“After the transition is before the transition” – Experiences of medically induced treatment discontinuation of disease-modifying therapies in people with multiple sclerosis: A qualitative descriptive study.

Robert Ammann

UniversitätsSpital Zurich

André Fringer (✉ mail@afringer.ch)

Zürcher Hochschule für Angewandte Wissenschaften <https://orcid.org/0000-0003-4950-7788>

Research article

Keywords: Multiple sclerosis, Disease-modifying therapy, Discontinuation of therapy, Patient experience, Qualitative description

Posted Date: October 14th, 2019

DOI: <https://doi.org/10.21203/rs.2.16027/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Treatment discontinuation and non-adherence are widely discussed topics in the context of multiple sclerosis (MS). However, little is known about the experience of medically induced discontinuation of disease-modifying therapies in people with MS. Serious side effects or treatment failure are possible reasons for discontinuation. Prevalence of treatment switches is high in people with MS. Doctors initiate almost 50% of treatment switches.

Methods: The aim of this study was to explore how people with MS experience medically induced treatment discontinuation. Using a qualitative-descriptive approach, ten semi-structured interviews were conducted with adult persons suffering from MS. Data analysis followed the procedure suggested by Saldaña. Open and axial coding were applied. The analysis was continued until it was possible to draw conclusions about participants' experiences and to answer the research question. At the end, the experiences could be synthesised into categories, resulting in a conceptual model.

Results: „ After the transition is before the transition “ was identified as central phenomenon. People with MS experience medically induced discontinuation as part of a cycle of repeated treatment switches. They get to know treatment options, develop criteria for treatment and decide about treatment, taking into account professional advice and personal preferences. Once treatment starts, health care professionals and people with MS assess whether it is well-tolerated and effective. If not, a decision about treatment discontinuation is necessary. Discontinued treatment implies that the cycle begins again. Health personnel initiates the cycle and supports patients with professional advice. Family and friends ensure that the perspective of people with MS is considered in the decision process.

Conclusions: Experiencing medically induced treatment discontinuation is a silent phenomenon requiring health care professionals' attention. Uncertainty associated with treatment adds to uncertainty of the disease trajectory. Knowledge can contribute to a feeling of control. Finding normality in the context of a treatment switch is essential. People with MS need continuing support from health care professionals beyond the moment of treatment decision.

Background

Multiple Sclerosis (MS) is a chronic inflammatory illness of the central nervous system characterized by a high degree of uncertainty with regard to progression [1]. Several types can be distinguished, among them relapsing-remitting, secondary-progressive and primary-progressive MS. About 80% of people with MS suffer from a relapsing-remitting type, possibly developing into the secondary-progressive type [2].

Worldwide, the number of persons affected by MS is estimated at 2.3 millions. The prevalence consists of 33 per 100,000 persons, varying between different regions due to environmental factors. In Europe, the prevalence is 108 per 100,000 persons, in Northern America 140 per 100,000 persons [3].

Since almost twenty years, relapsing-remitting MS can be treated by means of disease-modifying agents [4]. Although healing MS is impossible, these agents can reduce the frequency of relapses and slow down the progression of the disease [1, 5].

In the last years, the number of available drugs steadily increased. Meanwhile, more than ten different disease-modifying agents are approved for treating relapsing-remitting MS in the USA or Europe, and several are under development [6]. More recent treatment options show higher effectiveness and are easier to apply. However, the risk for serious side effects is elevated [7].

Disease-modifying therapies are intended for continuous treatment. From the medical point of view, the following indications require to interrupt treatment: an agent proves to be ineffective with regard to disease progression, serious side effects occur, and neutralizing antibodies probably reducing therapy effectiveness are detected [8]. Undesirable side effects possibly leading to medically-induced discontinuation comprise, for example, depression [9], rising risk for progressive multifocal leukoencephalopathy [10], hepatotoxicity [11] or changed blood values [12].

Treatment switches in disease-modifying therapies are common. According to Bonafede et al. [5], almost one fifth of people with MS change the therapy already during the first two years. During the entire course of disease, 75% of people with MS change their disease-modifying therapy at least once, 14% switch three times or more [13]. Therapy discontinuations are initiated either by persons with MS or by attending physicians for medical reasons. In a recent study up to 42.5% of treatment discontinuation was physician-driven [14].

The higher the number of available disease-modifying therapies, the more probable is a switch [13]. Currently, „no evidence of disease activity“ is discussed as a new treatment goal [15]. „No evidence of disease activity“ means a lack of visible disease activity in imaging and clinical controls. This treatment goal may result in increasing frequency of treatment switches on medical advice.

The phenomenon of treatment discontinuation in people with MS has been broadly researched for a long time under the name of „non-adherence“ [16]. Adherence is defined as active, voluntary involvement of patients in a mutually accepted treatment plan leading to intended preventive or therapeutic results [17]. With regard to disease-modifying therapies, non-adherence means that people with MS stop treatment on their own initiative.

