The best methods of communicating clinical trial data to improve understanding of treatments for patients with Multiple Sclerosis

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Abstract

Background. Patients’ understanding of treatment risks and benefits is a prerequisite for shared decision-making. Yet, patients with Multiple Sclerosis (MS) do not accurately understand treatment information provided in regular clinical consultations.

Objective. To identify the best methods of communicating clinical trial data to improve MS patients’ understanding of treatments. To also examine the relationship between patients’ understanding with decisional conflict, individual traits and MS symptoms.

Design. A repeated-measures study was employed. Patients were presented with hypothetical treatment risks and benefits from faux clinical trials. Treatments were communicated using absolute terms, relative terms and numbers needed to treat/harm. The presence of baseline information with each method was also manipulated. Patients’ understanding and conflict in treatment decisions was assessed. Individual traits and MS symptoms were also recorded.

Participants. A sample of relapsing-remitting MS patients from NHS sites in the UK.

Results. Understanding was better when treatments were communicated in absolute terms (M=3.99, SD=.93) compared to relative terms (M=2.93, SD=.91, p<.001) and numbers needed to treat/harm (M=2.89, SD=.88, p<.001). Adding baseline information to all methods significantly improved understanding (M=5.04, SD=.96) compared to no baseline information (M=1.50, SD=.74, p<.001). Understanding was not related to conflict in treatment decisions (r=-.131, p=.391). Numeracy, IQ and cognitive impairments were significantly related to patients’ understanding of treatments.

Conclusion. Treatment risks and benefits should ideally be communicated using absolute terms, alongside baseline information. MS patients with low numeracy, low IQ and reduced cognitive skills should be supported during treatment education.
Introduction

Shared decision-making is advocated in patient-centred healthcare as an ideal approach for making treatment decisions [1,2]. A prerequisite to shared treatment decisions is patients’ understanding of available treatments. Accurate treatment knowledge can ensure patients engage with the decision-making process [3], choose a treatment that aligns with their values [2], and adhere to their chosen treatment [4]. Good treatment knowledge can also reduce decisional conflict, which encompasses the feeling of uncertainty in a treatment choice [5-7]. However, not all patient groups show accurate understanding of treatment risks and benefits.

Multiple Sclerosis (MS) is a chronic inflammatory condition of the central nervous system, often leading to advanced neurological disability [8,9]. Patients with MS are faced with important decisions about disease-modifying drugs (DMDs), which can help delay disease progression. However, MS patients find it particularly challenging to understand DMD information during routine healthcare [10]. One reason may be the complex risk-benefit profiles associated with DMDs. For instance, while some DMDs are moderately effective with low risks, other DMDs offer higher efficacy in exchange for higher risks to patients [11]. It is also possible that individual traits and some MS symptoms can confound patients’ understanding of treatments. Intelligence, numeracy and health literacy can typically influence comprehension of treatments [12-15]. Cognitive deficits, prevalent in 40-70% of MS patients [15], can further affect understanding [16]. Other commonly experienced MS symptoms, such as depression, anxiety and fatigue [17] may also influence understanding, but have not been previously assessed. It is essential then that understanding of DMDs be improved for MS patients.

Understanding of treatment information derived from clinical trials can be affected by the methods in which this is communicated. Differences between risks and benefits experienced by a patient group taking a new treatment and another patient group taking a placebo during a clinical trial, can be
communicated in absolute terms (conveying true differences), relative terms (conveying proportional differences) and numbers needed to treat/harm (conveying the average number of patients to take the treatment for one person to experience an outcome). Absolute terms have been shown to improve understanding compared to other methods in non-clinical [18,19] and clinical populations [20,21]. With the addition of baseline information (i.e. the original number of patients in both groups that experience the risk or benefit), understanding improved regardless of the method [18,19,21]. The only study conducted with MS patients found better understanding when baseline information was added to absolute terms, but did not examine other methods [22]. There is still a need to systematically investigate all methods with MS patients.

This study is the last of three experiments investigating optimal methods of communicating treatment information to MS patients, to culminate in an educational intervention. Previous two experiments examined numerical and graphical methods, type of frequencies and ways of framing treatment risks and benefits. The main objective of the current study was to identify the best method of communicating clinical trial data. Specific hypotheses were as follows: (i) absolute terms would improve understanding, (ii) baseline information would improve understanding, (iii) patients’ decisional conflict would reduce with better understanding, and (iv) individual traits and cognitive impairments will be associated with understanding.

Methods
Participants

Patients were recruited from two UK National Health Clinics (NHS). Patients diagnosed with relapsing-remitting MS, taking a DMD, able to provide informed consent and meet study sensorimotor task demands were included. There was no selection on the basis of cognitive impairment. Patients were
excluded if their condition or medication had changed in the last four weeks, or if they had a significant medical and/or psychiatric condition besides MS. Patients had visual acuity of at least 20/70 [23]. The study received ethical approval from the NHS Research Ethics Committee.

