Medication Choice and Management Decision Making Considering Family Planning for Women Living with Multiple Sclerosis.

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Authorship statement

‘I, Lubna Essam Almouzain, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.'

Supervision This PhD was supervised by Dr. Fiona Hamilton (primary supervisor), Prof. Fiona Stevenson (secondary supervisor), and Dr. Declan Chard (secondary supervisor).

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Abstract

Background

Multiple sclerosis (MS) is a chronic inflammatory demyelinating and neurodegenerative disorder that affects women more than men. Most women are diagnosed during their childbearing years when they have not yet completed their family. Starting disease modifying drugs (DMDs) is vital in some MS cases to control the disease and prevent further disability. Choosing whether to start treatment or to complete their family first, or choosing to continue, stop, or switch treatment to conceive are all tricky decisions for both healthcare providers and women with MS. This difficulty arises from the novelty and management complexity of DMDs, not to mention the personal circumstances of patients which need to be taken into consideration in order to eventually reach a shared decision.

Aim

To explore and understand the holistic decision-making experience of treatment choices and family planning for women living with MS, to facilitate an improvement in the quality of the processes and decisions involved.

Objectives

1. To identify the available literature on the effects of switching and managing treatment to allow for pregnancy in women with MS.
2. To explore the real-life experiences of women with MS when choosing, switching, or managing medications, and how they arrange their family plans accordingly.
3. To explore the experiences of key healthcare providers (HCPs) who support these women in such decisions.
4. To identify available resources to help women with these decisions.

5. To explore what women needs to see in decision tools to help them with decisions through evaluation of an available online decision aid.

Methods

The methods were selected to match the objectives: Objective 1 was addressed via a systematic review; Objectives 2, 3, and 4 were reached through qualitative interviews with women with MS and their HCPs (consultants, nurses, and pharmacists); and Objective 5 was attained through qualitative Think Aloud sessions with women with MS.

Results

The systemic review showed the scarcity of published research focusing on medication decision-making when planning pregnancy, as well as its effect on a woman's MS. The interview studies showed that despite the importance of this area, it still needs more attention and standardisation of services to create a better care experience. The lack of all kinds of resources (time, information, human) for this for both women and their HCPs is also a challenge. The interviews highlighted the importance of the timing of decisions and patient readiness to decide, which has been found to be regularly compromised by the biographical disruption caused by illness. The Think Aloud sessions collected very useful ideas from its primary users to amend the online MS Trust tool. This serves as an important outcome/output of this thesis.

Conclusion

This thesis sheds light on medication management as it intersects with family planning decisions, and addresses the need for service standardisation, more patient-friendly information resources, the consideration of patient readiness to make decisions, and an updated usable digital aid that helps women with such complex decisions.

Impact statement

This thesis, with its four studies, explores the holistic experience of treatment decisions considering family planning of women with multiple sclerosis (MS), with the goal of improving this experience in the future.

It has highlighted how this area is scarce in data and how much more research is needed on treatment initiation and the management (switching) decisions in terms of women being able to conceive, as well as in terms of the impact of this on the disease and the quality of the decisions.

The qualitative studies of this thesis also addressed the gap in the existing literature by looking holistically at the treatment/family-planning decision-making experience in the UK for both women and their Healthcare Providers (HCPs). Highlighting the needs, challenges, and areas of development in the clinical service in this area is a first step in the process of improving the decision-making experience for both parties.

The research employed the sociological lens of biographical disruption to explore accounts of decision-making experiences. The study concluded that these decisions are linked to multiple critical times, when multiple disruptions to biography can occur. Readiness to decide is key for better quality decision-making experiences and better final decisions. Through this, the study highlights the importance of readiness assessments, which are currently not being undertaken by clinicians nor by patients. There is currently no standardised, validated tool for this assessment. This highlights the importance of future research for developing and validating an assessment tool. It also creates an opportunity for charity and support groups intervening to help women understand the importance of readiness in making these decisions in terms of the impact it will have, thus helping them to self-assess their readiness to make these decisions.

Finally, it also worked towards fulfilling one important need highlighted by both parties: a clear and helpful knowledge resource or decision aid. The study qualitatively evaluated the MS Trust decision aid tool for its usefulness for decision-making in terms of the use of DMDs in light of family planning wishes. The evaluation resulted in the collection of very useful insights from the tool main users (women with

MS), and clearly showed that the tool was useful for DMD choices more generally, but not when considering family planning.

The results and recommendations of this study have been provided to the MS Trust to consider during their upcoming tool update. This is another step towards improving the quality of the decision-making experience for women with MS who are planning a pregnancy, which was the main aim of this thesis.

Outputs of the study

Peer-reviewed publications

Almouzain L, Stevenson F, Chard D, Rahman NA, Hamilton F. Switching treatments in clinically stable Relapsing Remitting Multiple Sclerosis patients planning for pregnancy. Mult Scler J Exp Transl Clin. 2021;7(1):20552173211001571.

Conference Presentations

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Almouzain L, Hamilton F., Chard D, Stevenson F. Medication Decision-Making in the Context of Family Planning for Women with Multiple Sclerosis in the UK: Explorative Qualitative Study. Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS)2022.

E-Poster Presentation

L. Almouzain, F. Stevenson, D. Chard, F. Hamilton. Perspectives of Healthcare Providers Concerning Current Practice in Supporting Women with Multiple Sclerosis in Reproduction and Treatment Decisions. European Committee for Treatment and Research in Multiple Sclerosis (ECRIMS)2022.

Oral presentations

Almouzain L, Stevenson F, Chard D, Rahman NA, Hamilton F. Decisions around Family Planning and Medication Choice in Relapsing Remitting Multiple Sclerosis. International Women in Multiple Sclerosis iWiMS Global Epidemiology Conference 2021.

Blog posts

L.Almouzain, Researchers are asking “How much do you know about pregnancy and MS?” National MS Society 2020. https://www.mssociety.org.uk/research/latest-research/latest-research-news-and-blogs/ectrims---lubna-almouzain

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List of Abbreviations

ABN	**Association of British Neurologists**
ADHD	Attention Deficit Hyperactivity Disorder
ADR	Adverse drug reaction
A & E	Accident and Emergency
ARR	Annual relapse rate
CALs	Combined active lesions
CIS	Clinically Isolated Syndrome
CNS	Central Nervous System
COVID-19	Corona Virus Disease 2019
CSF	Cerebro-spinal fluid
DA	Decision Aid
DMDs	Disease Modifying Drugs
EBV	Epstein Bar Virus

EMA	The European Medicines Agency
FDA	The Food and Drug Administration
GA	Glatiramer Acetate
Gd+	Gadolinium enhancing lesions
GMC	General Medical Council
GP	General Practitioner
HAART	Highly Active Antiretroviral Therapy
HCPs	Health Care Providers or Practitioners
IFN	Interferon
IPDAS	International Patient Decision Aid Standards Collaboration
JCV	John Cunningham virus
MP	Methylprednisolone
MRI	Magnetic Resonance Imaging
MS	Multiple Sclerosis
NHS	National Health Service

NICE	The National Institute for Health and Care Excellence
NMP	Non-medical Prescriber
NPA	National Pharmacy Association
NTZ	Natalizumab
PC	Personal Computer
PML	Progressive multifocal leukoencephalopathy
PPI	Patient and Public Involvement
PPMS	Primary Progressive Multiple Sclerosis
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines.
PROSPERO	International Prospective Register of Systematic Reviews.
RCT	Randomized Controlled Trial
RID	Relative Infant Dose

RIS	Radiological Isolated Syndrome
ROB-2	The revised Cochrane risk of bias tool for used for randomised trials and a risk of bias assessment tool was used for randomised controlled trials.
RRMS	Relapsing Remitting Multiple Sclerosis
SDM	Shared Decision Making
SPC	Summaries of Product Characteristics
SPMS	Secondary Progressive Multiple Sclerosis
Th1	T helper 1 cells
Th2	T helper 2 cells

Chapter 1. Introduction to Multiple Sclerosis

1.1. Introduction

This chapter will outline the context for the complexity of treatment and family planning decision-making in multiple sclerosis (MS). It will present an overview of multiple sclerosis to provide an understanding of the nature of this illness, the evolution of its treatment over the years, the novelty of these treatments, and finally the existing literature on reproduction and MS. The chapter will end with a list of the different treatment/reproductive decisions that may be faced by women, highlighting how intertwined and important they are and how this decision need to be taken holistically.

1.2. Multiple Sclerosis

Multiple sclerosis is a chronic inflammatory demyelinating neurodegenerative disease where the body's own immune cells attack the myelin sheath of the nerve cells in the central nervous system (1). Patients can present with range of different symptoms depending on the damage location in the nervous system (2). The symptoms of MS are diverse and include sensory symptoms like numbness, fatigue, vision deficits, muscle weakness, bladder and bowel problems, impaired balance, spasticity, walking difficulties, sexual problems, mental, cognitive and emotional challenges (3-8). The disease is usually characterised by attacks or relapses of symptoms (9) followed by periods of stability which are called remissions (9). a relapse is defined as a period of neurological impairment with new symptoms or a worsening of previously-established symptoms, lasting for at least 24 hours with an absence of infection or fever (10). Many people with MS will eventually develop disabling and progressive symptoms. However, the symptoms experienced vary from patient to patient, as well as the course of the illness (11, 12). The response to different treatment also varies between patients and can be unpredictable.

1.3. Epidemiology, aetiology, and risk factors

In 2023, Atlas of MS epidemiological data, MS was estimated to affect 133,780 people in the UK and 2.9 million people worldwide(13, 14). The first onset typically occurs between the ages of 20-40, which is the childbearing age, with a 3:1 female to male ratio (1, 15). A precise aetiology of MS is still unknown. A gene-environment interaction is thought to increase the risk of MS (16). MS is not a direct hereditary disease, but having a family member with MS can increase your chance of developing MS, as a family history of MS was reported in 15-20% of cases of MS patients, which is higher than the prevalence in the general population. In other words, having a first or second-degree relative with MS will increase the risk of having it (17). Environmental factors that have been shown to provide an increased risk in genetically-susceptible people are Vitamin D deficiency (18, 19), viral infection – specifically the Epstein Bar Virus (EBV) (20), obesity, and smoking. These have all been shown to have some association with the disease but not enough to cause the illness on their own (16, 18).

1.4. MS Subtypes

There are four main disease phenotypes describes by the International Advisory Committee on Clinical Trials of MS, which were established in 1996 and revised in 2013 (10).

The first is Clinically Isolated Syndrome (CIS), which is the first acute clinical demyelination event, and has a variable rate of conversion to definite MS of 30-82% (10, 21). The second is Relapsing Remitting MS (RRMS), which is the most common form of the disease, as 85% of people with MS will be initially diagnosed with RRMS. In this form, patients go through periods of relapses (exacerbations), that will consist of one or a combination of neurological symptoms, followed by periods of remission which vary in length and magnitude (not all patients have a full recovery, and some are left with residual damage from relapses). Secondary Progressive MS (SPMS) is a progressive form of MS that initially starts as RRMS and then transitions to SPMS after gradual worsening and disability progression. Finally, Primary Progressive MS

(PPMS) is where gradual worsening and disability accumulates without an initial course of RRMS (10).

Radiologically Isolated Syndrome (RIS) is a possible MS precursor that is not considered an MS phenotype. It is defined as having only radiological evidence of the disease (MRI lesions), but no symptoms (10).

1.5. Diagnostic process

Diagnosis of MS is typically established based on the McDonald criteria. These criteria were first developed and published in 2011 by a team lead by the neurologist W. Ian McDonald (9). These criteria have been revised and updated multiple times, the last update of which was in 2017. The criteria employ clinical examination, laboratory tests, and an MRI scan to establish an MS diagnosis (9), but assume that diseases that can mimic MS have already been excluded. Patients will usually present with one of the common symptoms of first relapses, which can be optic neuritis (vision problems), sensory problems, balance issues, and gait problems. In the UK, patients' first interactions with the health team after developing symptoms will either be through their General Practitioner (GP) or Accidents and Emergency (A&E), who then refer them to a neurologist for further investigation (22).

A diagnosis of MS requires evidence of central nervous system CNS damage disseminating in both time and space. This means that the patient needs to have evidence of CNS damage happening at two different times or more (dissemination in time) and evidence of damage in two different areas of the CNS (brain and spinal cord) or more to fulfil the criterion of dissemination in space.

Dissemination in time can be evidenced through a second relapse, the appearance of new active lesions together with old inactive lesions in a contrast MRI scan, or through a positive cerebro-spinal fluid (CSF) test for oligoclonal bands, which predict future relapse sufficiently to fulfil the dissemination in time criterion (23). The dissemination in space criterion can be fulfilled by either having a new relapse with new symptoms, suggestive of damage to a new area of the CNS, or through evidence of having a new lesion in a new area of the CNS in an MRI scan (9).

1.6. MS pharmacological treatment

MS treatment branches into three main areas: relapse management with steroids, symptom management medications, and disease modifying drugs (DMDs). Pulsed steroids are used during a relapse to help induce remission and restore function in a shorter amount of time (11). Symptom management medications are drugs that can be prescribed to treat a symptom caused by MS. For example, baclofen is a muscle relaxant that is frequently prescribed for the muscle spasms caused by the disease (24, 25). In comparison, disease modifying drugs (DMDs) are used to decrease relapse rates, slow the progression of the disease and slow the accumulation of brain lesions and disability (26-28). In 1993, the first DMD interferon beta – 1b (IFN beta - 1b) – was proved to be effective in controlling relapsing remitting forms of MS(29). Since then, treatments for all forms of MS (RRMS, PPMS, and SPMS) have been developed and licensed.

In 2015, the Association of British Neurologists (ABN) published guidelines for prescribing disease-modifying treatments in multiple sclerosis. Based on these guidelines, DMDs can be classified as either: moderately effective (reduce relapses by 30%), more effective (reduce relapses by 50%), and highly effective (reduce relapses by 70%) (30).

DMDs can also be categorised according to the route of administration: self-injectables (subcutaneous or intramuscular), oral therapy, and intravenous drips. They can also be categorised according to regimen into life-long treatments and short-term treatments (also called inductions), which are given in cycles. Each treatment has its indications, so a patient may not be eligible for all treatments. This is decided by the healthcare team looking after a patient, who will select a few options the patient is eligible for according to the patient's individual MS course (31). Since most DMDs also come with their own unique profile of route of administration, frequency, side effects, risks and benefits, patient involvement in choosing the treatment that best suits their life (choosing from treatment options they are eligible for, as per their HCP), can be very beneficial for ensuring their adherence to treatment (32, 33).

1.7. Multiple sclerosis and reproduction (history, MS and pregnancy, post-partum, breastfeeding)

Historically, pregnancy in MS has been a controversial topic (34-36). In the past, women were discouraged from becoming pregnant due to concerning aspects such as the impact the stress of pregnancy might have on disease progression, possible adverse pregnancy outcomes, the fear of passing MS on to offspring, and disability issues that can be even more challenging in cases of a lack of partner or family support (35-37). In 1998, the PRIMS study, was the first large prospective cohort multicentre observational study to assess the impact of pregnancy and delivery on the course of MS (38). This study confirmed a decrease in the relapse rate during the pregnancy period, especially the third trimester, compared to the pre-pregnancy year. A two-year follow-up showed that pre-pregnancy disease severity was the only predictor for post-partum relapses, meaning that patients who were struggling with severe disease before conception were found to have a higher chance of post-partum relapses (39, 40). MS activity decreases during pregnancy are thought to occur because of female immune system changes, influenced by high oestrogen levels, which cause a shift from the T-helper 1 (Th1) cells that attacks myelin to the T-helper 2 (TH2) cells that secrete anti-inflammatory cytokines and down-regulate Th1 cells. After delivery (the first three months post-partum), oestrogen levels drop and the immune system goes back to its normal functioning (Th1 increases again), which was found to be associated with an increased chance of relapse (41).

As the post-partum period is a critical time for women with MS due to the increased risk of relapse, some studies support the immediate resumption of medication to protect the mother from post-partum relapses, suggesting that breastfeeding would not be effective in preventing relapses (42, 43). On the other hand, recent evidence has suggested that breastfeeding can protect from post-partum relapses and has thus encouraged breastfeeding, but only if done in an exclusive manner that induces lactational amenorrhea (loss of menses) (40, 44-46). Exclusive breastfeeding means that the infant will only be fed breast milk without the support of formula. This also includes feeding the infant expressed breast milk. The protection that is linked to

lactation amenorrhea will fade with the return of menses as breastfeeding is reduced (when the baby starts to depend less on breast milk and starts solid food) (45).

1.8. DMDs' compatibility with pregnancy and breastfeeding

Assuring medication safety during pregnancy and breastfeeding is one of the most difficult areas of medicine. This is because ethically, experimenting with treatment on pregnant or breastfeeding women is challenging due to risks to the child. Thus, data about drug safety and compatibility with pregnancy is always gathered from case reports and the pregnancy outcomes of accidental pregnancies that pool in drug pregnancy registries, together with conclusions drawn from studying both the treatment mechanisms of action (how much it can interfere with foetus organogenesis and impact DNA), drug pharmacokinetics (its permeability across the placental barrier to the foetus and its concentration) (47), and the change in drug pharmacokinetics due to female physiological changes during pregnancy (increased plasma volume and body fat) (48, 49). The data on medication safety during breastfeeding is thus usually determined by balancing the risks and benefits in terms of the following factors: the medication mechanisms of action, side effect profiles, pharmacokinetics (factors anticipating presence in breastmilk), and animal or human reports. A high volume of distribution and a high molecular weight both suggest that medication presence in milk is unlikely. Low oral bioavailability and a relative infant dose (RID) of less than 10% both predict the safety of the medication for use by a breastfeeding mother (50, 51).

Generally, the older the drug, the more is known about it. With MS, the oldest medications available are the interferons (IFNs) and glatiramer acetate (GA) (available for nearly thirty years now). Both had their pregnancy/lactation warnings lifted after enough literature showed no increased harm to the foetus or infant when used (52-55).

When a woman has clinically stable MS with previously mild symptoms, it can be an easy decision to stop DMDs and start trying to conceive, or to continue using one of the two licensed moderately effective treatments (IFNs or GA) when needed. However, it is not this easy or straightforward for every woman with MS due the

disease's variability, unpredictability, and the novelty of some of the treatment options. Teriflunomide and cladribine are both teratogenic drugs, meaning that if they are taken during pregnancy, they can cause serious birth defects in the foetus. They are thus contraindicated in pregnancy (56, 57). They both also require a long wash-out period before conception: two years for teriflunomide (without medicated accelerated flushing), and six months after each course of cladribine (55-58).

natalizumab and Fingolimod are high and medium potency medications, respectively, that expose patients to a higher risk of relapse and rebound when stopped (59-63). Fingolimod is a teratogen too and using it during pregnancy is therefore contraindicated (64, 65), women taking Fingolimod who want to get pregnant are thus more suited for a treatment switch rather than discontinuation to avoid disease rebound (30, 55). In comparison, natalizumab is increasingly used if needed but should be stopped by the last month of pregnancy to avoid haematological abnormalities in infants (55, 65, 66).

With the rest of the DMDs, it is usually a risk-benefit weighing process with sometimes complex management plans. As data about dimethyl fumarate is lacking, it is recommended to avoid it during pregnancy and to stop taking it when trying to conceive (without a wash-out period) (55, 67).

Anti-CD20 treatments such as and ofatumumab are now used until confirmation of pregnancy and may be continued if needed, based on the latest Association of British Neurologist (ABN) guidelines on Anti-CD20 use during pregnancy and breastfeeding (55, 68-70).However, these treatments are not yet licenced as safe to continue during pregnancy by EMA or FDA, which can put some legal liabilities on clinicians in case of any adverse events. This was merely an exemplary overview of some of the treatments available to demonstrate the complexity of such treatment management when thinking about and planning for a family. Other treatments from the same therapeutical class can vary a bit in management, specifically in their wash-out periods.

1.9. Switching DMDs

There are a number of occasions when switching DMDs is indicated. The most important reason – and therefore the easiest case of decision-making – for switching is when a patient has a breakthrough in disease activity, meaning that the DMD used has failed (71). Other reasons include not tolerating the DMD's side effects and compliance issues. Finally, another argument for switching is family planning while using a DMD that is not compatible with pregnancy and breastfeeding. This is particularly important for women who struggle with a severe disease that mandates the continuity of treatment during pregnancy and breastfeeding (71).

Switching DMDs is a difficult decision in itself because a) you still cannot predict the response of a patient to the new treatment (72), and b) a proper wash-out period (waiting for the right amount of time after stopping the old DMD before starting the new one) is required for some treatments when switching (73). A wash-out period is vital, especially when using DMDs that cause lymphocyte depletion. It ensures the recovery of lymphocytes to avoid the cumulative effects of both the old and new DMD, preventing infection. Waiting too long, however, can put the patient at risk of relapse. This is one of the difficult decisions HCPs face (73). The French MS Society developed guidelines to help with switching treatments. However, these guidelines did not consider switches made for the sake of family planning, where de-escalating treatment can be an option (73). In contrast, a very recent consensus paper on switching was published in 2022, which touched on switching strategies when planning pregnancy in a couple of statements, considering both options of induction strategy or de-escalation therapy depending on patient disease activity. However, this paper discussed all different switching reasons, approaches and wash out periods and was not focused in depth on pregnancy and breastfeeding (74).

Even if the decision to switch is an obvious one to make because a treatment is failing and the patient is relapsing while using one DMD or struggling with side effects, the choice of medication remains difficult.

Switching to conceive is even trickier as many factors such as time needed to conceive, level of protection provided by pregnancy to each different woman and whether it is enough to protect her without the need of treatment are all adding layers

of complexity to the decision. Women with MS who decide to get pregnant are usually either living with a mild form of MS, meaning that stopping the use of DMDs during pregnancy and breastfeeding should not be a problem, or are women with a severe case of the disease who have reached some kind of stability and control over their MS and have thus thought about family planning. The latter case, switching after reaching stability, is the more difficult instance. These women are usually either trying for pregnancy after completing cycles of induction treatments (such as cladribine), or are in between cycles after washing out, (the period used to flush treatments out of the body), and switch to ani-CD20 or natalizumab (not licensed but increasingly used during pregnancy by HCPs. De-escalating to pregnancy-safe options (interferons or GA) that are licensed by the EMA and FDA is also an option to consider(74).

De-escalating treatment is usually only discussed in the existing literature in the context of aging MS patients (patients aged 55 years or older) whose higher-efficacy DMDs are causing them more risks than benefits (75-77), until it was recently mentioned in the switching consensus paper in one of the statements(74, 75). For patients with severe MS, de-escalating treatment can be expected to be risky, especially if the patient does not fall pregnant quickly, thereby not gaining the extra protection afforded by the hormonal pregnancy state (39).

1.10. Decisions around treatment and family planning

When starting DMDs, HCPs will give patients a few options that they are eligible for according to their preferences. If family planning is a current priority, the decision has to be made as to whether to start trying for pregnancy and postpone treatment (if possible), to start treatment and postpone family planning, or to start a treatment that is compatible with pregnancy.

However, if family planning was not considered earlier when choosing a treatment option, or a change in a patient's circumstances has occurred; decisions regarding treatment management need to be made. This requires a number of questions to be asked, such as whether it is a good idea now in relation to their MS, whether they are candidates for stopping or switching treatment, and whether they would feel comfortable conceiving while on medication, even when a DMD is claimed to be

compatible with pregnancy. It also requires calculations to be made as to how long they need to stay on contraception for until the medication is cleared out of their system (wash-out period) before they can start trying for pregnancy.

The post-partum period, the most at risk period when women are prone to relapse, also needs to be considered. This requires decisions to be made by the patient, such as whether to breastfeed and to postpone the resumption of treatment or to not breastfeed and start back on treatment, and whether they want to breastfeed and use the breastfeeding-compatible treatment options or not. Moreover, when starting one of the treatments that cannot be used during pregnancy and possibly for a long period afterwards, patients need to decide whether they want to have more children before starting such a treatment and whether they have enough time in their fertility window to start this treatment now and postpone completing their family until later.

There are also other kinds of decisions that arise from a less planned approach, such as when accidental pregnancies occur while using a contraindicated or teratogenic DMD. This requires a decision to be made as to whether to keep this high-risk pregnancy or terminate it. These are very difficult decisions to make, especially considering the disease's variability, uncertainty, and the novelty of the drugs being used. This does not even take into account women's different personal circumstances and stories that will also impact those decisions.

1.11. Summary

This chapter has provided an overview of MS, its treatment, and how treatment choices and family planning are intertwined and impact each other. It also examined the multiple critical decisions that are often faced by women with MS. This experience needs to be explored holistically in order to be able to recommend interventions that can improve this process.

The next chapter will introduce the different decision-making approaches and highlight the role of shared decision-making in the DMD and family planning decision experience. This will form the basis of the explorative empiric work of this research.

Chapter 2. Introduction to Shared Decision-Making (SDM) in Multiple Sclerosis

2.1. Introduction

This chapter will set shared decision-making (SDM) in the DMD and family planning decision-making experience and highlight the importance of implementing SDM in this context. It will begin with short explanations of different decision-making approaches, followed by explanations of why SDM is important in chronic illness both generally and more specifically for MS decisions complicated by family planning wishes. The chapter will finish by introducing decision aids as tools which support the SDM process.

2.2. Treatment Decision-Making approaches (paternalistic, informed, or shared)

Historically, in the 60s and 70s, decision-making by HCPs was the predominant approach in the treatment decision-making process (78). This approach puts the responsibility of making decisions on the HCP only, without involving the patient. This is also called the paternalistic approach in treatment decision-making.

From 1990 onwards, patients started to engage more in their health choices, and other approaches like informed decision-making and shared decision-making started to evolve (78, 79). In informed decision-making, the HCP provides the patient with the needed information to allow the patient to make a decision. In comparison, in shared decision-making, there is more of a two-way communication of preferences and information between patient and HCP, which leads to an agreement on the best treatment option (79). In practice, it is difficult to always stick to one model in the decision-making process with every patient as this is not an ideal world. For example, a HCP who mostly follows a shared decision-making approach, might still find themself leading the decision when the patient does not want to be involved in the decision-making process (78).

2.3. Shared decision-making in chronic illness

Shared decision-making (SDM), is the process of making treatment decisions that takes into consideration both healthcare provider advice about the options which are in a patient's best interest, and patients' preferences (80). This offers a middle ground between the paternalistic and the informed decision-making models (80).

SDM is increasingly used in the management of chronic illnesses where treatments are expected to be taken for long time (possibly for life), and where adherence to these treatments becomes a challenge that impacts both patient health outcomes and costs (81). Adherence to medicines is defined by NICE as "the extent to which the patient's action matches the agreed recommendations" (82). When patients are given the chance to choose the medication or treatment that suits their values, beliefs, and preferences, together with a regimen that best fits into their life, an increased adherence to treatment can be expected (80, 81, 83). Involving patients in the decision-making process also empowers the patient, giving them a sense of control over the illness and increasing their motivation to adhere to the treatment plan (81).

Moreover, shared decision-making was also found to positively impact the HCP-patient relationship, which has been found to be the basis of successful treatment. When HCPs actively involve their patients in the decision-making process through effective communication, this will contribute to increased trust, loyalty, and respect between the two parties and thus positively impact a patient's adherence and health outcomes (81, 84).

The SDM approach is particularly suitable in the case of preference-sensitive decisions where there is no best option of treatment, meaning that the preferences of the patients are particularly important. This is frequently the case with MS (85, 86).

2.4. Is the SDM model suitable for making MS decisions?

The subsequent section will address why SDM model fits so well with the MS decision-making process.

2.4.1. The lack of a best treatment option (preference-sensitive decisions)

Preference-sensitive decisions occur when there is no best treatment option, meaning that the preferences of patients are then of greater importance in choosing a treatment that best fits into their life, in that this increases the chance of adherence to treatment, improves health outcomes, decreases all health costs, and enhances their quality of life (86-90).

In the case of MS, nowadays there are multiple treatment options (DMDs) available to control and slow down the progression of the disease. These DMDs come with different efficacies, routes of administration, regimens, side effects, and pregnancy compatibility profiles. It is also important to re-stress that the response of patients to each DMD cannot be predicted. Some treatments can therefore work well controlling the disease of patient A but not patient B. It is also important to take into account the variable nature of the course of the illness in each person (See Chapter 1). A patient can be eligible for several treatments which are of comparable efficacies, thus making MS treatment decisions preference sensitive. The SDM model therefore suits the MS decision-making process (90).

For example, an MS patient can be eligible for both Drug A (daily tablet) and Drug B (weekly injections). If the patient works in a job that requires a lot of travelling, it may be challenging to adhere to a treatment involving any of the self-injectable DMDs that need to be kept refrigerated. The patient may therefore do better with tablets that can be easily packed when travelling. In contrast, injectables may suit another patient who does not do a lot of travelling and usually struggles to adhere to daily regimens, as injectables need to be administered less frequently than tablets. Family planning adds another layer of complexity to this, as explained in Chapter 1. Discussing the place family plans have in a patient's timeline in relation to their treatment is therefore vital. This can only be considered when both the HCP and patient actively participate in the process of communicating information and preferences during the decision-making process using the SDM model.

2.4.2. Capacity to make treatment decisions.

Multiple sclerosis is a condition that can impact cognition domains such as memory, processing speed, and executive functions (91, 92). Capacity refers to the ability to

understand and use information to make decisions. In the context of clinical decision making specifically, it is the ability to understand information about the treatment options available and weigh up the risks and benefits in order to make a decision about the best treatment plan (93). The Mental Capacity Act of 2005 has been in force in England and Wales since 2007 to safeguard and promote the patients' rights in the decision-making process (94). Patients should not be considered incompetent unless they have demonstrated an inability to use, understand, and weigh up information, as well as to communicate a decision, despite the support and help provided (94, 95). The impact of MS on cognition may or may not occur at any stage of the disease at different levels. However, cognitively-intact MS patients are competent to make decisions just like the healthy population (92). Thus, while MS can cause cognitive deficits that can impact decision-making abilities in some patients, it is not considered a disease that will always cause decisional incompetence.

2.4.3. The impact of emotions on decisions

Another aspect in the existing literature that has been suggested to have an impact on decisions is emotions. There are two types of emotions which can impact decisions: integral emotions (emotions related to the stress of having to decide) and incidental emotions (any other emotions unrelated to the making of a decision). Both can influence the decision-making process (96, 97). Indeed, an emotional component can influence any kind of decision being made (98, 99).

MS is a disease that can cause a patient much emotional turmoil, from emotions of shock, fear, and grief when diagnosed (100), to the worry of the unknown and fear about its progression and the disability it might cause (101). MS can also cause a more complex emotional response, including emotional bluntness and neuropsychiatric disorders such as anxiety and depression (6, 100-102).

In summary, while MS is a disease that does not yet have a cure, there are several DMDs with different profiles available. As there is often no clear best option treatment, however, this makes the SDM model the best fit for decision-making in relation to MS (103). MS can impact a patient's cognition, emotions, and mental

health, which all can impact decision-making ability (104, 105). Despite this, however, patients can make their decisions with help unless they are severely impacted by MS and assessed by an HCP as lacking the capacity to make these decisions. This suggests that SDM is the most appropriate model for MS decision-making. The informed decision model can be too difficult to conduct in instances of cognitive deficiency, as the decision is solely made by the patient in this model. Similarly, the paternalistic approach is only suitable if it has been proven that the patient lacks the capacity to make their own decisions according to an HCP assessment.

2.5. The role of decision aids (DAs) in SDM

As directed by The General Medical Council (GMC) in their Good Medical Practice Guidelines, HCPs need to try as much as possible to help and support patients in making their own treatment decisions (106). This support and help can include any type of visual or auditory explanatory methods (decision aids), which can help patients better understand the information, as well as the benefits and risks of a treatment, allowing them to make a decision (95).

NICE defines decision aids as tools that can be used to support the discussion between HCPs and patients about preference-sensitive treatment decisions, which the patient can then take with them to consider them further after the discussion (86). The main goal of decision aids, as per NICE, is to summarise the available evidence relating to the effectiveness, safety, and practical factors of the treatment options, and to present that information in the easiest possible way for patients. This allows patients to understand the information so that, with support from their HCP, they can weigh up the risks and benefits of each option (86).

Decision aids come in different formats. They can be printed on paper or available online as a simple webpage or sophisticated computerised program. Tables, figures, videos, and pictures are all popular forms of decision aids (107). Decision aids are a vital part of the SDM process, in that it simplifies the bulky medical information provided so that patients can better understand the material. This thus allows for an improved decision-making experience and hopefully improve the quality of the decision (108). The efficacy of such tools can vary, however, and they often come

with their own challenges as they are time-consuming to prepare and update and can also be costly (109).

According to the International Patient Decision Aid Standards Collaboration (IPDAS), the effectiveness of any DA is measured by the extent to which the tool improves the quality of the decision-making process or the decision quality (110). The existing literature has shown that DAs can help to increase a patient's knowledge about their conditions, decrease decisional conflicts, help their expectations for a treatment to match the reality, and increase their contentment with their decision, meaning fewer regrets. However, the evidence that DAs help to improve the decision process and decision quality is still a growing area of research (107, 109, 111, 112). As such, it still lacks the standardised assessment methods for the measurement and reporting of effectiveness outcomes, although this is currently under development through the IPDAS (108).

2.6. Decision aids for MS decisions

Multiple sclerosis is one of the chronic illnesses that, as discussed earlier, requires a lot of decisions to be made both on the first day of diagnosis and further down the line. Decision aids have always been part of the MS care in the UK, especially when starting on DMDs. When discussing starting a new treatment or switching to another one, HCPs both highlight the options and discuss them with the patient and send the patient home with leaflets and booklets about these options to help them consider their options before finally making a decision.

There are many MS charity organisations globally. The MS Trust and the MS Society, which are both based in the UK, have been keen to develop and disseminate these pre-prepared decision aid booklets that are given to patients to take away by their HCPs. The organisations also have their own websites that publish articles, educational programmes, blogs, and different resources that can be ordered for free as a paper booklet mailed to their mailbox or as a pdf downloaded on their devices. These resources offer information about all life aspects of living with MS, such as dealing with symptoms, life changes, sexual life, breaking the news of MS to children,

MS and pregnancy, and other topics that can help patients with their decisions and other life aspects (113, 114).

Nowadays, with the growth of digital health sector, decision aids are also increasingly digitalised. Sophisticated decision models are being developed to help both patients and healthcare providers make decisions. Multiple prototypes of DAs for DMD choices that have been developed and tested for feasibility, usability, and effectiveness and found to increase patient knowledge and reduce decision conflict. However, long-term outcomes, especially patient adherence to treatments and the quality of these decision processes are not always studied and reported (108, 115-118).

Both the MS Trust and the National MS Society have published online decision aids on their websites. At the time of writing, these are digitalised, simplified forms of the DMD booklets that help patients with their DMD choices (119, 120). Although the focus of both DAs is to help patients choose a DMD, both only included a brief information section about family planning compatibility within the tool. That being said, the National MS Society tool includes pregnancy planning as one of the filtering questions upon which the recommended choices of treatment are based, while the MS Trust tool has included this as a criterion for comparing suggested DMDs. This only appears after the options have already been filtered and generated though. Both lack a detailed timeline for treatment management when considering family planning (120).

This thus presents an opportunity for digital DAs to be developed further to help patients with MS with the decision of whether or not to have children. The development of prototypes for DAs and the testing of their usability and efficacy has previously mainly focused on DMD choice more generally. Only one study focused on developing and testing a paper-based DA for family planning decisions in relation to MS (regardless of treatment) (121). This survey compared those who used the DA to make a decision about family planning with controls who made this decision without the help of the DA. The study results showed a decrease in patient's decision uncertainty (decisional conflict) using the decision conflict scale which is a widely used tool that reflect patients' level of being informed, uncertain, values, support and the quality of the decisions. The results showed also an increase in patient's

knowledge about pregnancy with MS as a result of the DA being used reported on the DA users' arm, this was assessed using a ten-question knowledge about pregnancy in MS questionnaire. There was no reported increase in anxiety or depression in relation to DA use(121).

Interestingly, there is currently no DA that helps patients to decide on a treatment plan in a way that considers and accounts for family planning by informing patients about the timeline and management of using DMDs when planning for pregnancy and through post-partum decisions.

2.7. The holistic decision-making experience in relation to DMD choices in light of family plans

When studying the decision-making experience, it is important to examine it holistically and to take family planning into account when deciding on a treatment plan, switching treatments, and managing treatments.

In a recent 2023 qualitative study of MS patients' experiences of family planning, the interviews were focusing solely on the family planning aspect, without considering the complications that may arise from treatment. In the study, women discussed their concerns when planning for pregnancy, such as passing MS on to children, the impact of DMDs on fertility and on their offspring, disease progression and management, as well as coping as a parent with MS (122). They also commented on the kind of support they need from their HCPs in this regard and how consistent this support should be (122). This study confirms the research undertaken by Ghafoori et al. in 2019 (37), and Prunty et al. back in 2008 (121). Although these are very informative studies which examine family planning decisions and patient needs around this, neither focus on the decision-making experience itself or the place of family planning within the treatment decision making experience.

DMD choices were also looked at separately, with the focus mainly being on the factors that matter the most to patients when choosing their treatment plan. As can be expected, the safety of treatments during pregnancy and breastfeeding was one of the important attributes reported (123, 124).

In another qualitative study in 2020, Manzano et al. interviewed 30 women to better understand the DMD-switching experience. The experience was described as emotional with a lot of risks and uncertainty. It also touched on patients stopping their use of DMD to conceive in one of the accounts, this account reported struggling with relapses. It was also reported that male patients do not have reproduction discussions with their HCPs like female patients do (72).

Studies about healthcare providers' perspectives on the holistic decision-making experience were largely absent in the existing literature. A large survey in the US, which was sent to both patients and neurologists, produced an evaluation of the treatment decisions despite of family planning (125). The study highlighted the importance of SDM for both parties for establishing a better patient-HCP relationship, promoting adherence to treatment, reaching better health outcomes, and enhancing quality of life. However, the survey did not allow for an in-depth examination of the nature of the experience. This could help to give HCPs a better understanding of this experience and thus highlight opportunities for improvement.

Chapter 3. Gaps in the literature and the thesis rationale

3.1. Introduction

As detailed in Chapter 1, MS is a chronic illness that often starts during a woman's childbearing age. Patients are thus often faced with multiple complex decisions to make, especially as treatment decisions are not easy to make due to disease variability, unpredictability, and the novelty of some drug options. The issues surrounding the safety of MS drugs during pregnancy were also outlined in Chapter 1, highlighting how difficult treatment decisions are in relation to family planning. Switching treatments to allow women to conceive is one management approach that has been found to be important and frequently arises in the Ms journey, with little published literature exploring the effects of switching treatments (as one of the treatment management modalities) on women's MS when stable on the current treatment and planning for pregnancy.

While the existing literature has examined treatment decision-making for patients with MS, studies have usually separated the issue of DMD choices from family planning decisions. Consequently, it is vital that this topic is studied more holistically, with more of a focus on the approach to the decision-making process itself, as this is seldom explored in existing research.

As noted in Chapter 2, there are a number of studies which have examined the importance of involving patients in their care plans through the SDM model as a way to improve adherence, health outcomes, and decrease costs for chronic illness. That approach was also positive in the case of MS but there was paucity in literature exploring how well this model is followed in real world through experience when choosing treatment for MS, more importantly when this is complexed with the family planning decision.

The role of decision aids (DAs) was also discussed in Chapter 2, bringing attention to their importance in SDM and their promising efficacy in improving the decision-making process and quality of decisions made. However, a standardised assessment of the outcomes of DAs is still lacking. DAs for MS have mainly been created to help patients with their DMD choices, but have not dealt with the intersection of DMD

choices and family planning. Key MS charity organisations have two important DAs for DMD decision-making that have a section on pregnancy and breastfeeding. In my thesis, I chose to evaluate the MS Trust tool and not the national MS society DA, and that was decided due to feasibility to access to the organisation with the help of my supervisor, Dr. Declan Chard who is a trustee of the MS Trust. The MS Trust has confirmed that it has surveyed MS patients on the usefulness of the tool and has undertaken usability testing, it has not yet conducted a thorough evaluation, especially in terms of the usefulness of the DAs in relation to pregnancy.

3.2. Research Aim

To explore and understand the holistic decision-making process in relation to treatment plans and family planning, as a way to facilitate an improvement in the quality of decision-making experiences and the decisions made.

3.3. Research Objectives

- To identify the existing literature on the effect a frequent decision made by women with MS has on their health outcomes: the decision to switch treatments when stable as a way to plan for pregnancy.
- To explore the full decision-making experience for women when choosing to start, switch, manage, or discontinue medications, as well as in relation to how they position their family plans accordingly.
- To explore the decision-making experience of key healthcare providers who support these women in such decisions.
- To explore women's needs in terms of treatment/family planning decision aids through an online qualitative evaluation of MS Trust online DMD decision aid.

Chapter 4. Systematic Review: Switching treatments for clinically stable relapsing remitting Multiple Sclerosis patients planning for pregnancy.

4.1. Introduction

Chapter 1 outlined the multiple reproductive decisions a woman may face through her childbearing years in light of an MS diagnosis and treatment. One of these complex decisions is switching medications. This can be done for a number of reasons such as treatment failure, intolerable side effects, adverse drug reactions, or for the purpose of conceiving. While the first three are largely not avoidable, switching DMDs to conceive can be a result of a change of plans in the patient's life. For instance, planning treatment with a high efficacy medication first, before trying to conceive when stable, could be the result of not having had a clear picture about the DMD/family planning complexities from the beginning. When a patient is stable as a result of a specific treatment (especially highly active treatments for women with active MS), de-escalating to a pregnancy safe, less active DMD (GA or INF) could mean expecting more disease activity, especially if the woman does not fall pregnant quickly. How well pregnancy can control the disease activity in these circumstances remains a question to be answered. As the decision of whether or not to switch treatments is a major one for women in relation to family planning, this is an area which needs more research.

The focus of this thesis will thus be looking at the effects of switching treatments in clinically stable MS patients planning for pregnancy. This is addressed through systematically reviewing available literature, with the purpose of helping to improve current clinical practices. This review was published in the peer-reviewed Multiple Sclerosis Journal in 2021 (126).