A study of the North American Research Committee on Multiple Sclerosis (NARCOMS) indicated that in 48.7% of cases, treatment switches in persons with MS occurred on the initiative of physicians, not of people with MS [13].

MS is a disease strongly marked by uncertainty and unpredictability [18]. Uncertainty is associated with cognitive, behaviour-related and affective burdens. For people with MS, disease-modifying therapies offer the hope to influence the course of disease [19, 20]. Probably as a response to uncertainty, people with MS experience a central need for control [21]. It is conceivable that they confront the discontinuation of a

disease-modifying therapy as a form of losing control. However, they also feel relieved when doctors recommend a change, for example if the therapy proved to be ineffective or distressing side effects occurred.

In the literature, the phenomenon of discontinuing therapies with disease-modifying agents has been primarily described with regard to the problem of non-adherence in people with MS. How the affected persons experience not self-imposed but medically induced treatment discontinuation has not yet been studied.

Aim

This research investigated how people with MS experience medically induced discontinuation of disease-modifying therapies. Gaining insight into these experiences may help health care practitioners to better support people with MS in the process of treatment switches.

Methods

To explore the experiences of people with MS, a retrospective qualitative descriptive design was appropriate [22]. Semi-structured qualitative interviews were performed, focusing on experiences with medically induced changes of disease-modifying therapies. Participants were offered to bring in additional issues of interest associated with the main topic [23]. An interview guide with key questions was developed. In the opening question of each interview participants were asked to narratively talk open about their experience of discontinuing a disease-modifying therapy due to medical reasons. The objective was to capture participants' perspectives.

Participants

To gain insight into participants' experiences with discontinuing different disease-modifying therapies, a purposive sampling strategy was suitable. People with MS were included if they were 18 years or older and able to describe their experiences in German. Additionally, at least one of their disease-modifying therapies had to be discontinued by their physician due to medical reasons.

The author identified potential participants during outpatient consultations. Ten participants, five men and five women, aged 24 to 55, were included (Table 1). Two participants had reduced working hours due to fatigue.

Table 1 Characteristics of the study sample

Participant	Age	Gender	Time since diagnosis	Changes of DMT ^a
Albert	25	M	1.8	1 (1)
Bill	38	M	0.8	1 (1)
Colin	55	M	6.8	2 (2)
Daisy	34	F	9.8	2 (1)
Eric	24	M	6.4	3 (3)
Fiona	28	F	5.2	4 (4)
Gina	50	F	4.7	2 (2)
Hanna	29	F	10.1	4 (3)
Iris	47	F	5.3	2 (1)
Kurt	45	M	2.1	2 (2)
Mean: 37.5		Mean: 5.3		Total: 23 (20)

^a Changes of disease-modifying therapy: Total number of changes of disease-modifying agents (Number of medically induced changes)

Participants' experiences encompassed a total of 23 changes of different disease-modifying therapies, 20 of which had been medically induced. Reasons for treatment switch included disease activity (12), serious side effects such as hepatotoxicity, depression or melanoma (4), and risk of progressive multifocal leukoencephalopathy (4). Discontinued drugs comprised Avonex, Betaferon, Copaxone, Gilenya, Rebif, Tecfidera and Tysabri. At the time of the interview, between 0.2 to 3.2 (mean: 1.3) years had passed since the last medically induced treatment switch.

Data collection

The first author conducted the interviews between February and April 2016. They lasted between 28 and 83 minutes (mean: 48 minutes). Participants were free to choose time and location for the interview. Most interviews took place in the office room of the MS outpatient clinic. Some participants chose coffee shops as interview location.

Data analysis

The first author audio-recorded all interviews and transcribed them verbatim according to Flick [25]. After each interview he took field notes including participants' statements after the audio recorder had been

turned off. Field notes and analytic memos written throughout the research process were included in the analysis.

To identify interrelated themes for deriving generalizations, the first author read the interview transcriptions several times [24]. Data analysis followed the procedure proposed by Saldaña [26]. Open and axial coding were applied, starting with the development of initial codes [27]. Codes were then grouped into subcategories and provisional categories. Data analysis was continued until it was possible to draw conclusions about participants' experiences and to answer the research question. At the end, the experiences could be synthesised into categories, resulting in a conceptual model. MAXQDA 12 was used to manage the data analysis.

To enhance the credibility of the analysis, the first author regularly discussed the results of the analytic process with the last author. In order to check the plausibility of the analysis, a peer debriefing was scheduled with a researcher not involved in the research process. This was a measure of analytic triangulation [25].

