Volume 1

THE LIVED EXPERIENCE OF SHARED MEDICAL DECISION MAKING IN PEOPLE WITH MS

By

JOANNA MATHEWS

A thesis submitted to the University of Birmingham for the degree of DOCTOR OF CLINICAL PSYCHOLOGY

Department of Clinical Psychology

School of Psychology

University of Birmingham

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Overview

This thesis is submitted in partial fulfilment of the requirements for the degree of Doctorate of Clinical Psychology (Clin.Psy.D) at the University of Birmingham. The thesis consists of two volumes.

Volume I This volume comprises three chapters. The first chapter is a systematic literature review and meta-analysis exploring the prevalence of depression and suicidal ideation in people with Multiple Sclerosis. The second chapter is an empirical study exploring the experience of shared medical decision making in people with MS. The third chapter is a public domain briefing document providing an accessible summary of both the meta-analysis and empirical paper.

Volume II Five Clinical Practice Reports (CPRs) are presented in this volume. The first report details the case of a 76-year-old woman experiencing low mood, formulated from cognitive-behavioural and psychodynamic perspectives. The second report presents a service evaluation, conducted in an Older Adult service to explore the extent to which inpatient dementia wards in a West Midlands health trust met the definition of 'dementia friendly' in accordance with national standards and guidance. The third report presents a case study of a 26-year-old female with Asperger's Syndrome who was experiencing low mood and outlines a psychological intervention drawn from schema therapy. The fourth report presents the process of consultation involved in implementing a positive behaviour support plan for a 46-year-old female with Down's Syndrome to illustrate clinical leadership in healthcare. The fifth is an abstract of an oral presentation given regarding a single case experimental design evaluating the effectiveness of a schema therapy-based intervention on reducing self harm behaviours in a 23-year-old female.

All names and identifying features have been changed to maintain confidentiality.

Dedication

This work is dedicated to Jamie Griggs. I'm so sorry the world never got to see your thesis.

Acknowledgments

Thank you to the six participants who gave their time and offered me such an honest insight into their lives. My research asked them to reflect at a time when they had a lot to consider, and I am full of gratitude that they took the time to do so.

Thank you to the clients who agreed for their work to be shared in my clinical practice reports, and in fact to all the clients I have worked with during training. I learned a great deal from them and wish them all safe and contented futures.

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To my parents, this course has reinforced that I am exceptionally privileged to have had the care, attention and opportunities you gave me. Thank you.

To Dave, I love you very much. Even though there was often a distance between us during this process, it has always felt like you have been alongside me. I am so grateful for both the emotional and practical support, and I am so proud of how we have coped and grown.

And to Charlie, if you ever happen to open Mummy's thesis then know I love you unconditionally from the top of your lovely little head to the tips of your lovely little toes.

Table of Contents

VOLUME I

Table of Contents

VOLUME II

LIST OF ILLUSTRATIONS

VOLUME I

LITERATURE REVIEW AND META-ANALYSIS

VOLUME II

CLINICAL PRACTICE REPORT 1

CLINICAL PRACTICE REPORT 2

CLINICAL PRACTICE REPORT 3

CLINICAL PRACTICE REPORT 4

LIST OF TABLES

VOLUME I

LITERATURE REVIEW AND META-ANALYSIS

EMPIRICAL RESEARCH PAPER

Volume I

Chapter 1
Literature Review and Meta-analysis: What is the prevalence of depression and suicidal ideation in people with Multiple Sclerosis?

Abstract

Background: Psychological distress, including depression and suicidal ideation, is thought to be elevated in people with Multiple Sclerosis compared to the general population although there is notable variation in prevalence estimates across the literature.

Aims: The current review aims to estimate the prevalence of depression and suicidal ideation in people with Multiple Sclerosis.

Methods: Systematic searches of three electronic databases were conducted using a search term strategy specific to depression, suicidal ideation and Multiple Sclerosis. Studies were screened against inclusion criteria, with included studies appraised for their methodological quality.

Results: Meta-analysis of seventy-four studies estimated the prevalence rate of depression as 32.1% (CI 28.5 to 35.7). However, there was substantial between studies variation and inclusion of additional moderator variables such as percentage of gender and disability did not reduce heterogeneity to an acceptable level. A number of aspects of quality significantly impacted the estimated prevalence rate and studies which were identified as low risk of bias estimated a prevalence rate of 25.9% (CI 13.12 to 38.86). Seven studies estimated the prevalence rate of suicidal ideation in MS of 14% (CI 0.07-0.21). However, problematic heterogeneity was observed (I^2=98%).

Conclusions: Data of a large number of patients indicate increased prevalence of depression and suicidal ideation in MS compared to the general population, however caution must be applied due to extreme variation between studies. Quality recommendations are made for future research with the aim of reducing sources of heterogeneity including for future studies to ensure target populations are a close representation to the national population and to ensure risk of non-response bias is minimal.

Keywords: systematic review, meta-analysis, depression, suicidal ideation, suicidality, multiple sclerosis.

Introduction

Multiple Sclerosis is a recurrent inflammatory disorder of the central nervous system, with a varying symptomatic course. The disorder is thought to impact 2.3 million people globally and is documented as one of the greatest causes of disability in young people, particularly in Europe and America (Kobelt, Thompson, Berg, Gannedahl, Eriksson, 2017). The disease course is most often categorised into three different types referred to as: relapsing remitting MS (RRMS), primary progressive MS (PPMS) and secondary progressive MS (SPMS). IN RRMS patients experience times where their symptoms get worse, followed by remission. In PPMS symptoms will get steadily worse. IN SPMS, patients will have previously experienced a pattern of symptomatic relapse and remission, which then shifts to a progressive presentation. In progressive MS types, where there is a higher level of increasing disability compared to RRMS, higher levels of depression and suicidal ideation are often reported (Chwastiak et al., 2002; Dennis et al., 2009; Sarısoy, Terzi, Gümüş, & Pazvantoğlu, 2013; Turner et al., 2006).

Multiple Sclerosis and depression

Depression is common in Multiple Sclerosis (MS), and is considered to be elevated compared with the general population (e.g. Siegert & Abernethy, 2005; Marrie et al., 2015). A complex interplay of variables is likely to underlie the comorbidity of MS and depression. Depression could be a response to a disabling and chronic disease, with the intermittent and debilitating nature of MS symptoms further exacerbating psychological distress (Amtmann et al, 2015). MS patients could also be at a heightened risk of developing depression by several psychosocial factors such as lack of social support, loss of status/identity or maladaptive coping styles (Rommer, Sühnel, König & Zettl, 2016). Emerging research has also suggested that neurobiological processes that take place in the course of MS, such as changes in brain structure and immunological and inflammatory pathways may contribute to an increased susceptibility to developing depression (Rojas, Sanchez, Patrucco, Miguez, Besada, & Cristiano, 2017; Morris, Reiche, Murru, Carvalho, Maes, Berk, & Puri, 2018).

Furthermore, people with MS are at an increased risk of experiencing chronic, as opposed to episodic depression, compared to the general population (Koch et al.

2015). In part this may be because associated symptoms of depression such as fatigue and lack of motivation adversely affect the disease course of MS. Several studies have highlighted that, when compared to persons with MS, persons with MS and depression experience reduced quality of life, poorer adherence to treatment regimens, reduced cognitive function, an increase in the likelihood of engaging in negative health behaviours and a direct pathophysiological effect on immunity (Zwibel, 2009; Bruce, Hancock, Arnett & Lynch, 2010; Nunnari et al., 2015; Marrie, Horwitz, Cutter, Tyry, Campagnolo & Vollmer, 2009; Mckay et al., 2018; Gold & Irwin, 2009). Thus, a vicious cycle is created whereby the symptoms of MS and the symptoms of depression are mutually exacerbated.

Boeschoten et al. (2017) conducted a meta-analysis of papers published up until December 2014 investigating the prevalence of depression and anxiety in Multiple Sclerosis, estimating overall prevalence of depression at 30.5%. Further subset analysis showed that there is a significantly higher prevalence rate of depression in studies that measured depression through self report symptom measures compared to studies which measured depression with formal diagnostic criteria. The authors noted a high level of heterogeneity in prevalence estimates and cited several possible reasons for this, including (1) whether the individual is receiving disease modifying therapies or anti-depressant treatment and (2) the type and course of MS. Sociodemographic data associated with depressive symptoms including: 1) participants marital status, 2) employment status and 3) gender were not analysed by Boeschoten et al. (2017) but may further address some of the heterogeneity in depression prevalence rates.

Multiple Sclerosis and suicidal ideation

Major depression is linked to an elevated risk of suicidal ideation, which in turn is linked to increased rates of suicide attempts and completed suicides (Pompili et al. 2012; Brown, Beck, Steer, & Grisham, 2000; Lewis, Williams, Koko, Woolmore, Jones & Powell, 2017). Suicidal ideation is recognised as a symptom of major depression, and as such features in popular screening questionnaires (Lonnqvist, 2000; Kroenke, Spizer & Williams, 2001; Beck, Steer & Brown, 1996). Suicidal ideation is elevated among patients suffering from physical illnesses (Kishi, Robinson & Kosier, 2001; Kavalidou, Smith & O'Connor, 2017), however prevalence

rates of suicidal ideation in MS appear to vary. One reason for this is likely to be the different methods utilised to measure suicidal ideation. Furthermore, a discrepancy between self-reported suicidal ideation and that disclosed to medical professionals is likely to exist due to patient fear of stigma or worrying the professional (Caine & Schwid, 2002). However, thoughts of suicide are one of the most accurate predictors of completed suicide, with an elevated risk in the first year of suicidal ideation progressing to attempting suicide (Kessler, Borges & Walters, 1999; Nock, Borges, Bromet. Cha, Kessler, & Lee, 2008).

The relationship between suicidal ideation and depression is well-established (Pompili et al., 2012), however it has been found that in the MS population, not all suicides have occurred in the context of depressive symptoms (Sadovnick et al., 1991). Thus, people can freely desire suicide, or a hastened death based upon a logical, carefully contemplated decision in the absence of depression or other psychiatric difficulties. This phenomenon has been termed 'rational suicide' (Onkay-Ho, 2014). There is limited research into this, however in one study of seventy-five MS patients, fourteen had experienced suicidal ideation but had mild or no symptoms of depression (Lewis, Williams, Koko, Woolmore, Jones & Powell, 2017). The same study also noted how depressive symptoms mediated the relationship between perceived and actual disability and a patient's experience of suicidal ideation.

Therefore attending to both depressive symptoms and suicidal ideation in MS is a priority for health professionals, as it may be that to appropriately investigate these symptoms may, to some extent, prevent avoidable suicides (Faber, 2003). In a systematic review of suicidality in MS patients, Pompili et al. (2012) identified several risk factors for suicide in MS patients, with male gender, social isolation, major depression and alcohol abuse all being related to a higher risk of completing suicide.

Suicide is globally estimated as the seventeenth leading cause of death (WHO, 2015). It is largely accepted that mortality rates are increased in MS compared to the general population however there is a lack of uncertainty as to the prevalence of suicide (Feinstein & Pavisian, 2017). The interpersonal theory of suicide (Joiner, 2005; Van Orden et al., 2010) suggests that suicidal desire emerges when individuals experience enduring feelings of perceived burdensomeness and a lack of

belonging. At a point when such an experience feels intractable and hopeless, if both suicidal desire and an acquired capability for suicide are present, then the risk of a fatal outcome increases. When applying this theory to an older adult population, Van Orden and Conwell (2011) found that physical health conditions were a strong contributor to both feelings of perceived burdensomeness and lack of belonging. In populations with long term health conditions, including Chronic Pain and Rheumatoid Disease, the theory also appears to identify those at risk of increased suicidality (Wilson, Heenan, Kowal, Henderson, Williams & Castillo, 2017; Shim, Song, Park, Lee, Go & Hahm, 2017). The theory has not been tested in patients with Multiple Sclerosis, however a qualitative study investigating suicidality in MS also appears to highlight increased dependence on others and the burden this may place on family members as a key theme (Karasouli, Latchford & Owens, 2014).

Aims

Given the links between depression and suicidal ideation, this systematic review and meta-analysis aims to both update Boeschoten' et al.'s (2017) findings on the prevalence rates of depression in MS, and where possible, include socio-demographic data not analysed in the existing meta-analysis to attempt to further explain heterogeneity in reported prevalence rates for depression. Despite publication in 2017, Boeschoten et al.'s search was actually conducted up to 2014, and thus a significant number of additional research papers have been published including one with a very large sample size of approximately 45,000 people with MS. Furthermore, despite attempts at sub-group analysis the level of heterogeneity in Boeschoten et al. (2017) was high (I^2=99.4%). Therefore, in this meta-analysis additional data which attempts to explore between study variation has been collected including: 1) percentage of study sample who are married; 2) percentage of study sample who are employed and 3) percentage of study sample who are university educated. Additional analyses of quality criterion will also be carried out.

Boeschoten et al.'s (2017) research also investigated the prevalence of anxiety in MS, however at the time of completing the literature searches for this study only two new studies had been published reporting prevalence rates of anxiety. Therefore, further analysis investigating the prevalence of anxiety in Multiple Sclerosis was not felt to be warranted at this time. The study also applies additional search criteria to

estimate currently unreported prevalence rates of suicidal ideation in MS populations with the hope of providing greater clarity on this important clinical phenomenon.

Method

Searches

Two separate systematic computerized searches in PubMed, EMBASE, and Psycinfo was completed in August 2017 for studies on 1) depression and 2) suicidal ideation in Multiple Sclerosis. A search strategy was developed which was adjusted for each of the databases: For the depression search, the medical subject headings (MeSH) terms ‘Depression’, ‘Depressive Disorder’, ‘Depressive’, ‘Mood Disorders’, ‘Distress’, ‘Psychological’, ‘Mental’, ‘Neurotic’ were combined with ‘Multiple Sclerosis’ and with ‘Epidemiology’, ‘Epidemiologic Studies’, and ‘Prevalence’. For the second search ‘Self-injurious behaviour’, ‘Suicide’ ‘Parasuicidal behaviour’, ‘Suicidal Ideation’, were combined with ‘Multiple Sclerosis’ and with ‘Epidemiology’, ‘Epidemiologic Studies’, and ‘Prevalence’. The search was supplemented with a free text word search of these terms (electronic search strategy is displayed in Appendix A).

Inclusion and Exclusion Criteria.

When selecting depression studies, the same inclusion and exclusion criteria outlined in Boeschoten et al. (2017) were applied. Therefore, studies investigating the prevalence of depression were included if they met the following criteria:

1) full text publication in English in a peer reviewed journal;
2) a sample size of ≥ 200 of outpatients with an MS diagnosis provided by an appropriately qualified clinician
3) report of a depressive disorder somewhere during the course of MS by a clinician, identified with (semi) structured interviews based on the Diagnostic and Statistical Manual of Mental disorders (DSM III/IV), the International Classification of Diseases (ICD-9/10) or the International Classification of Primary Care (ICPC) on depressive disorders, or clinically significant depressive symptoms identified with self-report questionnaires with appropriate psychometric quality (no sub-scales or self-report diagnosis); and

4) provision of sufficient information to calculate prevalence rates e.g. sample size and number or percentages of depressed patients.

Studies were excluded if they

1) contained errors in the calculation or presentation of the results
2) included patients under the age of 16 years
3) included only patients who had been diagnosed with Clinically Isolated Syndrome, a first episode of neurological symptoms lasting at least 24 hours which may be an indicator of MS and
4) included an epidemiologically selective sample. For example, case report studies or small case cohort studies may select on the basis of atypical presentation and intervention studies preselect participants on the basis of health status.

The same inclusion and exclusion criterion were applied to the suicidal ideation search with the following exceptions: 1) a sample size of ≥ 150 of outpatients with an MS diagnosis was included, instead of ≥200 in the depression group, and 2) studies which measured suicidal ideation using participant self-reports were also included. A reduction in the minimum participant number was felt to be necessary because of a lack of empirical literature in the topic area and it was felt that the inclusion of more studies was important to explore this under-researched area. It is also documented that recruiting significant numbers of participants can be difficult due to the sensitive subject matter when investigating suicidality, and this may account for the limited literature (Akhurst et al., 1996; Powis, 2002) Self-report measures were included because there are currently limited methods for measuring suicidal ideation. Patients have been found to underreport suicidal thoughts, to not worry physicians, and thus to get an accurate understanding of the prevalence of suicidal ideation, self-report measures should be included (Caine & Schwid, 2002).

Table 1: Selection criteria for primary studies

Exclusion criteria	*Rationale*
Multiple Sclerosis Group *The clinical sample group must have received a diagnosis of MS according to Macdonald or Posner criteria in at least 75% of cases. Papers which included a high percentage of participants with Clinically Isolated Syndrome (CIS) were excluded.*	To ensure that the research is estimating prevalence in the appropriate clinical group, people with MS. Ensuring recorded diagnosis of MS aims to also reduce heterogeneity (which is likely to dissipate the differences reported in the research). CIS patients were excluded because, it was felt that patients would not be experiencing the same chronic condition associated to an MS diagnosis, and risk increasing overall heterogeneity.
Article Type *Review articles, reviews, theoretical frameworks or models, clinical guidance papers, commentaries, test development or tool validation papers, single and group case studies, clinical protocols and qualitative studies were excluded.*	Articles of these types do not provide the data required for meta-analysis.
Sufficient Summary Data *Studies are required to provide sample size and number or percentages of depressed patients*	Provision of sufficient information to calculate prevalence rates
Adulthood *Samples were limited to individuals who were over 18 years old, though participants may have received their MS diagnosis in childhood.*	This is in accordance with the exclusion criteria established by Boeschoten et al. (2017) and aims to reduce heterogeneity across studies.
Depression Group *Report of a depressive disorder somewhere during the course of MS by a clinician, identified with (semi) structured interviews based on the Diagnostic and Statistical Manual of Mental disorders (DSM III/IV), the International Classification of Diseases*	This is in accordance with the exclusion criteria established by Boeschoten et al. (2017). Exclusion of self-reporting depression aims to remove studies with persons with sub-clinical depression.

(ICD-9/10) or the International Classification of Primary Care (ICPC) on depressive disorders, or clinically significant depressive symptoms identified with self-report questionnaires with appropriate psychometric quality (no sub-scales or self-report diagnosis)	
Suicidality Group *Studies which measured suicidal ideation were measured using self-report questionnaires or were recorded on the patient's medical records*	There is a recognition that the inclusion of patients self-reporting suicidal ideation may increase heterogeneity. However, there are currently a lack of validated measures capturing suicidality as well as evidence that participants under-report in clinical settings (Caine & Schwid, 2002).
Sample size *Depression analysis: ≥ 200 of outpatients with an MS diagnosis* ***Suicidal ideation analysis:*** *of ≥ 150 of outpatients with an MS diagnosis*	This is in accordance with the exclusion criteria established by Boeschoten et al. (2017) and aims to reduce 'small study effects' (Sterne, Gavaghan & Egger, 2001). Suicidal ideation studies were reduced to a minimum of 150 participants because recruitment of significant numbers of participants can be difficult due to the sensitive subject matter, and this may account for the limited literature (Akhurst et al., 1996; Powis, 2002)

Selection of studies - Depression

The systematic literature search returned 854 studies published between November 2014 and August 2017. Two-hundred and eighty-five duplicate publications were excluded. Eighty-nine studies were excluded due to not being published in English or published in full text in a peer reviewed journal article. After this the first author (JM) screened all remaining abstracts on selection criteria. Four-hundred and twenty-six were excluded due to irrelevant subjects. Fifty-four studies were excluded due to containing less than the designated participant number. Five studies were excluded because they contained data which had been included in the previous meta-analysis. Sixteen studies from the search were included in the final meta-analysis. These were

added to the existing 58 studies extracted in Boeschoten et al.'s (2017) analysis. In case of indistinctness, full texts were consulted. Reference lists of the selected articles were checked to identify further articles, but no further articles were identified utilising this method.

Several authors reported outcomes from the same cohort of participants over several articles. In cases of multiple reporting of outcomes, the most recent publication with the largest sample size was included, with sample size given priority over publication year. Our updated search returned studies which reported data that had already been published in alternative empirical papers included in Boeschoten et al. (2017)'s analysis. The same rules of inclusion were applied, whereby if the sample size of a new paper exceeded that of a paper included in the original analysis it would be included in the new analysis and the existing paper would be removed.

Selection of studies – suicidal ideation

The systematic literature search returned 213 studies published between August 1965 and August 2017. Forty-one duplicate publications were excluded. Twelve studies were excluded due to not being published in English or not available in full text in a peer reviewed journal article. After this all remaining abstracts were screened on selection criteria. One hundred and forty-three were excluded due to irrelevant subjects. Fourteen studies were excluded due to containing less than the minimum sample size.

Of the selected studies, 7 studies wereincluded in the final meta-analysis on suicidal ideation. The same quality check process was applied.

Data Extraction

All data was extracted by the author. The reliability of selection processes and data extraction was checked by another rater on a 10% random sample of the studies identified in the electronic searches. The level of agreement was 100%.

It is anticipated that event rates will be reported as the number of participants with and without depression in a sample of persons with MS. If selected studies provided event rates for a comparator group, then this data was also extracted to calculate a relative risk effect.

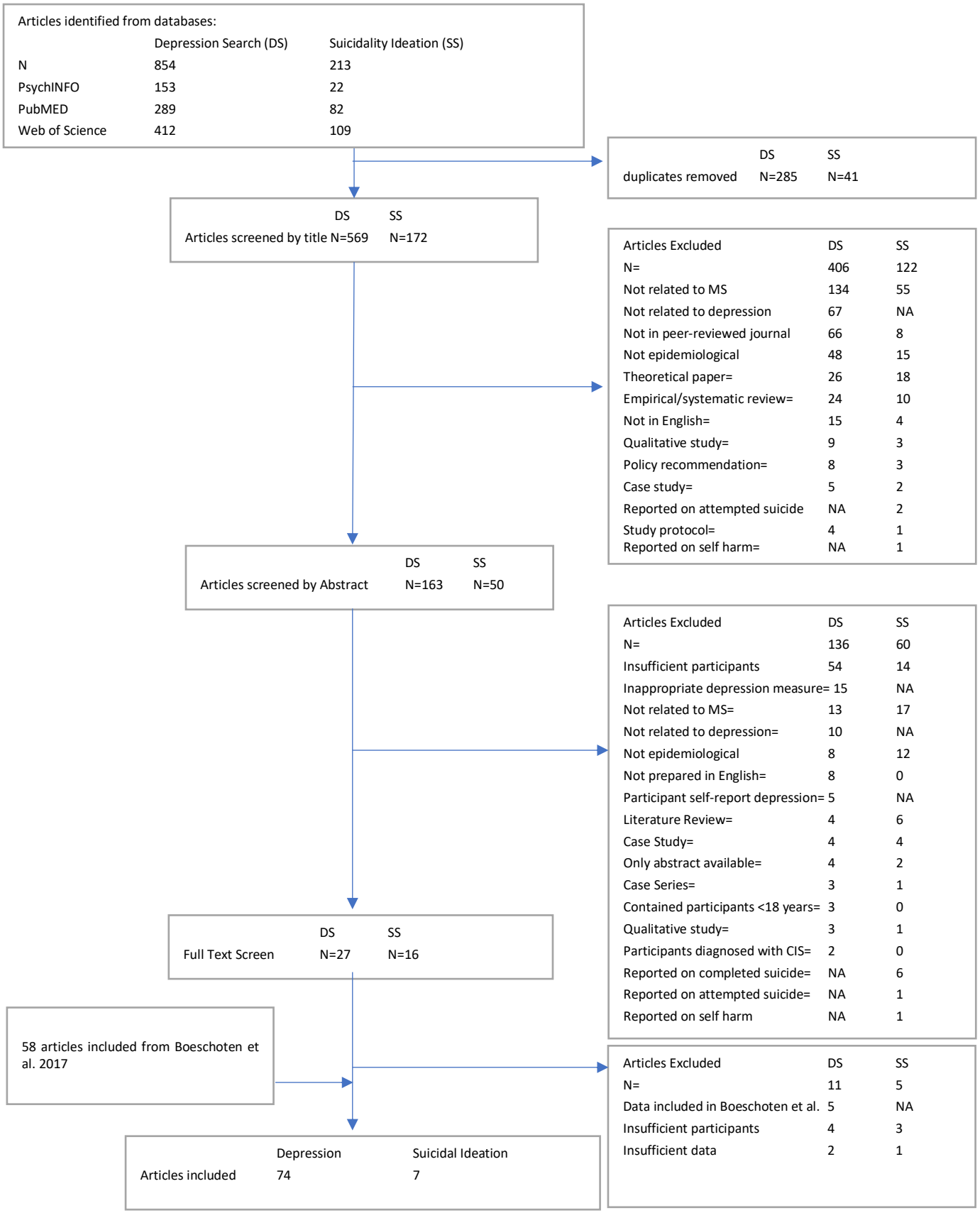


Figure 1: Application of inclusion and exclusion criteria

Quality Framework

Hoy et al.'s (2012) quality criteria was utilised to identify and assess risks of bias in the selected studies. Hoy et al. developed the quality criteria to assess the risk of bias specifically in prevalence studies. Items 1-4 in the checklist assess a study's external validity (e.g. selection bias, representativeness to population) and items 5-10 assess a study's internal validity (e.g. bias related to analysis and bias related to measurement). The quality checklist has been widely used in systematic reviews investigating prevalence in health populations, and had been used in Boeschoten et al.'s (2017) meta-analysis investigating the prevalence of depression in MS. The quality criteria has been critiqued for not assessing participant number (Munn, Moola, Riitano & Lisy, 2014), however because the study inclusion criteria in this analysis set a minimum participant number, this was not felt likely to be problematic in this meta-analysis.

As part of the quality check, all included studies were marked on each item as either a high or low risk of bias. Where relevant, if there was insufficient information this was documented as an unclear risk (see Table two). An overall quality mark was calculated: 2 points for each low risk item, 1 point for an unclear risk (where relevant) and 0 points for high risk items, with a possible maximum quality score of 20.