Materials

Patients were presented with a hypothetical disease with progressive characteristics similar to MS. Two hypothetical treatments were provided for this disease. Treatment risk-benefit profiles were based on DMD clinical trials [e.g. 24,25], to mimic real clinical decisions. Risks and benefits were presented for 1, 2 and 5 years of taking the treatment. Each treatment had one minor risk (e.g. flu-like symptoms), one adverse risk (e.g. kidney failure) and one benefit (delays in progression of disease symptom).

Design

A repeated-measures design was employed. Treatment risks and benefits were communicated using six different methods: absolute terms, relative terms and numbers needed to treat/harm, each with or without baseline information (see figure 1). Three methods were randomly assigned to each treatment at the beginning of the study. Treatment order was counterbalanced between patients using a latin-square design [26]. The study was conducted with the chief investigator (GR). The session took between 1.5-2 hours and included multiple breaks for patients as required.

Measures

Primary outcome measure.

Understanding

Six questions assessed understanding immediately after a treatment risk or benefit. Questions were author-developed but adapted from previous studies [27-29]. Patients first reported the number of people who experienced the risk/benefit of the treatment over the three time periods. Answers were
deemed correct if within 10% of the precise value [27,28]. Patients then stated the differences in risks/benefits between the treatment and placebo group over the three time periods. This was a multiple-choice question, with one correct answer out of four possible options.

Secondary outcome measures.

Decisional conflict

Patients were asked to make a treatment decision: choose a treatment, choose no treatment or state that they were unsure. Conflict in decisions was recorded using the patient-reported Decisional Conflict Scale (DCS), validated for use in healthcare decisions [5]. The scale consists of 16 items divided into 5 subscales: uncertainty, feeling uninformed, values, support and effective decision.

Individual traits and MS symptoms

Patient demographics, disease variables and disability status [31] were recorded. A short 8-item word recognition task assessed health literacy: the Rapid Estimate of Adult Literacy in Medicine - Revised [32] (REALM-R). Numeracy was assessed by the arithmetic subtask from the Verbal and Spatial reasoning scale [33] (VESPAR). Hospital Anxiety and Depression Scale [34] (HADS) assessed affective MS symptoms, and has been validated for use with MS patients [35]. Fatigue was assessed via the patient-reported Fatigue Severity Scale [36] (FSS), originally developed for the MS population [36]. The Wechsler Test of Adult Reading scale [37] (WTAR) measured premorbid intelligence, which is not altered by cognitive deficits [38]. The Brief International Cognitive Assessment for Multiple Sclerosis [39] (BICAMS) identified cognitive impairments.

Analysis

Sample size estimates were based on a questionnaire which found large effects on MS patients’ understanding [40]. Since only a few questionnaire items specifically assessed treatment knowledge, a
medium effect size (Cohens d of 0.5, [41]) was assumed. It was estimated that for an alpha of 0.05 and power of 0.80, a minimum of 45 patients were required.

All statistical analyses were conducted in SPSS 21. A two-way ANOVA assessed the impact of methods on patients’ understanding of treatments. Bonferroni corrections were applied for pairwise comparisons. Pearson’s product-moment correlations examined the relationship between understanding with standardised DCS scores, individual traits and MS symptoms.

Results

Of 82 eligible patients approached for the study, 45 patients agreed to participate (54.9% response rate). Patient demographics are reported in Table 1.

The effect of (i) methods and (ii) baseline information on understanding

Average understanding scores for each method were as follows: absolute terms (baseline, M=5.40, SD=1.03; no baseline, M=2.58, SD=1.22), relative terms (baseline, M=4.98, SD=1.39; no baseline, M=0.89, SD=0.96) and numbers needed to treat/harm (baseline, M=4.76, SD=1.32; no baseline, M=1.02, SD=1.12).

When collapsing across baseline and no baseline conditions, there was a significant main effect of methods on patients’ understanding, F(2,88)=36.03 p<.001, partial $\eta^2=.45$. Understanding was greater for absolute terms (M=3.99, SD=.93), compared to relative terms (M=2.93, SD=.91, p<.001) and numbers needed to treat/harm (M=2.89, SD=.88). There was no significant difference between relative terms and numbers needed to treat/harm (p=.745).
When collapsing across methods, there was a significant main effect of baseline information on patients’ understanding, $F(1,44)=577.74$, $p<.001$, partial $\eta^2=.93$, with greater understanding for baseline information ($M=5.04$, $SD=.96$) than no baseline information ($M=1.50$, $SD=.74$).

There was a significant interaction between methods and baseline information $F(1,44)=9.62$, $p<.001$, partial $\eta^2=.18$. Adding baseline information to all methods improved understanding.

(iii) Relationship between understanding and decisional conflict

There was no significant correlation between understanding and patients’ decisional conflict ($r=-.131$, $p=.391$) or any DCS subscales.

(iv) Relationship between understanding with individual traits and MS symptoms

Patients mostly showed symptoms of fatigue and cognitive impairments (see supplementary table). Understanding was significantly correlated with numeracy ($r=.517$, $p<.001$), premorbid IQ ($r=.434$, $p<.01$), information processing speed ($r=.439$, $p<.01$) and verbal memory ($r=.409$, $p<.01$).

