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Patient centered decision making: Use of conjoint analysis to determine risk–benefit trade-offs for preference sensitive treatment choices

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ABSTRACT

Understanding patient preferences facilitates shared decision-making and focuses on patient-centered outcomes. Little is known about relapsing–remitting multiple sclerosis (RRMS) patient preferences for disease modifying therapies (DMTs). We use choice based conjoint (CBC) analysis to calculate patient preferences for risk/benefit trade-offs for hypothetical DMTs.

Methods: Patients with RRMS were surveyed between 2012 and 2013. Our CBC survey mimicked the decision-making process and trade-offs of patients choosing DMTs, based on all possible DMT attributes. Mixed-effects logistic regression analyzed preferences. We estimated maximum acceptable risk trade-offs for various DMT benefits.

Results: Severe side-effect risks had the biggest impact on patient preference with a 1% risk, decreasing patient preference five-fold compared to no risk. (OR = 0.22, $p < 0.001$). Symptom improvement was the most preferred benefit (OR = 3.68, $p < 0.001$), followed by prevention of progression of 10 years (OR = 2.4, $p < 0.001$). Daily oral administration had the third highest DMT preference rating (OR = 2.08, $p < 0.001$). Patients were willing to accept 0.08% severe risk for a year delayed relapse, and 0.22% for 4 vs 2 year prevented progression.

Conclusion: We provided patient preferences and risk–benefit trade-offs for attributes of all available DMTs. Evaluation of patient preferences is a key step in shared decision making and may significantly impact early drug initiation and compliance.

1. Introduction

More than 2.3 million people worldwide and 317,000 in the United States have multiple sclerosis (MS) [1]. The majority of patients at diagnosis have the relapsing–remitting multiple sclerosis (RRMS) subtype [2,3] characterized by neurological flares followed by periods of stability. MS is a progressive disease, which over time, can result in severe physical and cognitive disability with decreased activities of daily living, quality of life, and autonomy [3–6].

Disease modifying therapies (DMTs) are considered the first line treatment for RRMS with proven clinical benefits including relapse reduction and decreased time to disability. Early initiation and adherence are shown to contribute to better clinical outcomes [7] and improved survival [8]; however, as with all drugs, patients must be willing to accept the associated risks with DMTs for their gains. Side effects can range from mild (flushing or injection site reactions) to severe (progressive multifocal leukoencephalopathy, life-threatening cardiac events, hepatotoxicity, or lymphopenia) [9–13]. Each available DMT on the market has its own unique risk and benefit profile challenging patients and providers to make trade-offs with each treatment decision. The complexity of choices may lead to patient uncertainty and confusion resulting in barriers to treatment initiation and adherence [14].

Physicians are moving away from a model of making treatment decisions for the patient to a shared decision-making model, which necessitates reviewing patient preferences [14]. Shared decision making models promote better outcomes for patients [15,16] and are especially

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important for RRMS patients for which multiple reasonable treatment options exist, with none clearly outperforming the others [14,17,18]. The most common approaches to evaluation of preference under risk are health state utility assessments (e.g. standard gamble, time trade-off and willingness to pay), and health state classification systems. More recently, contingent valuation methods such as conjoint analyses, have emerged as a method for measuring preference under risk because they better reflect patients true decision-making behavior [19,20]. Understanding patient preferences helps facilitate the shared decision-making process, promotes preference sensitive care, and places focus on patient centered outcomes [17]. Little is currently known about RRMS patient preferences for DMTs. The objective of this study is to use choice based conjoint (CBC) analysis to calculate the relative patient preferences for the current risk and benefit attributes of hypothetical DMTs and to quantify patient willingness to accept DMT-associated risks for benefits gained.

2. Material and methods

2.1. Study sample

Patients with a diagnosis of RRMS were recruited via telephone between April, 2012 and January, 2013 prior to their scheduled tertiary medical center MS clinic appointments. Our target sample size was 300 patients based on the number of attributes and levels included in our conjoint measure [21]. Inclusion criteria were age over 18 years, RRMS diagnosis confirmed by medical chart review, and patient's willingness to participate and sign a consent. The computerized utility and conjoint portions of the study were completed in the clinic, but patients had the option of mailing back the disease and treatment paper-based questionnaires if they were fatigued or needed more time. Upon completion, patients received $20 USD for their participation. All patient data for the study were de-identified and kept securely and the study was approved by the University Committee on Human Research.

