
Patient Perspectives on Disease-Modifying Therapy in Multiple Sclerosis

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*The purpose of this study was to understand factors contributing to the decision-making processes of individuals with multiple sclerosis (MS) regarding the use of disease-modifying therapy (DMT). Semi-structured qualitative interviews were conducted with 18 individuals with MS. Qualitative interviews revealed two major themes: opting for and opting out of DMT. Participants indicated that stable health, predictability, and perceived control were reasons to be on DMT. They also indicated that taking DMT is not without personal cost, both financial and psychological (eg, denial, fear, and uncertainty). Fear of needles and side effects, not feeling “sick enough,” the costs of medication versus benefits, and discouragement from physicians were given as reasons for opting out of DMT. Participants also reported that restarting DMT after they had stopped was difficult, especially if they felt better when not using DMT. Early treatment of MS with DMT, especially for those with relapsing-remitting MS, is strongly supported by published findings. Although participants in our study revealed significant barriers to initiating and adhering to DMT, recent advances in clinical practice and improved coverage for treatment costs should reduce these barriers. *Int J MS Care*. 2006;8:11–18.*

Multiple sclerosis (MS), a chronic and often disabling disease of the central nervous system, affects at least 400,000 people living in the United States. MS occurs through a process of destruction of the myelin sheath that protects the nerves and enables rapid transmission of nerve impulses in the brain and spinal cord. This progressive demyelination is initially an inflammatory process that ultimately leads to the destruction of the nerve axon itself. The initial inflammation is called an exacerbation and can often be treated with medications to reduce inflammation, which may result in less residual damage. MS is characterized by a complex array of symptoms, including physical and cognitive changes, and typically presents with a relapsing-remitting course. However, after an average of 15 years, most people experience a secondary progressive phase in which the course either becomes continuously progressing or progresses between exacerbations.¹

MS is now thought to be an immune-mediated disorder that develops from a complex interaction of early exposure to multiple viruses and genetic vulnerability.^{2,3} Although the role of the immune system in MS is not fully understood, several immunomodulatory drugs have been developed. Disease-modifying therapy (DMT) has been shown in clinical trials to

alter the course of MS by reducing the number and severity of attacks by more than 30%, reducing disease activity (ie, development of lesions) by up to 75%, and prolonging the onset of disability by nearly 40% in individuals with both relapsing-remitting MS (RRMS) and secondary progressive MS.^{2,4-7} Less is known about the effectiveness of these medications on primary progressive MS.

Known as the ABCR drugs (Avonex, Betaseron, Copaxone, and Rebif), these DMTs have changed the way clinicians manage RRMS.⁴ Based on the convincing results of clinical studies, the executive committee of the medical advisory board of the National Multiple Sclerosis Society published a statement advising that an immunomodulator (ABCR drug) be started as early as possible after a definite diagnosis of MS with a relapsing course. Furthermore, they recommend that this treatment be considered for select patients who experience the first attack if they are at high risk for MS.⁸

Early treatment is essential, because neurological damage is irreversible. Researchers generally agree that individuals with MS should be treated with DMT as soon as possible after diagnosis.^{4,6-10} Despite clear recommendations, a 2002 survey reported that only 50% of all MS patients in the United States and 60% of those with RRMS are using DMT. Of those who decide to start DMT, between 12 and 25% discontinue therapy.¹¹ Mohr et al.¹² reported that many patients who begin treatment will discontinue DMT within a few months

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or may opt out altogether because of side effects, self-injection anxiety, and concerns about the cost-effectiveness of treatment. Patient lack of knowledge about DMT, lack of visible results or improvements in functional status, low self-efficacy, and cognitive or physical impairment have also been reported to influence therapy adherence.^{12–15} In addition, physician attitudes about treatment, both positive and negative, and the availability of medical support staff (eg, MS specialty nurses) affect whether patients adhere to DMT.^{13,15}

Decision making is grounded in the personal and social context of people's lives, and it involves complex psychological processes and multiple (sometimes conflicting) goals and expectations.¹⁶ To better understand which factors contribute to the decision-making process of individuals with MS regarding the use of DMT, we used a qualitative research approach to examine this issue from the individual's perspective.