Discussion

Patients’ ability to understand treatment information is a prerequisite for effective shared decision-making [1,2]. Yet, MS patients do not accurately understand treatment risks and benefits in regular clinical practise [10]. The current study sought to determine the most effective method of communicating treatment information derived from clinical trials to MS patients. As predicted, absolute terms led to better understanding of treatments compared to other methods. Baseline information substantially improved understanding for all methods. However, understanding was not related to patients’ conflict in treatment decisions.
Understanding of treatments was low when communicated in relative terms and numbers needed to treat/harm. Relative terms usually result in larger figures than absolute terms and may be misinterpreted for the latter. This is supported by patients’ likelihood of selecting a treatment when benefits are communicated in relative terms instead of absolute terms [42]. Low understanding for numbers needed to treat/harm may be explained by its similarity to the 1-in-X format (e.g. 1 in 20, 1 in 75), shown to reduce understanding of treatments [43,44]. These methods should be avoided when communicating treatments to MS patients.

The current study showed no relationship between patients’ understanding of treatments and decisional conflict or the DCS informed subscale, inconsistent with previous studies [5-7]. The absence of this relationship may be a result of differences in perceived knowledge measured by the DCS and objective understanding assessed in the current study [5,7]. Although the DCS has been validated for real and hypothetical decisions [5], it is also possible that patients’ decisional conflict may differ for decisions which can have real consequences. Nevertheless, MS patients expressing low conflict in decisions should not be assumed to have good treatment knowledge.

As predicted, understanding of treatments showed a relationship with patients’ numeracy and premorbid IQ. Health literacy did not show a relationship, possibly due to the measure being too short. With regards to MS symptoms, only cognitive impairments showed a relationship with patients’ understanding. A simple assessment of cognition within clinical practice, such as BICAMS [56], could help identify patients requiring support during treatment decision-making. However, this study was not powered to detect relationships between understanding and MS symptoms. Thus, support for patients with affective symptoms and fatigue should not be ruled out.

Findings of the current study should be interpreted in light of its limitations. First, hypothetical treatments were provided to avoid risking patients to new or conflicting information about current medication. However, outcomes may differ for real treatments in which patients feel emotionally
invested and should be evaluated in future work. Second, treatment information was provided in a setting not reflective of a regular consultation, to allow for a systematic assessment of different methods. With the best methods established and incorporated into an educational intervention, future work can implement this in real consultations. Finally, the effect of fatigue and cognitive burden on study outcomes cannot be excluded. Possible effects were minimised by providing breaks and counterbalancing treatments between patients. Fatigue could have influenced scores on BICAMS [44], which was always conducted last in the study. Since BICAMS as a stringent measure identified only mild cognitive impairments in the current patient group, any cognitive burden may have had only a small effect on study outcomes.

Conclusion

The current study is the first to evaluate the best methods of communicating treatment risks and benefits derived from clinical trials to MS patients. Good understanding was evident for treatments expressed in absolute terms and with baseline information. MS patients with low numeracy, low IQ and cognitive deficits should be supported during treatment education.
References


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<th>n (%)</th>
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Methods to communicate clinical trial data

In a clinical trial, 1000 MS patients were given drug A and 1000 MS patients were given a placebo.

**Baseline information**

“150 patients taking drug A experienced risk B, and 50 patients taking placebo experienced risk B”.

**Absolute terms**

“100 more patients taking drug A will experience risk B”

**Relative terms**

“2 times as many patients taking drug A will experience risk B”

**Numbers needed to harm**

“10 patients would have to take drug A for 1 patient to experience risk B”

**Figure 1** Example showing the following methods to communicate clinical trial data: baseline information, absolute terms, relative terms and numbers needed to treat/harm; Example of treatment risk only

Actual study contained hypothetical treatment names and a potential risk (e.g. liver failure)
**Supplementary table**  Patients impaired on assessments (n=45) and correlations between individual traits and MS symptoms with total understanding score

<table>
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<tr>
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<th>Max score</th>
<th>Mean (SD)</th>
<th>Patients impaired, n(%)</th>
<th>Correlation with understanding</th>
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<td>Numerical reasoning</td>
<td>25</td>
<td>16.36 (3.80)</td>
<td>3 (6.7)</td>
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<td>7.42 (1.32)</td>
<td>6 (13.3)</td>
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<td>Anxiety</td>
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<td>6.27 (3.98)</td>
<td>5 (11.1)</td>
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<td>Fatigue</td>
<td>63</td>
<td>44.00 (13.47)</td>
<td>22 (48.9)</td>
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<td>36.69 (8.46)</td>
<td>3 (6.7)</td>
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<td>Info processing speed</td>
<td>110</td>
<td>56.62 (12.62)</td>
<td>14 (31.1)</td>
<td><strong>.439</strong></td>
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<td>Verbal memory</td>
<td>80</td>
<td>49.07 (12.43)</td>
<td>15 (33.3)</td>
<td><strong>.409</strong></td>
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<td>Visual memory</td>
<td>36</td>
<td>21.16 (6.46)</td>
<td>23 (51.1)</td>
<td>.287</td>
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* = indicates significance at the p<.05 level; ** at p<.01 level; *** at p<.001 level; correlations in bold accepted as significant