and level on the choices made by participants can be estimated.
- The specific design (Case-3, multi-profile case) simulates a real choice situation between different hypothetical multi-attribute treatment alternatives (**Figure 1**).

Figure 1: Example of a DCE Scenario

	Treatment 1	Treatment 2	Treatment 3
Mode of Administration	Self-injection into muscle	Self-injection into skin	Taking a pill
Frequency of Administration	3-4 per week	2-3 x daily	1 x daily
Monitoring	Regular blood-test	Regular blood-test	None
Local Side Effects	None	Rash, itching, swelling	None
Systemic Side Effects *(occur in at least 10% of applications)*	When starting therapy flush and gastro-intestinal problems for approx. 1 month	Flu-like symptoms for approx. 1 day after medication	Flush, chest-tightness, anxiety, rapid heart beat or breathing difficulty
Please mark the one best option… Treatment I like best:			X
… and the one worst option! Treatment I find worst:		X	

Study Population

- 1,426 MS patients were recruited from 38 neurological practices in Germany instructed to include only RRMS patients.

Assessments

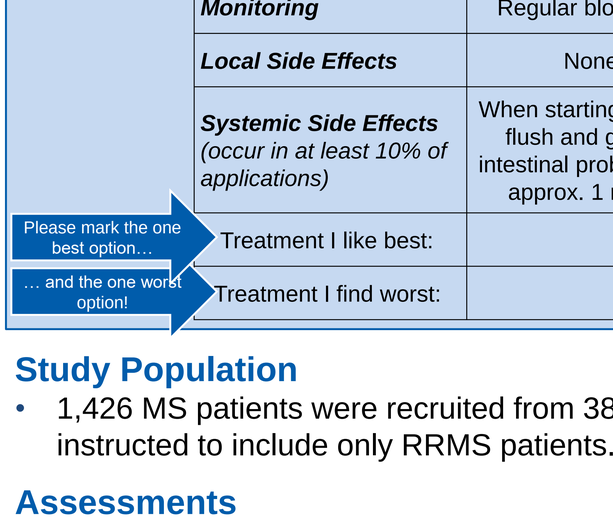
- Age, age at diagnosis, sex, date of last relapse, current and previous medication with DMDs, self-reported health status (measured by the EQ-5D).
- Continuous population variables (e.g., age) were tested with analysis of variance (ANOVA) categorical variables (e.g., sex) with Chi²-tests.
- Each questionnaire included 8 orthogonally varied DCE scenarios.

RESULTS

Study Population.

- On average, patients were 42 years of age with 10 years of disease duration.
- ~75% of the patients were females, that were significantly younger at time of diagnosis than males (*M* = 32.1 vs. 33.8 years; ANOVA: *p* = .005).
- Those results are in line with previous evaluations[3,4] in MS and therefore suggest a representative study sample.

Figure 2: Current DMD Status



- The majority of patients (~53%) currently receive DMDs approved for baseline therapy in the EU (mainly *interferon*-β, *glatiramer acetate*).
- ~25% of the patients receive DMDs indicated for escalation therapy in the EU (mainly *fingolimod*, *natalizumab*).
- ~17% do not receive DMDs; however 87% of them have previously received such treatment.
- ~90% report prior experience with parenterally administered DMDs from current or previous medication.

- Patients without current treatment rate their health status as measured with EQ-5D significantly lower than patients on DMDs (see **Table 1**; ANOVA controlled for age and disease duration: $p < .001$) and also report more recent relapses (see **Table 2**; *Chi*²-test: $p < .001$).

Table 1: Current Health Status (According to EQ-5D)

	Baseline	Escalation	other	no DMD
EQ-5D Summary Index	.86	.85	.91	.79

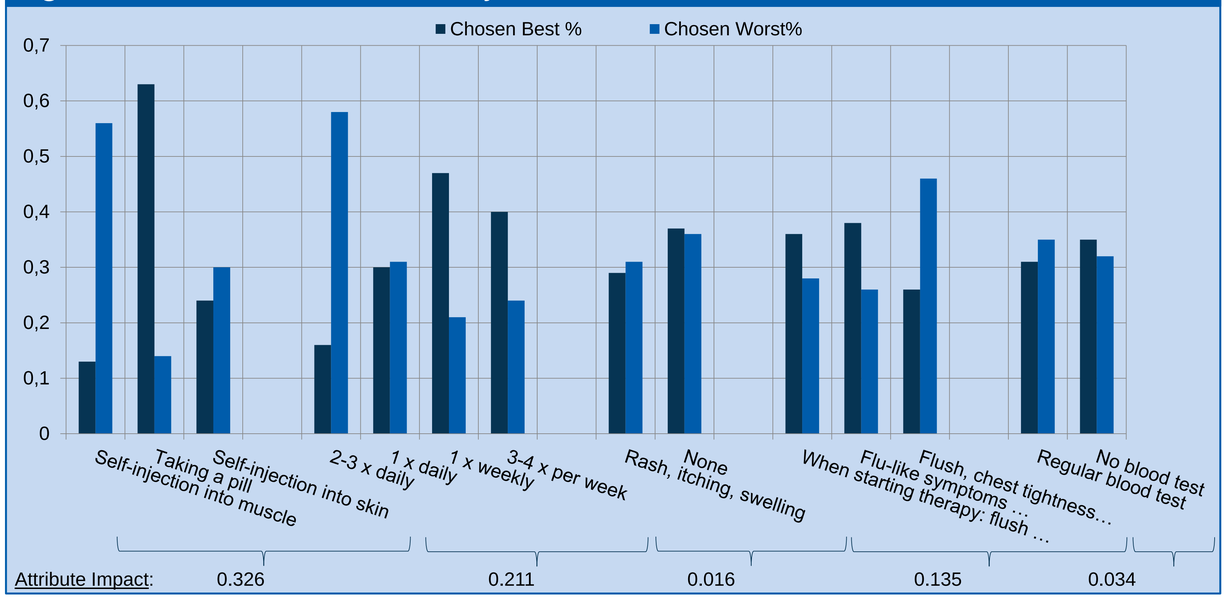
Table 2: Disease Activity and Health Status by Treatment Status, Total n=1,327