Table 2: Quality framework applied to assess risk of bias. Adapted from Hoy et al. (2012)

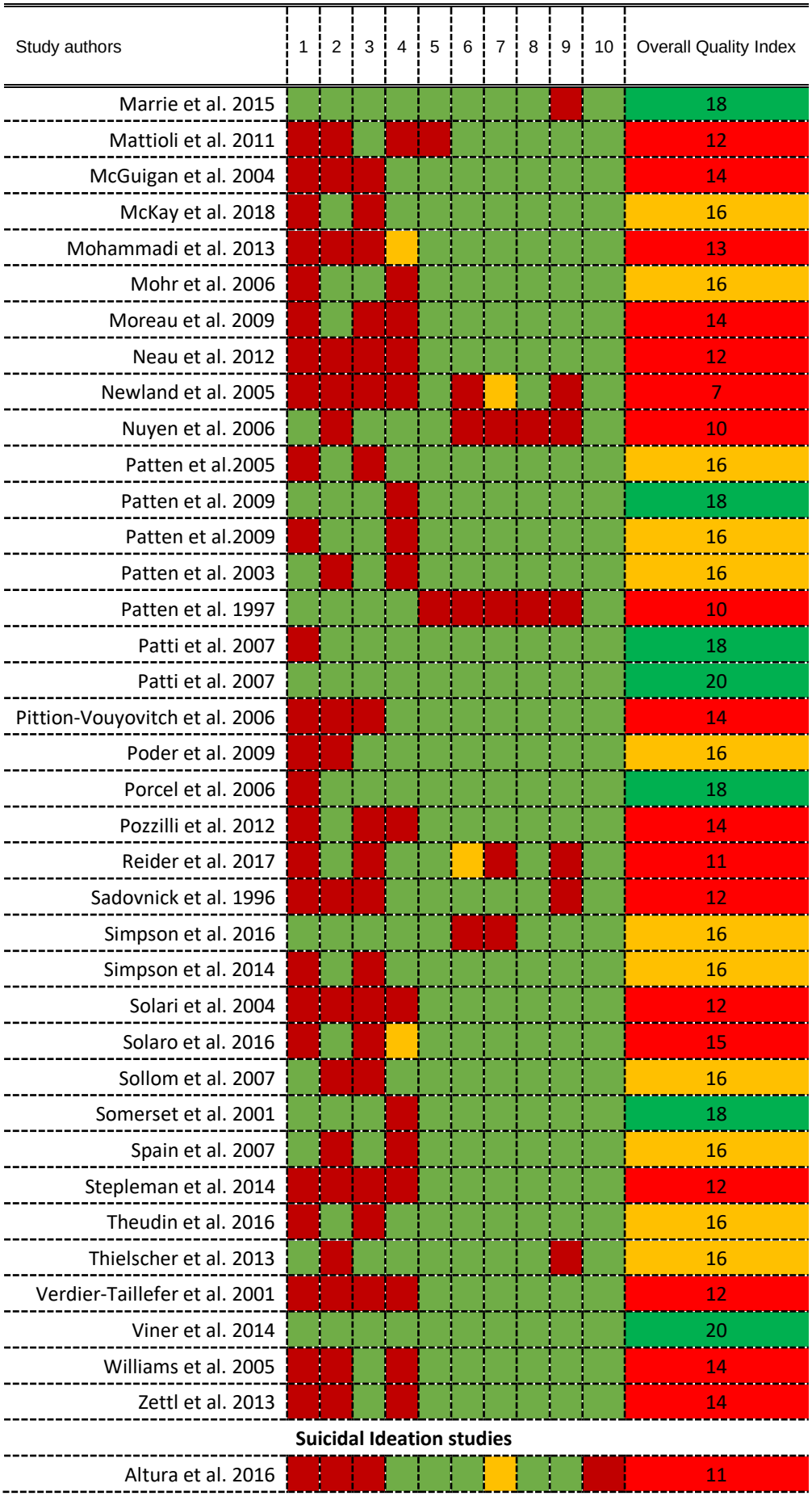
Domain	Details	Risk of Bias
Was the study's target population a close representation of the national population in relation to relevant variables?	The study's target population refers to the group of people or entities to which the results of the study will be generalised. The criterion investigates whether the target population identified in a study is a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation	High Risk- The study's target population was a specific population that is clearly not representative of the national population, such as a small single-site MS clinic. Unclear Risk- It is unclear regarding the study's target population. The study recruits from multiple sites but does not report on relevant variables Low Risk- The study's target population was a close representation of the national population, with reference explicitly made to this in the method section.
Was the sampling frame a true or close representation of the target population?	The sampling frame is a list of the sampling units in the target population and the study sample is drawn from this list.	High Risk- The sampling frame was a list of just one group (for example only females/only war veterans/only individuals with PPMS) within the overall target population. In comparison, the target population is of comprised many groups. Low Risk- The sampling frame was a true or close representation of the target population and was a list of almost every individual within the target population.
Was some form of random selection used to select the sample OR was a census undertaken?	A census collects information from every unit in the sampling frame. In a survey, only part of the sampling frame is sampled. In these instances, random selection of the sample helps minimise study bias.	High Risk- A census was NOT undertaken, AND some form of random selection was NOT used to select the sample. Low Risk- A census was undertaken, OR, some form of random selection was used to select the sample (e.g. simple random sampling, stratified random sampling, cluster sampling, systematic sampling).
Was the likelihood of non-response bias minimal?	Non-response bias is the variation between the true estimate of prevalence of the original sample list (people who are invited to participate in the study) and the estimated prevalence from those actual respondents. Most often, this form of bias is created by refusals to participate or the inability to reach some respondents. Hoy et al. define a study be at a low risk of non-response bias, if the response rate reported is >/=75%, or evidence of an analysis that showed no significant difference in relevant demographic characteristics between responders and non-responders.	High Risk- The response rate was <75%, and if any analysis comparing responders and non-responders was done, it showed a significant difference in relevant demographic characteristics between responders and non-responders or response rates were not reported. Unclear Risk- Response rates was reported as >/=75%, however participants completed only partial parts of the datasets so unclear about true non-response bias Low Risk- The response rate for the study was >/=75%, OR, an analysis was performed that showed no significant difference in relevant demographic characteristics between responders and non-responders
Were data collected directly from the subjects (as opposed to a proxy)?	Research shows a systematic underreporting of symptoms when caregivers are questioned, as compared to patient self-assessment.	High Risk- In some instances, data were collected from a proxy Low Risk – Data was collected directly from participant at the time the research was being conducted
Was an acceptable case definition used in the study?	The study clearly defines the parameter: depression or suicidal ideation.	High Risk – A case definition of 'depression' or 'suicidal ideation' was not stated in the research paper Unclear Risk – The paper reported on the measure or diagnostic criteria that conceptualised 'depression' or 'suicidal ideation' but did not provide cut off scores or enough information on the diagnostic process. Low Risk – A clear case definition of 'depression' or 'suicidal ideation' was specified in the research paper which was defined by a cut off score on a symptomatic measure or by clear diagnostic criteria

Domain	Details	Risk of Bias
Was the study instrument that measured the parameter of interest shown to have reliability and validity (if necessary)?	The study instrument had been shown to have reliability and validity (if this was necessary), e.g. test-retest, piloting, validation in a previous study, etc.	High Risk- Studies which did not adequately outline a diagnostic criterion, or which used symptom measures which had not been validated or tested for reliability Unclear Risk- A measure or diagnostic tool has been used which currently has not been stringently validated or checked for reliability. Validated measures which have been translated into a foreign language (and no available reliability or validity research has been conducted on the translated version) were also marked as an unclear risk. Low Risk- A measure or diagnostic tool has been used which has been shown to be reliable and valid
Was the same mode of data collection used for all subjects?	The mode of data collection is the method used for collecting information from the subjects. The most common modes are face-to face interviews, telephone interviews and self-administered questionnaires.	High risk – Mode of data collection varied across participants. For example, some subjects were interviewed over the telephone and some filled in postal questionnaires. Unclear Risk – The mode of data collection appears to be the same method (i.e. interview with participants), however there is not a clear description in the methodology, and thus there is some ambiguity over the consistency of data collection Low risk- Mode of data collection was consistent across all participants.
Was the length of the shortest prevalence period for the parameter of interest appropriate?	The prevalence period is the period that the subject is asked about e.g. "Have you experienced low back pain over the previous year?" The longer the prevalence period, the greater the likelihood of the subject forgetting if they experienced the symptom of interest (e.g. low back pain). Thus, the shortest prevalence period for the event was appropriate (e.g. point prevalence, one-week prevalence, one-year prevalence)	High risk – No prevalence length for depression or suicidal ideation was reported, or the prevalence period was over one year Low risk- A prevalence length was specified in the studies of one week to one year
Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	There may be errors in the calculation and/or reporting of the numerator and/or denominator.	High risk – The paper did present numerator(s) AND denominator(s) for the parameter of interest but one or more of these were inappropriate. Low risk- The paper presented appropriate numerator(s) AND denominator(s) for the parameter of interest (e.g. the prevalence of low back pain).

A randomly selected 10% of the studies were reviewed for quality by an independent rater. The level of agreement was 88%. Disagreements between the rating were resolved by discussion between the two raters. If resolution could not be achieved by discussion, then the dispute was taken to a third rater for adjudication.

Table 3: Risk of biased based on quality framework

Study authors	1	2	3	4	5	6	7	8	9	10	Overall Quality Index
Depression studies											
Amtmann et al. 2015											16
Asano et al. 2013											18
Bamer et al. 2008											14
Beal et al. 2007											16
Brenner et al. 2016											18
Buchanan et al. 2003											18
Carta et al. 2014											14
Coyle et al. 2014											14
Da Silva et al. 2011											14
Demakis et al.2009											14
Dickstein et al. 2015											12
Duquin et al. 2008											12
Ensari et al. 2014											16
Ferrando et al. 2007											18
Frickska-Nagy et al.2016											15
Greeke et al. 2017											15
Hakim et al. 2000											20
Harel et al. 2007											14
van der Hiele et al. 2012											18
Holden et al. 2011											16
Horton et al. 2010											10
Jensen et al. 2014											16
Jick et al. 2015											9
Johansson et al. 2007											18
Johansson et al. 2014											16
Jones et al. 2012											16
Kang et al. 2010											14
Kargarfard et al. 2012											18
Kehler et al. 2009											4
Koch et al. 2015											12
Lo Fermo et al. 2010											14
Lobentanz et al. 2004											10
Lorefice et al. 2015											13
Maier et al. 2016											12
Marck et al. 2017											7
Marrie et al. 2009											10
Marrie et al. 2013											18


Study authors
1
2
3
4
5
6
7
8
9
10
Overall Quality Index
Marrie et al. 2015 18
Mattioli et al. 2011 12
McGuigan et al. 2004 14
McKay et al. 2018 16
Mohammadi et al. 2013 13
Mohr et al. 2006 16
Moreau et al. 2009 14
Neau et al. 2012 12
Newland et al. 2005 7
Nuyen et al. 2006 10
Patten et al.2005 16
Patten et al. 2009 18
Patten et al.2009 16
Patten et al. 2003 16
Patten et al. 1997 10
Patti et al. 2007 18
Patti et al. 2007 20
Pittion-Vouyovitch et al. 2006 14
Poder et al. 2009 16
Porcel et al. 2006 18
Pozzilli et al. 2012 14
Reider et al. 2017 11
Sadovnick et al. 1996 12
Simpson et al. 2016 16
Simpson et al. 2014 16
Solari et al. 2004 12
Solaro et al. 2016 15
Sollom et al. 2007 16
Somerset et al. 2001 18
Spain et al. 2007 16
Stepleman et al. 2014 12
Theudin et al. 2016 16
Thielscher et al. 2013 16
Verdier-Taillefer et al. 2001 12
Viner et al. 2014 20
Williams et al. 2005 14
Zettl et al. 2013 14
Suicidal Ideation studies
Altura et al. 2016 11

Study authors	1	2	3	4	5	6	7	8	9	10	Overall Quality Index
Dickstein et al. 2015											12
Ferrando et al. 2007											17
Lo Fermo et al. 2010											6
Strupp et al. 2016											10
Turner et al. 2006											13
Viner et al. 2014											11

Data analysis

Separate meta-analyses were conducted to calculate an overall estimated prevalence of depression and suicidal ideation in people with Multiple Sclerosis using the generic inverse variance method. This was implemented using the Metafor package (Viechtbauer, 2010) in the R statistical programming language (R Core Team, 2019).

Transformation of effects for calculations and back transformation for presentation

The event rates and, where relevant, relative risk estimates in selected studies were log transformed prior to numerical synthesis however, unless otherwise indicated, the values presented in tables and figures have been back-transformed to their original format for clarity of presentation.

Omnibus Test

The omnibus test can be calculated using either the fixed effects or the random effects models. The fixed-effect model is calculated on the assumption that the true effect size for all studies is identical, and the only reason the effect size varies between studies is sampling error. Also, all studies are assumed to have equivalent power to measure the effect. Therefore, the fixed effects model used only sample size as a measure of study precision. Information in the smaller studies is largely ignored when assigning weight to each study since larger studies provide better estimates of prevalence.

In contrast, under the random-effects model the goal is not to estimate one true effect but to estimate the distribution of possible effects (the range of which may

reflect variation due to the idiosyncratic characteristics of the individual or the unique circumstances of measurement of the effect). This means that we cannot discount a small study by simply giving it a very small weight as the estimate provided by that study may be imprecise, but it is information about the effect that no other study may have estimated. By the same logic we cannot give too much weight to a very large study. Our goal is to estimate the mean and distribution of the effect in a range of studies, and we do not want that overall estimate to become dominated by “merely” the larger studies. Therefore, the random effects model weights studies by sample size and heterogeneity. Studies with smaller sample sizes, who are reporting effects that are discrepant with the rest of the literature are the most penalised.

In addition to the random effects model, the quality effects model was also calculated (Doi & Thalib, 2008). The random effects model assumes that the precision of a study estimate is a function of sample size and heterogeneity, with smaller sample sizes and studies that show marked deviation from the meta-analytic synthesis being penalised. The quality effects model builds upon the random effects model to model the precision of a study estimate as a function of sample size, heterogeneity and an explicit rating of “risk of bias” pertinent to the specific issue under review. In this review the quality effects model was calculated using the total score from the risk of bias ratings. Accordingly, the quality effects model weights against studies with a greater risk of bias, and the comparison with the random effects model allows for the estimation of the attenuation due to sub-optimal methodology.

Normalisation and variance stabilisation

The simplest and most commonly used method for calculating the between studies variation (tau) for fitting the random effects model is the DerSimion and Laird method. However, this method assumes that the random effect is normally distributed in the population and therefore the effects sizes reported in the primary studies should also approximate a normal distribution. If the assumption of normality cannot be maintained, then the Restricted maximum likelihood estimator has been shown to be more robust to violations of the normality assumption. The distribution of the study effects will be examined using a QQ plot and the DerSimion and Laird tau will be used if data demonstrate normality and the Restricted maximum likelihood estimator tau will be used if data are not normally distributed.

Estimating heterogeneity

The random effects model separates between studies variation in two types: true variation in the effect; and heterogeneity. Therefore, heterogeneity refers to variation from the meta-analytic synthesis that cannot be attributed to true variation in the prevalence of depression in MS, and may reflect methodological variation in the studies, measurement error or uncontrolled individual difference factors within the body of literature.

In order to quantify heterogeneity in the reported analysis, Cochran's Q, Higgins I^2 and Tau were computed using the inverse-variance method. High levels of heterogeneity suggest that unknown and uncontrolled factors may be influencing the estimates of prevalence. Borenstein et al. (2009) recommends the use of Higgins I^2 to decide if further exploration of study heterogeneity is required. Benchmark values of <50%, <75% and >75% have been suggested to reflect low, moderate and high heterogeneity respectively (Higgins, Thompson, Deeks, and Altman, 2003). Given the high variation of depression measures and high levels of participant heterogeneity in clinical research it was decided that a Higgins I^2 of 75% or higher should be the cut-off for the presence of unacceptable heterogeneity. Should heterogeneity across studies included in the meta-analysis exceed this threshold then subgroup analysis or meta-regression will be conducted to further explore the causes of this uncontrolled variance.

Identifying Influential Studies

To examine whether any studies were exerting a disproportionately high influence on the overall meta-analytic effect, a "one left out" procedure was conducted. The impact of removing each study in turn is analysed with the aim of identifying individual studies with a disproportionate influence on the overall metanalytic effect. If omitting a study results in a change in the synthesis greater than 10% of the synthesis for the complete set of studies, then the omitted study is deemed to have a disproportionate influence. Disproportionately influential studies will be re-examined for risk of bias or unrepresentativeness and omitted from the overall analysis if necessary.

Publication Bias

Meta-analysis provides ways to estimate the likelihood and potential impact of

publication bias. In the present analysis, publication bias was assessed by visual examination of Funnel Plots. If publication bias is identified, its impact will be estimated using a “trim and fill analysis” (Duval & Tweedie, 2000). The trim and fill procedure builds on the assumption that publication bias would lead to an asymmetrical funnel plot. The trim and fill procedure attempts to simulate the impact of publication bias by adding the minimum number of effects to area of the funnel plot associated with publication bias until symmetry is no longer present.

A Fail-safe N will also be calculated using the Rosenthal method (Rosenthal, 1979). This is an estimation of the number of missing studies that would need to be retrieved for the effect to be no longer significant.

Moderator Analyses

Subgroup analyses were conducted on each of the outcomes to explore heterogeneity. These variables included continent of study, percentage of females, age of participants, percentage of participants in employment, percentage of participants who had a university education, percentage of participants who were married, MS disease duration, measure of participant disability estimated by the EDSS, type of MS diagnosis (primary progressive, secondary progressive or relapse remitting). In the depression analysis measurement of depression (symptomatic or diagnostic) was also included as a moderator variable. For categorical variables, each variable was split into minimal groupings to control for overestimation of differences. A subgroup analyses will be conducted for categorical variables and a meta-regression will also be conducted continuous variables.

Results

Prevalence of depression

Seventy-four studies reported prevalence of depression (defined as a depressive disorder or a score above a defined cut-off on a depression rating scale) in a total sample size of 170239 persons with MS. Sample sizes ranged from 201 (Carta et al. 2014) to 44452 (Marrie et al. 2015). The distribution of the study level reports of prevalence of depression conforms to normal expectations, see QQ plot below, and

confirms that the DerSimonian-Laird estimate of between study variation is appropriate.

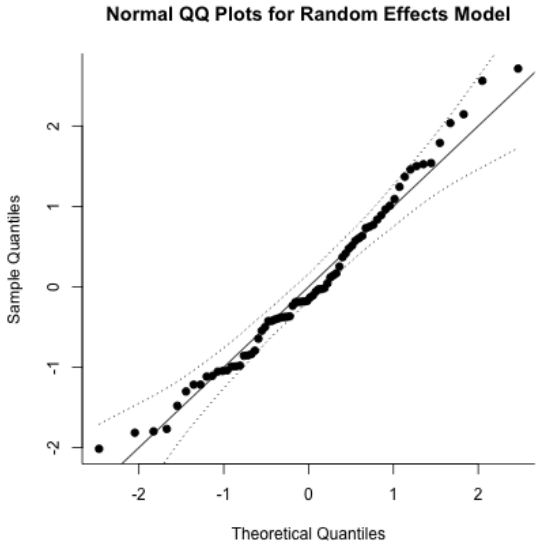


Figure 2: QQ plot of study level effect. If distribution is normal, then study level effects should be within the 95% CI of the QQ plot

Figure Two reports the random effects synthesis of these 74 studies, with an estimated prevalence rate of 32.1% (CI 28.5 to 35.7). However, there was substantial between studies variation which could not be attributed to true variation in the prevalence of depression in persons with Multiple Sclerosis (Higgins I^2 = 99.7%). The current level of heterogeneity replicates a similarly high level reported in Boeschoten et al.'s (2017).

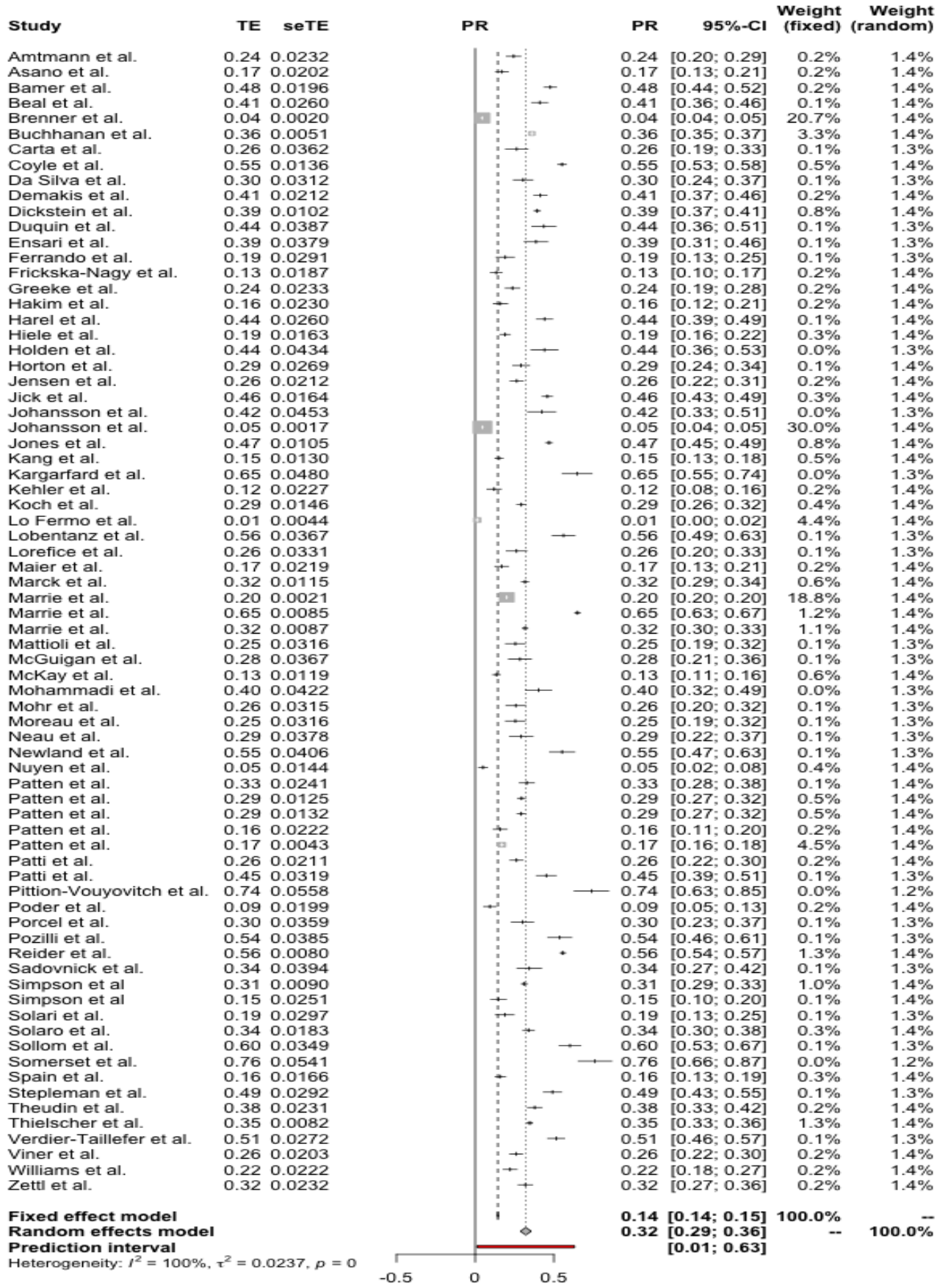


Figure 3: Forest plots for depression prevalence rates in Multiple Sclerosis

The Baujat et al. (2002) scatter plot in Figure 4 portrays the contribution of each study to the overall heterogeneity statistic on the x-axis and the standardised difference of the overall treatment effect with and without each study on the y-axis plotted. Accordingly, studies plotted in the upper right-hand corner of this chart are exerting a large effect on the meta analytic synthesis and are discrepant with the main body of the literature. Five studies were selected as possibly exerting a disproportionate influence over the meta analytic synthesis (Somerset et al., Marrie et al., Pittion-Vouyovitch et al., Lo-Fermo et al., and Kargarfard et al.).

Four studies (Somerset et al., Marrie et al., Pittion-Vouyovitch et al., and Kargarfard et al.) appear to influence the meta analytic synthesis by overestimating the prevalence of depression. All the studies utilised symptomatic self-report measures and include questions which measure fatigue, a symptom associated with MS. This may have resulted in inflated depression scores. Furthermore, all four studies reported a prevalence for individuals who met criteria for mild depression as opposed to many studies which defined depression as a moderate cut off score or above.

In the case of Lo Fermo et al. the study was removed because it appeared to have disproportionate influence on the meta analytic synthesis by underestimating the rate of prevalence. This study included retrospective data from one MS clinic and only identified records where patients qualified for a Major Depressive Disorder. The authors noted all the depressed participants also displayed suicidal ideation, suggesting that milder forms of clinical depression may not have been recorded in this study.