Methods

Qualitative research methods were chosen for this study because they enable examination of issues related to MS from the perspective of the study participant. Qualitative methodology is the inductive step in research and leads to hypothesis seeking and theory building. These methods have yielded valuable information that has been used to further theory development and shape clinical practice in numerous health-related fields. Phenomenological research is one qualitative method that enables examination of human experience without the inclusion of preconceived ideas or assumptions.¹⁷ The focus of phenomenology is the description of lived experiences of individuals in their everyday lives, revealing the meaning of the experiences. Phenomenological research is guided by the use of subjective and first-person experience as a source of knowledge. Its main theoretical premise is that the meaning of an experience can only be understood if it is presented within the context in which it occurred. During a series of semistructured interviews, the participant shares the information he or she feels is most crucial.

Participants

In qualitative methodology, the number of subjects typically ranges from 6 to 20, and explicit sampling strategies are not used. For this study, subjects were drawn from a pool of individuals who had volunteered to participate in future research when responding to our large survey of people with MS in metropolitan Seattle, Washington. The original survey was distributed by the MS Association of King County on our behalf. Eighteen participants (16 women, 2 men) were interviewed for the current study (Table 1). All participants volunteered, and none were remunerated. Note that 10 participants completed at least one follow-up interview 6 months after the first interview. Participants were not selected based

on whether they were undergoing or had undergone DMT or on which medication they had taken or were currently taking. The average age of participants was 43 years (range 27–62 years), and average time since diagnosis was 8.1 years (range 3–16 years). Most (16) subjects were diagnosed with RRMS (based on self-report) at the time of the interviews. Only one individual reported secondary progressive and one reported primary progressive MS. All participants completed an informed consent form approved by the University of Washington institutional review board. As part of the consent process, participants were told that they could discontinue participation at any time. Although not all of the individuals in our study would have been good candidates for DMT at the time of their interviews, all of them had strong feelings, both positive and negative, about being on DMT.

Interviews

Interviews were conducted by two of the researchers between 2000 and 2003. One of the researchers took the role of primary interviewer. The other contributed to the interview when appropriate and kept field notes that included any pertinent observations about the participant at the time of the interview. Interviews were 60–90 minutes long and took place at a location that was most convenient for the participant, ie, the University of Washington or the participant's home or work setting. All interviews were audio recorded. Interviews were semistructured and open ended. The interviewers occasionally used prompts or questions to guide the participant back to the focus of the study.

Participants were asked to describe their everyday experiences of living and working with MS. The purpose of the interview was carefully explained and reviewed when necessary. This explanation introduced the notion that the participant was the expert and the interviewer was interested in understanding what it was like to live and work with MS. Each interview began with broad questions such as, *Tell me what a typical workday is like for you.* When the participant mentioned the subject of drug therapy for MS, the interviewer asked additional questions and guided the participant to fully describe his or her experiences regarding use of DMT, the decision to begin drug therapy, and issues surrounding the costs and benefits of that therapy.

Questions were presented in neutral terms to minimize potential bias. The interviewer encouraged the participant to elaborate freely on the topic and asked for further description or definition when information shared was vague or unclear. The interviewer continually reflected on the information communicated by the participant to ensure understanding and emphasize the importance of the information being given. Interviews were continued until a saturation level had been reached. Saturation was reached when further interview-

