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Faith, Hope and Fallacy

An Idiographic Exploration of the Experiences of People with Multiple Sclerosis Participating in Research Trials.

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Glossary

Sub-types of Multiple Sclerosis

The following explanations are included to assist the reader in understanding the three main sub-types of multiple sclerosis (MS) (Dobson & Giovannoni, 2019) which are referred to throughout this thesis.

Relapsing Remitting MS - RRMS is the most common form of MS. Approximately 85% of pwMS are initially diagnosed with RRMS. It is associated with relapses or flare-ups of neurological symptoms, followed by periods of recovery or remission.

Primary Progressive MS – PPMS is typically associated with gradual accumulation of progressive disability from the start. This primary progressive onset is diagnosed in 5 -15% of people with MS.

Secondary Progressive MS - SPMS typically develops 10 -15 years after RRMS onset, with a gradual evolution from episodic relapse to gradual progressive disease. SPMS is therefore characterised by a reduction in relapses with progressive worsening of symptoms (accumulation of disability) over time, with no obvious signs of remission.

Other Relevant Terms or Commonly Used Abbreviations

MS – multiple sclerosis

PwMS – person or people with multiple sclerosis

MRI – magnetic resonance imaging

DMT – disease modifying treatment or therapy

IPA – Interpretative Phenomenological Analysis

PPMS, RRMS, SPMS – the main subtypes of multiple sclerosis as described above.

GT – Grounded theory

TA – Thematic analysis

Abstract

Faith, Hope and Fallacy

An Idiographic Exploration of the Experiences of People with Multiple Sclerosis Participating in Research Trials

Multiple sclerosis (MS) is a heterogeneous degenerative disease of the central nervous system. It is usually diagnosed in people between 20 and 40 years of age. MS is the most common cause of non-traumatic disability in the young adult population and affects two to three times as many women than men. It is estimated that there are over 110 000 people living with MS in the United Kingdom. Currently MS has no cure although available disease modifying treatment (DMT) options have increased significantly over recent years. In order for these treatments to have gained authorisation for use, many clinical trials have been undertaken involving people with MS (pwMS). However, little is understood about the experience of participating in MS research. Moreover, evaluation of experience of taking part in research has been largely conducted using impersonal survey approaches to assess study conduct satisfaction or barriers to recruitment. Whilst there is extensive published literature cataloguing the nomothetic outcomes of completed MS DMT trials, the experiences of people with MS taking part in MS research has not previously been the specific focus of research.

In this thesis, interpretative phenomenological analysis (IPA) has been employed to understand the experiential *meaning* that exists for pwMS in taking part in MS research. Six semi-structured interviews have been conducted involving four participants who were recruited to long-term trials of pharmacotherapeutic interventions. Two participants were interviewed twice, one of whom had taken part in a study that was terminated prematurely. Interpretative phenomenological analysis of participant accounts revealed three key themes which comprised: benefits and harm of trial participation (physical and psychological), human connectedness within the trial setting, and aspects of self in connection with trial participation. The findings of this thesis indicate that self-efficacy (or activation), control, hope, altruism trust, power, therapeutic misunderstanding, enhanced care and shared decision making are important for pwMS taking part in research. Findings will be helpful to research clinicians to better understand research participation from the participant frame of reference and to improve communication, participant understanding and experience going forward.

Chapter I

Introduction and Reflexive Incursion

'The particular eternally underlies the general, the general eternally has to comply with the particular'

Goethe (Hermans, 1988)

Brief overview

This thesis is based on an interpretative phenomenological analysis (IPA) of the experiences of people living with multiple sclerosis (MS) who are taking part in MS research. MS is a relatively common life-long incurable neurodegenerative condition with cumulative physical and cognitive decline. Each participant who takes part in an MS treatment (drug) trial contributes efficacy and safety data collected *from* them which collectively constitutes the overall research dataset. In this study I am turning the periscope to explore how the trial plays its part in the life of the participant. The study's aim is to uncover what meaning MS trial participation has for people with MS taking part in research, on an individual basis; to hear the voices of people with MS who enter MS research studies.

In introducing this thesis, I will firstly present myself as the analytical instrument within the interpretative process, in terms of my own background and experiential influence on my epistemological stance. A brief overview of MS, the extent of MS research and the existent limitations of the understanding of research participation *per se* will expound the rationale for the research, and the unique contribution that this thesis will contribute to current understanding of research participation. A short synopsis of IPA and its applicability to this research study followed by the value of a coproductive collaboration in research is included. Finally, a brief overview of ensuing chapters completes my introduction to this thesis.