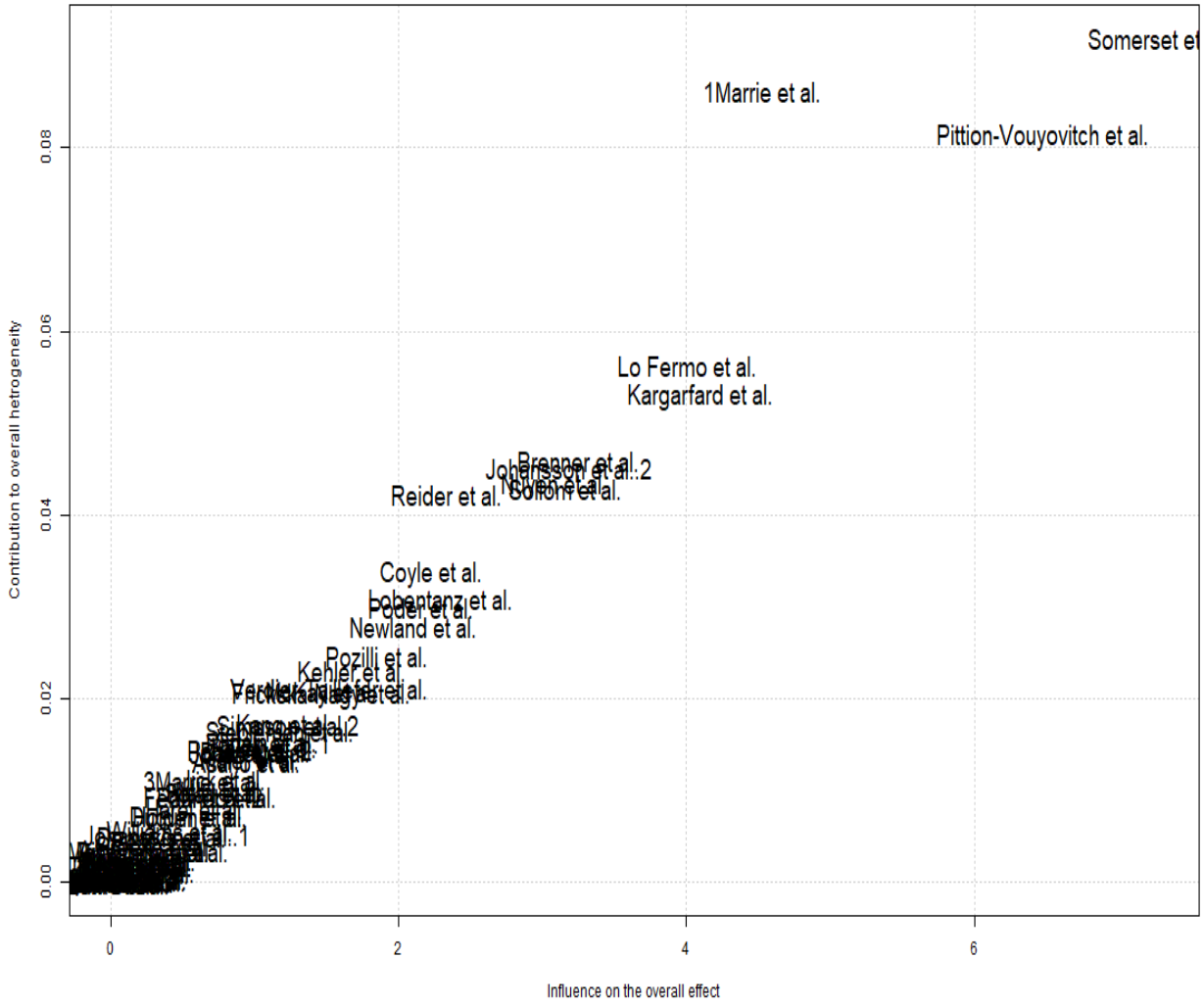


Figure 4: Baujat et al. (2002) scatter plot of study level influence

When the meta analytic synthesis is calculated omitting the studies with disproportionate influence (Somerset et al., Marrie et al., Pittion-Vouyovitch et al., Lo-Fermo et al., and Kargarfard et al.) the random effects model decreases to a prevalence of 30.5%, but heterogeneity remains substantial (Higgins I2 = 99.6%). These four studies were omitted from subsequent analyses.

As a substantial amount of heterogeneity remains between the primary studies, a series of sub-group analysis were conducted to attempt to identify the cause of between study variation in prevalence estimates.

Attenuation due to risk of bias

Table four explores the impact of methodological variation by examining the difference in prevalence and heterogeneity estimates for studies rated as low or high risk on each of the ten criteria for risk of bias.

Table 4: Sub-group analysis: attenuation due to risk of bias

Sub-group analysis		**Number of studies**	**Random Effects Model**		**Heterogeneity**			***Between groups comparison***
			Prevalence	95% CI	Higgins I^2	Tau^2	Cochran's Q	
Target population are a close representation of national population	High Risk	47	0.33	0.29-0.36	98.6%	0.02	2326.27	*Q=6.50 p=0.01**
	Low Risk	19	0.25	0.20-0.29	99.0%	0.01	4441.07	
Sample frame a close representation of target population	High Risk	28	0.31	0.24-0.38	99.3%	0.04	4153.1	*Q=0.10 p=0.80*
	Low Risk	39	0.30	0.24-0.36	99.7%	0.04	12441.4	
Random sampling or census data	High Risk	35	0.35	0.30-0.40	98.5%	0.02	2210.17	*Q=6.80 p=0.01**
	Low Risk	32	0.26	0.21-0.30	99.7%	0.02	9359.64	
Bias due to attrition/non-response	High Risk	26	0.35	0.30-0.40	97.3%	0.02	931.85	*Q=4.40 p=0.03**
	Low Risk	33	0.28	0.23-0.33	99.7%	0.02	11324.81	
Data collected directly from participant	High Risk	6	0.20	0.11-0.29	99.6%	0.01	1368.45	*Q=6.40 p=0.02**
	Low Risk	61	0.32	0.27-0.37	99.5%	0.04	12955.51	
Acceptable case definition	High Risk	8	0.28	0.20-0.37	99.1%	0.02	748.66	*Q=1.35 p=0.24*
	Low Risk	58	0.31	0.27-0.35	99.5%	0.02	12507.17	
Reliable and valid measures	High Risk	10	0.26	0.15-0.36	99.6%	0.03	2260.5	*Q=0.82 p=0.37*
	Low Risk	53	0.31	0.26-0.35	99.5%	0.02	11436.99	

Sub-group analysis		Number of studies	Random Effects Model		Heterogeneity			*Between groups comparison*
Same method of data collection used for all participants	High Risk	4	0.19	0.08-0.30	98.4%	0.01	181.83	*Q=3.98 p=0.04**
	Low Risk	62	0.31	0.27-0.35	99.6%	0.03	16364.81	
Appropriate shortest prevalence length	High Risk	13	0.29	0.18-0.39	99.8%	0.04	6311.51	*Q=0.13 p=0.66*
	Low Risk	52	0.31	0.26-0.36	99.5%	0.04	9542,97	
Prevalence rate calculated appropriately	High Risk	5	0.35	0.21-0.48	99.4%	0.10	104.47	*Q=0.03 p=0.86*
	Low Risk	64	0.30	0.26-0.34	99.6%	0.02	16298.47	
Overall quality rating	High Risk	35	0.34	0.29-0.39	99.2%	0.02	4038.94	*Q=2.89 p=0.09*
	Low Risk	34	0.28	0.23-0.34	99.7%	0.02	9852.74	

Several methodological variations attributable to individual risk of bias significantly affected the estimate of the prevalence of depression in persons with Multiple Sclerosis. Studies rated as a high risk of bias estimated a significantly higher prevalence rate than studies rated as a low risk of bias in the following criterion: 1) the target population was not a close representation of the national population (Q=6.50, *p*=0.01); 2) the sample was not randomly selected or from a census (Q=6.80, *p*=0.01); and 3) the study displayed high non-response rates (Q=4.4, p=0.03). However, studies judged to have a high risk of bias in two of the criteria also calculated a significantly lower estimate of prevalence than studies rated as a low risk of bias:1) was data was collected directly from the participant (Q=6.40 , p=0.02); and 2) was the same method of data collection used across all participants studies (Q=3.98, p= 0.04). Some caution should be applied when interpreting all findings because heterogeneity remained high across all analyses. However, tentatively it can be interpreted that certain methodological biases may result in both an overestimation and an underestimation of prevalence rates.

With an aim of estimating the meta analytic effect on an unbiased literature base, an analysis was run on studies which were identified as low risk in the following quality criterion:

1) the target population was not a close representation of the national population
2) the sample was not randomly selected or from a census
3) the risk of non-response bias was minimal
4) data was collected directly from the participant
5) the same method of data collection used across all participants studies

Eight studies met this inclusion criteria, and the random effects synthesis of these studies estimated a prevalence rate of 25.9% (CI 13.12 to 38.86). This is a reduction in prevalence estimate of 6.3% compared to the overall calculated prevalence estimate. Heterogeneity remained high across the selected studies (Higgins I^2 = 99.7%).

Attenuation due to conceptualisation of depression

Analysis of potential moderating variables was undertaken to investigate the potential influence of study characteristics, clinical variables and sample demographics on heterogeneity and explaining variance observed. Subgroup analyses were used for categorical variables and meta-regression analyses were conducted for continuous variables.

Disorder vs. symptom

Twenty-one studies reported prevalence rates of a depressive disorder identified with (semi) structured interviews, ICD or ICPC codes, and/or by a clinician. Forty-

eight studies used a cut-off on a depression rating scale to assess clinically significant depressive symptoms. The meta analytic prevalence of a depressive disorder was 27% (95% CI = 22%–32%) with a range from 4% (Brenner et al.) to 55% (Newland et al. 2005). Prevalence of clinically significant depressive symptoms was higher compared with the prevalence of a depressive disorder with an overall meta analytic prevalence of 32% (95% CI = 27%-36%) and range from 9% to 76%. The difference between these groups was not found to be significant and heterogeneity remained high across both groups (diagnosis group, I^2 =99.8%; symptom group, I^2 =98.83%).

Clinically significant depressive symptoms

Studies varied in the tools used to measure depression. The most widely utilised measures were the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), variations of the Beck Depression Inventory Scale (BDI; Beck, Steer & Brown, 1996), the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the Patient Health Questionnaire (PHQ; Spitzer, Kroenke & Williams, 1999), which attempt to capture the frequency of depressive symptoms over a one-two week period. Even when studies utilised the same measure, there was often a variation in the cut off scores utilised to calculate the prevalence of depression. In total there were 20 different combinations of measure and cut off scores utilised across 48 studies. Subgroup analyses for different assessment scales showed the highest average prevalence rate for studies BDI-SF (0.39%; 95% CI = 0.25%-0.54%) and lowest for studies using the HADS (cut-off > 10) (0.16%; 95% CI = 0.09 – 0.23). The difference between measures was statistically significant (Q=32.22; p<0.001*)*. Table 3 shows the estimated prevalence rates of all measures.

Measures were included if 3 separate studies used the same clinical measure and cut off rate. When analysing between sub-groups, all measures showed high levels of heterogeneity (I^2=80.9%-98.7%). In Boeschoten et al.'s (2017) study heterogeneity was lower for studies which utilised the PHQ-9, however this was not replicated in this analysis (I^2=95.8%).

Table 5: Sub-group analyses for studies investigating prevalence of depression

Sub-group analysis		Number of studies	Random Effects Model		Heterogeneity			Between groups comparison
			Prevalence	95% CI	Higgins I^2	Tau^2	Cochran's Q	
Measurement of depression	Diagnosis	21	0.27	0.22-0.32	99.8%	0.01	10212.43	Q(1)=1.96 *p=0.16*
	Symptom	48	0.32	0.27-0.36	98.3%	0.02	2773.67	
Symptom assessment method	HADs (cut off >7)	9	0.26	0.16-0.36	98.7%	0.02	638.69	Q(5)=32.22 *p*<0.001
	HADs (cut off >10)	4	0.16	0.09-0.23	87.2%	0.00	23.42	
	BDI SF (cut-off > 3)	3	0.39	0.25-0.54	93.7%	0.02	31.66	
	BDI (cut off >9)	3	0.39	0.29-0.49	80.9%	0.01	10.46	
	CES-D (cut-off > 15)	9	0.40	0.34-0.47	96.2%	0.01	210.19	
	PHQ-9 (cut-off > 9)	6	0.26	0.19-0.34	95.8%	0.01	118.92	
Diagnostic assessment method	DSM-IV MDD Diagnosis	5	0.28	0.17-0.38	94.2%	0.01	68.67	Q(1)=1.08 *p=0.29*
	ICD-10 Depression	7	0.21	0.12-.0.29	99.9%	0.01	6024.96	
Study design	Longitudinal	23	0.28	0.24-0.33	99.7%	0.01	6890.28	Q(1)=1.35 *p*=0.25
	Cross-sectional	46	0.32	0.28-0.36	98.9%	0.03	4187.51	
Study Location	Europe	30	0.30	0.26-0.34	99.5%	0.01	5465.21	Q(2)=0.21 *p*=0.85
	US/Canada	33	0.31	0.27-0.35	99.3%	0.01	4294.11	
	Rest: Middle East, Asia, Australia	6	0.29	0.22-0.37	97.7%	0.01	217.80	

Diagnostic criteria for depression

Studies varied in the criteria utilised to diagnose depression. Seven studies documented physician diagnosis however did not report details on criteria used. Information on prevalence times was also often lacking. Five studies defined depression as that diagnosed according to DSM-IV criteria for Major Depressive Disorder and 7 studies used retrospective data from databases documenting depression as defined by ICD-10. Heterogeneity remained high across all studies which applied diagnostic criteria (I^2 = >97%) and there was no significant difference between prevalence estimates.

Other sources of attenuation

Study design

Studies were grouped by study design: cross-sectional and longitudinal. Cross-sectional was defined as a study assessing prevalence of depression based on a single time point measurement. Longitudinal was defined as a study taking data at more than one time point. Forty-six studies with a cross-sectional design reported a meta analytic prevalence rate of depression of 32% (95% CI=0.28-0.36). Twenty-three studies with a longitudinal design reported a meta analytic prevalence rate of depression of 28% (95% CI=0.24-0.34). Heterogeneity remained high across both groups (cross sectional group, I^2 =99.2%; longitudinal group, I^2 =99.7%).

Region

Regions were defined to replicate Boeschoten et al.'s (2017) analysis: North America, Europe and Australia, Middle East and Asia together. These were combined due to limited studies in the latter regions. There was no difference between the meta-analytic prevalence rates recorded between regions (see table 3 for data). Heterogeneity was > 97% for all subgroups.

Participant demographics

Data regarding participant demographics was analysed by conducting individual meta-regressions to understand whether any variables contributed to understanding

the variance displayed across studies. Table 4 outlines all variables analysed in the meta-regression. Heterogeneity remained high however gender and scores on the EDSS were calculated to contribute approximately 4% and 5% respectively to the variance observed. Controlling for either variable was calculated to not significantly impact heterogeneity.

Table 6: Moderator analyses for studies investigating prevalence of depression

Moderator analyses	Number of studies	Random effects model		Heterogeneity			Moderator
		Prevalence estimate	95% CI	Higgins I^2	Tau^2	R^2	
Gender (% female)	63	0.31	0.28-0.35	99.6%	0.02	4.14%	QM=0.42 *p*=0.51
Age (mean)	60	0.32	0.28-0.36	99.5%	0.03	0.00%	QM=0.60 *p*=0.43
% university educated	17	0.29	0.18-0.40	99.7%	0.06	0.00%	QM=0.42 *p*=0.51
% employed	20	0.31	0.25-0.38	97.9%	0.02	0.00%	QM=0.17 *p*=0.67
Reported level of disability (EDSS)	22	0.28	0.21-.35	98.7%	0.02	5.05%	QM=1.48 *p*=0.22
% of relapse remitting MS	40	0.32	0.27-0.37	98.5%	0.03	0.60%	QM= 1.02 *p*=0.31
% of primary progressive MS	35	0.34	0.28-0.39	98.5%	0.03	0.00%	QM=0.22 *p*=0.63
% secondary progressive MS	34	0.33	0.27-0.38	98.4%	0.03	0.00%	QM=0.06 *p*=0.80
% married	27	0.34	0.29-0.39	98.4%	0.02	0.00%	QM=0.13 *p*=0.72
Disease duration	40	0.30	0.26-0.35	97.7%	0.02	0.00%	QM=0.74 *p*=0.39

Prevalence of suicidal ideation

After full-text assessment, the literature search investigating the prevalence of suicidal ideation in Multiple Sclerosis identified seven articles. This meta-analysis included a total sample size of 6097 MS patients. Sample sizes ranged from 151 (Altura et al. 2016) to 3823 (Dickstein et al. 2015). As can be seen in figure 4, the random effects model calculated a prevalence rate of suicidal ideation in MS of 14% (CI 0.07-0.21). However, problematic heterogeneity was observed (I^2=98%), suggesting that there may be uncontrolled sources of variance influencing meta-analytic effect that require further investigation.

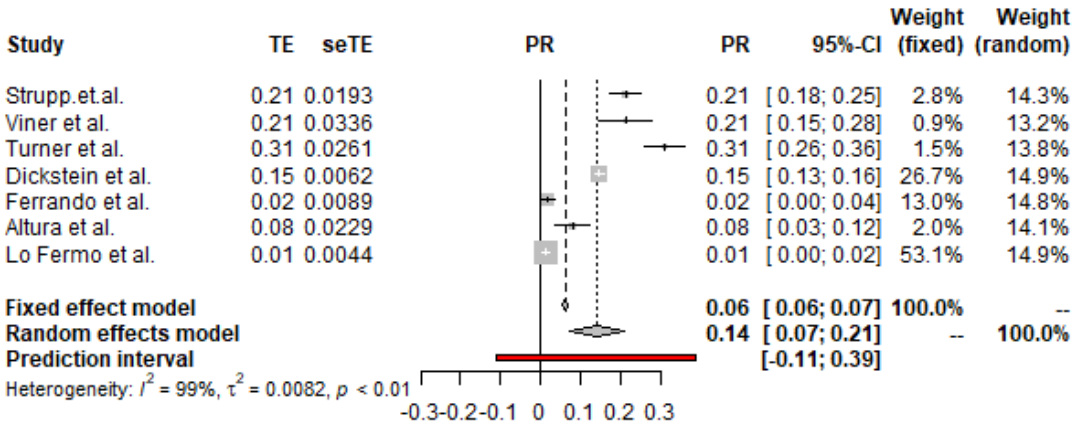


Figure 5: Forest plots for suicidal ideation prevalence rates in Multiple Sclerosis

The Baujat et al. (2002) scatter plot in Figure six portrays the contribution of each study to the overall heterogeneity statistic on the x-axis and the standardised difference of the overall treatment effect with and without each study on the y-axis plotted. Accordingly, studies plotted in the upper right-hand corner of this chart are exerting a large effect on the meta analytic synthesis and are discrepant with the main body of the literature. It was identified that Turner et al. (2006) may exert a disproportionate influence over the meta analytic synthesis. When the meta analytic synthesis is calculate omitting this study with disproportionate influence then the random effects model decreases to 11.2% (CI 4.28 – 17.96) prevalence, but

heterogeneity remains substantial (Higgins I2 = 98.8%). This study was omitted from subsequent analyses.

As a substantial amount of heterogeneity remains between the primary studies, a series of sub-group analysis were conducted to attempt to identify the cause of between study variation in prevalence estimates.

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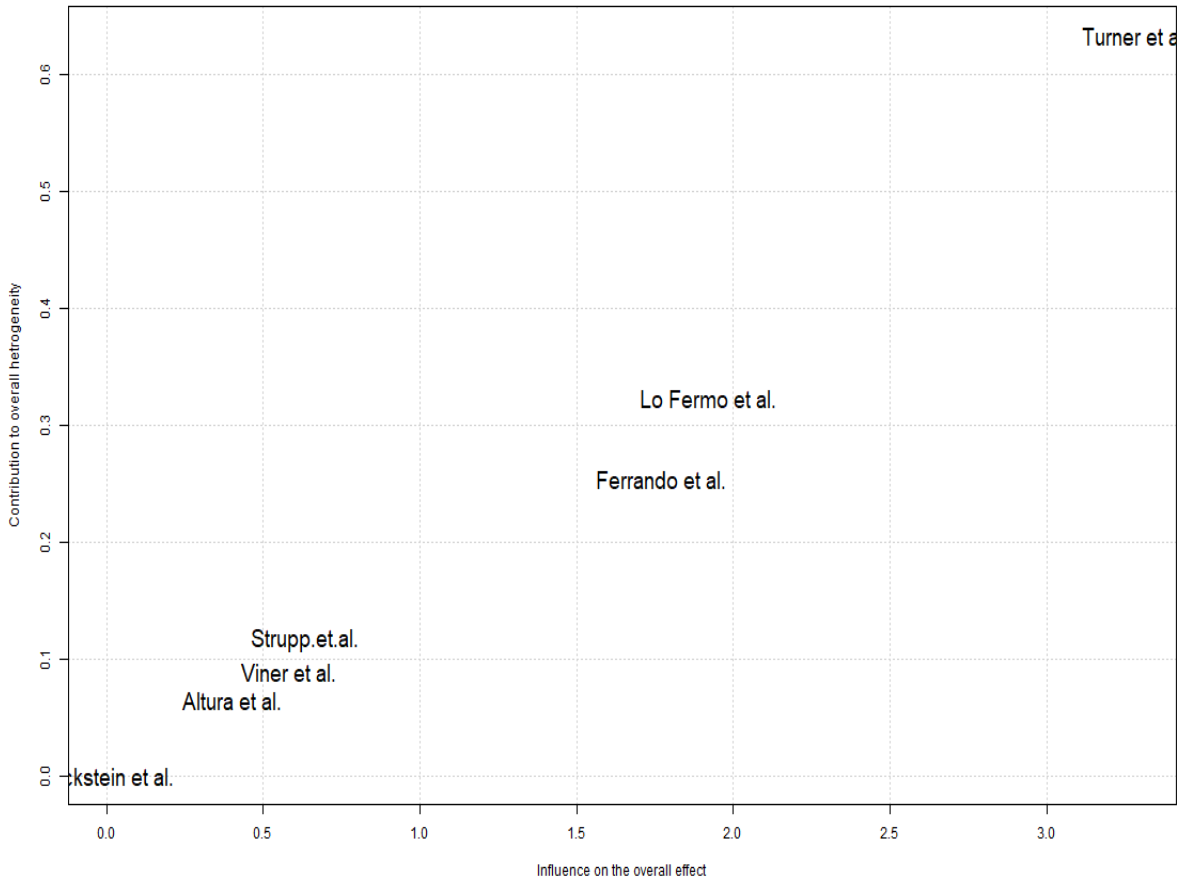

Figure 6: Baujat et al. (2002) scatter plot of study level influence

Moderator analysis: further investigations into heterogeneity

Analysis of potential moderating variables was undertaken to investigate the potential influence of study characteristics, clinical variables and sample demographics on heterogeneity and explaining variance observed. Subgroup

analyses were used for categorical variables and meta-regression analyses were conducted for continuous variables.

Attenuation due to risk of bias

The quality was assessed for all studies according to Hoy et al.'s (2012) criteria outlined in the method section. Six studies were assessed as having high risk of bias, and one study as low risk. Several methodological variations attributable to individual risk of bias significantly affected the estimate of the prevalence of suicidal ideation in persons with Multiple Sclerosis. Studies rated as a high risk of bias estimated a significantly higher prevalence rate than studies rated as a low risk of bias in the following criterion: 1) bias due to non-response/attrition studies (Q=8.45, p<0.01) and 2) stating an appropriate shortest prevalence period studies (Q=,8.44 p<0.01). However, studies judged to have a high risk of bias in two of the criterion also calculated a significantly lower estimate of prevalence than studies rated as a low risk of bias:1) was data collected directly from participant (Q=9.19, p<0.01); and 2) was the same method of data collection used across all participants studies (Q=9.19, p<0.01). However, given the low number of studies (and particularly that in all significant criterions one of the comparator groups only contained one study) it is difficult to draw meaningful conclusions from these findings. Thus, significant differences may be due to one outlier study as opposed to a true difference. Therefore, to provide further analysis on the quality of the included papers, the paper's overall quality score was included as part of a meta-regression. A quality score was assigned to each paper based on Hoy et al.'s (2012) ten criterion. 2 points was assigned to a study with a low risk of bias in each criterion, 1 point for unclear risk (where relevant) and 0 points if the study was deemed to have a high risk of bias. The maximum quality score is 20. Heterogeneity did not reduce when quality scores were controlled for (I^2=99%).

Table 7: Sub-group analysis: attenuation due to risk of bias

Sub-group analysis		Number of studies	Random Effects Model		Heterogeneity			*Between groups comparison*
			Prevalence	95% CI	Higgins I^2	Tau^2	Cochrans Q	
Target population are a close representation of national population	High Risk	6	0.11	0.04-0.18	98%	0.01	416.78	
Sample frame a close representation of target population	High Risk	4	0.13	0.01-0.24	97.8%	0.01	138.55	Q=0.27 *p*=0.60
	Low Risk	2	0.08	-0.04-0.21	99.3%	0.01	142.17	
Random sampling or census data	High Risk	4	0.11	0.01-0.20	99.2%	0.01	372.68	Q=0.00 *p*=0.99
	Low Risk	2	0.11	-0.07-0.30	96.8%	0.02	31.40	
Bias due to attrition/non-response	High Risk	1	0.21	0.15-0.28	-	-	-	Q=8.45 *p*<0.00
	Low Risk	4	0.08	0.02-0.14	97.2%	0.00	108.41	
Data collected directly from participant	High Risk	1	0.01	0.00-0.002	-	-	-	Q=9.19 *p*<0.00
	Low Risk	5	0.13	0.06-0.21	97.8%	0.01	182.61	
Acceptable case definition	Low Risk	6	0.11	0.04-0.18	98%	0.01	416.78	
Reliable and valid measures	High Risk	2	0.11	-0.08-0.30	99.0%	0.02	102.03	Q=0.00 *p*=0.99
	Unclear risk	4	0.11	0.02-0.20	98.0%	0.01	153.65	
Same method of data collection used for all participants	High Risk	1	0.01	0.00-0.002	-	-	-	Q=9.19 *p*<0.00
	Low Risk	5	0.13	0.06-0.21	97.8%	0.01	182.61	
Appropriate shortest prevalence length	High Risk	1	0.21	0.18-0.25	-	-	-	Q=8.84 p<0.00
	Low Risk	5	0.09	0.02-0.16	98.9%	0.01	351.09	
Prevalence rate calculated appropriately	High Risk	2	0.04	-0.02-0.11	87.6%	0.00	8.05	Q=0.49 p=0.48
	Low Risk	2	0.11	-0.08-0.31	98.8%	0.01	84.51	

Sources of attenuation: other variables

Sub-group analysis was conducted on relevant sub-groups to explore heterogeneity. Four studies measured suicidal ideation using Q9 of the PHQ-9, one study utilised a likert scale and one study recorded individual's self reports to medical professionals. When omitting the studies which did not utilise the PHQ-9, heterogeneity remained high (I2 =98.5%). Prevalence of suicidal ideation was significantly higher in the studies which used the PHQ-9 self report compared to the study which measured prevalence using reports to medical professionals in patient notes (Q=5.08, *p*=0.02). Three studies were conducted in North America, Two studies in Canada and two in Europe. Heterogeneity remained high across regions (I2>90%). There was no significant difference observed between prevalence estimates based on region of study.