4.2. Background

While pregnancy and breastfeeding both reduce the risk of relapses in women with MS (127-129), they do not appear to do so to the same degree as some disease modifying drugs (DMDs). In women with more active MS who have achieved clinical stability on higher efficacy DMDs, there is a concern that despite the protective effects of pregnancy, there remains a significant risk of relapse. The decision to switch treatments is thus more suitable than completely stopping treatment when planning a pregnancy (130). Indeed, women on certain DMDs such as Fingolimod are encouraged to switch treatments to a safe DMD rather than completely stopping treatment in order to avoid the return of the disease and rebounds (59, 61, 71, 131-137).

Concerns about the potential foetal effects of DMDs may lead some women to stop or delay treatment until their families are complete, or switch their DMDs (138). Some DMDs are known to be teratogenic (such as fingolimod, cladribine, and teriflunomide), meaning that they need to be stopped or patients need to switch treatments with variable wash-out periods. Emerging safety data now means women with MS who are planning a pregnancy are increasingly being encouraged to continue some DMD treatments. Both glatiramer acetate (GA) and interferons (IFN) are increasingly continued during pregnancy and breastfeeding after the removal of their pregnancy contraindication by the EMA (139-143). However, these treatments are only moderately effective treatments, meaning that switching to them from higher efficacy treatments is considered “de-escalation”. This can thus be expected to increase the risk of relapse.

All other DMDs are still not licensed for use during pregnancy. However, some (such as natalizumab and ocrelizumab) are being used by clinicians according to the current safety reports and a patient’s level of risk (70, 141). Nonetheless, women may refuse to use treatments that are still not licensed for use during pregnancy, and thus choose to completely stop or switch to the moderate efficacy injectables (GA or IFN).

At the time of writing, there has been no other systematic review that looks at the effects of switching DMDs, particularly in stable MS patients for the purpose of planning a pregnancy. Existing reviews either examined the safety of DMDs in

pregnancy (144), the main reasons for switching DMDs (145, 146), or studied the available treatment switch options due to pregnancy planning without evidence of the possible clinical impact of the switch (147).

A guideline paper on pregnancy planning for multiple sclerosis patients in the UK has been published that advises on medication management when planning for pregnancy and breastfeeding (141). In 2022, an updated guide by the Association of British Neurologists (ABN) reviewed the use of anti-CD20 in the family planning context (148), with the recommendations based on the consensus opinion of experts. However, this review did not seek to systematically review the existing literature on the effects that switches in treatment, resulting from pregnancy planning or otherwise, have on women with MS (e.g., relapse rates and new lesions being found in MRI scans).

The effects of switching to another DMD type when a patient is clinically stable on another DMD is thus unclear. The available studies in this area are controversial and variable. While multiple studies have compared different pairs of medication switches, some included patients who had switched medication due to treatment failure. This means that disease activity may have influenced the results, making escalation therapy more appropriate and making the patient less suitable for pregnancy planning (149). Others included both stable and unstable patients (150) or included different MS types (clinically isolated syndrome, relapsing remitting, primary progressive, secondary progressive) who switched therapies (151). Due to this variability, these studies consequently produced conflicting results, even though the treatment switches were the same.

4.3. Objectives

To review the evidence for the effects of switching from various DMDs to interferons and GA on the disease activity in people with stable RRMS wishing to conceive.

4.4. Methods

This systematic review was planned according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines (PRISMA) and registered in the

International Prospective Register of Systematic Reviews (PROSPERO). The registration number is CRD42020172912 (see Appendix 1 for the registration). PROSPERO was updated when the review was published.

4.4.1. Search Strategy

I developed and refined the search strategy for this review multiple times with the help of the librarian S.P who works at the Royal Free Library campus.

A comprehensive search was run using the following databases: Medline, Emcare, Embase, CINAHL, SCOPUS, and Cochrane Library. Non- English papers were screened using the English abstract and if relevant then translated and included. No limits were applied. In addition, a manual search for the references included in the relevant articles was conducted. The full search strategy can be seen in Appendix 2.

4.4.2. Inclusion and exclusion criteria

All study designs were included where participants fulfilled the following criteria:

Table 1. Inclusion Criteria

Inclusion Criteria	Comments
1- Adults with a confirmed Relapsing Remitting multiple sclerosis diagnosis according to the McDonald criteria (9).	
2- Using any type of DMD.	
3- No evidence of on-treatment relapses leading to a decision to	Patients who switched for other reasons such as side effect intolerances, a wish to conceive, and changes in life circumstances were all included. Only those

change DMDs (in stable patients).	switching because of suboptimal treatment efficacy (treatment failure) were excluded.
4- Switching to one of the pregnancy-safe DMD options (IFN or GA).	As this research is focused on the switching of DMDs for the purpose of conceiving, only switches to one of the drugs that are licensed for use during pregnancy are included (IFN or GA). Drugs that are sometimes used in clinical practice, but are unlicensed for use in pregnancy e.g., natalizumab, were excluded. The fact that these DMDs are not licensed for use during pregnancy, makes many women opt out using them when planning a pregnancy. Another reason for excluding switching to more effective unlicenced treatment is that the negative impact on MS when switching between higher efficacy treatments is expected to be much less because in this case patients will not be "de-escalating" treatment and thus the decision will not be as tricky in relation to impact on MS. Conversely, de-escalating from higher efficacy treatments to pregnancy licensed options (IFN or GA) to conceive is a difficult decision when stable on the current pregnancy unsafe treatment. A decision that requires weighing benefits and risks for both mother's health and foetus safety. It is particularly hard when women are not comfortable to switch to a more effective unlicenced treatment, thus opting for de-escalating for the pregnancy licenced treatments. This is my focus in this review, to know the clinical impact of such switch on these women health.
5- Following up with patients for at least six months	

after switching DMDs.	

Table 2. Exclusion Criteria

Exclusion Criteria	Comments
1- Reviews, editorials, book chapters, commentaries, replies, and conference abstracts for which the full texts were not available.	The authors of conference abstracts that matched the inclusion criteria were asked if their work had been published.
2- Studies looking at progressive disease, clinically isolated syndrome (CIS), and those that did not specify the type of Ms.	Progressive Ms can be very limiting for people's lives due to gradual accumulation of disability. Although patients can get pregnant, it is unlikely due to worsening of symptoms and disability accumulation(9). As for CIS, as a large portion of patients will be doing well at this stage and therefore may not be on any treatment, it is not yet considered a confirmed diagnosis of Ms (9).These cases were thus excluded to avoid bias.
3- Studies of patients who only switched DMDs for unclear reasons or treatment failure, where those switching due to treatment failure could not be separated from those switching for other reasons (switches made for reasons other than treatment failure, such as side effects, safety concerns, or patient preference were considered for inclusion).	This review is solely looking to examine the dilemma that women go through when stable on their current medications but need to switch (with all the risks involved) to conceive.

4.4.3. Data management and studies screening

Referencing was managed using Endnote X9 software. The screening process was carried out using Rayyan (an internet-based platform). The screening of initial article titles and abstracts prior to the screening of full articles was conducted by myself and my colleague NA. NA was a second reviewer for 10% of the studies at both stages. Eligible articles were included independently and blindly. Any conflicts were resolved firstly through meeting with NA and then through meeting with my supervisors.

4.4.4. Data extraction

The following data were extracted: country, setting, study design and methods, sample size, baseline characteristics, duration of follow-up, previous DMD regimen, new DMD regimen, primary outcome which is annual relapse rate (ARR), secondary outcomes which are expanded disability status scale (EDSS Score), new magnetic resonance imaging (MRI) lesions, and finally the main reasons for switching.

4.4.5. Quality assessment

4.4.5.1. To assess the quality of RCTs

The revised Cochrane risk of bias tool for used for randomised trials and a risk of bias assessment tool was used for randomised controlled trials (ROB2) (152).

4.4.5.2. To assess the quality of pre-post cohorts

The National Heart, Lung, and Blood Institute (NIH) quality assessment tool was used to assess before-after (pre-post) cohort studies with no control group (153). The tool consists of 12 questions (see Appendix 4 to review the questions). The answers were illustrated using a multi-colour graph (**Error! Reference source not found.**). Positive answers indicated a high quality and were represented in green, while negative answers indicated a low quality and were represented in red. Questions with “not determined” or “not reported” answers indicated a neutral effect on quality and were represented in orange. Question 12 asks if the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.). The question states: Did the statistical analysis consider the use of individual-level data to determine effects at the

group level? This question was not applicable for all the studies and was thus removed from the graph below.

4.4.6. Data synthesis

The data were narratively synthesised to address the results found in the eligible articles. Tables were used to present the data from the articles and outcomes. A multi-colour figure was created to represent the quality of each of the included studies. Meta-analysis was not possible due to the high heterogeneity between studies.

4.4.7. Review update methods

In May 2023, I started to run an update for the review. Another meeting with S.P the librarian was held to revise my search strategy that I have used before, to make sure the strategy is still valid as some databases can have some minor changes to their operators. I searched the same databases, and the search was restricted by date to include papers from 2019 to May 2023 only.

Papers were exported to and managed by Endnote. When screening the papers, I strictly followed the same inclusion and exclusion criteria.

4.5. Results

4.5.1. Search results

The search was run on 31 March 2020 and identified 2298 articles. After duplicate removal and a title-abstract screening, 1210 records were eligible for full-text screening. From this, 1109 were excluded. An additional two (154)articles were also identified during the manual reference searching of the eligible papers. The search strategy included grey literature, and for those five abstracts identified, I contacted the authors to get full texts for potential publications identified by the search, three of them declined to send the papers because they were in the process of publication at the time and two did not respond back to my emails. Seven articles that matched the

inclusion criteria were included in the end. After updating the review in May 2023, none of the new papers had met the inclusion criteria to be added to the review.

4.5.2. Overview of included papers

The seven papers which were included consisted of four pre- and post-cohort studies, two case reports and one RCT. Studies were conducted from the years 2006 to 2017. One study took place in Spain(155), three in Italy(154, 156, 157), two in the United States of America (158, 159) and one in Switzerland(160). Sample sizes were small ranging from one patient in both case reports and up to 40 patients in Rossi et al. cohort(156). In all seven papers, the main reason for switching treatment was adverse drug reactions and particularly increased risk of progressive multifocal encephalopathy (PML) when using natalizumab. Only one patient in one study decided to switch to plan pregnancy(154).

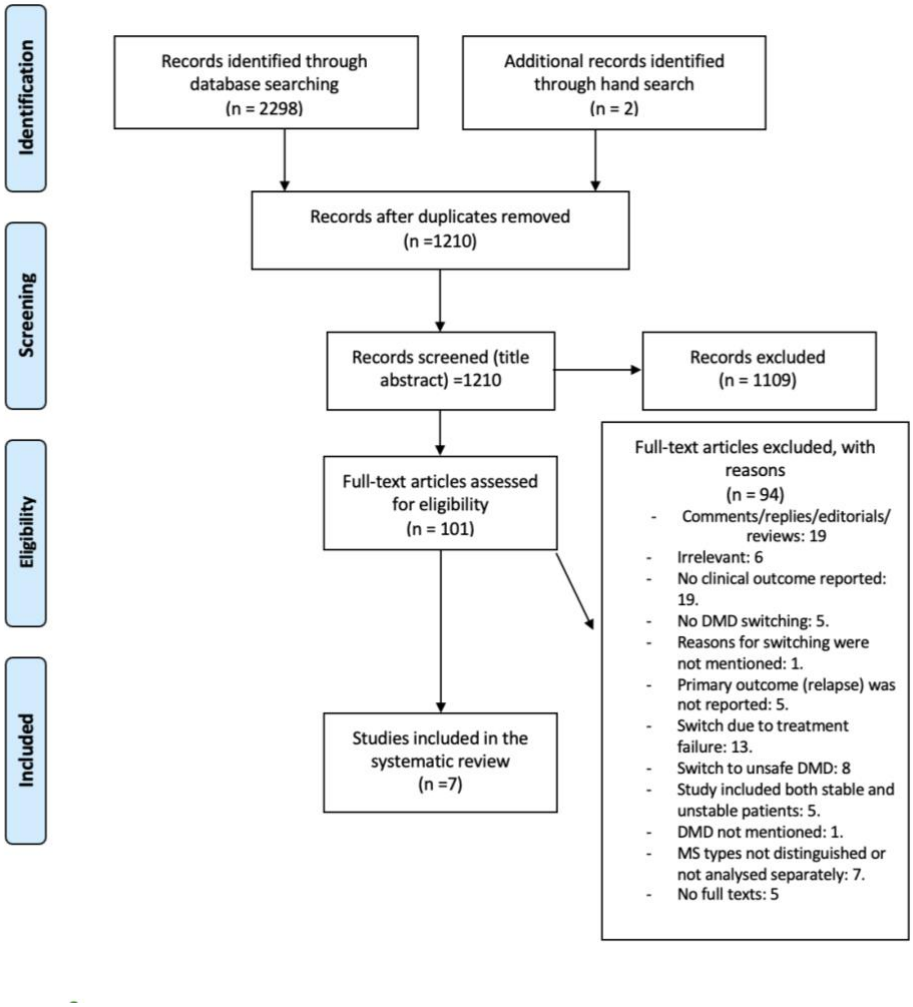

Figure 1 PRISMA flow diagram

The included articles consist of four pre-post cohort studies with no controls, two case reports, and one RCT (Table 3, Table 4, Table 5). When assessing the quality of pre-post cohort papers, three studies achieved more than 50% positive responses (72.7%, 63%, 63%). Negative responses accounted for only 9% (one question) in all three studies. The open label design used in the Caon et al. and Rossi et al. studies was problematic because the assessors' statuses were not mentioned, and participants were non-blinded while de-escalating from a potent medication like NTZ (156, 159). This may have influenced their reporting of symptoms. In comparison, the Magraner et al. study did not test for significance(155). The most common unreported information was power calculation, as all of the studies had small sample sizes ranging from 11- 40 participants(154-156, 159). It is not clear if all the eligible patients

were included in three of the studies because none of them reported this information(154, 156, 159). The fourth cohort by Ferre et al., is the only study judged to be poor-quality according to the assessment tool: it scored only 45% positive responses, while receiving 36% negative responses and 18% neutral responses. It is published as a brief communication and lacks the detail necessary for a quality assessment. A request was made to the author for a more detailed version but as there was no reply, the paper was assessed according to the available information(154).

Only one Randomized Controlled Trial (RCT) was included in the review and assessed for quality using the ROB-2 tool to be low risk in all areas except one (bias due to deviations from intended interventions), with some concerns due to masking, as only the assessors were blinded to the intervention while patients and carers were not(160). For the full assessment, see Appendix 3.

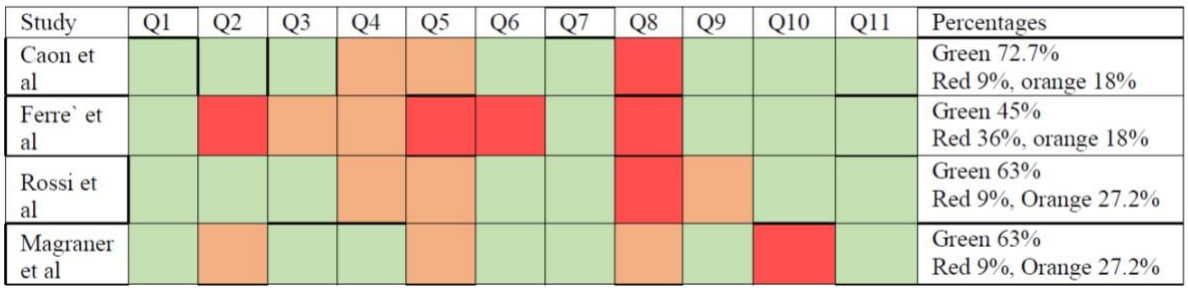

Figure 2 Quality assessment of the included pre-post cohort studies

Q: Question

Table 3. Characteristics of included observational studies.

Reference	Year	Extracted sample size	Switch pair	F/u	ARR on Rx1	ARR on Rx2	Mean EDSS score change	Mean number of new lesions	Reason for switching
Caon et al.	2006	23	IFN β- 1a To GA	mean 37.5 m	0.61 ± 0.6	0.47± 0.4^	-0.42*	NA	ADR
Ferre` et al.	2015	14, 12 switching to GA, 2 switching to IFN	NTZ to GA or IFN	32 m	0.03	1.5*	NA	Mean number of Gd+: 3.1*	Fear of PML, positive anti-JCV, pregnancy
Rossi et al.	2013	40	NTZ to GA	12 m	0.06 ± 0.2	0.6±0.8 1.3±2.1°¨	+0.09*	Mean number of CALS 2 ±1.36°	Risk of PML
Magraner et al.	2011	11	NTZ to MP 3m then GA	mean = 10 m, 6-18 m (outcomes at 6m interval)	0	0.045	+0.34	Mean number of Gd+: 3.6±6.3?	completed 2 years of treatment, 2- ADR,

IFN: interferon, GA: glatiramer acetate, NTZ: natalizumab, MP: methylprednisolone, m: months, NA: not available, F/U: Follow up, ARR: annual relapse rate, EDSS: Expanded Disability Status Scale, Rx: treatment, PML: progressive multifocal leukoencephalopathy, JCV: John Cunningham virus, ADR: adverse drug reactions, Gd+: gadolinium enhancing lesions, CALs: combined active lesions ^: non-significant, *: statistically significant, °: not reported, ¨: ARR adjusted to treatment duration.

Table 4. Characteristics of included RCT

Reference	Year	Design	Sample size	Intervention group: switchers	Control: Stayers	F/U	ARR in switchers	ARR in control	Median EDSS change switcher	Median EDSS change control	Median n of new lesions in switchers	Median n of new lesions in stayers	Reasons for switching
Gobbi et al.	2013	1:1 randomised; assessor blinded	IFN B= 9 NTZ= 10	Switch to every other day subcutaneous (s.c.) INFB 250 microgram.	continue monthly NTZ 300 mg, IV	12 m	0.4°	0°	0.5°	-	N of nT2L (6m): 1.5* (12m): 0^ N of Gd+L (6 and 12m): 0^	N of nT2L (6m): 0* (12m): 0^ N of Gd+L (6 and 12m): 0^	Risk of PML.

IFN: interferon, GA: glatiramer acetate, NAT: natalizumab, IV: intravenous, m: months, NA: not available, F/U: follow up, ARR: annual relapse rate, Rx: treatment, EDSS: Expanded Disability Status Scale ,PML: progressive multifocal leukoencephalopathy. nT2L: new T2 lesion, Gd+L: gadolinium enhancing lesions, ^: non-significant, *: statistically significant, °: not provided.

Table 5. Characteristics of included case reports

Reference	Year	Age	Gender	Disease duration	Rx1	Duration Rx1	Rx2	Duration Rx2	Relapses	EDSS score change	New MRI Lesions	Reasons for switching
Berkovich et al.	2017	39	F	4 Y	IFN-β 1a SC	2 Y	GA	1 Y	0 for 1 Y	+2	Yes	1- tolerability 2- ADR
Gaetani et al.	2017	25	F	9 m	IFN-β 1a IM	9 m	GA	5 Y	0 for 5 Y	NA	NA	ADR (Flu-like symptoms)

IFN: interferon, GA: glatiramer acetate, Y: years, m: months, NA: not available, F: Female, EDSS: Expanded Disability Status Scale , MRI: magnetic resonance imaging, Rx: treatment, ADR: adverse drug reaction.

4.5.3. Switching strategies

4.5.3.1. Switching from natalizumab to glatiramer acetate (de-escalation)

Two observational studies examined the effect of switching from NTZ to GA on disease activity. Ferre et al. tested the effect on clinical disease activity using the Annualised Relapse Rate (ARR) measurement, and the radiological activity using the mean number of new enhancing gadolinium lesions (Gd+) in an MRI scan before and after switching (154). Both the ARR and Gd+ increased after switching to GA, reaching statistical significance (at 0.05). However, this study is judged as poor quality due to missing information (it was published as a brief communication) (154).

The other study by Rossi et al. included 40 participants and measured disease activity according to ARR, time adjusted ARR, Combined Active Lesions (CALs) in the MRI, and EDSS score change. The ARR while on NTZ was (0.06 ± 0.2) and rose to (0.6 ± 0.8) and (1.3 ± 2.1) with unadjusted ARR and treatment duration adjusted ARR, respectively. New CALs were (2 ± 3.6) at month 12 of the MRI assessment, without evidence of a rebound. The mean EDSS score change from baseline to the end of the follow up was very small but statistically significant. Both differences in ARR and mean CALs while on NTZ and after switching to GA increased but the significance was not calculated. Instead, the study reported decreased clinical and radiological activities after switching to GA compared to the pre-NTZ period, both of which were statistically significant. This study thus showed the safety and tolerability of GA and its ability to prevent disease rebound without maintaining the same efficacy as NTZ (156).

4.5.3.2. Switching from natalizumab to glatiramer acetate after “bridging”

In the study by Magraner et al., switching from NTZ to GA after “bridging” with methylprednisolone for three months was tested for the effect this had on the disease activity as a protocol that aimed to prevent disease rebound during the NTZ interruption periods that take place when patients have a risk of developing Progressive multifocal leukoencephalopathy (PML). PML is a severe demyelinating event caused by the John Cunningham Virus (JCV), a latent childhood infection that

reactivates for a number of reasons, including the use of immunomodulatory medications such as NTZ (161).

Data were provided for each participant, which allowed me to exclude those switching due to treatment failure. While 11 patients who switched treatment due to the risk of Progressive multifocal leukoencephalopathy (PML) having used NTZ for two years already were included, the other seven patients who experienced relapses while using NTZ (not stable) were excluded. The ARR changed from 0 to 0.045, while the mean change in EDSS score was +0.34 and the mean number of the new Gd+ was (3.6 ± 6.3). However, on assessment, a substantial risk of study bias was identified. All the changes in measures were assessed from the point of stopping NTZ and six months after stopping it (155). This is very likely an insufficient period to assess the effects of a treatment change, as exposure treatment with GA alone was effectively only done for three months (methyl prednisolone was given for the first three months). Equally, the biological effects of NTZ last for approximately 12 weeks, while the changes it makes to the cerebrospinal fluid distribution of immune cells may persist for up to six months after discontinuation (160, 162, 163).

4.5.3.3. Switching from natalizumab to IFN-ß 1b (de- escalation)

The effect on disease activity of de-escalation from NTZ to IFN-ß 1b was studied by Gobbi et al. in a one-year randomised rated blinded controlled pilot trial. The number of relapses reported was used to calculate the ARR in switchers, and it was higher than non-switchers (0.4 and 0, respectively).

The EDSS score increase ranged from 0.5–1.5 with a median of 0.5 in the switchers, while no progression was recorded in the NTZ group. Radiologically, no new lesions were reported in the control NTZ group in all MRI scans. The number of new lesions (T2 and/or Gd+) in the IFN group ranged from 0-12, but the only significant difference between the groups was the number of new T2 lesions reported at month six. The study concluded that IFN could not maintain the efficacy of NTZ but exerts some anti-inflammatory effects that made all three reported relapses mild and non-disabling (160). Studies of this on a larger scale are needed to confirm these findings, as this RCT was limited due to its small sample size. It also had some quality concerns because only the assessors were blinded.

4.5.3.4. Switching from IFN to GA

Changing between first line injectables – specifically from IFN to GA – was assessed in one pre-post cohort, a case series report, and a case report that fulfilled our inclusion criteria.

Caon et al. found that the ARR was reduced by 23% after switching from IFN to GA due to toxicity, although this reduction did not reach statistical significance (159).

A case report of a 25-year-old woman with relapsing remitting MS who was initially using IFN-ß-1a for nine months and then switched to GA due to the flu-like side effects, showed clinical stability on GA for five years, although radiological activity was not reported (157).

Lastly, a 39-year-old woman who had had relapsing remitting disease for four years switched from IFN-ß-1a to GA due to the side effects. One-year outcomes showed no relapses but confirmed new MRI lesions and a + 2 increase in the EDSS score (158).

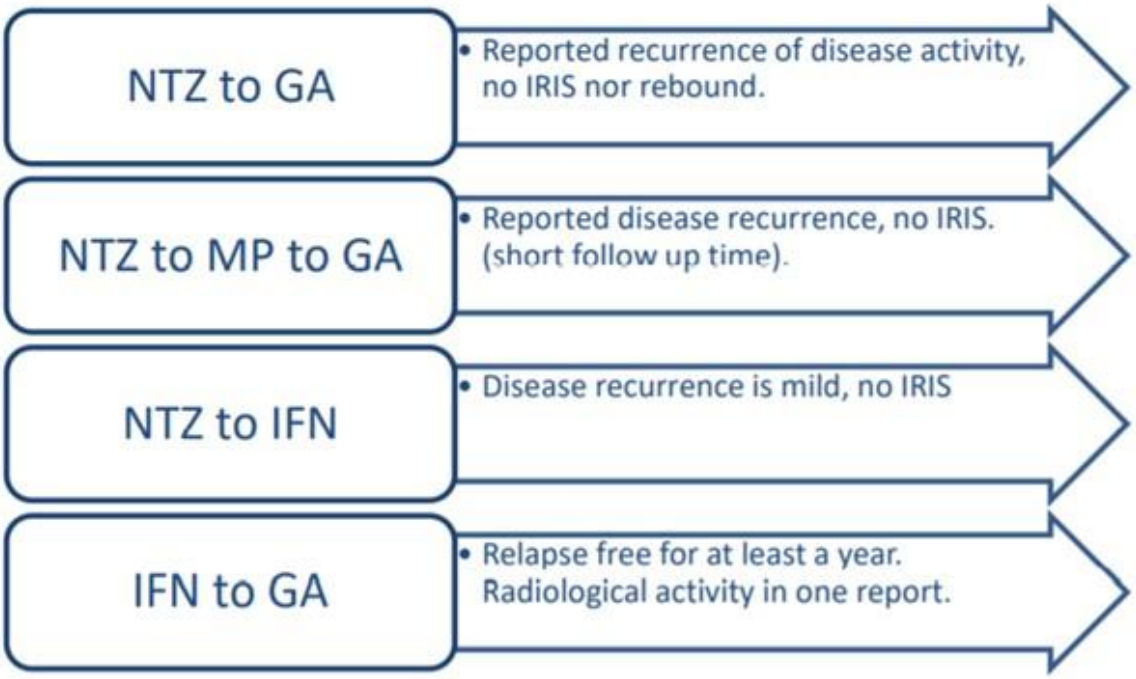

Figure 3 Switching strategies according to the review results.

4.6. Discussion

This review found two main DMD switching strategies in people who were stable on treatment and switched from a higher potency drug to drugs licensed for use during pregnancy (GA or IFNs), or switching between interferons and GA. The findings confirm that the risk of relapse when switching matches the medication's known efficacy. In other words, when switching from a higher potency medication like NTZ to a lower efficacy one (de-escalating treatment), chances of relapses are higher. Nothing in these findings causes one to question the recommendations of the UK consensus on pregnancy in multiple sclerosis (55). However, the most striking finding is how little high-quality information there is about the relapse risk associated with changing treatments. Furthermore, none of the included studies identified specifically considered this in the context of pregnancy and the reduction in relapse risk associated with pregnancy and breast feeding.

When balancing risks, it is worth noting that people on higher potency treatments will tend to have had more active disease before starting these medications. The study

by Alroughani et al., which followed up on 99 pregnancies, measured the ARR before and during pregnancy. Of these pregnancies, 21 of the participants were using Fingolimod, 24 used NTZ, 42 used IFN, 2 used teriflunomide, 1 used DMF, and 9 were taking no medication. Seventeen relapses occurred during pregnancy. Of these, 70% of them happened in patients who used either NTZ or Fingolimod before conception (130). This reconfirms the fact that for patients with a previously more active disease which has been controlled with more potent medications, switching treatments (and in the case of NTZ, now continuing) rather than stopping treatment entirely may be preferable. In addition, there are now two treatments available that can induce a sustained response after only two courses of treatment (cladribine and alemtuzumab). While they cannot be used during pregnancy due to the teratogenic risk, conception is advised to be attempted from six (cladribine) or four (alemtuzumab) months after a cycle of treatment. This may be preferable to using a lower potency drug during pregnancy.

GA and IFNs are considered of comparable efficacy (164-166). While evidence of the effects of switching between them appears consistent with this, this is of less interest than it was previously, as both treatments can now be continued during pregnancy (52, 143, 167-169).

Only one high potency treatment (NTZ) was identified as being stepped down to GA or IFN. However, there are now a lot more treatment options with a higher potency than GA or IFN being commonly used in clinical practice. People with MS now also have a choice between treatments that can induce and sustain remission after two courses (alemtuzumab and cladribine) and others that maintain remission when regularly taken such as interferons, fingolimod, and natalizumab.

While the recent UK consensus guidance paper on pregnancy with MS adopts a pragmatic approach (which is supported by the limited data identified), an optimal approach to DMD management in women planning pregnancy is yet to be established. To help women make informed shared decisions about pregnancy and DMD management, we need a more robust evidence base that includes managing the full range of commonly used treatments. Direct evidence of DMD efficacy during pregnancy, compared with pregnancy alone is still lacking (65, 142, 143, 158, 167).

Studies where a switch in DMDs was prompted by side-effects were included here, but only where patients were not also having relapses. While this is not the case with pregnancy planning, treatment side effects, per se, are unlikely to substantially bias the comparison of the risk of relapse before and after switching, except where this affects treatment compliance. However, if such studies had been excluded, only one out of the seven identified would still have been included, further highlighting the paucity of data directly applicable to pregnancy planning.

In addition to highlighting how few studies there are on treatment switching, it should also be noted that those identified were small in size, so one has to be cautious about generalising the results. Furthermore, a formal meta-analysis was not possible due to the limited treatment overlap between the studies, with only one study being an RCT.

4.7. Conclusion

The results of the few studies that have been published on switching treatments in clinically stable relapsing-remitting patients appear to be predictable based on a medication's known efficacy, and thus highlight the risk of de-escalation. This makes switching when stable a difficult decision to make for both women and HCPs, highlighting the importance of discussions about family planning happening as early as possible to reduce unnecessary switches that may cause complications later on.

Chapter 5. Empirical work methodology

5.1. Introduction

The previous chapter highlighted the paucity of literature on the clinical effect of switching treatments when patients are stable for the purpose of planning a family. This ambiguity and risk highlight the importance of the DMD/family decision-making experience in trying, as much as is possible, to plan ahead for the future as a way to avoid the necessity of treatment switching. It is therefore very important to explore this experience holistically, and from all participating parties' points of view, in order to understand the process as well as the patients' challenges and needs. This understanding could then facilitate the improvement of the quality of both the experience and the decisions made.

5.2. Study Design (Why qualitative?)

Based on the literature review, and as explained earlier in Chapter 2, the experience of medication choice and family planning decision-making is an understudied area about which little is known. These decisions have big impact on the disease activity and patients' life choices. As I explained before in the previous chapters, DMDs are relatively new and as shown in our review, few studies have been done to assess the effect of switching a stable patient to a safe (but less effective DMD) before they try to conceive. The review also showed that the effect of switching DMDs on the disease activity depends on the baseline efficacy of these DMDs. Therefore, de-escalation increases the risk of relapses (see Chapter 4). With little known about the safety of the new DMDs during periods of conception, pregnancy and breastfeeding, and variable effects of switching, decisions around DMD choice and family plans gets very complex for both women with MS and their healthcare providers supporting these women during the experience. We do know the concerns these women have when deciding (such as effect of MS on fertility), but we still do not know how they take the decision and what can influence or sway their decisions.

We do know that switching treatment can impact the MS course, but we do not know how HCPs reach a decision to switch, how decisions generally are made from the HCP point of view, the challenges they face, and the needs for a better experience for both women with MS and their supporting HCPs.

It is very important to understand the process of choosing DMD in depth from the very beginning, and how family plans are incorporated throughout treatment journey.

Qualitative research is the method of choice to answer questions about experiences, meaning and perspective; enabling such an explorative study that holds a lot of subjectivity, disease variability, life stories variabilities, feelings and beliefs across participants (170). Qualitative research is a very powerful tool to voice out those feelings and beliefs then use them to understand the experience to help enhance it. In my study, both women with MS and their health care providers perspectives were studied to gain a full picture about the experience(171).

5.3. Interviews with women with MS (Why semi structured interviews?)

I chose to conduct a 30-40-minute online video-recorded semi-structured interview with women with MS (see Appendix 14 for interview questions) for a number of reasons. Firstly, women with MS have a range of disease activity and disability levels, so talking about their family planning and treatment experiences (which can be the source of emotions and pain) in focus groups could create tension and resentment and could also impact the amount of information disclosed by the women (self-censoring). Topic sensitivity and MS variability thus meant that the one-to-one interview format was preferable over the focus group method so as to provide the women with the privacy they needed (172). Secondly, exploring experiences through interviews allows for the collection of different accounts (stories) rather than the exploration of ideas and opinions with the purpose of reaching consensus through focus group discussions.

Semi-structured interviews offer a degree of structure while also allowing for some flexibility in the ordering of the questions and the word use. This was thus a suitable

method for this topic in order to give the patient the space to talk about their experiences and to provide some depth, while at the same time keeping the conversation on the right track so as to meet the study objectives (173-175). Online interviews were the only option due to COVID restrictions as these interviews took place between March and May 2021. The interviews were conducted in the form of video calls so the participants' body language and expressed emotions could be recorded, as these were highly reflective of their feelings about their experiences and the decisions they made. Lastly, participants were given the option of having their partners attend the interview to give those affected by brain fog and memory problems some help recalling events, or for emotional support, if needed, or even for technical troubleshooting purposes. The interviews were conducted using a secure UCL account via the Microsoft Teams platform.

5.4. Think Aloud sessions with women with MS (Why Think Aloud?)

After finishing the interview with each woman, I conducted a 15-minute Think Aloud session to evaluate the MS Trust decision aid tool provided on their website. The tool is used to help with DMD choices via a shopping-like experience. Filters are provided to reduce the number of options, and a comparison between up to three drugs is possible. I chose this tool because according to the MS Trust, MS nurses are increasingly encouraged to direct patients towards it to help with their DMD choices. I was able to reach the Head of information and Engagement at the MS Trust through the help of my supervisor, DC, who is one of the MS Trust trustees. This, together with the opportunity to materialise the results of this research through their tool update and amendment project, made the MS Trust tool the preferred choice over the National MS Society's one.

Think Aloud is a method of testing usability by asking the participant to speak their thoughts while being given a task to perform (3). While it can track the time needed to complete a task as well as some other statistics, this was not the aim of the research here. Rather than using the method for usability testing, the focus of this

research was instead to qualitatively evaluate the tool from the perspective of the tool's main users by examining the following:

- The women's general opinions of the tool (easy/hard, interface, pros/cons, etc.) and its suitability for their variable MS-related needs.

- How useful the tool is for choosing DMDs while considering family planning (this was assessed by the women's understanding and interpretations of the pregnancy recommendations of their chosen medication).

- The women's recommendations, stemming from their own needs and thoughts.

5.5. Interviews with HCPs (Why interviews?)

I conducted one-to-one 15–30-minute online video-recorded semi-structured interviews with different HCPs supporting MS patients (see Appendix 17 for the interview questions). The interview duration was a pragmatic choice, allowing enough time for all the questions to be asked but without taking up too much of the HCPs' time. The choice of interviews over focus groups was also a pragmatic solution for the HCPs' busy schedules. This allowed each HCP to choose a suitable time for their interview. Again, the interviews were conducted online in order to accommodate COVID restrictions and the interviews consisted of video calls so that the HCPs' body language could be observed. Likewise, the interviews were conducted using a secure UCL account via the Microsoft Teams platform.

5.6. Participants and the sampling of women with MS

Although MS affects both genders, the fact that it affects women in a bigger ratio is the one reason to direct the research to them. While male patients' treatments and family plans can be affected in some cases when using certain medications, conception tends to have more of an impact on female patients' health and treatment plans for longer periods of time (pre-conception, pregnancy, breastfeeding, and postpartum), whereas this would only have an effect on men with MS during pre-

conception and conception. These factors, together with the restrictive childbearing age of women, make their decisions even more difficult and complex.

5.6.1. Inclusion criteria

I used purposive sampling to allow me to examine the different experiences. The aim was to interview 10-15 **women** living with relapsing remitting multiple sclerosis **(RRMS)** from each of the three sub-groups or until data saturation and thematic saturation were reached.

Data saturation refers to the degree to which new data repeat what was expressed in previous data limiting the value of conducting more interviews during data collection. Thematic saturation unfolds during analysis when no more codes or themes are identified in new data. Both are integral parts of naturalistic qualitative inquiry (176-178). In my data, data saturation was reached after 25 interviews where no new data were identified. Interviews were stopped for a month to start preliminary thematic analysis. After creating a draft of codes and themes, six more interviews took place to ensure thematic saturation.

<u>The sub-groups were as follows:</u>

- Participants who have experienced pregnancy +/- breastfeeding, whether they are planning for more or not.

- Participants who have not started a family yet but wish to do so.

- Participants who have not started a family yet but are not considering it.

5.6.2. Exclusion criteria

Men with MS: As discussed earlier, although, male patients' experiences are important, the only major concern for men is the possible fetotoxicity caused by DMDs, and this can be managed during the period of pre-conception (if needed) (179). This thus does not give rise to the same complexity and challenges as for women. Accordingly, the focus of this research is the complications women with MS

experience in relation to their family plans, DMD choices, and management during periods of pregnancy, breastfeeding, and postpartum.

Progressive MS: Having a progressive type of MS can be severely disabling. As such, people living with it are unlikely to choose to get pregnant as the disabling effects of the disease makes it physically challenging to carry and care for a baby (34). That does not mean that women with progressive Ms do not start families, but it is very unlikely. In addition, as RRMS constitutes 85% of all MS cases, it makes sense for the research to focus on women with RRMS.

Women with RRMS who are currently pregnant or currently breastfeeding: This decision was taken to avoid creating any conflict or confusion, especially because participants were going to be asked to do a "Think Aloud" session about an online decision aid after their interview (see Chapter 10), which would give them the opportunity to read about the use of certain medications during pregnancy and breastfeeding. While the website provides a summary of the product characteristics (SPC) of each drug, it offers a very cautious approach to the use of DMDs that may contradict the doctor's advice given to participant, which is likely based on direct experience and practice.

5.7. Participants and the sampling of HCPs

A range of different HCPs are involved in the choice of DMDs, all of whom have different roles at different points in the process. MS consultants, MS pharmacists, and MS nurses are the main HCPs who support MS patients during treatment decisions. The aim was thus to speak to these three specialties, preferably working at different NHS trusts across the UK, in order to further explore how family planning fits into the process of care when helping women with MS choose DMDs, particularly from the perspective of their different professional roles and duties.

Snowball sampling (also known as chain referral sampling) is an effective sampling method when a sample is not easily accessible or not readily available (180). This was used to reach as many HCPs as possible in an effective way, as they are usually busy and were even busier during the pandemic. One of my PhD supervisors, who is a consultant neurologist, and a colleague of his who is an MS

consultant nurse, work at The National Hospital for Neurology and Neurosurgery, Queen Square, London, and used their connections and networks to spread the word about this research study.

I also tried to recruit via social media. Although research on this method is still growing, there is promising evidence of it is high efficacy compared to conventional methods, particularly for reaching hard-to-reach groups (181-183).

I contacted The Head of Research at the MS Society. While she offered to advertise the study in February's newsletter, that was very late in my PhD timeline.

I also tried to reach one pharmacist who had been particularly helpful in providing pregnancy planning and medication management advice to one of the MS patients in the study (she sent my email to him), but he did not reply.

My aim was to interview five participants from each specialty (five consultants, five MS nurses, and five pharmacists). This was an estimate based on the research question (exploring experience), data collection method (interviews), and analysis method (thematic analysis). The study also sought to sample from different areas across the UK to get a wider insight of what is available to women with MS.

5.8. Recruitment procedures for women with MS

Social Media

I started my recruitment through social media, specifically Twitter and Facebook. A descriptive advertisement for the study was prepared (see Appendix 8), approved by the UCL ethics committee, and disseminated via a Twitter account by mentioning different MS societies and support groups across the UK. They then responded by retweeting and spreading the advertisement. Facebook MS groups were also used, although this was challenging, because these groups are private and usually for people diagnosed with MS to share their experiences. Posts about things such as research adverts are thus often considered to be spam.

MS Trust

Another channel I used for the recruitment was the MS Trust charity, who boosted the post advertising the study through their social media accounts on multiple occasions.

A link to the application was provided in the advertisement. Through these two recruitment channels, 55 women registered for the interviews using the provided link. An email was sent to each eligible woman with the study information sheet, privacy notice, and a consent form for them to read, sign, and send back. Only two replied to this email and returned their signed consent forms. Despite another round of emails being sent as reminders and attempted calls to the women via the contact number they had given in the application form, no further women completed forms to participate in the study.

Research Recruiting Agency

Due to the specific inclusion criteria for this study, it was difficult to recruit without scanning potential participants to check their eligibility criteria. The multiple layers of procedures and paperwork also affected the number of participants cultivated from the first round of recruitment through social media, as people registered their interest by answering a few questions. This might have made some of the participants think that this was all that was needed from them. To make the recruitment process more efficient, I decided to use a research recruiting agency, SAROS, which is a recruitment agency approved by UCL. It was agreed that 40 women in total would be recruited according to the pre-discussed criteria. The agency took care of recruiting, scanning for eligibility, organising, booking interview time slots, and even getting the signed consent forms from participants through their secure password-protected file transfer system. This gave me the peace of mind to focus on the interviews, transcription, and analysis.

An online “one 4 sale” voucher of £25 was also sent via email or mail (depending on participant preference) to all the participants as a gesture of gratitude. This was handled by myself and not by the agency.

5.9. Recruitment procedures for HCPs

A short and concise summary about the study was prepared and sent together with the participant information sheet, local privacy notice, and informed consent sheet (seeAppendix 12,Appendix 13, andAppendix 15) via my UCL email to a few contacts of one of my supervisors (DC) and his colleague nurse.

HCPs who were interested in participating contacted me directly via email and an online interview date/time was arranged that suited both of us. Each participant was also asked after their interview to promote the study to their colleagues. This helped to secure two more interviews.

The consent forms were either signed electronically or verbally taken at the beginning of the interview.

5.10. Ethical approval for the studies

All the research materials (protocols, topic guides, participant information sheets, consent forms, and local privacy notices) were approved by the UCL Research Ethics Committee Office (See Appendix 6 Appendix 11,Appendix 12,Appendix 13,Appendix 14 and Appendix 15 Appendix 15 for the study materials).