Ethical considerations

The cantonal Ethics Committee of Zuerich approved the study (KEK-ZH-Nr. 2015–591). The participation of the interview partners was completely voluntary. All participants signed an informed consent and were aware that they could withdraw their participation at any time without suffering any consequences. The first author knew most of the participants due to his work as a MS nurse at the outpatient clinic. Due to this vulnerable situation and to ensure neutrality, other MS nurses performed the recruitment.

Results

Experiencing treatment discontinuation: After the transition is before the transition

Four categories depicting the central phenomenon of a cycle of change—*„After the transition is before the transition“*—were identified: *„Getting to know therapy options“*, *„Deciding for a therapy“*, *„Experiencing therapy“*, and *„Experiencing treatment discontinuation“*. The cycle of change occurs in the context of three further categories: *„Living with MS—experiencing the course of disease“*, *„Living one's life—The disease is not in the centre“*, and *„Environment“* (Fig. 1).

Fig. 1: Experiencing medically induced treatment discontinuation: After the transition is before the transition.

Getting to know therapy options

Getting to know therapy options implies acquiring knowledge about medication and developing criteria for therapy decisions.

Acquiring knowledge about therapy options

To take a decision, people with MS need to know several therapy options. They obtain information from brochures received by health care professionals as well as by internet searches.

Discussions with health care professionals are of very high importance. People with MS report that they are dependent on their specialist' expertise: „*Finally, if precise information is necessary, I certainly trust the doctors*” (Daisy).

Developing realistic expectations with regard to medication is required to decide about therapies. During the course of the disease, people with MS familiarize themselves with the fact that they cannot anticipate if a certain drug will be effective:

„*That is precisely the problem. Nobody can tell you if the drug may have a positive effect—you simply have to (breathing in deeply) decide. What is good and what is bad—nobody knows. So you only can hope to make the right choice*” (Colin).

People with MS learn to have to give a medication a try. If drugs prove to be not effective enough, other therapies are discussed and chosen.

Developing criteria for therapy decisions

People with MS start to develop criteria for a therapy decision. For example, they try to estimate if possible side effects would be tolerable for them. They supplement information received by health care professionals with their own thoughts. In doing so, discussions with relatives and friends are very significant:

„*For me, it is very important to receive feedback from different persons. During the consultation I only hear the medical point of view. Surely, this is superb as a point of departure. But for balancing the pros and cons, I prefer to hear also the opinion of people in my own environment—people who know me as a person*” (Fiona).

Sharing their everyday understanding of the disease and the medication with significant others provides a contrast to the medical perspective in consultations with health care professionals.

Deciding for a therapy

Therapy decisions are in the focus of the cycle of change. Within this framework, people with MS are challenged to decide on the beginning and discontinuation of therapies. After experiencing various

changes, the voice of people with MS becomes stronger in the decision-making process.

Therapy decision

As a rule, several medications are at the disposal. Some people with MS regard the neurologists' recommendation as the most decisive factor in their decision: „I did not study medicine, so I follow the doctors' decisions" (Bill).

However, most people with MS decide themselves on the basis of their neurologists' recommendation. After the decision, the experience with the new medication begins (see below „Experiencing therapies")

Deciding for therapy discontinuation

If the current therapy does not proof its value because, for example, disease activity in form of relapses or lesions are visible, people with MS are confronted with the decision to stop therapy.

In some cases, neurologists decide for treatment discontinuation due to serious side effects. Bill, for example, had a massive elevation of liver enzymes a few weeks after the therapy had started. After excluding other reasons for elevated liver enzymes, the attending neurologist decided to disrupt the therapy: „*The neurologist called me and asked me to stop it*" (Bill). This shows that serious side effects can lead to therapy decisions taken without the participation of people with MS.

However, most decisions are discussed with the affected person. In the context of a Tysabri therapy, a change is debated not later than two years after the start as the risk for a progressive multifocal leukoencephalopathy increases after more than 24 administrations. In this situation, some people with MS ask for a second opinion:

„Then they recommended that I change but I did not want to do so. I asked for a second opinion at another neurologist's. He recommended me even more so to stop it. Due to these medical recommendations I stopped it, although I would have liked to go on (laughing)" (Fiona).

A second opinion offers the chance to integrate an additional perspective. Exchanging views with relatives and friends can also be understood as a way of obtaining a second opinion. Thus, people with MS feel more secure that their decision is right for them.

One's own voice gets stronger

Due to experiencing changes, people with MS develop expertise with regard to several medications. In case of renewed therapy decisions, they express themselves more determined with regard to several medications and make their voice heard:

„And when they again observed some activity I was told to think about stopping the drug. But I thought: No, it's enough with stopping suddenly if it does not have an effect from the beginning. There is no reason why not to give it a chance" (Fiona).

Fiona experienced several changes. She had relapses under various medications. From her point of view, the current medication is clearly more effective than the preceding ones. On the basis of this experience, she is determined not to start another cycle of change. Her descriptions are different from other people with MS who experienced only one treatment discontinuation. Fiona argues on an equal footing with neurologists.

