Perspectives and experiences of Dutch multiple sclerosis patients and multiple sclerosis-specialized neurologists on injectable disease-modifying treatment

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Background: The adherence to treatment with injectable disease-modifying drugs (DMDs) in multiple sclerosis (MS) may benefit from adequate information provision and management of expectations. The communication between patients and physicians is very important in this respect. The current study investigated the perspectives and experiences of the MS patients and neurologists concerning the choice and course of treatment with DMDs in the Netherlands.

Methods: The MS patients (aged 18–60 years; diagnosed with MS at least a year ago, currently treated with injectable DMD treatment) and MS-specialized neurologists (practicing for ≥3 years, treating ≥15 MS patients/month on average, and spending >60% of their time in clinical practice) were asked to complete semistructured Internet-based questionnaires. The neurologists in this study were not necessarily the treating neurologists of the participating MS patients.

Results: In all, 107 MS patients and 18 MS-specialized neurologists completed the questionnaires. The MS-specialized neurologists in this study reported discussing most of the suggested treatment goals with their patients. The MS patients indicated that certain important treatment goals, ie, reduction in disease progression, reduction or prolongation of time to long-term disability, and reduction in new magnetic resonance imaging lesions, were not discussed with them. More than one-quarter of the patients (27%) would appreciate more information about their treatment. We found evidence for suboptimal patient adherence to MS therapy (23% indicated taking a treatment break) due to diverse side effects, lack of efficacy, or practical issues. As compared to these patient reports, the scale of poor adherence was overestimated by more than half of the neurologists (on average, 30% estimated treatment breaks).

Conclusion: The MS patients and MS-specialized neurologists in this study differ in their experiences and perspectives on information provision and adherence to DMDs. Education programs and up-to-date information on MS treatments for both neurologists and patients may be helpful in improving patient involvement and patient–physician communication.

Keywords: multiple sclerosis, disease-modifying treatment, opinion, adherence

Introduction

Several injectable disease-modifying drugs (DMDs) are available for the treatment of multiple sclerosis (MS) aimed at decreasing the frequency and severity of relapses and limiting disease progression. These drugs are often prescribed in an early stage of the disease. Many studies demonstrate poor adherence to long-term therapy.1-3 The World Health Organization defines adherence as “the extent to which a person’s...”
behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider”. In the MS patients, treatment adherence to DMDs varies between 52% and 63%. The reasons to discontinue treatment are a perceived lack of treatment effect, side effects, fatigue, and depression. Treatment adherence may benefit by offering people with MS better information about the effects of the treatment and more involvement in the choice of treatment. A recent study suggests that the perspectives of patients and physicians concerning the choice and course of treatment with DMDs may differ significantly. Patient adherence to treatment was overestimated by the physicians. One in five MS patients reported that the different treatment options were not discussed with them prior to the selection of a DMD by their medical team.

In order to improve information about the available treatment options and improve communication between a patient and a physician, it is important to compare the experiences and perspectives on treatment of both groups. As an addition to the study of Rñon et al, the current study focuses on the Dutch situation. We also made an inventory of the patients’ and neurologists’ preferred methods to gather or share information about treatment goals. We have the following research questions:

- What are the patient perspectives and experiences on DMD treatment initiation and continuation?
- What are the neurologist perspectives and experiences on DMD treatment initiation and continuation, and to what extent are these similar to the patient perspectives and experiences?

**Methods**

**Recruitment of respondents**

Patients affiliated with the National Multiple Sclerosis Foundation were directly invited to participate in the Dutch MS Choices Survey through invitation by email. Advertisements were placed in the quarterly newsletter “MS Nieuwslijn” and on the websites of the National Multiple Sclerosis Foundation (www.nationaalmsfonds.nl and www.msyoung.nl). Patients participating in the web-based Dutch Multiple Sclerosis Study, a prospective long-term assessment of health-related quality of life and disabilities in MS, were informed via email. The study information and the consent form were available and could be downloaded from the website. The information given to the potential participants concerned the purpose of the study, the eligibility criteria, the kind of data to be obtained, where the data were to be stored, and who was the principal investigator. No incentives were offered.