Table 8: Subgroup analysis for studies investigating prevalence of suicidal ideation

Sub-group analysis		Number of studies	Random Effects Model		Heterogeneity			Between groups comparison
			Prevalence	95% CI	Higgins I^2	Tau^2	Cochran's Q	
Measurement of suicidal ideation	Q9 PHQ-9	4	0.11	0.03-0.20	98%	0.08	153.64	Q=5.08 *p*=0.02
	Report to medical professional	1	0.01	0.00-0.002	0	NA	NA	
Study Location	US	2	0.08	-0.04-0.21	99.3%	0.01	142.17	Q=0.44 p=0.80
	Canada	2	0.14	0.01-0.27	90.7%	0.01	10.72	
	Europe	2	0.11	-0.08-0.31	99.0%	0.02	102.03	

Participant demographics

All included studies in the meta-analysis except Lo Fermo et al. reported descriptive statistics on gender and age of participants and four of the studies reported on marital status of participants. Each was inputted as a separate meta-regression. Heterogeneity remained high when both gender and marital status were individually controlled for (I^2 > 98%; R^2 = 0%). When mean age was controlled for heterogeneity reduced to 82.14% (R^2=80%), which is still considered problematically high. However, the variance explained by including this moderator was significant.

Table 9: Moderator analyses for studies investigating prevalence of suicidal ideation

Moderator analyses	Number of studies	Random effects model		Heterogeneity			Moderator
		Prevalence estimate	95% CI	Higgins I^2	Tau^2	R^2	
Gender (% female)	5	0.13	0.06-0.21	97.7%	0.01	0.00%	QM=0.00 p=0.97
Age (mean)	4	0.13	0.06-0.21	82.14%	0.04	80.22%	QM=12.75 p<0.01
% married	3	0.14	0.09-0.20	83.17%	0.06	0.00%	QM=0.98 p=0.32
Overall quality score	6	0.11	0.04-0.18	99.0%	0.10	0.00%	QM=0.00 p=0.93

Discussion

Summary of findings: depression

The aim of this systematic review and meta-analysis was to estimate the prevalence of depression and suicidal ideation people with MS. This review is an update of a previous meta-analysis on depression in MS by Boeschoten et al. (2017). In addition to the studies reported in Boeschoten et al.'s analysis this review included an extra 82483 participants across 16 studies. The meta-analysis estimated a prevalence of depression in MS of 32%, which although slightly higher, is generally in line with Boeschoten et al.'s (2017) estimate. Heterogeneity was problematically high in all analyses of depression prevalence estimates. This was recorded in Boeschoten et al. (2017) and inclusion of additional moderator variables such as percentage of gender and disability did not reduce heterogeneity to an acceptable level. Thus, conclusions drawn from the analysis should be interpreted with caution.

Subgroup analysis of Hoy et al.'s (2012) quality criteria showed that high risk of bias in five of the criterions significantly impacted the estimated rate of prevalence. When only studies which were at a low risk of bias in these five criterions were included the meta-analytic prevalence of depression was calculated to be 25.9%. Thus, it may be that this estimate is a more accurate predictor of the overall prevalence of depression in MS. However only eight studies met this stringent 'high quality' check, and thus some caution should be taken in interpreting these findings.

Summary of findings: suicidal ideation

When investigating suicidal ideation, the meta-analysis estimated prevalence at 14%. For the suicidal ideation analysis, 6097 MS patients were included across seven studies. There are no known review studies estimating prevalence of suicidal ideation in MS. Despite the small number of studies included in this meta-analysis heterogeneity was problematically high and meta-regressions did not reveal the source of heterogeneity.

Clinical implications

Overall, it appears that rates of depression both as a diagnosed disorder (26%) or as a clinically significant symptom (32%) are higher than the general population (Bromet, Andrade, Hwang, Sampson, Alonso & de Girolamo, 2011; Patten & Schopflocher, 2009). The estimated prevalence for depression as a diagnosed disorder and as a clinically significant symptom are similar to other chronic medical illnesses such as Parkinson's (Reijnders, Ehrt, Weber, Aarsland & Leentjens, 2008). Although caution should be applied due to the high heterogeneity observed in the analysis, elevated levels of depression in people with MS compared to the general population should be addressed with both increased research into the area and support to patients. Treatment for depression should be in accordance with NICE guidelines, thus acknowledging the chronic condition the person is experiencing and include pharmacological and, where beneficial, psychological intervention (NICE, 2009).

In a systematic review and meta-analysis of seven studies exploring the use of cognitive behavioural therapy (CBT) for depression in MS, Hind, Cotter, Thake, Bradburn, Cooper, Isaac and House, (2014) found a medium size treatment effect for CBT when compared mainly with those who received 'standard care', were waiting list controls or received other supportive therapy. Furthermore, ensuring screening for depression is carried out as part of regular clinical practice in MS clinics and outpatient services could ensure that depression is recognised in patients.

Similarly, prevalence of suicidal ideation appears to be elevated compared to the general population. In our review, the opportunity for people with MS to self-report

suicidal ideation using a symptomatic measure such as the PHQ-9 showed a significantly higher prevalence rate than when reporting directly to doctors. Given the small number of studies, caution should be taken in drawing conclusions from this, however tentatively this could support Caine & Schwid's (2002) findings that patients may underreport suicidal ideation for fear of concerning medical professionals. Regular screening of suicidality in clinical practice is imperative and appropriate training should be provided for clinicians to ensure patients are asked whether they are experiencing any thoughts about suicide. Raising awareness of the risk of suicidal ideation in people with MS and ensuring support is available should be managed both at a local and national level.

Limitations of the research

In the analyses of suicidal ideation, a limitation is the small number of studies included which limits the power of statistical analyses. Even in the depression analysis, which contained many studies, no included moderator explained a significant amount of the high levels of heterogeneity. Thus, in both analyses some caution should be taken in interpreting findings.

Furthermore, the setting of a minimum participant number to reduce selection bias (>200 for depression studies; >150 for suicidal ideation) meant that our meta-analysis has not included high quality, small studies. This may also mean studies which investigated prevalence rates in countries with lower populations of people with MS (such as Central and South America) were also unintentionally excluded. As an alternative, a criterion could have been added to the quality measure to reflect on low participant-number studies so these studies could have been included.

Recommendations for future research

The high levels of heterogeneity recorded across depression and suicidal ideation studies means drawing meaningful conclusions is difficult. Being able to explain such heterogeneity in the future would therefore be of value. Future studies could help to address this by ensuring consistent outcome measures and cut-off points are utilised. Whilst not to a significant level, meta-regression suggested that disability as measured by EDSS and gender did explain small levels of variance in the prevalence estimate, so future studies ensuring this data is gathered and reported as

would help future reviewers, Furthermore research investigating the relationship between these variables and levels of depression in MS would be of value.

When researching the prevalence of depression in MS, the meta-analysis showed that risk of bias in five of criterions in Hoy et al.'s (2012) quality checklist significantly impacted the meta-analytic prevalence rate of depression. Therefore in future, studies investigating the prevalence of depression in MS should ensure:

1) the target population is a close representation of the national population
2) the sample is randomly selected or from a census
3) the risk of non-response bias is minimal
4) data are collected directly from the participant
5) the same method of data collection is used across all participants studies

Continued research investigating the prevalence of suicidal ideation in MS populations would be helpful to contribute to a developing literature base. Furthermore, a more in depth understanding through qualitative exploration of people with MS's experiences of suicidal ideation would help to provide further insight into what contributes to, as well as what helps people to manage, this phenomenon.

When investigating suicidal ideation, selected studies were often at a high risk of bias. This was largely due to samples that were not representative of the wider population, and uncertain reliability and validity in measurement of suicidal ideation. The use of the PHQ-9 appears to be a helpful way of studies gathering data on both depressive symptoms and suicidal ideation to contribute to the literature, however the PHQ-9's validity in accurately capturing suicidal ideation is limited (Na et al. 2018). Therefore, future research utilising validated measures such as the Beck Suicide Scale (Beck & Steer, 1993) or completing validation analysis on the one-item PHQ will help to provide further insight into the very important understanding of how prevalent suicidal ideation is in people with MS.

Conclusion

This study has contributed to literature that reports increased prevalence of depression and suicidal ideation in MS. However, caution must be taken in drawing meaningful conclusions from data due to high heterogeneity. Sub-group analysis of Hoy et al.'s (2012) quality criteria shows risk of bias in five of the criterions significantly impacts meta-analytic prevalence rate. Therefore, recommendations are made for future research to ensure future studies investigating the prevalence of depression in MS are designed with these criterions in mind. Extensive sub-group analyses and meta-regression did not reveal explanations for variance in the depression or suicidal ideation meta-analyses. Thus, researchers agreeing more consistent methods of measuring depression and suicidal ideation, with a focus on a consistent use of measures and cut off scores may all help to provide further clarity in the future.

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Chapter 2
Empirical Research Component

The Lived Experience of shared medical decision-making in people with MS

Abstract

Background: People with MS are presented with a complex choice between differing partially effective treatment options. Each treatment option has varying side effects and impacts upon the patient's quality of life. It is increasingly recognised that medical decision making should be facilitated by a process known as Shared Decision Making (SDM) between patient and medical professionals.

Aims: To explore how people with MS experience the medical decision-making process, paying particular attention to underlying mechanisms which may facilitate shared decision-making.

Methods: Six semi-structured interviews were conducted with people with MS who were in the process of medical decision making. Interview data was analysed using Interpretative Phenomenological Analysis.

Results: Three super-ordinate themes emerged from the data, 'Facing MS', 'Assimilating a New Identity' and 'Imagining a future'. Overall, it appears that people with MS consider relatively objective factors such as side effects and the practicalities of administering medication as suggested by behavioural economic models of decision-making, however values are assigned in a more existential context whereby a person assigns value on costs and benefits on what would 'fit' in with life. Shared decision-making is aided by professionals acknowledging this process.

Keywords: Multiple Sclerosis, shared decision making, decision making, qualitative.

Introduction

The treatment of Multiple Sclerosis

Multiple Sclerosis is a recurrent inflammatory disorder of the central nervous system and is thought to impact 2.3 million people globally. It has been documented as one of the greatest causes of disability in young people particularly in Europe and America (Feign & GDB 2015 Disease and Injury Incidence & Prevalence Collaborators, 2016; Rosati, 2001). Symptoms associated with MS can have a detrimental impact on quality of life and tend to worsen over time (Jongen, 2017). However, patients' experiences of MS are highly variable due to both symptomatic variation and the type of MS diagnosed.

The three most common types of MS diagnosed are: relapsing remitting MS (RRMS), primary progressive MS (PPMS) and secondary progressive MS (SPMS). In RRMS patients experience times where their symptoms get worse, followed by remission. In PPMS symptoms will get steadily worse. In SPMS, patients will have previously experienced a pattern of symptomatic relapse and remission, which then shifts to a progressive presentation. Treatment for MS is therefore dependent on the type of MS diagnosed and the individual experience of the patient. In PPMS and SPMS, treatment will largely focus on the alleviation of specific symptoms associated with MS. This is usually by steroids. However, with RRMS, whilst no cure exists and steroids are still utilised to treat symptoms associated with relapse, treatment options which aim to reduce the frequency and severity of relapses are becoming increasingly available (Ha-Vinh, Nauleau, Clementz, Regnard, Sauze, Clavaud, 2019). These treatments are known as disease modifying therapies (DMTs).

When offered DMTs, patients with MS are presented with a complex choice between differing partially effective treatment options. Each treatment option has varying side effects and impacts upon the patient's quality of life. Some DMTs also result in a small risk of patient exposure to life threatening adverse risks including liver failure, leukaemia and a progressive viral disease of the brain, progressive multifocal leukoencephalopathy. Research has shown that when taken as prescribed, DMTs generally improve a patient's quality of life and increase life expectancy (Jongen, 2017; Kingwell et al. 2019). However, of all patients eligible for DMTs, between 25% and 50% of people choose not to initiate treatment (Grytten et al. 2012; Margolis, Fowler, Johnson, Kassed & Kahler, 2011; Remington G, Rodriguez Y, Logan D, Williamson C, Treadaway K, 2013). The choice not to initiate medication is thought to be linked to the intermittent nature of MS symptoms, the side effects often experienced due to these medications and a perceived lack of medication efficacy (Carder, Vuckovic & Green, 2003; Visser & Van Der Zande, 2011).

Shared Decision Making

It is increasingly recognised that medical decision making should be facilitated by a process known as Shared Decision Making (SDM) between patient and physician (Charles, Gafni & Whelan, 1999). Makoul & Clayman (2006) suggest that SDM occurs when the following criteria are met:

1) both patient and health professional acknowledge the need for a decision to be made

2) that the best available evidence concerning the risks and the benefits of every option is made aware and is fully understood

3) that the decision made takes not only the professional's recommendations but also the patient's values and preferences into account.

NHS England identifies that SDM is an appropriate intervention when there is more than one reasonable course of action and the decision involves trade-offs (NHS, 2019). However, a systematic review of research investigating SDM in the NHS highlights two key barriers to the implementation of SDM: organisational barriers and barriers which arise during the decision-making interaction (Joseph-Williams, Elwyn & Edwards, 2014). Organisational barriers are generally outside of patients' or clinicians' control, for example: time, continuity of care, healthcare setting. Barriers which arise during the decision-making interaction are often relational in nature and include patients feeling unable to share in the decision-making process, difficulty trusting health professionals, and a desire to be a 'good' patient. The authors conclude that SDM requires both the provision of knowledge to patients, but also to ensure patients feel empowered to participate in the decision-making process.

Shared Decision Making in MS

Specifically in MS, SDM has been shown to be helpful to patients making a choice about DMTs, with 90% of patients stating they preferred making an autonomous or shared decision, as opposed to medical professionals taking a paternalistic approach (Kasper, Köpke, Mühlhauser, Nübling & Heesen, 2008). However, there have been challenges to understanding the process of SDM. In a narrative review of the literature, Ben-Zacharia et al. (2018) noted that a marked lack of standardisation of SDM contributes to a wide range of interpretations of what constitutes SDM. Furthermore, research findings are not yet robust enough to conclude whether SDM

significantly impacts the medical decisions patients make. However, the authors do conclude that SDM does look like a “promising approach” to supporting patients with MS.

Currently research is significantly lacking in understanding a patient’s experience of SDM in MS. Heesen, Köpke, Solari, Geiger & Kasper (2013) outlined that a patient’s locus of control and reported self-efficacy are not significantly associated with patient decision making and that other antecedents to decision making, including cognitive styles, personality traits and cognitive and social competencies are under-researched. Research investigating a patient’s attitude and understanding of risk, show inconsistent findings on their impact on medication choice (Prosser, Kuntz, Bar-Or & Weinstein, 2002; Heesen et al. 2010).

With these challenges in understanding how patients with MS make decisions, the growing field of behavioural economics has aimed to model patient decision making in MS to offer further insights. Jarmolowicz et al. (2018) asked patients with MS to report the likelihood of taking medications with a range of efficacies, and side-effect probabilities and severities. The authors found that the likelihood of people with MS taking medication that will halt disease progression in the future is likely to be impacted by probability discounting; a propensity to devalue a delayed reward in the face of low probability short term variables. Hence, a person appears to weigh up the costs (side effects, routines) of taking medication versus the long-term benefits associated with DMTs, and commitment to take medication takes place when significant enough value is found in the benefits of medication versus the costs of side effects. The author’s three-dimensional model suggests that patient’s weighting of probability and severity of medication side effects, and efficacy of the DMT, are all significantly likely to impact the patient’s decision to take a DMT. So, the long-term

benefits of DMTs are diminished for those patients who place a high value on the severity and probability of side effects. Studies such as these provide an important overview into medical decision making. However, in this study, side effect severity levels were labelled generically (mild, moderate and severe) which offers limited ecological validity. Furthermore, the task of making hypothetical choices can often be different to when faced with a real-life complex decision (Camerer & Mobbs, 2017). Therefore, challenges exist in drawing meaningful conclusions from the research when, for example, looking to apply findings to tailor service delivery.

IPA studies investigating SDM in heart disease (Borg Xerueb et al. 2016) and genetic testing for Huntington's disease (Smith, Michie, Stephenson & Quarrell, 2002) suggest that patients' lived experience of SDM is a more complex and emotional process than that outlined in behavioural economics, whereby there is "not a 'correct' result to the decision-making process", but rather an outcome that feels in line with a person's values (Smith et al. 2002; p. 142). Two qualitative studies which have adopted a phenomenological approach have been conducted investigating MS patients' experiences of choosing between DMTs. Lowden, Lee & Ritchie's (2014) adopted Colaizzi's (1978) procedure for analysis and identified one superordinate theme whereby coming to a decision was part of a process of coming to a "redefined self". A second study, this time using IPA, found four emergent themes: Constant confrontation with the disease; managing inevitable decline; hope of delaying the progression of the disease, and; the importance of social support (van Capelle, van der Meide, Vosman & Visser, 2017). Whilst there was an overlap in emergent themes between the two studies, there was a marked difference between whether decision making is a predominantly individual or social experience.

Whilst existing studies offer some insight into patient experiences, there were several methodological limitations in both studies:

1) Both studies had heterogeneous samples in the context of what stage of the decision-making process participants were at. Some participants were still deciding (and studies reported that these people had chosen not to take DMTs), some participants had decided but not commenced taking DMTS, some participants had been taking DMTs for up to 6 months.

2) The majority of participants in both studies had commenced DMTs and this is likely to impact participants' retelling of their decision-making process, biased by their experience of the medication and any potential side effects.

3) The study by van Capelle et al. (2017) is published in an online journal and offers little detail about the emergent themes and lacked any tangible clinical implications from the research findings.

4) The ten research interviews in the study by van Capelle et al. (2017) were conducted by three different interviewers. This is likely to influence the direction of questioning in interviews and, given the double hermeneutic process, also influence the subsequent themes that emerged.

4) In the Lowden et al. (2014) study, the interviewer was known to several participants. This is likely to have influenced participant's retelling of their experience, particularly when reflecting on the experience of SDM.

A further qualitative exploration of patients' experiences of shared decision making in the context of MS treatment could inform future research into understanding MS patients' approach to medication choices and aid SDM for patients within a clinical setting. This study uniquely recruited participants after a medication workshop (for

details see recruitment section in method section) with the aim that participants were all at a similar point in their decision-making process, reducing heterogeneity in the sample. Thus, the aim of the current research was to explore the lived experience of people with MS engaging in the shared decision-making process of whether to take DMTs, paying particular attention to what facilitates shared decision-making. Furthermore, it would be of interest to identify if similar themes emerged to the existing IPA studies, as this would offer an opportunity to meta-synthesise data.

Methodology

Interpretative Phenomenological Analysis (IPA)

Interpretative Phenomenological Analysis (IPA) is increasingly used within health research (Brocki & Wearden, 2006). The methodology takes both a phenomenological and double hermeneutic stance, as it is concerned with the participants' lived experience and how they, and the researcher, interpret or make sense of their experience (Smith & Osborn, 2003; Smith, Flowers, & Larkin, 2009). Within the research aims stated, it is felt that IPA will therefore offer an opportunity to understand individuals' unique experiences, whilst also understanding how a person's decision-making is socially constructed as a 'patient' who belongs both to their own social and family network, an MS clinic and wider NHS system, and a broader society. By gaining an understanding of patients with MS and their experiences of medical decision making, it is hoped that this research will offer a richer understanding of a complex decision-making process. In the future, it is hoped this will support professionals and services to offer and deliver the best care for people with MS.

Ethics

The research was submitted and approved by the HRA Research Ethical Committee (17/SC/0308) and by the local NHS site (see appendix 1 for approval). The research was logged with and sponsored by the University of Birmingham's Science, Technology, Engineering and Mathematics Ethical Review Committee. Informed consent was sought (see appendix 2 for consent form), and participants were made aware of their right to withdraw at any point during the research including up to two weeks after the interview had taken place. Participants were provided with a participant information sheet prior to taking part in the study. This was distributed by MS nurses working at a large NHS teaching hospital in the Midlands who were not linked to the research team.

All data collected was stored in password protected files and all personal information about the participants was stored separately from the data in a locked file and kept at the NHS site where the research took place. Participants' anonymity and confidentiality was ensured by using pseudonyms for participants. Where participating, significant others were informed that their data would not contribute to the analysis of emergent themes, but quotations could be used if it supported themes which emerged in the IPA analysis. Participants provided informed consent to quotes from their transcripts being used in the research thesis. Participants were also made aware that the research would be available in line with University of Birmingham regulations for the storage of ClinPsyD theses, and that research findings may be published in a scientific journal. Given the nature of the research topic, participant distress was monitored by the researcher throughout the research interviews. Whilst some participants did become upset during interviews, none of the

participants became so distressed that the participant or researcher felt it was necessary to stop the interview.

Inclusion criteria

The inclusion criteria for the sample were as follows: patients who had been diagnosed with RRMS and who had experienced a relapse of their MS symptoms in the six months prior to the interview which, after assessment by a Consultant Neurologist, qualified them for DMTs. All participants were aged 18 years and over, able to provide informed consent, and able to complete their interview without an interpreter. All participants had been diagnosed with MS for at least one year.

Participant recruitment

MS nurses purposively recruited six patients from an outpatient MS clinic located at a large teaching hospital in the Midlands. The MS clinic has a set protocol in place for patients who qualify for DMTs (see figure 7). Initially participants who qualify for DMTs will have an appointment with a Consultant Neurologist, where they are informed of this and provided with an information booklet which details all MS medications funded by the NHS clinic. Patients then meet with an MS nurse to discuss the DMTs available to them and ask any questions they have. After this, patients can self refer for a medication workshop. This is facilitated by two MS nurses. Each DMT is presented, showing patients the routes of administration, frequency of medication administration, mechanisms of action, and safety and tolerability profiles. Most people attend this workshop with an idea about which DMT, if any, they would like to take and then plan for the delivery of one of the DMTs with the MS nurses at the end of this workshop. Some patients choose not to take any DMTs and do not attend the workshop. Other people may attend the workshop but

have not come to a firm decision at the end of the workshop. All patients who have not decided or choose not to take DMTs are monitored in six monthly reviews with a consultant neurologist. They have the option to take DMTs in the future should their symptoms associated with MS continue to meet eligibility criteria for DMTs.

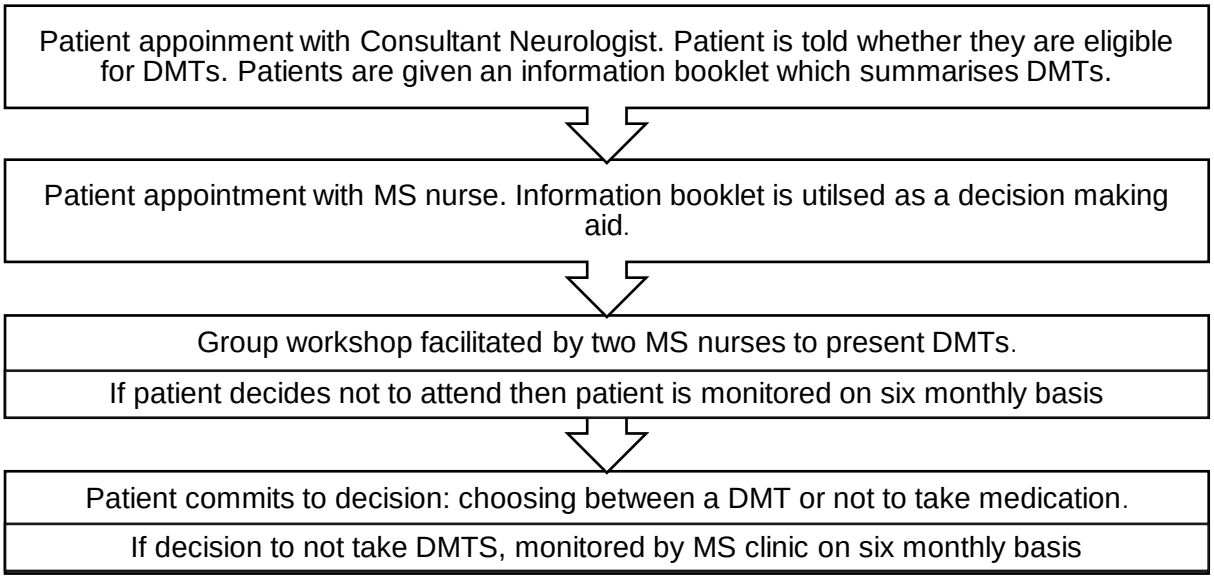

Figure 7: Flow diagram to show MS clinic's protocol for the shared decision-making process of whether to take DMTs, and if so which DMT to take

All participants in the current study had attended these appointments and the medication workshop. Participants were informed about the research taking place in a screening appointment with an MS nurse before the workshop. It was explained that the researcher had no connection with the hospital and was conducting research as part of a doctoral thesis.

To recruit study participants, the researcher attended fourteen medication workshops, and attendees were directed to make contact with the researcher after the workshop should they wish to participant in the study. In total, thirty-eight people

attended the medication workshops. Eleven people approached the researcher. Five people were not eligible for the following reasons:

1) Three people were not eligible because their MS diagnosis had occurred less than one year prior to attending the medication workshop.
2) One person was involved with secondary care mental health services and, after a preliminary conversation between the researcher and the potential participant, it was decided that the interview may be too distressing for the participant.
3) For one person, English was their second language and would not be able to articulate their experience fully in English.