Experiencing therapy

After initiating a new therapy, the probationary period of the medication begins. If it proves to be effective, it is followed by a quiet period without discussing further changes. However, in case of side effects or further disease activity, discontinuing the current therapy and determining a new medication is discussed again.

The medication has to prove its effectiveness

If persons with MS start to take their medication, they have been informed about possible side effects or have read about them. However, they do not know, whether these side effects will really affect them or not. After starting the medication, a comparison between expectations and experiences takes place. Some side effects compromise quality of life in such a way that they dominate the potentially positive consequences of therapy for the further course of disease:

„There is a point when the threshold of pain is reached. I would have preferred to have another relapse instead of such strong side effects. It does not make sense to be even more affected by a drug that should prevent something“ (Iris).

People with MS know that—from the professional view—a treatment switch is followed by a latency period until it is possible to decide whether the chosen medication proves to be effective and can be continued:

„I hope that this preparation is just as effective as Gilenya. And I hope that there are less lesions or no lesions at all. But you do not know overnight“ (Bill).

Only after completion of the probationary period, people with MS can assume that it is possible to continue with the new medication.

The medication works well

If a medication proves to be effective, a period of rest begins. From the point of view of people with MS and health care professionals, this represents the aspired goal at the time of selecting a disease-modifying therapy. If people with MS can remain in this period of stability, they leave the cycle of change for a moment:

„Since then I really did not have anything. I felt excellent. I could drive a bike, go on a walk. I could do everything. If you reach this state again, you get used to it and of course you enjoy it“ (Colin).

However, if people with MS experienced several therapy discontinuations, they express themselves reserved also in such phases: *„Let’s see how it will go on. I hope for some rest in the coming years“ (Fiona).* For Fiona, experiencing the cycle of change means that her situation can change at any time. Even in a phase of stability, an idea of possible instability shines through.

Change becomes an issue

All participants have experienced that the phase of stability can lead to a phase when change becomes an issue again. The temporal dynamic of upcoming changes is various. Some changes cast their shadows for a long time. This also applies to changes discussed on the basis of a risk evaluation in Tysabri therapy:

„The neurologists recommended me to stop Tysabri due to the risk for progressive multifocal leukoencephalopathy. I personally wanted to continue with Tysabri. We had two discussions. In the first discussion, I said that I did not want to change. In the second one my partner was present. He also said: The risk is high, so let’s try it now. So I agreed to change therapy for a second time“ (Hanna).

In other cases, the decision for discontinuation occurred abruptly. Once a melanoma was detected during the annual control, Gina was told to stop Gilenya on the same day.

Experiencing treatment discontinuation

After the decision for a change, people with MS precisely assess the situation. They come to different conclusions, depending on the plausibility of the change, its foreseeability over a long time or experiences with previous therapies. Experiencing discontinuation also includes the feeling that now the whole cycle of change begins again.

Evaluating the discontinuation

If the decision for discontinuation occurred without precaution, it can be very stressing for people with MS: *„My world broke down as they told me to stop it“ (Gina).* Gina was confronted abruptly with the discontinuation. Like a relapse it crashed into her life—suddenly and uncontrollably.

It depends on the experience and assessment of the discontinuation if it is comprehensible for people with MS: *„They do not want to see any more lesions. They want to reach something and I do not know what it is. It is for insiders“ (Albert).* Albert could not follow the discussion in the medical consultation. He reported about not knowing what the neurologist wanted to achieve. From his point of view, professionals discuss something he cannot understand. He feels excluded.

Some people with MS experience discontinuation in a positive way. This can be the case if relapses occurred under previous therapies. However, if treatments were effective and well-tolerated in the past, discontinuing therapy leads to a feeling of regret. Notwithstanding how people with MS evaluate the change, it is a setback to the beginning of the cycle of change.

Everything begins again

After the change, people with MS have to deal with choosing a medication again. They must get acquainted with new knowledge and once more decide about therapy: *„Now we start again from the beginning, the whole way“ (Gina).*

If people with MS experienced disease activity under various therapies in the past, they are deeply concerned with the question if there is an effective therapy for them at all:

„Is another therapy really effective? Or will it fail again? This uncertainty remains. Do we have to change again? And how many possibilities do remain at all? (Kurt).

While talking about their experiences, participants' statements were often followed by laughter. They utilized laughing when they reported serious experiences associated with medically induced change of medication. For example, Gina mentioned that she could not take her previous drugs for a longer time: *„I took the medication for two years until it had to be stopped. I hope that this will not become a repeating pattern (laughs)“ (Gina).*

Laughing expresses Gina's uncertainty about being able to continue the current medication for a longer time although it is well-tolerable. Previous experiences with discontinuation taught her that there is no certainty at all to continue with a therapy infinitely.