Neurologists were included based on the following criteria: practicing as a neurologist for ≥3 years, treating at least 15 MS patients/month on average, and spending >60% of their time in clinical practice. Based on these criteria, we decided to invite all MS-specialized neurologists from the Dutch Society of MS Neurologists (N=33). They were approached by Leo H Visser and asked to participate in this study. Twenty-two neurologists were willing to participate, and finally, 18 neurologists completed the questionnaires.

Inclusion criteria for patients included being diagnosed with MS at least a year ago, aged between 18 years and 60 years, and currently being treated with an injectable DMD. Patients included in this study were not necessarily treated by the neurologists. It should be noted that Dutch MS patients can choose to be treated by any neurologist, and thereby have access to an MS-specialized neurologist. The study was approved by the Medical Ethical Committee of the St Elisabeth Hospital in Tilburg. All respondents gave informed consent by means of a checkbox online.

**Data collection**

The survey consisted of one questionnaire for patients (see the Supplementary materials) and one for neurologists (see the Supplementary materials). They were based on the questionnaires designed by Rñon et al who conducted a similar survey in seven countries, ie, Australia, Canada, France, Germany, Italy, Spain, and the UK. The questionnaires inquired about the type of treatment, treatment initiation, supply, factors involved in the choice of treatment, treatment goals, sources of information used and needed, side effects, adherence (measured by inquiring about treatment interruptions and discontinuations), opinions about newly available oral treatments, and what factors are important for treatment continuation.

The data were collected between July 2014 and June 2015. Patients completed a semistructured Internet-based questionnaire that took ~20 minutes to complete. The study was performed using the LimeSurvey software, an open-source online application operative on the MS4 Research Institute’s platform. The items of the questionnaire were fixed. The responses were automatically captured. To protect the personal data from unauthorized access, various mechanisms were used to comply with the European Union regulations concerning online medical data, including the use of a personal username and a strong password, separation of answers from questions in the database of personal information, each screen having a username and password.
protection, virtual private network tunneling, 256-bit encryption, and the encryption of the participants’ identities via unique 15-digit codes. Automated checks on completeness were done before questionnaires could be submitted. The respondents saw an overview of all questions and answers before submission, and they could change the answers before submitting. After submission, changes were no longer possible. Only completed questionnaires were analyzed. The help desk (MAH) contacted respondents by phone in case they did not succeed in completing questionnaires. No methods were used to adjust for a nonrepresentativeness of the sample.

The questionnaire consisted of 47 closed-ended questions (each with two to ten possible answers) and two open-ended questions. In a question concerning factors involved in deciding what treatment to take, the importance of a given factor was questioned on a scale from 1 (not important at all) to 5 (extremely important). The Internet-based questionnaire for neurologists took ~15 minutes to complete. This questionnaire consisted of 27 closed-ended questions (each with two to nine possible answers) and seven open-ended questions, mostly concerning an estimate on the percentage of patients involved.

When clicking the hyperlink needed to start the online questionnaire, the inclusion criteria were first checked using several closed-ended questions. When the patient met all the inclusion criteria, an informed consent was presented. If informed consent was given, the link to the questionnaire was provided by email.

Results

Demographics

In all, 107 MS patients and 18 MS-specialized neurologists completed the questionnaire.

<table>
<thead>
<tr>
<th>Table 1 Factors in deciding what treatment to take (patient report)</th>
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</thead>
<tbody>
<tr>
<td><strong>Factors for treatment choice</strong></td>
</tr>
<tr>
<td>How effective the treatment would be in reducing relapses</td>
</tr>
<tr>
<td>How effective the treatment would be in reducing disease progression</td>
</tr>
<tr>
<td>Possible side effects from taking the treatment</td>
</tr>
<tr>
<td>How the treatment would be taken</td>
</tr>
<tr>
<td>How frequently the treatment would be taken</td>
</tr>
<tr>
<td>How it could affect your quality of life</td>
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<tr>
<td>Long-term safety profile of the treatment</td>
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<tr>
<td>Availability of a patient program (offering instructions for administration)</td>
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<tr>
<td>Other factor</td>
</tr>
</tbody>
</table>

Notes: Importance is scored on a scale from 1 (not important at all) to 5 (extremely important). Mean (SD) is noted. Patient-rated importance scores all varied between 1 and 5.

