

Appendix S1. Analysis categories

Part A. Theory-based categories (n=5):

- 1) *type of nonadherence* (intentional and unintentional)
- 2) *reasons for nonadherence* (attitudes toward behavior, subjective norms and perceived behavioral control)
- 3) *handling of nonadherence* (active or passive)
- 4) *factors which could have had a positive influence on adherence*
- 5) *reasons for adherence* (attitudes toward adherence behavior, subjective norm and perceived behavioral control)

Part B. Final main categories (n=21) derived from interviews in first- and second-line-treated pwMS

Nonadherence

1. Conscious or unconscious

Medication

2. Positive/negative toward medication in general
3. No/burdensome side effects
4. No/tiredness of medication
5. To be reminded about the disease
6. Strong/weak believe in medication effectiveness
7. Inner barriers against realization of treatment
8. Organisational barriers

Illness beliefs

9. Negative/positive illness beliefs toward MS in general
10. Negative/positive illness beliefs toward own disease

Treatment decision

11. Autonomous or physician-focused role
12. Lack of information
13. Dissatisfaction with role in decision making process
14. Negative attitude of social environment
15. Social pressure, responsibility for others
16. Loss of/trust in physician

Own view on adherence

17. Active or passive Handling of nonadherence
18. Experience of nonadherence as deliberating

What would have been helpful

19. Information support
20. Adequate support in decision making
21. Support in treatment implementation

Table S1. Interview guide ADEPT

	Topic	Question/content	Reason
	Initiate interview	Thanks for participation, welcome	Warming up
1	Introduction	Psychologist in the MS unit, research project	Get to know each other, elicit trust
2	Topic of the Interviews	It is about finding out why patients stop taking their medication/do not take it regularly, not in the right dose. The aim is not to condemn you, but: To improve the choice of medication/ to find parameters that should be considered when deciding on therapies. About 50% of the prescribed drugs are not taken. It is therefore more the rule than the exception not to take a medicine. We would like to better understand why this is the case and - as already mentioned - make it possible, for example, that things can be considered early during the decision-making helping patients to find the right drug for them..	Minimize worries, fears
3	Sociodemographic and MS demographic data	- How old are you? - Since when do you know about your diagnosis? When was the diagnosis made? - Marital status, children - Educational attainment - Occupation - Social environment? Are you rather a sociable person? Friends? - PDDS self-assessment: Interviewer should read items aloud	General parameters that could have an influence. Social environment: Does the person have contact persons? How strong is the person connected?
		- Which doctor looks after you for MS? Is there a main contact person? - Are you satisfied with this person? - Have you already been treated by this person - When did you make your therapy decision? If not, why not? And: Was there a main contact person (e.g. also for questions)? And how was the relationship to this person? Has this changed at any time?	If the patient did not have a main contact person, he may not have been so well informed. If the relationship with the counselor changes, the adherence behavior may also change.
4	Treatment start	- Did you start medication immediately after the diagnosis? When did you start? And when did you start the medication that was discontinued? This is basically then, the medication history: - When you started the drug: How have you been? - Did you stick to the plan from the beginning? Or did you deviate from it from time to time? Why?	Many different drugs. Possibly tiredness of drugs

		- What did you experience after the first intake of the drug?	If strong side effects appeared early, patients possibly more accessible for nonadherence.
5	Form of nonadherence	- Deviations: Since when? - What kind? E.g. taken less (dose), taken less often (frequency, also dose)?	
6	Reason for nonadherence	- What was different at that time from the start of the medication? (consciously nonadherent or possibly changed life circumstances + stress)	Hypothesis: Dealing with other things became more important and therefore the treatment moved into the background or also: getting other information (e.g. during training) and therefore changing behavior (cognitive dissonance).
		- What was too much? Side effects? Be reminded of illness?	Are these reasons identical to the things listed at the beginning? If so, then they could be risk factors.
7	Theory of planned behavior	Do you remember the decision for the last drug before going on an MS pill? I would like to discuss this decision with you in more detail (e.g. interferon before, dimethyl fumarate then the decision for interferon, because it was then aborted). I'd like to have a little thought game with you: I want to know what you believe and what had an influence on your treatment decision at that time. Back then: How was it then? (If possible, without taking today's view into account.) When you put yourself back into the situation when you made the decision: - <u>Cognitive</u> : How did you think about therapy? e.g. What was your attitude toward medication? Did you think that the medicine is working for you? (Disease model, illness beliefs) Do you still remember the Pro+ counterarguments? Where did you get your information from? - <u>Social Norm</u> : Who else was involved in the decision? How did you talk about the decision?	Was it an informed decision? If so, many counterarguments could lead to nonadherence at an early stage (quasi as a continuation of skepticism) if they were not well processed.