The approval given by the UCL Research Ethics Committee Office (UCL Ethics Project ID Number: 18923/001, see Appendix 6) covered both the interviews with the women with MS and the interviews with the HCPs. This ethical approval was initially only granted for a period of one year. Due the COVID situation and the effect it had on HCPs specifically, as mentioned before, things moved at a slower pace and the interviews with the HCPs were not completed on time. It was therefore necessary to apply for an extension to the ethical approval for one more year, which was granted (see 0 for the extension confirmation).

5.11. Data governance for both studies

The recruitment was conducted using the secure UCL emailing system. Research documents were sent using it and signed consent forms are stored on the UCL secure “N” drive in a folder that can be accessed by myself only.

The video-recorded interviews were conducted using the UCL secure account via the Microsoft Teams platform. Microsoft Teams was chosen over Zoom, as per UCL research ethics advice. It explains that when using Teams, data are processed and saved in Microsoft Data Centres in Europe, which are compliant with GDPR. This is not the case when using Zoom, as data are stored in the United States servers before coming back to the UCL UK server. Thus, UCL advised the preference of using Microsoft Teams over Zoom(184, 185). Recorded interviews were saved on the Microsoft Stream UCL cloud for the period of transcription. The original videos were deleted from the cloud after the completion of the transcription and checks.

The transcripts were automatically generated by Microsoft Stream so there was no third party involved in the transcription process. The manual checking and de-identification of the transcripts was performed by me. The de-identified transcripts are kept on a secure UCL drive and will be kept there for 10 years, as agreed upon by the ethics committee, to allow for post-publication reflection.

The SAROS recruiting agency sent documents and consent forms directly to my UCL email in a password protected files using their secure folder sharing system. These shared folders get automatically deleted after 48 hours.

5.12. Patient and Public Involvement (PPI)

Public involvement is where members of the public (in this case women, with MS), contribute to different parts of the research (designing, developing research material, analysing, or disseminating). This has been found to improve the quality of research, provide different perspectives, and only research what really matters to this cohort, thereby using the resources more efficiently (186).

I ran two different rounds of PPI recruitment at different times during the study. Each round had its unique objective and the PPI for each one was recruited through different channels.

Round One

Purpose: To find out what MS patients prefer to be called in the context of the study. Since the study is done outside of the clinic, it made since to find something else other than “patient” to call the participants in the research.

Channel: I used my twitter account to ask whether MS patients like to be called an “MS warrior” or not. And if not, what else they would prefer to be called when outside of the MS clinic. The reason for asking about the term “MS Warrior” specifically, was that I saw some MS patients on Twitter referring to themselves as MS warriors in their profile bios. This made me curious as to whether this is a term that the majority prefers. Having mentioned multiple MS charity accounts and MS support groups accounts in the post to increase its reach, good insight was provided by 18 MS patients. Most of them preferred the term “people living with MS” over “MS warrior”, as the latter involves a win/lose situation which they would rather not have to face. They also reflected on using the term “warrior” as depicting being in a battle with MS as an enemy to fight, which was not preferred by most of the responders. A couple of people used the interesting term “MS manager”, elaborating that this makes more sense as they are managing their MS daily. However, this was not the predominant term used by the responders.

Result: I referred to the patients in the study as “women living with MS”.

Round Two

Purpose: To review and assess my methods, interview questions, and practicalities with a woman with MS.

Channel: social media (Twitter and Facebook) was again utilised here. A patient and public involvement request (see Appendix 9) was prepared and disseminated using the Twitter account. One woman applied for the position of the PPI representative (GW). The objectives of her position and expectations were explained to her via email.

Aim: To conduct two online video calls, the first of which was aimed at reviewing and discussing the methods used and the interview questions, while the second was aimed at reviewing the results and themes and seeking any possible different points of view or interpretations.

The PPI representative was paid in line with the INVOLVE rate (£ 25/hour).

Results:

The first meeting: This meeting had a duration of 60 minutes and was conducted using the Microsoft Teams secure platform. GW suggested sending the interview questions for the participants one day before the interview to help them better prepare and to allow them to recall important dates and events related to the questions. She did not like the idea of the participants' partners attending the interview, but this seemed very subjective to GW's case, so it was decided that it would be left as an option for the participants. She found all of the questions clear and reasonable, so she did not amend anything.

The second meeting: This meeting had a duration of 40 minutes and was conducted using the Microsoft Teams secure platform. GW received a document with a summary of the results to review and comment on (of both the interviews and the Think Aloud sessions). GW agreed with all of the results, finding them very valid and logical. She also related to many points through her own experience. She also gave similar opinions and recommendations regarding the MS Trust DA tool.

5.13. The interview process (women with MS)

Every interview started with some small talk about the participant's day or the weather in order to break the ice. Consent issues were also discussed briefly, especially the fact that the interview would be recorded. The participants were given the time to ask any questions they had about the documents they received earlier by email. The information about the data governance was explained again and the permission to start the video recording was given. A topic guide was used as a roadmap during the interview. This was developed at the beginning and was amended slightly down the line as some participants added some important parts to the picture that needed to be included, such as their experiences of a time they had the family planning discussion with their health team and the effect this had on their decisions. Questions were asked to address the following areas of the decision-making experience:

- Their diagnosis story and the effect it had on their life decisions, especially family planning.

- The time this topic was discussed with a health team and the effect this had on their decisions.

- Factors and aids which helped with their decisions.

- Challenges they faced during the process.

- In what ways they would improve their experience.

The Think Aloud sessions followed. A link to the MS Trust decision tool was sent to the participants, a brief explanation was given about what this tool is for (without explaining how to use it), and the task of using the tool to help them choose a medication was set. The women were given the chance to navigate and comment on any part of the tool freely. If they did not mention the pregnancy element, however, this was actively asked about. They were also asked if they had any recommendations about what could be changed to improve it.

At the end of these sessions, the participants were thanked for their time and asked for their help in spreading the word about the research. The thank you voucher was also sent to them via email or by post, depending on their preference.

5.14. The Think Aloud process (women with MS)

At the beginning of the session, the link to the tool was sent to participants, and they were asked to share their screens with me so that I could see their navigation process together with their facial expressions in the corner of the screen. The task they were set was to use the tool as if they are going to choose a DMD to start on soon or to switch to, and to voice any thoughts they had while browsing the tool. I also reassured that I was not part of the team who developed the tool, but rather part of the team amending it, thus giving them the space to provide their honest feedback without any pressure.

At the beginning of the session, after allowing for a couple of minutes for the women to look at the interface, they were asked to give their first impressions of the tool. Subsequently, the women were then allowed free reign to navigate the tool and to use it while commenting on the aspects that mattered the most to them (content,

interface, navigation). The sessions were video recorded and auto transcribed using Microsoft Stream, after which they were thematically analysed.

The themes were inductively identified from these sessions across all areas, except with the commentary on the pregnancy recommendations section within the tool, which they were actively asked about if they did not proactively mention it.

The only challenge faced here was the technical difficulties some women encountered, especially those who were not that familiar with Teams. These challenges were overcome by either having someone with them to help them with the technical issues or by providing help myself when needed.

5.15. The interview processes (HCPs)

Every interview started with some small talk about their day; this provided some insight into how busy or ready they were for the interview and helped to break the ice at the same time. The consent issues were discussed briefly, after which point the HCPs were given time to ask any questions, they had about the documents they had received earlier by email. The information about the data governance was explained again and the permission to start the video recording was given. A topic guide was used as a roadmap during the interview. This was developed at the beginning and was updated after the completion of the MS patients' interviews as these generated important ideas to be explored further with the HCPs, such as the right time to discuss family planning and the effect the patients' mindsets at the time of this discussion had on their decisions. Questions were asked to address the following areas of the decision-making experience:

- Current practices and the role of HCPs in supporting MS patients in choosing a DMD in relation to their family plans.

- Patients' concerns during the process and the questions they most frequently ask their HCPs.

- The information resources available to both HCPs and patients.

- The challenges faced by HCPs when supporting patients with such a decision, as well as any suggestions they had to achieve better practices.

At the end of each interview, the HCP were thanked for the time they had given to the study and were asked for their help in spreading the word about the research. The thank you voucher was then also sent to them via email.

5.16. Analysis

5.16.1. Analysis as undertaken for studies (interviews and Think Aloud)

The following steps summarise the procedure used to thematically analyse the data, using both Microsoft Word and Microsoft Excel software:

1. I read over all the transcripts while simultaneously listening to the recordings to check for any errors, to add punctuation, and to add notes about some of the important gestures or emotions shown by the participants that were not explicitly clear in the automated transcript. This helped to add to the context and story of what the participants were saying.

2. I selected two of the richest HCPs transcripts and six of the women with MS interview transcripts to be read again and to discuss the different possible codes and themes therein with my supervisors.

3. I ran a virtual data clinic in the department to look at one woman's transcript which was particularly rich in information together and to listen to any possible different interpretations by other people from different backgrounds.

4. The transcript coding was completed in two stages:

    - The initial coding was completed using Microsoft Word by highlighting the codes with marked colours and adding the code names and any further elaborations as a comment. At this point, the same two transcripts were sent to the supervisors after being coded for another discussion and for further amendments of the codes.

    After agreement on the codes to be used, I independently carried on coding the rest of the interviews using the same method.

    - The second phase consisted of transferring the codes into an Excel spreadsheet together with the quotations that illustrate them. This step helped

me to look at everything in one place and then to identify possible themes. It also facilitated the finding of specific quotations in a timely manner instead of having to go through the transcripts again.

5. The themes were then further developed by creating another Excel spreadsheet to demonstrate the themes together with the quotations illustrating them. This step allowed me to check all of the data in one place to make it easier to judge the accuracy of the themes and also for ease of extracting these quotations when writing.

6. The Codes and Themes spreadsheets were sent to my supervisors for review. This was followed by further discussions to finalise those themes.

7. I had wide areas and aspects to cover with my questions, where codes and themes under each area were all identified inductively. The in-depth analysis of accounts using biographical disruption theory was inductive too, but came at a later stage of the analysis because I did not expect or consider use of any theory earlier and so did not directly ask or probe about the impact of disease on identity and thus decision-making. However it was strong enough to be identified throughout the accounts. The use of this theory in particular was recommended by my supervisor Fiona Stevenson who is a medical sociologist. Following my initial inductive analysis, F.S. directed me to literature on biographical disruption which I found helpful to organise and frame the responses from women. As this theory was only identified after data collection was completed. I did not ask directly or probe about the impact of disease on identity and thus decision, however it was strong enough to be identified throughout the accounts.

5.17. Trustworthiness and rigour in methods

In a naturalistic paradigm, qualitative methods (design, data collection, and analysis) have certain criteria that need to be met in order to fulfil the requirements of trustworthiness and rigour, as with the positivist paradigm (quantitative methods) (187, 188). Four criteria were proposed by Lincoln and Guba to assess qualitative methods for trustworthiness: credibility, dependability, transferability, and

confirmability. This section will explain how each of these aspects was addressed and fulfilled in these studies (187).

5.17.1. Credibility

Credibility is defined by how confident a researcher is about the findings and how genuine these findings are. This resembles the concept of internal validity for quantitative research. In this research, credibility was ensured through the peer reviewing of the study's methods, data, coding, and theme generation by my supervisors and other colleagues in the department during the data clinic. This was achieved by sharing a few of the transcripts with them for them to independently code, whereafter meetings were held to discuss and finalise the codes and themes.

In my work, credibility was also ensured by debriefing with a PPI member at two different points of the research (before starting the interviews to discuss the study's methods and after the analysis to discuss the results).

5.17.2. Dependability

Dependability, or consistency, is the process that produces dependable findings and can be repeated by other researchers. This resembles the concept of reliability in quantitative research.

In my work, dependability was ensured through research transparency by providing detailed information about all of stages of the process in this chapter. The documentation of the transcripts, the different stages of coding, and the theme identification has also been kept for reference. All the data were utilised by including quotations from all the transcripts without any bias toward certain stories or participants. Only one transcript was excluded from the analysis because the woman interviewed seemed very ignorant about MS and its treatment and was quite young to be thinking about family planning or be interested in it. She also provided irrelevant answers to the point that I suspected that she maybe only participated in the study for the compensation, and that she might not have MS at all.

5.17.3. Transferability

Transferability is defined by how applicable these findings are for other populations, settings, and contexts, which is similar to the concept of generalisability or external validity in quantitative research.

In my work, I sought to explore a varied range of stories and contexts. The women were thus recruited from all different parts of the UK in order to have maximum range of experiences geographically that will reflect medical care in those different areas. In addition, detailed demographic data of the participants has been provided. A moderate sample size was planned during the recruitment phase (40 women) and data saturation was reached after interviewing 32 women, whereupon the interviews were stopped. The interviews with the HCPs may be less transferable, however, due to smaller sample size of 8 HCPs from 6 NHS centres across the UK, with no luck recruiting a HCP from Wales. These limitations are discussed in detail with reasoning, see Limitations from chapter 11.

5.17.4. Confirmability

Confirmability or neutrality is ensured by the researcher addressing the potential impact of their background on their findings. This corresponds to objectivity in quantitative research, although this cannot be achieved in qualitative research as there will always be a relationship between the inquirer (researcher) and the object (participant) (187-189). However, it is nonetheless important to make sure that a researcher's findings represent the participants' viewpoint and not their own.

In my work, confirmability was ensured through early checks being made to transcripts with my supervisors to make sure that my interviewing style was not leading or restrictive. The advice I received from them also helped me to make positive improvements to my style. Watching and re-watching the first few interviews also helped me to identify moments when I felt I was being too directive or even giving participants space to talk in a way that derailed the roadmap of the interview. This thus helped me to avoid these mistakes later on.

The analysis of the results was also undertaken within the supervisory team and was repeated several times to ensure its rigour. The supervisory team also had diverse professional backgrounds (a GP, a sociologist, a neurology consultant), and I am a

pharmacist, which helped to view the analysis from different aspects and angles. The following section will outline in-depth how I minimised the impact of my background on the findings.

5.17.4.1. Reflexivity

As a pharmacist holding a master's degree in clinical pharmacy who has worked both in hospital and university settings, I have both a clinical and academic pharmaceutical background. However, this expertise was not gained in the UK, which was both an advantage and a limitation at the same time. On the one hand, I had to learn about the UK health system from scratch which took time and effort. On the other hand, this helped to minimise any possible bias that could occur if my background was in the NHS.

Before starting the interviews with the HCPs, I made sure to attend the specialised MS clinics run by trust A as an observer to gain a better understanding of the workflow, highlight areas that need to be explored more, and refine my interview questions to get the most out of these interviews. While this required extra time and effort, this was an important step for preparing myself for the interviews. It was also necessary to ask for more details during the interviews, which ultimately provided the data with more depth.

During my interviews with women with MS, I presented myself as a "researcher" and concealed my clinical pharmaceutical identity to avoid getting asked clinical questions and for advice by the participants, which I would not be allowed to answer due to my status as a "PhD student" in the UK. As a clinician, it was difficult in some instances to see women holding onto outdated ideas about pregnancy with MS or about treatments which impact their family plans and not intervene or give advice. However, in such cases, I gently encouraged them to refer back to their HCP to enquire more about certain topics and to read more around the issue. There were no occasions where women needed urgent intervention that would have required contacting their health teams.

During my interviews with the HCPs, I introduced myself as an academic with a clinical pharmacy background to encourage them to talk more freely about technical and specific medicinal issues if they wanted. However, I also made sure to tell them

that I had never practised in the UK in order to provide them with a judgement-free space to talk openly.

Likewise, I do not believe that my background derailed the analysis of the data in any way as my background is not within the NHS, so it was objective and reflective of what had been said in the interviews by the participants. The only impact I would say of my role is that with my background of clinical pharmacist capabilities and drug knowledge, I was surprised that the pharmacist's role in this DMD/family planning decision making experience was more of a non-patient facing role. I believe that a clinical specialised pharmacist has the potential to have a very important patient facing role in the patient journey of the DMD/family planning decision-making experience, which is still under-utilised. This is examined in detail in the discussion chapter (see Chapter 11). However, this did not impact the study methods or results by any means.

Chapter 6. Overview of the treatment decision-making experience in the context of family planning for women with Multiple Sclerosis in the UK: an explorative qualitative study

6.1. Introduction

The systematic review in Chapter 4 showed the paucity of information available about the effect of switching medications on women with stable MS trying to conceive. Switching could be difficult for those de-escalating treatment as the clinical effect of switching is expected to match the medication's headline efficacy, meaning that a switch from a higher efficacy to a lower efficacy drug will likely result in less control over disease activity. While switching can be inevitable sometimes, for instance in the case of drug ineffectiveness or intolerable side effects, in the case of family planning this could be reduced by having a good treatment plan in place from the start that takes family planning into consideration. This would reduce the need for women with MS to switch DMDs when stable in order to conceive. This study explores the real-world experiences of women with MS when choosing DMDs in the context of family planning. As part of this study, I interviewed women with MS to understand the context in which these treatment decisions were made (either starting, switching, or stopping a certain treatment, as well as any other reproductive decisions, as explained in Chapter 1), factors which impacted their decisions, their challenges and needs, and finally the decision-making process itself (how these women made these decisions, what influenced, aided, or swayed their decisions, and the impact of their state of mind when making these decisions on their experience).

6.2. Objectives

In order to support the overarching aim of improving the treatment/family planning decision-making process, the objectives of this study were as follows:

1- To explore the current experiences women with MS have had during their DMD choice/family planning decision-making processes.

2- To identify the sources of the basic knowledge women living with MS have specifically about pregnancy and breastfeeding with MS, the effects these periods have on their disease courses and treatment plans, and vice versa.

3- To explore their concerns, fears, and thoughts about choosing a DMD and considering their reproductive plans.
4- To describe their needs in order to help them make decisions about their treatments and family plans.
5- To explore the impact their state of mind towards their illness had on their decisions.

6.3. Results

In total, I interviewed 32 women. After interviewing 25 women, I had reached data saturation, meaning that there were no new information or data demonstrated during interviews. I stopped interviewing for a month, and started thematic analysis of the data, and once agreed on a draft of codes and themes, I resumed interviews to confirm thematic saturation. Six more interviews were confirming reaching thematic saturation and interviews were stopped. As I previously mentioned, one transcript was excluded from the analysis because the woman interviewed provided irrelevant answers to the point that I suspected that she maybe only participated in the study for the compensation, and that she might not have MS at all. This is possible as the participants were recruited by the research agency. Consequently, only 31 transcripts were analysed.

Of these participants, 15 women had experienced pregnancy and breastfeeding, of which three women wanted more children and 12 women felt that their family was complete. In comparison, 16 women did not have children, with nine reporting that they were planning to do so. Lastly, seven women reported that they did not want to have children. Further details about the study's sampling and recruitment process are available in Chapter 5 (on methodology).

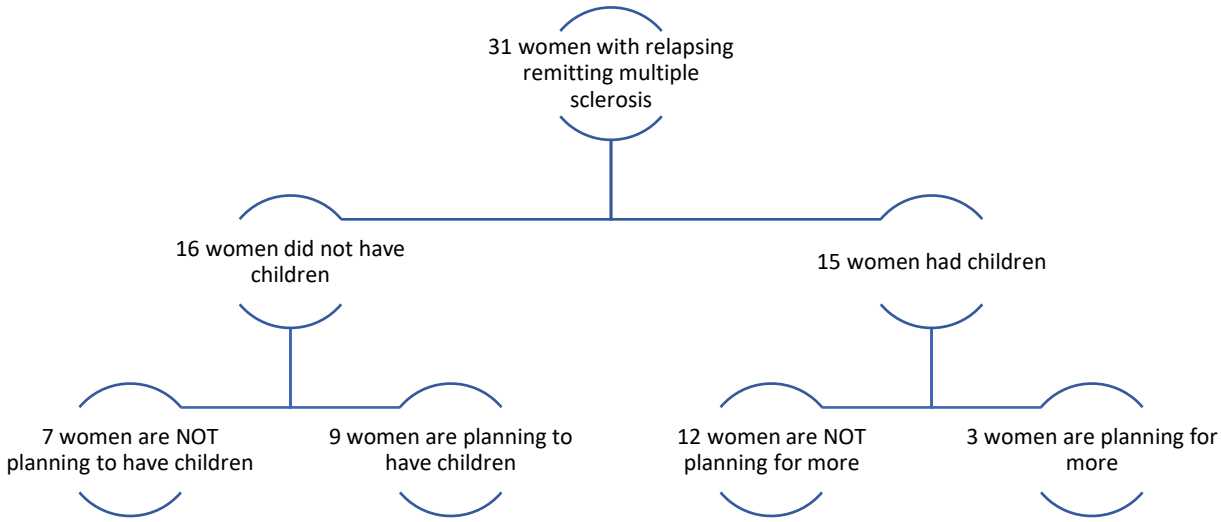

Figure 4 The subgroups of women interviewed, categorized according to their current and future family planning.

6.3.1. Demographics

The study recruited 31 women with Relapsing Remitting MS who were diagnosed at a mean age of 30. Most of participants were still employed full-time (15 women), while the rest either worked part-time (11 women) or were self-employed (two women). Only four of the women were homemakers. At the time of interviews, 17 women had partners while the rest were single. The majority (25/31) had used and/or were still using a DMD. While the sample was recruited from different areas across the UK, most of the participants were of a white British ethnicity (26/31), although some ethnic minorities were also included (five women). All women spoke English as their first language except three for whom English was not their first language but were able to convey their ideas clearly during interviews. Specific data about the participants' locations and ethnicities were not collected from the patients during recruitment. However, these data were revealed during interviews.

Table 6. Participant demographics

Age at the time	Range	24-49
of interview	Mean	37
Age at diagnosis	Range	16-42
	Mean	30
Occupation	Full-time	15/31
	Part-time	11/31
	Self-employed	2/31
	Homemaker	4/31
	Medical	3/27
	Non-medical	24/27
	Child-related*	7/27
	Non-child-related.	20/27
Social status	Single	14/31
	With partner	17/31
Number of children	0 none	15/31
	1 child	10/31
	2 children	5/31

	3 children	1/31
DMD use	Yes	25/31
	No	6/31
Ethnicity	White British	26/31
	Other	5/31

*A child-related job is any job that involves any relationship with children. In the sample, this included teaching, midwifery, child protection services, and child minding.

6.3.2. Themes

During the interviews, the complex process faced by the women of choosing a DMD in the context of family planning was evident. These concerns branched into several smaller aspects. Themes and subthemes were inductively identified. The following are the main themes:

1- Factors affecting family plans: any factor that the women talked about and considered when planning their family.
2- Factors affecting DMD choice: any aspects the women considered a high priority when choosing their medication.
3- Decision process: how the women experienced the holistic decision-making process, e.g., Did they make a decision and how did they feel about it? How much were the women involved in this decision? How proactive were these decisions in taking future plans into account?
4- Decision aids, influences, and information resources: any kind of help, aid, tool, or influence that had a major effect on the women's decisions.
5- Mental health and their state of mind during the process: the effect their mental health and state of mind had on the decision-making process, as well as the implications this had on their decisions.
6- Changes in family plans: any changes made to family plans due to the MS diagnosis and treatment.

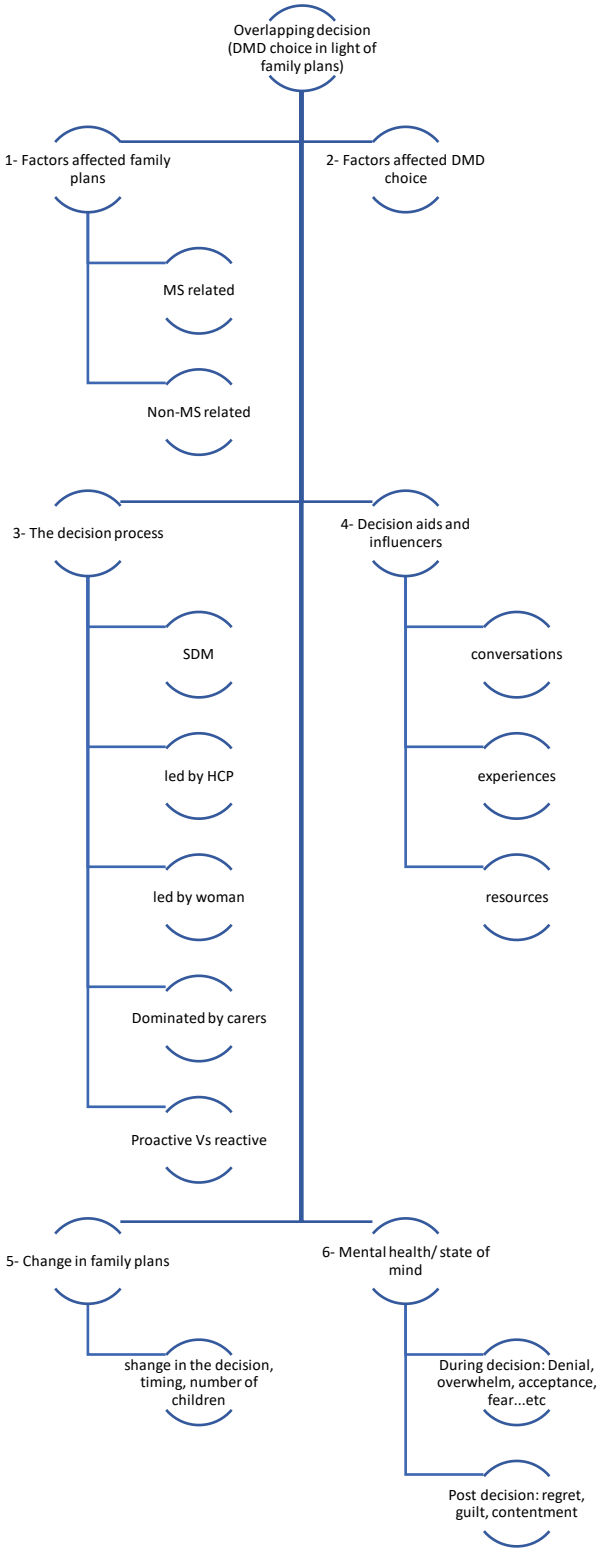

Figure 5 Theme mapping showing the themes and sub-themes of the overlapping decisions made in relation to treatment choices and family planning.

Figure 1 **KEY - DMD: disease modifying drugs; MS: multiple sclerosis; SDM: shared decision making; HCP: healthcare practitioner.**

6.3.2.1. Factors affecting family plans.

Before looking at our focus which is the complexity of the decision in relation to DMD choice and family plans, it is important to address the factors that women with MS mentioned that affected both aspects separately (family planning and DMD choices). In the interviews, the women talked about factors both related to and not related to MS which affected their final family planning decisions.

6.3.2.1.1. Non-MS-related factors affecting family plans.

Table 7. Descriptive statistics of the women's ages at the point of diagnosis (data is normally distributed)

	Min	Max	Mean	Median	Mode	Standard deviation
Age at diagnosis	16	44	30.40	30	30	6.61

Age

By 2019, the average age at which a woman from the general population has her first child had risen to 29 years old in England and Wales (190). Women usually receive their MS diagnosis in their late twenties to mid-thirties (191), a period in which, according to the previous survey, many women have not yet started their families. This study's sample had normally distributed data for age at diagnosis, with a mean of 30 years and a standard deviation of 6.61 years. Only four women (12.5%) had started their families before diagnosis, whereas 28 women (87.5%) had received their diagnosis before they started their families, which is in line with the general population numbers.

These numbers also highlight how age is one of the major factors that women have concerns about when deciding about motherhood, especially for women with MS who have already hit their mid-thirties, as expressed in the interviews by the women in this study. Participant (P) 11, for example, a 36-year-old divorced woman who did not have children at the time of the interview, raised her concerns about her age:

P11: “I am 36 and that feels a bit iffy time wise."

Indeed, the interviews suggest that age is always part of the equation when it comes to women with MS making a decision about family planning. It was seen as being a major factor for a number of different reasons. For instance, the women discussed the effects of ageing on both their fertility and parenting abilities, as both get harder down the line, not to mention the effect age has on MS symptoms and in relation to a drop in energy levels. When DMDs was discussed, the women talked about the implications that the length of a treatment and washout periods could have for the time they have left in their fertility window. Their decisions were also complicated by lots of other factors such as MS activity and their current relationship status. P3, who had to put family plans on hold to start treatment, linked her age to her DMD choice, describing the decision as frightening due to her age:

P3: "it's quite frightening when I'm 35 to make that choice to put that [having a second child] on hold”

Relationship challenges (not related to the diagnosis with MS)

The women also reported that relationship issues such as non-stable relationships, short-term relationships, break ups and divorces, same-sex relationship challenges, and complicated long-distance relationships as a factor which impacted their family plans, irrespective of having MS.

P4, a 47-year-old woman who was not in a long-term relationship until recently, talked about this as a reason for not having children:

P4: “a few years ago I kind of concluded it was never going to happen for me anyway [becoming a mother] because I wasn’t in a long-term relationship”

Similarly, P32 expressed how pregnancy is something that would need to be a planned process for her anyway, irrespective of having MS, due to her sexual orientation:

P32: “I’m also gay… so if I were to decide to get pregnant anyway, it would be a whole procedure”

Other health conditions and priorities

Some of the women also had to make a decision based on other priorities. The women interviewed who live with other physical or mental health conditions, for example, or those with a child or a husband with special needs, disability, or mental illness, stated that they found it difficult to grow their families due to this. P2 is a 35-year-old woman who has a six-year-old child living with ADHD and a husband who has a disability. When choosing her treatment plan and making a decision about her family plans, she decided, together with her husband, not to have more children for a number of reasons, including prioritising her health, in order to be able to take care of her child, husband, and, of course, herself.

P2: "I worry that I could ever relapse after birth, so that is something that can happen… also having a 6-year-old. He's also got ADHD";

"he's [her husband] classed as disabled himself"

Financial commitments

Factors such as not having a family house or focusing on building a career were also raised in the interviews as issues which affected their decisions to not start a family. P5, a 25-year-old woman who talked about her decision to start a family or treatment first, decided to start treatment first because she and her partner had not bought a house yet and that was their current priority:

P5: "in our relationship we want to move house and then have a baby and I think because we're not there yet, we've both sort of thought. Let's start the treatment now."

Desire to become a mother

This was a factor for many of the women interviewed, those who had children and those who wanted to become a mother at some point in their lives. However, not all

of them were able to materialise this wish, as some reported being childless either by choice or due to circumstances.

Some of the women decided to start a family despite having MS and irrespective of their MS activity and the consequences of this decision. P16 had very active MS and was on Tysabri when it was still new and only a few people were taking it, and still decided to disregard her doctor's advice to not get pregnant. She reported that she decided to stop all of her treatments and try to conceive because she wanted to become a mother:

P16: "I ignored him [her consultant] because I wanted to have a baby.";

"I think when you want to have a baby you want to have a baby."

Some of the women even reported having such a strong desire to become mothers that they would consider having a child without having a partner, whether through sperm banks if necessary, like P11, or with a partner who was not going to be around due to a complicated long-distance relationship, as with P22. P11 discussed having a baby without the support of a partner, even though this would be difficult to manage alongside her MS:

P11: "If I wasn't with someone, I potentially would still try and have start family like on my own.";

"if my MS doesn't settle down (A) Is it a good idea to kind of put more responsibility on myself and like bring another person to the equation? and then (B) if I'm on my own without a partner and my MS is really active like is that just like a crazy thing to do?"

On the other hand, some of the women chose not to have children for reasons unrelated to their MS. Some of the women talked about how they had never viewed themselves as mothers, while others considered it would be very demanding to have children themselves and instead were interested in fostering and helping their spouses or other family members with their children. While MS was one of their considerations when choosing to remain childless, it was not always presented as

the main reason for them. P14, a 44-year-old woman who was diagnosed at the age of 42, decided not to have children before her diagnosis:

P14: "I was never the kind of girl that sort of dreams of being a mother".

Others reported wanting to have children but were unable to due to various life circumstances such as reaching the age of menopause, not having long-term relationships, having very active MS, and having financial problems. P22, a 42-year-old woman, was childless despite her desire to have children due to not having a stable long-term relationship, in addition to her role as a carer for both of her parents, who struggled with cancer for a long time before passing away last year:

P22: "my brain probably put that on the back burner in this sort of sense of it's just too much, too difficult to even contemplate that…. Which feels like I missed opportunity?"

6.3.2.1.2. MS related factors affecting family plans.

Current MS activity

Some of the women also reported that they felt that they had to choose between their health and motherhood, whether this was due to their MS currently being unstable and struggling with relapses, or a fear of developing further relapses due to stopping treatment to conceive, or even during postpartum. P12, for example, a 38-year-old woman with active MS, was not stable and was on Tysabri when she started to think about starting a family. Her consultant advised her to give Tysabri time to work and control the disease before trying to conceive:

P12: "we did talk about it, but he [the consultant] said just get on top of things, give Tysabri chance to work"

MS Stability

On the other hand, reaching MS stability also reportedly affected a number of the women interviewed in different ways. While it made some of them confident enough to try to conceive as they felt better and more comfortable in their health and abilities, it made others feel concerned about risking the stability they had gained in relation to their MS for the chance to conceive:

P10: "I've been so well on Rebif. It kept me unbelievably well...I was quite happy and felt really healthy and well at the time. So, I thought this is the time to do it [try to conceive], so came off it."

P31: "do I really want to rock the boat by coming off this [coming off DMDs]?"

Fear of future progression and disability

This was the most frequent factor reported in the interviews. The fears some of the women discussed about the effect of family plans on their MS was not necessarily medically accurate, as some of them still saw pregnancy as an extra stress on their bodies, thus believing that this stress would eventually cause a relapse. These fears thus ran contrary to the fact that MS activity actually tends to decrease during pregnancy (38). Indeed, those who had a good understanding of MS were more fearful about the postpartum period, which is considered a riskier time for women with MS. They reported that the risk of relapsing and suffering from disability during the first three months postpartum can be overwhelming, especially when trying to adjust to their new life as a mother to a new-born. These doubts pushed some of the women to decide not to have children and to instead prioritise their own health and/or their current children and family, if they had them. P3, a 35-year-old woman with one child, wanted more children but decided to put trying for another baby on hold to start treatment, a decision that was driven by the fear of a postpartum relapse whilst having a new-born:

P3: “My husband says, what? What use am I? If I'm really poorly or with no energy or having a relapse with the new baby? Life is going to be so difficult."

Effect of the condition on their ability to be a parent

Women with active MS tend to be very mindful about their physical and cognitive abilities that affected their daily lives. Energy levels, fatigue, and brain fog thus played a big role in the decisions of some of the women. They questioned their ability to become a mother, which is a very demanding 24-hour job that requires total mental and physical focus. Some of the women who had limited energy levels thus chose to avoid this energy expenditure and instead sought to direct their energy towards other priorities:

P14: “I have limited energy and that’s always been the case and so I couldn't… I couldn’t spare the resource to be a parent.”

Safety Concerns

Some women also reported that they had safety concerns when it comes to their physical abilities. They expressed how scary it would be to suddenly lose their grip or fall when holding the baby. P1, a 28-year-old woman who had not started a family yet but wants to have children, expressed doubts about her abilities and concerns for the safety of her baby:

P1: “if I ever had a child and suddenly that symptom came back…. You know if you like carrying a baby or something like that and then all of a sudden, my legs buckled.”

Burden of care

Some of the women also expressed that they hated the idea of burdening their partners and children with their care, and so decided not to have more children or even not to have children at all. For example, P22, a 42-year-old single woman who

has no children and works at children's services, reflected upon her career and questioned the fairness of having children as carers:

P22: "is it even fair bringing a child? Into a world, when I might end up having them caring for me?"

In contrast, this factor was a strong motivator for others interviewed to have more children to split the burden of caring for the mother between siblings, instead of one child having to take on all of the responsibility. P28, a 42-year-old woman who already had a daughter before her diagnosis, decided to have her second child after her MS diagnosis in order to split the burden of care between two children instead of putting the entire burden onto only one child:

P28: "having a daughter already made me more determined to have a second... I didn't want her to have to look after me all by herself."

Similarly, P4 looked at having children as creating a potential support network. As a 47-year-old woman who does not have any children or siblings (although she did recently get into a long-term relationship), and has parents who are old and sick, she expressed that although she does not desperately feel the need to become a mother, she sometimes feels the need to have them as a support system for herself when she needs care in the future. She described her worries as "selfish":

P4: "my worries by MS are more probably selfish, really. It was a bit like, well, there's nobody to look after me as I get older."

Relationships challenges (due to MS diagnosis)

Many of the women discussed the full support they had received from their partners when diagnosed. This included their care and understanding of the impact the disease has on their life decisions, especially family plans and medication choice. In contrast, an MS diagnosis was reported to have put some relationships to the test,

and some even fell apart after diagnosis for a number of reasons. The overwhelming new demands of their partner's health was reported as a key factor that played a role in this in some of the women's stories. For instance, P24 reported that while she initially had her partner's support at the beginning, with him taking her to the appointments, filling in her forms, and listening to her, he eventually got tired and overwhelmed, so she had to arrange to be picked up by her parents from the hospital because he was spending time with his friends and refused to come home when she received her diagnosis, at the time she needed him the most:

P24: "I knew it was getting too much for him and basically, I rang my parents who lived away, to come and collect me and take me home because I knew that he'd had enough of supporting me. It was too much for him."

Fear of disability and the future implications of the disease on the marriage was another concern that caused the partner of P21 (who was 20 then) to leave her when he knew about the possibility of her being disabled in the future:

P21: "the thought that I was just going to end up in a wheelchair in a couple years…. so, my partner was a bit….[she showed a facial expression reflecting her partner's shock]."

Similarly, the women interviewed who were single professed their doubts about the idea of finding the right partner (especially after an experience of a breakup after diagnosis) who will firstly accept their condition, and secondly be serious enough to start a family. P21, who is currently single, described telling any prospective partner about MS as a "confession", especially after her breakup experience because of the diagnosis:

P21: "I suppose…. for me it became almost like a burden of this big confession. If I went into a new relationship."

Likewise, MS also affected P19's self-confidence in her relationship and the way she feels within herself, to the extent that she was the one who initiated the breakup with her partner after her diagnosis:

P19: "if I'm not feeling good within myself, how can I offer… you know, myself to anybody else";

"I was the one who initiated the breakup"

Passing MS on to offspring

Although MS is not considered a hereditary condition, families with MS have a slightly higher risk than the general population of having children who develop MS (17, 192). Even though the women were aware of this, it was still reported as a source of concern when deciding whether to have a family. Some of the women decided to have children despite the slight risk, but talked about how guilty they would feel if any of their children gets it. P28, a woman who had two children, expressed her fear of any of her children getting MS and how guilty she would feel if that happened:

P28: "I will feel very guilty if either of them actually has it."

This was a notable that the decision to have children was harder for those who have other family member with MS. P1 and P32 are both daughters of women with MS. The fact that they have inherited their mothers' condition thus made them doubtful about the idea of having children. Both women have lived the experience of having these small odds directly apply to them. They thus found it difficult to reconcile themselves with the statistics, probabilities, and numbers on MS when they themselves are examples of the possibility of genetic inheritance with MS.

P1: "it's not hereditary… but my mom has MS, so for me it's like a big thing of all… God, I wouldn't want to pass it on again to like somebody else … a child!"

MS stigma

MS stigma is one of the more interesting factors reported by some of the women in terms of affecting their family plans. Some of the women were afraid of being

stigmatised for thinking about pregnancy and children while being poorly. Fear of family and friends' judgment was thus a challenge. P21, for example, recounted that a cousin with MS was judged by her family when she got pregnant twice despite it negatively affecting her health:

P21: "the response from the family was, you know she is stupid for getting pregnant again"

Many of the women also referred to another aspect of the MS stigma, which is association of MS with wheelchair use. This anticipation of future disability thus made them think again about their family plans. P9, for instance, talked about how the thought of her ending up in a wheelchair dominated her concerns and thus affected her family plans:

P9: "Do we need to think about it now [having children]? Generally, I was paranoid that I'm in a few years' time I was going to be in a wheelchair."

Starting DMDs

Deciding to start a family when living with a chronic disabling condition like MS is already difficult in itself, as explained by the women interviewed. Adding DMDs to the equation makes this even more difficult as these medications are relatively new, meaning that there is not enough safety data yet about most of the higher efficacy ones during pregnancy and breastfeeding. This does not even account for other aspects of medication management which also need to be considered, such as the time needed for them to start exerting an effect on the body, the treatment duration (long vs induction cycle treatment) needed to achieve disease stability, the wash-out period needed before starting to try to conceive, the rebound effect when stopping some medications, and the time needed to start another medication if switching. All of these aspects combined with the MS activity itself and patients' life circumstances make these overlapping decisions quite difficult to manage without decision aids that encourage the shared decision-making approach.

The interviews thus sought to gain further insight into the women's experiences of having to choose a medication and accordingly plan or change a current family plan to suit their new health conditions and life changes. Some of the women chose to go with their instinct and start a family first despite the risks, as with P16 (see 'desire to become a mother' theme), while others chose to start treatment first and postponed pregnancy until reaching a level of MS stability that allows them to stop their treatment in order to conceive, as with P12 (see 'MS activity' theme).

In other instances, some of the women accidently got pregnant and had to deal with the stress and fear of having a high-risk pregnancy, as with P20, a 39-year-old lady who fell pregnant while using a DMD. She spoke about the stress she lived with knowing that her baby had been exposed to an unsafe treatment for three weeks:

> *P20: "stressing cause like I probably took it for about 2-3 weeks, I found out that I was pregnant, and I was worrying if it would affect the baby"*

Conversely, others had to continue their medications during their pregnancies after having weighed up the risks and benefits of this with their health team, knowing that it is never absolutely safe to be on a medication while pregnant. P11, who planned to start Tysabri to control her active MS and to conceive while using it, talked about the idea of taking medication during pregnancy and her doubts over whether it is "safe":

> *P11: "with the Tysabri. Although you can take it when you're pregnant. So, it's a bit like is it really, OK? Isn't it just better not to be taking anything?"*

This overlap between these two big decisions (starting treatment and starting a family) is the focus of this thesis. It seeks to demonstrate the complexity of the multiple interacting factors presented in these stories, the variability in the weight of the factors across these stories, the decision fluidity (in that women might decide something now and change their decisions soon after), and the importance of considering the high rate of unplanned pregnancies (45% in Britain) when choosing any DMD.

6.3.2.2. Factors affecting DMD choice

When it came to choosing a DMD, the women reported a number of different factors which influenced the decisions they made. Efficacy was one of the most frequently mentioned and important aspects according to the women interviewed, as was the weighing up of a DMD's efficacy against its side effect profile. Some of the women stated that they preferred the drug that has a higher efficacy in controlling their condition where possible, while others were hesitant to use them after reading more about their side effect profiles. For example, one of the serious side effects of using medications such as natalizumab, even if rare, is Progressive Multifocal Leukoencephalopathy (PML) (161). This kind of serious side effect pushed some of the women away from using medications such as this despite their efficacy.