Abbreviation: SD, standard deviation.

Treatment decisions and initiation

Patient involvement

Most of the neurologists (83%; 15/18) believe that patients should select their treatment after discussing the options with their physician. In all, 72% of the neurologists (13/18) stated that their patients were fully involved in the decision process. The other 28% (five of 18) stated that their patients were fairly involved.

Overall, 59% of the patients (63/107) stated that they were responsible for the selection of their treatment after discussing the treatment options with their medical team. In 27% of the patients (29/107), treatment options were discussed and a treatment was recommended by their physician. A total of 14% of the patients (15/107) reported that their treatment was selected for them without any discussion of the options.

Time to treatment initiation

Most neurologists, ie, 78% (14/18), initiated treatment within 6 months after diagnosis and the remainder within 12 months. Most patients, ie, 62% (66/107), reported initiating treatment within 6 months after diagnosis. Almost one-quarter of the patients (24%; 26/107) initiated treatment >12 months after being diagnosed with MS.

Factors important for treatment choice

Factors that are considered important by patients for deciding what treatment to take are listed in Table 1. The effectiveness of the treatment for reducing relapses and effectiveness of the treatment for reducing disease progression are selected by, respectively, 51% and 54% of the patients and are both considered highly important; mean (SD): 4.5 (0.9). Treatment frequency (selected by 41%) and possible side effects of the treatment (selected by 40%) are selected as third and
factors, respectively. How the treatment affects the quality of life and the long-term safety profile are selected by a lower percentage of patients, but are rated highly important. Other factors mentioned by the patients included “how to preserve the medication during travel” and “effects on fatigue”.

Table 2 lists which treatment goals are being discussed according to both patients and neurologists. The neurologists discuss most of the suggested treatment goals with their patients. However, a much lower number of patients indicate that these treatment goals have been discussed with them, especially concerning the reduction in disease progression, the reduction or prolongation of time to long-term disability, and the reduction in new magnetic resonance imaging lesions. In all, 27% of the patients would like to have more information about their treatment, via either the neurologist (21%), the MS nurse (15%), a patient organization (6%), a brochure (12%) or a website with accurate information (13%).

Most neurologists, ie, 56% (ten of 18), would appreciate materials to discuss treatment goals with their patients, eg, brochures (30%), websites with accurate information (50%), medication choice models (10%), or expert panel summaries of the literature (11%).

Table 2 Treatment goals discussed according to patients and neurologists

<table>
<thead>
<tr>
<th>Treatment goals</th>
<th>Percentage of patients (N=107) indicating that the treatment goal was sufficiently discussed with them</th>
<th>Percentage of neurologists (N=18) indicating that they discussed the treatment goal with their patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longer between/less frequency of attacks/episodes/flare-ups</td>
<td>76</td>
<td>89</td>
</tr>
<tr>
<td>Decrease in severity of attacks/episodes/flare-ups</td>
<td>72</td>
<td>83</td>
</tr>
<tr>
<td>Reduction in disease progression</td>
<td>69</td>
<td>94</td>
</tr>
<tr>
<td>Maintains current status/condition</td>
<td>76</td>
<td>72</td>
</tr>
<tr>
<td>Prevents symptoms getting worse (eg, cognition, fatigue)</td>
<td>65</td>
<td>61</td>
</tr>
<tr>
<td>Long-term disability is reduced/prolongs time to long-term disability</td>
<td>55</td>
<td>94</td>
</tr>
<tr>
<td>Reduction in new MRI lesions</td>
<td>54</td>
<td>94</td>
</tr>
<tr>
<td>Less reduction in total brain volume</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>Improvement in quality of life</td>
<td>57</td>
<td>50</td>
</tr>
</tbody>
</table>

Abbreviation: MRI, magnetic resonance imaging.
previous Tysabri use; one of eleven). Two of eleven patients did not know the reason.

Side effects in general
In all, 80% of the patients reported experiencing side effects from the MS treatment at some point during their treatment. In 50%, these side effects have affected their daily life. Flu-like symptoms (selected by 36%), tiredness/lethargy (selected by 28%), and injection-site reactions (selected by 24%) affected daily life the most.