Reflexive Stance

I commenced this thesis with a feeling of disquiet, the very use of the word 'I' quickened my pulse such is the indoctrination of traditional scientific teaching. I have journeyed from a discipline where the very premise of the first-person pronoun is not deemed acceptable in academic writing. Yet here this entire work is focussed on individuals -the participant, the experiential-expert coproducer, the researcher, the reader. I should not be surprised that I feel challenged on many levels as a traditional scientist embarking on a wholly unfamiliar journey in qualitative landscapes. Reflexivity itself challenges the traditional principles of science with its emphasis on professional distance and objectivity versus subjectivity and engagement inherent in qualitative work (Davis, 2020; Freshwater, 2005). I also confess that when I first started on this path, I would have struggled to explain the difference between reflexology and reflexivity! Reflexivity is now a concept that I have embraced and found resonance with (less so reflexology as I do not like my feet to be touched).

It has been a personal revelation that ***no*** research is free from the assumptions, biases, or the individual character of the researcher (Berger, 2015) who is an integral component of the research process and findings (Horsburgh, 2003). The essence of self is inherently entwined in all stages of qualitative research, from design, through implementation, data capture and interpretation. It seems obvious to me now that findings cannot and do not emerge spontaneously from data but are sculpted by the choices the researcher makes in enacting the research (Davis, 2020). Reflexivity is the is the *'active acknowledgement by the researcher that [their] own actions and decisions will inevitably impact upon the meaning and context of the experience under investigation'* (Horsburgh, 2003) and provides epistemological context for the research (Davis, 2020). Reflexive awareness requires researchers to be cognizant of assumptions about ontology (what there is to know) and epistemology (how one can come to know).

Here I present my reflexive stance by critically and transparently reflecting on how 'I' am entrenched in the choice of methodology, the research process itself, subsequent findings and interpretation. Given my positivist background I reconcile this essential aspect of qualitative research by recognising that one would expect to have access to, or at least a rudimentary understanding of the inner workings of any instrument of analysis employed in any research arena. If we equate researcher presence as bias then, as Freshwater (2016)

asserts, the bias of any researcher can never be fully known. Only what we are consciously aware of may be expressed which can only every be an incomplete depiction. Acknowledging these limitations, my hope is that here I may shed some light on the lenses through which I perceive the world and by which I construct this thesis.

Come, walk with me

(Brontë, 1996)

What of my contextual self is of relevance for you, the reader, to understand is for you decide as I commit my innermost workings to sit upon a virtual shelf for anyone to judge – am I representing just the aspects I wish the reader to access, or my darkest thoughts like an antithesis of Facebook?

I find myself, perhaps inevitably or at least understandably, comparing my own health(-care) experience to those whom I have interviewed. In the same way that humans are sense making creatures (Smith et al., 2009), people naturally look for common ground and make comparisons between their own circumstances and those of others (Frith & Frith, 2007). At times I am consciously, and unconsciously, employing my own experiences as a frame of reference. With this in mind, please allow me to take you back to the Summer of 2001; I was 31 years old with a new baby and a dying father when I felt the ground beneath my feet further shift and contort. Horizons are funny things - they are constantly shifting, changeably lit and always out of reach. On a shadowy wet day that I remember only too well I saw my horizons darken. And the cause of this angst? It does not sound so remarkable when committed to paper, but at the time I was felled by the hard cold dread of life-changing illness. My foot drooped, I could not raise it. I absolutely **knew** with complete certainty that I had MS. I was terrified. I was beside myself. I bargained (quite with whom, I do not know) and lashed out like an injured animal. Did I go and seek medical help? – held back by fear, I did not. Did I share my fears with family or friends? – I did not. I remained in a state of angry paralysed dread until my foot mobility returned to its normal status. If it happened again, I reasoned, *then* I would seek help – for now there was nothing to see. For months, probably years, I felt dry mouthed fear at every potential symptom in case *it* returned (spoiler alert – it didn't). I found resonance of that fear, of that anger, of that

premise of 'it' and the shifting horizons in the accounts of the participants as will be recounted in the findings section.