Table 1. Characteristics of study participants

Identifier	Age (y)	Sex	Type of MS	Time since diagnosis (y)	Occupation	Employment status	Interviews (n)	Mobility	Drugs
AA	29	F	RR	5	Administrative assistant	Full time	5	Good	Discontinued Copaxone
BL	46	F	RR	16	Loan underwriter	Full time	5	In wheelchair	Betaseron
BO	55	F	RR	8	Bank operations	Part time	1	Slow	Betaseron
DS	32	M	RR	8	Student/software engineer	Part time + school	1	Good	Copaxone
EP	34	F	RR	4	Project manager	Part time	4	Good	Copaxone
GG	27	F	RR	5	Store manager	Full time	1	Good	Copaxone
GH	46	F	RR	15	Systems analyst	Part time	5	Slow	Copaxone
GL	62	M	PP	11	Insurance broker	Retired early	1	Slow	None
MD	38	F	RR	3	Manufacturing	On disability	1	Good	None
ML	56	F	RR	16	Paralegal	Retired	1	Slow, uses cane	None
MR	38	F	SP	16	Receptionist	4 days/wk	3	Uses walker, wheelchair	None
PK	35	F	RR	5	Investigator	Full time	3	Good	Avonex
PW	40	F	RR	4	Communications specialist	4 days/wk	2	Good	Discontinued Avonex
SP	54	F	RR	9	Administrative assistant	On disability	2	Good	Avonex
ST	58	F	RR	8	Teacher	Retired early	1	Uses cane	None
TC	40	F	RR	4	Consultant	Stopped working	3	Good	Betaseron
WD	38	F	RR	5	Web designer	Full time	1	Good	Avonex
WL	39	F	RR	4	Volunteer coordinator	Stopped working	2	Good	Copaxone

MS = multiple sclerosis; PP = primary progressive; RR = relapsing remitting; SP = secondary progressive

ing did not yield any information that was not shared by previous participants.

Analysis

The recorded interviews were transcribed verbatim. Accuracy of the transcripts was verified by one of the interviewers, who also transcribed any portions of the interview that were difficult to understand. Data analysis was consistent with the principles outlined by Benner.¹⁷ Each manuscript was read several times to grasp the essence of the entire interview. The interviews were then reread several more times to identify ideas or opinions about the experience of working with MS. This information was used to develop an initial coding system that reflected what participants felt were important issues related to drug therapy and MS.

The Ethnograph software package,¹⁸ a computerized indexing system, was used for the organization and coding of

a large amount of textual information gathered in this project. Initial coding identified all information having to do with the use of medications for treatment of MS. As the transcripts were reread, common themes began to emerge. For example, the transcripts revealed that a fear of needles was one factor related to not using DMT. Initial coding of the interviews was completed separately and in groups by each of the authors.

Summary descriptions of the themes presented in each interview were drafted to facilitate finding similarities and differences among the interviews. Initial themes were carefully reviewed and discussed by the entire research group. Each author brought a unique perspective to the interviews and moved the interpretation process forward beyond any one person's views. The trustworthiness of the analysis was enhanced by the research team's commitment to challenge each others' biases and honor the perspectives of the partici-

Table 2. Issues discussed by participants

Theme	Example
Opting for DMT therapy	
Perceived benefits of DMT	
Stable health and predictability	Physical wellness; even keel, less worry
Being in control	Improved confidence; proactive
Concerns and difficulties associated with DMT	
Financial cost and insurance	Gratitude for insurance; fear of changing jobs
Denial and fear	Issues of denial; inner strength
Uncertain outcomes	No tangible evidence
Opting out of DMT intervention	
Dislike of needles	Awaiting oral therapy
Not sick enough	Minimal symptoms; waiting for change
Fear of side effects	Others' experiences; feeling normal
Cost vs benefit	Minimal symptoms
Physician discouragement	Uncertain effectiveness

DMT = disease-modifying therapy

pants. This process continued until all of the authors agreed that the themes had been interpreted accurately, reflected the information provided in the interviews, and answered the questions posed by the study.

The findings were further validated during follow-up interviews with the participants.¹⁷ A summary of the initial interview and its interpretation was reviewed with the participant, who was asked to comment on the validity of the interpretations offered. The research team then reviewed these comments, and themes were adjusted, if necessary, to incorporate participant feedback. The remainder of the follow-up interviews focused on changes that may have occurred in participants' circumstances since the initial interview.

Results

Opting for DMT

Eleven participants reported being on DMT at the time of the interviews. The perspectives of participants who opted to initiate DMT fell into two major themes: perceived benefits and personal cost of DMT. Within each theme, we identified several subthemes (Table 2).