Information sources
Most patients indicated using the neurologist (73%), the MS nurse (63%), or the nurse from their patient support program (42%) as a source to get more information on how to manage their MS treatment more effectively (Figure 2). Other sources included online sources or websites (used by 57% of the patients), the MS society or association (used by 27%), and the manufacturer’s website (22%).

New treatment/innovation
On the question “Which new treatment/innovation do you believe would be likely to benefit you most, as an MS patient, if it was available?”, most patients answered “oral therapy” (34%) or “do not know” (34%). In those who answered “oral therapy”, the majority (78%) explained that this is because they would not have to take injections any more. Of all patients, 89% would still make the choice of

Figure 1 Main reasons why MS patients may take a break or stop their injectable MS treatment according to the neurologists.
Notes: Horizontal axis denotes the percentage of neurologists who consider the indicated reason as the main reason. Multiple selections are possible.
Abbreviation: MS, multiple sclerosis.

Figure 2 Sources or services used by the patients to get more information on how to manage the MS treatment more effectively.
Notes: Horizontal axis denotes the percentage of patients using the source. Multiple selections are possible.
Abbreviations: MS, multiple sclerosis; GP, general practitioner.
injectable medication if oral medication was going to be less effective (Figure 3).

On the question “Which treatment-management interventions do you believe would be likely to benefit MS patients the most if they were available?”, most neurologists (39%; seven of 18) answered “new specific biological therapies”, followed by an “other” type of treatment, ie, “a treatment with effect on disease progression” given by 22% (four of 18) of the neurologists (Figure 4).

**Discussion**

This study was aimed at examining patient and neurologist perspectives and experiences concerning treatment initiation and continuation of injectable DMDs. In the study by Riñon et al,7 a substantial disparity was found between the views of patients and neurologists concerning treatment with injectable DMDs, although there were many differences between the countries involved (ie, Australia, Canada, France, Germany, Italy, Spain, and the UK). DMD benefits are generally considered the greatest when the treatment is started early in the disease course.8 In accordance with the timing of treatment initiation in Spain (82%), 78% of the MS-specialized neurologists in the Netherlands initiated treatment within 6 months after diagnosis. Patient experiences were fairly similar to the neurologists’ perspective; 62% reported initiating treatment within 6 months after diagnosis. However, although none of the neurologists in our study initiated treatment after 12 months, 24% of the patients indicated starting treatment >12 months after being diagnosed with MS. It is unclear why patient and neurologist perspectives differ in this respect, but this discrepancy was also found in the study by Riñon et al. One hypothesis is that these patients decided themselves to start treatment at a later time. Another hypothesis concerns differences between general and MS-specialized neurologists. The neurologists in this study were not necessarily the treating neurologists of the MS patients who participated in

![Figure 3](https://www.dovepress.com/)

**Figure 3** Answer to the question “What new treatment/innovation do you believe would be likely to benefit you most, as an MS patient, if it was available?”.

**Notes:** Horizontal axis denotes the percentage of patients choosing the treatment. Only one selection is possible.

**Abbreviation:** MS, multiple sclerosis.

![Figure 4](https://www.dovepress.com/)

**Figure 4** Answer to the question “Which treatment-management interventions do you believe would be likely to benefit MS patients the most if they were available?”.

**Notes:** Horizontal axis denotes the percentage of neurologists choosing the treatment. Only one selection is possible.

**Abbreviation:** MS, multiple sclerosis.
the study. Immunomodulating therapies in the Netherlands can be prescribed by general neurologists as well as MS-specialized neurologists. The questionnaire was filled in by patients who were treated by either an MS-specialized neurologist or a general neurologist. As only MS-specialized neurologists participated in this study, it is possible that these neurologists advised patients to start treatment earlier than the general neurologists.