Fitting the DMD into their existing lifestyle was also important to the women interviewed. The ease of a DMD's administration, the frequency of taking it, the hospital visits needed for either administration or monitoring purposes, and how manageable it is, all affected their decisions.

The method of administration certainly influenced some of the women in their decisions. The women with a needle phobia, for example, looked for the oral option, while others with adherence issues looked for a less frequently administered DMD. In fact, these factors not only affected their decisions when choosing a medication, but also affected their decisions in relation to switching treatments, which comes with its own risks.

Of course, family planning was one of the most-considered factors when choosing or switching DMDs for those planning for a pregnancy, in addition to all of the other factors previously mentioned.

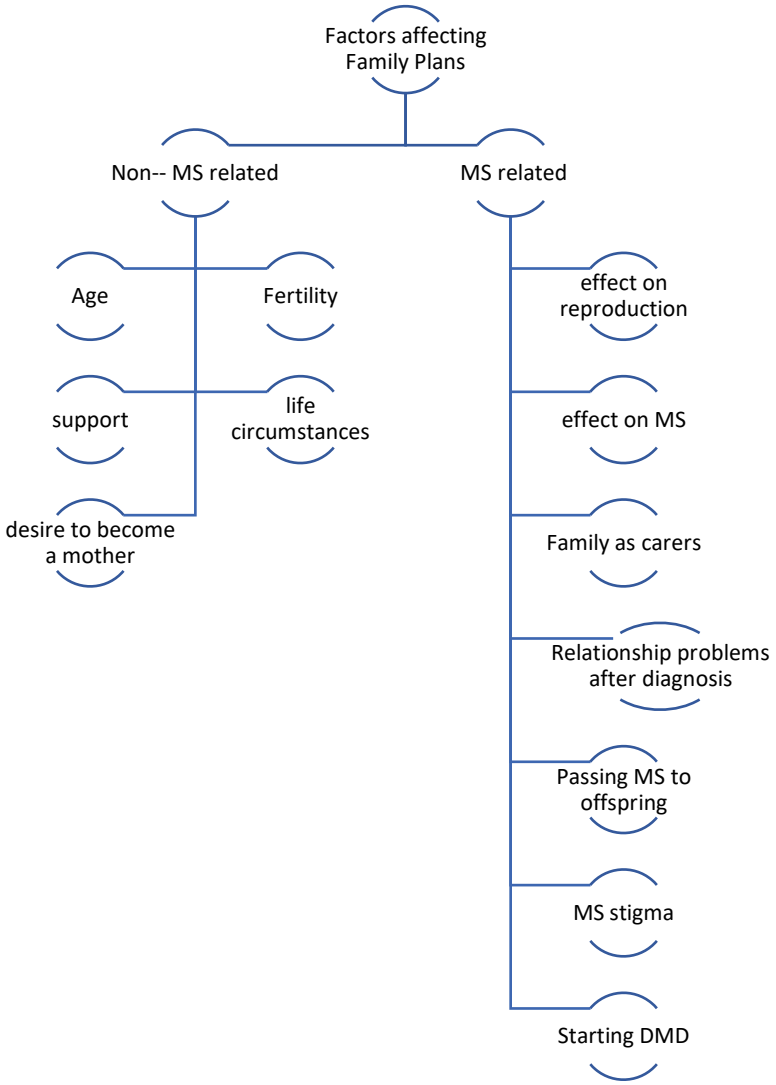

Figure 6 The mapping out of the sub-themes under the "factors affecting family plans" theme.

6.3.2.3. The Holistic Decision-Making Process

When discussing the ways in which they approached the decision-making process itself, the women described a number of different approaches during their interviews. The first section below will look at the extent to which the women were involved in the decision-making process, and the second section will reflect on the extent to which the participants together with their HCPs accounted for the future when choosing a treatment.

When examining the **extent of the women's involvement** in the decisions made, four main approaches were identified:

1- **Shared Decision Making (SDM)**: Some of the women reported how strategically they had planned their treatment options and timelines in line with their family plans with the help of their HCP. These women had a good relationship with their healthcare team due to mutual trust and understanding, as well as the women being empowered by resources and education on MS. This kind of rapport led to the reaching of a shared decision which combined HCP expertise with the women's own preferences. P10, for example, a 37-year-old married woman who has one child, shared a good example of this shared decision-making process. She noted how treatment and the reaching of a level of stability with her MS helped her to feel confident about planning a pregnancy with her husband when it was the right time for them as a couple. She also noted that she referred to her consultant to help her with her a treatment/conception plan and a risk/benefit weighting:

P10: "well we [herself and her husband] had decided that it was time to have a family… so I went to speak to my doctor, and he had said OK will stop Rebif now. He did speak to me about; you know the possibilities of there being a relapse, but you know, we outweighed it."

It should of course be noted that this is an optimal scenario which is not the case for every woman.

2- **The women leading the decision-making process:** Some of the women shared that they preferred to and felt more comfortable with taking the lead with their treatment and family planning decisions. For P14, this was a result of mistrust in healthcare systems because of a past medical error. This led her to exclude HCPs from the decision-making process entirely:

P14: "I had a bad relationship with ...medical institutions"

Another example of this was given by P10, who after receiving conflicting advice from a consultant and a nurse in relation to whether breastfeeding

would act as a protection from postpartum relapses, chose to follow the nurse's advice to breastfeed because this is what she wanted to do anyway (confirmation bias):

P10: "I didn't say, well you said this, and you said that I just thought well, I'm going to make my mind up anyway and I had wanted to breastfeed."

3- **HCPs leading the decision-making process:** Conversely, some of the women found the shared decision-making approach a bit overwhelming and confusing and felt more comfortable leaving this to their HCP. They expressed how difficult and daunting this process was for them, especially with multiple different options being offered to them, each with different aspects to consider:

P21: "I wasn't aware that you would make your own choice on medication, I found that really weird."

In some cases, women with higher disease activity also experienced HCPs taking the lead in the way of treatment and family planning decisions in order to control the disease activity as a priority, unless the women insisted that they wanted to prioritise family planning. For example, P1 was a 28-year-old single woman who was diagnosed with MS after a major relapse where she could not walk and lost all feeling in areas of her body, with two long spinal lesions found in an MRI scan. As a result of this, P1 was not offered any options by her HCP as her very active MS needed to be controlled urgently:

P1: "because I had such a severe relapse. They put me straight onto Ocrevus, I wasn't allowed to take any other kind of medication"

4- **Carers dominating the decision-making process:** Some of the women had a partner/carer during the decision-making process who largely dictated their treatment or family planning decisions. P27 was a 27-year-old woman who was diagnosed at the age of 16. Her mother refused to start treatment in order to try homoeopathic remedies first. P27 ended up with more MS activity, shown as

three new lesions in her MRI scan, in less than a year, which finally made her mother change her mind, especially after the hospital admission of the homeopathic therapist himself. Although the mother did not directly make any decisions for her daughter in the way of family planning, her rejection of any treatment in the beginning and the patient's health deterioration as a result of this, could have affected P27's family planning decisions later on as a result.

P27: "my mother wanted to start with like more homoeopathic remedies"

Similarly, other stories told in the interviews also revealed dominating partners who took the decision against their wives' wishes to not have more children. P3, a 35-year-old woman who had one child before diagnosis and was trying for a second with multiple miscarriages, was swayed by her husband's decision that she should start treatment to keep her healthy for her family, despite her wishes to have more children:

P3: "my husband has to weigh up, we want another child, but my health…"; "I'm finding it harder cause I want another one [child]."

When looking at the extent to which the participants and their HCPs accounted for the future when choosing a treatment, two main approaches were evident: proactive and reactive. It is notable that in some of the cases, the women did not receive a proactive educational approach about their treatment and family planning options during the decision-making process, which then had implications for their plans. These women mainly reported being asked by their HCPs if they wanted to start a family and if they answered "no", no further questions were asked about their reasons for this answer or the proposed timeline for such a plan in the future. In the interviews, a number of the women revealed that there was a hidden story behind their refusal to have children, such as being given outdated advice many years ago by their HCP upon diagnosis that they should refrain from pregnancy, fear generated by negative stories read online or heard from other people with MS, or simply being ignorant of the services available to them and thinking about the issue of family planning as a non-medical matter that a HCP could not help with. It is important to

note that this was not the case for the majority of the women. However, it does seem that a few of the women interviewed made decisions that did not match their wishes due to a lack of proactivity from both the women and/or their HCPs. P21 was a 42-year-old woman who was diagnosed with MS 20 years ago. When talking about her diagnosis consultation, she expressed how her consultant's warning about pregnancy was still ringing in her head. She thus never asked about family planning in relation to her MS despite her wish to become a mother. When asked about her feelings toward her decision she expressed her sadness and regret:

P21: "he said DON'T HAVE CHILDREN!";

"That always stuck in my head from the age of 20";

"regrets along the way";

"sad that it didn't happen"

On the other hand, P17 did not know that planning a family is something that she could get help and advice about from her HCP, and noted that she would not want to "bother" her health team with this:

P17: "if I've got a problem with my MS and I feel that's why I go to the nurse, but things like that [planning pregnancy], I don't really want to bother them about"

6.3.2.4. Decision aids and influences

The combined decision-making process of choosing a treatment *and* deciding about family plans is complex. The women mentioned a number of variable factors that played different roles with different priorities for them, as previously mentioned earlier in this chapter. Indeed, the process itself was described differently by participants, with different time frames from the starting point of having their first relapse to receiving a diagnosis and choosing their medication. This is likely due to the difference in the health services provided in different locations across the UK and by different HCPs (some received the most comprehensive details from their consultants, others from nurses, but rarely from pharmacists). This was also affected

by the women's different priorities and levels of understanding of the MS information they received, as well as their different life circumstances, naturally. Despite this high variability in the women's stories, they all used at least one decision aid and/or had at least one decision influencer that swayed their decision.

As outlined in Chapter 2, a decision aid is defined by NICE as tools that can be used to support the discussion between HCPs and patients about preference-sensitive treatment decisions, which the patient can then take with them to consider them further after the discussion which is very important in the SDM model (86, 107). On the other hand, influence as defined by Cambridge dictionary is to affect, change how someone develops, thinks or behaves.

During the interviews, a variety of decision aids and decision influencers were identified that helped the women during the process of deciding on treatments and family plans.

1- Decision aids:

When the women were asked about the information resources decision aids, they had access to in relation to the overlapping area of DMD choices and family planning, they mentioned the following:

a. **Paper-based resources:** The women all received paper resources in the form of DMD booklets prepared by charity organisations and given to them by their HCPs. Some also used the leaflets enclosed with medications to read more on the subject, or even received DMD-specific booklets by mail for each eligible option. These paper resources, were reported by women interviewed, to be daunting, and confusing. They also reported that the information provided about the management of DMDs during conception, pregnancy, and breastfeeding is not comprehensive enough for them to make a decision. P5, a 25-year-old woman who plans to have children in the future, talked about her DMD choice experience and how the booklets did not provide any detailed information about pregnancy:

P5: "I have to compare the treatments is this booklet that she gave me when I first got diagnosed... mentions nothing about pregnancy. Which isn't very helpful."

b. **MS charity websites:** The MS Trust and MS Society websites appeared to be at the top of the list of the online resources used by the women. The women largely described these websites as a good and non-scary information resource:

P17: "I did go on to the MS Trust and the MS Society websites are really good and they are quite accurate. They're not scary at all."

c. **Online forums and Facebook groups:** These sites and groups were another resource the women talked about. As much as some found them helpful as they provided them with greater exposure to other people's experiences, others found them to be full of negativity, with lots of horror stories attributed to the disease's high variability:

P9: "I'm quite happy to chat to people on forums."

P4: " When I was first diagnosed, I did join lots and lots of support groups online on Facebook and I found them a blessing and a curse really."

d. **Google:** Using search engines to research further was also reported and frequently linked with negative outcomes such as scary studies, horror stories, and untrustworthy information. For instance, P8, a 33-year-old single woman who wants to have children in the future, talked about how she googled to see if she could have children, given her diagnosis of MS:

P8: "Like I googled it straight away, like if I've got a MS, can I have a baby? What does that mean for me?"

P17: "Google stuff that makes it even worse."

2- Decision influencers

a. Conversations

Variable content: During the interviews, the women reported that conversations were one of the most important decision aids in helping them to make a decision. Discussing their treatment options and family plan positions in relation to a timeline, together with the benefits, risks, and their life circumstances, helped them to get through the process. A number of the women reported having such conversations with both an HCP to get some professional advice, before discussing it with a partner or close family member.

Notably, the women who took the HCPs' advice on board, used it to reassure themselves about any information they had received from other sources, which gave them more confidence in their decisions. However, the content and timing of these conversations varied a lot across the interviews, and the only clear denominator in these conversations was a HCP asking if a patient was planning a family or not, discussing the safety of certain medications during pregnancy, and explaining their postpartum relapse chances.
P22, a 42-year-old woman who was diagnosed at the age of 39 and wanted children but was not in a relationship at the time, described the family planning discussion with her health team as a "brief" and in relation to her choosing a treatment option:

P22: "We did discuss it briefly when I was kind of picking treatment options."

Similarly, P26, a 36-year-old woman who had had one child after diagnosis, found it hard to remember any clear details about any family planning conversations with her HCP, but recalled that any family planning discussions were tied to discussions about treatment safety:

P26: "I do remember there were some questions asked, or if I will have children if I want to have, I think I remember that… In terms of like treatments, I've been told that is a safe treatment in terms of pregnancy and everything."

It is important to note here, however, that most of the time the women found it hard to recall the content of these conversations. This could be attributed to the time which had passed since they had these conversations, brain fog and memory problems, and the existence of multiple information sources, or it could be due to the fact that the main points made during these consultations were not made clearly or strongly enough to be remembered.

P18, for instance, clearly struggled with memory problems and brain fog (she found it hard to recall a lot of the events she was asked about). When asked about her family planning conversations with any HCP, she reported that she could not remember the details.

P18: "the MS nurse I spoke to. I did have a discussion with… a… doctor can't remember anyway"

Moreover, the women who were not using any DMD tended to not have such detailed conversations about family planning. P23, a 46-year-old woman who did not have any children and was not planning to have any, was never on any treatment, and thus reported not having any family planning conversations with an HCP:

P23: “I've never had a conversation with an MS professional about family planning."

On the other hand, P13, a 41-year-old woman who had had one child after diagnosis and had never been on any DMDs, reported that her neurologist

actively offered her general information about the possibility of postpartum relapse:

P13: I was told I believe by my neurologist that there could be a potential of an episode If you know when I give birth."

HCP involvement: MS consultants and nurses were the most repeatedly reported HCPs who had participated in these decision support conversations with the women about DMDs and family planning. Only one woman reported that a pharmacist was involved in her planning experience. It is perhaps worth noting that this participant showed a uniquely high level of understanding of the details of her treatment plan together with her family plan:

P11: "the best person I spoke to about these kind of medication decisions is that they've gotten MS pharmacist, and I spoke to him on the phone a few times."

b. Experience: As opposed to the previous sub-theme, some of the women noted that they preferred to hear from other **women with MS** who went through similar decision-making processes. The impact of these lived experiences appeared to have changed some of the women's decisions completely, from not wanting to have children to going for it, and vice versa. P31, a pharmacist, was influenced by other women's experiences rather than by a colleague (HCP). She reportedly made the decision not to have children, before changing her mind after meeting a woman with MS on a plane who talked about her positive experiences with MS and having children:

P31: "what swayed me has been other people's insights, if I hadn't met that lady on the plane that time probably might not have tried initially"

The women were also drastically influenced specifically by the **experiences with MS of people they were very close with.** Those who had a sister, mother, or a

friend with either “good” or “bad” MS, as described by them, were swayed by their MS experiences, despite any information they had received that contradicted their experience. P21, for instance, decided not to have children because of her experience with her cousins who had “bad” MS, and for whom having children and being pregnant led to a worsening of their MS:

P21: "Two female cousins and one of them made herself worse by being pregnant."

One other form of experience which was described in the interviews, was the **previous self-experience** of these women. This included, for instance, women who had tried a specific medication and were unable to tolerate it, and would not switch back to it for the sake of family planning due to their own experiences with it. Likewise, the women who did not do well during pregnancy and postpartum, reported that they thought it would be a bad idea to repeat the experience again. P26, a woman who had had a severe postpartum relapse, was not planning for another child because of her fear of this repeating:

P21: “I can relate to myself...my own experience. This is when it first happened [post-partum relapse]. It happened really badly and uh, and yeah, I am really, really really scared that it will repeat.”

c. **Psychotherapy:** A few of the women reported using a number of different resources that while not directly helping them decide on an DMD option and with family planning, helped them more in other aspects that prepared them mentally for making a decision. Group CBT therapy sessions, for example, helped one woman with acceptance, commitment, and her life decisions in terms of helping her with her mental readiness to make a decision. Others treated their underlying mental health conditions such as anxiety and depression with therapy in order to help them accept and then prepare them to process the decisions they were making about their treatments and family plans. P28, a 42-year-old married woman who had one child and suffered from postnatal depression but wanted a second child after her MS

diagnosis, explained how one CBT course helped her overcome her fears and make a decision

P28: "it's called action on living, it's acceptance and commitment therapy, and they told me it's a bit like CBT";

"So if you took away all that, what would you do? What would you say? What? What things would change? So I was thinking about if I hadn't had post-natal depression… if I hadn't had MS…? What was my plan? And so, I wrote down, we were going to have a second child."

6.3.2.5. Mental health and state of mind during the process

The women's mental health and states of mind during the decision-making process are also both important aspects of the process, as the interviews showed that this drastically affected their final decisions.

Mental health: This is very important when making a decision. Anxiety and depression can affect a person's decision-making capacity and the final decisions they make (105, 193). This can also be heightened by the stress the decision-making process brings, as one of the participants reported. P30, a 32-year-old married woman who wanted to have children, talked about her anxiety, how it worsened when she needed to make decisions, and how counselling helped her to deal with it:

P30: "I do have quite bad anxiety anyway, and any major decision or change brings that up";

"I do get counselling for that because often the worst thing will not happen."

State of mind during the process: This is very important as well. At the time of diagnosis, it is usual for patients to go through a lot of different emotions and different states of mind, such as of denial, fear, anger, and confusion (100). Similarly, postpartum periods and relapse periods are just as confusing and overwhelming as

the initial diagnosis period. In both of these periods, women go through big life changes, and yet it is also these times when they are usually expected to make decisions about starting/restarting/switching treatments.

Thus, when it comes to making these decisions, most women are neither mentally nor emotionally ready to make decisions about two such complex aspects of their lives (family and treatment). Indeed, some of the women reported that they consequently regretted the decisions they made.

P10, a woman with MS who had a relapse 18-months postpartum (while she was breastfeeding), had to stop breastfeeding and restart treatment while simultaneously having to decide about her future family plans in order to choose a suitable DMD. Due to how frightening and overwhelming these circumstances were for her, she decided not to have a second child and to go for a high efficacy treatment that cannot be used during pregnancy and needs a long wash-out period. She reported how her fatigue, sleepless nights, and the signs of relapse she was having (pins and needles), lead her to make a decision from a place of worry and being overwhelmed. She expressed her regret about not having a second child, especially now that her age stands in the way of her wishes:

> *P10: "baby wasn't sleeping so we were very low on energy and couldn't make any decisions or have any time to talk about anything. And so, it just seemed like I just both of us agreed that we didn't know that we could do it.";*
>
> *"I still regret our decision quite often."*

6.3.2.6. Changes in family plans

MS undoubtedly affected these women's initial family plans. For instance, it affected the **time** at which they wanted to have children. Some had to start a family sooner than they had planned so as to be able to be a parent and run around with the children when they were still strong and healthy, while with others, their active disease necessitated a period of treatment that meant postponing their family plans or even cancelling them entirely.

P24, a 49-year-old woman who had to conceive earlier than she had planned in order to follow her neurologist's advice upon diagnosis that she should do it sooner rather than later. She was not ready at that time due to her career and some marriage challenges, but decided to prioritise becoming a mother:

> P24: "I was 30 years old. My career was taking off. I wasn't ready for maternity leave";
>
> "I'm gonna have to change plans here. I can't wait some 35, 36. I'm gonna have to have children sooner than we'd planned.";
>
> "I need to divorce him right now, but my decision was very much swayed by… I need to have children now and I'm already married to this guy."

MS also affected **the number of children** the women had planned. As a result of this, the majority of the women had fewer children than they had planned to have before their diagnosis. Diagnosis also massively influenced their decisions about becoming a parent in the first place:

> *P16: "Originally I thought I would have three children…. But once I have my second son, I was able to see that I've been so ill with both of them. I'm very lucky. I've got two healthy boys."*

6.4. Discussion

The interviews demonstrated the complexity of the treatment and family planning decisions women with MS needed to make through the granular view of all their stories and circumstances. It also highlighted the multiple overlapping layers and inter-related factors involved in the decision-making process, making the process of deciding on both DMD and family plans very difficult. The study thus not only confirmed the findings of the existing literature in terms of the concerns women with MS faced when planning their families, but also provided additional qualitative depth to this area of research by underlining the complexity of such decisions. While MS-related factors such as fear of disease progression, passing the disease on to

offspring, coping with parenting, and dealing with MS symptoms are naturally key areas of concern for women with MS, issues surrounding family planning in relation to choosing DMDs are as crucial as MS-related factors when making these decisions. It is thus vita that the processes of making decisions about DMDs and about family plans are linked discussions (37, 194).

This study was also the first to focus on the holistic decision-making process itself, the experiences these women went through, the different decision aids used during this process, and the influence(r)s which swayed these women's decisions.

The interviews confirmed that conversations with HCPs were of upmost importance to the women due to the scarcity of information elsewhere when looking at the decision holistically. However, the women also had very variable experiences across different practices in different locations in the UK. Most of them did not report receiving a detailed specialised consultation about family planning and DMD choices, with these topics instead being briefly embedded during regular consultations. Furthermore, not all of the women who received such a session were able to recall the details of it. While this phenomenon could be the result of a number of factors such as not being mentally ready to hear about these topics at the time, memory problems caused by MS, and the fact that the sessions took place a long time ago, it could also reflect the quality of the sessions provided.

The information that the women could most recall being offered was about medication safety during pregnancy and postpartum relapses. Only a few of the women were able to provide more details about being given information about a treatment/family timeline, plans, plan B, and the management of these DMDs during the family panning journey. The content, timing, and the HCPs leading (consultants, nurses, or pharmacists) these sessions varied. In addition to this, the rapport and trust built up with their HCPs impacted the value of these conversations for the women and thus impacted their final decisions. Indeed, patient-HCP trust has been demonstrated to improve the efficiency of prescribed treatments and to increase patient satisfaction, which in turn will improve the quality of the decision-making experience (195, 196).

Some of the women also demonstrated some level of ignorance about what HCPs could provide them with in the way of support for their decisions. Some also held

onto outdated information and shut themselves off to further information despite their wishes. These cases highlight the importance of education and awareness, together with proactive in-depth conversation.

The study also emphasised the importance of choosing the right time for these conversations to happen. Treatment decisions usually take place in three critical periods when treatment initiation or management is prompted (diagnosis, relapse, and postpartum). However, it is during these periods that women are not in the proper state of mind to make such decisions due to shock, denial, or feeling overwhelmed. It is thus very important to identify when women are having these challenges and triage them to the right service in order to help them get back their balance and stability before deciding on any plans. Of course, it is worth bearing in mind that this is not always possible, especially when patients' MS reactivates and they need fast intervention. It is thus crucial to find a time that is both soon enough to prevent relapses, but also gives women time to absorb the diagnosis and accept it, recover from a relapse, or settle after delivery. However, this can be tricky to estimate and be decided on by a HCP, especially given their limited time.

Other women's experiences constitute a second decision aid that the participants in this study used. These stories were valued by many participants, especially those with a medical background who understood the science but needed confirmation from people who had lived a similar story and faced similar decisions. While some of the women found it difficult to read and listen to negative stories, it also positively encouraged other women to make the right decision for them.

Resources that discuss family planning together with treatment options and management in lay language are scarce. The women talked about both the paper and online resources they used that discussed each topic separately but found nothing that provided guidance on both issues together. This then places more responsibility with the HCPs, as they remain the main source of information on these topics, as confirmed by a survey of 332 patients with MS across the USA, UK, France, Germany, Italy, and Spain. In this survey, 81% of the participants indicated that their HCPs are their main source of information when making decisions about family planning (197).

6.5. Conclusion

This chapter offered a granular view of the women's experiences when choosing medication in relation to having children. The interviews confirmed the findings of the existing literature about the main concerns women with MS face here. This study was the first to focus on the holistic decision-making experience itself, however, positioning HCPs as the main resource of information, highlighting the scarcity of resources available to patients, and variability in the decision-making experience. It also demonstrated the complexity involved in these treatment decisions and how it cannot be separated from family planning decisions. Lastly, the study also drew attention to the impact women's states of mind and mental health had on the decision-making process and the final decisions made during these critical decision-making periods.

Chapter 7. Exploring commonalities between the accounts of the impact of decision-making – An in-depth analysis using a biographical disruption framework

7.1. Introduction

The previous chapter detailed a descriptive analysis of factors women consider when deciding on treatment in relation to family planning, alongside exploring the decision aids and influencers involved. The factors, identified in themes, are in line with what is already known from the existing literature regarding concerns women have about having children when they receive a diagnosis of MS. The concerns that impact these decisions include a patient's own health, their child's health, coping with parenting, the availability of a support system, and societal attitudes and judgement over their decision to have children (37, 198, 199). The main factors women consider when choosing treatments in relation to family planning, such as treatment safety during pregnancy, were also outlined.

The interviews also shed light on the decision-making experience with regards to treatment choices in combination with family planning, and the interaction between these decision-making processes. This encompassed the level of patient involvement and proactivity during the decision-making process, resource availability, finding the best time to discuss these kinds of decisions, and the effect patients' states of mind have on their decisions during this time.

This chapter will provide an in-depth analysis of the accounts given by the women in the interviews, using the biographical disruption model developed by Bury (1982) (200). Biography combines both "self" and "identity". "Self" has been described in the literature as the internal perception and a reflection of one's internal thinking, an internal persona, while "identity" in contrast is shaped by social interaction and imposed as a label, known as a public persona (201). Biographical disruption theory, as described by Bury, is the disruption to a patient's biography (self and identity) due to the development of chronic illnesses.

In the case of MS, this disruption can take place during multiple critical times of the course of MS: when patients are first diagnosed, when they struggle with a relapse, and after giving birth when the risk of relapse is higher. These three periods are usually when decisions about treatment and family planning are discussed. The analysis of the decision-making process through the lens of the biographical disruption model, will thus give insight into the impact this disruption has on the self, identity, and decisions, as well as into the role of context in this process.

7.2. An in-depth interpretation of the women's accounts using Bury's biographical disruption framework

Before applying this framework, it is important to highlight the reasons I chose this theory to analyse my data. First, the decision to choose this theory was reached during supervisory meetings with the guidance of my supervisor Fiona S, who is a medical sociologist. This was agreed on after identifying and discussing the idea of the disease impacting identity and thus decision making and decisions during these meetings which was translated by Fiona S to this choice of theory, who recommended I read further into this.

When reading more about the theory, I found how Bury's sample was very comparable to the sample I used in my study which also made this theory a good fit. Bury had developed his theory using data from semi structured interviews with 30 patients who had Rheumatoid arthritis and who were referred to rheumatology outpatient clinics. Rheumatoid arthritis is a chronic inflammatory disease that can have episodes of both flare ups and remissions, resembling the nature of the disease of the relapsing remitting form of MS (See Chapter 1 for a RRMS definition) (202, 203). As with MS, Rheumatoid arthritis is also more prevalent in women. In his sample, 83% (25/30) of the participants were thus women, mostly aged between 25 and 54 years, which is also close to the age range of the sample used for this study (200).

When analysing the accounts using the lens of biographical disruption, the following themes and subthemes were identified:

1- Biographical disruption to self
    a. Motherhood with reduced capabilities
    b. Stigma around disabled mothers
2- Biographical disruption to mother-self
3- Biographical flow to mother-self

7.2.1. The biographical disruption caused by diagnosis to the self and its impact on decisions.

Bury's theory of biographical disruption is based on the effect the onset of chronic illness as an acute disruptive event (diagnosis) has on a patient's perceived self, career, relationships, and future.

In my sample, when women were speaking about their experience of receiving a diagnosis of MS, they reported how shocking this experience was for them, how they felt that their bodies were failing them, the grief they felt for the life they have lost or might lose, the feeling of being overwhelmed by the amount of information they received, the expected changes that will happen to their life and to their careers, relationships, and future, and being overwhelmed by the decisions they needed to make in such a short space of time. For instance, some had to stop doing their favourite sports due to disability, some experienced a breakup with a partner due to lack of self-esteem after diagnosis or having to give up a demanding job in order to adjust to their new self. Some of the women also discussed the experience of having to shield during COVID.

Bury describes the diagnosis disruption as consisting of three stages which unfold due to chronic illness. The first stage is the disruption of taking assumptions for granted. This is when the first symptoms start to creep in.

In my sample, when interviewed, the women talked about this stage of disruption caused by experiencing these first symptoms (such as vision problems), how scared, unsure, and overwhelmed they were, and even how prone some of them were to assuming that the worst would happen.

The second stage according to Bury, is the stage of living with the pain of acknowledging that you have the condition, living the day-to-day symptoms, and then asking the questions “why me?” and “why now?”.

According to the accounts in my study, this stage was shown to be full of denial, grief, and feeling overwhelmed. With MS, receiving a diagnosis usually ushers in a period where treatment initiation may be discussed, and consequently also family planning. Two big decisions to be made, right when women are still in the middle of this second stage of biographical disruption experience.

P12 was a 38-year-old woman who was diagnosed at the age of 24 after having optic neuritis (inflammation of the optic nerve caused by demyelination), meaning that the illness manifested itself as vision problems (first stage). During that time, she was preparing for her wedding. She talked about the effect of the shock of the diagnosis on her life, stating that “it was all a blur”, as well as the effect this had on the way she perceived herself, feeling like she was “put together wrong”. She also talked about receiving a lot of information at once, how overwhelming that was, what her worries and her family’s concerns were, and how differently she saw everyone else at that point:

P12: “You go through a process of shock and trying to come to terms with it. Trying to understand what's going on?”;

“That time I was being, flooded with a lot of information. There's a lot of other people you're trying to come to terms with seeing them differently. Trying to handle like my family trying to deal with their concerns and worries”;

“You just feel like you're put together wrong.”

Indeed, P12 was one of the women who talked about making decisions from a place of grief, denial, and disruption. She started on weekly injected interferons to make it through her wedding but stopped afterwards because she felt that they made her feel worse. Without communicating with her healthcare team, she decided to come off the treatment in order to go back to her “normal” life (second stage of denial). When asked about the reasons and circumstances for deciding to come off the treatment, she expressed that reflecting on that decision now, she has realised that this was part of her grieving process at the time. She is currently not happy with that decision as she perceived this had a negative impact on the course of her MS:

P12: "It's the part of the grieving process of coming to terms with having MS in your life";

"I just want to have a normal life. I want to go and have my job and work. You know when I marry my husband and you know spend some time with him. I wanted to put it [MS] on one side. I didn't want it to have to become my only thing. I think about every day. So yeah, that was the reason. I just more that I just was trying to ignore the diagnosis for a while."

Interviewer: "so you were off medication for this period of time?"

P12: "Yeah, sadly yeah."

The last stage of disruption, as described by Bury, is the stage of using resources to cognitively cope with the changes by tolerating the disruption and coming to terms with their new capabilities, the 'new normal', and developing practical strategies to get through the day (200). In my sample, P12, for example, talked about this stage of trying to cope, and how her consultant helped her to make better decisions by introducing her to the key concept of re-normalising her life as much as possible. Re-normalising helped P12 to make the decision to re-start treatment in order to control her MS, and as a result feel better and more confident in her re-negotiated self, as well as making the decision to start a family:

P12: "He just said that this is a really good chance for you to slow this progression down as much as you can and have as normal life as possible, and that was really what I wanted to hear… normal life";

"because of Tysabri. I was well enough, and I felt confident enough that I could have children with MS."

7.2.2. Biographical disruption to the mother self caused by diagnosis

When Bury's theory applies to the disruption to self-perception when diagnosed with chronic illness, in my sample, the disruption of the diagnosis was extended to impact also the mother self and how women perceived their selves as mothers after the diagnosis.

The "mother self" is a woman's construction of their maternal subjectivity. This study recruited 31 women to share their experiences of making treatment and family planning decisions. This included both women who had already had children and those who did not know whether they were planning for more, in order to cover all kinds of decision-making experiences. In the accounts given, the impact of an MS diagnosis on the women's perception of their mother self was evident. Some of the women assumed, anticipated, and constructed their mother self as soon as their diagnosis was made, while others constructed this subjectivity before and then after experiencing motherhood with MS. These women tried having children after diagnosis and decided either to have more (mainly with positive experiences) or not to have more after experiencing how MS impacted their capabilities and thus the way they see themselves as mothers. Both groups attributed their decisions to their disrupted mother self.

Whether this subjectivity was anticipated (at the time of diagnosis) or experienced (postpartum), it is important to note that both of these times are critical, as they are when treatment and family planning decisions usually take place. Thus, biographical disruption occurs in a way that can impact those decisions.

Subthemes under biographical disruption to mother self are the following:

7.2.2.1. Motherhood with reduced capabilities

The women who made the decision not to have children or who were still in doubt about their decisions, talked about their reduced capabilities due to MS in a way that makes or might make motherhood even harder. This thus led them to form this subjectivity about themselves as mother, stemming from their reduced capabilities, disability, or even the anticipated effects of the disease on their capabilities in the long run.

P14, a woman with a mild MS that does not require treatment with DMDs, chose nevertheless not to have children because of her limited energy and high fatigue due to her MS, among other reasons. P14 thus formed a mother subjectivity about herself, reflecting her own beliefs about motherhood and her reduced capabilities. She explained that she cannot meet these high standards of motherhood, as for her, being a mother in this society means sacrificing more, something that she could not afford to do with her low energy levels:

P14: "you do pay to be a mother… in our society mother still sacrifices more";

"I don't have that much there to sacrifice because like I say I've only got just enough [energy] to do what I want to do."

7.2.2.2. The stigma around disabled mothers

One of the main aspects of diagnosis which impacted the mother subjectivity and the women's decisions, is the fear of society judging women for their decision to have children while living with a disabling illness. The stigma around MS being disabling, and the idea of being in a wheelchair sooner or later, burdening others, and not being able to take care of their children, are all things which impacted the way the women constructed their mother identity. In these cases, their sense of self was thus shaped by social beliefs and judgement rather than by their own views of their self and their capabilities.

P9, a 40-year-old married woman who was diagnosed with MS at the age of 29, spoke about how when she was first diagnosed, she was paranoid about becoming wheelchair-bound and how this would affect all aspects of her life including having children, despite the fact that becoming a mother was not a short-term plan at that time. Even though she and her ex-husband started to slowly grow apart and the fact that family planning was thus slowly disappearing from their conversations, she expressed that every time she had one of these small chats with him about having children, the "MS Label" was always there in the background:

P9, answering the question, "What had the diagnosis changed in her life?":

"I was paranoid that I'm in a few years time I was going to be in a wheelchair"

Interviewer: "So about the family planning. So what was your decision can you tell me more about that?"

P9: "We'd never really discussed kids we we always lived by selfishly, being independent[…] We had lots of little chats, natural chats.[about having a baby] […], I was conscious about it and all the little chats that we had. I was always

conscious of this thing, this label this disease that's going on in the background of me."

Even though P9 listed a few different reasons that stopped her from becoming a mother, she ended her answer by mentioning the "labelling" effect of the illness that was always hovering in the background. This ties in with her previous answer about her fear and paranoia about her possible fate of being in a wheelchair, a symbol of disability, which is self-labelling and self-stigmatising.

P21, a 42-year-old woman, had a first (unconfirmed) diagnosis at the age of 20, when her doctor at the time advised her not to get pregnant to avoid relapses. She had her confirmatory diagnosis at the age of 36 when she had to start DMDs. Upon being asked whether she had considered family planning at this point, she stated that she had not because she was impacted by both her first consultant's advice and her cousin's experience with MS. She noted that her cousin made her health worse by having children, and that all of the family judged her for being "stupid" for doing so:

P21: "I was then affected, by m…I've got female cousins ended up getting MS as well. One of them made herself worse by being pregnant, so the response from the family was, you know almost like she is stupid for getting pregnant again, and because it was making her worse. It's listening and hearing things like that…and you're thinking, is it? Is it better just not to do it?"

As a result, she decided not to become a mother as she suggested that she would also be judged for having children while having MS, which also contributed to shaping and forming her mother identity.

7.2.3. Biographical flow or continuity within the mother subjectivity

Some of the women in the sample formed a capable maternal subjectivity despite the impact of the illness. This was common in the case of mild illnesses, which resulted in the disease having a minimal impact on their self-recognition, both

generally and in terms of their maternal subjectivity. P13 was a 41-year-old woman who was not using any DMDs and living with a mild form of MS. She had had a child after diagnosis and was planning for more. She also did not suffer a postpartum relapse. She thus talked about how her maternal subjectivity was not impacted by the disease at all, due to the mildness of her illness and symptoms, to the point where she forgets that she has MS in the first place:

> *P13: "I always plan to try to be a mother, so I'm not sure whether me having multiple sclerosis would have been enough to stop me from trying to plan a family.";*
>
> *"I 95% of the time forget that I have multiple sclerosis."*

Mild illness, with almost no symptoms and no treatment complications, suggests biographical flow rather than disruption, as there was no disruption to start with.

Cultural beliefs and norms were another aspect that was identified as impacting the self and the mother subjectivity of one of the women. According to P16, believing that being a mother is the expected choice of any woman regardless of circumstance, had a strong impact on the formation of her maternal subjectivity. This was also further shaped by the influence of culture and society (204, 205).

P16's husband comes from a traditional Asian background where the norm is to have big families and more than two children. Although she was struggling with severe illness and was on an experimental treatment at that time, she decided to follow the traditional model for women and have two children. When asked about the factors she considered when she made the decision to have children, following the traditions and family norms that she would get married and then have kids was one main factor. She also talked about the influence of her husband's background preferring big families:

> *P16: "I think it was just a kind of quite a traditional family and it was gonna be married by 30, so we got married, we kind of had it all planned out. Then I got pregnant."*
>
> *Interviewer: "So did he help you? What was his role in your decision?"*

P16: "My husband? [confusing laugh that sounds a little bit sarcastic] I think he was on the same page really? I mean, he's one of seven. My husband is [Asian background], so he's very traditional background where everyone's you know gets married, has three to seven children. So he was quite happy to… have the babies."

This suggests that traditions, norms, and societal expectations can form and shape the mother identity and make women fake the continuity of her normal mother identity in order to fulfil these expectations, instead of listening to their own bodies' needs and capabilities in a way that would help them to form a more realistic identity and ultimately impact their decisions. P16 talked about how lucky she was to have her boys, but also about how her MS deteriorated after each baby and how difficult life has become for her as a mother with active Ms.

7.3. The importance of context and fluidity in the decision-making process within Bury's framework

When interpreting these accounts of women's decision-making processes through the lens of biological disruption, it was of an upmost importance to highlight the two common elements within the accounts, context and biographical fluidity, as these elements are two important parts of biographical disruption.

7.3.1. Context

Context is one fundamental element in all of the accounts because different contexts lead to different self-perceptions. Williams has looked at the role of context in the biographical disruption theory, arguing that context has an impact on the level of biographical disruption caused by chronic illness (206). Context is also a major factor in the medical decision-making process, in that contextualising decisions is encouraged to ensure better outcomes. Indeed, Saul J. et al. has explored the importance of contextualising medical decisions in order to individualise care.

Contextualisation is identifying what is relevant to the immediate medical problem in a patient's life, including their cognitive abilities, emotional state, cultural background, spiritual beliefs, economic situation, access to care, social support, caretaker responsibilities, attitude to their illness, and relationship with healthcare providers (207). Indeed, the contextual categories of emotional state and attitude towards illness are strongly related to the notion of biographical disruption.

For example, some of the women in my sample were diagnosed with a severe disabling relapse, which consequently made them experience a high level of negative emotions and attitudes towards their illness in relation to their family plans. P1, for instance, stated that:

*P1: "the fact that I had such like debilitating symptoms so early on that I was really **nervous** that if I did have children and then I had another relapse, cause they said if I had another incident with my another attack on my spine I would probably have much worse than like walking abilities and things like that."*

In contrast, P13, who lives with a milder form of illness without the accumulation of any disability and frequent relapses, demonstrated a better emotional state to the point where she almost forgot she even had the illness, as explained earlier, consequently did not perceive herself as disrupted, meaning that her decisions were less influenced by biographical disruption. It should be noted, however, that disease severity does not automatically equate to greater disruption to the mother self, as with P16. This makes context immensely important in the decision-making process because it impacts biography. This is in line with Williams' and Saul's conclusions (206, 207).

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7.3.2. Biographical fluidity

As is referenced in the name of RRMS itself (relapsing remitting form of MS), together with MS's high variability between patients in symptoms, disease course, and response to DMDs, change is an inevitable part of living with MS. A patient can always unexpectedly relapse, adding a new symptom/disability to their course of illness and thus shaking the boat of normality reached earlier. This continuous

change in self-subjectivity (disruption and renegotiation after each relapse) is what will be referred to here as biographical fluidity. Indeed, biographical fluidity across the disease course was evidenced in the women's interviews, which confirms Larsson's theory about chronic illness as a recurrent disruption rather than as a one time disruption (diagnosis time) (208). This change in the disease course can cause a change in self-subjectivity and thus the decisions the patient makes. Since relapse is another indication for DMD switching, decisions about treatment and family planning will be part of the patient's medical care again at a time when self-disruption may occur again. The postpartum period is also another time of disruption in the life of women with MS. A critical transitional time for any mother, and more specifically for MS mothers as their risk of relapse increases, this is a period when decisions about breastfeeding and treatment resumption need to be made.