Living with MS: Experiencing the course of disease

The change of medication occurs in the context of experiencing a chronic condition. People with MS live with their disease and assess its course. Experiencing the cycle of change and the course of disease mutually influences each other. A phase of rest and stability can occur on the level of the cycle of change as well as on the level of the course of disease. If stability is achieved on both levels, people with MS experience a period of *double* rest. However, in case of disease activity and discussions concerning therapy, people with MS experience *double* uncertainty.

Experiencing the course of disease has an impact on therapy decisions. People with MS judge the degree of disease severity and accordingly decide which therapy seems to be effective for them. After experimenting with medications not preventing disease activity, Kurt changed his view about Tysabri. One year before, he rejected a change in favour of Tysabri due to the risk for progressive multifocal leukoencephalopathy. However, two months before the interview, he finally agreed to take Tysabri.

Living one's life: The disease is not in the centre

Living one's life regardless of the disease is important for people with MS. They have relationships, start a family, train for a profession, set goals, have dreams and try to realize them.

Several persons with MS succeed in living their life while pushing the disease aside, despite the uncertainty: „*Let's see how it will go on. I always try to make sure that my disease does not become the centre of my life*" (Bill). For several reasons, some people with MS are less able to live their life independently of the disease. Kurt experienced two treatment switches within one year due to disease activity. Double uncertainty associated with the cycle of change and disease activity prevents him from living his life.

Coping with the cycle of change also consists of finding normality under the conditions of the new medication. The aim is to develop a daily routine and to live one's own life. The disease is part of this life but not the dominating element: „*When I get up in the morning, I do not think: I have MS. I live an absolutely normal life*" (Iris). Despite uncertainty, people with MS try to shape their lives as normal as possible".

Environment

Significant others

Relatives and significant others play a central role in experiencing the cycle of change. They support people with MS with getting to know medications and bring in their own evaluations into the decision-making process:

„*Then the change back to Tysabri became an issue again. I myself would have liked to give Tecfidera a little bit more time to have an effect. But after pressure from my partner and my mother, I decided to return to Tysabri*" (Eric).

As far as complex therapy decisions are concerned, significant others know people with MS better than anyone else. Therefore, their evaluation is particularly valuable for people with MS. They ensure that individual concerns of persons with MS are considered in the decision-making process and personal as well as professional perspectives are matched with each other.

Health care professionals

Health care professionals have a dual role. Their professional estimations result in medically induced treatment discontinuation. Additionally, people with MS depend upon professionals' expert advice.

Participants reported that they highly appreciate regular contacts with health care professionals. In case of uncertainties in dealing with medication, it is important to have a phone number and contact persons

to call at any time: „*I could always have called them. This gave me a feeling of security*” (Hanna).

In the context of medically induced treatment discontinuation, people with MS cherish health professionals being at their disposal if they need support. This is related to the fact that „after the change” can always be „before the change”.

Central phenomenon

The analysis of the collected data revealed a central phenomenon: People with MS experience medically induced treatment discontinuation as part of a cycle of change, whereby „after the transition is before the transition” (Fig. 1).

In consultations with health professionals, people with MS get to know medications. They develop therapy estimations and adjust their decisions to personal criteria and recommendations of health professionals. After the beginning of a therapy, it becomes apparent whether the medication is effective or not. If it is not effective, treatment switching comes to the fore. At the end, people with MS experience treatment discontinuation and the cycle starts again from the beginning. However, people with MS are not at the same point as they were during the previous decision-making process. Acquired knowledge, previous decisions and the experience of discontinuation have a decisive influence on them.

For people with MS there’s a fundamental fact about their experience of disease-modifying therapy: The cycle of change has no ending. Therapy switches can become a necessity again at any moment in time.

Discussion

This qualitative-explorative study investigated how people with MS experience medically induced treatment discontinuation. The results indicate that people with MS experience discontinuation as part of a cycle of change. This finding has not yet been described in the literature. In the noisy discussion about non-adherence, the scientific community has neglected the many people with MS who continually take their medication but are confronted with therapy discontinuation for medical reasons.

In a study about the experience of Interferon therapy, Miller and Jezewski report about a patient whose therapy had been discontinued due to severe depression. The patient told that physicians „had taken away” something from her [20]. In their previous study Miller and Jezewski mention another person whose therapy had been discontinued for medical reasons [28]. Despite this anecdotal evidence, the lack of scientific results indicates that experiencing medically induced treatment discontinuation from the view of people with MS is up to now a „silent phenomenon” probably not noticed by health care professionals [29].

Several phases of the cycle of change are described by other authors as well. Various studies confirm that people with MS develop their own criteria for therapy decisions [6, 28, 30]. Hanson et al. [31] indicate that for neurologists’ criteria like effectiveness, security and tolerability have higher priority in their

therapy decision than patient preferences. They confirm that professional and personal views can diverge. In a study by Ceuninck van Capelle et al. [32], people with MS emphasize the significance of relatives in therapy decisions and experiences of disease-modulating therapies.