However, my most seismic shift in horizons was during the hinterland of knowing, post-surgical excision, that I had confirmed thyroid cancer but not yet knowing what type of thyroid cancer had been lurking in my body, insidious and pervasive. Not knowing whether I would 'lose my battle' within months, whether I would live under the shadow of recurrent cancer for the rest of my days or whether I could potentially be cured. Those were days of brave faces and dark thoughts. Facing such uncertainty crystallised what was of value to me. As before, I reasoned and I bargained, and I feared. I *needed* to believe that I would survive, in whatever state, at whatever cost in order to usher my children into adulthood – I felt that my 'self' became largely irrelevant.

Here I am five years later. Every day, every twinge, every swallow I evaluate my body for unbidden cellular intrusion. The bone pain in my foot – is that a metastatic lesion? or a new primary cancer resultant of my, ironically, carcinogenic cancer treatment? That swelling in my gum, that grinding in my swallow, that twitch in my muscle, the increased fatigue, each of these bodily insults I evaluate. The quote from one of the qualitative evaluations of a woman's MS experience resonates – the author conducted a phenomenological analysis of the experience of a woman who has been recently diagnosed with MS. Poignantly, the woman each morning when she wakes checks her body to assess if it is still functioning (Finlay, 2003). The not-knowing on a daily basis of how and when my body will let me down is a burden that I feel that I share with those with MS, and other long-term conditions. Fatigue is often heralded as one of the most common, impactful and pervasive consequences of MS (Tur, 2016). Having no thyroid, my enervation is the unseen but direct consequences of my missing gland. I have adjusted; I work from home so that I may take breaks to sleep in the day, I work extended hours to compensate for my slowed sludge-filled brain. My notes are voluminous to retain the thoughts, words and concepts that my brain will not. Unlike the unstable quagmire of MS, my horizon has shifted but is stable, for now. And I am lucky, I have choices, and options and solutions and I am here. When, later, participants talk of not being understood, their plight unseen, I feel solidarity and empathy to their predicament. I do not and I cannot begin to understand what it is actually like to have MS, to face a future with MS. Regardless, even if I could understand, what it is like for

one will be different for every other. I can only snatch glimpses, or draw some small parallels that help me to, as far as possible, put myself in the shoes of the study participants. A coproductive approach with people with MS who have taken part in research brings further understanding of the study phenomena in question (MS research participation) to the study design, implementation, and interpretation.

'Compassion is not a relationship between the healer and the wounded. It's a relationship between equals. Only when we know our own darkness well can we be present with the darkness of others. Compassion becomes real when we recognise our shared humanity.'

(Chödrön, 2007)

At different points within this thesis, it may be that my demographic details and cultural background are relevant to a greater or lesser degree; to what extent may vary with each scenario. I am a white British middle-aged female, married to a white male of similar age with two grown up children. I am from the Northwest of England and feel strong allegiance for the region. My education and qualifications have focused on the applied natural sciences. After graduating in microbiology, I have been employed in clinical research, regulatory, medical information and medical affairs roles within the NHS and pharmaceutical industry for my entire career. I have been extensively involved in delivering other people's clinical (positivist) research across the decades, and so this study is my first foray into being the actual researcher. These roles and experiences have significantly shaped my prior and hitherto firmly entrenched epistemological stance.

As a traditional scientist my scientific belief system is founded in 'rationality, logic and facts'; hypothesis testing is the accepted core principle of evidence-based medicine citing study after study to represent the scientific 'truth' in medicine (Chalmers, 2013). My experience of the nomothetic approach concerns clinical trials with quantitative endpoints assessing the effects of different pharmacotherapeutic interventions on different outcome measures in different diseases or conditions. The parlance of clinical research within Pharma or an NHS setting includes terms such as accrual (participant recruitment), *taking* informed consent, recruiting to time and target, failing screening, eligibility criteria. These trials result

in averages, median values, TEAEs (treatment emergent adverse events), SAEs (serious adverse events), subgroup analyses, post-hoc analyses and further such measures. This approach reduces the human research experience to little more than 'a confidence interval' or a 'p value'. Kastenbaum (1985) describes the resultant output as the '…*indeterministic statistical zones that construct people who never were and never could be'* (quoted in Datan et al., 1987). By representing the statistical average, the accepted study endpoints, the research output neither signifies nor relates to any single individual. This has comprised the majority of and remains my professional world. However, on embarking upon my doctoral studies and looking at the research world through an entirely unfamiliar set of lenses has ultimately led to my almost epiphanic journey to gratefully embrace the complementary value (Bateson, 2002; Pope & Mays, 1995) of the appropriate application of qualitative methodology.