P12 is a good example of this fluidity of biography and sense of self across the course of MS, as well as in terms of the impact this can have on decisions down the line. P12's decision to abruptly stop treatment after she initially started treatment to get through her wedding, is a decision she considered to come from a place of grief (reflective of biographical disruption due to diagnosis). A period of re-normalisation and self-renegotiation then made her decide to restart DMDs, which made her well and confident in herself and abilities to be a mother with MS. Then, when an ectopic pregnancy and losing one of her fallopian tubes was an added further doubt towards her mother-self, together with her MS, this made her stop trying for a while. She described how counselling finally helped her to overcome these challenges and self-doubts, and helped her make decisions that were right for her and involved having children.

P12: "because of Tysabri. I was well enough to, and I felt confident enough that I could have children with MS."

P12: "I got pregnant really quickly and then ended up very quickly, it was an ectopic pregnancy …that was another time I was just thinking Oh my goodness is this right? Should I be having children? But then I had time to grieve and come to terms with it and I had counselling."

7.4. Discussion

Diagnosis with MS can be shocking, saddening, and overwhelming for many women. It comes with a lot of change and disruption in all different aspects of a woman's life.

The focus of this study was to examine the way in which women perceive themselves as mothers after knowing they have MS, and how this constructed maternal self and identity influenced their family planning and treatment decisions. Those who were suffering from reduced abilities, fatigue, or severe illness with frequent relapses, had doubts about their ability to fulfil the standards they held about motherhood and consequently decided to remain childless. In contrast, for those women who were living with mild MS or were very much culturally encouraged to believe that motherhood is the expected course of action from women, the disease had less impact on their maternal subjectivity. The fear of judgement from society was an external societal influence that shaped the maternal subjectivity and impacted family decisions too. These findings are in line with what Parton et al. found when interviewing mothers living with MS and exploring how women with MS perceive their subjectivity as mothers (209). The difference between this study and Parton et al.'s study, however, in that my sample included both women who were not mothers yet and those who are already mothers (they experienced motherhood and know their mother-self). This allowed for an exploration of the first group's assumptions and expectations about their mother-self in light of their MS. This study has also taken into account both retrospective and prospective points of views, while the women's stories in Parton et al.'s study were all explored retrospectively, meaning that they interviewed women who had experienced motherhood and expressed their maternal subjectivity based on their experiences rather than on their assumptions about what they might do. Parton et al. also categorised the women in the study to fall under the themes of "failing mother" or "normal mother". Although a similar categorisation could be applied using the participant's own words, the decision was made not to categorise the participants using any kind of labels, and instead describe the reasons that underpinned their subjectivity and justified their decisions.

An extra dimension was also added to this research by linking biographical disruption and the construction of self-subjectivity to the decision-making process,

introducing and incorporating the elements of context and biographical fluidity within the biographical disruption framework, and by examining how these elements impact the decision-making process in relation to both choosing treatments and family planning. Improving the decision-making process, especially in relation to treatment choice, is known to improve compliance and thus lead to better health outcomes and quality of life for patients.

This chapter has also shown that different patient contexts impacted the level of disruption the disease caused. This is in line with Williams' arguments. Indeed, this was particularly evident in the accounts of P12 and P13, for whom their different levels of disease severity, different cultural beliefs, different emotional states and disease attitudes, and different contexts, impacted how they constructed their maternal selves and impacted the final reproductive decisions: to go childless and to have two children, respectively.

Biographical fluidity reinforces Larsson's arguments about chronic illness as a recurrent disruptive event that can cause recurrent self-renegotiation. This is a pattern that clearly manifests itself with MS patients every time they face a disruptive event. This chapter has thus highlighted the three key periods of disruption in the MS journey which were also evident from the women accounts: the news of diagnosis, the failure of treatment that mandates switching (relapse), or the restarting of treatment after delivery when a postpartum relapse is an expected event. It is in these three key periods when decisions around treatments and family planning are usually discussed and made, even though the disruption experienced could impact a patient's self-subjectivity and thus their treatment and family planning decisions. Many women may thus not be ready to make such big decisions.

The findings of this study suggest that, under the umbrella of biographical disruption caused by the illness, readiness to make decisions is more likely when normalisation or self-renegotiation is established. Lowden et al. looked at the treatment decision-making experience of MS patients using voice-recorded interviews and positioned readiness to decide as occurring after patients have reached the stage of self-renegotiation and re-normalisation. They thus argued that readiness only occurs sometime after diagnosis, suggesting that patients are less ready to make decisions early on after diagnosis (210). This was evident in P12's story demonstrated earlier.

Indeed, a number of interviewed women mentioned how not feeling ready to make these decisions at that time impacted their decisions and their satisfaction about these decisions later down the line.

It is thus very important to assess the readiness of women with MS to make these decisions. An appreciation of the level of biographical disruption caused by these disruptive events (diagnosis, relapse, or postpartum) can help when assessing a patient's readiness. Unfortunately, there is currently no systemic way or universally-validated tool to assess readiness. Unlike capacity, the ability to make the decision, which can be assessed by healthcare providers in accordance with the Mental Capacity Act (MCA), readiness is still a matter of professional judgement (93).

This study suggests that women who are closer to the final stage of disruption (coping), are more likely to be ready to make these decisions, with hopefully fewer regrets. Revisiting a woman's sense of self before making DMD and family planning decisions, not only at the point of diagnosis, but also after each disruptive event (all three key times), is thus vitally important.

Considering the limited resources (time and human resources) HCPs have and the lack of an objective assessment tool of readiness, education about patients' readiness to decide may best suit the work done by charity organisations and support groups in future. Discussing the sense of self after each disruption and sharing stories about decisions that have been made and the places they were made from, could be helpful for both those who are still at the beginning of their MS journey or for those in the middle of a disruption and not aware of this yet.

7.5. Conclusion

MS does cause biographical disruption for women, including to the mother-self. This disruption can impact both treatment and family planning decisions. However, the level of biographical disruption also depends on the patient's context, which is an important consideration in the medical decision-making process. Biographical disruption is also not restricted to the time of diagnosis. Rather, it is concurrent with any disruption to a patient's health that causes deviation from the norm. These three critical times of disruption with MS are diagnosis, relapse, and postpartum,

highlighting the biographical fluidity of the disease. Readiness to make decisions is part of the decision-making experience with MS.

Chapter 8. Think Aloud evaluations of the MS Trust online DMD decision aid in a family planning context: amendments and recommendations for improvement.

8.1. Introduction

The interviews with the women highlighted the importance of decision aids for such complex decisions, particularly in light of the scarcity of such resources (see Chapter 6). As a key aim of this thesis is to explore the decision-making process in order to facilitate its improvement, it was important for the study to examine a good available DA and evaluate it in the context of DMD and family planning decisions. The MS Trust is a charity that supports MS patients from diagnosis onwards in their MS journey, providing services and decision aids for MS patients that cover all aspects of living with MS. These comprise paper-based treatment decision aids and information booklets as well as online resources. This thesis is particularly interested in investigating the MS Trust's online DMD choice decision tool. The tool helps people with MS look at all the DMD options available to them to start or switch to. It uses a shopping-like interface which applies filters to narrow down the DMD options. The tool also allows patients to compare up to three drugs head-to-head across different aspects such as the route of administration, side effects, monitoring, and pregnancy recommendations. I chose this tool because I was able to reach the Head of Information and Engagement at the MS Trust through the help of my supervisor, DC, who is one of the MS Trust trustees. The opportunity to materialise the results of this research through their tool update and amendment project, which made the MS Trust tool the preferred choice over the National MS Society's one.

The aim of the Think Aloud sessions is thus to explore women's thoughts and opinions about the tool to identify recommendations which can then be passed on to the MS Trust, who are planning to update the tool. This will thus help to improve the quality of the decision-making experience for its users.

It is important to note that this research was begun at the beginning of my PhD in 2019 and was completed near the end of 2022. The MS Trust's tool updating project

was intended to begin earlier but was held back during COVID and was resumed in early 2023. All the screenshots used in this study were date/time-stamped to show the actual date/time they were taken.

8.2. The tool (history, brief description of the interface and its functions)

Given the number of DMD options available to people with MS, each with a different efficacy, side effect profile, regimen, administration route, and management and monitoring plans, making decisions about treatment options is difficult. Pregnancy planning adds an additional level of complexity to this. In 2014, work on the MS Trust DMD online tool was started. It was created by the MS Trust Information Team, in conjunction with the digital agency Blackbaud, following an in-depth evaluation of the treatment information available to patients in January 2013. Patients with MS and HCPs were involved in this work at an early stage, as well as in reviewing the performance of the final tool. This online decision aid had been live for seven years at the time of my research, helping patients with their DMD choices as part of the SDM approach. It lays out all of the DMD options in a shopping interface format, where “customers” (in this case, the patient) can use filters to narrow down their options according to their preferences.

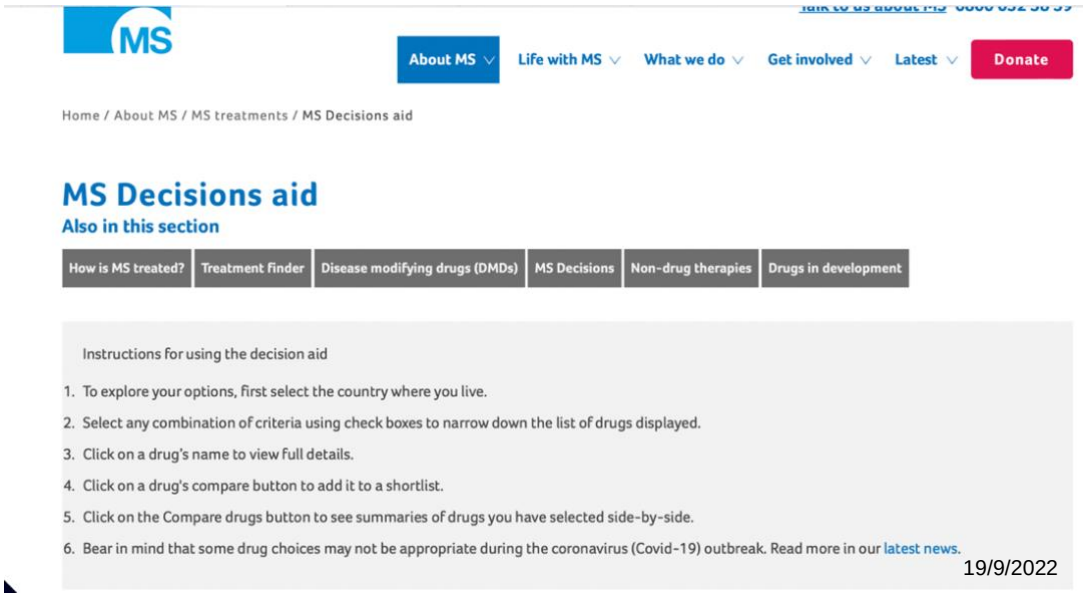
It is important to mention that there are slight differences in the interface of the PC version and the smartphone version. These will be highlighted throughout this chapter where relevant, supported by screenshots.

This chapter will first provide a quick tour of the tool to explain its different functions and to give as close a picture as possible as to what a patient sees. Lastly, in the results section, this chapter will discuss the thoughts and opinions expressed/shared by the women in this study during the Think Aloud sessions.

8.2.1. Instructions

Upon reaching the home page of the tool, users find instructions for the tool’s use, presented as six-step written directions in a grey box at the top of the tool page. The

instructions section in both the PC and smartphone version is shown in Screenshots 1 and 2, respectively.



Screenshot 1MS Decision aid home page (PC view)

Screenshot 2 MS Decision aid home page (smart phone view)

8.2.2. Filters

The filters appear on the left-hand side in the PC version when scrolling down, and by clicking the “Search and Filter” tab in the smartphone version. Both include the following criteria, using exactly the same wording:

- **Nation** (England, Northern Island, Scotland, Wales): to filter according to DMD availability in their country.
- **What type of MS is the drug for?** (Clinically isolated syndrome, Active RRMS, Very Active RRMS): to filter medications according to MS type and DMD eligibility criteria.
- **How Do I take the Drug?** (Self-injection, Pill, Intravenous infusion (drip) in hospital): to filter according to the preferred route of administration).
- **How often do I need to take the drug?** (Daily, six monthly, several times a week, weekly, fortnightly, monthly, annually): to filter according to the preferred frequency of treatment.

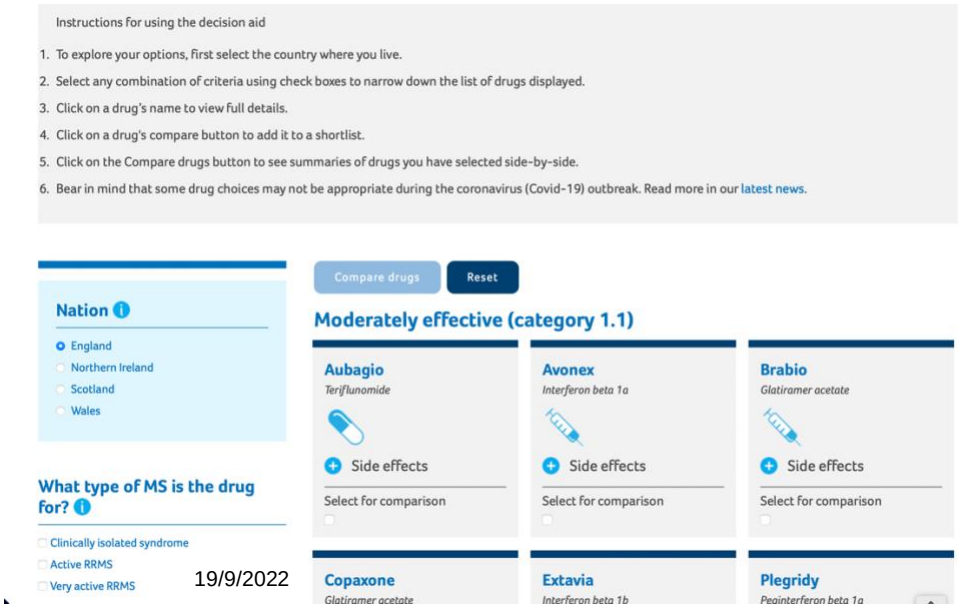
- **How often do I need to visit a clinic for regular monitoring and tests?** (More than monthly in the first year, every month, every 3 months): to filter according to preferred monitoring frequency.

Upon checking one of the filters' boxes, the page will automatically refresh and the list of available DMDs will be narrowed down accordingly. Screenshots 3 and 4-5 are of both the Filters and the DMD categories in the PC and smartphone versions, respectively (see 8.2.3 DMD categories).

8.2.3. DMD categories (the body of the tool)

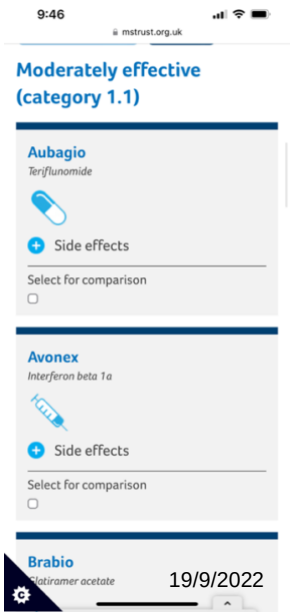
The DMDs which appear are categorised by efficacy at the centre of the screen. They are located just below the instructions in the PC version and can be viewed by scrolling down on the smartphone version. The DMDs are categorised by efficacy into the following groups:

1- Moderately effective (category 1.1)
2- More effective (category 1.2)
3- Highly effective (category 2.0)



Screenshot 3 The filters and DMD categories (PC view)

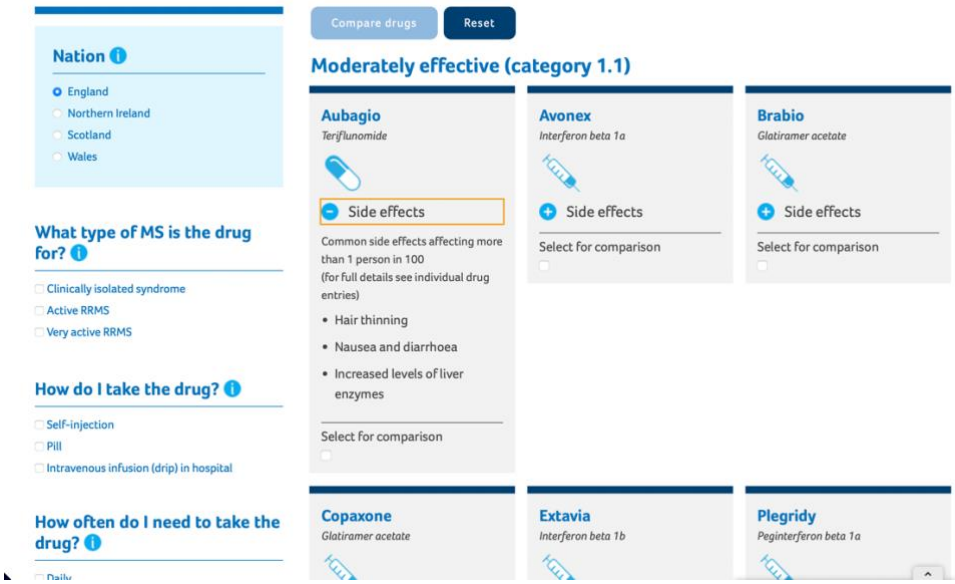
Screenshot 4 The filters and DMD categories (smartphone view)



Screenshot 5 DMD Categories (smartphone view)

8.2.4. Side effects (drop list) function

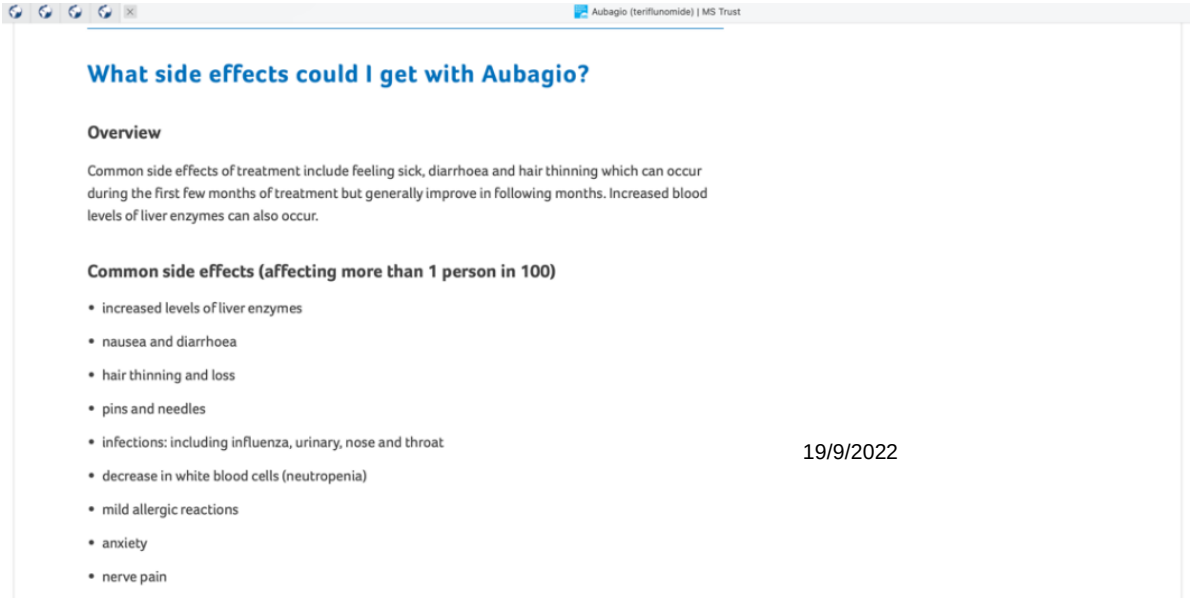
Clicking on the plus button in each drug overview section will show a short list of the common side effects of this drug, while rare or severe side effects can be found when clicking on the drug name to read more detailed information about it.



Screenshot 6 Side effects shortcut tab (PC view)

8.2.5. Detailed drug information

By clicking on any treatment name, another page of detailed information will appear.



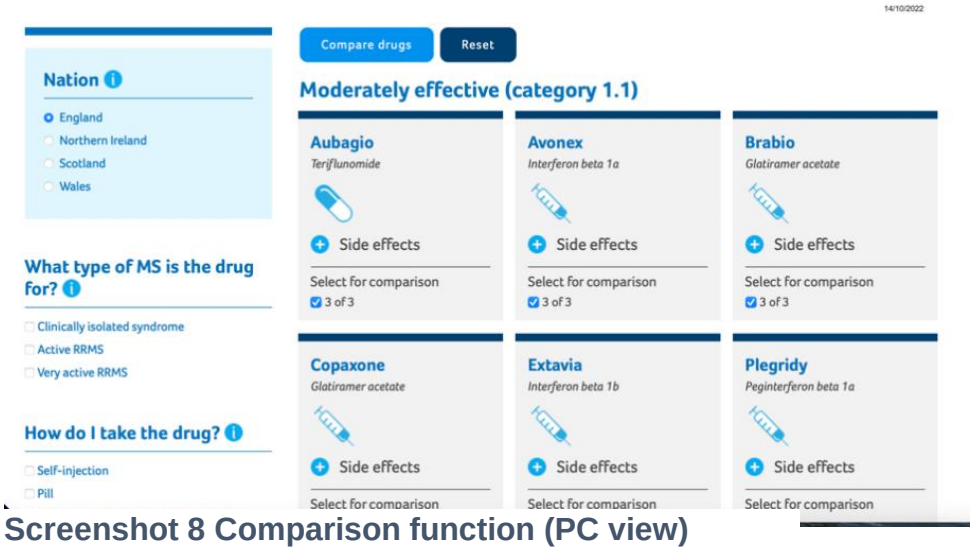
Screenshot 7 Detailed drug information page (PC view)

8.2.6. Comparison Function

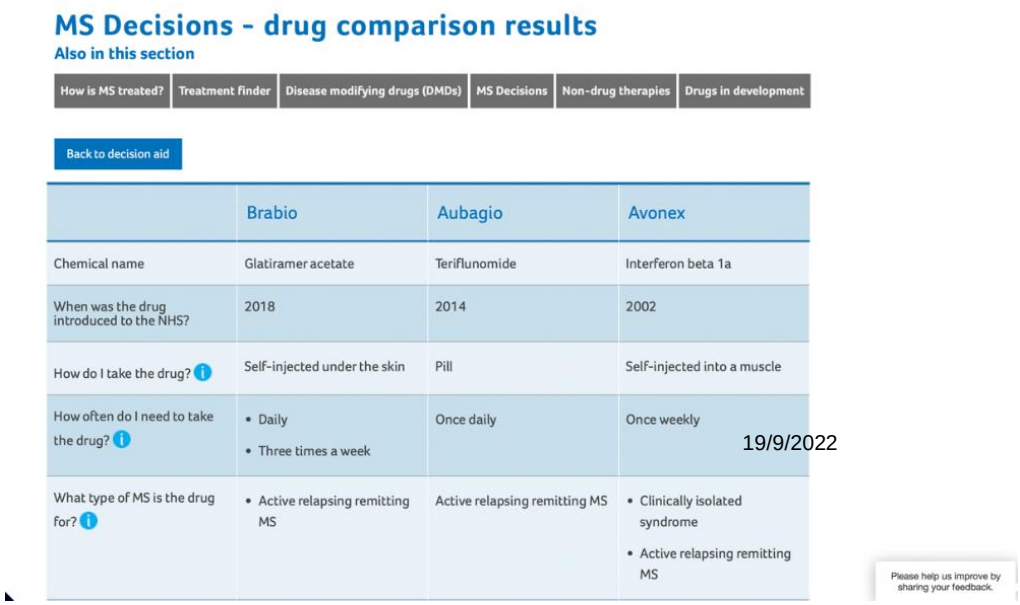
By checking the small white box under each drug and then selecting the “compare” option, the user can compare up to three treatments in one go. The comparison criteria for each drug includes the following:

- The drug’s chemical name
- Its date of introduction to the NHS
- How to take the drug (route of administration with a “more information” tab to explain the terms (self-injection, pill, and intravenous drip)
- How often the drug is taken (frequency), with a “more information” tab to explain the terms (daily, several times a week, weekly, fortnightly, monthly, and annually).
- What type of MS the drug is used for, with a “more information” tab to explain the terms (clinically isolated syndrome, active relapsing remitting, and very active relapsing remitting).

- The efficacy of the drug in reducing relapses with a “more information” tab to explain the terms (moderately effective, more effective, and highly effective).
- Its side effects, with a “more information” tab in order to explain that these side effects are only the most common ones and to look for other side effects under each treatment page.
- Its less common but more serious side effects.
- Whether the drug requires clinic visits for monitoring, with a “more information” tab that explains the reasons for that.
- Whether it is safe for conception and pregnancy, with a “more information” tab that explains the statements (you must not become pregnant during treatment, and pregnancy is not recommended during treatment).
- Additional information.



Screenshot 8 Comparison function (PC view)



Screenshot 9 Comparison page (PC view)

8.2.7. Pregnancy and breastfeeding recommendations within the tool

Pregnancy recommendations can be found either by clicking on the drug to view the full detailed information for that drug (in which case the pregnancy and breastfeeding information will be located under the heading “Conception and pregnancy”), or can be found in the comparison table when comparing multiple DMDs under the “Conception and pregnancy” criterion There is an “i” (for “information”) button next to the “Conception and pregnancy” title that provides an explanation for the statements made in this category. The statements used are:

1- “Pregnancy is not recommended during treatment”: this is explained further as “your MS team may recommend you stop taking a DMD when trying to become pregnant and during pregnancy. If you have a high risk of relapse, your MS team may recommend remaining on treatment.”
2- “You must not become pregnant during treatment”: this is further explained as “Treatment must not be started if you are pregnant or planning to become pregnant in the near future.”

Conception and pregnancy **You must not become pregnant during treatment** Treatment must not be started if you are pregnant or planning to become pregnant in the near future. **Pregnancy is not recommended during treatment** Your MS team may recommend you stop taking a DMD when trying to become pregnant and during pregnancy. If you have a high risk of relapse, your MS team may recommend remaining on treatment.	Pregnancy is not recommended during treatment	You must not become pregnant during treatment	Pregnancy is not recommended during treatment

Screenshot 10 The conception and pregnancy category in the comparison table of the tool

8.3. Objectives

1- To use the Think Aloud techniques to explore the women's opinions and thoughts about the tool's content, interface, navigation, and how useful it is specifically in the context of family planning.

2- To synthesise patients' recommendations to improve the tool in a way that supports women's treatment choices and the management of treatment when planning for pregnancy.

3- To pass these recommendations on to the MS Trust so they can take the suggestions into consideration when updating the tool.

8.4. Results

None of the participants were familiar with the tool, although two had seen it before but a long time ago so they needed to do the think aloud session to be able to feed back about it. "

The data are presented according to the four main areas which were identified from the Think Aloud sessions and illustrated in the following theme mapping figure (see **Error! Reference source not found.**).

1- The women's first impressions during their initial exploration of the tool.
2- The women's commentary on the following elements of the tool:
    a. Instructions
    b. Filters
    c. Comparison and side effects functions
    d. Pregnancy and breastfeeding information
3- The women's comments about the interface.
4- The women's recommendations for improvement.

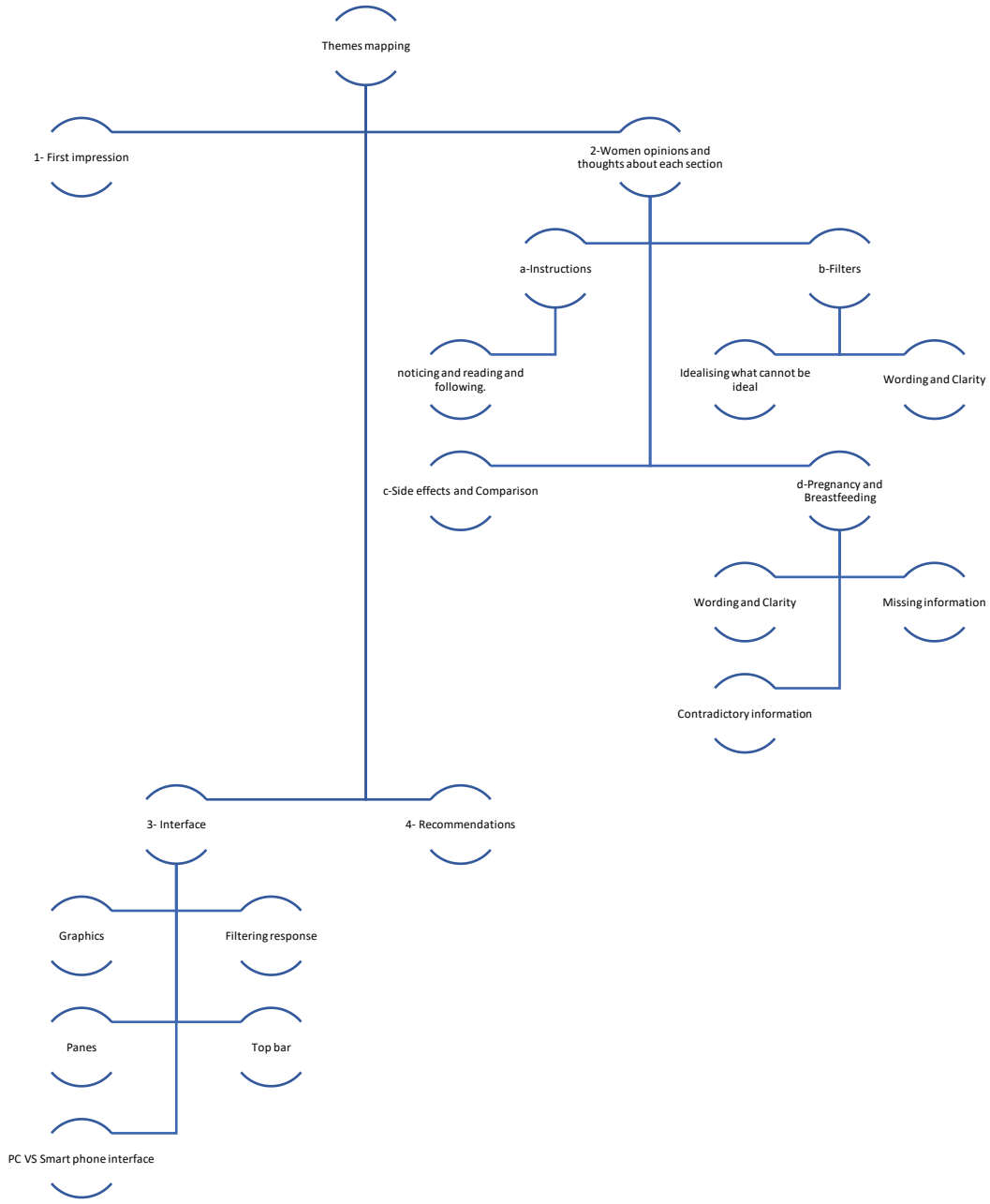


Figure 7 Theme mapping of the women's Think Aloud session on the MS Trust decision aid.

8.4.1. Theme 1. First Impressions

During their initial investigation of the tool, most of the women found the tool confusing due to a lot of information being presented all in one go. This was clear in their body language (cross-looking faces, heads tilted in a questioning way) and in the fact that many of the women performed multiple random up and down scrolls

through the page. A number also verbally expressed confusion by asking for help and instructions from me. As the interviews were video-recorded, this allowed me to not just to view but also review their body language and facial expressions.

P1, a 28-year-old woman, verbally expressed her confusion a few minutes after looking at the first page of the tool:

P1: "I was a little bit confused as to…. where I start"

A few women, however, reported that it was "nicely laid out", "fresh" and "simple":

e.g., P14, a 44-year-old participant: "it's nice it is very nicely laid out."

Only one woman (P13) started with a question rather than expressing an opinion:

P13: "The first thing I'm thinking is, what is a decision aid?"

The term "decision aid" was not mentioned or explained in any of the tool sections. The term was not self-explanatory for P13, which is a fundamental issue that was accordingly identified.

8.4.2. Theme 2. The women's commentary on each section of the tool

While using the tool, the women expressed their thoughts about each section and function they encountered and used. Therefore, this theme branches into sub-themes, organised according to the relevant sections. This then branches further into the main comments the women had about each section.

8.4.2.1. Tool instructions

Noticing, reading, and following the tool instructions

Ten women (9/30) **noticed the instructions section and took the time to read it carefully** before starting to use the tool. This was observed by myself because the video call allowed me to see both their facial expressions and body language, together with their shared screen. Those who took the time to read the instructions stopped by the instructions for a couple of minutes. Some of them read them out

loud while others whispered them. It is clear that those that took the time to do this definitely understood them because they could execute the instructions well afterwards. No time measurements were taken of this as this will vary according to a number of factors, including the effect MS has on cognition and the retaining of information. 12 women (12/30) **noticed the instructions, stopped at them and maybe started to read a couple of words, but then skipped them right away** in order to use the tool. Although most of these women were able to work through the tool without reading all the instructions points, three of the women had to go back and read the instructions because the tool was not self-explanatory to them. Four women (4/30) **did not notice the instructions at all**, directly scrolling down to the body of the tool without stopping at the instructions at all. One of them needed to be directed to them by me and still struggled to understand how to use the tool, even when directed to the instructions box and after having read the instructions. Lastly, two of the women (2/3) **noticed the instructions but expressed that they found it challenging to retain all six instructions in one go due to brain fog and affected memory.** This was in line with the views expressed by them during the interview, where they had difficulties recalling certain events and stopped to find the right word when talking**.** As a result, they instead read the instructions and applied them step by step by scrolling up and down between the body of the tool and the instructions.

8.4.2.2. Filters

The most common comments expressed by the women when using the filter function were categorised into the following sub-themes:

- Idealising what cannot be ideal.
- Wording and clarity

Idealising what cannot be ideal

When answering the filter questions, the women mostly chose the combined options most convenient for them, such as a drug that can be taken less frequently, with fewer hospital visits, together with their preferred route of administration. Due to the fact that all of the women interpreted the filters as questions that all needed to be answered in order to generate a recommended option, and because there is no ideal

drug, many of the women were left with no DMD options that matched their preferences because they had used too many filters. P1 voiced this idea while reading the filter questions:

P1: "How often you want to take the drugs? Like, why would you choose to take a drug several times a week if you had an ideal world?"

This demonstrates the need for compromise when choosing an MS medication. While this was the aim of the tool, this was not successfully achieved because the current design eliminates options instead of ranking the DMD options according to what best fits the preferences inputted into the filters by patients.

Wording and clarity

For many of the women it was not clear what the questions (filters) were for. The questions were not defined as "filters" on the website on the PC version, as opposed to on the smartphone version where these questions are labelled as "filters". The instructions also used the word "criteria" rather than "filters", making it even more confusing and less clear. The instructions currently read: "Select any combination of criteria using check boxes to narrow down the list of drugs displayed." The instructions, however, do not indicate that you can choose more than an option for each filter, that you can skip filters that are not/less important to you, and the fact that you can skip them entirely if you wish. In addition to this, many of the women skipped the instructions or only skim read it. As a result, many them did not understand the purpose of these filter questions and thus asked for clarification from myself about this:

P25: "I'm not quite sure in terms of this [pointing with the cursor at FILTERS]. What this is for?!"

Interviewer: I'll explain more to you, it's more like a shopping interface.

P25: "aaaaahhhhh"

The wording of the filter function was also commented on for being confusing and not getting across the purpose of the tool. The filters use the present tense when asking as if the patient is already using an DMD (for instance, “how do I take the drug?”). This phrasing caused confusion as it assumes that the user is currently using a treatment, when it should be asking about the user’s future treatment preferences:

> *P9, talking about the wording of the filters: “It’s easy for me because I take no drugs currently, so it’s all to do with the future. I think if people take drugs, they might get a little bit confused”.*

It is worth noting that some of the women struggled to answer the question about their MS type. This is because patients are not always aware whether their MS is active or very active to begin with, and there was no category for stable or inactive RRMS, even though people with these MS types could be candidates for switching their DMDs, for instance. The information button that explains and defines what clinically isolated syndrome, active, and very active MS are, was also not easily noticed by the women. In fact, even after reading the explanations, some of them still found it difficult to understand.

P3, for example, viewed herself as having active MS. But when she selected the active filter option, she was surprised that her medication (the one she is currently using) did not come up as an option for active MS. Instead, she found it under the very active MS category. This made her realise that her consultant had diagnosed her as very active rather than active, but according to her, she was unaware of this.

> *P3: “I don’t think that needs to be there [MS type filter] because I picked myself as active, not very active, but clearly my consultant thinks I’m very active, so I mean… yeah, and I don’t even know I am. I don’t know.”*

8.4.2.3. The side effects and comparison functions

Unlike the instructions and the filters, the side effects drop list, and the comparison function were clearer for the women. While a few needed some guidance with the comparison tool, the majority found and used it efficiently. The feedback about these

two functions was quite positive as the women found them “very useful”, “helpful”, and “good”. Some of the women did not like the use of medical jargon such as “lipoatrophy” without an explanation or hyperlinking, however, and others stated that the serious side effects, such as risk of developing PML, put them off and scared them.

8.4.2.4. Pregnancy and breastfeeding information

The women’s comments about the pregnancy and breastfeeding part of the tool were categorised into the following sub-themes:

- Recommendations: wording and strength
- Contradictory recommendations
- Missing information

Recommendations: wording and the strength of the given advice

The women generally thought that the conception and pregnancy recommendations in the comparison table were not clear enough. The two available recommendations are:

- You must not become pregnant during treatment.

OR

- Pregnancy is not recommended during treatment.

When comparing the two phrases, some of the women found the first statement to be very clear and firm in a preventative clear manner, but provided minimal hope and gave them more to worry about due to the lack of a given time frame. In contrast, they felt that the second statement is less firm but not clear enough about the consequences. Both of the phrases lack any kind of time frame, which was important to the participants in order to give them reassurance, decrease their worries, and help those with a tight fertility window with their decision.

P17, a 38-year-old woman, expressed that reading these phrases panicked her. She thus suggested that a time frame should be added:

P17: "would probably want a timeline in there to say when I could have a baby because it would probably panic me at the moment."

Similarly, P11 mentioned how the inclusion of a time frame is vital for a person like her, considering her age and circumstances (36-years-old and not currently in a long-term relationship):

P11, "Pregnancy is not recommended during treatment, but it doesn't give you any any idea on how long you have to wait? Where is actually someone in who's my kind of age would want to know that? Because if it was not recommended, but then you've got to wait five years afterwards. Someone in my position would, therefore, not consider that an option".

In response to being asked about the clarity of the pregnancy recommendations, P30 also expressed that she felt that the phrase "not recommended" is not clear as "must not":

P30: "I think for… 'you must not become pregnant', yes…. but that [pointing to 'pregnancy is not recommended during treatment'] is not pretty clear."

The women thus recommend the use of clearer phrasing and the addition of a suggested time frame.

Contradictory recommendations

The women who had used medications during their pregnancies found it concerning to read that the medication they had been told to use during pregnancy is not recommended for use during pregnancy. P7, for instance, noted that according to the tool, pregnancy is not recommended during the use of copaxone, which

contradicts her HCP's recommendations when she had her two children while using copaxone a few years ago. Although P7 had already given birth to healthy children, reading this left her concerned:

> P7*:* "there's always said the same thing to me, that copaxone *y*ou can stay on it during *like trying to get pregnant on, you can stay on it while you're pregnant, so this is this something completely different... So yeah, that's a bit concerning..."*

This contradiction between the tool's restrictive recommendations (which follow exactly what is written in the Summaries of Product Characteristics SPC) and real-time healthcare practices which follow updated primary literature and reports and are based on weighing up the benefits versus risks of any treatment, left the women confused and with more questions, rather than the tool being a place for them to find answers and reassurance.

Missing information

The women also expressed that because these recommendations are very brief and to the point, they would not help them to make a decision, especially if family planning is a priority. The following information was not covered by the tool: medication management, the time needed for a treatment to work, the time needed for a treatment to get flushed out of the system, guidance about what to do if a pregnancy accidently occurred while using a treatment and what implications this would have for their health and the health of their developing foetus, as well as breastfeeding recommendations.

P11, a 36-year-old well-informed participant (who had a comprehensive DMD/family plan) found that the information about conception and pregnancy missed vital information about what to do if she accidentally got pregnant while using a treatment:

> P11*:* "Basically what I want to know is if I accidentally got pregnant on when taking either these drugs, what are you meant to do?"

P20 similarly found the conception/pregnancy section to be too general and missing a lot of the important information needed to make DMD/family planning decisions:

> *P20: "I don't think this information is kind of made … to help you decide if you're planning to start a family, or to have another child cause there is no much information about pregnancy and conception, there is much more information for everything else"*

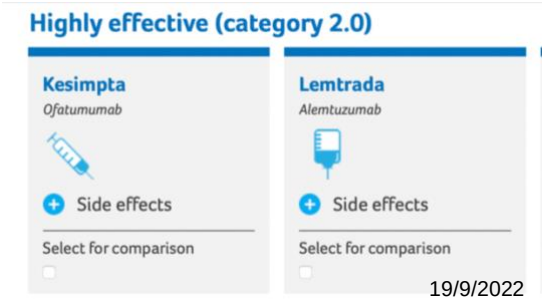
8.4.3. Theme 3. The interface

The women's main comments about the tool's interface were categorised into the following sub-themes:

- Infographics and colours
- Automatic filtering response
- Panes
- Top bar
- PC vs smartphone version differences

8.4.3.1. Graphics (infographics and colours)

While most of the women liked the colours and graphics, especially the ones representing the route of administration (pictures of a pill, a syringe, and a drip), some found it quite tricky to differentiate between the syringe and the drip using only the graphics.



Screenshot 11 Graphics of both the syringe and IV drip.

One woman's toddler, who was sitting on her lap during the interview, commented "Too blue!!" while pointing at the screen. This comment matched P5's opinion that the monochrome colour scheme does not help to distinguish the different drug efficacies. She thus suggested having each category in a different colour. Some women also commented on the grey colour of the instructions box, which they felt did not stand out enough because of the colour choice.