The researcher being present for the workshops also aimed to build rapport with participants and to begin to immerse herself in the participant's context.

Procedure

Participants were interviewed directly after attending a medication workshop, in a private room located in the hospital. Participants were invited to attend alone, or with a significant other if they would prefer. It was explained that if a significant other was present, questions would be directed towards the participant, but significant others could take part. The researcher conducted semi-structured interviews following Smith, Flowers & Larkin's (2009) IPA guidelines. Each interview lasted between 42 to 90 minutes and each participant had one individual interview. Each interview followed the same semi-structured interview schedule (see appendix 3). The interview schedule was developed from the research questions and a review of the literature, following consultation with two experts by experience and one MS nurse. A Consultant Neurologist and a Clinical Psychologist reviewed the interview schedule

in their capacity as research supervisors. The semi-structured interview enabled the researcher to develop rapport with participants through the flexible format, allowing questions to be reflexive and informed by the interaction and the topic area.

IPA analysis

The interviews were audio-recorded and transcribed verbatim by the researcher. The transcript was analysed using IPA, adopting the procedure outlined in Smith, Flowers & Larkin (2009). The transcripts were read through twice. Transcripts were then re-read simultaneously alongside listening to the audio-recording of each interview in order to engage at an intersubjective level with the data. Initial noting was completed, paying attention to ideas, feelings and observations. Sections where the significant other present talked for long periods were not analysed, because the study aim was to understand the lived experience of persons with MS. The transcripts were re-read and a detailed line-by-line analysis with a focus on noting descriptive experiences, linguistic and phenomenological interpretations to develop emerging themes. This was repeated for each transcript before the emerging themes were then clustered and ordered into ordinate and super-ordinate themes. Transcript excerpts (corresponding to emergent themes) were then grouped together under themes. Transcripts were re-read for a final time to check against the internal validity of the themes and supporting excerpts. Appendix four shows the grouping of themes and sub-themes and the links between themes which emerged from this process.

Validity and quality

To assess the validity and quality of qualitative work Yardley's (2000) guidelines were followed. The guidelines set out four principles and how to apply these to IPA

studies. The principles are: (1) sensitivity to context; (2) commitment and rigour; (3) transparency and coherence; and (4) impact and importance.

Sensitivity to context

Sensitivity to the context of the research was established by becoming familiar with existing literature. Furthermore, the researcher met with experts by experience and MS nurses prior to the interviews to both consult on the development of an interview schedule and to understand the likely challenges people with MS face. The researcher attended the medication workshop that each participant attended to further understand the preceding context of the interview. In staying close to the participants' perspectives, the semi-structured design of the interviews allowed them maximum opportunity to tell their own story and hold their place as experts of their lived experience. Also, the in-depth analysis of the data and using verbatim quotes to support results allows the voice of the participant to be heard and for interpretations to be checked.

Commitment and rigour

In-depth analysis was conducted (see section 2.6) and triangulation was achieved via peer support from trainee clinical psychologists also conducting IPA research and regular meetings with supervisors. Interpretations were checked throughout each stage of the analysis and final themes (and the supporting data) were checked and agreed with supervisors and peers. A reflective journal was also kept (see appendix 7 for excerpt), with the aim of 'being with' the participants and the data, whilst simultaneously attempting to understand the position and context from which a person's claims make sense (Smith et al. 2009).

Transparency and coherence

Ethical implications have been considered and communicated to participants through an approved participant information sheet (see appendix 5 for participant information sheet). The description of the analysis process used for the study, use of verbatim quotes to support themes and the inclusion of an audit trail covering all the themes also allows for the study to be considered transparent and coherent.

Impact and importance

The discussion section of the study includes a sub-section discussing the study's clinical applications to ensure an outcome of the research is the provision of impactful and important recommendations to benefit the research participants.

Reflexivity

Shaw (2010) recommends that to elucidate the research processes a reflexive account is included. The reflexive account is written in first person prose as a more natural narrative style fitting with the aim of exploring the researcher and their experiences in relation to the research.

"I am a 30-year-old White British female trainee clinical psychologist with a specialist interest in long term health conditions and their impact on wellbeing. I am married and, at the time of commencing interviews, am 28 weeks pregnant. My partner and I are both healthy and with no long-term health conditions. Growing up, a close friend's mother was diagnosed with MS, and I have several memories of how this condition impacted their family. The research, particularly the research interviews, put me in touch with my deep love for my partner and our unborn child as well as the hopes I have for both my own and my family's future, and the fear of how illness may

subvert these hopes. Being witness to the experiences of the participants who have received a diagnosis of MS and were now making decisions about their medication made me think about the unpredictability of health, and how a long term condition can impact present day experience and a person's individual and familial hopes for the future. This universal experience allowed for intersubjective moments within the interviews, and my obvious pregnancy appeared to particularly deepen these moments with those people who had children. I believe my pregnancy brought up memories in them about their plans for children, and how this predated their MS diagnosis. At times this connection made it hard to 'stick to the schedule' when I was with them, in that moment of sharing, not just as a researcher or clinical psychologist in training but as a person. Furthermore, the distress that participants had experienced at various points made me think of my friend and her mother, and how I wish I had been able to provide more support to them. However, whilst this experience informed my feelings and explores my motivation towards the research it was the participants and their data which led the interpretations and results of the research."

Participant details

Six participants were recruited and interviewed. Four of the participants chose to have a significant other also attend the interview. Table nine details participant information. Pseudonyms have been attributed to the participants to protect confidentiality and anonymity. Where a significant other is quoted in the analysis, they are quoted in their relational role to the participant (e.g. 'Andi's partner'). Where it was felt that it may compromise a participant's anonymity, job roles have been changed or removed and some quotes have also been anonymised..

Table 9: Participant information detailing demographics and medication choice

Participant Pseudonym	Participant Age	Disease Duration	Current decision to take DMTs, and if so which DMT	Comorbidities	Significant Other Present?
Sara	51-60	1 year	No medication	None	Yes
Rachel	21-30	1 year	Yes-Copaxone	None	Yes
Alex	31-40	18 years	Yes-Copaxone	None	No
Andi	41-50	1 year	Yes-Avonex	None	Yes
Talia	31-40	1 year	Yes-Tecfidera	Depression	Yes
Marie	21-30	6 years	Yes-Avonex	Epilepsy, Underactive thyroid	No

Results

Results Overview

Table 10 outlines the three superordinate themes and respective subthemes which emerged from the IPA analysis. Below is a narrative account, exploring super-ordinate and ordinate level themes, with relevant illustrative quotes from participants included.

Table 10: Superordinate and subthemes which emerged from IPA analysis

Superordinate Theme	*Theme*	*Participants*
1. Facing MS	1.1 Accepting there is no cure	All participants except Rachel
	1.2 The absence of current symptoms vs. preventing future unknown damage	All participants
	1.3 The importance of informed support	All participants
	Taking Action*	All participants except Marie and Alex

2. Assimilating identity as a person who takes medication	2.1 Medication confirms I am an 'ill person'	All participants except Andi
	2.2 Asserting independence	All participants except Andi
	2.3 The importance of roles & responsibilities	All participant except Talia
3. Imagining a Future	3.1 Facing MS in 'black and white': the information booklet	All participants
	3.2 Living with the side effects: creating a personal hierarchy	All participants
	3.3 Future Plans	All participants

*Reported in appendix 6. It was decided the theme did not fit with the overall research aims

Superordinate theme 1: Facing MS

All the participants discussed how their experience of medical decision making forced them to think about their MS diagnosis. From our analysis this had four different components. Firstly, to make a decision all participants had to come to terms with there being no cure for MS. Secondly, participants reflected on how medication was offering improvement to an unknown future decline, often in the absence of symptoms in the present. Thirdly, there was a recognition that to face MS in a safe, contained way, it was important to have access to informed support. Finally, for all participants except Marie and Alex, the opportunity to make a decision about medication represented a way of taking action against their MS. However, this theme appeared to capture an experience specifically relating to those newly diagnosed with MS and was therefore not felt to be relevant to the current research aims. Further information on this sub-theme is included in appendix 6.

Theme 1.1: Accepting there is no cure

All the participants except Rachel talked about how deciding about medication had made them face the reality that there is no cure for MS. For Andi, Sara and Marie it was a shock that medication would not eradicate their symptoms. Andi explained:

"because on the mention of medication, for me, as a non-medical person, medication deals with the condition and that's it. But you realise afterwards, the condition is never going to change. Nothing anybody can do can sort out the condition…you realise that actually the medication isn't about curing what's there, because nothing is going to do that. Erm, so it was a more measured approach afterwards…Initially I was, thought 'oh, bloody hell' I mean you know, 'the medication doesn't cure me?'" (Andi, line 141).

For Andi, prior to his experience of medical decision making, a simple mental construct of medication existed, whereby medication cured disease. He identified as "non-medical" which highlighted that prior to making the decision between DMTS he had never had to think or understand the complexities of illnesses such as MS and their treatments. The simple response: "Oh bloody hell", highlighted the shock at having to address this. However, the realisation appeared important in him being able to deliberate and come to a more 'measured approach'. Andi narrated his experience in the past tense which appeared to represent him having come to an understanding about the lack of cure. Similarly, Talia outlined an acceptance at the lack of cure and had even found some hope in coming to terms with this fact:

"whatever happens with it, yeh, I'm not gonna put my hopes and say 'oh, it's gonna cure me, oh it's gonna do this' because there is no cure for it, but if I start taking it and it makes my life a bit easier then that's a good thing isn't it." (Talia, line 353)

However, for Sara, Alex and Marie coming to an understanding that MS had no cure was a much more emotive subject. Sara's distress about the lack of cure was much more tangible at the time of the interview, and she talked about her thought process in the present tense:

"Well, I suppose, you know, it's this business of it's not a cure, it's just managing the disease and you know that but I suppose you're sort of…[sigh] you want it to be much more don't you, and so you think 'why do I want to take', as I said, 'why would I want to take a drug that could potentially make me feel quite grotty for a while?'" (Sara, line 205)

Sara's sigh during this exert captured the hopelessness she felt having contemplated that medication cannot cure her MS. Her linguistic shift from first to second person suggested this may be linked to the superordinate theme of identity; having deliberated that medication cannot cure MS forced Sara to also face that *she* was a person with an incurable illness. Furthermore, Sara seemed ambivalent about taking a medication if it will not cure the illness, particularly when it could have several side effects. This dilemma is shared by Marie: "Yeh, the like, there's no guarantee is there, there's no cure. And because there's no cure and you're like…you know, then…Because I've, now that I've, um…" (Marie, line 43). Marie tailed off in her explanation as she faced the idea that there was no cure for her MS. In a similar way to Andi, she is perplexed by the concept that medication could not fix the problem. In fact, during her interview Marie referred to a lack of a cure on three separate occasions, including in her final response: "No I think that's all it. That's, I think, it. And I hope there is a cure one day…" (Marie, line 390). Despite many reflections on her life with MS and what influenced her medication choice, a fundamental desire remained that one day she will not have to make such a decision. There is a sense that Alex shared this desire, though her distress at a lack of a cure is instead channelled into anger:

"I'm very frustrated with the whole 'MS is getting much better at managing relapses and managing symptoms' but what they're not good at is they haven't managed to find anywhere close to the root cause of it and that bugs the hell out of me…I appreciate the body is a very complicated system. But it is just a system…And, in reality, how I would solve problems at work… and they can be really complicated… problems, I'll map it out…I will then start to find the root cause. And I understand the

body is a complicated system, but it is just a system. It's just a system." (Alex, line 144)

Alex felt angry at her lack of control over MS. Interestingly, Alex's analogy of the body as a mechanical system conflicted with the feeling, human being she describes herself as. However, there was a desire to reduce her symptoms and experience down to something she understood, giving her back some control when discussing the uncertainty of a future where no cure for her MS exists. To Alex, a problem that cannot be solved is unsafe and highlights her vulnerability. Potentially this felt unsafe, and interestingly what Alex connected with was her anger. Again, the link between identity and the lack of cure appeared, as Alex positioned herself as adept at solving complex problems in her field. Alex, like Andi, is 'non-medical' and was not responsible for this failure to find a cure. This links to a potential drawback for patients outlined by Joseph-Williams et al. (2014) in their narrative review of SDM whereby patient involvement negates a comforting opportunity to 'blame' clinicians for 'bad' outcomes; there was a comfort for Alex in separating herself from the inescapable lack of cure and blaming health professionals responsible for this.

Theme 1.2: The absence of current symptoms vs. preventing unknown future damage

All the participants talked about coming to an understanding that DMTs reduce the frequency and intensity of future relapses. For many of the participants, by the time they made the choice to take medication, symptoms associated to their relapse had subsided. Despite this, for Andi it was a straightforward decision to try to protect against future decline:

Andi: …if you've got something and there's medication to help then you take it. Really. That's really it. Um, for me the big issue is to, well I've got relapsing remitting MS, to try and avoid or reduce the chance of getting Progressive, and that's what these drugs do so…it's almost like a no brainer…

Andi's partner: …it's immensely manageable and if he didn't take anything it would be alright. For us there's always that danger that -

Andi: - It'll get worse.

Andi's partner: So, we want to prevent that. (Andi, line 93)

At the time of interview, for Andi and his partner, though his MS symptoms were minimal, preventing future decline was worth any potential side effects and difficulties associated with taking medication. There was a suggestion in both his partner's involvement in this section of the interview and in their language ('us' and 'we') that for Andi this theme was relational. Perhaps his role as a husband and a father means a greater value was placed on limiting future decline over short-term side effects and discomfort [linking to theme 2.3].

However, for Rachel the dilemma as to whether to begin medication, when in the present she is largely unimpacted by her MS, required more deliberation:

"I think because you can't necessarily see what's going on, doesn't mean nothing is going on…no, well, I mean I haven't had a relapse or any symptoms for about 6 months so it's a bit "why are you going to go for a drug that's got side effects…why would you do that when I've been feeling ok for six months. I get tiredness and things like that…but why would you do it? It's not until someone explains it, and it's like, well you don't actually know." (Rachel, line 51)

Rachel had a decision to make where she must commit to the possibility of feeling more unwell in the short-term taking medication, than her current state at interview not taking medication. It is in stark contrast to Andi and his partner's priorities outlined above, suggesting there is a split between those who feel that anything is worth halting future decline, compared to those who question the value in potentially

feeling ill in the present. This links to the probability discounting model outlined by Jarmolowicz et al. (2018), whereby people weigh up the costs and benefits of situations in the present and future. For Rachel the risk of the unknown future decline was enough for her to tolerate side effects in the short term. However, for Sara, the opposite was true:

"I certainly don't feel in any way, erm, ill or at the moment any symptoms I was shocked to find that the second scan still showed some inflammatory response going on…y'know it is this business of having got to the age of nearly sixty-one and not being on any medication at all, is there that, you know, reluctance to start medication." (Sara, line 7)

The disconnect between Sara's own subjective experience of wellness and the medical evidence suggesting decline was a prominent theme during her interview. There was perhaps an important meaning attached to her 'wellness'; stating her age (which she did on two occasions during the interview) suggested that her experience of making the decision also brought into focus what it meant to age and perhaps become more prone to illness [linking to theme 2]. In Marie's case it has taken the severity of her relapses to increase before she has been convinced by the value of taking medication:

"I said "no I'm not going to have the treatment". Then I had another relapse, and then I was like, I was really poorly during that relapse and was like 'I have to go for this treatment if this is what's going to make me better, because I can't go through this relapse again'. It was, erm, severe damage to this eye of mine [points to right eye] I still don't know what would be correct for me because it's a lot of confusion of treatments. Erm, there's a lot of symptoms, then there's a lot of risks, and then there's no promises. So, that's why." (Marie, line 33)

Marie's experience highlighted the fluid nature of symptoms experienced by people with RRMS and how this may influence decision-making: at the height of a relapse,

the severity of symptoms motivated her to take medication as she realised the impact that MS has on her life.

Theme 1.3: The importance of informed support

All the participants reflected on how talking to other people had helped them to face their MS diagnosis, and was an important part of their decision-making process. Everyone except Talia identified that their MS nurse was a source of informed support and the role required both provision of information and a space to reflect, as Andi and his partner discussed:

"she [MS nurse] dealt with the softer, lifestyle things. I think with MS it's a life rather than, er, an acute illness that you have to sort out. It's something that's got to incorporate into our whole life, and she gave that life bit. 'How about your life?'

Andi: Yeh, it was actually [surprised]. I mean the website's very good and these things [holds medication booklet] are very good but when you actually have someone sitting there with you, telling you practically and then you can, you know, bash ideas off and say "look what about this" that was extremely helpful." (Andi, line 167)

Support from MS nurses allowed participants to face their MS and manage the anxiety that comes with this process but also allowed participants to begin to imagine their futures taking medication [linking to theme 3]. It appears there is an importance in transferring from written information documenting facts [theme 3.1] about the medication to a dialogue where more personal questions can be asked which seems to be emphasised by Andi's partner's repetition of 'life'. The calculated, logic-based decision that is set out in the information booklet must become something more akin to a heuristic; suggesting that the decision-making process takes place in the context of a person's life, not simply in the rational weighing up of pros and cons.

For Alex and Marie, who had managed MS for considerably longer than the other participants, a trusting relationship with their MS nurses had developed. Both participants placed great importance on what their MS nurse offered both in terms of practical advice and emotional support:

"…I spoke to [MS nurse] as well, at length, when I was in hospital. She came to talk to me about them. Because when she came up to see me, lovely lady that she is, um [laughs], I've known her for 17 years now so I feel like she's kind of – we're – um, and we kind of went through all of them together anyway…" (Alex, line 214)

Alex's affection towards her MS nurse was apparent, and her pauses as she searched for the right term to label their relationship illustrates the strong rapport they have; to Alex her MS nurse appeared to be more than that of a health professional, though professional boundaries meant she was not a friend. This relationship appears to develop over time, so Sara, who received her diagnosis six months before her interview, saws the nurses as "helpful" but in "work mode" (Sara, line 397). Over time then the role of the MS nurse appears to develop from allowing a person to face MS, to forming a working relationship with them. The formation of this relationship may offer a chance to build a new construct of the patient-health professional dynamic from the traditional paternalistic model to an SDM model.

Andi, Marie and Sara also discussed different medication options with friends or family members with a working knowledge of MS. There appears to be an added advantage in seeking informed support from friends and family as opposed to professionals which Andi outlines:

"…There's a very good friend of mine who just happens to be our family GP. So, he actually popped round yesterday. So whenever he's around, obviously he referred me initially and all the rest of it, so yeh chatting with him is nice because it's not only, I'm not chatting to a doctor, I'm chatting to an old mate and he's known me…" (Andi, line 317).

Where possible then, discussing medical decision making with a knowledgeable, trusted friend or family member appeared to help the participants face the facts of having MS, but also to do so in a way that ensured their own existing identity is considered [linking to theme 2]. So, for Andi, when he talked about 'chatting to an old mate,' one may interpret that it was important for Andi to have someone understand both who he was before his MS diagnosis, as well as to help to redefine who he is as a person with a long-term condition. The informality of the description appears to highlight the comfort he gains from this.

One of the participants alluded to why it may be important for the person to be informed; those with a lack of information had views that were unhelpful:

"…like, they see it in a different way, they don't see it scientifically. But then that's not their fault, because they don't have all the information or they haven't been educated in that way to know about it…sometimes you get told "because you don't pray, it's why it's happening" and "if you pray it will be better" [chuckle] so, that me-, that, it, that can be a bit of a challenge…" (Anonymised participant, line 199)

Furthermore, there may be a desire to protect friends and family members from the process of facing MS and medical decision making. Sara explained "…my attitude is I don't want to burden them with the decision-making process. Because ultimately, it will be my decision…" (Sara, line 133). Similarly Rachel wants to ensure she has understood her MS and the decision, before explaining it to those close to her: "…if I'm explaining MS to someone who doesn't know what MS is, I'm using the terms that she's [MS nurse] used in the appointment I've had with her. It's education..." (Rachel, 134). There was an importance on having knowledgeable sources of support to facilitate an individual facing MS to make decisions about medication. This

had important consequences for the individual making the decision as well as their wider network.

Superordinate Theme 2: Assimilating a new identity

All the participants discussed how medical decision-making had forced them to think about their own identity and assimilate how taking medication for a long-term illness fitted in with how they viewed themselves. There appeared to be three key aspects of this theme. The first was participants accepting what it meant to be an 'ill' person and the impact this had on identity. This in turn linked to the second sub-theme, asserting independence, which appeared to be a key coping response to the illness identity. The third sub-theme was how roles and responsibilities were important in preserving a person's identity, and again linked to theme 2.1, how this helped a person to adjust and see themselves as more than an 'ill' person.

Theme 2.1 Medication confirms I am an ill person

All the participants except Andi reflected on how medical decision-making had forced them to think about their concepts of 'wellness' and 'illness'. All the participants elaborated that due to the relapse-remission pattern of RRMS, when in remission participants felt 'well', and it is only at the time of a relapse severe enough to require medication that there was a recognition that they have an illness, and consequently that they themselves are an 'ill' person.

For Alex, who had experienced a number of relapses, there was a clarity in her awareness of this: "When I don't take any drugs, I think I'm ok. So, there's a real direct, causal link between me being ok and not taking drugs." (Alex, line 188) There was a recognition that her illness can exist without impacting how she viewed

herself; she was ‘ok’. However, when she is taking medication this confirms her illness, and this appeared to be a distressing shift. Alex distanced herself from the identity she inhabited when taking medication and described herself in the third person: “she’s sick and she’s not going to be very well. Erm, and she’s the lady who’s out of control. Whereas Alex who doesn’t go to the hospital is in control” (Alex, line 312). For Alex there was a complete split of her personality brought about by taking medication: there is a ‘well’ Alex who is in control and an ‘ill’ Alex who is not. Interestingly, Alex was so keen to remove herself from the illness role that when at appointments she positions herself alongside the medical staff: “most people think I’m a nurse to start off with anyway because I’m taking notes and I’m being efficient” (Alex, line 420). For Alex, the concept of a patient being efficient and in control is so removed from her ‘out of control’ experience that she instead must adopt the role of someone treating the problem.

Talia, Rachel and Sara all also described some level of distress in the split between ‘well’ person and ‘ill’ person. For Talia the shift to that of an ‘ill’ person means she sees herself as more fearful:

“…I feel like I’m suffocating inside myself. I’m getting more and more scared now in myself so, before, I could walk on the road and go “yeh, I could jump off a rope swing or whatever”, now I’m, I mean, I’m getting trapped in it…” (Talia, line 88)

MS appeared to take on an identity of its own in Talia’s description, as if MS was engulfing Talia’s old vision of herself. Consequently, the emotional experience of fear is highlighted. The image of her jumping from a rope swing conjured the idea of someone who was carefree and adventurous. This was juxtaposed with the ‘trapped’, ‘suffocated’ person who is ill and takes medication. Similarly, Rachel felt like there was a change in her, and during the decision-making process she “…was

having to paint a face on, a happy face…" (Rachel, line 78). Her description of 'painting a face on' suggested that she felt that she was presenting a false sense of self. For Sara this transition between well person and ill person resulted in such ambivalence towards taking medication that it had not been possible to come to a decision:

"…but it is just this [pause] making the decision when you feel as well as I do. And also, that in this last six months, I've made real changes to my life where I feel that I am definitely leading a healthier, certainly physically more active, erm, and less stressful existence. And, of course, when you're not feeling unwell…I've never up to date have had to have any sort of drug therapy, for instance the taking of high dosage of steroids…I feel well." (Sara, line 49)

Theme 2.2: Independence

All the participants apart from Andi talked about how the decision to take medication was one that required individual reflection, and this appeared to be linked to their identity as an independent adult. Given the emotive process outlined in Theme 2.1 where participants had to come to terms with an 'illness identity', it is understandable that participants wished to assert their independence. For example, with some pride Rachel reflected on her decision-making process: "I did it all on my own. I told my mum about it on the way here" (Rachel, line 19). Taking ownership of the decision-making process allowed Rachel to assert her independence. Conversely Sara's difficulty in coming to a decision was at odds with her previous independence:

"…Well, again, I'm…I'm someone who doesn't, I really don't, I'm not, er, someone who seeks advice erm, you know, "what would you do?", you know, I'm not. You know, I'm very much someone who makes their own mind up…" (Sara, line 90)

For Alex, independence could be found not just by taking ownership of her decision making but by her MS as a whole:

"…I'm very protective over my MS. Um, and it's my MS, it's not anybody else's. It's mine. And I think there's a very, like control, it goes back to control, it's all about me protecting my MS, and everybody else can bog off because it's mine. And it's nobody else's. And in reality, nobody else can help me anyway…" (Alex, line 446)

Interestingly then, for Alex the illness identity outlined in theme 2.1 could even be harnessed to assert her independence; she appeared to be saying 'even though I am ill, the illness is mine and I am in control'. Similarly, Talia's need for independence distanced her from other people: "I don't wanna contact my MS nurse. I don't wanna contact the specialist, I don't wanna contact the doctors. I've got my medication." (Talia, line 102). However, whilst for both Alex and Talia asserting independence may be a protective mechanism to defend against feelings of vulnerability, it may also increase their risk of feeling isolated and denying a need for help.

Theme 2.3: The importance of roles and responsibilities

All the participants talked about the roles and responsibilities they have. Not only did they present important practicalities to consider when imagining a future [linking to theme 3], but, for everyone except Sara and Talia, they were an important part of assimilating an identity as someone who takes medication.