Experiences with disease-modifying therapies are described in various studies [20, 28, 33]. Miller and Jezewski point out that for people with MS, disease-modifying therapies are associated with the hope to influence the course of disease [20] and to maintain control over their body [28]. However, in the current study, people with MS reported that the desired control is not guaranteed in the cycle of change. From their point of view, the temporal and event-related uncertainty of the course of disease [34] is also characteristic for the experience of medical treatment. In the cycle of change, people with MS are confronted with temporal uncertainty. They must expect the next treatment discontinuation of treatment without knowing when it occurs. On the other side, event-related uncertainty can arise as well. This is the case if the next treatment discontinuation is already decided without knowing whether the new therapy is effective and tolerable or not. Therefore, the experience of stability in the cycle of change is always fragile and uncertain.

As in the transition framework proposed by Schumacher, Jones & Meleis [35], people with MS may experience phases between switches from one therapy to another as stable periods, whereas the processes of discontinuation are characterized by feelings of disorientation and uncertainty. People with MS need new knowledge to cope with the transition to the next disease modifying therapy.

According to Mishel [36], uncertainty emerges if situations offer too few indications for affected persons to understand and to categorize what is going on. Uncertainty intensifies if situations present themselves repeatedly in a different way. In contrast, uncertainty diminishes if processes keep on repeating themselves. This is evident in the current study with people with MS experiencing a series of treatment switches. They seem to be more sure of themselves and articulate their preferences in the decision-making process more clearly. Knowledge contributes to a feeling of control. Based on knowledge, affected persons can develop a „cognitive structure“ [37] enabling them to interpret events like discontinuing therapy.

Another strategy to cope with uncertainty consists of maintaining a stable social and mental state [37]. People with a chronic condition search for normality and routine amid changing situations. Penrod, Hupcey, Shipley, Loeb und Baney [38] describe how caring relatives at the end of life try to achieve a feeling of normality by searching for reliable patterns. It is conceivable that people with MS use similar strategies in order to find a new form of normality while experiencing treatment discontinuation and change of medications. Memories about previous possibilities to find a new and tolerable medication in the past could perhaps contribute to trust in future opportunities allowing a daily life routine with another medication.

Findings from this study could be relevant for other chronic conditions as well. Health care tend to overrate the degree of accordance between their own and the patients' point of view. With regard to treatment, professional criteria can differ from patients' personal criteria [31]. Additionally, therapy

switches can lead to uncertainty [39]. Therefore, caring for patients experiencing medication changes should not be considered as trivial.

Limitations

This is the first study to address the experience of medically induced treatment discontinuation in people with MS. The results are valuable to educate caregivers about the lived experiences of the target group.

The descriptive qualitative study design and the small sample size affect the transferability of findings. Possibly, people with MS experiencing treatment discontinuation due to lymphopenia or neutralizing antibodies may have reported additional experiences.

The convenience sample represents a further limitation. It is probable that people with difficult medication-related experiences were reluctant to participate.

All participants were interviewed at one single point of their discontinuation experience. Kurt's narrative seems to indicate that the perception of risks associated with a certain drug changes over time. After reaching the phase of stability and peace, the outlook on the discontinuation is different from the phase of imminent decision-making. To demonstrate changing experiences over time, the study should be repeated with a longitudinal qualitative design [40].

Recommendations for practice

Health care professionals should be aware of the uncertainty experienced by people with MS in the cycle of change [18]. As Jackson [41] points out, telling hidden stories allows the narrators to experience themselves as persons with opportunities for action. Health care professionals should invite people with MS undergoing a therapy switch to tell their stories. From the narratives, professionals can deduce conclusions about the degree of uncertainty people with MS are exposed to. More qualitative research is needed to understand how feelings of people with MS evolve in the process of transition from one medication to another and to identify interventions which help people with MS to cope with transition processes.

Support for coping with therapy switches should not be restricted to the time of treatment decision-making. Health care professionals should be at the patients' disposal during the whole cycle of change.

Conclusions

This exploratory qualitative study for the first time gives voice to people with MS talking about their experience of medically induced treatment discontinuation.

The study demonstrates that people with MS experience medically induced discontinuation of disease-modifying therapies as part of a cycle of change, whereby new changes can

always follow previous changes. In addition to the uncertainty of the course of disease, people with MS also face uncertainty concerning further treatment.

With the increasing number of available disease-modifying agents and changed expectations concerning therapeutic success, medically induced discontinuation of disease-modifying therapies could become even more prevalent in the future.

If health care professionals succeed in reducing uncertainty associated with the cycle of change, more people with MS could live their lives irrespective of their disease.