8.4.3.2. Automatic filtering response

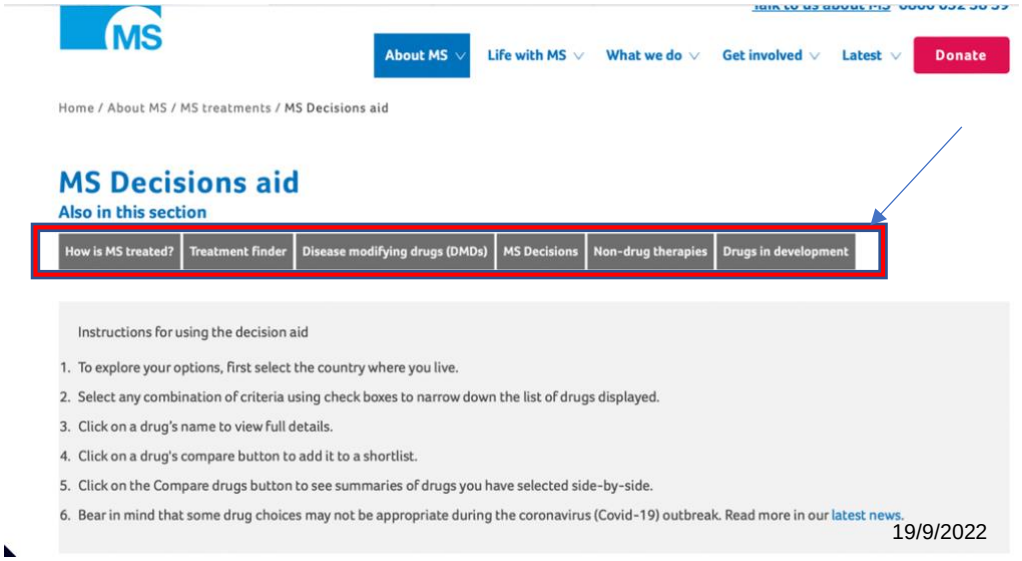
When selecting an option in the filter tool, the tool immediately applies the filter and refreshes the page to show the remaining filtered down DMD options, before the user has finished making all of their selections. This proved to be confusing for some of the women, who would have preferred it if they could have selected all of the filters they wanted to first, before the recommended options then appear at the end.

8.4.3.3. Panes

In the comparison table, the first column and the first row are not frozen. For users who might suffer from brain fog and memory problems such as MS patients, it was therefore a bit challenging for the women to remember which drug the displayed information related to. This meant that the women had to keep scrolling up and down the page in order to remind themselves which drug was being discussed. Some of the women verbally expressed their annoyance while others did so via confused or frustrated facial expressions.

8.4.3.4. Top bar

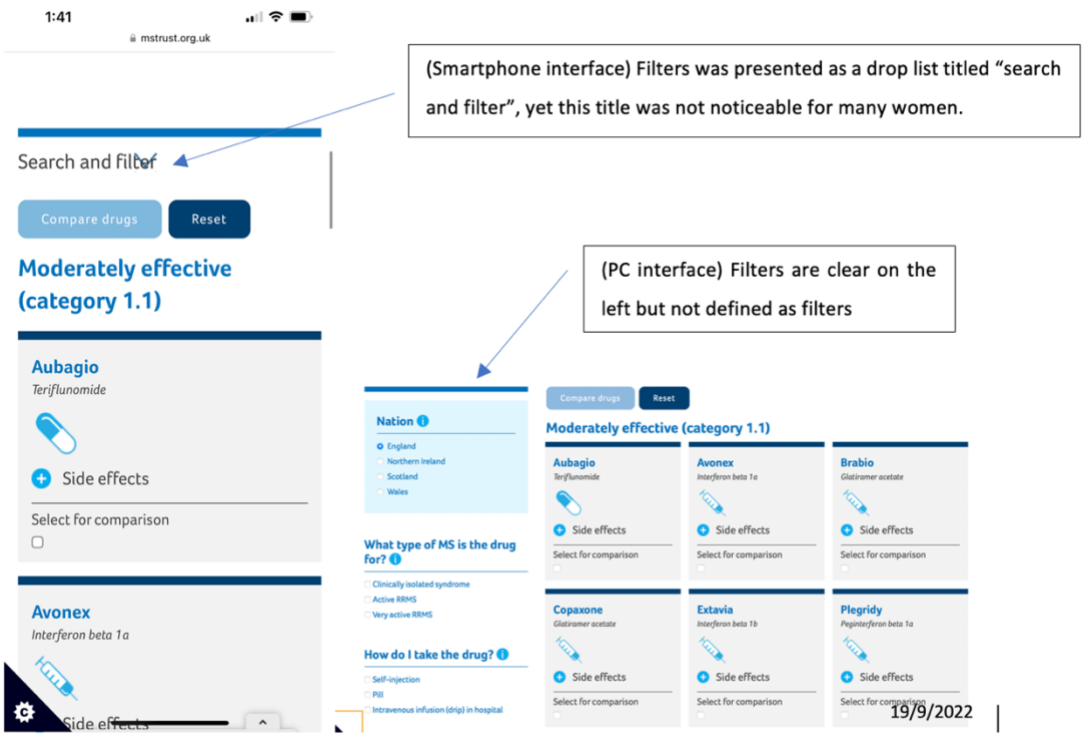
Some of the women were also confused by the top bar which takes you completely out of the tool because they thought that it was part of what needed to be explored.



Screenshot 12 The top bar which is not part of the tool

8.4.3.5. PC vs smartphone interface differences

The interface of the filter tool in the PC version is slightly different from the way it looks in the smartphone version. The main difference that affected the ease of use was the way the filters were presented. The women who used their phones to navigate through the tool found it harder to find the filters in the first place, even though it was labelled with the title “search and filter” on the drop list (see Screenshot 12). In comparison, the filter tool was easier to find in the PC version. However, the fact that this is not labelled as “filters” confused some of the women. When I directed smartphone users to find filters, they had the same comments as the other women who used their laptops about the idealising, wording, and clarity issues which were discussed earlier.



Screenshot 13 A comparison of the differences between the mobile interface and the laptop interface

8.4.4. Theme 4. The women's recommendations

The women had a number of very insightful ideas for how to improve the tool to match their needs and help them in the decision-making process. These recommendations were conveyed to the MS Trust who considered some of them in their first phase of the tool updating project, and will look at the rest during the coming updating phases. The following sections outline their recommendations for each area of the tool:

8.4.4.1. Instructions section

1- Replacing the written instructions with an automated tutorial before you begin using the tool (something similar to the tutorials you get when using a new app which take you on a tour of the app and describe and define every tab and its function).

2- Adding the option of having the instructions read to you out loud as an accessibility function.
3- Being given the instructions in a pre-recorded video that explains how to use the tool and its various functions.
4- Having the instructions on a separate page first so that you first need to read them before clicking next to take you to the tool. This would decrease the amount of information provided in one go, thereby decreasing the distractions and making sure that users notice the instructions and take the time to read them before moving on to the tool.

8.4.4.2. Filters

1- Labelling the filter options as “Filters” in the PC version, where the filters are currently represented as questions at the side and are not defined by their use.
2- Adding a pregnancy/breastfeeding filter.
3- Adding a checkbox after each question which users can tick if that filter is not that important or relevant to them. Alternatively, making it clear in the instructions that you DO NOT need to use all of the filters. This will give users some more flexibility and decrease the probability of ending up with no options.
4- Using a quiz-like interface to select the filters, where each question is presented separately one after the other. This will break down the large amounts of information presented all on one page into separate pages, which would better accommodate users suffering from brain fog and focus and memory problems by helping them to understand each bit separately.
5- Re-wording the filter questions so that they use the future rather than the present tense in order to avoid confusing those who are currently using DMDs and exploring their switching options, e.g., “How would you prefer to take the drug?” rather than “How do I take the drug?”.

8.4.4.3. The side effects and comparison functions

1- A “learn more” tab for almost piece of information given in the comparison table that hyperlinks to other pages within the website which provide more information about the section. For instance, a “learn more” tab for the side effects information given which explains more about the rare side effects and

the other side effects which are expected to ease away with time, as well as more about what to do if you experience any of the more serious side effects. Similarly, a “learn more” tab that explains elements such as what the different efficacies mean and what the year a drug was introduced into the NHS means for the patient, i.e., whether the newer a drug is, the better, and vice versa.

2- A lay language explanation of technical jargon and medical terms such as “lipoatrophy”.
3- Adding information about the monitoring requirements for the rare and serious side effects in the comparison table.
4- Adding a filter asking about the user’s preferred medication storage requirements, as this is one of the most important factors for some patients when deciding on a treatment, especially for those who travel a lot, for example, and thus would not want to carry a cool bag around for medications that require refrigeration.

8.4.4.4. Pregnancy and breastfeeding information

1- Having a dedicated separate tool that helps with the family planning decision.
2- If the same DMD decisions tool continues to be used, adding family plans as a filter.
3- More information about the required wash-out period before conception, the risks to the foetus when exposed to treatment, and what to do if you accidently get pregnant while using a treatment, as well as more in-depth breastfeeding recommendations in the comparison table and for the pregnancy and conception recommendations. This could be a hyperlink to another page about DMD management during the periods of conception, pregnancy, and breastfeeding.
4- Adding a time frame to each recommendation, e.g., rather than just “pregnancy is not recommended”, which is a phrase that holds no hope or promise, having a statement such as “pregnancy is not recommended during treatment and for X amount of time after stopping treatment”.
5- Adding the phrase “ask your HCP for more information” to the recommendations for the DMDs which require complicated treatment

management to decrease the level of anxiety a user may feel and to give them some hope for an available solution.

8.4.4.5. Other (Miscellaneous)

1- Using a freeze pane function in the comparison table for the row which details the drugs names and the column which details the comparison criteria for easier navigation.
2- Clearer infographics for a drug's route of administration, especially for the syringe and drip graphics.
3- Using different colours for the different medication efficacy categories.
4- Using percentages for the different efficacy levels instead of the more vague terms 'moderate', 'high', and 'very high' categories.

8.5. Discussion

The Think Aloud sessions with the women highlighted a number of areas of potential development in the tool, specifically in terms of helping users with their treatment choices in relation to family planning.

While the women found the tool useful when choosing a DMD more generally, it was less useful in relation to family planning decisions as it can confuse and raise more questions rather than providing answers and reassurance. This was due to the inclusion of some outdated information and other restrictive recommendations which contradicted what their healthcare teams had explained to them after weighing up the risks and benefits of a treatment. Many treatments that are not yet licensed are now increasingly being used during pregnancy with specific management plans in place. This may have some legal implications for the website though if it was to declare a drug as safe for use during pregnancy. However, it should be possible to reword and update the pregnancy and conception section of the tool so that it gives as much information as possible in order to also support the advice given to users by HCPs (which is usually supported by new developments in the literature on the subject, as well as stemming from real practice and an assessment of a patient's individual risks and benefits), alongside the existing SPC recommendations.

Some of the women also asked for more information to be included about family planning and DMD management, such as a timeline of when to stop treatment and contraception and when to start trying to conceive. This was particularly important to those with a tight fertility window due to their age, as knowing the length of time they need to wait after stopping treatment and before they try to safely conceive will help these women to plan ahead, especially in relation to their treatment choices (for example, avoiding treatments that require a long wait before trying to conceive). They also wanted to know what course of action to take if they accidentally fell pregnant while on a treatment, as well as what to expect. This is particularly important given that a 2018 report from Public Health England found that 45% of pregnancies in Britain appeared to be unplanned, with one third of births being unplanned or ambivalent. While there is no data about the prevalence or rate of unplanned pregnancies for women with MS, Smith et al. conducted an observational chart review to identify risk factors for unplanned pregnancy in order to identify a target population for family planning counselling (211). They found that 32% of the 45 patients in their sample had an unplanned pregnancy, of which 16/20 were exposed to DMDs during pregnancy. Moreover, the proportion of those who had received family planning counselling was lower for the unplanned pregnancies. Both young age and being unmarried were found to be the main risk factors for unplanned pregnancies, which explains why these women did not receive detailed family planning counselling in the first place. This highlights the importance of both/either family planning counselling being offered to women with MS by HCPs and/or information being provided to these women about what to expect when unplanned pregnancies happen during DMD use, such as through DAs like the MS Trust tool. This would hopefully help to decrease DMD-exposed unplanned pregnancies as much as possible.

The women also commented on the wording and the strength of the recommendations given, wanting clearer and more comprehensive statements rather than summative ambiguous ones. This thesis therefore proposes that the DMD recommendations be further categorised into four instead of only two groups:

- Safe and licensed to be continued during pregnancy.
- Safe to continue during pregnancy but NOT licensed.

- Not recommended (can be used after weighing up the risks vs the benefits of this with a HCP and with proper management).
- Contraindicated (teratogenic or harmful to the foetus).

The women also shared insightful suggestions for further changes which could be made to the tool's interface and presentation to reflect their own needs. Cognitive issues such as brain fog and memory difficulties, such as difficulty retaining large amounts of information, were highlighted during the sessions. This was evidenced in the way in which some of the women struggled with reading and retaining the lengthy instructions and getting confused due to the bulky home page because of the many elements available to read and work through in one go. The women's recommendations thus included starting with an automated tutorial, video, tutorial, or the instructions being read out. They also suggested that a segmented quiz-like interface for the DMD filter tool would be easier to use as this would break down the large amounts of information given into smaller portions that can be worked through one by one.

Lastly, the women expressed the importance of family planning for them and how this can play a major role in their DMD choice. As this needs to be considered as early as possible when choosing a DMD, they suggested adding this as a filter option in the current tool or even creating a separate tool for those considering family planning.

8.6. Conclusion

Decision aids are very important for helping women with MS to make shared decisions about their treatments and family planning. The MS Trust DMD decision tool is an excellent tool that helps women with this. However, it is not currently possible to filter the DMDs according to a user's family plans. The tool's content also more generally needs updating, especially in relation to the "Pregnancy and conception" section. In particular, the recommendations need to be reworded to provide clearer recommendations which do not contradict HCP advice. The tool's interface also needs to be updated to meet the users' cognitive needs.

Chapter 9. Perspectives of Healthcare Providers (HCPs) on the current practices for supporting women with MS in their reproductive and treatment decisions

9.1. Introduction

The previous chapters (see Chapter 6 and Chapter 7) have detailed how complex the DMD decision-making process is for women with MS, particularly if family planning decisions are included in this process. They also showed how underexplored these kinds of decisions are. Both decisions (treatment choice and family plan) are affected by both MS-related and non-MS-related factors. This decision-making process can be helped through different forms of support, such as reading the information provided on leaflets or websites, talking with other women with MS on forums, or even going to group counselling or workshops. The interviews also highlighted the importance of the role healthcare professionals (HCPs) play in the decision process, especially in terms of providing women with information which they struggle to access elsewhere The women interviewed (see Chapter 6) named their MS consultants, MS nurses, and pharmacists as the professional kind of support they received during the process. HCPs are thus an important information source for patients. Combining both their expertise and a patient's preferences, they lay out the most suitable treatment options for patients and help them navigate through them. HCPs are also the first point of contact from which patients can then be referred to other professionals that can support their other needs (psychotherapy, fertility clinics, etc). Therefore, it was important to also hear from HCPs and look at the process from their point of view in order to shed light on the challenges they face and how this could have an effect on the quality of care received by their patients and the life decisions they consequently make. This will thus help to identify areas to improve.

9.2. Aim and objectives.

The overarching aim of this thesis is to improve the holistic DMD and family planning decision-making experience for women with MS.

In this study, the main objectives are as follows:

1- To describe the perceived role HCPs play when supporting women with MS in their decisions about treatments and family planning.
2- To better understand the process of decision, and the position of such an area in the structure of healthcare.
3- To identify the resources available for both patients and HCPs which is specially catered towards women of childbearing age with MS who are choosing their DMDs.
4- To identify the challenges HCPs face during the treatment choice and family planning decision making process.

9.3. Findings

I was able to interview eight HCPs in total instead of fifteen. This included five Neurology consultants with a subspecialty or interest in MS, two MS nurses, and one MS-specialised pharmacist. This study thus explored the practices followed in four different NHS trusts in England, one in Ireland, and one in Scotland. Although trusts may vary in the healthcare systems offered, their area coverage, and the number of MS patients treated, and that these differences could indeed affect the quality of care provided, the aim of this study was to gain an overview of the main MS practices implemented across different areas of the UK, rather than comparing the services and facilities of different trusts. However, the impact of these differences may have on patients will still be highlighted where relevant.

Of the HCPs interviewed, three (a consultant, a pharmacist, and a nurse) worked for the same trust. This trust runs a pioneering service dedicated to providing family planning support for people with MS. This was thus done to better understand how this service works and explore the role of each of the HCPs in the family planning pathway. This trust will be referred to as **(Trust A).**

Table 8. Sample demographics (Healthcare Providers)

Participants	MS-specialised Pharmacist Ph 1 *	Consultant C 1	Consultant C 2 *	MS Nurse N 1 *	MS Nurse N 2	Consultant C 3	Consultant C 4	Consultant C 5
Geographical location of trust	England	England	England	England	England	England	Scotland	Ireland
Existence of a dedicated service for family planning	YES	NO	YES	YES	NO	NO	NO	NO

HCP: Healthcare Provider; Ph: Pharmacist; C: Consultant; N: Nurse (Ph1, C2, and N1 work in the same trust that provides the family planning service), *: work at Trust A.

9.3.1. Themes

To understand the process from a HCP perspective, the participants were interviewed about four fundamental areas. Sets of themes were inductively identified under each of these areas:

1- Current role of each HCP
2- Resources
3- Decision making process
4- Challenges

These themes are expressed in both Figure 8 and Figure 11.

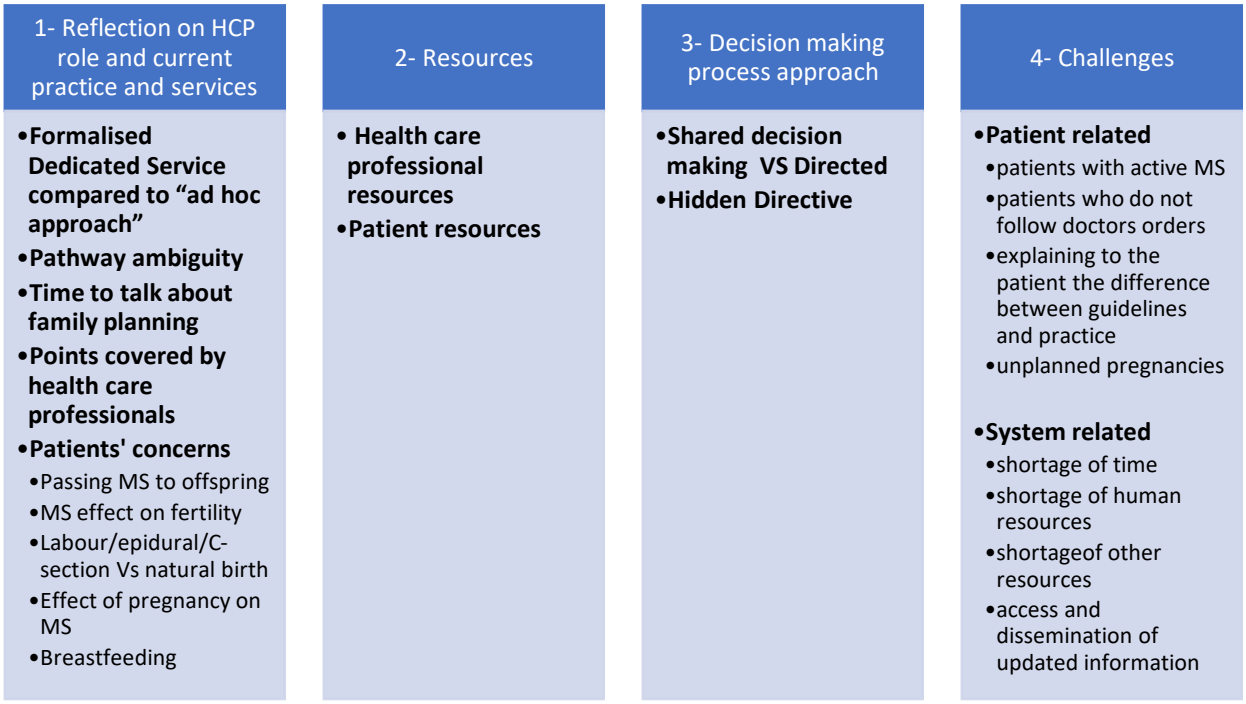


Figure 8 Themes inductively identified within the decision-making experience from a HCP perspective under the four main areas of exploration.

9.3.1.1. Reflections on HCP role and current practice and available services

The interviews were begun with an open question about the HCP's role and the current practices they employ to support women with MS when they are making decisions about their DMDs and family plans. The HCPs identified five main themes which were then explored in depth with them during the interviews:

9.3.1.1.1. A formalised dedicated service compared to an "ad hoc approach".

One of the six trusts (Trust A) included in the study sample had a specialised service dedicated to helping women with MS with their DMD choice decisions and family planning decisions. None of the other HCPs interviewed either had such a formalised service or could even identify another trust that provides such a service. Instead, they reported that such a service was offered more on an "ad hoc", informal basis within consultations. The overall impression given by the interviews with the HCPs was that there is a lack of a consistent service for this purpose, meaning that the

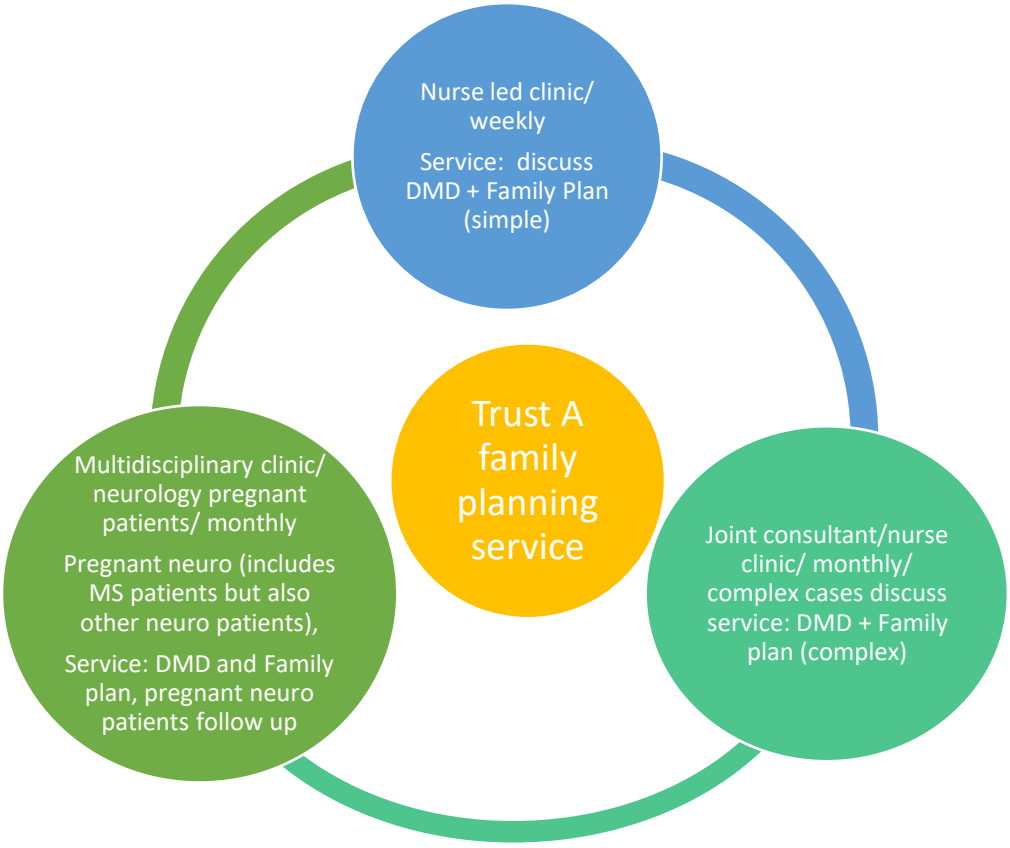
extent and type of care offered to MS patients is reliant on where patients live (in terms of their likelihood of being able to access a coherent healthcare package) and the ‘goodwill’ and individual interests of healthcare staff.

Trust A (dedicated MS service)

The three HCPs (Ph1, C2, and N1) who work at Trust A talked about this service in detail. There is a nurse-led clinic that gets run weekly by an MS-specialised nurse to discuss and set out a plan and even an alternative plan for a patient’s DMD options in relation to their family plans. These options are suggested by the MS consultant. A joint consultant/nurse clinic also gets run monthly to look at the more complex cases that needs further investigation and adjustment. This is in addition to a multidisciplinary clinic staffed by a Neurology consultant, an Obstetrics consultant, a midwife, and an MS nurse, that runs monthly to look after neurology patients who are currently pregnant or considering their family plans. The latter clinic is more general than the former two, as HCPs will see any neurological patients who are pregnant or planning pregnancy (epilepsy, MS, brain tumours, etc.). The team looks at all of the medications a patient is on and how best to manage them (titrate, stop, or switch). This is followed up by anomaly scans, especially for those with high-risk pregnancies, as well as the HCPs answering any patient questions. An illustration that details the specialized services for family planning and medication choice and management within Trust A as described by HCPs working there is presented in Figure 8.

C2, the lead of the Trust A family planning pathway, stated how her interest in helping with family planning and DMD choices was formalised into a dedicated service:

> *C2: "I've always been interested in how to support them, and that's recently been formalised that I'm now sort of in charge of the pathway."*



Key: DMD: Disease modifying drugs

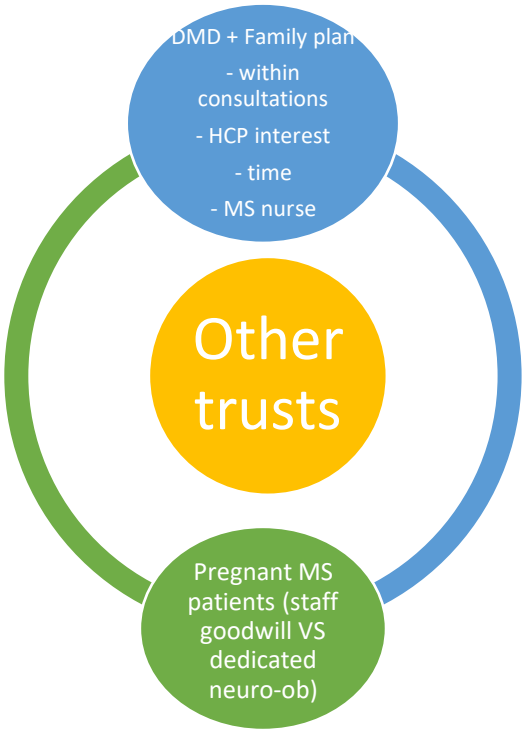
Figure 9 Illustration of the Trust A specialized disease modifying drugs/family planning services.

The other trusts at a glimpse

In comparison, in the other trusts, the current practice is to provide help with family planning and DMD choices in a non-formalised manner. These services are thus mainly embedded within the regular patient consultation appointments, see Figure 10. C3, for example, talked about how informal the DMD choice-family planning support service is at their trust:

> *C3: "it's embedded within the services we provide. There's no custom service for it"*

This approach might be affected by the level of investment the HCP has in this area, as well as the average consultation times and frequency at their trust. It may also be influenced by the HCP's own judgement about the childbearing potential of woman with MS. This will be discussed in greater depth later on in this chapter. When it comes to pregnant MS patients, some of these trusts will thus support them in a more informal manner that largely depends on the goodwill of the staff who see pregnant MS patients and support them in a "friendly" fashion, while other trusts may be fortunate enough to have a specialised neurology obstetrician that formally looks after those patients. This thus creates non-standardised care and variability across the trusts. Indeed, the provision of extra appointments for pregnant women is not the general standard of care according to the consultants interviewed. Due to the lack of time these HCPs have, only patients at risk of relapse who have switched between certain DMDs before pregnancy, or those labelled as having a high-risk pregnancy, (unplanned pregnancy while on unsafe medication) will be offered scarce resources such as extra appointments with MS nurses during their pregnancy and anomaly scans.



Key: DMD: Disease modifying drugs, HCP: health care professional, MS: multiple sclerosis

Figure 10 Illustration of other trusts' disease modifying drugs /family planning services.

9.3.1.1.2. Pathway ambiguity

Trust A

At Trust A, the roles of each HCP as well as the objectives of each clinic and pathway are all very clear, especially when it comes to referrals. A consultant will discuss the most appropriate DMD options with a patient and depending on their current family plans and the complexity of their case, they will be either referred to the nurse-led family planning clinic for simple cases or to the specialised family planning consultant-led clinic to discuss this further. Trust A also has two MS-specialised pharmacists that work side by side with the consultants and nurses to provide care. However, their role is more in the background and non-patient-facing, with their focus mainly being on checking patients for their eligibility for a particular DMD suggested by the consultant, ordering the lab work related to that, educating patients about the DMD use, asking about their family plans, and dealing with contraception. As the pharmacists are not tasked with discussing family planning and DMD choices in detail, they will instead refer any patient who expresses the wish to start a family to one of the family planning clinics, especially if those family plans are not compatible with the suggested DMD options. Ph1, a pharmacist for Trust A, talked about referring a patient to the nurse-led clinic when she showed interest in family planning:

> *Ph1: "... Whenever you're trying to conceive....and then that's when I mention the specialised nurse [nurse name] and that pathway.".*

The other trusts

In contrast, the trusts which lack this formalisation in their family planning service present an ambiguous pathway for dealing with family planning and medication management. Patients are either referred to an MS nurse to talk with if needed, and sometimes to a consultant, while others could be seen by another consultant who has an interest in this area of medicine and thus will talk about family planning with a patient at length. This is thus a lengthy unclear process. However, this could also

be due to the novelty of this area of care, as prior to the development of these new treatments, treatment management was simpler and required less planning. C3, in particular, expressed how the unclear the family planning pathway is:

C3: "I will have a general discussion with the patients. I will talk about pregnancy. I'll refer them to the MS Decisions website. They'll have an opportunity to go on that and look at the drugs. They'll get contacted by a nurse. They'll go through the conversation with the nurse who will answer any questions. Sometimes they'll come back to me."

9.3.1.1.3. Time to talk with women about family planning.

All the HCPs expressed the importance of choosing the right time to talk about family planning and its impact on women's decisions. Within this theme, the HCPs talked about four main sub-themes, which were identified as follows:

Patient acceptance and mental readiness at the time of the conversation: The HCPs talked about different and patient-specific the level of acceptance after diagnosis is from one woman to another. During the diagnosis consultation, the conversation may be dominated by denial and thus prevent any further information uptake. The HCPs expressed that they only seek to talk about family planning when they see that a woman is ready to hear and take in the information.

Making use of the longer diagnosis appointment: The HCPs reported that diagnosis appointments are often longer than other clinics across all of the trusts, varying from 30-45 minutes. Despite this, however, the HCPs reported that there still may not be enough time to address the issue of DMD choices and treatment management in relation to family plans in any detail. Some of the HCPs stated that they would take advantage of the longer appointment to discuss family planning and DMD choices, but that this is also dictated by a patient's level of acceptance of the diagnosis and their readiness to absorb more information at that point. This

reinforces and confirms the importance of the previous sub-theme (mental readiness).

Indeed, C2 (a consultant from Trust A) talked about the importance of mindset and how it can be difficult to talk about family planning during a diagnosis consultation because of the different levels of patient acceptance:

C2: "if I can see the patient is, you know, finding it very emotional, difficult, even accepting they have a condition, I may leave it [meaning the family planning conversation]."

Similarly, C5, a consultant from a trust with conventional services, talked about importance of patient readiness before discussing treatment and family planning. However, they also explained that the next appointment would be with the nurse, meaning that if the patient was not ready for this conversation during the diagnosis appointment, this is a missed opportunity to talk with patients about family planning:

Interviewer: "breaking the news of having MS itself could be too much to handle for some patients. So how do you feel adding the bit of family planning to that in that consultation? What's the effect usually on patients?"

C5: "The way the service runs here is that I have a conversation with them and then they'll come up with in the next sort of week or two to meet the MS nurses who will go through it all again. It's individual. Some people are well ready […] people are not so ready, and you sort of pick that up….you should go along, but I do try to have a little bit of a conversation [….]. So, I suppose an ideal world. It might be two separate appointments. UM, telling some of them they have MS and then treatments. But actually, lots of people are ready to move on and ready to go, right?"

Talking about family planning when starting on DMDs: It was noticeable that all of the HCPs highlighted the importance of talking about family plans in the context of patients starting DMDs. The safety consideration is a top priority for them that

necessitates having this discussion with patients. The importance of having a discussion about family planning with women who are not starting DMDs was only mentioned by one of the HCPs after some probing. C6, for example, described a patient starting a DMD as “the trigger” to talk about family planning, and thus being less proactive with patients who are not starting a DMD:

C6: “No, I think if somebody if somebody wants to talk about talk to us about pregnancy, we would go through all of that with them. We talk about what happens during pregnancy, what happens after pregnancy. We talk about breastfeeding etc. I think prescribing medication is often the sort of trigger to have that conversation. But if somebody is thinking of starting a family, they'll often bring it up… So, some of them, will, some of them won't.”

C3 likewise mentioned medication as one of the most important factors that push HCPs to prioritise the family planning talk:

C3: “if we're talking about prescribing any medication. We would have that conversation.”

The childbearing potential and social set-up of a patient: The HCPs also mentioned age and social set-up as a factor that might push them to bring up the topic of family planning sooner rather than later. For example, a woman of childbearing age being in a long-term relationship would cause HCPs to bring this topic up earlier:

C3: “I guess the first thing is to understand where they are with family planning. So, before anything really will sort of make inquiries about their social set up, who they live with, how many children they have. If they have children, if they want more children”.

However, HCPs such as Ph1 also highlighted that it is very important to remember that circumstances can change between consultations and that it is therefore important for HCPs to be proactive in order to pick up on these changes:

Ph1: "I know you don't want babies at the moment, but you know your circumstances might change over the years, and therefore it's important to be proactive."

9.3.1.1.4. The variability of the points covered by HCPs during family planning discussions

When asked about the main points that they make sure to cover during this discussion, all the HCPs mentioned the compatibility of DMDs with family planning. This confirms the importance given to the third theme (talking about family planning when starting on DMDs) by HCPs.

All of the other points mentioned by the HCPs when interviewed varied from one HCP to another, despite the importance placed on these topics by the women when they were interviewed (see Chapter 6). These topics include wash-out periods, breastfeeding, contraception, fertility, labour and delivery, and the postpartum period. The lack of standardisation across the UK about the topics which need to be covered means that not all patients will be given a full picture of the topic, especially if they did not actively ask about certain topics because of their dependence on other information resources, or because they simply assume that MS will not affect their family plans.

This variability between HCPs was also not limited to the topics mentioned earlier, but also in the recommendations made by the HCPs, especially around areas of controversy in the existing literature. For example, the lack of consensus as to whether breast feeding offers women protection against MS relapses in the postpartum period, is not routinely mentioned to patients. This can create confusion for patients when receiving conflicting advice from different HCPs, even within the same trust and within the same period of time. A situation similar to this was recounted by one of the women with MS in the other study (see Chapter 6)

Fertility is not affected by MS, however having children is made complicated by the medications used to control MS. These two key pieces of information are very important for better MS and pregnancy outcomes. Notably, these are points that C2 (the head of the family planning service pathway at Trust A) makes sure to convey to their patients during consultations. This also forms the foundation of Trust A's services:

C2, “MS doesn't affect fertility. UM, that they are very much able to get pregnant. It's very much about getting the disease well in control and helping them choose a path that allows the MS to be relatively well treated."

In contrast, the HCPs from the other trusts that lack the same formalised service, did not emphasise these points clearly enough, even though some of them mentioned one of them or talked around the concepts.

9.3.1.1.5. Concerns MS patients have according to HCPs

In most trusts, the family planning conversation only happens later when patients are expected to have had the time to read and know more about their condition. Despite this, the HCPs reported that patients still worry about the following issues:

The effect of MS on fertility and the passing of MS on to offspring: although these concerns have well-established answers in the existing literature and can be readily found in different online resources, for instance, the HCPs reported that these questions are still at the top of the list of what female patients ask about. This suggests that patients may bring this up as a way of seeking professional reassurance from an HCP, rather than because they could not find answers to these questions themselves online.

Labour/epidural/C-section vs natural birth: while these obstetric concerns are also well-documented in the literature, it appears that patients still worry about this issue according to the HCPs.

The effect of pregnancy on MS: although it is well known now that pregnancy does not increase the risk of long-term disability and that the risk of relapse decreases during pregnancy, sometimes relapses during pregnancy do happen for women with highly active MS (38). This risk, even if small, still concerns many women. These fears are made worse by the highly variable nature of the disease.

Breastfeeding: this remains one of the top concerns women with MS have when they talk with their HCPs about their family plans and treatment options according to the HCPs interviewed. It also remains an area of controversy in the literature, however, which explains why women still worry and ask about this.

C4 listed some of her patients' concerns in the interview:

> *C4: "they worry about passing MS, they worry about fertility...issues with IVF...miscarriages...impact of being pregnant on their long-term MS.";*
>
> *"they're often really worried about the labour and stuff"*

9.3.1.2. Resources for helping patients with DMD choices and family planning.

In this section, resources that help women with MS decide are branched into two main branches:

- The recourses HCPs provide for women
- The resources available for HCPs to help them with the decision

9.3.1.2.1. The resources HCPs provide to patients to help them with their decisions

Trust-specific resources

Only Trust A has their own resources which are prepared by their HCPs and cater specifically to the needs of their services. These resources are sent to patients via email prior to family planning service clinics to prepare them for the discussion. HCPs will then discuss a patient's DMD options afterwards during the clinic and answer any questions patients might have before finally

reaching an informed shared decision about a patient's medication choices and family plans. There is a separate PowerPoint presentation for each DMD, and patients will receive the presentations of the DMDs they are eligible for, as per their consultant's order. For example, N1 from Trust A talked about their trust-prepared resources:

> *N1: "So the separate ones for the medications and then ordering include a slide or two depending on which drug it is about planning and the do's and don'ts. Sort of pregnancy. Sort of breastfeeding."*

The HCPs from the other trusts did not report using any specific resources or handouts prepared by their own trust team that can help patients with the joint decision of family planning and medication management. N2, for example, talked about their lack of trust-prepared resources:

> *N2: "we don't have specific resource material, really that is designed from our centre"*

Other resources (HCPs, charity websites, scientific articles)

All of the trusts (including Trust A) used the resources (DMD booklets, websites) produced by charity organisations such as the MS Society and the MS Trust to provide patients with some more information in a lay language. Although the charity resources offer information about individual DMDs and information about pregnancy and breastfeeding, they do not, however, provide comprehensive information about DMD management and treatment timelines when considering pregnancy:

> *C4: "there's some information on MS Society and MS Trust... on DMT generally, we always direct those patients to those two for their DMT reading, There's a bit on pregnancy."*

Some of the HCPs also reported handing out the UK consensus guidelines and other scientific articles about specific topics to those patients who want more specialised data and statistics:

N1: "if they want some more detailed information, I'll always also send the consensus guideline."

This practice highlights the scarcity of available resources and increases the risk of misunderstanding or the misinterpretation of information by patients because of the very scientific language such articles use. In relation to this, C3 talked about an ongoing trust project of translating these guidelines into simple lay language so that they can be easily understood by patients. This would certainly be a step towards a better practice. C5 similarly stated that they believe that professional conversations with their healthcare team is the main resource that patients rely on:

C5: "they are in general very much guided by us."

This was certainly evidenced to an extent by the interviews with the women with MS. However, the interviews also demonstrated that the women sometimes also trusted and valued the experiences of other people with MS more than practitioners' scientific recommendations.

9.3.1.2.2. Resources available for HCPs to help them guide the decision-making process

Trust A have their own HCP-directed resources which aim to help HCPs guide patients with their DMD management in relation to family planning. These resources provide the HCPs with information about key topics such as the transitional period when switching DMDs before conception, the wash-out periods for different DMDs, and when exactly patients need to stop using contraception and start trying to conceive. These resources are all easily accessible to them alongside neat, organised schedules prepared for them

by their MS-specialised pharmacists with reference to the most up-to-date primary literature.

In contrast, when HCPs from the other trusts were asked about the resources provided for them, some of the HCPs mentioned the lack of resources directed towards them as HCPs when helping patients with DMD management for the purpose of family planning. They also expressed that being up-to-date in this area is quite challenging as recommendations change quickly, so having specialised easily-accessible resources would be very helpful. C5, for example, expressed how challenging staying up-to-date and accessing new information is for them:

> *C5: "some information about drug safety in pregnancy from the various pharmaceutical based registries. They're not easy to find in the literature."*

9.3.1.3. The decision-making process (shared decision-making vs directed decision-making)

When the consultants were directly asked in the interviews about the decision-making approach they follow in this area, they all answered that they follow a Shared Decision-Making (SDM) approach, as this is well-known to promote better treatment adherence in MS patients (90), and because this is necessary when medication choices are made more complicated due to family plans (see Chapter 2 for further details about SDM in relation to MS). C3 described the SDM approach best when he used the term "steer" to describe their role as HCPs, as consultants give the patient multiple options of DMDs that are considered to be their best choices for their disease activity, the patient chooses from this shortlist according to their preferences and priorities. Consultants will inform patients about the best plan for their current MS activity but will never force any treatment option on them. This shows the importance of patients being educated about their condition in order to make the right decision for them, whereupon HCPs can then support them later

down the line. However, when more generally talking about patients making decisions about their DMD options during other parts of the interviews, I noted a subtle directive approach. For instance, C2 (the head of the family planning pathway at Trust A) seemed sceptical when asked about the MS Trust digital decision aid (212) and whether or not she refers her patients to it as a way to help them with their decision. She stated that she feels anxious about patients having access to the full list of DMDs through the tool because this can make them ask questions about the other options that they were not discussed with the HCP before because they are not eligible for them:

> *C2: "I have some anxiety. They will go onto it and then, So what about all these other ones? Which? Which will they have to go through? Why not suitable?"*

This more directive approach was also evident when C1 expressed that he often tells his patients that breastfeeding is not protective. While the breastfeeding effect on postpartum relapses is still an area of controversy in the literature (42, 44, 45), this imposition of C1's own opinions on the patient rather than introducing the information to the patient as still controversial, points to a more directive approach.

> *C1: "Uh, I often also mention that breastfeeding is not protective."*

9.3.1.4. Challenges HCPs face when supporting MS patients

During the decision-making process, HCPs face several different challenges. These have been categorised in two main themes:

- Patient-related challenges
- System-related challenges

9.3.1.4.1. Patient-related challenges

The HCPs talked about several patient-related challenges they face in their clinics when providing this type of care. The first area where HCPs face this type of challenge is with **patients with active MS** who are stopping their treatments during pregnancy, with the resulting risks to their health that comes with this. Those patients will either be switched to a pregnancy licensed DMD, continue using their unlicensed DMD during pregnancy in order to protect the mother from any relapses, or stop their treatments completely to prevent foetal exposure to the medication.