Andi, Rachel, Talia and Sara reflected on their roles within the family and how this impacted their decision making. For Talia, Andi and Sara there was a similar responsibility referred to: protecting members of their family from their illness. Again, whilst the illness itself could be forgotten about when a person was not symptomatic, medication brought an unavoidable confrontation with MS into not just the participants' lives, but their families too [linking to theme 1]. One participant explained how so far, they had not told their children about the diagnosis but the

decision to choose an injectable medication meant it was unrealistic for them now to not be informed:

"…mmm, I think in talking about the kids, because it's not been obvious. But I suppose when you're taking injections, they will ask what it is. So, I don't know, it might become an issue. But for the moment we haven't told them." (Anonymised participant, line 344)

There was a recognition that to take a long-term medication becomes part of not just an individual's view of themselves but also impacts how others seem them. Similarly as a mother, even to grown up children, Sara highlighted the tendency to put the family's needs above her own: "when you've worked and brought up a family, women do have this business of putting themselves, you know, you're the last one to, or you do things for yourself last don't you" (Sara, line 353). There is a sense that whilst adults may be able to come to terms with the reality of MS, as a parent there is a responsibility to protect children from the impact of the disease and to continue with as normal a life as possible. However, it may be this semblance of normality actually helps to ground the adults, as Andi's partner describes: "yes I was anxious about what was happening but actually after you get on with the kids, you get on with life and everything and you think 'it's ok, it's alright'" (Andi, line 146).

Superordinate Theme 3: Imagining a future

All the participants appeared to work through future scenarios, thinking about how potential medication options would fit into their lives. This process began for all participants by consulting the information booklet given to them at their first appointment. Then, for participants to make a decision, they weighed up side effects, and considered future plans. Participants then pictured how taking their chosen medication would fit into these imagined scenarios.

Theme 3.1: Information booklet and its role in decision-making

All the participants described how they had engaged with an information booklet given to them at an earlier appointment which is designed to support decision-making. For everyone except Andi, participants indicated that they had consulted the booklet numerous times in between their appointments. Rachel describes how it helped to be able to return to the information:

"…I'd always, kind of, picked the book, have another flick through, I'd leave it for a couple of weeks, and I'd pick it back up again. So, I probably have read through it quite a few times. So, for me to get to that decision, I probably have read it and gone over it quite a few times to decide that's the one that I want… "(Rachel, line 102)

For Rachel, the presence of the booklet helped her to comes to terms with her need to take medication and allowed her to deliberate the decision at convenient times. Alex elaborated on how the information provided allowed her to feel more in control: "It's a table. It's data. It's almost like putting a graph and data in front of me and that brings it right into my world." (Alex, line 282). For Rachel, Talia and Alex , at a time when they must face a lack of a cure and an unknown prognosis [linking to theme 1.1 and 1.2], the information provided by the booklet offered both a reassuring factual 'certainty' and a helpful tool in the decision-making process. However, the same facts left other participants feeling overwhelmed. For example, Sara explained that all the information in the booklet "being there in black and white" was "quite frightening" (Sara, line 243). There is a sense that the information booklet draws attention to the complexity of the decision. Andi's partner elaborated on the difficulty with reading the information booklet: "And in there [points at booklet], it's not a real-life recollection…the sessions are what brought it to life." (Andi, line 213). It appeared that participants must digest the facts presented in the booklet, take what

is relevant to them and then attempt to translate this into ‘real life’. It appeared that the group workshop facilitated by MS nurses helped this process.

The act of digesting information may then provide everyone with different dilemmas and signified the start of participants imagining their future as someone who takes medication. Furthermore, the booklet appears to be symbolic of the participant having to play a role in a shared decision, as opposed to the more traditional patient role where a doctor advises a patient which medicine to take. For Alex, this was an emotive process:

“…Erm, terrified is too strong. But it’s definitely towards that end. Um, incredibly nervous that I’d make the wrong decision…you kind of put doctors and nurses on a pedestal, because they’re the people who know what drugs it is, and you give them that responsibility. Because you do that from when you’re very young…but now all of a sudden, forty years later, now I’m being told “which drug would you like?”. And it’s just – I haven’t got a clue.” (Alex, line 357)

For Alex there was a vulnerability in translating the data of the booklet into a working, real-life choice. This is somewhat emphasised by the image of her as a young girl being told what to do, compared to the clueless adult she described in the present. Similarly, for Marie, the difficulty in translating information had led her to simply ask her MS nurses’ opinion on which medication take: “so I’ll just take that one rather than reading loads and going even more mad. Yeh.” There is a recognition then that whilst SDM allows participants to factor in personal considerations, it also may be an additional source of anxiety at an already overwhelming time.

Theme 3.2: A personal hierarchy of side effects

All the participants discussed their experience of weighing up the side effects and referred to the side effects of medication having some impact on their decision. Each

person appeared to prioritise different side effects, given their own personal situation. The thought process is described with some clarity by Alex:

"…so, which is the best one of these drugs for me? Er, because of the side effects I could absolutely point out the ones which are the worst. But it's that 'how do I know which one is the best for me?'…So, I ruled everything out, um, from the pills so Aubagio and Lemtrada – all sorts of different reasons – and then I ruled out Avonex because it's IM [intramuscular], and then so I had a choice of five in the middle. And, in reality, four of them had flu-like symptoms which definitely leads me to Capaxone. And it was literally that. So, I yeh, ruled out the worst first and see what happens or not…" (Alex, line 369)

The short, clear phrasing suggested that the method of creating a hierarchy of side effects gave Alex a framework to tackle the difficult multi-faceted decision, thereby reducing earlier anxiety raised when facing MS [theme 1]. The reference to "all sorts of different reasons" is picked up by all the participants. For Alex, Andi and Rachel the side effects deemed to be the most acceptable were based on those that were thought to have minimal disruption on their parental or work responsibilities [linking to theme 2.2]. For example, Andi identified that the flu-like symptoms associated with one medication were in fact less likely to impact his job less than gastrointestinal problems associated with another:

"…I'm usually out at court most working days and I know they said, you know, for example the diarrhoea just leaves loose motions rather than full blown dia-, well, but still, I don't want to be sitting in court waiting for my case to come on and be "oh, I've got to go" whereas Friday night it's always home, you know, family time, take injection and take some medication, you know, erm, ibuprofen or whatever, before going to bed and hopefully that will be it...." (Andi, line 74)

Andi appeared to imagine a future where he is taking the medication and picturing the impact of a side effect. For him the unpredictability of gastrointestinal problems, and the potential disruption it may cause was of greater importance. This was somewhat emphasised in Andi's imagined future by the image of the formal surroundings of a court. Interestingly, this was juxtaposed against the much more

comfortable, secure image of his family and their Friday night routine, when he thinks about the flu-like symptoms that could occur from the medication he has chosen. The medication isn't perfect, but the side effect appears to be something that in Andi's imagined future, with management, could become an extension of the existing normality.

For Talia and Marie existing mental and physical health conditions also contributed to participants' constructing a mental hierarchy of medication side effects. Talia took antidepressant medication and was clear that for any medications that increase the vulnerability of experiencing depression she was resolute: "when you read up about the side effects, that's somewhere I'm not willing to go." (Talia, line 168). Marie was prescribed other medication for underactive thyroid and epilepsy:

"…Erm, erm the reason that erm it's got less side effects, so the side effects are extremely low. And it's not a medication I have to take orally, because I'm quite tired of taking oral medications. Because my mouth is now, like, it's got a particular taste in it and I can't taste flavours anymore. It affects how I taste flavours and…even my speech and everything. That's why I hate medication. I hate taking pills. Because I already have to take enough and I don't want to just, like, add on more. Yeh…." (Marie, line 112).

Marie's response highlighted how medication treating comorbid illnesses may impact a mental hierarchy of medication side effects; her decision making is impacted by the intrusiveness of existing side effects. Comparative to the other medications she takes, she viewed the impact of any side effects from the DMTs as 'extremely low', which differs from other participants who described the same set of medication side effects as "terrifying". The severity of side effects is therefore likely to be valued proportionate to other difficult symptoms the participant is managing.

Participants also referred to recalibrating their hierarchy of side effects if new information emerged. Andi recognised that for a time he favoured taking oral

medication, however when he further understood the implications of the side effects he opted for an injectable:

"…we were thinking of the oral medication particularly because it's much easier, and I thought with the side effects I might be able to live with those more than the injection. But then after the chat today, we, I thought, perhaps, going for the injections was probably better. Simply because the, erm, I think the side effects are probably going to be a bit more manageable" (Andi, line 34)

Theme 3.3: Life plans

All the participants made some acknowledgment to how making a decision about medication had made them consider future life plans. Talia, Marie and Rachel all referred to medication and its impact on their ability to have children. For Rachel this was one of the most important factors in her medication choice:

"…you're either looking after your health or you're deciding to have another child so it's a bit like the option is taken away. It felt like it was taken away from me a little bit…it was horrible. Not that we're planning any time soon but then it was a bit like…when you're told you can't do something, it makes it a lot worse…" (Rachel, line 92)

Rachel's experience of having to decide between having a child and commencing medication found a productive compromise; one of the medications can be continued during pregnancy. However, for another participant the impact of medication had dramatically shaped her future plans:

"…they're not suitable for women having babies. But I don't have any intention of having babies…I don't think I'll find an individual who can keep up with all of this [laughs]. …It has definitely impacted my, er, relationship status because I feel very insecure when I have to approach a new individual and then talk to them about my medication and talk to them about my medical history and it's not very interesting because there's a lot behind it. Especially in my community, they always look for a fit and well woman rather than, not a woman who's going to last for a few years…I always take it [medication] in private." (Anonymised participant, line 124)

To this participant, the decision to take medication was linked to a future without a long-term relationship, and of marking her out as someone unsuitable for marriage and motherhood. There was a sense of shame in the image of taking the medication in private, hiding from her community that she was not a 'fit and well woman'. The participant's emotion was palpable throughout, as she reflected on her vision for the future and how these were restricted because of her illnesses and her need to treat them. The current decision to take more medication had thrown this into sharper focus. However, later in this interview the participant also talked about a future ambition to travel:

"…I do hope to travel on my own, and just have time to myself, yeh, and I think that will make me happier. When I am happier, I do feel I'm better and then, when you're better you see that improvement in the pain because that pain just disappears…" (Marie, line 224)

There was a sense that travelling was hopeful: it could offer independence and freedom [linking to theme 2.2], as well as offering an alternative to traditional path of relationship, marriage and children that her community expects. Another participant also had ambitions to travel, specifically sailing around the world, and there was a direct link to her medication:

"I think the only thing that, the only thing that annoyed me was that there wasn't a Copaxone that didn't need to be stored in the fridge. The fridge is a big one. I do sailing on yachts, and the problem is, is the fridge is a thing you tend not to have. Um, but we'll sort it out [laughs]. There's ways and means of sorting it out…the problem is about skin site reactions. Erm, it's not great if you're wearing a bikini [laughs]. And I know that sounds a bit kind of vain and everything like that…if I'm wearing a bikini on a boat and I've got red things all over my legs then I'm just going to have to brave it out. I'm just going to have to go "you know what, if they're there, they're there". We'll see how successful I am on that" (Anonymised participant, line 104)

The participant's imagined future was impacted but was still possible, and she appeared confident in her ability to solve problems. However along with the practicalities of storing the medication, the participant also had to contend with picturing side effects in her imagined future. In her day to day life it was possible to cover the skin site reactions and therefore hid signs of her illness, however in this imagined future, a bikini revealed these. It is interesting that both in the image of a bikini and in earlier mentions of child-rearing the participant group highlight gender-specific plans; as if their imagined futures have forced them to consider what it means to be a healthy female.

For all the participants their medication choice resulted in them thinking about their hopes for the future and required them to find a way of successfully reimagining the future with their chosen medication now part of the scenario. For the main part plans for the future seemed like a source of hope, however for Sara her MS diagnosis and qualifying for DMTs had bought her dreams of the future in to the all-too-real present:

"I retired. Um, I was a physiotherapist and I had my own business, um, and decided that, you know, I'd been doing that for over 40 years and enough was enough, I was stopping and whilst I'm fit and well do things for me and my family [becomes tearful] whilst I can." (Sara, line 173)

There is an acknowledgment then that making a decision about medication can force participants to think about the future; should medication 'fit' into their routines and future plans there is more confidence in making a decision, however if it does not this can be a source of anxiety and hopelessness.

Discussion

The aim of the current research was to explore the lived experience of people with MS making a shared decision about medication. This was done by analysing semi-

structured interviews using IPA. The analysis has demonstrated that the decision-making process a person with MS faces when choosing between multiple DMTs is often complex and emotionally demanding. Three superordinate themes were interpreted from the data: (1) Facing the realities of MS; (2) Assimilating a new identity, and (3) Imagining a Future.

Comparison between our findings and the existing literature

There are similarities between aspects of the findings from this research and the existing literature. One of our superordinate themes, Facing MS, appears to have similarities with the constant confrontation with illness superordinate theme outlined in van Capelle et al. (2017), particularly in the recognition of a lack of cure and in the unknown prognosis patients with MS face. This is perhaps unsurprising given the impact these aspects of MS are likely to have on any individual, regardless of a patient's circumstances. The second superordinate theme extracted in this research, assimilating a new identity, appears to have many similarities to Lowden et al.'s (2014) one overarching theme: patients developing a new, 'redefined self'. Our findings drawing parallels between both existing phenomenological research papers, as well as identifying different themes. This may partially be a result of the double hermeneutic principle present in IPA: Lowden et al.'s (2014) nursing background, and van Capelle et al.'s (2017) interest in ethics of care are likely to influence the analysis process, in the same way that psychological theory and my own experiences as a trainee clinical psychologist are likely to influence my own experience of the participants' recollections.

Our research noted a much more future-focused aspect of decision making whereby participants needed to consider many aspects of their potential medication and

whether they ‘fit’ with an imagined future. Lowden et al. (2014) do highlight aspects of this in subthemes: weighing and deciding what's important and evaluating symptoms and fit with quality of life. However, in our analysis Imagining the Future felt like an experience with its own psychological nuances, linked to - but separate from - understanding one’s own identity. In our research, the emergence of this theme felt more in line with cognitive decision-making theories, whereby data presented on medication is translated to real life heuristics (akin to seminal work by Daniel Kahneman and Amos Tversky; e.g. Kahneman & Tversky, 1979). This partially fits with the probability discounting model outlined by authors such as Jarmolowicz et al. (2018), whereby a person appears to weigh up the costs (side effects, routines) of taking medication versus the long-term benefits associated with DMTs, and commitment to take medication takes place when significant enough value is found in the benefits of medication versus the costs of side effects. However, the findings from this research suggest that many of the costs and benefits associated with the decision are much more subjective than behavioural economic models tend to appreciate and are made by each participant in the context of their own life. The participant does consider relatively objective factors such as side effects and the practicalities of administering medication, however they occur in a more existential context whereby a person assigns value on costs and benefits on what would ‘fit’ in with life. Shared decision making appeared to be aided by professionals acknowledging this process.

Strengths and limitations of the research

A strength of the research conducted was the time point where participants were captured for interview: within an hour of attending a medication workshop. In five of

the six interviews, this meant the interview was conducted straight after the person had committed to their decision to take a specific DMT. In one interview, the participant had attended the medication workshop and was still undecided. Therefore, the participants were able to reflect on their decision-making with a fresh perspective, without being tainted by retrospective bias, had more time elapsed between making the decision and data collection. The method of recruitment also aimed to provide access to a homogenous sampling group as participants would likely be at a similar point in their decision-making process.

However, a source of heterogeneity within the sample was the varied time that had elapsed for participants since they had received their MS diagnosis. With hindsight, the medication review group was likely to bias towards those newly diagnosed and considering medication for the first time; individuals who had previously relapsed and taken DMTs are likely to feel more confident in making the decision without attending the group provided. It was felt by the research team that given the aim to understand patient experience of decision-making in MS, including a varied length of time since diagnosis would help to understand the insights into all patients, as opposed to understanding what it is like to make a decision about medication for this *first* time. However, the themes showed some clear differences between those making a decision about medication for the first time (Sara, Rachel, Andi and Talia) and those who have managed relapses previously (Alex and Marie) so it would be of use to ensure more homogeneity in a sample's experiences of relapses or perhaps compare a sample of people choosing between DMTs for the first time compared to those who have made the choice before. Furthermore, the specific recruitment window of participants meant that the research was also biased against the recruitment of people who chose not to take DMTs. Sara was the only participant

whose current decision at the time of interview was to not take medication, and perhaps because of this Sara's interview was very different to other participants. Given that 25-50% of people choose not to take DMTs it is important that the experience of these patients is heard too (Grytten et al. 2012; Margolis et al. 2011). Potentially, recruiting participants through organisations outside the NHS, such as the MS Society or MS groups on social media may help to ensure the inclusion of these groups in future research.

A further strength of the research was the involvement of several stakeholders in the design of the study. People with MS, MS nurses, a Consultant Neurologist and two Clinical Psychologists were consulted at various stages when designing the recruitment strategy and interview schedule. It is hoped that this ensured that the interview process felt relevant, convenient and valuable to participants and feedback from participants generally did confirm this was the case.

Clinical Implications

Our sample size was very small, and every caution must be taken in generalising such a small sample, particularly given the idiographic nature of analysis (Smith & Osborn, 2003). However, it does appear that health professionals have an important role to play in supporting a person with MS to engage with SDM. Firstly, our research shows that patients need a combination of relevant information to both weigh up potential medications and understand what medication 'fits' in context of their life. Therefore taking time to understand a person's context including: what roles or responsibilities they have, what future plans they have, whether they have any friends or family who have an understanding of MS will all influence the decision, and how much support they will need from health professionals to engage in the SDM

process. Ensuring this kind of information is gathered in clinical sessions will help to facilitate SDM.

In our sample, the value in the relationship between MS nurse and patient was apparent, but our findings suggested that fostering trust in professionals can take time. This may be particularly critical for patients who find themselves having to adjust their life plans (as Sara did) or who have previous experience of mental health problems (like Talia). This tentative finding does appear to fit with existing research, which suggest that those in transitionary phases of life and who have a previous history of mental health problems may be more at risk of experiencing excessive emotional distress in ill health and may find participating in SDM more challenging (Kim & Moen, 2002; Holt-lunstad & Uchino, 2015; Joseph-Williams et al., 2014). Therefore, ensuring MS nurses and medical professionals are adequately trained in empowering people to participate in SDM would be of great value. Health professionals can do this in part by ensuring relevant mental health history is also sought as part of assessment and asking about any notable transitions. Equally, acknowledgment of the importance of the relationship between MS nurse and MS patient is crucial; whilst pragmatically it may help to have multiple contacts to liaise with, patients appeared to appreciate building a relationship with one particular staff member. Therefore, if significant appointments could consistently be offered by a named nurse this may empower patients further to engage in shared decision making. Alternatively, a clinical psychologist working within the MS clinic could offer both a reflective space for people with MS to consider the multi-faceted decision and supervision to MS nurses to formulate patients who are finding the SDM process challenging. This could help to ensure ‘hard to reach’ patients with MS do not miss

out on appropriate support and would fit with the ‘multidisciplinary MS care unit’ described by Soelberg-Sorenson et al. (2019).

It may be that the provision of low-level psychological support to patients may be a useful resource as it may prevent avoidable longer-term anxiety and depression. This research suggests that it would be particularly helpful to facilitate discussions about how a person can assert independence and the important roles they have. Furthermore, the support could help to facilitate a person with MS developing a meaningful relationship with their MS nurse or seeking out a knowledgeable friend or relative (Methley, Campbell, Cheraghi-Sohi & Chew-Graham, 2016; Kidd et al., 2017; Kellett, Webb, Wilkinson, Bliss, Ayers & Hardy, 2016). This could take place outside of the MS clinic setting, and, given the value participants placed on people who had a working knowledge of MS, may be a valuable role for expert patients or mentors. There is a paucity of research investigating this kind of provision though certainly rates of these mental health problems are higher in MS populations than the general public (Boeschoten et al., 2017).

In our research there was a divide between participants who found the information booklet providing statistical information on DMTs helpful and those who did not, and in fact conversely found the information provided was a source of anxiety. It may be helpful for health professionals to acknowledge that this difference exists when offering their patients this type of decision-making aid. People with MS could also be made aware of alternative sources of information to aid SDM. For example, ensuring people with MS can contact their MS nurses or accessing an expert patient may again help to minimise anxiety in those people with MS who are finding the reported statistical information overwhelming.

Future Research

Given the similarities which have emerged between this study and the two existing IPA studies (Lowden et al. 2014; van Capelle et al. 2017), it would be helpful to conceptualise the experiences of individuals with MS further, potentially using Grounded Theory, which employs larger scale qualitative studies with bigger sample sizes to generate “a theoretical-level account of a particular phenomenon” (Smith et al., 2009 p. 201). Alternatively, a meta-synthesis could be conducted on the existing studies to analyses convergence and divergence in identified themes. It would be of further interest to understand the multiple perspectives involved in the decision-making process: medical professionals, nurses, patients’ significant others. This would help to further understand the shared decision-making process in MS and to help its successful application in an MS setting.

Conclusion

The research provides a contribution towards understanding the experience of people with MS making a decision about medication. It is hoped that the findings, recommendations for future research, and clinical implications make a meaningful contribution, not only to the literature but also towards improving the experience of individuals with MS.

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Chapter 3
Public Briefing Document

Psychological Aspects of Multiple Sclerosis: Reviewing the prevalence of depression and suicidal ideation and understanding the experience of shared medical decision-making

Public Briefing Document

Psychological Aspects of Multiple Sclerosis: Reviewing the prevalence of depression and suicidal ideation and understanding the experience of shared medical decision-making.

This document provides an overview of the thesis submitted in partial fulfilment of the requirements for the degree of Doctorate of Clinical Psychology (Clin.Psy.D.) at the University of Birmingham. This paper presents a summary of a literature review and meta-analysis investigating the prevalence of depression and suicidal ideation in people with Multiple Sclerosis, and a research paper exploring the experiences of shared medical decision-making in people with Multiple Sclerosis.

Overall context

Psychological distress, including depression and thoughts of suicidal, is generally thought to be higher in people with Multiple Sclerosis (MS) compared to the general population. Several studies have shown that people with MS who are also depressed experience poorer quality of life, do not stick to their treatment regimens well, experience poorer cognitive function, and are more likely to engage in negative health behaviours such as smoking and drinking alcohol excessively. However, it is unclear from current research how common both depression and thoughts of suicide are in people MS as the evidence varies greatly. No comprehensive review has attempted to estimate how common thoughts of suicide are in people with MS. One paper, published in 2017 looked at how common depression is in people with MS and reviewed studies published up to 2014. It found increased levels of depression compared to the general population but noted several challenges in accurately estimating how common depression is in people with MS.

The treatment of MS presents a complex choice for patients with many partially effective treatment options available. The choice not to take medication is thought to be linked to the irregular nature of MS symptoms, the side effects and a perceived lack of medication effectiveness . It is increasingly recognised that medical decision making should be facilitated by a process known as Shared Decision Making between the patient and medical professionals.

Literature Review and meta-analysis

Introduction

This review, conducted as a “meta-analysis”, where data from multiple reviews is examined, aimed to address the gap in knowledge around how common thoughts of suicide are in people with Multiple Sclerosis (MS). The review updated the findings of an existing meta-analysis which investigated how common depression is in people with this condition.

Method

Systematic searches of three electronic databases were conducted to identify all the relevant studies investigating how common depression and thoughts of suicide are in people with Multiple Sclerosis. A statistical procedure known as meta-analysis was carried out, which combined the data from seventy-four studies estimating how common depression is in people with MS and seven studies estimating how common thoughts of suicide are.

Findings

The results of the meta-analysis estimated the rate of depression in people with MS as 32.1%. However, it is difficult to truly estimate how common depression is for several reasons including because the fact that the studies reviewed measured depression in different ways. Also, the quality of the studies varied; studies which were rated as good quality estimated that around 26% of people with MS experience depression. Seven studies estimated that 14% of people with MS experience thoughts of suicide. However, the samples of people with MS in these studies differed in the severity of their MS, their ages and genders all of which are also likely to impact the likelihood of a person experiencing suicidal thoughts.

Conclusions

Results from this review, which look at data from a large number of people with MS, indicate that depression and thoughts of suicide are more common in

people with MS compared to the general population. However, caution should be applied in interpreting these results due to the many differences between the studies in terms of how they were conducted and who their participants were. Future studies in this area should ensure that those included in research reflect the diverse population of people affected by MS and directly survey people with MS when measuring depression and thoughts of suicide.

Research Study

Introduction

When choosing between medications for MS, known as disease modifying therapies (DMTs), people with MS are presented with a complex choice between different options, many of which are only partially effective. Each treatment option has varying side effects which impact upon the patient's quality of life. It is increasingly recognised that medical decision making should be facilitated by a process known as shared decision making between the patient and the medical professionals involved in their care. This involved patients actively engaging in decisions about their treatment, with health professionals providing support and information to ensure patients can make an informed choice. Of all people eligible for DMTs, between 25% and 50% of people choose not to initiate treatment. This is thought to be linked to the irregular nature of MS symptoms, the side effects of the medications and a perceived lack of medication effectiveness. However, little is known about the psychological processes which help patients in their shared decision making. To address this gap, the current study aimed to explore how people with MS make decisions about their treatment, paying particular attention to aspects that may facilitate shared decision making.

Method

Six semi-structured interviews were conducted with people with MS who were in the process of medical decision making. Interview data was analysed using a method known as Interpretative Phenomenological Analysis (IPA), which allows for in-depth exploration of the individuals' unique lived experience, which is organised into themes

Findings

Three over-arching themes emerged from the data, 'Facing MS', 'Assimilating a New Identity' and 'Imagining a future'. Overall, it appears that the people interviewed considered relatively objective factors such as side effects and the practicalities of administering medication when making their decisions., They appeared to do this by considering the costs and benefits of what would 'fit' in with

life. Shared decision-making was aided by professionals acknowledging this process.

Conclusion

Shared medical decision-making is a complex and meaning-laden process for people with MS. It involves the person coming to terms with having a long-term health condition, understanding the impact of this on their identity and future plans, and considering carefully the impact of medication decisions on their everyday lifestyle. The study recommends that where possible patients have contact with a named nurse as this is likely to encourage patients to participate in making decisions about their care. In addition, the study suggests that a clinical psychologist working within MS clinics would be beneficial for both patient's wellbeing and in encouraging shared decision making.