		<p>What were the social influencing parameters? Were you under pressure from the family or neurologist, for example?</p> <p>What were the experiences with medication in general in your social environment (attitude to medication, orthodox medicine, bad experiences, etc.)?</p> <p>- <u>Expected behavioral control</u>: Were problems addressed in implementation? (Self-efficacy)</p> <p>Today about then: What would you say today, what was it really like?</p> <p>- The same questions about cognition, social norms and expected behavioral control once again</p> <p>Change: When did one of the parameters change?</p> <p>Today: How is it today? If you imagine that you would have to answer the same question again today (with the same disease status as then). How would you then evaluate the 3 areas individually?</p>	
8	Self-perception	<p>- Would you have thought of yourself that you could be someone who stops therapy? (self-image)</p> <p>- Have you ever encountered anything like this in other cases? (different medication, different area of life) How did it work / how was it there?</p> <p>- How do you feel about it? E.g. relief, because side effect is gone, feelings of guilt, anxiety</p>	<p>Behavior shown so far in real terms is the best predictor for future behavior.</p> <p>How is the nonadherent behavior evaluated?</p> <p>If necessary, include the planned behavior at appropriate points during exploration.</p>
9	Own presumption	<p>- Looking back: Is there anything that would have needed you to make your decision differently so that it would fit your current behavior (no drug or other medication)? Or do you think you made the same decision anyway?</p>	<p>So was there a change in a person's behavior (we couldn't predict that beforehand)? Or were the parameters already there beforehand (then we could have predicted that).</p>

Table S2. Factors influencing adherence/nonadherence in first-line PwMS

Categories (quote)	<i>N</i>	<i>percentage</i>
1. Burdensome side effects (“When I didn’t take the injection. I didn’t have flu-like symptoms and could handle my daily routine at the next day quite well.”)	9	9.59
2. Belief in medication effectiveness (“I was well aware of how I felt without taking the medication.”)	9	7.35
3. No/marginal side effects (“I had a skin rash once. But it was gone after a short period time already.”)	9	5.48
4. Positive Illness-Beliefs (“I actively wanted to do something against my disease.”)	9	5.23
5. Adequate support in decision making process (“No one ever forced me to take medication.”)	9	4.73
6. Adequate information (“I read a number of studies and had sufficient knowledge on the different treatment options.”)	9	3.61
7. Positive attitude toward medication (“When there is medication available you should take it.”)	9	1.87

N = number of interviews for which the respective category was coded. *percentage* = relative frequency of the coded units within a given category coded for all first-line interviews compared to the total number (803) of coding units.

Table S3. Factors influencing adherence/nonadherence in second-line PwMS

Category (quote)	<i>n</i>	<i>percentage</i>
1. Positive illness beliefs (“I consider the medication to be important. It’s my body.”)	12	8.42
2. Belief in a highly active disease (“I suffer a lot from the disease. I want to do everything to avoid further deteriorations.”)	12	8.35
3. Belief in medication effectiveness (“At the moment I’m quite optimistic. I just realized that Lemtrada helps.”)	12	7.59
4. Positive attitude toward medication of social environment (“A friend that also suffers from MS recommended to me to take the medication. He also benefits from it.”)	12	7.34
5. No/marginal side effects (“I always tolerated the infusion quite well.”)	12	6.32
6. Trust in physician (“Let’s say it this way: I had trust in my doctor, I trust the clinic, so why shouldn’t I take it.”)	12	4.89
7. No tiredness of medication (“The injection was like brushing my teeth, daily routine.”)	12	4.3
8. Adequate support in implementation (“The nurses offered me their support in case that there is something I would need.”)	12	4.13
9. Lack of belief in medication effectiveness (“I stopped believing in its effectiveness when I developed another lesion despite I took the medication regularly.”)	12	4.13
10. Negative attitude toward medication of social environment (“And then my doctor advised me to discontinue it. It seemed as if it didn’t help.”)	12	3.46

n = number of interviews for which the respective category was coded. *percentage* = relative frequency of the coded units within a given category coded for all first-line interviews compared to the total number (1186) of coding units.

Table S4. Distribution in the relative frequencies of main cited categories for first-line and second-line PwMS

Categories	First-line PwMS (N=9)	Second-line PwMS (N=12)
Intentional nonadherence	n = 8 (5.2%)	n = 3 (0.3%)
Burdensome side effects	n = 9 (9.6%)	n = 10 (5.7%)
Belief in a highly active disease	n = 6 (2.7%)	n = 12 (8.3%)
Adequate support of therapy implementation	n = 6 (1.2%)	n = 12 (4.1%)
Support and sense of responsibility for others	n = 2 (0.5%)	n = 11 (3.1%)
Positive illness beliefs (self-efficacy, active patient role)	n = 9 (5.2%)	n = 12 (8.4%)
Lack of belief in medication effectiveness	n = 7 (3.6%)	n = 12 (4.1%)
Trust in physician	n = 8 (1.7%)	n = 12 (4.9%)

n = number of patients in the respective group that reported a coded unit referring to the category. Percentages refer to the frequency of coding units named in each category in relation to the total number of coded units in each group (elements in first-line patients: 803; elements in second-line patients: 1186).