> *C2: "The tricky ones are the high activity and the ones who have to switch."*

On the other hand, in practice, some potent medications such as natalizumab is increasingly used during pregnancy, despite the fact that it is not yet licensed as being safe during pregnancy. As a result, convincing patients to continue using these while pregnant in order to prevent relapses is another challenge for HCPs, as they are having to push back against the instinct mothers have to protect their babies. Consequently, many refuse to take any kind of medication during pregnancy, which again puts them at risk of relapse and MS deterioration.

This gap between what is written in the guidelines and the SPC recommendations and what happens in practice based on primary research and a drug's mechanism of action, also make things even harder for HCPs. On the one hand, following rigid guidelines may put the patient at risk. On the other hand, going against the guidelines may put the HCP at risk of legal liability. This was expressed as a concern by some of the HCPs interviewed, as the key issue of care in this matter is to maintain the balance between controlling a patient's MS and keeping the mother healthy, while also keeping the developing foetus safe and healthy too:

C4: "God knows how it's taken however many years to get a beta interferon labelled as safe in pregnancy or relatively safe. You know it's too slow… We will harm the patients if we stick rigidly with the guidelines."

Non-compliant patients are another challenge. The HCPs stated that despite all the conversations, plans, and options offered to patients to maintain this balance, **some patients just choose not to follow doctors' orders**. While they can provide information, give advice, and support patients during the decision-making process, it is ultimately still the patient's decision, even if this is not always the optimum choice from a healthcare provider perspective:

C3: "we have women who get pregnant on drugs when they're being told not to."

The occurrence of **unplanned pregnancies** for patients with MS also remains a challenge which HCPs face, even with the most well-planned and informed patient decisions and treatment plan. N2, for example, talked about an anxious patient of hers who accidently got pregnant while using ocrelizumab, which at that time was "not recommended to conceive while using it until 12 months after last dose" (55). The patient had had fertility problems for a long time and thus considered this pregnancy a "miracle*".* Indeed, patient fertility problems are likely the main reasons for patients being less careful with contraception, forgetting that spontaneous pregnancies can still happen to infertile people (213). N2 thus needed to support this patient in both containing her emotional breakdown and, in her decision, as to whether to keep the baby she had always wanted and was not able to have for a long time, while also factoring in the risk to the foetus due to the DMD exposure. This was thus very challenging for N2. Similar stories of unplanned pregnancies while patients were using unsafe treatments were also told by all of the other HCPs. Indeed, cases such as this were also reported by some of the women with MS interviewed (see Chapter 6).

C3: "I used to probably only bring it up when someone said to me I'm thinking of start trying for baby and now I that's way too late because one in six pregnancies are not planned you know."

N2: "There are patients who are really systematic, you know are planning their lifestyle but. OK, let's say, for instance, patients who accidentally get pregnant."

9.3.1.4.2. System-related challenges

One of the main system-related challenges the HCPs reported was **not having enough time to cover everything.** Consultants who see patients during their diagnosis consultation only have around 30-40 minutes (consultation time varies across the trusts) with a patient, during which time they have to cover a lot of information about the disease and the implications it could have for their lives, their DMD choice, and contain any emotional breakdowns that may happen. After this, they only see patients once a year, in a 20-minute session that should cover what has happened in the past year. Nurses see patients twice a year, but still have a lot of things to cover, which may lead to any in-depth family planning consultations being shelved, especially if a patient has not expressed any clear family plans.

Ph1: "Time is the first one because there's so many other things to cover."

In addition to the limited time HCPs have with patients, a **shortage of staff** is another problem HCPs face. In the context of treatment choices when patients are considering their family plans, a multidisciplinary clinic is really needed due to the complexity of these decisions.

N2: "I agree, uh, we have, you know, shorts staff. I really, really, you know… deprived of more clinics with regards to follow ups and we are really short of staff"

A shortage of other resources is another challenge HCPs face, particularly from the point of view of pharmacists. Ph1, for instance, stated that administering DMDs to patients at the right time postpartum being a priority, this is a challenge due to the insufficient number of infusion wards. Moreover, although pregnant women with MS are booked in for their postpartum resumption of DMDs, due dates are not guaranteed and adjusting to their new lives with an infant causes a lot of women to miss their DMD resumption infusion appointments. Rebooking another appointment can be a lengthy process, however, and the more time is taken for patients to resume their DMD treatments after delivery, the more the patients are put at risk of relapses (214). This again highlights the importance of proper patient education about the possibility of postpartum relapses and patients being supported in making their decisions regarding DMD resumption and breastfeeding:

> *Ph1: "It's really important to coordinate that giving birth and then getting them back on treatment before they have a postpartum relapse."*

Another resource which is in short supply for both HCPs and patients is accessible up-to-date information about DMDs and family planning, as noted by C5. The existence of practitioners who still follow the outdated practice of stopping all DMDs during pregnancy is another obstacle for HCPs to overcome, in terms of needing to identify any outdated information patients have received previously and then helping them to unlearn this information:

> *C5: "information about drug safety in pregnancy from the various pharmaceutical based registries. They're not easy to find in the literature."*

Another issue MS-specialised HCPs face is the **dissemination of updated information about DMDs and family planning** to other healthcare

professions that may also support MS patient care. Midwives, for example, are key healthcare providers for MS patients during their pregnancy journeys, but rather than reassuring them, midwives tend to lack the necessary knowledge about the effect MS has on pregnancy, labour, anaesthesia, and delivery modes. N1 and C4 both stated that they usually provide letters for the midwives to confirm that an MS pregnancy is considered a normal pregnancy, and that patients can have an epidural and go into normal labour and natural delivery. While this is well-established information in the literature on MS, this does not seem to be accessed nor disseminated to other practitioners supporting MS care readily enough.

> *C4, talking about questions she receives from midwives: "midwives are more worried than they need to be in there, taking all your extra appointments stating that it is a high risk!! It's not high risk for the vast majority! It's a normal pregnancy!"*

9.4. Discussion

These interviews with HCPs who support women with MS demonstrated that with the exception of Trust A, there is no dedicated service to help HCPs and patients with the decision-making process in relation to DMD choices and family planning. Most of trusts in the study's sample (except Trust A) thus provided this service in an "ad hoc" manner, which results in a high variability of care.

The interviews also highlighted the lack of standardisation across the trusts in a number of aspects, including consultation times, referral pathways, service availability (neuro-obstetric), the resources used by HCPs and those provided to patients, and the topics covered by HCPs during DMD-family planning conversations.

The interviews also demonstrated that the timing of this conversation is vital, in that this conversation should be had as soon as possible after diagnosis,

but only when patients also appear to be mentally ready and accepting of their diagnosis. Delaying this conversation for too long might result in a higher possibility of patients switching DMDs later on to conceive, which comes with its own risks, as discussed in Chapter 4 Delaying the conversation beyond the initial diagnosis consultation, however, can also sometimes mean that women miss the opportunity to have this discussion with their consultants until their next appointment in 12 months' time. Having said this, patients do still have the chance to discuss this with their MS nurses in the meantime.

Unplanned pregnancy is another reason why it is important to have this discussion as early as possible with all childbearing-aged women, regardless of their social set-up and family plans, and especially if they are starting a DMD. There is currently no data about the prevalence or rate of unplanned pregnancy for women with MS. However, in a survey of 590 Danish women, 10% reported an unplanned pregnancy while using DMDs (215).

Indeed, the HCPs interviewed identified multiple challenges that they face which prevent them from providing this service in a standardised manner. The system-related challenges mentioned included short consultation times and a shortage of staff which makes specialised and multidisciplinary clinics difficult to actualise with their current caseload ratio (216). On average, there was only one nurse available per 379 people with MS in the UK in 2018. This places quite a big load on these nurses, which may lead to some tasks, such as social intervention or medication recommendations and prescriptions, being left undone (216).

On the other hand, the patient-related challenges reported were related to the complexity of women with active MS wanting to start a family while on DMDs, which required them to either stop a patient's treatment and thus risk the mother's health, or switching treatment, which also comes with its own risks. Switching treatments is always a challenge, regardless of whether a patient's MS is either stable or non-stable, which further underlines the importance of incorporating family plans into treatment plans as early on as possible. This

again underscores the need for further research in this area, as was already identified in Chapter 4. Unplanned pregnancies also force HCPs to try to bridge the gap between the rigid guideline recommendations and real practices. While sticking rigidly to these guidelines might cause harm to their patients, not following them might make HCPs legally liable. However, conveying and explaining this to patients while lacking clear specialised resources is thus extremely challenging. Furthermore, in the absence of such resources, the provision of information, practices, and outcomes in this area will be very variable, which again highlights the need for standardisation.

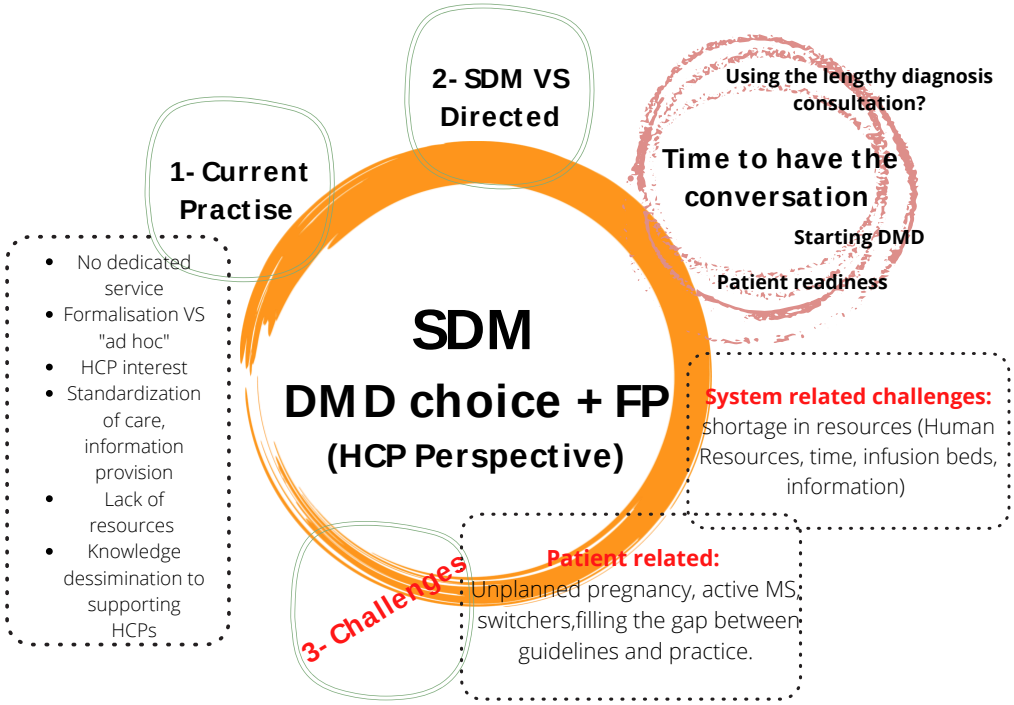


Figure 11 The DMD and family planning decision process (from a HCP perspective)

9.5. Conclusion

DMD choices and family planning is a very important aspect of MS care. However, it is still delivered in a non-standardised manner, which creates great variability in the care provided. While the readiness of a patient to have these DMD/family planning discussions is important, it is equally important to have this conversation with every woman of a childbearing age regardless of her social set-up and active family plans.

What is needed to support women with these decisions, is the formalisation of this service, run by a multidisciplinary team. This is currently lacking, however, due to resource shortages.

Chapter 10. Evaluation of the MS Trust DMD Decision Aid in the context of family planning: the HCP perspective

10.1. Background

Chapter 8 examined the findings of the Think Aloud sessions with the women interviewed in relation to the MS Trust DMD decision aid. To complete the picture, it was thus vital to also examine HCPs' opinions of this tool, both in general and in the context of family planning. Unlike with the women's study, however, the very limited time of the HCPs meant that similar Think Aloud sessions were not possible. The HCPs were thus asked questions about the tool during their interviews (see Chapter 9; the interview questions can be found in Appendix 17).

10.2. Objectives

To explore HCPs' opinions of the MS Trust DMD decision tool, especially in the context of family planning, as well as whether or not they use this tool in their clinics.

10.3. Methods

Discussions about the tool was either independently raised by HCPs when they were asked during the interview about the available resources that they direct their patients to, or the HCPs were prompted to do so if they did not mention it themselves. The HCPs were also asked about whether or not they refer their patients to the tool, and what their reasons were for or for not referring them towards it. They were also specifically asked about the role the tool plays in helping women to choose a DMD in the context of family planning.

For the full methodology, please refer to Chapter 5.

10.4. Results

In total, six HCPs (five consultants and a nurse) were asked about the decision tool during their interviews in relation to questions about available resources. P1, was the first HCP I interviewed and at that time, a decision to take HCP perspective about the tool was not taken yet.

<u>Consultant 1</u> (C1) stated that he does not usually direct his patients towards it. It is worth noting, however, that when asked about some of the details of the tool, he admitted that he had only looked at the website a day before the interview.

Interviewer (I): “Do you think this tool is helpful for them?”

C1: “I think I think so. I think so, yeah, uh, when people come back for further follow up, they've usually had a look at it and I think it is a good website.”

I: “How about the family planning part of it? At the website.”

C1: “Actually, uhm, I don't think I've specifically directed people towards that, but uhm but there is stuff on there.”

“In preparation for this…. Actually, I was looking at the website…. actually, funny enough yesterday, and maybe it's been updated, but I'm not sure.”

<u>Consultant 2</u> stated that while they use the tool for helping women with their DMD choices, they do not use it to help with family planning due to the small number of options available and the differences between the website’s recommendations (which follow the legal licensing guidelines) and real practices.

C2: “So yeah, I do I do, I do but I don't usually with pregnancy”

“On my normal MS clinic, I would use that quite a lot. In my pregnancy clinic. I don't use it so much.”

“Pregnancy, DMD selection is a smaller selection to start with, and I think the information you know if you go to tysabri, for example, the official information is so that it's unsafe in pregnancy.”

<u>Nurse 1</u> (N1) stated that she used to recommend the tool but does not anymore because she finds it outdated now. As for family planning, she finds it confusing because of the restrictive recommendations that sometimes do not match real practices.

N1: “Historically we've always recommended that I, I think of late just with sort of funding. It's not being kept that up to date…But it's, it's great as a I would say maybe more outside of pregnancy we would tend to sort of use that more because I think some of the information about the licensing of treatments and I think for patients it can be quite scary reading information in a trusted sort of source that says this is contraindicated in pregnancy, don't do this for breastfeeding, then it can be really confusing time for them.”

<u>Consultant 3</u> (C3) stated that they find it nice and useful, but not for family planning.

C3: “I don't know how great it is on family planning, but it's It's quite nice.”

<u>Consultant 4</u> (C4) stated that they use it when helping women to choose a DMD, but again not in terms of family planning.

C4: “I haven't looked at it in terms of that [family planning] so much we use it anyway, but in terms of I haven't really thought about. Yeah, I think it's I don't. I don't know in terms of family planning, I think it's a good. The decision aid is good…. Generally”

<u>Consultant 5</u> (C5) stated that while she does not usually use the tool, she is aware of it. She prefers to use information booklets instead, although she is not sure if the booklets are up-to-date or not.

C5: “I haven't used it very often in clinic I've got the MS Trust booklets has only the DMT in the back of it, so I sometimes start with that. No, it can be. It can be out of date. In fact, I'm not entirely sure whether we have a completely up to date one now”.

10.5. Discussion

In terms of the interviews, the HCPs were split into two main groups:

1- Those familiar with the tool who think that it is helpful for choosing DMDs, but not in the context of family planning. The following reasons were given for this:

a. The information is outdated.
b. It highlights the contradiction between the rigid SPC recommendations and real practices in which the risks vs benefits are weighed up, thus confusing patients.

2- Those who know about the tool but are not familiar with it, and do not usually direct patients to it, meaning that they did not have a lot to share about the tool.

The HCPs who were familiar with the tool suggested the need for the content of the tool to be updated or amended in a way that helps women with MS to choose a DMD in the context of family planning. They also highlighted the importance of finding a middle ground when presenting pregnancy recommendations, so that the contradictions between the guidelines and real practice does not confuse patients.

However, as this tool can help women with choosing a DMD, regardless of their family plans, it still remains a good resource for patients. The fact that some of the HCPs were not very familiar with the tool highlights the need for information about the tool to be more widely disseminated to increase its reach. Indeed, this is particularly in light of the fact that the MS Trust booklets that some HCPs are still handing are often outdated or get lost by patients, not to mention the effect of printing that amount of paper on the environment.

10.6. Conclusion

The HCPs expressed the opinion that the MS Trust decision aid is a good tool to direct patients to, but not in the context of family planning, as the tool can be outdated and confusing when it comes to its pregnancy recommendations which matches the women's opinions of the tool. Some of the HCPs were also not familiar with the tool, which points to the need for better dissemination.

Chapter 11. Final Discussion: The Holistic Decision-Making Experience in terms of DMD choices and family planning – joining the dots, providing recommendations, and the implications of this study for improving the decision-making experience.

11.1. Introduction

This chapter will summarise the main findings of the studies, link them together, and discuss them in light of the available literature in order to provide an overall picture of what the current DMD and family planning decision-making experience looks like. Possible areas of improvement will also be identified. The strengths and limitations of this research will also be examined. Finally, this chapter will conclude with recommendations for both future research and practical suggestions for improving the decision-making process.

11.1.1. Overview of the main aims and objectives of this thesis:

Aim:

To explore and understand the holistic decision-making experience of treatment choices and family planning for women living with MS to facilitate an improvement in the overall quality of the process and the decisions made.

Objectives:

- To identify the available literature on the effects that switching and managing treatments for the purpose of pregnancy has on women's MS.
- To explore the real-life experiences of women when choosing, switching, or managing their medications and how they manage their family plans in accordance with their overall lives.

- To explore this same experience from the point of view of the key healthcare providers who support women in making these decisions.
- To identify the resources and decision aids available to help women with these decisions.
- To explore what women want in a decision aid through a qualitative evaluation of a current online decision aid.

11.2. Summary of all the studies' findings

The studies conducted for this thesis sought to explore the choice and management of DMDs in relation to family planning decision-making. The systematic review explored the effects switching DMDs for the sake of pregnancy can have on stable patients, as one of the most complicated reproductive decisions frequently faced by women and their HCPs regarding their treatments and family plans. Objective clinical outcomes (relapse rate and new lesions) were consequently reviewed to determine the implications such a decision can have on women's health. The review only included seven articles, highlighting the paucity of literature on this topic. However, of these articles, all confirmed that switching treatments, especially when de-escalating to less effective DMDs, will likely decrease control over the disease, leading to higher risks of relapses.

As this need to switch medications can be the result of patients and HCPs not accounting for future family plans when first choosing a treatment, gaining a better understanding of the decision-making process was important. This was achieved through the in-depth interviews with women with MS. This provided descriptive accounts of this experience and highlighted the factors, approaches, decision aids, and influencers that play a role in the decision-making process. It also identified and explored the impact of patients' mental readiness to make these decisions using the biographical disruption approach. A lack of trusted knowledge resources and decision aids such as online pages or paper booklets that help with both decisions (DMD choice and family planning) simultaneously was one of the main issues highlighted by the women interviewed and their HCPs. This thus informed the next

study, which sought to evaluate the MS Trust online DMD decision tool. This evaluation offered key insights from the tool's primary users (MS patients), which could help to improve the existing tool or provide a good basis for developing a new tool. Indeed, these recommendations were communicated to the MS Trust for them to consider when updating their tool. Lastly, the HCP interviews highlighted the practical and clinical challenges of this decision-making process from a professional point of view.

11.2.1. The main findings of the systematic review

The systematic review identified only seven papers that matched the inclusion criteria, with only one of these seven papers directly discussing the issues of switching treatments for the sake of pregnancy (159). This highlighted the paucity of the data available on the effects of women switching when stable in order to get pregnant, and the importance of further research being done into the time it takes to fall pregnant, the different treatment options used, and the effects the different types of switches have on women's MS. This is thus necessary for improving the decision-making experience for women with MS.

11.2.2. The main findings of the women's interviews

The interviews confirmed that the existing literature's findings in terms of the concerns and fears women face when deciding on treatment and family plans, this research makes an important and novel contribution in exploring the decision process, feelings, needs, resources, and influences involved in the DMD-family planning decision-making process. The main findings of this study were as follows:

- The decision-making process varied in a number of ways between the participants depending on the area of the UK they received their care and the available resources provided.
- The different levels of knowledge, proactivity, and involvement of each participant in this process.

- The key decision aids (influencers) were the past experiences of others and themselves, as well as HCPs and charity websites (the MS Trust and the MS Society).
- The decision-making experience is complex, heterogenous, and fluid, which can make it more difficult.
- The biographical disruption which MS causes can affect the decisions made by women with MS and the timings of the decision-making process.

11.2.3. The findings of the MS trust decision tool evaluation

Charity organisations such as the Ms Trust and the MS Society were both frequently reported as trusted sources of information. While both run a digital decision aid for DMD choices, I was able to collaborate with the MS Trust to run a qualitative in-depth evaluation of this tool to specifically look at the tool in relation to family planning decisions. The women with MS I interviewed found it very helpful, practical, and more environmentally friendly than the printed DMD booklets. The usefulness of this tool was restricted to the DMD choices, however, with both the women and the HCPs reporting it as not particularly useful for choosing a treatment in relation to family planning due to its conservative and unclear pregnancy and conception recommendations. The women also highlighted potential improvements to the tool's usability and interface stemming from their own cognitive needs due to MS.

11.2.4. The main findings of the HCP interviews

These interviews sought to explore the decision-making experience from a HCP perspective. The main findings of this study were as follows:

- DMD-family planning services are mainly provided in "ad hoc" manner, with these discussions embedded into regular consultations.
- The quality of these services also depends on the HCP level of interest and investment in this area.

- The service pathway in trusts that lack a formalised service is ambiguous.
- Not all trusts have support teams (e.g., Obstetrics) who would have the time and the goodwill to provide support service.
- The time at which these services are provided rests on finding a compromise between patient readiness and the limited time in consultations with HCPs together with constrains in terms of how often they can meet.
- Patient involvement in this process varies (while HCPs aim to use the SDM model, they are often more directive when it comes to severe cases).
- Current practices vary due to a lack of standardisation of care due to the non-formalised services offered for DMD choices/family plans (except for one trust).
- The main patient resources according to the HCPs are HCPs themselves and charity websites.
- Decision aid resources for HCPs can be difficult to access and find (only one trust had their own prepared resources for both patients and HCPs).
- Patient-related challenges when providing this service include patients with active MS, accidental pregnancy, bridging the gap between SPC guidelines and practice, as well as conveying this clearly to patients.
- System-related challenges all stem from a shortage of resources.
- In conclusion, the decision-making experience is usually non-formalised, non-standardised, highly variable, and with few resources, which makes it harder for HCPs.

11.3. Discussion of the key areas of improvement recommended to increase the quality of the decision-making experience – linking the women's and the HCPs' perspectives.

The section will expand upon the areas that need improvement in relation to the current treatment/family planning decision-making experience, merging both the perspectives of the women with MS and their HCPs.

11.3.1. The scarcity of the literature in this area

The availability of literature on this topic is very scarce in most areas. The existing literature is not substantial enough to come to any major conclusions or make any recommendations that could help with this decision-making process. This is further exacerbated by the paucity of detailed information and decision aids on this topic in accessible lay language that can be easily understood by patients. Likewise, the HCPs interviewed also commented on not having access to information resources on this topic that could help make consultations easier and save them a lot of time. The existing literature on the role of decision aids in improving the decision-making experience for both women with MS and HCPs is scarce (see Chapter 2). Finally, the decision-making experience provided by UK health services for MS patients is also an understudied topic. This will be examined further in the following section.

11.3.2. Variability in care

11.3.2.1. Variability in the study sample (women with MS and HCPs)

All of the studies included in the systematic review suggest that the current decision-making experience for all involved parties (both patients and their supporting HCPs) is hugely variable. The women I interviewed reported different timelines in terms of consultations and family planning conversations, different conversational content with varying levels of details, and different levels of their involvement in the decisions. This all points to services of varying quality too.

The HCPs I interviewed also reported the same level of variability from their perspective. Different centres have different services, for example, whether they have a specialised clinic for patients planning to get pregnant. Different centers also have variable numbers of staff serving variable numbers of different patient populations depending on location e.g., rural versus urban. HCPs also drew attention to the current shortage of staff and the workload crisis for both neurologists and MS nurses (217). The variability in the levels of interest shown by HCPs and trusts towards the area of DMDs and family planning was also highlighted by the interviews, as the more interested a HCP is in this area, the more likely they will be

to provide more details, education, and support in this regard to patients. All these factors create the conditions for variation in the care provided and also impact HCPs' abilities to fulfil the SDM model in relation to supporting patients in the decision-making process.

11.3.2.2. The importance of variability within the SDM model

Some variability can be inevitable and important in the SDM model. This is called behavioural variability, which includes the different personalities of patients, disease courses, life circumstances, values, and preferences. This is normal, expected, and needs to be accounted for during the decision-making process, especially with respect to preference-sensitive decisions like those faced by MS patients (218). When it comes to healthcare services, however, the process itself needs to be standardised and controlled as much as possible to reduce variability and ensure safety and equity in the care delivered, which is one of the NHS's main values (218, 219).

11.3.2.3. Variability in the NHS services provided to MS patients.

A recent 2021 Getting It Right First Time (GIRFT) report on Neurology services across the UK, reported that MS services were struggling with the variability of the care pathways provided in major areas such as access to MS nurses and access to treatments (220). Unfortunately, the existing literature evaluating NHS services focuses on DMDs, and family planning for MS patients is minimal. This may be a result of this service still being in its formative stage. Studies of other supportive services and descriptions of more general experiences of MS services can provide some insights.

In 2019, a UK-wide survey of 8000 patients with all types of MS about their needs was conducted by the National MS Society. Of these, 89% of patients reported having access to a key HCP (consultant or nurse) in the past 12 months. However, the access rate varied between UK nations by 10%, reinforcing the huge variability in care across the UK (221). This survey also showed how access to specialised services such as emotional support services was unavailable to 44% of the patients

surveyed. Although this is still not a direct evaluation of the availability of DMD/family planning services, not having access to emotional support services undoubtedly will impact patients' treatment/family planning decisions (221). However, these surveys focused on service access rather than overall experience.

When looking at evaluating the service experience itself, the literature largely focused on either diagnosis (222, 223) or palliative care experiences (224), leaving a gap in the research of the period in between which DMD management and family planning experiences can fall (225, 226). Edmonds et al. looked at patients' experiences of such services back in 2007 using interviews. In this study, patients reported a lack of continuity and co-ordination of care, as well as a lack of information about services, aids, and adaptations, welfare benefits, and end-of-life issues. Overall the participants described their experiences as a "struggle" (227).

11.3.2.4. The importance of standardisation

A reduction in the variability of care can be achieved through the standardisation of a formal specialised service dedicated to helping women with their treatment choices and treatment management in relation to family planning. Standardisation ensures that effective, safe, and affordable care is delivered, and has been proven to improve the quality of received care, the fundamental aim of this thesis. This in turn requires a greater workforce to actualise this standardisation in a real-life setting, as the current workload crises is a barrier to this (228, 229). Having a specific pathway for DMD and family planning decisions will give women more time to think about, discuss, and make their decisions. More frequent consultations would also help with building rapport between patients and HCPs. Furthermore, having a dedicated team providing such a service would also provide more defined roles for the HCP team and ensure less stressful first-time consultations as consultants can then focus on other aspects of care and defer to the specialised clinics in this regard.

11.3.3. The SDM approach in practice

As discussed in Chapter 2, SDM is the treatment decision-making approach of choice for MS (230). This is even more necessary when family planning decisions are also added to the mix, making these decisions even more complex. However, given the current picture we have established of the treatment/family planning decision experience and the current MS services, implementing an SDM approach seems very challenging and cannot perhaps be applied in every situation in real-life settings, which again impacts the overall quality of the process and the outcomes of the decisions made.

As establishing a good physician-patient relationship is an important part of SDM, as explained in Chapter 2, the current shortage of available staff, services, and high caseload presents another challenge for HCPs, as it is very difficult to establish trust when consultants barely see individual patients once a year. This then also puts more pressure on MS nurses, who have more frequent interactions with patients (a twice-yearly review, and patients can communicate with them when needed), adding to their already high caseload (216). It is important to note that HCPs report consulting using SDM wherever possible.

11.3.4. The underutilisation of pharmacists in the process

Currently, the pharmacist's role very much resides in the background of the DMD/family planning decision making process, having more of a non-patient-facing role (231). This was concluded through my clinical observation time, when I attended clinics and observed the flow of service and the main practitioners' roles and was also confirmed during the interviews with both women and HCPs.

11.3.4.1. Pharmacists in the data collected by these studies.

Out of the 31 women interviewed, only one reported getting direct help and support in the DMD/family plan decision-making process from a specialised MS pharmacist. Similarly, only one out of the four trusts examined in the study's sample had two specialised MS pharmacists, one of whom was interviewed. However, this

pharmacist explained that their role is more related to assessing patients' eligibility for their chosen treatments before treatment starts, the therapeutic drug monitoring of patients' blood (TDM) and attending multidisciplinary team meetings (MDTs) to discuss certain cases with the rest of the team, as well as more administrative formulary drug approvals and drug information-related work. A very minimal patient-facing role was thus reported within the decision-making process, with only contraception (in relation to DMDs and family planning decision) options being discussed with the pharmacist. That could also be because of this trust's pre-defined roles when running specialist clinics for DMD and family planning choices, however, which are led by a consultant and an MS nurse. The MS pharmacist thus stepped down from this patient facing role within the context of the decision-making process in this trust, meaning that they aid and support the medical team during the process without directly helping patients.

Several attempts were made to contact the MS pharmacist that had helped one of the participants of the first study of women with MS, but these were not successful. An interview would have helped to offer more insight into his role, as he had provided the participant with multiple phone consultations to discuss her DMD options in relation to her family plans, which is a patient-facing role. This stands in contrast to the MS pharmacists working in the trust with the specialised service clinics.

11.3.4.2. Specialised MS clinical pharmacists, and non-medical prescriber (NMP) pharmacists

The increased incidence of MS diagnoses and the high caseload on both neurologists and MS nurses highlights a space specialised MS clinical pharmacists could be more involved in to share out the workload, especially in the case of non-medical prescriber pharmacists who are licensed to prescribe medication and can thus decrease the workload of neurologists too. In a retrospective 6-month service evaluation of a pharmacist-led clinic (non-medical prescriber pharmacists) which was published on the MS Trust website, revealed that 75% of the consultations the pharmacists provided were about prescription renewal/drug monitoring. They also

conducted pre-initiation counselling (14%) and treatment initiation consultations (9%). This study concluded that NMP pharmacists were very able to lead such consultations and stressed how useful this is for decreasing the workload on both consultants and MS nurses, which is extremely high for both (1815 patients per consultant and 315 patients per full-time MS nurse). However, it also showed that the main role of pharmacists was still drug monitoring, with less treatment counselling provided (232). Decreasing the workload of HCPs would thus likely result in better HCP outcomes such as greater job satisfaction (233), lower staff turnovers, and the overall provision of a better service experience for both patients and HCPs (234). It would therefore also positively affect patient outcomes by increasing patient safety (fewer adverse drug events) (235), improving treatment adherence, and increasing the number of positive patient health outcomes (236).

11.3.4.3. The need for drug experts

With the increasing number of specialty drugs being approved for use with MS in the NHS and an increase in the complexity of the decisions having to be made, especially in relation to pregnancy and breastfeeding, it is increasingly difficult to establish long-term treatment plans and ensure pregnancy/breastfeeding safety (see Chapter 1). There is thus a clear need for drug experts who can help with these decisions. Making proper use of pharmacists' knowledge of pharmacokinetic and pharmacodynamic knowledge of drugs and their different mechanisms of action, could help with making preliminary predictions about the safety of certain treatments and ensuring the proper management of treatments during pregnancy and breastfeeding, especially when evidence-based data is insufficient and risk versus benefit evaluations need to be made.

11.3.5. When should HCPs talk to patients about DMDs/family plans? Assessing patient readiness

The time at which these decisions are made is an important factor in the outcome of the decision-making process for both women and their HCPs. There are three time

periods during the MS journey that are critical: diagnosis (starting treatment), relapse (treatment failure requiring switching), and postpartum (increased chance of relapse and treatment management decisions need to be made in relation to breastfeeding). Patients, together with their HCPs, are often expected to make these treatment/family planning decisions during these key periods, even though these periods often cause emotional and biographical disruption and thus impact the decisions made (See Chapter 6).

While HCPs can assess the mental capacity of their patients using an assessment tool (the Mental Capacity Act), readiness to decide cannot be assessed yet with a specific tool. Much work has been done in the field of HIV treatment in trying to measure patient readiness to make a decision about whether or not to start highly active antiretroviral therapy (HART) (237). A number of different approaches have been used to develop different tools that relate readiness to different variables such as the time needed to make a decision (238), a patient's level of knowledge of the illness (the more knowledgeable, the more ready the patient is) (239), and the likelihood of patient adherence to treatments (240), using visual scales and behavioural questionnaires (241). Unfortunately, however, much of this research appears to be incomplete and thus none of the approaches has been adopted for universal use in clinical settings (237).

However, another study in the field of breast cancer, an evaluation of a web-based decision aid to assess the readiness of a patient to make a decision about getting a mastectomy, reported an increase in patient readiness when using this DA. This study used knowledge, deliberation process and surgery intentions measures to assess readiness and simultaneously highlighted the importance of DAs (242).

In the field of MS, Lowden et al. have explored the decision-making experience when choosing an MS treatment. The core theme of this study was "redefining the self" and demonstrating how patient emotions, biography, and readiness to decide are intertwined. Indeed, this confirmed the relationship between the biographical disruption caused by MS and patient readiness to decide. It also highlighted the importance of decision aids in helping patients with these complex decisions. Readiness was thus positioned as a key part of the treatment decision-making

process which comes right after self-renegotiation in the overall process. This supports the conclusions made earlier in Chapter 6. However, the study did not provide any insights on how to assess readiness (210).

This again highlights the paucity of the existing literature on assessing readiness to decide in the field of MS. This is reflected in the fact that a validated universal assessment tool for readiness has not been developed yet.

11.4. Strengths

This is the first study, to my knowledge, to holistically focus on the decision-making process of treatment choices in relation to family plans in the life of women with MS, rather than studying each of these decisions separately. In doing so, this thesis has highlighted the paucity of the existing studies on treatment switching and the impact it can have on patients with stable MS when planning pregnancy. It also provided the first in-depth analysis of women's experiences of this process. This builds upon the conclusions of the existing literature by looking at the process in which these decisions are made and highlighting the reasons and emotions behind the decisions made. It also explored the decision-making process through the lens of the biographical disruption framework to gain further insight into the decisions made by these women in relation to their self-subjectivity. This was consequently the first work to touch upon the relevance of this theory for the treatment/family decisions made by women with MS.

This thesis also examined this decision-making process from the perspective of healthcare providers to gain a full picture of the process and to address the joint issues and challenges discussed by both parties. This could thus help to improve the decision-making experience for both.

The interviews also highlighted the importance of decision aids in making patients feel more confident about their decisions, as well as examining how HCPs are far too busy to be the only relied-upon trusted source of information for patients. It also demonstrated the extent to which both women with MS and HCPs trust charity websites. As a result, a collaboration with the MS Trust was begun to evaluate and

update their decision-making online tool. The qualitative evaluation of this DA tool in terms of its usefulness in relation to DMD choice/family planning also generated recommendations for improvements which could be made. The Think Aloud method was thus a fantastic way to get extensive reviews from the tool's users, unlike conventional surveys that provide much less in-depth data.

11.5. Limitations

11.5.1. Critique of Recruitment

The number of HCPs interviewed was quite small (eight HCPs). This consisted of five consultants, two MS nurses, and an MS-specialised pharmacist. The HCPs were recruited from six different NHS trusts around the UK (one from Scotland, one from Ireland, and the rest from England). While this provided some variety, this was not enough to gain enough insights from all three professions (consultants, nurses, and pharmacists) in each country. It also needs to be noted that it was not possible to recruit any HCPs from Wales. This was partly because the busy schedules of HCPs were made even busier due to the COVID outbreak when the recruitment took place.

There is also the possibility of bias of interest from both the participants and HCPs taking part in this research as a recruitment agency was used to recruit women with MS and snowball sampling was used to recruit HCPs using one of my supervisor's networks, together with the help of an MS nurse. It is thus possible that the participants and HCPs who were recruited were more interested in this area and topic than others who were not recruited. This means that their experiences of this area may be better than is the case in other trusts, where HCPs might not be as interested in this area. It is thus possible that the opinions, thoughts, demands, and explanations of the participants may be biased by their hyperfocus on this area.

11.5.2. Critique of Methods

When examining the results of the interviews with the women with MS, it was not possible to provide more details on the decision-making process using the biographical disruption framework, as this element was only identified during a later in-depth analysis of the accounts. Although I did not proactively ask or probe participants about this, the importance of this underlying framework was strong enough to inductively be present at various points in some of these women's stories.

The Think Aloud sessions conducted with the participants to evaluate the MS Trust's decision aid were very informative and resulted in a comprehensive evaluation of each part of the tool. This provided very insightful criticism and recommendations for improvement stemming from the primary users' needs. As HCPs are part of the decision-making process too and in some cases do also refer their patients to this tool, their evaluation of the tool was very vital too. However, due to the limited time the HCPs had during COVID (in terms of both the recruitment and the interviews), it was very difficult to arrange both a 15-minute-interview and then another 15-minute Think Aloud session. Consequently, they were only asked about the tool during their interviews. While this offered some insight into HCPs' opinions of the tool, there was little time to explore the reasons behind this. Furthermore, some of the HCPs also did not seem to be very familiar with the tool, at which point the Think Aloud sessions would have been very useful for encouraging them to engage more directly with the tool.

11.6. Future research

- In order to develop more optimal management approaches, more studies are needed which explore the effects of different treatment switches on MS and examine the efficacy of DMDs during pregnancy on those who chose to continue treatment compared to the pregnancy protection offered without the use of any DMD.
- The women's interviews revealed the impact of emotions in terms of biographical disruption and self-renegotiation on the women's decisions, despite not probing for it. More qualitative work is thus needed in this area to better understand and adjust for emotions and biographical disruption during the three main periods when DMD/family

planning decisions are to be made (diagnosis and choosing treatments, relapse and switching treatments, postpartum and returning to treatments).

- As the HCP interviews relied on a very small sample, expanding this study to include more trusts around the UK nations would help to provide better insights into the HCP experience.
- A comparative study of the decision-making experiences of the women who received care from Trust A's specialised service and the experiences of those at other trusts (non-specialised variable care) would help to generate more rigorous results which could support the importance of service specialisation.
- More quantitative work (including surveying) is needed to offer further insights into the experience in the areas of service availability, consistency, and access to DMD/family planning service.
- More work is needed on decision aid development that helps in the DMD choice and management considering family planning that provides what women expresses as needs such as safety, timeline, and action.
- Further work also needs to be done in the development of tools for assessing the readiness of patients to make decisions about treatment, specifically in relation to MS.

11.7. Implications for real-life practice

- When considering the findings of this thesis together with the GIRFT report and the Neurology Now reports, and in order to support a robust SDM approach to pregnancy planning in MS, suitably trained specialists, with adequate time available, are needed. This will also make it more feasible to set up specialised DMD/family planning multidisciplinary services (such as the service run by Trust A) that could dedicate their time and effort to this area.
- The further training and involvement of MS-specialised pharmacists in this process could be one of the key solutions to the MS consultant/MS nurse workload crisis and to also make the specialized treatment choices and family planning service more feasible.
- It is also important to increase patient access to emotional support services. This could either be through the NHS (with enough resources) or through charity

organisations and support groups who can run educational sessions, emotional support group therapy and CBT programs.

- The development of a self-assessment tool to help patients assess if they are ready to make decisions about treatments and family plans is crucial. As readiness is not yet an outcome that can be objectively measured by a specific, validated, universal tool, this highlights an opportunity for academics, charity organisations and tool developers. This could be, for example, an educational document defining readiness, explaining the importance of it, and the consequences of making decisions when not ready, for example. This could be followed up with an assessment of a patient's knowledge of DMD in relation to family planning and the time taken by patients to deliberate as a way to assess readiness. It would also be useful to include the stories and experiences of other patients in this about when and how they felt ready to make these decisions.
- Charity programs and campaigns to raise awareness about decision making readiness, which may include educational sessions, workshops for both women and HCPs and support groups that focus on importance of readiness.
- Increase patient awareness of the shared decision making approach and the importance of decision aids, with training on how to use online decision tools such as MS Trust or National MS society tools that can enhance the decision making experience if patients have known and trained on how to use them.

11.8. Conclusion

Improving the holistic decision-making experience of treatment choice and family planning for women living with MS was the main goal of this thesis. It started with a systematic review to show importance of DMD/family planning decisions through looking at the effect of one of these decisions, which is switching DMD when stable, on the health outcomes.

Exploring the experience showed both the HCPs and majority of the participating women preferred the SDM approach of decision making. Despite this, however, this approach is still not always taken or is not possible. The women highlighted those conversations with HCPs, family members, and other people with MS influenced

their decisions. They also talked about how their own previous experiences or others' experiences also had a great impact on their decisions. The information resources most heavily relied on by both the HCPs and the patients were reported to be both the HCPs themselves and charity websites. However, much of the responsibility is still on HCPs.

One of the most important and original approaches of this thesis is the examination of the impact of emotions and biographical disruption on patient readiness to make a decision and thus the quality of the decision-making process and the quality of the final decisions, especially during the key periods of disruption during the MS journey for both patients and HCPs. Despite the importance of patient readiness, however, there is still no universally validated tool for this.

This research has also highlighted the fact that the decision-making experience as a delivered service for both MS patients and HCPs is hugely variable and is provided in an "ad hoc" manner. The key to reducing this variability to ensure equity and quality of care may be greater standardisation of formal services across the UK and an increase in the resources available.

The availability of information resources and decision aids are important tools of SDM, to support an improved decision-making experience. These are currently in short supply. While the MS Trust's decision tool is a good example of a decision aid, it is not tuned to choosing DMDs in the context of family planning. The tool may also benefit from some changes to its interface in light of users' cognitive needs. These recommendations were shared with the MS Trust to consider it during the next tool update.