Abbreviations

MS: multiple sclerosis

Declarations

Ethics approval and consent to participate

The cantonal Ethics Committee of Zuerich approved the study (KEK-ZH-Nr. 2015–591). All participants signed an informed consent.

Consent for publication

Not applicable

Availability of data and material

Data collected for this study are not publicly available.

Competing interests

The authors declare that they have no competing interests.

Funding

This study received no funding.

Authors' contributions

RA was responsible for defining the research question, for drafting the study proposal and the data collection. RA and AF were responsible for data analysis. RA was responsible for the drafting of this paper representing a summary of his master thesis. RM and AF read and approved the final manuscript.

Acknowledgements

The authors would like to thank the people with MS for sharing their experiences about medically induced medication changes. They also wish to thank Dr. Diana Staudacher for her feedback on a draft of this paper.

References

1. Compston A, Coles A. Multiple sclerosis. *Lancet*. 2008 Oct 25;372(9648):1502–17.
2. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple Sclerosis. *New England Journal of Medicine*. 2000;343(13):938–52.
3. Browne P, Chandraratna D, Angood C, Tremlett H, Baker C, Taylor BV, et al. Atlas of Multiple Sclerosis 2013: A growing global problem with widespread inequity. *Neurology*. 2014 Sep 9;83(11):1022–4.
4. Killestein J, Rudick RA, Polman CH. Oral treatment for multiple sclerosis. *Lancet Neurol*. 2011 Nov;10(11):1026–34.
5. Bonafede MM, Johnson BH, Wenten M, Watson C. Treatment patterns in disease-modifying therapy for patients with multiple sclerosis in the United States. *Clin Ther*. 2013 Oct;35(10):1501–12.
6. Kremer IEH, Evers SMAA, Jongen PJ, van der Weijden T, van de Kolk I, Hiligsmann M. Identification and Prioritization of Important Attributes of Disease-Modifying Drugs in Decision Making among Patients with Multiple Sclerosis: A Nominal Group Technique and Best-Worst Scaling. *PLoS One* [Internet]. 2016 Nov 3 [cited 2017 Jul 1];11(11). Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5094791/>.
7. Heesen C, Solari A, Giordano A, Kasper J, Köpke S. Decisions on multiple sclerosis immunotherapy: New treatment complexities urge patient engagement. *Journal of the Neurological Sciences*. 2011 Jul 15;306(1–2):192–7.
8. Coyle PK. Switching therapies in multiple sclerosis. *CNS Drugs*. 2013 Apr;27(4):239–47.
9. Feinstein A, O'Connor P, Feinstein K. Multiple sclerosis, interferon beta–1b and depression A prospective investigation. *J Neurol*. 2002 Jul;249(7):815–20.
10. Salhofer-Polanyi S, Baumgartner A, Kraus J, Maida E, Schmied M, Leutmezer F. What to expect after natalizumab cessation in a real-life setting. *Acta Neurol Scand*. 2014 Aug;130(2):97–102.
11. Thomas RH, Wakefield RA. Oral disease-modifying therapies for relapsing-remitting multiple sclerosis. *Am J Health Syst Pharm*. 2015 Jan 1;72(1):25–38.