Perceived Benefits of DMT

Stable health and predictability. For some participants, DMT was clearly the best choice because they had fewer exacerbations, could anticipate a more stable course, and felt more confidence in their ability to manage MS. Their responses were consistent with enhanced self-efficacy with respect to their MS. BL, a wheelchair user, described it clearly:

Before I was on the Betaseron, if I got a bad flare up, I couldn't even walk.... Taking the steroids would

put it off, but it was hard going through that. I don't have the need for it as much now. I am on an even keel; I don't get worse; I don't get better, just stay the same, which is nice, because I don't have to worry about the bad parts. I hope it keeps working.

EP described the comfort of having her MS stable and predictable:

My neurologist told me that I was neurologically boring the last time I went to see him and that is a good thing...really nice to hear. The medication that I am on [Copaxone] must be working. I am just lucky I guess.

For EP, enhanced health and a predictable course were important:

I think that my confidence level around the MS has increased because of the success I have had with the Copaxone.

Being in control. Some of the participants noted that their choice to take DMT leaves them feeling proactive and in control. For example, BL said:

I guess I am the kind of person who likes to...know what is going on and to be in control...that medicine has really worked.... I don't worry that I am going to get worse, so I am trusting that medicine.

For GG, getting on a regimen felt proactive:

I got right on the medicine, and I felt like, OK, I am doing something.

WL felt she had a narrow range of issues around MS over which she has control:

There's so little I can do medically but take my medicine and stuff...I'm trying to have as much...control as I can.

GH wants to be in control of the decision-making process:

I am like a doctor's nightmare. I demand information. Don't tell me to take this and then not tell me anything else or explain anything.

Concerns and Difficulties Associated With DMT

Participants reported several concerns and difficulties about personal costs associated with being on DMT.

Financial cost and insurance. The cost of medications can be substantial, and access to health insurance is critical. For example, EP's concerns about paying for medications has meant that she is afraid to leave a job she is unhappy with:

I'm afraid of losing the good health insurance coverage that I have. Although my husband has good insurance coverage, the coverage for Copaxone is not good. With my insurance, I paid almost nothing for Copaxone, and I mean that is big when your drugs cost \$10,000 a year.

PK describes the circle of needing the medications to work and needing work to have health insurance to pay for the medications:

If I can't work and pay the bills, where am I going to get medical insurance?

Denial and fear. Taking DMT drugs required some participants to confront their own denial and face their attitudes toward disability, injections, and drugs and caused them to think about MS more than they otherwise would. For example, AA observed:

The first time I realized that I might be taking Copaxone injections, I was really upset. I just really had to work through a lot of stuff with it. Take the injections every day and stuff. That was a lot of my problem, and really just overcoming my own denial.

PK reported that taking her medications required her to think about having MS:

When I started on the Avonex about 4 months ago, it brought up a lot of feelings for me. I...had this healthy denial and I only had these little episodes, but then half my face and scalp went numb, and I had a lot of pain and they diagnosed me with relapsing-remitting MS. Then I went on the Avonex. I am not in healthy denial anymore. I kind of think about it constantly; I am worried about the future.

AA, who eventually discontinued DMT, echoed similar sentiments:

What I did know is that it made me feel like an invalid to do a shot every day... So, if I was doing the DMT drugs every day, then I'm thinking about it (MS), you're owning it, you're being it every single day.

TC explained how difficult the injections are for him:

[G]iving yourself shots is a stressful thing in itself. I had told the doctor originally... "Do you not understand that I come from the generation that was taught it was bad to stick your body with a needle?" And all of a sudden you have to do it every other day and...oh don't you feel good about yourself.

WD acknowledged the two sides of the injections:

...and that shot! I mean, who likes to give themselves a shot? No one. But I can do it, and I'm thankful for it. Every Friday, I'm thanking all those researchers that gave up their time and their energy to develop this.

Uncertain outcomes. For some participants, uncertainty about whether the medications were having the intended effect contributed to ambivalence and distress. For example, DS was not sure whether to attribute his current stability to medications:

I've been on Copaxone since May, which is supposed to stabilize symptoms, but they might have been stable all along.

AA observed that there have been no perceivable benefits of DMT for quite some time:

After, what, 2 years, I can say, okay, I haven't had an episode this whole time, so it must be working. But, like in the next 6 months or a year, I don't know if I will really see it. Because, when you are doing [DMT treatment] you know no difference if you do it or you don't. In other words, you don't feel better if you do.