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Appendix 1 : PROSPERO Registration

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

Back

Dear Mrs. Almouzain,

Thank you for submitting details of your systematic review "Effect of switching disease modifying drugs on relapse rate in stable relapsing remitting multiple sclerosis patients" to the PROSPERO register. We are pleased to confirm that the record will be published on our website within the next hour.

Your registration number is: CRD42020172912

You are free to update the record at any time, all submitted changes will be displayed as the latest version with previous versions available to public view. Please also give brief details of the key changes in the Revision notes facility and remember to update your record when your review is published. You can log in to PROSPERO and access your records at https://www.crd.york.ac.uk/PROSPERO.

Comments and feedback on your experience of registering with PROSPERO are welcome at crd-register@york.ac.uk

Best wishes for the successful completion of your review.

Yours sincerely,

PROSPERO Administrator
Centre for Reviews and Dissemination
University of York

Appendix 2 : Systematic Review Search Strategy

A comprehensive search was run through the following databases:

- Ovid Medline ® and Epub Ahead of Print &In Process & Other Non-Indexed Citations and Daily, 1946 to 31 March 2020
- Emcare, 1995 to 31 March 2020
- Embase, 1974 to 31 March 2020
- SCOPUS, up to 31 March 2020.
- CINAHL, up to 31 March 2020
- Cochrane Central, up to 31 March 2020

The following is the search strategy I followed for <u>Medline</u>:

1. Multiple Sclerosis, Relapsing-Remitting/
2. ((relaps* or remit*) adj3 multiple sclero*).mp.
3. 1 or 2
4. (Disease modifying adj2 (agent* or drug* or therap*) adj3 (switch* or substitut* or de-escalat*)).mp.
5. (Disease modulating adj2 (agent* or drug* or therap*) adj3 (switch* or substitut* or de-escalat*)).mp.
6. (immuno* adj3 (drug* or therap* or agent or treat*) adj3 (switch* or substitut* or de-escalat*)).mp.
7. interferon-beta/ or interferon beta-1a/ or interferon beta-1b/
8. Glatiramer Acetate/
9. 7 or 8
10. Drug Substitution/
11. 9 and 10
12. ((Drug or therapy or treatment or medication) adj3 (switch* or substitut* or de-escalat*)).mp.
13. ((interferon* or rebif* or avonex* or betaseron* or extavia*) adj3 (switch* or substitut* or de-escalat*)).mp.

14. ((copaxone* or glatopa* or glateramir acetate) adj3 (switch* or substitut* or de-escalat*)).mp.
15. 4 or 5 or 6 or 11 or 12 or 13 or 14
16. 3 and 15

Appendix 3 Quality assessment of the included RCT

1- **ROB2 tool**
2- **NIH tool**

Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Version of 22 August 2019

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2-N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.

Study details

Reference	

Study design

X Individually-randomized parallel-group trial

☐ Cluster-randomized parallel-group trial

☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental:		Comparator:	

Specify which outcome is being assessed for risk of bias	
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.	

Is the review team's aim for this result…?

☐ to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)

☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

☐ occurrence of non-protocol interventions

☐ failures in implementing the intervention that could have affected the outcome

☐ non-adherence to their assigned intervention by trial participants

Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

☐ Journal article(s) with results of the trial

☐ Trial protocol

☐ Statistical analysis plan (SAP)

☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)

☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)

☐ “Grey literature” (e.g. unpublished thesis)

☐ Conference abstract(s) about the trial

☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)

☐ Research ethics application

☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)

☐ Personal communication with trialist

☐ Personal communication with the sponsor

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		Y / PY / PN / N / NI
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI

1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI

2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI

Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?		NA / Y / PY / PN / N / NI
2.4. [If applicable:] Were there failures in implementing the		NA / Y / PY / PN / N / NI

intervention that could have affected the outcome?		
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?		NA / Y / PY / PN / N / NI
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns

Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		Y / PY / PN / N / NI
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI

Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		Y / PY / PN / N / NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have		NA / Y / PY / PN / N / NI

been influenced by knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales,		Y / PY / PN / N / NI

definitions, time points) within the outcome domain?		
5.3 ... multiple eligible analyses of the data?		Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Appendix 4 National Heart, Lung, and Blood Institute (NIH) quality assessment tool for before-after (pre-post) with no control group cohort studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?			
2. Were eligibility/selection criteria for the study population prespecified and clearly described?			
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?			
4. Were all eligible participants that met the prespecified entry criteria enrolled?			
5. Was the sample size sufficiently large to provide confidence in the findings?			

Criteria	Yes	No	Other (CD, NR, NA)*
6. Was the test/service/intervention clearly described and delivered consistently across the study population?			
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?			
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?			
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?			
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?			

Criteria	Yes	No	Other (CD, NR, NA)*
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?			
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			

Answers for included pre and post cohorts were demonstrated in Error! Reference source not found.

Appendix 5 Systematic Review Publication

MSJ Experimental Translational Clinical

Review Article

Switching treatments in clinically stable relapsing remitting multiple sclerosis patients planning for pregnancy

Lubna Almouzain, Fiona Stevenson, Declan Chard, Nur Abdul Rahman and Fiona Hamilton

Abstract

Background: The decision to have children can be complex, particularly for people with multiple sclerosis (MS). A key concern is the use of disease modifying drugs (DMDs) during pregnancy, and how continuing, stopping or switching them may affect the mother and child. In people with active MS, stopping medications puts the mother at risk of relapse and disease rebound.

Objectives: Review evidence on the effect of different switching strategies in people with stable relapsing remitting MS (RRMS).

Methods: We searched MEDLINE, EMBASE, EMCARE, CINAHL, SCOPUS, Cochrane Library up to March 2020. Only papers in English were included and no other limits were applied. Seven articles were included: four cohorts, two case reports and one randomized controlled trial (RCT).

Results: Two strategies were found: de-escalating, which was associated with an increased risk of relapses, and switching between first line injectables, with no change in relapse rate observed.

Conclusion: Evidence on the effect of switching strategy on disease course in stable RRMS patients planning for pregnancy is scarce, but when switching, current evidence suggests the risk of relapses mirrors known medication efficacy.

Keywords: Multiple sclerosis, relapsing-remitting, substitute, switch, interferons, glatiramer acetate

Date received: 16 February 2021; accepted: 21 February 2021

Appendix 6 Empirical Studies UCL Ethical Approval

UCL RESEARCH ETHICS COMMITTEE
OFFICE FOR THE VICE PROVOST RESEARCH

9th October 2020

Department of Primary Care and Population Health
UCL

Cc: Lubna Almouzain

Dear Professor

Notification of Ethics Approval with Provisos
Project ID/Title: 18923/001: Knowledge, views and needs of people with multiple sclerosis around reproductive decision making

Further to your satisfactory responses to the Committee's comments, I am pleased to confirm in my capacity as Chair of the UCL Research Ethics Committee (REC) that your study has been ethically approved by the UCL REC until **9th November 2021.**

Ethical approval is subject to the following conditions:

Notification of Amendments to the Research
You must seek Chair's approval for proposed amendments (to include extensions to the duration of the project) to the research for which this approval has been given. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing an 'Amendment Approval Request Form'
http://ethics.grad.ucl.ac.uk/responsibilities.php

Adverse Event Reporting – Serious and Non-Serious
It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (ethics@ucl.ac.uk) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Joint Chairs will decide whether the study should be terminated pending the opinion of an independent expert. For non-serious adverse events the Joint Chairs of the Ethics Committee should again be notified via the Ethics Committee Administrator within ten days of the incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Joint Chairs will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Final Report
At the end of the data collection element of your research we ask that you submit a very brief report (1-2 paragraphs will suffice) which includes in particular issues relating to the ethical implications of the research

i.e. issues obtaining consent, participants withdrawing from the research, confidentiality, protection of participants from physical and mental harm etc.
In addition, please:

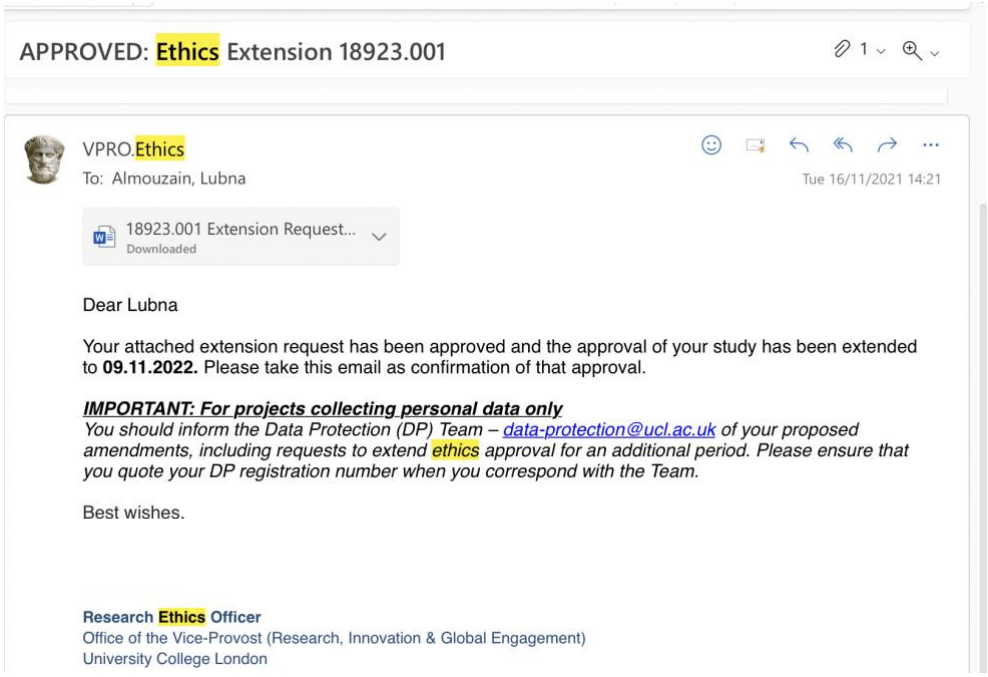
- ensure that you follow all relevant guidance as laid out in UCL's Code of Conduct for Research: https://www.ucl.ac.uk/srs/file/579
- note that you are required to adhere to all research data/records management and storage procedures agreed as part of your application. This will be expected even after completion of the study.

With best wishes for the research.

Yours sincerely

Joint Chair, UCL Research Ethics Committee

Appendix 7 Ethics approval extension confirmation



APPROVED: Ethics Extension 18923.001

VPRO.Ethics
To: Almouzain, Lubna
Tue 16/11/2021 14:21

18923.001 Extension Request...
Downloaded

Dear Lubna

Your attached extension request has been approved and the approval of your study has been extended to **09.11.2022.** Please take this email as confirmation of that approval.

IMPORTANT: For projects collecting personal data only
You should inform the Data Protection (DP) Team – data-protection@ucl.ac.uk of your proposed amendments, including requests to extend ethics approval for an additional period. Please ensure that you quote your DP registration number when you correspond with the Team.

Best wishes.

Research Ethics Officer
Office of the Vice-Provost (Research, Innovation & Global Engagement)
University College London

Appendix 8 Advertisement for Patients Recruitment Through social media

Population Health Sciences, Institute of Epidemiology and Health Care, Primary Care and Population Health Department, E-Health Unit.

UCL

Do you have Multiple Sclerosis?
Do you want to share your experience, concerns, and challenges about taking decisions regarding family planning?

We are exploring your concerns and needs when taking reproductive decisions and taking your opinion of an online digital decision aid tool. **Your participation is valuable!**

What to expect when participating:

1. 30-40 minutes online interviews.
2. 15-20 minutes talk aloud session when you use the online digital aid and give your opinion while using it.

Interested?

Please fill the following registration form:

Registration form.

And send it to:

We will email you with all information that you need to know before your participation.

2- You can participate if:

- You are female
- Diagnosed with MS
- Whether you experienced pregnancy/breastfeeding before or not.

You **cannot** participate if you are currently pregnant or breastfeeding.

This study has been approved by the UCL Research Ethics Committee: Project ID number: 18923/001

Please note that emailing us with your interest and filling the registration form does not commit you in any way.

Appendix 9 Patient and Public Involvement (PPI) Advertisement

Opportunity: Explorative Study Around Reproduction Decision Making with Multiple Sclerosis.

UCL PCPH

UCL

About the opportunity: We are studying knowledge, concerns and needs of people living with multiple sclerosis (MS) when taking the decision to start a family. Our aim is to tackle their needs to help them in taking these vital (pregnancy, breastfeeding, drugs stop or change) decisions considering their disease status, medication used and the support they have. We are looking for 2 PPI members with different opinions and experiences. This will help us to understand patients' needs from all perspectives.

What the role involves

PPI members are required to attend virtual team meetings in all study stages:

- Discussing the idea, explaining from your point of view the most important objective to comprehensively cover (concerns when taking the decision, knowledge to take the decision, other needs?)
- Review the interview questions to match patients' different needs and concerns.
- Check for questions clarity and appropriateness of the language used.

What you will bring

- We are looking for Relapsing Remitting Multiple Sclerosis adult patients.
- Interested in MS and shared decision making.
- Having different experiences, needs and concerns when it comes to family planning.
- Good communication skills.

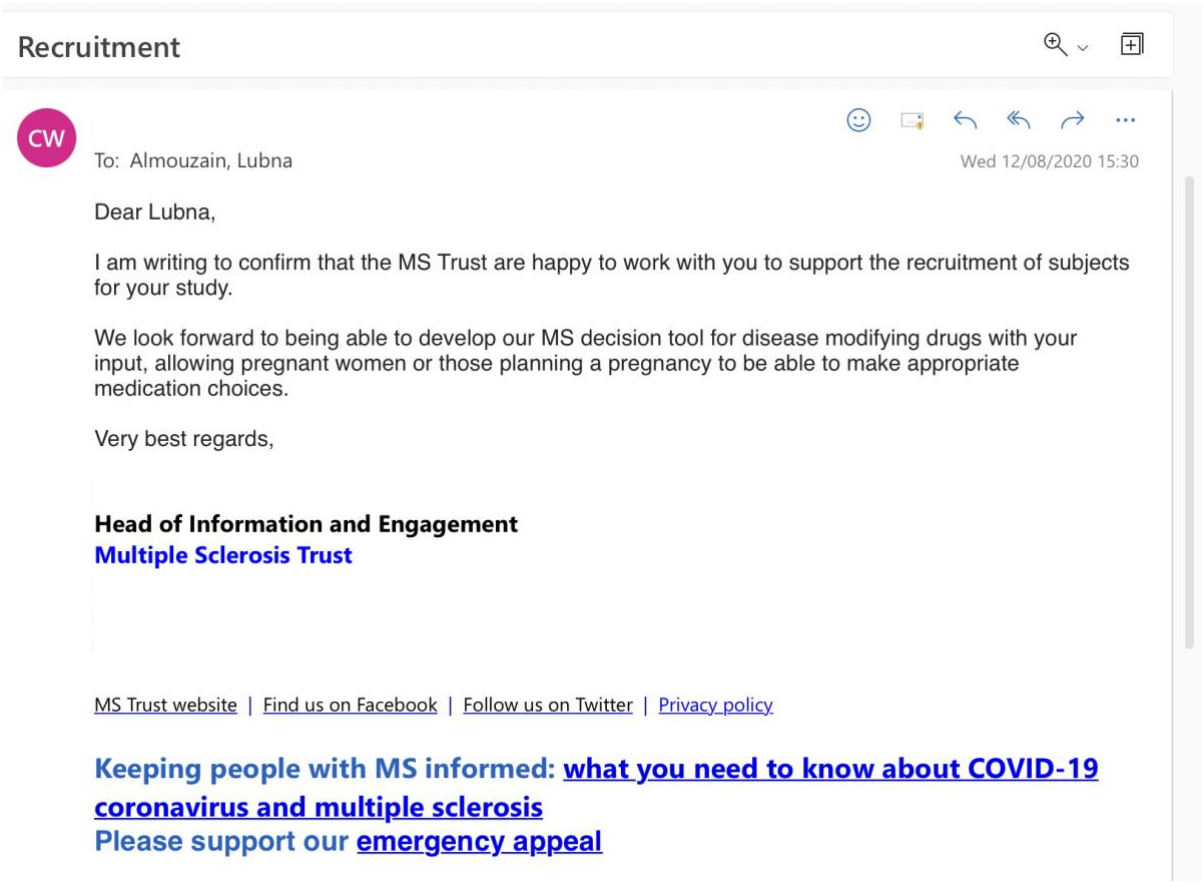
Practicalities

- ✓ **Time:** 2 x 60 minutes online Microsoft Teams meetings, including an initial first piloting meeting and a mid-study meeting. You can access the meetings using a link sent to your email, you will need a laptop with webcam and microphone, or you can use your smartphone.
- ✓ **Length:** Study will take 8-12 months, we prefer you attend both meetings whenever is possible, if your contribution is interrupted for any reason, kindly inform us by email as soon as possible before the assigned meeting time.
- ✓ **Payment:** (25£/ hr) will be paid for each member, 2 hrs pay will be given for 90 mins meetings (if needed)

Applying

Please send a few sentences to Lubna Almouzain explaining your interest in the study at

Appendix 10 MS Trust Letter of Confirmation of the Collaboration



Recruitment

CW

To: Almouzain, Lubna

Wed 12/08/2020 15:30

Dear Lubna,

I am writing to confirm that the MS Trust are happy to work with you to support the recruitment of subjects for your study.

We look forward to being able to develop our MS decision tool for disease modifying drugs with your input, allowing pregnant women or those planning a pregnancy to be able to make appropriate medication choices.

Very best regards,

Head of Information and Engagement
Multiple Sclerosis Trust

MS Trust website | Find us on Facebook | Follow us on Twitter | Privacy policy

Keeping people with MS informed: what you need to know about COVID-19 coronavirus and multiple sclerosis
Please support our emergency appeal

Appendix 11 Consent Form (participants)

Consent Form for Adults Living with Multiple Sclerosis Research Study

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: Knowledge, Views and Needs of Multiple Sclerosis Around Reproductive Decision Making.

Department: Primary Care and Population Health
Name and Contact Details of the Researcher(s):
Lubna Almouzain, PhD student Primary Care & Population Health, University College of London, London, UK.
Supervisors:
Fiona Hamilton
Fiona Stevenson
Chard Declan

This study has been approved by the UCL Research Ethics Committee: Project ID number: 18923/001

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes mean that I DO NOT consent to that part of the study. I

understand that by not giving consent for any one element that I may be deemed ineligible for the study.

		Tick Box
1.	*I met the inclusion criteria and confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions which have been answered to my satisfaction.	
2.	I would like to take part in the individual online video recorded interview.	
3.	I would like to take part in the digital tool talk aloud assessment that follows the interview.	
4.	I understand that I will be able to withdraw my data prior to data analysis **(2 weeks from the date of interview).**	
5.	I consent to participate in the study. I understand that my personal information *(name, age, gender, and medical condition)* will be used for the purposes explained to me. I understand that according to data protection	

	legislation, 'public task' is the lawful basis for processing.	
6.	**I understand that my information will only be used for this project**	
7.	I understand that all personal information which might carry a risk of identification will be removed and that all efforts will be made to ensure you cannot be identified	
8.	I understand that my data gathered in this study will be stored anonymously and securely and it will not be possible to identify me in any reports nor publications.	
9.	I understand that my information may be subject to review by responsible individuals from the University for monitoring and audit purposes.	
10.	I understand that my participation is voluntary and that I am free to withdraw prior to analysis of my data without giving a reason **(2 weeks from the date of the interview).**	
11.	I understand the potential risks of participating and the	

	support that will be available to me should I become distressed during the research.	
12.	I understand there are direct benefits to myself from participating, but the results will help people like me in the future.	
13.	I understand that the data will not be made available to any commercial organisations.	
14.	I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.	
15.	I consent to my interview being video recorded and understand that the recordings will be: • Stored temporarily in UCL secure drive and in a password protected folder. • Viewed and shared with the research team only. • Not shared with any third party. • Transcribed by the research team using automated Microsoft Teams	

	transcription service. • Destroyed following transcription.	
16.	I agree that my medical team may be contacted if any unexpected results are found in relation to my health.	
17.	I am aware of who I should contact if I wish to lodge a complaint.	
18.	I voluntarily agree to take part in this study.	
19.	I understand that anonymised transcripts of my data will be stored in UCL secure drive for the period of 20 years.	
20.	I wish to receive a summary of the findings	

If you have any concern that cannot be resolved by the researcher please contact Dr. Fiona Stevenson, Secondary Supervisor
Professor of Medical Sociology Primary Care & Population Health, University College of London, London, UK.

Name of participant

Date

Signature

Appendix 12 Consent Form (HCP)

Consent Form for Health Care Providers

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: Knowledge, Views and Needs of Multiple Sclerosis Around Reproductive Decision Making and Medication Choice and Management.

Department: Primary Care and Population Health

Name and Contact Details of the Researcher(s):

Lubna Almouzain, PhD student Primary Care & Population Health, University College of London, London, UK.

Supervisors:

Fiona Hamilton

Fiona Stevenson

Chard Declan

This study has been approved by the UCL Research Ethics Committee: Project ID number: 18923/001

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes mean that I DO NOT consent to that part of the study. I

understand that by not giving consent for any one element that I may be deemed ineligible for the study.

		Tick Box
1.	*I meet the inclusion criteria and confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions which have been answered to my satisfaction	
2.	I would like to take part in the individual online video recorded interview.	
3.	I understand that I will be able to withdraw my data prior to data analysis **(within 2 weeks from the date of interview).**	
4.	I consent to participate in the study. I understand that my personal information *(name, age, gender)* will be used for the purposes explained to me. I understand that according to data protection legislation, 'public task' is the lawful basis for processing.	

5.	I understand that my information will only be used for this project	
6.	I understand that all personal information which might carry a risk of identification will be removed and that all efforts will be made to ensure you cannot be identified	
7.	I understand that my data gathered in this study will be stored anonymously and securely and it will not be possible to identify me in any reports nor publications.	
8.	I understand that my information may be subject to review by responsible individuals from the University for monitoring and audit purposes.	
9.	I understand that my participation is voluntary and that I am free to withdraw prior to analysis of my data without giving a reason **(within 2 weeks from the date of the interview).**	
10.	I understand there are no direct benefits to myself from participating but the results will help others the future.	

11.	I understand that the data will not be made available to any commercial organisations.	
12.	I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.	
13.	I consent to my interview being video recorded and understand that the recordings will be: • Stored temporarily in UCL secure drive and in a password protected folder. • Viewed and shared with the research team only. • Not shared with any third party. • Transcribed by the research team using automated Microsoft Teams transcription service. • Destroyed following transcription.	
14.	I am aware of who I should contact if I wish to lodge a complaint.	

15.	I voluntarily agree to take part in this study.	
16.	I understand that anonymised transcripts of my data will be stored in UCL secure drive for the period of 10 years	
17.	I wish to receive a summary of the findings	

If you have any concern that cannot be resolved by the researcher please contact Dr. Fiona Stevenson, Secondary Supervisor
Professor of Medical Sociology Primary Care & Population Health, University College of London, London, UK.

Name of HCP participant
Date
Signature

Appendix 13 Local Privacy Notice

LOCAL PRIVACY NOTICE

1. Introduction

Institute of Epidemiology and Health Care/ Primary Care and Population Health Department ("we" "us", or "our") respects your privacy and is committed to protecting your personal data.

Please read this Privacy Notice carefully – it describes why and how we collect and use personal data and provides information about your rights. It applies to personal data provided to us, both by individuals themselves or by third parties and supplements the following wider UCL privacy notice(s):

- General privacy notice when you visit UCL's website
- Student privacy notice
- Staff privacy notice
- Research participants for health and care purposes privacy notice

We keep this Privacy Notice under regular review. It was last updated on 19 August 2020.

2. About us

Institute of Epidemiology and Health Care/ Primary Care and Population Health Department is part of University College London (UCL).

UCL, a company incorporated by Royal Charter (number RC 000631), is the entity that determines how and why your personal data is processed. This means that UCL is the 'controller' of your personal data for the purposes of data protection law.

3. Personal data that we collect about you

Personal data, or personal information, means any information about an individual from which that person can be identified. It does not include data where the identity has been removed (anonymous data).

We may collect, use, store and transfer different kinds of personal data about you. This may include:

- Your name and contact details.
- ‘Special category’ data about you (this include details about your sexual orientation, information about your health and used medications).

4. How we use your personal data

We will only use your personal data when the law allows us to. Most commonly, we will use your personal data in the following circumstances:

- To register you as a participant and to manage our relationship with you.
- Research study that we are doing about knowledge base, concerns and needs of people with multiple sclerosis when taking reproductive decisions, we need to video record our online interviews for research purpose. These videos will be used for transcription and will be deleted after completion of de-identified transcripts.

Where the processing is based on your consent, you have the right to withdraw your consent at any time by contacting us using the details set out below. Please note that this will not affect the lawfulness of processing based on consent before its withdrawal.

We may also use anonymised data, meaning data from which you cannot be identified, for the purposes of:

- Education and research; or
- Fundraising and promotional purposes.
- Anonymised data may also be used in published reports or journals and at conferences.

5. Who we share your personal data with

Your personal data will be collected and processed primarily by our staff and UCL (Access to your personal information is limited to staff who have a legitimate need to see it for the purpose of carrying out their job at UCL.). We will not share your personal information with any third party.

6. Lawful basis for processing

Data Protection Legislation requires that we meet certain conditions before we are allowed to use your data in the manner described in this notice, including having a "lawful basis" for the processing. The basis for processing will be as follows:

- Consent. You have given us your consent for processing both your personal data and special category data.

7. International transfers

We do not transfer your personal data outside the European Economic Area (EEA).

8. Information security

We have put in place appropriate security measures to prevent your personal data from being accidentally lost, used or accessed in an unauthorised way, altered or disclosed. We have established procedures to deal with any suspected personal data breach and will notify you and any applicable regulator of a breach where we are legally required to do so.

9. Data retention

We will only retain your personal data for as long as necessary to fulfil the purposes we collected it for, including for the purposes of satisfying any legal, accounting, or reporting requirements. We will keep your personal data according to the Records Retention Schedule.

10. Your rights

Under certain circumstances, you may have the following rights under data protection legislation in relation to your personal data:

- Right to request access to your personal data;
- Right to request correction of your personal data;
- Right to request erasure of your personal data;
- Right to object to processing of your personal data;
- Right to request restriction of the processing your personal data;
- Right to request the transfer of your personal data; and
- Right to withdraw consent.

If you wish to exercise any of these rights, please contact the Data Protection Officer.

Contacting us

You can contact UCL by telephoning +44 (0)20 7679 2000 or by writing to: University College London, Gower Street, London WC1E 6BT.

Please note that UCL has appointed a Data Protection Officer. If you have any questions about this Privacy Notice, including any requests to exercise your legal rights, please contact our Data Protection Officer.

11. Complaints

If you wish to complain about our use of personal data, please send an email with the details of your complaint to the Data Protection Officer so that we can look into the issue and respond to you.

You also have the right to lodge a complaint with the Information Commissioner's Office (ICO) (the UK data protection regulator). For further information on your rights and how to complain to the ICO, please refer to the ICO website.

Appendix 14 Participant Information Sheet

Participant Information Sheet for Adults Living with Multiple Sclerosis

UCL Research Ethics Committee Approval ID Number: 18923/001

Title of Study: Knowledge, Views and Needs of Multiple Sclerosis Around Reproductive Decision Making.

_____

Department: Primary Care and Population Health

_____

_____ **Name and Contact Details of the Researcher(s):**
Lubna Almouzain, PhD student Primary Care & Population Health, University College of London, London, UK.
Dr. Fiona Stevenson, Secondary Supervisor
Professor of Medical Sociology Primary Care & Population Health, University College of London, London, UK.

1. **Invitation Paragraph**

   'You are invited to participate in my qualitative research project. This is part of my studies towards a PhD. In this information sheet, I will explain about this project and what you would be asked to do. Kindly read the following information carefully and discuss it with others if you wish. I am happy to answer any questions you have. Thank you for reading this.'

2. **What is the project's purpose?**

   Starting a family is a life changing decision, especially for people living with multiple sclerosis who face the additional challenges of disease and medication management. As more people with MS are considering pregnancy and breastfeeding, I am trying to understand the level of knowledge, views and needs people need to make their decisions.

3. **Why have I been chosen?**

   I am interested in talking to women diagnosed with relapsing remitting MS who are (i) considering having a child, (ii) have had a child, or (iii) have made the decision not to have children.

4. **Do I have to take part?**

It is up to you whether or not you want to take part in my study. If you decided to take part, you will be asked to sign a consent form. You can withdraw from the study at any point up to the analysis of data (2 weeks from the date of the interview) by sending an email. You do not need to provide a reason.

5. What will happen to me if I take part?

You will be interviewed on your own (unless you want someone with you). The interview will last up to an hour. You will be asked some questions about your current knowledge regarding pregnancy and breastfeeding with MS. I will ask for your views, concerns, challenges and needs when taking the decision whether to start a family or not and how can medications be managed during these periods. The interview will be followed by a 15-minute session using a digital decision-making tool. This is an online tool that helps people with MS choose their preferred medication according to the type of MS they have, availability of medications in UK, route of administration and frequency of taking medication. We are planning to add pregnancy/breastfeeding plans to the tool, so you can choose your medication according to that too and you will be asked to give your opinion of the current tool, how do you want to see the tool after adding the reproductive plan? Your ideas? Views and thoughts for a better experience and interface.

<u>Logistics and technical requirements</u>
I will conduct the interview and it will be online because of the current COVID-19 pandemic.
This is to ensure the safety of both yourself and me. You will receive an online invitation on your email with the link to the meeting, we are using the secure Microsoft Teams online platform. You are required to have a good internet connection, a web camera, and a microphone, you can also use your smartphone if you wish. You are not required to download Microsoft teams as you can enter the interview using the provided link through your internet browser.

6. Will I be recorded and how will the recorded media be used?

Your interview will be video recorded using (MS Teams) and will be saved on a UCL secure Microsoft Stream drive. Your videos will only be viewed or shared with my supervisors and will be deleted when I have written up (transcribed) the data.

The video recordings will be transcribed using Microsoft Streams automated transcription service and will be immediately deleted after the completion of transcription. I will take out any identifying information of the transcripts and use these for my analysis. The results of the study will be written up for my thesis, published in

journals and presented in scientific conferences. No other use will be made of the data without your written permission. The transcripts of the recordings will be kept on a secure drive at the University in a password protected folder for 10 years, this time period allows us to publish the work and go back to the data to answer researchers questions after publication. Only myself and my supervisors will have access to the transcripts.

7. What are the possible disadvantages and risks of taking part?

There might be a possible discomfort answering some questions if you have had negative experiences regarding pregnancy and family planning. That will vary from person to person depending on individual experiences and personalities. You can always take a break, ask for family support or skip the question that caused discomfort for you.

8. What are the possible benefits of taking part?

There are no immediate benefits for you as a participant but with your help we hope we can better understand the different needs of people living with MS when starting a family to find solutions that help them take decisions with confidence.
We are also offering a voucher to the value of £25 as a token of gratitude for your participation.

9. What if something goes wrong?

If you have any problem you should let me know as soon as possible via email. If I cannot help you can contact Prof Fiona Stevenson, who is my supervisor and the Head of the Research Department of Primary Care and Population Health If that is not satisfactory you can contact the Chair of the UCL Research Ethics Committee.

10. Will my taking part in this project be kept confidential?

All data collected from you during this project will be strictly confidential, you will not be identifiable in any of the project reports, publications or conference presentations. I will use data which has had any identifying features removed for analysis, reports and publications. No third party will handle the data as the transcription will be done by myself using the Microsoft Teams automated transcription service.

11. Limits to confidentiality

I have a duty to report any possible harm or danger I become aware of to the relevant authorities, I may contact your health

care team if needed. I would inform you of any decisions that might limit your confidentiality.

12. What will happen to the results of the research project?

The results will be part of my PhD thesis and will be published in scientific articles and presented in national or international conferences. It will take almost a year to get results from this study.

13. Local Data Protection Privacy Notice

Notice:

The controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

This 'local' privacy notice sets out the information that applies to this particular study. Further information on how UCL uses participant information can be found in our 'general' privacy notice:

The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the 'local' and 'general' privacy notices.

The categories of personal data used will be as follows:

Name
Age
Gender
Biometrics (face and voice identification in video recordings)

The lawful basis that would be used to process your *personal data* will be performance of a task in the public interest.

Your personal data will be processed following collection and any identifying details removed when the data are transcribed. We will delete your video recordings following transcription and securely archive the anonymised transcripts at UCL for 20 years.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk.

14. Who is organising and funding the research?

This research is sponsored by University College of London (UCL), United Kingdom, and funded by King Saud University (KSU), Saudi Arabia.

15. Contact for further information

Please feel free to contact Lubna Almouzain or her supervisor, Dr. Fiona Stevenson. for any further information, concerns or clarification.
If you are happy to take part in this project, please complete and sign the electronic copy of the consent form, and send it to me.

Thank you for reading this information sheet and for considering taking part in my research study. ----------

Appendix 15 HCP Information Sheet

Participant Information Sheet for HCPs Supporting People Living with Multiple Sclerosis

UCL Research Ethics Committee Approval ID Number: 18923/001

Title of Study: Knowledge, Views and Needs of Multiple Sclerosis Around Reproductive Decision Making and Medication Choice and Management.

Department: Primary Care and Population Health

Name and Contact Details of the Researcher(s):
Lubna Almouzain, PhD student Primary Care & Population Health, University College of London, London, UK.

Dr. Fiona Stevenson, Secondary Supervisor
Professor of Medical Sociology Primary Care & Population Health, University College of London, London, UK.

1. Invitation Paragraph

'You are invited to participate in my qualitative research project. This is part of my studies towards a PhD. In this information sheet, I will explain about this project and what you would be asked to do. Kindly read the following information carefully and discuss it with others if you wish. I am happy to answer any questions you have. Thank you for reading this.'

2. What is the project's purpose?

Starting a family is a life changing decision, especially for people living with multiple sclerosis (MS) who face the additional challenges of disease and medication management. As more people with MS are considering pregnancy and breastfeeding, I am trying to understand the process of the joint decision of family planning and medication choice and management, level of knowledge and needs of MS patients to make their decisions.

3. Why have I been chosen?

I am interested in talking to health care providers (MS consultants, MS specialist nurses, MS specialist pharmacists) supporting women diagnosed with relapsing remitting MS who are (i) considering having a child, (ii) have had a child, or (iii) have made the decision not to have children).

4. Do I have to take part?
It is up to you whether you want to take part in my study. If you decided to take part, you will be asked to sign a consent form. You can withdraw from the study at any point up to the analysis of data (2 weeks from the date of the interview) by sending an email. You do not need to provide a reason.

5. What will happen to me if I take part?
You will be interviewed on your own (unless you want someone with you). You will be asked about your role supporting these women in their decisions about medication and family planning, the decision aids available for them that you offer, challenges you face during the process and your suggestions for a better experience. It will be a 30–40-minute video recorded online interview, via Microsoft Teams secure Platform.

Logistics and technical requirements
I will conduct the interview and it will be online because of the current COVID-19 pandemic. This is to ensure the safety of both you and me. You will receive an online invitation on your email with the link to the meeting. We are using the secure Microsoft Teams online platform. You are required to have a good internet connection, a web camera, and a microphone, you can also use your smartphone if you wish. You are not required to download Microsoft teams as you can enter the interview using the provided link through your internet browser.

6. Will I be recorded and how will the recorded media be used?
Your interview will be video recorded using (MS Teams) and will be saved on a UCL secure Microsoft Stream drive. Your videos will only be viewed or shared with my supervisors and will be deleted when I have written up (transcribed) the data.

The video recordings will be transcribed using Microsoft Streams automated transcription service and will be immediately deleted after the completion of transcription. I will take out any identifying information of the transcripts and use these for my analysis. The results of the study will be written up for my thesis, published in journals and presented in scientific conferences. No other use will be made of the data without your written permission. The transcripts of the recordings will be kept on a secure drive at the University in a password protected folder for 10 years, this time period allows us to publish the work and go back to the data to answer researchers' questions after publication. Only myself and my supervisors will have access to the transcripts.

7. What are the possible disadvantages and risks of taking part?

There might be a possible discomfort answering some questions That will vary from person to person depending on individual experiences and personalities. You can always take a break or skip any questions.

8. What are the possible benefits of taking part?
There are no immediate benefits for you as a participant but with your help we hope we can better understand the different needs of people living with MS when starting a family to find solutions that help them take decisions with confidence.
We are also offering a voucher to the value of £25 as a token of gratitude for your participation.

9. What if something goes wrong?
If you have any problem, you should let me know as soon as possible via email. If I cannot help you can contact Prof. Fiona Stevenson, who is my supervisor and the Head of the Research Department of Primary Care and Population Health. If that is not satisfactory you can contact the Chair of the UCL Research Ethics Committee.

10. Will my taking part in this project be kept confidential?
All data collected from you during this project will be anonymised, you will not be identifiable in any of the project reports, publications, or conference presentations. I will use data which has had any identifying features removed for analysis, reports, and publications.
No third party will handle the data as the transcription will be done by myself using the Microsoft Teams automated transcription service.

11. Limits to confidentiality
I have a duty to report any possible harm or danger I become aware of to the relevant authorities, I may contact your health care team if needed. I would inform you of any decisions that might limit your confidentiality.

12. What will happen to the results of the research project?
The results will be part of my PhD thesis and will be published in scientific articles and presented in national or international conferences. It will take almost a year to get results from this study.

13. Local Data Protection Privacy Notice

Notice:
The controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted.

This ‘local’ privacy notice sets out the information that applies to this study. Further information on how UCL uses participant information can be found in our ‘general’ privacy notice:

The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the ‘local’ and ‘general’ privacy notices.

The categories of personal data used will be as follows:

Name
Age
Gender
Biometrics (face and voice identification in video recordings)

The lawful basis that would be used to process your *personal data* will be performance of a task in the public interest.

Your personal data will be processed following collection and any identifying details removed when the data are transcribed. We will delete your video recordings following transcription and securely archive the anonymised transcripts at UCL for 20 years.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance.

14. Who is organising and funding the research?
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15. Contact for further information.
Please feel free to contact Lubna Almouzain
or her supervisor, Dr. Fiona Stevenson for any further information, concerns or clarification.

If you are happy to take part in this project, please complete and sign the electronic copy of the consent form, and send it to me.

Thank you for reading this information sheet and for considering taking part in my research study.

Appendix 16 Participant Interview Questions

Interview Questions

The decision

1- How does MS diagnosis affect your life plans?
Probes: How do you think it affects it? Can you give an example? Why do you think it affected your decision?
Prompts: Do you think it affected your reproductive and family plans? (Planned number of kids before and after diagnosis, the decision itself, the timing).

2- How do family planning and DMD choice inform and affect one another in your case?
Prompts: timing, plans, treatment

3- Can you tell us more about the decision process (choosing the medication and family plans)?
Probes: What did you consider when taking decisions?
Prompts: mother health, baby's health, negative experience, disability, disease progression, medication use, support, energy levels, non-MS related, hereditary,

4- What is the Major factor/person/tool that helped you decide?
Probes: How did it help you? In what ways? Why do you think so?
Prompts: HCP conversations, decision approach, time,

5- How do you feel about your decision?
Probes: would you do things differently?
Prompts: any regrets?

Knowledge

6- What do you know about pregnancy and breastfeeding safety for women living with MS?
Probes: Why do you think so? Where do you usually seek information on this regard from?
Prompts: contraception, fertility, post-partum, hereditary, medication safety.

Support

7- Can you tell me about your support system and their role in the decision?
Probes: How did your support system helped you with your decision?
Prompts: family, friend, partner, HCP, social groups…

Needs

8- How do you think we can help women living with MS take an informed decision regarding family planning with confidence?

Probes: Can you give me an example? Can you tell me more?

Prompts: Health Care providers counselling (nurse, physician, pharmacist)? Internet, workshops, digital aids, etc.

9- Do you think you want to add any more information on this topic that we might have missed?

End of interview questions and start of the talk aloud session.

Thank you again for your valuable participation. These data will be used anonymously as previously discussed and agreed upon in the information sheet and consent. Please do not hesitate to ask any question you have.

Appendix 17 HCP Interview Questions

Interview Questions

1- Can you describe your role as (Consultant, Pharmacist, Nurse) in the decision- making process regarding MS patients' reproductive plans and medication choices considering those plans?

Probes: Can you give me an example? How do you help patients?

Prompts: the decision is (shared, one sided), systems, referrals.

2- How would you describe the current practice when helping women with MS to make treatment decisions in the context of their family plans?

Probes: Can you give an example? Why do you think this is the case?

Prompts: Do you have a specialised service for this concern?

3- How can we enhance our practice on this regard?

Prompts: Workshops? GP care? supportive care? digital aids? Obstetricians? Standardization?

4- What are the main knowledge resources people with MS use in the context of pregnancy/breastfeeding and MS?

Probes: Why do you think so? Can you give me an example? Pros and cons? How does it impact patients' care and decision process? (Unwanted pregnancies, not getting pregnant while they wish for it,)

Prompts: online, booklets, HCP advice

5- What do you think are the main concerns and challenges patients have when taking the decision to get pregnant/breastfeed when they live with MS from your point of view?

Probes: Why do you think this can impose a concern/challenge? Can you tell me more?

Prompts: lack of knowledge, health care system, mother health, baby's health, negative experience, disability, disease progression, medication use, family support, energy levels, non-MS related?

6- What are the challenges you face as an HCP (consultant-nurse-pharmacist) when doing your role helping MS patients with their decisions?

Probes: Can you elaborate more about that?

Prompts: Mental status of the patients? Rapport? Time? Documentation?

7- How do you think we can help women living with MS take an informed and confident shared decision regarding family planning and medication management?

Probes: Can you give me an example? Can you tell me more?

Prompts: Health Care providers counselling (nurse, physician, pharmacist)? Internet, workshops, digital aids), things you can do (not in the system yet) to help in the decision and wish to be implemented.

8- What do you think of the MS Trust digital tool?

Probes: Why do you think so? Can you explain? How can we overcome/ promote this?

Prompts: Do you know another better digital aid? Why do you think it is good? How can we enhance? What are the barriers in such tools?

9- Is there anything you think we haven't covered with our questions that you want to add?

End of interview questions

Thank you again for your valuable participation. These data will be used anonymously as previously discussed and agreed upon in the information sheet and consent. Please do not hesitate to ask any question you have.