12. Gold R, Kappos L, Arnold DL, Bar-Or A, Giovannoni G, Selmaj K, et al. Placebo-controlled phase 3 study of oral BG-12 for relapsing multiple sclerosis. *N Engl J Med*. 2012 Sep 20;367(12):1098–107.
13. Perrin Ross A (ed.). Advising patients about disease-modifying therapy selection and switching. Counseling Points [Internet]. 2015;10(3). <http://iomsn.org/counseling-points/> Accessed 3 Sept 2017.
14. Lanzillo, R., Prosperini, L., Gasperini, C., Moccia, M., Fantozzi, R., Tortorella, C., ... R. I.Re.MS study group. (2018). A multicentre observational analysis of PERSISTENCE to Treatment in the new multiple sclerosis era: the RESPECT study. *Journal of Neurology*, 265(5), 1174–1183. <https://doi.org/10.1007/s00415-018-8831-x>.
15. Sormani MP, Muraro PA, Saccardi R, Mancardi G. NEDA status in highly active MS can be more easily obtained with autologous hematopoietic stem cell transplantation than other drugs. *Mult Scler*. 2016 Apr 26.
16. Menzin J, Caon C, Nichols C, White LA, Friedman M, Pill MW. Narrative review of the literature on adherence to disease-modifying therapies among patients with multiple sclerosis. *J Manag Care Pharm*. 2013 Feb;19(1 Suppl A): S24–40.
17. International Organization of MS Nurses (IOMSN) (Ed.). Case Management in Multiple Sclerosis. A stage-by-stage guide to MS care for nurse case managers [Internet]. n.d. <http://iomsn.org/publications/> Accessed 3 Sept 2017.
18. Kroencke DC, Denney DR, Lynch SG. Depression during exacerbations in multiple sclerosis: the importance of uncertainty. *Mult Scler*. 2001 Aug;7(4):237–42.
19. Corbin JM, Strauss A. Unending work and care. Managing chronic illness at home. San Francisco: Jossey-Bass; 1988. 358 p.
20. Miller C, Jezewski MA. A phenomenologic assessment of relapsing MS patients' experiences during treatment with interferon beta-1a. *J Neurosci Nurs*. 2001 Oct;33(5):240–4.
21. Yorkston KM, Johnson K, Klasner ER, Amtmann D, Kuehn CM, Dudgeon B. Getting the work done: a qualitative study of individuals with multiple sclerosis. *Disabil Rehabil*. 2003 Apr 22;25(8):369–79.
22. Neergaard MA, Olesen F, Andersen RS, Sondergaard J. Qualitative description - the poor cousin of health research? *BMC Med Res Methodol*. 2009;9:52.
23. Silverman D. Interpreting qualitative Data. 3rd ed. London: Sage; 2006.
24. Miles MB, Huberman AM, Saldaña J. Qualitative data analysis. A methods sourcebook. 3rd ed. London: Sage; 2014. 381 p.
25. Flick U. An Introduction to Qualitative Research. 4th Edition. Los Angeles: Sage; 2009. 528 p.
26. Saldaña J. The coding manual for qualitative researchers. 2nd ed. London: Sage; 2013.
27. Sandelowski M. Whatever happened to qualitative description? *Res Nurs Health*. 2000 Aug;23(4):334–40.
28. Miller CE, Jezewski MA. Relapsing MS patients' experiences with glatiramer acetate treatment: a phenomenological study. *J Neurosci Nurs*. 2006 Feb;38(1):37–41.

29. Kolbe N, Kugler C, Schnepf W, Jaarsma T. Sexual Counseling in Patients With Heart Failure: A Silent Phenomenon: Results From a Convergent Parallel Mixed Method Study. *J Cardiovasc Nurs*. 2014 Dec 3.
30. Visser LH, Heerings MA, Jongen PJ, van der Hiele K. Perspectives and experiences of Dutch multiple sclerosis patients and multiple sclerosis-specialized neurologists on injectable disease-modifying treatment. *Patient Prefer Adherence*. 2016 Apr 26;10:659–67.
31. Hanson KA, Agashivala N, Wyrwich KW, Raimundo K, Kim E, Brandes DW. Treatment selection and experience in multiple sclerosis: survey of neurologists. *Patient Prefer Adherence*. 2014;8:415–22.
32. Ceuninck van Capelle A de, Meide H van der, Vosman FJH, Visser LH. A qualitative study assessing patient perspectives in the process of decision-making on disease modifying therapies (DMT's) in multiple sclerosis (MS). *PLoS ONE*. 2017;12(8):e0182806.
33. Miller CE, Karpinski M, Jezewski MA. Relapsing-Remitting Multiple Sclerosis Patients' Experience with Natalizumab. *Int J MS Care*. 2012;14(1):39–44.
34. Wilkinson HR, das Nair R. The psychological impact of the unpredictability of multiple sclerosis: a qualitative literature meta-synthesis. *British Journal of Neuroscience Nursing*. 2013 Aug;9(4):172–8.
35. Schumacher KL, Jones PS, Meleis AI. Helping elderly persons in transition: A framework for research and practice. 1999; Available from: <http://repository.upenn.edu/nrs/10>.
36. Mishel MH. Uncertainty in illness. *Image J Nurs Sch*. 1988;20(4):225–32.
37. Miller JF. Coping with chronic illness. Overcoming powerlessness. 3rd ed. Philadelphia: F. A. Davis Company; 2000.
38. Penrod J, Hupcey JE, Shipley PZ, Loeb SJ, Baney B. A Model of Caregiving Through the End of Life: Seeking Normal. *West J Nurs Res*. 2012 Mar;34(2):174–93.
39. Chambers JA, O'Carroll RE, Dennis M, Sudlow C, Johnston M. "My doctor has changed my pills without telling me": impact of generic medication switches in stroke survivors. *J Behav Med*. 2014 Oct;37(5):890–901.
40. Calman L, Brunton L, Molassiotis A. Developing longitudinal qualitative designs: lessons learned and recommendations for health services research. *BMC Med Res Methodol*. 2013 Feb 6;13:14.
41. Jackson M. The Politics of Storytelling. Violence, transgression and intersubjectivity. Copenhagen: Museum Tusculanum Press; 2002. (Critical anthropology; vol. 3).

Figures

Living with MS –
experiencing the course of
disease

Figure 1

Experiencing medically induced treatment discontinuation: After the transition is before the transition.