2.2. Measures

Patients completed two computer based utility measures (CBC and standard gamble) and two paper based questionnaires on their demographics (age, gender, ethnicity), disease characteristics (time since diagnosis, functional abilities, relapse frequency), disease knowledge and current and previous DMT use.

This paper is focused on analysis and discussion of the main CBC analysis measure and its relationship to the demographic and disease-based questions. CBC, similar to discrete-choice experiments, is an increasingly used methodology to assess patient preferences in healthcare decision-making [22–24]. CBC is a systematic method of eliciting risk–benefit trade-offs that can be used to quantify the relative preferences and risk acceptance for attributes of medical interventions, such as medications [21]. It is grounded in the theory that patients will choose the combination of attributes that maximizes utility (a quantifiable preference based valuation). The total utility associated with a patient choice is a summation function of the utilities contributed by each attribute of that choice, these are also known as part-worth utilities [21,25]. The choices that patients make thus can implicitly reveal the relative preferences for attributes or specific characteristics of a medical intervention [19,26]. Our CBC survey was constructed to mimic the treatment decision-making process and trade-offs in a patient's own DMT choice. The hypothetical DMTs presented in the instrument were based on all possible combinations of DMT attributes rather than asking patients to choose a particular DMT currently available.

2.2.1. Determination of attributes and levels

The CBC attributes and attribute levels were identified based on the results of our group's pilot study (n = 50) [27], where we used a ratings based conjoint method to evaluate eight attributes with four levels each. Based on the results of this pilot study we were able to omit two attributes and one level within four of the six remaining attributes because they did not significantly impact patient preferences. This allowed us to construct a shorter task set, reduce patient burden and increase the reliability of results. For the final CBC instrument we included six attributes of DMTs – three benefits and three risks – with three to four levels each (Table 1). These attributes and levels were selected based on DMT clinical trials, current clinical literature, and consultation with neurology clinicians [9–13,27]. We tested a broad probability range of DMT attribute levels rather than the limited range from current medications to assess the linearity and thresholds of patient preference scores.

2.2.2. Description of instrument content

Each patient choice included the 3 benefits (relapse reduction, progression prevention and symptom improvement) and the 3 risks (common and severe or life-threatening side effects of DMTs (not the disease itself), administration). The attribute levels for the 2 choices were varied for the patient for each decision task, so they would weigh the different risks and benefits between the choice pairs. The common side effect levels were grouped by like symptoms 1) neurological which includes changes in mood, feeling depressed or anxious, 2) pain related symptoms which includes headache, muscle/joint aches, and 3) infection related symptoms which includes bladder infection or flu. Severe side effects included different probabilities (0 to 1%) of severe disability or death related to all the DMTs. Administration included a combination of route and frequency of the available DMT; 1) oral pill daily, 2) intramuscular shot weekly, 3) subcutaneous injection daily, and intravenous infusion monthly. How patients felt, was divided into three symptom improvement groups: 1) none, 2) mild, and 3) substantial, but rare. Delaying progression of MS symptoms was presented for a period of time of either two, four or 10 years. Preventing relapse, the primary outcome of clinical trials, was expressed as the time span in which a patient would experience one relapse; one relapse per one, two or five years.

2.2.3. Development of choice based conjoint (CBC) preferences

The CBC was developed using Sawtooth Software [28,29] and followed conjoint analysis good-practice guidelines [23]. We chose a random, full profile CBC design to maximize the information that could be obtained for each response. There were 10 possible choice profiles that each contained 20 choice tasks per patient [29]. The levels of

Table 1
DMT attributes and levels.

Attribute	Levels
Delay progression This medication can prevent the symptoms of MS from getting worse for ____.	• 2 years • 4 years • 10 years
Prevent relapse Most patients on this medication experience 1 relapse every _____.	• 1 year • 2 years • 5 years
Improve symptoms Patients taking this medication feel ___.	• No improvement • Mild improvement • Substantial, but rare improvement
Common side effects The most common side effects associated with this medication are:	• Headache, muscle/joint aches • Increased risk of infection (bladder, flu) • Changes in mood (feeling depressed or anxious)
Severe side effects _____ patients die or become severely disabled from a side effect of this medication	• 0 out of 1000 • 0.5 out of 1000 • 1 out of 1000 • 10 out of 1000
Administration This medication is administered as _____.	• An oral pill taken once daily • An intramuscular shot weekly • A subcutaneous injection daily • An intravenous infusion monthly