Much of my tenure in the NHS and within industry has been directly involved with MS, PwMS, MS clinicians or MS disease modifying treatments. In my hospital role I found myself responsible for setting up a research team to deliver neurology research studies, the focus of which was pwMS. Trials had complex and demanding criteria, with gruelling regimes of partially tested treatments with many associated unknowns – but without these studies the treatment options for pwMS cannot advance or improve. In industry I have been responsible for providing medical and clinical support to MS clinicians regarding MS treatments produced by my employing pharmaceutical company. These discussions often involved detailed explanation of clinical trial results and how such aggregate results might apply to the individual patient with MS.

Clinical research is a mandated regulatory requirement of pharmaceutical licensing. It is widely acknowledged that research participation is a positive experience, but it seemed that the participants voice is largely commuted to comment only when requested to do so, and only on aspects of research conduct, and participant satisfaction of facilities etc. Indeed, one of my deep-rooted fears on embarking on this research study was that I would garner similar insight regarding parking convenience and suggestions for the improvements of the facilities or beverages. [Note - Hospital tea does carry what I can only convey as 'essence of shredded vegetables peelings' and so I would concur that such feedback would be entirely

reasonable; the therapeutic value of a good ‘cuppa’ although not necessarily grounded in substantive scientific evidence, would be uncontested by most…]

Within my NHS research role, patient or participant experience consisted of a brief questionnaire completed by eager contributors posted into the slotted lid of a shoe box. The feedback, where positive was received with self-congratulatory complacency incorporated into annual performance reviews. Where research team performance was found lacking it was met with grumbling resentment, improved magazine provision (now banned from a microbiological health and safety perspective), or in the most radical of outcomes, a coffee machine for the research facility waiting room. The intent of this study is to take a deeper dive into research participation from the perspective of pwMS who take part in research; how the individual participant feels, what meaning research participation has for them individually, how they made sense of the research, or whether there is a deeper significance to them. The essence of this is depicted in Diagram 1 (page 8) to help illuminate the rationale behind this thesis.