Last relapse	Baseline n=744 (%)	Escalation n =352 (%)	Other n=9 (%)	no DMD n=222 (%)
within last 6 months	147 (19.8%)	75 (21.3%)	2 (22.2%)	77 (34.7%)
within last 6-12 months	109 (14.7%)	66 (18.8%)	1 (1.1%)	32 (14.4%)
within last 12-24 months	180 (24.2%)	85 (24.1%)	1 (11.1%)	34 (15.3%)
>24 months	308 (41.4%)	126 (35.8%)	5 (55.6%)	79 (35.6%)

DCE Analysis

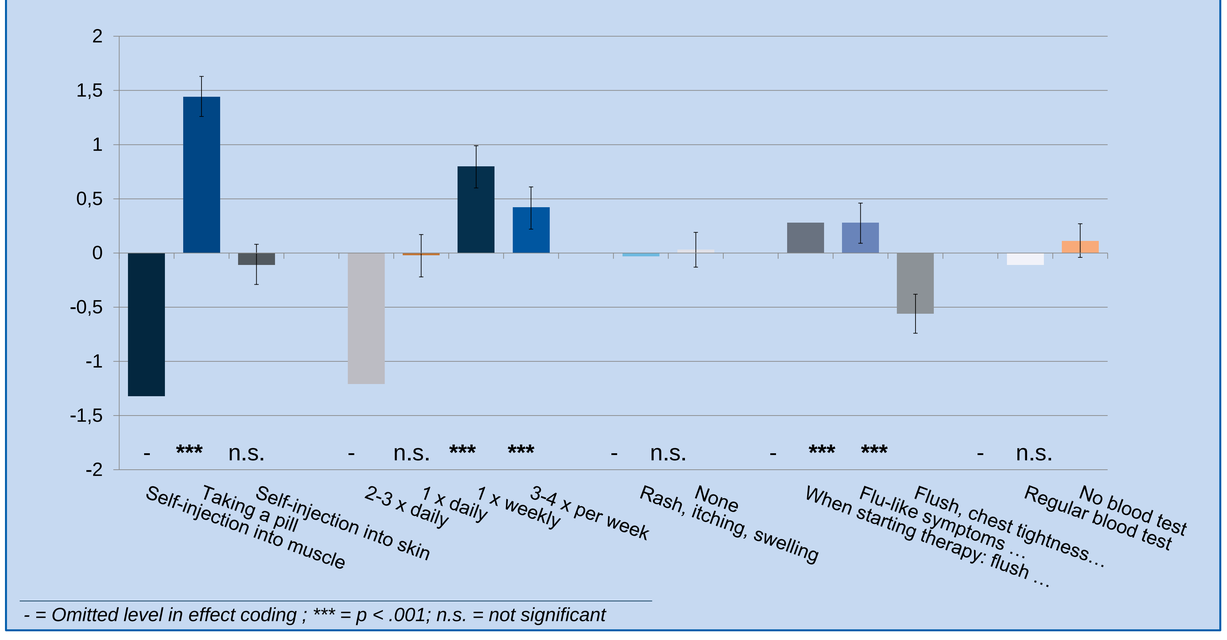
- 1,153 patients (81%) completed the DCE and were included for final analysis.
- Count analysis[5,6]:
  - The Best-Worst-Difference score (BW-Diff) is defined as the difference of times an attribute level is chosen as best minus the times it is chosen as worst across presentations, (i.e., Chosen Best % – Chosen Worst %). It reflects the average influence of an attribute's level on patients' decisions.
  - The average impact of an attribute is calculated as the sum of the absolute values of BW-Diff scores divided by the number of levels.

Figure 3: DCE Results Count Analysis



- Regression analysis predicts the counts of chosen best-worst pairs (adjusted by trials x participants) to estimate the levels' part-worths[7].
  - The natural log of adjusted counts is a linear function of the difference in utility and can be modelled with a linear model. Effect-coded attributes and levels are used as predictors of the natural log. Part-worths can be interpreted as rate of change in choice frequency implied by a level.

Figure 4: DCE Results for Part-Worths (Regression Analysis, Paired Method)



*- = Omitted level in effect coding ; *** = p < .001; n.s. = not significant*

CONCLUSIONS

- In a representative RRMS sample with prior experience with parenteral modes of administration, count and regression analysis yielded that mode of administration was the most important attribute guiding patients' preferences, with 'oral application' being most desired (selected as best in 63% of the cases).
- Notably, the studied systemic side effects, such as flu-like symptoms or gastrointestinal disorders were only half as important as mode of administration for patients' choice (cf., attribute impact in count analysis).
- The second most relevant attribute was frequency of administration, with 'administration once a week' being the most preferred attribute level (in 47% of the cases).
- Our data indicate that for RRMS patients, the most important attributes of MS disease modifying drugs are route of administration (oral being the number one choice by majority) and frequency of administration (with intake once a week being the most preferred), probably because these aspects meet the patients' need for low treatment burden in daily life.

DISCLOSURES

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