Appendices

Empirical Paper

Appendix 1 - Ethics approval letter

Health Research Authority

Ms Joanna Hanks
Trainee Clinical Psychologist
Email: hra.approval@nhs.net

University of Birmingham
School of Psychology
Edgbaston
B15 2TT
31 July 2017

Dear Ms Hanks,

Letter of HRA Approval

Study title:	**Patients' and physicians' experiences of decision-making in Multiple Sclerosis: A multi-perspective IPA design**
IRAS project ID:	**216807**
Protocol number:	**RG_16-156**
REC reference:	**17/SC/0308**
Sponsor	**University of Birmingham**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity

and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.

- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices

The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators"*, issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/.

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **216807**. Please quote this on all correspondence.

Yours sincerely

Alex Thorpe

Senior Assessor

Email: hra.approval@nhs.net

Copy to: *Mr Sean Jennings, Sponsor's Representative*

[redacted]

Appendix A - List of Documents

The final document set assessed and approved by HRA Approval is listed below.

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Advertisement (MS Society)]	1	07 April 2017
Covering letter on headed paper [Cover letter]	1	16 December 2016
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Certificate]		
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Confirmation]		
Interview schedules or topic guides for participants [Interview Schedule]	1	16 December 2016
IRAS Application Form [IRAS_Form_02062017]		02 June 2017
IRAS Application Form XML file [IRAS_Form_02062017]		02 June 2017
IRAS Checklist XML [Checklist_04072017]		04 July 2017
Other [Dr Ruth Howard CV]	1	16 December 2016
Participant consent form [Participant consent form]	3	10 March 2017
Participant consent form [Participant consent form]	3	10 March 2017
Participant information sheet (PIS) [Patients]	5	31 July 2017
Participant information sheet (PIS) [Physicians]	5	31 July 2017
Research protocol or project proposal [Project protocol]	5	03 July 2017
Summary CV for Chief Investigator (CI) [Chief Investigator CV]	1	16 December 2016
Summary CV for student [CI CV]	1	16 December 2016
Summary CV for supervisor (student research) [Supervisor, Chris Jones CV]	1	16 December 2016
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Flow chart of study]	1	06 February 2017

Appendix B - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in

England, please refer to the, *participating NHS organisations*, *capacity and capability* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections in this appendix.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Joanna Hanks

[redacted]

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	The Participant Information Sheet has been updated to meet HRA Assessment Standards. Text has been added to explain the data retention period.
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	[redacted] If more sites are added to this study,

Section	HRA Assessment Criteria	Compliant with Standards	Comments
			then a Statement of Activities and Schedule of Events would be expected.

4.2	Insurance/indemnity arrangements assessed	Yes	Sponsor insurance will cover design, management and conduct while not on NHS premises. Conduct while on NHS premises will be covered by NHS indemnity. The insurance certificate expires on the 31st July 2017 but a letter from the sponsor explains that the policy will be renewed on the 1st August 2017. Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study.
4.3	Financial arrangements assessed	Yes	No funding will be provided.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
Section	**HRA Assessment Criteria**	**Compliant with Standards**	**Comments**

6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

If this study is subsequently extended to other NHS organisation(s) in England, an amendment should be submitted to the HRA, with a Statement of Activities and Schedule of Events for the newly participating NHS organisation(s) in England.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.

This is a single site study sponsored by the site. The R&D office will confirm to the CI when the study can start.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).

A Principal Investigator is appropriate for this study and has been identified at the single participating site.

GCP training is not a generic training expectation, in line with the HRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken
If the investigator meets participants at their homes and medical professionals in their offices, then no HR Good Practice Pack arrangements are required. If the investigator meets participants on NHS premises, then a Letter of Access and appropriate Occupational Health and DBS clearances would be expected.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix 2 – Consent form

UNIVERSITY OF BIRMINGHAM

Title of Project: Patients' and physicians' experiences of decision-making in Multiple Sclerosis: A multi-perspective IPA design

Researcher: Jo Hanks, Dr Chris Jones, Dr Ruth Howard & Dr John Woolmore

Please initial box

1. I confirm that I have understood the information for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time during the research interview, without giving any reason, without my own medical care being affected. ☐

3. I understand that the research interview will be audio-recorded. ☐

4. I understand that following the research interview I will have a two-week period for reflection. The researcher will then contact me at which point I may withdraw my interview entirely or in part, without giving any reason, without my own medical rights being affected. ☐

5. I understand that the data collected during this study will be looked at by the researcher and relevant others at the University of Birmingham to ensure that the analysis is a fair and reasonable representation of the data. Parts of the data may also be made available to the NHS team responsible for my family member's care but only if any previously undisclosed issues of risk to me or my safety should be disclosed. ☐

6. I understand that direct quotes from my interview may be published in any write-up of the data, but that my name or identifying information such as age and gender will not be attributed to any such quotes and that I will not be identifiable by my comments. ☐

7. I agree to take part in the above study. ☐

.....	.....	.....
Name of participant	Date	Signature
.....	.....	.....
Name of researcher	Date	Signature

Appendix 3 – Interview schedule

Can you tell me about what happened when you were offered medication for your MS?

- What was involved?

- Then what happened?

- Who said what?

- How quickly did the decision happen?

- Where did it happen?

Who did you talk to when you were thinking about what to do?

- Who was helpful to talk to?

- What did they say that was helpful/unhelpful?

- If no mention of medical professionals - What did the consultant say? What did you think of what the consultant advised?

Potentially draw out a map of people to understand exactly who is involved

What was the most important thing to consider when making decisions about your treatment?

- Was x more important than y?

- How did you manage the different things to consider?

- Did you do anything to try to help you make the decision?

How did it feel to make that decision?

- What did you find challenging?

- What helped you when you felt that way?

What was the most challenging thing about making the treatment decision?

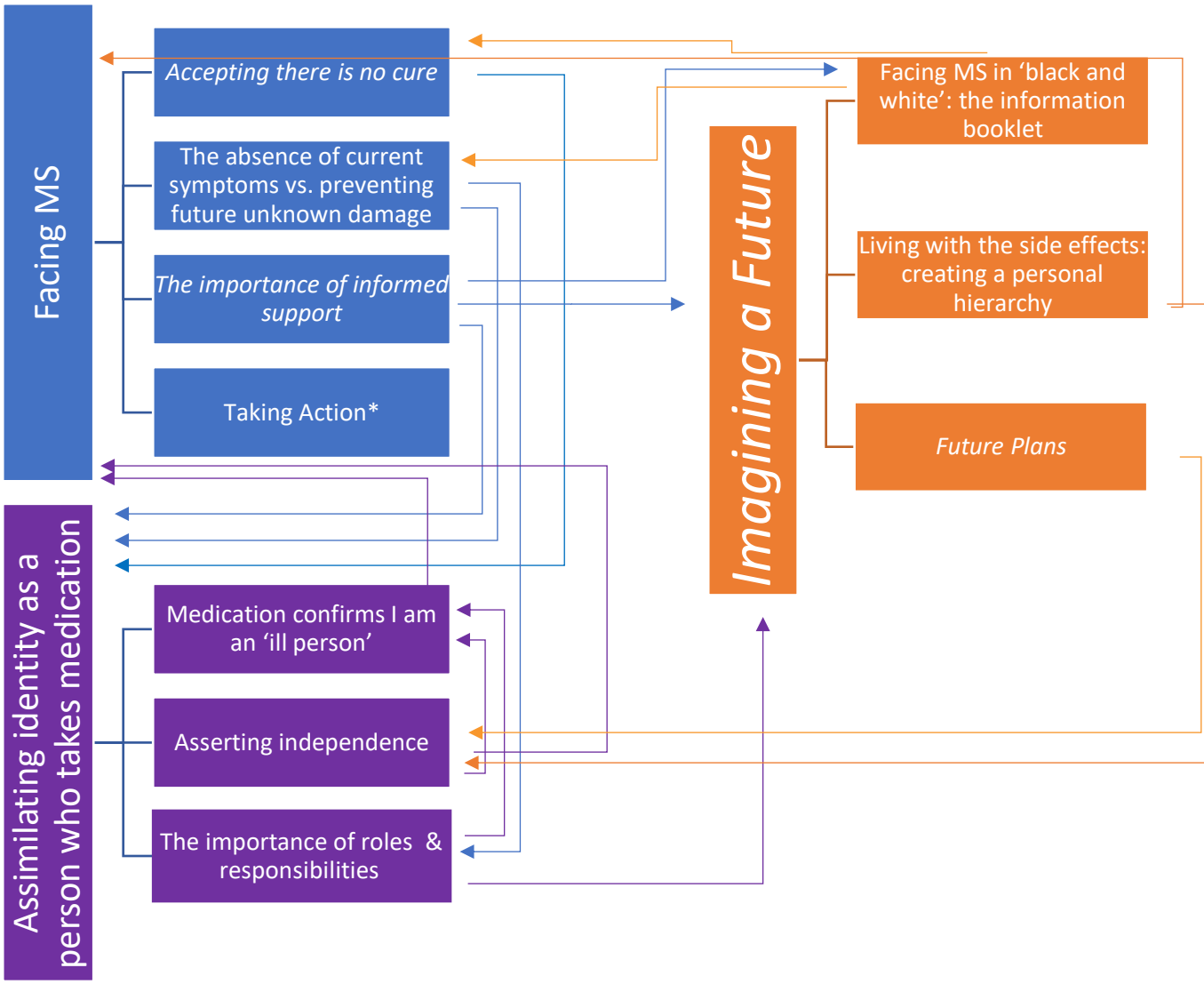
- How did you manage that?

- Who helped to manage that?

If you were advising someone in the same situation you were in what would you say?

-Any things you wish others had done differently?

Appendix 4 - Summary of themes, sub-themes and links between



Appendix 5 - Participant information sheet

Title of Project: Patients' and physicians' experiences of decision-making in Multiple Sclerosis: A multi-perspective IPA design

Researcher Team: Jo Mathews, Dr Chris Jones, Dr Ruth Howard & Dr John Woolmore

Reviewed by: REC South Central – Oxford A

My name is Jo Mathews and I am a trainee clinical psychologist. As part of my training I am conducting a research project and I am inviting you to take part. I would like to know more about how patients with MS and MS physicians make decisions about treating MS.

- **What is the purpose of this research?**

The purpose of the research is to gain a greater understanding of how patients and physicians experience the decision-making process when deciding on treatment options for MS.

- **Why have I been invited to take part?**

You have been invited to take part because you have been diagnosed with Relapse Remitting MS for over two years and you have recently made a decision about your treatment (for example, choosing to take medication, choosing to change medication or choosing to discontinue medication).

- **What will happen to me if I agree to take part?**

If you decide to take part, you will be invited to attend an interview with me which will last approximately 45 minutes. It can take place at a location convenient for you – perhaps at the location of your MS clinic or your home. This interview will be audio recorded. I will ask you about what factors you took into consideration when making decisions about your MS treatment. We are also interested in understanding what helped you to make the decision you made and whether there were any difficulties you faced when making the decision. Direct quotations from your interview may be used when I write up the study for my qualification; I will discuss this with you, and I will ensure that no identifying details are attached to the quote(s). From the time of the interview to checking you are happy with the transcript, the length of participation is approximately 6 weeks. There are no direct risks associated with taking part in the study.

- **What will happen if I do not want to carry on with the study?**

Participation in the study is entirely voluntary and you can withdraw from the study at any point before or during the interview, and up to two weeks after the interview. Your care will not be affected if you do not choose to take part or if you withdraw.

- **What are the benefits of taking part?**

While there are no direct benefits to you by taking part in this study, the findings help doctors working in MS to support patients in making their treatment decisions. The findings will also be an important addition to the literature on shared decision-making in MS.

- **What will happen to the results of the research study?**

The results of the study will be written as part of my thesis for my Doctorate in Clinical Psychology. The results may be published in an academic journal, and will be shared with those who have an interest in this area of healthcare, including researchers, doctors and patients

- **Will my taking part be confidential?**

Yes. Your interview will be audio recorded and transcribed. The recording of the interview and the transcription will be kept confidential and stored in line with the University of Birmingham's data governance policies. The study is sponsored by the University of Birmingham. Should you be required to travel to the interview then your expenses will be reimbursed.

- **What happens if I have any concerns or would like to make a complaint?**

If you have any concerns or wish to make a complaint about the research, then you can contact my research supervisors as follows:

Dr Chris Jones's email: C.A.Jones@bham.ac.uk, Dr Ruth Howard's email: R.A.Howard.20@bham.ac.uk

Alternatively, you can speak to someone from the Patient & Advice Liaison Service (PALS):

Tel : [redacted] Email : [redacted]

In person: PALS office, [redacted]

- **What happens if I have any questions?**

If you would like to discuss any aspect of this research with me, please contact me by email [redacted]

Or if you have more general enquiries about taking part in research and would like to speak with someone unconnected to the research project then you can contact the MS Society on 0808 800 8000 or speak with your MS nurse.

Appendix 6 – THEME 1.4: Taking Action

This theme was not included in the final analysis as it was felt to not be fully aligned to the research aims. It instead appeared to capture all of the newly diagnosed (<1year) participants' experience to gain some control over their diagnosis and 'take action' by making a choice to take medication.

For all the participants except Marie and Alex the decision to take medication was viewed as a way of taking action to manage their MS. For Andi, Rachel, and Talia, who were all taking DMTs for the first time, there was a remarkable similarity in the urgency in their responses:

"…to me, all this is – all I want – yes, I've got MS, you've spoke about it, you've told me what's happened, just give me my medication and let me get on with things…" (Talia, line 90)

"…I thought, 'well, why delay it? Let's just get on with it'…" (Andi, line 374)

"…yeh, I think I'm finding I just want to finish this bit of it and get on to it and start the drugs and get it all started…" (Rachel, line 111)

For these three participants, commencing medication is a way of actively moving on from their MS diagnosis. Sara, who also qualified for DMTs for the first time, also refers to this transition despite remaining ambivalent towards taking medication. In Sara's current experience, the process is of 'getting on' is much more complex:

"…Erm, I'm not explaining this very well, but you know, I suppose the wait, um, and the wondering, is probably more nerve-wracking than getting on and dealing with

what you've got to deal with. Um, which will be when I've finally made the decision and am getting on with taking the treatment, it'll be better than the process of having to come to terms with it and make that decision. You know, I'll find that easier than this bit probably…you know you've made the decision you're going forward with it and that'll be it. That'll be fine. But it's this nebulous time at the moment that I'm, you know, finding it a little bit tricky. [becomes tearful] …" (Sara, line 293)

Sara's emotional discharge highlights the depth of what it means to her to decide whether to take medication. She displays an awareness that she is likely to be less anxious when she has committed to a decision (be it not taking medication or choosing between medications). Yet what it means to deliberate the medication choices outlined in this report: to face MS [theme 1], assimilate an identity with MS [theme 2] and imagine a future with MS [theme 3] are too much so she is forced instead to remain in the "nebulous" place of debating her options. Throughout her interview, Sara's linguistic phraseology mirrors this 'nebulous' state as she questions herself, pauses, and searches for the correct words.

Conversely Rachel's elaboration on her state is clear and concise: "it's always there still at the moment. But I can start the drugs and try and get to my new normal" (Rachel, line 78). There is still a sense of MS lurking, but one senses that Rachel is on the verge of moving from the 'nebulous' place that Sara experiences to the comparative safety of a 'new normal'. It is of interest that this theme only emerged for the participants who were experiencing their first treatable relapse. Taking action did not emerge as a theme for Alex in her current experience, but during her interview Alex reflected on her first time taking DMTs:

"…I needed to do something about this disease, so in 2002-2003, I was very much on a charge to try and do something because there's nothing you can do about this disease in reality. Erm, and I think I was on such a mission…so I just needed to do something so I, kind of, went into it with a bit, er, gung-ho attitude last time…" (Alex, line 16)

It is possible to speculate that for those participants whose diagnosis is relatively new, medication choice offers an opportunity to act, and gain some semblance of control over a situation that feels very out of control. Perhaps the participants who had received their diagnosis several years ago have in fact arrived at their 'new normal' and medical decision-making is in fact part of that normality, as opposed to precluding it.

Appendix 7: Reflective Log excerpt

I conducted interview four an hour after interview three so I'm quite tired after today. Both interviews lasted for over 45 minutes, so it felt like a lot of people's experiences to take on. I think from now it would be best to complete the remaining two interviews on two separate days.

Participant four was very young. Or at least she felt much younger than other participants (in age she is actually only three years younger than P1). It is the first participant who qualified for second line treatment (although she has opted for first line) and it really hit home how disabling MS can be. I felt very, very sad after the interview as I think the speed at which this participant is relapsing and how young she was when she received a diagnosis are risks for a worse prognosis.

At times it was difficult to follow P4's line of thought and I wondered if this was a side effect of the relapse. The interesting thing was P4, despite being the youngest participant, had had her MS diagnosis the longest to date. There was something noticeably different in how she talked about the MS, as if it were part of identity. She was fused with the MS. She was also much more embedded in MS support channels and recorded her own YouTube videos. I thought this was a really positive part of the interview, and on listening back to the recording am clearly wanting to talk more about this to minimise some of my own discomfort at the severity of the participants relapses. There's a whole channel of exploration in the source of support online and the energy notably picks up in both the participant and I as we talk about this.

The participant appeared quite comfortable with me and she seemed quite keen to discuss her thought processes around medication.

Another interesting thing that has not come up so far was around cultural responses to MS. I had not realised that in a strict Hindu community, a participant's MS would be interpreted as recompense for a participant's misdemeanour in a past life. It made me wonder about how this would have impacted her experience of diagnosis and the disconnect between the decisions she makes about her care and her family life. I wonder if this is why YouTube is such a good outlet for the participant as it gives her a chance to voice things that otherwise would not be heard.

The future is definitely something that has now been voiced by all participants and may well be a - superordinate theme.

Appendix 8: Master table of themes

Superordinate Theme: Facing MS

1.1 Accepting there is no cure

Sara (line 205): I suppose, you know, it's this business of it's not a cure, it's just managing the disease and you know that but I suppose you're sort of…[sigh] you want it to be much more don't you,
Sara (line 80): again, they absolutely say to you "it is not a cure", it is just in a sense a manage the condition and keep you, hopefully, as well as you possibly can for as long as they can. Umm, and so, yeh, it's all there, I…I hear it and that, but actually when you hear it spoken and said like that then it, you know, it does register erm to a larger extent really.
Alex (line 144) Absolutely, absolutely. I – I'm very frustrated with the whole 'MS is getting much better at managing relapses and managing symptoms' but what they're not good at is they haven't managed to find anywhere close to the root cause of it and that bugs the hell out of me.
Alex (line 152): Yes. Yes. Yes. I appreciate the body is a very complicated system. But it is just a system. We are a function of our inputs and our outputs. Whether they're from a mother or a father or whatever. Those are all inputs into our system. And, in reality, how I would solve problems at work, engineering problems, and they can be really complicated engineering problems, I'll map it out, I'll have inputs and outputs, and therefore I have noises, and if I can eliminate noises I will then start to find the root cause. And I understand the body is a complicated system, but it is just a system. It's just a system.
Alex (line 160): Oh, I'm completely frustrated. I can't believe that I've challenged doctors, I've challenged, um, psychiatrists, everybody, going "this is just ridiculous". I, I can't – there are some very intelligent people around and there seems to be this complete focus on management of the disease, not trying to find a cure for it. And I've done my research [laughs]. And I find that very frustrating.
Talia (line 18): It's annoying because you've been told about something that can't be cured, and then "we'll give you all the help you want", but when it comes to the help, you don't exist. You don't.
Talia (line 353): Whatever happens with it, yeh, I'm not gonna put my hopes and say "oh it's gonna cure me, oh it's gonna do this" because there is no cure for it, but if I start taking it and it makes my life a bit easier then that's a good thing isn't it.
Andi (line 133): For me, as a non-medical person medication deals with the condition and that's it. But you realise afterwards, the condition is never going to change. Nothing anybody can do can sort out the condition. It's about managing how it is and hopefully pushing back, erm, it progressing any further. So, there was that realisation as well, wasn't there [to P3a] and you realise that actually the medication isn't about curing what's there, because nothing is going to do that. Erm, so it was a more measured approach afterwards.
Andi (line 141): Yeh, I think it did. Initially I was…thought "oh, bloody hell" I mean you know, "the medication doesn't cure me?" and then you realise "Oh

ok, well…"
Marie (line 43): Yeh, the like, there's no guarantee is there, there's no cure. And because there's no cure and you're like…you know, then…Because I've, now that I've, um…
Marie (line 72): But these medications are just going to help me. They're not gonna…they're not gonna resolve the issue. They're just gonna help me.
Marie (line 371): I think it was more upsetting. Yeh, it was more upsetting. Ok, you've got this condition and then you have to go through all this to get better. And then it's not going to cure, and yet you have to go through all of this. I think it was more emotional things and stuff like that.
Marie (line 390): No, I think that's all it. That's, I think, it. And I hope there is a cure one day. That's why it's good to have these things to research about it. Why has it happened? What's behind it? Some people say it's genetic, some people say what is the cause, we just don't know, do we? Knowing the cause would be helpful.

1.2 The absence of current symptoms vs. preventing unknown future damage

Rachel (line 44): yeh, well I came here today either going for the drug I've chosen, or nothing at all. The reason that I've kind of swayed…the reason I've got the doubt is because you can't see anything or experience anything doesn't mean nothing is happening to me.
Rachel (line 51): I think because you can't necessarily see what's going on, doesn't mean nothing is going on
Rachel (line 54): No, well, I mean I haven't had a relapse or any symptoms for about 6 months so it's a bit "why are you going to go for a drug that's got side effects, that's going to make you feel anxious, that…it's going to make you feel hot, why would you do that when I've been feeling ok for six months. I get tiredness and things like that…but why would you do it? It's not until someone explains it, and it's like, well you don't actually know
Rachel (line 62): Yeh, it's still there. Like she said, it's just managing the future I suppose, now really isn't it.
Rachel (line 69): you don't know what's going on to say no. You don't know what's going to happen in the next five years. Just because I'm ok today doesn't mean…next year I might not be, and you don't know.
Rachel (line 73): Yeh, I think that's what I've found hard with the whole diagnosis anyway, it's very uncertain. No one can tell you what you're going to be like in a few years' time. And that's the most difficult bit, not knowing what the future holds.
Andi (line 93): erm…[pause, laughs] well it's just I suppose, if you've got something and there's medication to help then you take it. Really. That's really it. Um, for me the big issue is to, well I've got relapsing remitting MS, to try and avoid or reduce the chance of getting Progressive, and that's what these drugs do so…it's almost like a no brainer.
Andi partner: It's probably the thing that hit home most about what that consultant said. It wasn't about the medication; it was that you should take something because this is going to prevent…later on. The progression of it. So, at the moment he manages really well. There's no, really, his relapses and remissions, there's no…well you wouldn't even know he had it. Just that pins and needles isn't it? So, it's immensely manageable and if he didn't take anything it would be alright. For us there's always that danger that…

Andi: It'll get worse.
Andi partner: So we want to prevent that.
Talia (line 353): If it keeps you out of a wheelchair, and it stops you falling over and brings feeling back to your hands and you don't burn yourself every time you go by a cooker, you don't drop your phone or smash glasses on the floor – if all that happens, or even if 50 percent of it happens then it's a benefit.
Sara (line 15): You know when you're feeling perfectly fit and well…do I really want to? You know why would you turn down, or why would I turn down something that is ultimately, hopefully, going to help, you know, really long term in keeping me well and as fit and able as I possibly can be.
Sara (line 47): well I mean it is, the fact that, as I say, that second scan that showed still ongoing, erm, inflammatory response there, so you know that there is damage still potentially going on [sigh] you know, why would I refuse it if it's going to stop that?
Sara (line 49): making the decision when you feel as well as I do.
Sara (line 57): when you read the side effects you think "oh God, do I…" you know. I feel well.
Sara (line 78): she's got friends who aren't on any medication and who are doing very well and then, unfortunately, two people who are taking drugs, both of whom have had quite severe relapses
Sara: (line 183) Exactly. So, I've been able to, I *have* been able to, sort of, push it to one side and not give it thought. Because, you know, if you were experiencing symptoms or whatever, of course you'd be much more focused on it, wouldn't you. So, in one way that's a good thing, in the other it's allowed me to do this ostrich thing and pretend that it's not actually going on.
Marie (line 33): And I said "no I'm not going to have the treatment". Then I had another relapse, and then I was like, I was really poorly during that relapse and was like "I have to go for this treatment if this is what's going to make me better, because I can't go through this relapse again". It was, erm, severe damage to this eye of mine [points to right eye], I remember that, and I was like "I should go for Lemtrada". But then, because I haven't had a relapse since... As I have gradually been going towards Lemtrada, like I said that infection interfered and gave me a setback again. I still don't know what would be correct for me because it's a lot of confusion of treatments. Erm, there's a lot of symptoms, then there's a lot of risks, and then there's no promises.
Alex (line 4): I've been really well for the last fifteen years, but over the last six to twelve months I've noticed a gradual decline in things, so I've had loads of urine infections, I've fallen over hence my broken arm, and various other things so it just, was, speaking with [MS nurse], my MS nurse, she just said "look, let's just get you back on to disease modifying therapies"
Alex (line 523): minor symptoms for want of a better word…that's my limit.
Alex (line 538): Maybe it might reduce those little ones as well which I hadn't considered to be relapses.