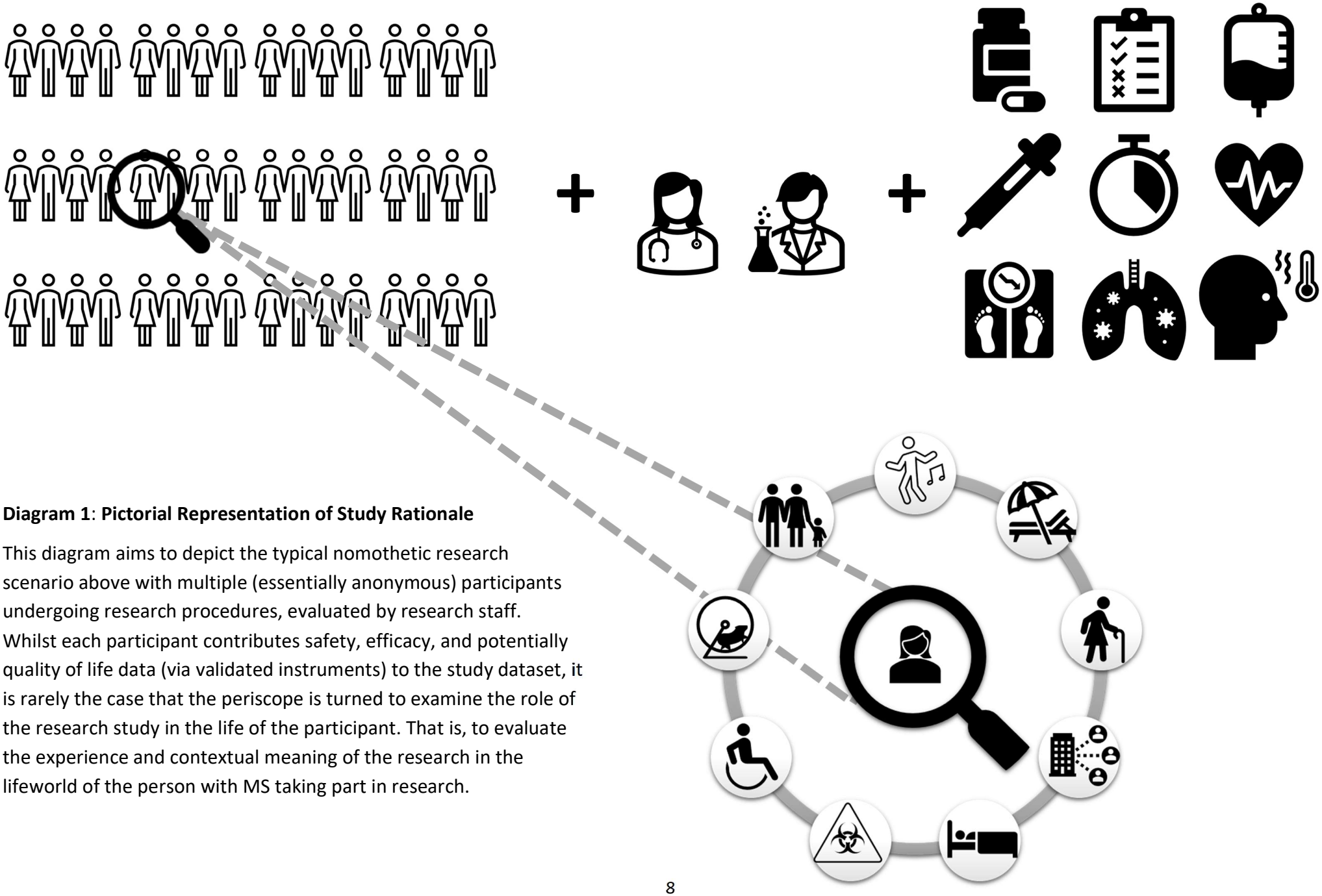


Diagram 1: **Pictorial Representation of Study Rationale**

This diagram aims to depict the typical nomothetic research scenario above with multiple (essentially anonymous) participants undergoing research procedures, evaluated by research staff. Whilst each participant contributes safety, efficacy, and potentially quality of life data (via validated instruments) to the study dataset, it is rarely the case that the periscope is turned to examine the role of the research study in the life of the participant. That is, to evaluate the experience and contextual meaning of the research in the lifeworld of the person with MS taking part in research.

Reflexive Reconciliation

Despite my shifting allegiance, I do not eschew the nomothetic approach but concur with the authors Bryman (2016), Pope & Mays (1995) and Silverman (2002) who each assert the complementary value and validity of both qualitative and quantitative approaches, appropriately aligned with epistemology of the research question. I have reconciled my antithetical epistemological positioning, in that both quantitative and qualitative research methodology, positivist and interpretivist stances simply provide different perspectives of relevance to health and illness in much the same way that an ordnance survey map, a street map, prose, or metrical composition might describe the same geographical space. Idiographic and nomothetic approaches should not be seen as conflicting, but as complementary (Hermans, 1988; Pope & Mays, 1995). As Bateson (2002) asserts, '*extra depth"* in some metaphoric sense is to be expected whenever information for *'two descriptions is differently collected or differently coded'* or in his summary wisdom *'two descriptions are better than one'*. This research brings together the disparate paradigms in a complementary manner whereby a person's lived experience of positivist population level research is examined in personal idiographic terms. This idiosyncratic approach is in alignment with traditional clinical practice in terms of the clinician-service user (doctor-patient) relationship. It is the individual patient who engages with the clinician, not the embodiment of Kastenbaum's constructed [research] persona as described earlier. The doctor-patient relationship is idiographic and often both interpretative and experiential. This resonance between the methodology utilised within this study and the participant relationship with the clinician has been recognised within the literature (Biggerstaff & Thompson, 2008); and discussed in greater depth in the methodology chapter.

Working in professional roles that essentially aim to address unmet patient need, in both the NHS and the pharmaceutical industry, I am constantly reminded of both the diversity and the subjectivity of human experience. The value of randomised controlled clinical trials is, to me, indisputable. The outputs from large-scale clinical trials are an essential facet of regulatory endorsement of medical interventions and new treatments to safely enhance patient care and people's lives; I also see that this is by no means the full picture nor the objective truth. Resultant of these trials, over the last 20 years huge advances have been made in the identification and availability of MS disease modifying treatments (DMTs) which

reduce both physical and cognitive decline in people living with MS. It is these very trials that have brought treatment options to the participants within this study, and which provide the situational context [MS research trials] for participants within this study. Further, it may be considered that insights from an idiographic approach may be regarded as enriching the general principles developed using the nomothetic approach, and feasibly could help to prevent incorrect ontological assumptions in positivist research approaches (Johnson et al., 2004).