Most neurologists (83%) in the current study believed that patients should select their treatment after discussing the options with their medical team. In the study by Riñon et al, only 58% shared this belief. None of the neurologists in the current study believed that patients should not be involved at all. Furthermore, 72% of the neurologists stated that their patients were fully involved in the decision process. This is high in comparison with most countries involved in the study by Riñon et al, where on average, 47% of the physicians stated such. Although most Dutch patients (86%) indicated being involved in the decision-making process, 14% reported that their treatment was selected for them without any discussion of the options. In the study by Riñon et al, this situation occurred in 28% of the patients. The preference of patients themselves not to be involved or the lack of treatment options in specific cases may have made this situation possible. In a previous study in the Netherlands in 2006, a similar percentage of patients (15%) stated that the information had been insufficient to make a proper choice when choosing treatment. Based on these findings, there is still a need for improving patient involvement and patient–physician communication.

**Treatment choice**

Patients considered both the effectiveness of the treatment for reducing relapses and the effectiveness of the treatment for reducing disease progression as the most important factors when deciding what treatment to take. Treatment frequency and possible side effects of the treatment were selected as third and fourth important factors, respectively. Although these factors are less often selected by patients as the most important factors in the choice of treatment, “how the treatment affects quality of life” and the “long-term safety profile” are rated highly important. In a recent study, patient preferences for injectable treatments in MS were gathered through a discrete-choice experiment, indicating trade-offs that people were willing to make. In that study, certain changes in injection frequency were as important to the MS patients as treatment efficacy. Although we did not conduct a choice experiment and the results cannot be easily compared, the MS patients in this study selected treatment efficacy as the most important factor when selecting a treatment, beyond injection frequency. Considering treatment efficacy, we found that reducing the number of relapses and reducing disease progression were considered almost equally (highly) important by the MS patients in the current study.

The MS patients and MS-specialized neurologists in the Netherlands differed in their experience on treatment goals that are being discussed. Treatment goals such as the reduction in disease progression (indicated as a very important factor in the treatment choice by the MS patients), the reduction or prolongation of time to long-term disability, and the reduction in new magnetic resonance imaging lesions are much less often discussed with patients than indicated by the neurologists. It seems debatable whether patients would explicitly remember all these various treatment goals being discussed with them. Still, the fact that the most important factor in the treatment choice, ie reduction in disease progression, is discussed with only 69% of the patients, while 94% of the neurologists indicate that this goal is a topic of discussion, is a finding of interest.

**Adherence**

Almost all neurologists (94%) in the current study felt that adherence is an issue when treating the MS patients. In contrast, in the study by Riñon et al, most physicians (59%) did not consider adherence as an issue when treating the MS patients. This is a remarkable difference, even more so when considering that adherence was operationalized in exactly the same manner in both studies.

The neurologists’ estimates concerning the percentage of patients taking a treatment break were very diverse, ranging from 5% to 80% of the patients. The neurologists estimated that on average, 16% discontinued treatment. In the current study, 23% of the MS patients reported taking a break from treatment for ≥1 day and 19% reported once having discontinued treatment. In the study by Riñon et al, the percentage of patients taking a treatment break varied between countries from 16% to 47%. The scale of nonadherence in terms of treatment breaks was overestimated by more than half of the neurologists participating in this study. The fact that almost all of our neurologists consider adherence as an issue in treatment with DMDs may have resulted in this overestimation, which is in sharp contrast with the high levels of underestimation found by Riñon et al. Another option is that the number of treatment breaks was underreported by the MS patients in this study. Providing socially desirable answers is a general issue when using self-report measures.
The true level of treatment adherence can only be verified in studies using more objective measures. Both neurologists and patients need adequate up-to-date information on this topic.

The patients and neurologists both noted side effects and lack of efficacy as the most important reasons for nonadherence. The neurologists mentioned injection-site reactions and flu-like symptoms as the two side effects with the greatest impact on treatment adherence, followed by mood changes. The patients named a diversity of treatment side effects as reasons to discontinue treatment. The association between adverse events, such as flu-like symptoms, injection-site reactions, and lipatrophy, and long-term adherence has been previously described.\textsuperscript{6,10} While neurologists view either a combination of physical and psychological factors (33%), physical factors alone (33%), or psychological factors alone (33%) as most likely reasons for nonadherence, the majority of patients noted physical factors as the main reason for nonadherence. This may be related to a reluctance to acknowledge the involvement of psychological factors by patients, or perhaps, patients perceive these factors as less relevant to treatment adherence. Previous studies found that cognitive impairment, depression, and needle phobia may negatively affect treatment adherence.\textsuperscript{6,10} The use of periodic checks with a simple questionnaire in the waiting room may help neurologists become more aware of their patients’ treatment expectations and barriers.\textsuperscript{11} Neurologists, MS nurses, and informative websites are the most commonly named sources of information for managing treatment with DMDs. More than one-quarter of the patients would like to have more information about their treatment, either via the neurologist, MS nurse, websites with accurate information, brochures or a patient organization.