BO feels that tolerating uncertainty of the outcome is a better choice than hoping that his MS would have a benign disease course:

The thing with Betaseron is that maybe it's working...but I know enough about MS that I could have had two episodes and nothing ever again. I don't know, but I am not going to take any chances.

Opting Out of DMT

Five participants chose not to take the disease-modifying drugs, and two had discontinued DMT. Reasons for opting out of DMT were dislike of needles, not being "sick enough," fear of side effects, cost versus benefit, and discouragement from physicians.

Dislike of Needles

Some participants chose not to take DMT medications because they found the process of self-injection intolerable. AA stopped injecting her medications:

I tell you, it is just like getting a big nasty bug bite every night.

GL was unequivocal:

No, I don't take any shots. I made that decision... and I said, "Doc I don't like needles, I will start doing that stuff when they give me pills," and I said, "Don't even bring it up again. I will tell you no."

AA also indicated that she would be willing to consider oral medications:

Have they come out with an oral Copaxone yet?

Not Sick Enough

For some participants, believing that they were not sick enough to profit from the medications played a role in their decision not to take or to discontinue DMT. AA:

I just feel I am not sick enough to do injections every day. So I kind of told myself that if I get another bout of optic neuritis or another one of the biggies, then I will go ahead and do it.

Even though she does not see herself as sick now, MR is willing to consider taking the medications:

I am willing to look at this issue over time... I am not having exacerbations even though they say chronic progressive now should be on it too, which is probably where they would put me.

MR is aware of the benefits of DMT, but her MRI looks good, and she does not see a reason to go on it now:

I'm not on any of the medications, and even though you can be stable clinically, sometimes there can be changes going on in the brain that you are not aware of, so I asked the neurologist [to] redo my MRI, just to make sure it looks okay. Because, if there was something alarming looking there, then I might reconsider if I wanted to go on the medication. And that all looked great, so [I didn't].

ST acknowledged that she allows herself to believe she has been misdiagnosed:

The doctor asked me, "Why have you been so unwilling to go under more aggressive medication?" I said, "Well I didn't want to disrupt what I had in the hopes that this would go away. I just choose to think that you misdiagnosed, but know intellectually that you did not."

Fear of Side Effects

Anticipating side effects played a key role in decisions to not start or discontinue DMT. MR believed that several acquaintances had significant side effects:

I know two people personally who have developed brain tumors after being on the ABC drugs.

PW found that she felt better when she discontinued DMT:

I was on Avonex. I did it for almost a full year. But around Christmastime, it got kind of hectic and I got off. I missed a couple because I go in once a week. And I found actually that I felt better... I read the literature; I understand that it's protecting you against something in the future. But that's my current struggle. I'm really having a hard time going back on it since I feel pretty good.

Cost Versus Benefit

ML explained the ambivalence about balancing the cost with uncertain outcomes (when asked if she was on any DMT):

Can't afford it. I mean quality of life is important to me, and if I'm putting out \$11,000 a year on a medication that may or may not work, my quality of life is really deteriorating.

GG noted that her physician was concerned about the cost versus benefit:

My other doctor was saying that they don't know about insurance, and it costs \$10,000 per year to pay for that medicine, and there is only a third of a chance that it could help you.

Physician Discouragement

Several participants understood their physician to recommend against DMT because their symptoms were stable. MR went for a second opinion to a neurologist reputed to be aggressive with his MS patients:

[E]ven at that time, he said, "You are stable. You are not having attacks. I wouldn't put you on them. We don't know the long term, what is going to happen."

Although currently opting to take DMT, three of our participants were originally discouraged by their physicians from starting it. For example, EP, who now takes Betaseron, had earlier inquired about the DMT medications:

He, my doctor, discouraged me actually, from going on the Betaseron.

PK, who currently takes Avonex, was told her MS was not severe enough to use DMT but now feels she was not well advised:

Eventually I was sent to a neurologist, and he told me that he thought this seemed very benign. I got the impression that it wasn't going to be a factor in my life, that I shouldn't expect to have any more attacks, or very few, very rare ones.