1.3 The importance of informed support

Sara (line 76): a great friend of mine, only in a voluntary capacity, not in any medical sense, is umm… works with the MS Society over in Solihull and so she's…she mixes with a lot of people with MS
Sara (line 83): Umm and my friend would never, ever advise me in any…she's just there giving me the facts with working with all these people. You know, it is your personal decision isn't it? What you do, what your choices are…and everything. So, I'm just…still mulling it over.
Sara (line 127): yeh, so yeh I do have, I do have friends that I do talk to but I'm not looking at, for advice from them, but just you know, talk to someone about it.
Sara (line 266): I mean you can, you read it all through but – yeh, on the emotional level, um, well certainly for me anyway, you know that's much more important and, you know, takes precedent really.
Sara (line 306): Well this particular friend I've got [tearful], I do find talking to her, you know, very useful.
Sara (line 397): the nurses are really helpful but they're in 'work' mode whereas patients, it is very different.
Sara (line 407): when you're thinking about making a decision about which therapy whether or not to have people willing to be there to talk about their experience with it. I don't know, my, I think it would be helpful. Well, certainly I feel it would be helpful.
Alex (line 214): I spoke to [MS nurse] as well, at length, when I was in hospital. She came to talk to me about them. Because when she came up to see me, lovely lady that she is, um [laughs], I've known her for 17 years now so I feel like she's kind of – we're – um, and we kind of went through all of them together anyway. So, the two of us went through them.
Alex (line 513): mainly because I spoke to [MS nurse] about it for about two hours. So that is that one on one time, you know, that was, well it was about two hours. She popped up to see me on her lunch break in hospital, sweetheart. Um, and we just talked through everything and had a chat and just talked about life and just put it all together and I think that gives me the control that I want to be able to explore things. So, yeh
Rachel (line 131): if I'm explaining MS to someone who doesn't know what MS is, I'm using the terms that she's [MS nurse] used in the appointment I've had with her. It's education.
Marie (line 11): I looked into the treatment, did my research, and obviously there was lots of research on it on Facebook, because there's a Facebook group where people actually have the treatment. So there's lots of questions I asked people: whether they regret taking the treatment, or what were their experiences.
Marie (line 164): I went about it because it was advised by my MS nurse [name], because she knows quite a bit about my relapsing and everything and she advised that one. She says "that's fine, you don't have to worry about Lemtrada, it's ok if you think it's not for you" and she thinks another one that could be suitable for me and then read about it is this one that she advised. And I'm like, she knows best about these medications, she's been in it or a while
Marie (line 178): um, I've got an uncle who's a pharmacist. His daughter is a pharmacist. And his sister, her husband is a pharmacist as well. So, we have got

medical people in the family. And discussing options with him is very helpful. Yeh, that's because he's in line with medication and everything. And I'm like his guinea pig as well. So, he finds it very interesting on how one medication to another, then how that works with that, what decisions are made between consultants and what they're doing. He finds it very interesting as well.
Marie (line 195): Because they don't understand it medically. They think it's more spiritually. They think it's happening because you don't, er, you're not, um, practicing or religious…Yeh, they think that becomes part of it, that's the reason for it. If you do practice your religion more than that would be a cure. Like, they see it in a different way, they don't see it scientifically. But then that's not their fault, because they don't have all the information, or they haven't been educated in that way to know about it. So, that can be a challenge to balance them both. Because it's hard to discuss and prove that, how do you explain all this? The complex, how complex it is. And it's a brain. Every individual that suffers from MS is going through something different but then you, but you, sometimes you get told "because you don't pray, it's why it's happening" and "if you pray it will be better" [chuckle] so, that me-, that, it, that can be a bit of a challenge.
Talia (line 237): speak to who? You can't talk to the doctors. The doctors say, "we've got 10 minutes to talk to you and it has to only be about one thing" and if you go in and talk to them, well your times up, that's it, some other time. Um, you're told you're going to have an MS nurse, you haven't got the foggiest who she is until you refer yourself to get one, and then when you get one she meets you and then when she phones you she doesn't know who you are.
Talia (line 245): It's about my MS nurse. I want to be able to talk to her about what is happening with me. I don't want to go, don't want to talk to [partner] and then [partner] goes "oh I don't want to see you no more, go and talk to someone about this". It's pushing me from pillar to post
Talia (line 271): I've been offered no help. So how do I feel? I've got my medication and that's good for me.
Talia (line 196): I mean I'm really lucky, because I've got a man who has medical knowledge and who can speak on the phone. I can't. Um, if it wasn't for [partner] I don't think everything would have gone in order.
Andi (line 114): I think the other thing was the fact that, like you said, after the initial meet with the doctor it was, kind of like, a lot and then we saw the nurse and that was a bit calmer. More focused. Yeh, and also a little bit like she gave us, "Don't worry you don't have to make the decision" and kind of made it more live. That nurse, I think for me the nurse, I've forgotten her name now, she gave the life to it. I think the doctor gave us the science [laughs], she gave us the practical. For us it was the life. What is this life going to look like.
Andi (line 159): The first meeting with the nurse was actually very, very helpful focusing on what you need to do and then today was actually very good.
Andi (line 175): when you actually have someone sitting there with you, telling you practically and then you can, you know, bash ideas off and say "look what about this" that was extremely helpful.
Andi (line 240): my, er, my cousin's husband is a neurologist and, er, I spoke to him about the diagnosis. Because again, the time between "you've got this" and seeing the Consultant is quite different.
Andi (line 317): There's a very good friend of mine who just happens to be our family GP. So, he actually popped round yesterday. So whenever he's around, obviously he referred me initially and all the rest of it, so yeh chatting with him is nice because it's not only, I'm not chatting to a doctor, I'm chatting to an old mate and he's known me. So, he's the only person that I personally have spoken to.

Superordinate Theme: Assimilating a new identity

2.1 Medication confirms I am an ill person

Rachel (line 39) : I think you always want to kind of look nice, look like there's nothing wrong with you
Rachel (line 78): , I was having to paint face on, a happy face. It's always there still at the moment. But I can start the drugs and try and get to my new normal.
Talia (line 87): everything is like, I feel like I'm suffocating inside myself. I'm getting more and more scared now in myself so, before, I could walk on the road and go "yeh, I could jump off a rope swing or whatever", now I'm, I mean, I'm getting trapped in it. To me, all this is – all I want – yes, I've got MS, you've spoke about it, you've told me what's happened, just give me my medication and let me get on with things.
Talia (line 190): I don't know what – how – how I've become scared of little things. I wasn't like this before.
Marie (line 137): Especially in the Asian community, they always look for a fit and well woman rather than, not a woman who's going to last for a few years.
Marie (line 143): I always take it in private
Marie (line 330): I don't like restrictions. I don't like, erm, commitments as such. You feel locked. You don't feel comfortable. And, it's like you have to do something. Yeh, I don't like that. I didn't like the sound of getting blood checks every month. Because I live far from here, I don't live close – it takes me 45 minutes to get here. And then impacting work pattern and whether there's improvements or not, and then the whole monitoring. It's a bit OTT, bit too much.
Sara (line 55): I've never up to date have had to have any sort of drug therapy, for instance the taking of high dosage of steroids. I haven't had any adverse reactions at all in my life
Sara (line 107): if I'm getting on with life and I don't think about it, I-completely because I feel so well, I can completely forget about it.
Sara (line 167): But it is that reluctance to, um, admit that you are ill and that you've got to go on medication for the foreseeable future. I've avoided it for sixty years, you know, here I am confronted with it. And, it, so it's, it's also, um, admitting that your aging, that you're not the fit, um, person you used to be.
Sara (line 182): So, I've been able to, I *have* been able to, sort of, push it to one side and not give it thought. Because, you know, if you were experiencing symptoms or whatever, of course you'd be much more focused on it, wouldn't you. So, in one way that's a good thing, in the other it's allowed me to do this ostrich thing and pretend that it's not actually going on. Um, but I have got to make a decision

Alex (line 85): I appreciate I've got MS, and I know it's not the biggest thing in the world, but it's just the continual taking of drugs. Erm, and I'm not very good at that – taking lots of pills…I don't see my MS as that bad.
Alex (line 188): When I don't take any drugs, I think I'm ok. So, there's a real direct, causal link between me being ok and not taking drugs. So that's something I've got to think about when I go back on this because there will be a mental kind of "are you sure about this?"
Alex (line 312): She's sick and she's not going to be very well. Erm, and she's the lady who's out of control. Whereas [P4] who doesn't go to the hospital is in control.
Alex (line 534): As soon as I get steroids then I know I'm having a relapse. And then I will say to people "I'm having a relapse". I will never say to people "I'm having a relapse" if I've just got shaky vision, or um shaky hands or fatigue. I think that's an ongoing symptom, not a relapse.

2.2 Independence

Talia (line 102): I don't wanna contact my MS nurse, I don't wanna contact the specialist, I don't wanna contact the doctors. I've got my medication. Do what they say. Get on with it.
Alex (line 401): I ended up looking up trials for it which I didn't understand 99% of it, but I thought I might, you never know! [laughs]. But it is that, um, that type of thing, because I'm data driven and I want to make sure I've got all the facts in front of me and then I'll make a decision.
Alex (line 446):] I suppose that I'm very protective over my MS. Um, and it's my MS, it's not anybody else's. It's mine. And I think there's a very, like control, it goes back to control, it's all about me protecting my MS, and everybody else can bog off because it's mine. And it's nobody else's. And in reality, nobody else can help me anyway. So you know it's just like "well, thank you, you can be there for me, that's brilliant, but" um, yeh there's this control thing and it may be that.
Rachel (line 19): I did it all on my own. I told my mum about it on the way here.
Rachel (line 138): and I found it better probably doing the research on my own because I'd already kind of come here with my decision of going for the medication, what I was going for, so it was just a case of weighing it all up.
Marie (line 90: I just talk about my experiences. Like this current experience, I haven't had a recent update of my MS, erm, story on there but I will definitely post this all out. And then I've chosen, I let go…like what I'm doing with yourself, this is what I'm gonna talk about. Why I opted for this, and why I thought this was the correct decision.
Marie (line 213): I think when I'm on my own, I enjoy myself a lot more. I'm a lot more happier. Because sometimes you need that break to just sit down, sometimes you're in pain and you know you wanna relax and whe- you're not tripping someone else. You're doing, you're working, you're moving on your own pace. And you're not being selfish. It's only you, you don't - , you wanna do what you want to do with that energy.
Sara (line 90): I'm someone who doesn't, I really don't, I'm not, er, someone who seeks advice erm, you know, "what would you do?", you know, I'm not. You know, I'm very much someone who makes their own mind up.

Sara (line 308): And, well no, just, sort of being by myself or walking and thinking about it when I'm on my own, that, you know, again, um again, coming to the decision myself, you know, I don't involve other people particularly in the process at all.

2.3 The importance of roles

Rachel (line 9): Yeh, I, erm, I've got a little boy he's just turned two so erm, obviously being sick or feeling rough (pause) it's not something you want when you've got a toddler

Sara (line133): My attitude is I don't want to burden them with the decision-making process. Because ultimately, it will be my decision. But also, the two men in the family are not good at this sort of thing at all. They're not good at, you know, confronting illness

Sara (line 233): in my professional lifetime I was always very pleased when patients took my advice, and did what they were told so why am I reluctant to do that for somebody else. You know, it's a completely different perspective.

Sara (line 353): when you've worked and brought up a family, women do have this business of putting themselves, you know, you're the last one to, or you do things for yourself last don't you, so it's not, it doesn't come easily to, er, sit there and think about it as a decision for yourself. I always try and do other things than focus on that. I've got to. So, yep

Andi (line 74): I'm a [redacted] so I'm usually out at court most working days and I know they said, you know, for example the diarrhoea just leaves loose motions rather than full blown dia-, well, but still, I don't want to be sitting in court waiting for my case to come on and be "oh, I've got to go" whereas Friday night it's always home, you know, family time, take injection and take some medication, you know, erm, ibuprofen or whatever, before going to bed and hopefully that will be it.

Andi (line 347): Well, I mean my father obviously he had diabetes so he was injecting. So, they have seen that in the family. So, when they see me doing that, they'll probably think the same thing, "he's got what Grandad had". But we might tell them, there we go.

Marie (line 233): I used to be a senior, um, staff member at Barclays and HSBC, done my degree, I'm quite professional, I'm quite well educated, um but then I was discriminated for my condition, for my MS and epilepsy.

Marie (line 240): I thought I'm going to drop everything, invest my savings into my business, erm, and then start my business, and it's been three years and it's successful. And I work on my own time pace. That's why I've done my own business, because then I can take my own breaks.

Alex: (line 19): I'm an [redacted], I'm process orientated, I'm an [redacted] so I solve problems – and I can't solve this one.

Alex (line 43): I still go to work, I still can do this, I've been promoted, you know I'm still on that kind of path, er, and erm I just kind of let MS do its own thing underneath.

Alex (line 546): if that means I don't go out for five, six weeks because the only thing I do is go to work, come home, sleep, go to work, come home, sleep, go to work, come home, sleep all weekend to make myself ready for Monday then that's what I do. So work is incredibly important to me.

Alex (line 553): Because then, in reality, I've only got two days that it may affect the next day. Whereas you know if I do it on Saturday, well it effects

Sunday, and it effects Sunday doesn't it. So I would prioritise work over home.

Superordinate Theme: Imagining a future

3.1 Information booklet and its role in decision-making

Sara (line 22): reading the book but perhaps you do need to read the book- booklet they give you first and then - so you've got some knowledge of what they're talking about beforehand
Sara (line 66): Certainly reading the handbook they gave me erm what, last August or September, and reading that handbook…I mean the side effects really register.
Sara (line 243): Again, when it's there in black and white, as I say, some of it is, quite frightening really.
Sara (line 425): That is definitely the difference between being given that literature which you've got to read and you've got to go through that process but then to hearing and them saying "well you know, in all the years I've been dealing with it I've had 10 people who've you know" um, you know, that is the sort of thing you need to hear. You need much more positive spin put on it, than that, those facts in the booklet that you know are a bit um, it is a bit off-putting, you know, it's quite frightening reading really.
Sara (line 432): I'm not criticising, you know, you need to have that information. You need it. You can't make the decision without it. But hearing the nursing team talking about it, and their experience of dealing with all the patients they see, you know that's where you get a much more, sort of positive theme.
Marie (line 32): Then when I got the Lemtrada pack and I read all the risks of the whole treatment…that terrified me. A little.
Marie (line 168): I'll just take that one rather than reading loads and going even more mad. Yeh
Talia (line 145): when you open the book up you've got a list of the drugs there and you've got the side effects and the symptoms, everything on it. And it's even got the ingredients on it. But, er, on the other side you've got the advanced version of the drugs
Rachel (line 101): I'd always, kind of, picked the book, have another flick through, I'd leave it for a couple of weeks and I'd pick it back up again. So, I probably have read through it quite a few times. So, for me to get to that decision, I probably have read it and gone over it quite a few times to decide that's the one that I want.
Rachel (line 117): then for someone to give you all these leaflets and break down what it is you're actually experiencing, I think then you do need that time to kind of gather your thoughts
Andi's partner (line 190): You'd never catch Andi sitting, taking the book, proactively reading through it. Andi would expect that I'd done that, and that I would then distil whatever the bits are to her.
Andi (line 207): I think so, I think you only get a general overview from these, the booklets. They don't really – what we wanted was that whole do you fi…the amount of people that are…do you, you know, because we asked those questions about "how many people would have, er, these side effects? Are

we talking about lots? Is it the main?"
Andi (line 216): it actually made you realise actually that these [details in booklet] are the little issues, and more practical basically on *how* they take it.
Alex (line 281): Um the table is the answer. [redacted] you're now basically bringing it into my world [laughs]. It's a table. It's data. It's almost like putting a graph and data in front of me and that brings it right into my world. And then I start questioning it with my [redacted]'s head on, not a [P4] head on. Um, and, um, the presentation of it is a little bit patronising, but that's ok [laughs]. But for me, anyway.
Alex (line 287): Yeh, I think, I think, um, I'm not quite sure how you do it but just the diagram of the injection, it's just a bit ridiculous. I'd actually prefer it to be more like it actually is, rather than a kind of, um, comical kind of, er, image. Um, I think also, um, this table, um, it doesn't have enough information on it.
Alex (line 357): Erm, terrified is too strong. But it's definitely towards that end. Um, incredibly nervous that I'd make the wrong decision. I've never made this decision in my life, I've got no experience of it, I've got no rationale that I'm any good at it because I've never done it before. There's no- I've got no basis to decide whether this was the right thing to do or not. Um, and it's, it just, that's why it's so strange. You kind of put doctors and nurses on a pedestal, because they're the people who know what drugs it is, and you give them that responsibility. Because you do that from when you're very young. Don't have any, what to say, conscious choice about it. But now all of a sudden, forty years later, now I'm being told "which drug would you like?". And it's just – I haven't got a clue.

3.2 A personal hierarchy of side effects

Rachel (line 5): Erm, so I'd kind of been narrowing down the side effects really.
Rachel (line 10): so it was more of the ones where I was avoiding flu symptoms and things like that and then it was also with the tablets, it was remembering to take tablets and to be taking them with food and things like that, you're just running round all the time so…(pause)
Rachel (line 29): It sounds quite vain but the hair loss wasn't something I wanted to experience at all because if I think you're already going through quite a lot with your emotions anyway…To have something like that, it's a lot…it's going to upset you a lot more isn't it
Rachel (line 150): No, I think it was kind of the side effects. I knew I was going for an injection.
Talia (line 86): It was something I said from the start. When I see my specialist in November, I said to him, erm, "I can't- ", it's not that I've got a fear of needles,
Talia (line 128): what are the side effects? Going to the toilet? I've got irritable bowel syndrome so, [laughs] that's a relief for me! And hot flushes, whatever, I can deal it. Because I've been dealing with it for the past two and half years. It doesn't make a difference to me.
Talia (line 137): It was the injections. Because they're the ones that, um, give you suicidal thoughts and stuff and because of how I am already [laughs] I don't need that.
Talia (line 167): maybe I could do that but when you read up about the side effects that somewhere I'm not willing to go.
Talia (line 230): They will be in little boxes, won't they. Morning, evening. Take. With an alarm on them.

Andi (line 33): So initially, when we came here today, we were thinking of the oral medication particularly because it's much easier, and I thought with the side effects I might be able to live with those ones more than the injection. But then after the chat today, we, I thought perhaps going for the injection was probably better. Simply because the, erm, I think the side effects are probably going to be a bit more manageable but also, erm, the way they work and how they deal with the relapses and things I think is better with the medi-with the, erm, injections.
Andi (line 43): I mean, the side effects of the oral medication was, you know, more gastro, you know, nauseous, bit of, you know, diarrhoea. Um it did say hair loss as well [laughs] but I thought "oh, trendy thing to have a bald head as a bloke now so that's fine". But no, it was like "ok fine". Whereas the other ones were like flu like symptoms, and I thought I didn't like the idea of suffering like that.
Andi (line 60): when they actually explained "this is what it actually is, it's easily managed by, you know, paracetamol" I thought "actually yeh, that's ok"
Andi (line 65): Bit too much. No, no not too much…as in…we'd require far more, or I'd require far more to perhaps try and manage those side effects, whereas with the injection, erm, the one we've chosen is the one we take once a week, so take it Friday night, which is what they suggested, and hopefully sleep it off. You know, bit of ibuprofen or paracetamol before going to bed and then hopefully by Saturday morning OK. But even if it is, it's, if it stays it just stays for that day and then actually I'm fine.
Andi (line 200): to be honest with you, for me it was when I realised that all the medications do roughly the same thing, so the only real issue is what fits into lifestyle and I'd always discounted injections straight away so it was just that, it looks, it's all about the, erm, side effects. And that was really it. And then when I saw the two sets of side effects again, I thought "yeh, bit of stomach upset, it's not going to be a problem". But, that's why I thought, you know, that's - For me that was what was important.
Andi (line 419): You have to…my view is always "look, they have to, medical staff have to tell us the diagnosis, the er side effects, no matter how rare they are. They have to tell us". Ok, that's fine. I accept that. I suppose it's me being ever the optimist "oh it's oh you know it's very rare so let's not worry about it".
Marie (line 48): Side effects can be permanent, and then you have to take medication to cure those side effects.
Marie (line 112): Erm, erm the reason that erm it's got less side effects, so the side effects are extremely low. And it's not a medication I have to take orally, because I'm quite tired of taking oral medications. Because my mouth is now, like, it's got a particular taste in it and I can't taste flavours anymore. It affects how I taste flavours and…even my speech and everything.
Marie (line 152): I think mood swings is probably the most, erm, thing I think I, er, do deal with quite a lot which is quite challenging because not everybody knows that you're having a mood swing or that's a side effect.
Marie (line 363): I think fatal side effects. It was more fatal, and not the guarantee of getting better. I think there were loads of side effects that I didn't even understand.
Sara (line 67): I mean the side effects really register.
Sara (line 360): "why wouldn't you?" and actually maybe I've been to focused on the negatives, you know the side effects, than the potential good that the drugs can do. You know that sort of just fly-away comment there, but it brings you up short and maybe I've focused too much on the negatives rather than the positives

Alex (line 58): skin site reactions. And they were horrific. And I've still got the scars on my legs from it, I can still feel it now, from 2002. Like these really hard lumpy bits. Um, now, theory goes I'd had no other side effects though. No hotness, no nothing. Nothing at all. Apart from these skin site reactions, which actually led last time to me running out of room [to inject]. And I'm nearly six-foot-tall so that's [laughs]. I'm literally just like "I've ran out of room, I can't, I can't go back to those sites". Because the sites, the sites before I reckon were three inches in diameter for each skin site reaction so you very quickly, I could only do two in one leg. And at that point, if you've got your seven in a week, you very quickly run out of room. And they would last for up to ten days, they wouldn't reduce at all. Um so now that it's three times a week, the theory is, in my head, that hopefully that will be better.
Alex (line 76): the flu-like symptoms were horrific. Um, and I ended up having a really dodgy injection where I obviously did something and, um, I just passed out. And I woke up kind of naked in my bed with a needle hanging out of my leg, which completely fried with my brain. Um, so that's gone [laughs]. That was definitely off. Um, the one, Rebif, was interesting, um, to me but again it's the flu-like symptoms. And they were just so horrible last time. I don't – I don't think I really want to have, or be, have so much paracetamol and ibuprofen.
Alex (line 91): So for example, brain infection, even if it's five people in the world, that's too much of a risk for me.
Alex (line 220): who knows why, um, but no, it's the flu-like symptoms that I can't do with Rebif.
Alex (line 270): So, it's just so strange, like, looking at a table going "which one shall I choose?" because in reality, what the hospital or the government or whoever is behind it is saying is "which side effect do you want?". I think. Anyway, that's how I see it. I say "right, which side effect would I like?" [laughs]. None of them are great, um, but that's how I see it. Um, because I don't see any difference really between injecting and taking a pill. Obviously, it's easier to take a pill but I didn't mind the actual effect of injection last time. I didn't get kind of emotional about it or anything like that. And now it's so much easier, it's just going to be a walk in the park hopefully. Um, but yeh, it's like "which side effect would you like?" [laughs] so, um, it's very strange, it's just a very strange feeling.
Alex (line 370): Er, because of the side effects I could absolutely point out the ones which are the worst. But it's that how do I know which one is the best for me?
Alex (line 373): So I ruled everything out, um, from the pills so Aubagio to Lemtrada – all sorts of different reasons – and then I ruled out Avonex because it's IM [intramuscular], and then so I had a choice of five in the middle. And, in reality, four of them had flu-like symptoms, which definitely leads me to Capaxone. And it was literally that. So, I, yeh, ruled out the worst first and see what happens or not.
Alex (line 593): I don't think that there is a best but there's definitely a worst. I think you can definitely look at those less common but serious side effects and go "well, there's nothing in that box but there's blood clotting disorder and kidney problems in that one, that's definitely worse than that". And definitely brain infection, not a good idea. Because that sounds serious.

3.3 Life plans

Rachel (line 83): For me I think it was, the drug I've gone for, if I did want to have another baby it's something I can continue taking. Um, because that was always something that if I came off the drugs to have a baby then you'd experience a relapse so at least you could carry on taking that drug. That's something that was a positive towards it as well.
Rachel (line 91): It's kind of like when I'm reading the booklet, it's not recommended with pregnancy so it's a bit like that choice is taken away from you because you're either looking after your health or you're deciding to have another child so it's a bit like the option is taken away. It felt like it was taken away from me a little bit. So, seeing that it was a bit like 'oh so I can still do it if I'm going down that path'.
Rachel (line 97): Oh, it was horrible. Not that we're planning any time soon but then it was a bit like…when you're told you can't do something, it makes it a lot worse.
Talia (line 117): he said to me "as long as you don't want any more children, this is the best one for you". And as all my children are grown up I don't, you know, I don't need more kids.
Andi (line 123): very upset about, you know, all the plans when we retire, have those plans all gone out the window? Hopefully they haven't.
Marie (line 124): Even with these treatments, they're not suitable for women having babies. But I don't have any intention of having babies. We [mother and P5] were just talking about it, and I could adopt one so it's not an issue.
Marie (line 128): don't think I'll find an individual who can keep up with all of this [laughs]. But it's why I keep myself busy. It concerns mum a lot. She always says, "yes you will, yes you will", she's looking forward to my wedding, but I'm like "mum, let's just forget about that". Yeh. I don't want to put anybody else through this misery [laughs].
Marie (line 218): I would love to travel on my own, have a chance to travel Europe on my own, explore Europe on my own, make new friends on my own. Because I'm a people person, I would speak to anyone so…I would like to do it on my own. That is something that I want, it is something, it's a big ambition I have, a big dream. Before time is up, before I end up in a wheelchair, I want to do it.
Sara (line 173): I mean, I retired. Um, I was a [redacted] and I had my own business, um, and decided that, you know, I'd been doing that for over 40 years and enough was enough, I was stopping and whilst I'm fit and well do things for me and my family [tearful] whilst I can. It's the thought of not being able to do those things that's…
[redacted] (line 105): The fridge is a big one. I do sailing on yachts, and the problem is, is the fridge is a thing you tend not to have. Um, but we'll sort it out [laughs]. There's ways and means of sorting it out. I: did you have conversations around that though, in how you might sort that out? Alex: Yeh exactly. I had a chat with my MS nurse before I came to this session, um, and I'm not going to go sailing round the world for at least another five years. So, you know what, it doesn't really matter.
[redacted] (line 247): We can do our dream of going sailing, then Capaxone I think may fit in a bit more. It's just the fridge I've got to sort out, and there's lots of things I can do for it.

[redacted] (line 258): if I'm wearing a bikini on a boat and I've got red things all over my legs then I'm just going to have to brave it out. I'm just going to have to go "you know what, if they're there, they're there". We'll see how successful I am on that.