At the time this survey was sent, oral medication as a first line treatment became available in the Netherlands (October 2014). One of the inclusion criteria was that patients had to be on injectable DMDs, and because of the recent introduction of first-line oral treatment, lack of experience with these new oral DMDs, and the ability to compare our data with the results of the study of Riñon et al, we decided to stick to the earlier defined criteria. Out of several potential future treatment options, many patients indicated that oral treatment would benefit them most as they would not have to take injections anymore. However, the MS patients in this sample would still choose to take injectables if oral treatment was going to be less effective. In this respect, it should be kept in mind that all the MS patients in this study were currently using injectable DMDs. Preferences may be different in patients who are not taking or stopped taking injectables. Neurologists indicated seeing most benefit in new specific biological therapies. Interestingly, one-quarter of the neurologists provided as alternative a potential future treatment that would have an effect on disease progression.

Limitations

Although this study provides new information on Dutch patient and neurologist perspectives on the use of DMDs, there are some limitations that were also mentioned in the study by Riñon et al.\textsuperscript{7} These are the unavoidable differences in the formulation of questions posed in the patient and neurologist surveys and the fact that the neurologists in this study were not necessarily the treating neurologists of the MS patients who participated in this study. Furthermore, the neurologists included in this study have treated many MS patients. There may be a larger discrepancy between patient–neurologist perspectives in neurologists with less clinical experience with the MS patients. Another limitation is the relatively low number of participating neurologists as compared to the relatively high number of participating MS patients. This is a direct result of our decision to invite only MS-specialized neurologists. In future studies, it would be interesting to also include general neurologists and aim at directly comparing the views of neurologists and the patients they treated. Finally, the results could not be specified in terms of disease characteristics (eg, disease duration, duration of DMD use, level of disability) as this information was not available. The diversity in patient experiences and perspectives may be related to diverse disease characteristics. However, a specification of perspectives in terms of disease characteristics was not the main focus of this study.

Furthermore, the field involved in the treatment of MS is rapidly changing and a comparable study should be done within a few years with the inclusion of the new available oral medications and the new injectables. This study may use a revealed or stated preference method to examine trade-offs in treatment choices that people are willing to make.\textsuperscript{9} Positive aspects are the representative number of included MS patients and Dutch neurologists specialized in MS. The questionnaire was adequately designed by Riñon et al\textsuperscript{7} and adapted in collaboration with the clinical experts.

Conclusion

We found some differences in the experiences and perspectives of the participating MS patients and MS-specialized neurologists concerning information provision and adherence to DMDs. Dutch MS neurologists are very supportive
of patient involvement and aim to discuss various treatment goals. The MS patients included in this study indicated that important treatment goals were not always discussed with them, and 14% reported that their treatment was selected for them without any discussion of the options. We found that the MS patients considered the effectiveness of the treatment for reducing relapses and the effectiveness of the treatment for reducing disease progression as the most important factors when deciding what treatment to take. As in the study by Riñon et al, we found evidence for suboptimal patient adherence to MS therapy, due to diverse side effects, lack of efficacy, or practical issues. As compared to these patient reports, the scale of suboptimal adherence was overestimated by more than half of the neurologists. In this respect, there may be a large focus on adherence in the Netherlands, but less access to adequate up-to-date information on this topic. Finally, it is important to stress that the neurologist is considered the most consulted source of information for treatment management by MS patients.

This information on patient and neurologist perspectives may be very helpful for health care professionals and professionals in health care education. Education programs for both neurologists and patients may improve patient involvement and patient–physician communication. There is a need for up-to-date information about possible treatments and treatment management. Accurate websites, brochures, medication choice models, and independent expert summaries of relevant scientific literature (indicated by neurologists) would be very helpful in this respect.

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Disclosure
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