Discussion

Early treatment of MS with DMT, especially for those with RRMS, is strongly supported by published findings in clinical studies and by longer-term data that have accumulated since DMT became available. Despite the benefits associated with DMT, some participants in this study (5 of 16) had never been on DMT and a few (2) had discontinued it. Of those who had never been on it, one participant had secondary progressive and another had primary progressive MS. Although less research indicates that DMT is effective for people with secondary and primary progressive disease, efficacy was not the primary motivation for opting out of DMT. Rather, the patients were concerned about self-injection or perceived themselves to not have symptoms that were sufficiently severe to justify it. The remaining three who had never been on DMT and two who had discontinued would probably benefit from it. All 11 participants who were on DMT had RRMS and presumably were appropriate candidates for this kind of therapy.

Participants in our study carefully considered the pros and cons of DMT before making a decision to begin, continue, or discontinue DMT. For individuals with a chronic disease such as MS, problems associated with adherence to medication are complex.¹³ This is especially true when the treatment being administered does not provide any immediate or obvious benefit and can have adverse side effects.^{13,14} In our study, respondents reported barriers to initiation and adherence to DMT treatment similar to those reported in previous studies (eg, cost, limitations of health insurance, difficulties with needles and self-injection, side effects).¹⁹ Our findings are also consistent with the reports that patients taking one of the disease-modifying drugs described feelings of control over their MS by taking the medication and feelings of hope for the future.¹⁵

The recurring concern voiced by both those who opted for and out of DMT was the lack of guarantee that DMT would make a significant difference in the long run. For those who experienced exacerbations before DMT, the decision to initiate and adhere to the therapy appeared easier because they could measure the benefits of the therapy by observing fewer exacerbations while on medication. For those who experienced no or infrequent flare-ups, seeing the benefits was more difficult, so the patients were frustrated with not knowing whether the therapy was working. Understandably, patients are uncertain about the long-term benefits of treatment, and the goal of preventing future disabilities is abstract. In particular, patients and/or their physicians may interpret the absence of current symptoms to mean that their MS will have a benign course, so patients may opt out of treatment. Any added disincentive (eg, cost, concerns about injections, possible side effects) tend to support the decision not to initiate

DMT, at least for the time being. Unfortunately, patients at the earliest stages of MS, with few symptoms, are the ones who could benefit the most from DMT.

In deciding whether to take or not take DMT, patients have to solve a complex equation. Each of the pros and cons is viewed through the lens of individual beliefs and experiences. The likelihood of opting for DMT might increase if more convincing evidence were available about the long-term efficacy of the therapy for that particular individual. Also, patients would probably be more likely to choose DMT if concerns were eliminated or reduced through patient education, provider counseling, or perhaps peer-to-peer support.

For some respondents in this study, the cost of DMT was a significant concern, even for those taking it. As noted by Johnson et al.,²⁰ people with MS are unemployed at a higher rate than would be expected given their age and education level, and finances are a key issue. Health insurance may not pay all or even part of the cost of DMT or may cover some medications and not others. Many states have “high-cost medication” pools, but the pools can be difficult to navigate. As of June 2004, Medicare coverage has been extended to include drugs, or biologics, used in the treatment of MS. The change has been implemented as part of a demonstration project under the amended Medicare law for 2004 and 2005, and permanent changes are being considered in the reauthorization of Medicare. In addition, several of the pharmaceutical companies that make disease-modifying drugs have programs for people who have low or very low income. Until the financial burden of DMT on patients is lowered, health care providers must inquire about the role of financial cost in making the decision to not take DMT. In cases where cost plays a significant role, referral should be made to a professional such as a social worker, MS nurse specialist, or financial specialist at the local MS Society who can help the patient identify funding options.

In conclusion, despite compelling support for the efficacy of early DMT intervention for RRMS to reduce the accumulation of lesion load and advancement of disability, some of our participants have opted out of DMT for various reasons. With early clinical support for patients regarding the financial and psychological issues of DMT and consistent efforts to educate patients about its beneficial effects on the progression of MS, we are optimistic that the barriers described by our study participants will continue to break down. □

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