We do not know what it *means* to someone diagnosed with MS to take part in research for their condition. And so this study seeks to understand how people with a lifelong neuro-degenerative condition experience the process of research and find meaning in what is anticipated to be a significant decision. IPA centres on experience and meaning making acknowledging the primacy of the participant's subjective experience and context.

Multiple Sclerosis

The participants contributing their experiences to thesis are people living with MS and taking part in an MS research trial. MS is a highly variable lifelong incurable neurodegenerative condition with gradual or sporadic accumulation of increasing physical and cognitive decline. Multiple sclerosis is the most frequent cause of non-traumatic neurological deficit in young adults (Dutta & Trapp, 2011). It is a relatively common neurological autoimmune condition affecting around one in every six hundred people, over 110,000 people in the UK and approximately 2.3 million people worldwide. It is most often diagnosed in the third or fourth decade, and it affects significantly more women than men (Thompson et al., 2018). MS has a highly unpredictable disease course and severity and, in most cases, leads to major physical incapacity, disability, co-morbidities and hugely impactful life changes.

For patients living with this incurable progressive condition the importance of taking a proactive approach in management of their illness has been recognised (Miller & Jezewski, 2006). Until relatively recently disease modifying treatment (DMT) options were extremely limited. More recently available treatments have improved levels of efficacy but in practice treatment often represent a trade-off in terms of balancing beneficial effects, lifestyle, convenience, side effects and treatment risks. Taking part in a study to assess the unknown

qualities of such a drug provides an added level of complexity to the decisional challenges already faced by someone trying to find the optimal way to manage such an impactful disease.

Multiple Sclerosis Research

MS research frequently employs positivist approaches to test pharmacotherapeutic interventions using randomised controlled trials as a key method. Such approaches may be guilty of considering the research participant as a passive resource (Armstrong & Morris, 2010) and do not provide any meaningful insight into the lived experience or meaning of that research for those taking part.

The main clinical trials registry (https://clinicaltrials.gov/) is a global database of medical studies involving human participants across the world, which currently lists over 2500 studies in MS, most of which are clinical trials or interventional studies. Although there is no equivalent central register of non-interventional studies, from the literature review in Chapter II it is evident that there is a wealth of non-interventional quantitative and qualitative research that have explored this condition.

The NHS constitution (Health, 2009) commits that the NHS will use *'research to improve the current and future health and care of the population'*, and critically *'to inform [patients] of research studies in which [they] may be eligible to participate'*. Whilst this is the intent there is a multiplicity and complexity of reasons why clinicians may not offer patients opportunities to participate in trials (Fletcher et al., 2012; Mairs et al., 2012; Nipp et al., 2019). Given the NHS's commitment to research, together with the volume of treatments that have been trialed in large scale international studies across the world, people living with MS are relatively (compared to many other conditions) likely to have been offered participation in a clinical trial. While MS research *per se* is extensive (Calabresi, 2018; Zhang et al., 2019) it is not known what meaning this research participation holds for pwMS.

Participant Experience of Research

From an interrogation of the literature that investigates research participation, it is evident that knowledge base in this area is evolving (Lee et al., 2012, Signorell et al.,2021), but has significant limitations. Studies researching participation often comprise generic and superficial analyses, procedural evaluations of study conduct (CISCRP 2017 www.ciscrp.org),

or motivation for participation; and which in practice rarely go beyond the categorical or descriptive. These provide participant experience from the research conduct perspective and not that of the participant.

Although there are some qualitative studies within the relevant domain, IPA and other interpretative methodologies are seldom utilised to consider the meaning of study participation – a synthesis of these data is included in PART C of the literature review chapter. Overall, neurological conditions are rarely the topic of research participation evaluation, and MS research participation specifically has scant representation within the literature. There is an isolated example which employed qualitative methods to explore participant experience of research which included a trial with people with primary progressive MS (Kerrison et al., 2008). However, Kerrison's work was not specific to MS and lacked the depth and richness of an IPA approach. Examples of qualitative approaches in the understanding of research participation (Harrop et al., 2016; Kerrison et al., 2008; Nelson et al., 2013) and limitations of such work are presented in Chapter II.

Qualitative Enquiry with pwMS

There is a growing corpus of qualitative literature offering meaningful enlightenment of the lived experience of having and living with MS (Boland et al., 2012; Borkoles et al., 2008) but this does not extend to the experience of having MS *and* taking part in research. As far can be determined from extensive examination of the literature there are no studies specifically exploring the contemporaneous lived experience of people with MS taking part in MS research.

Interpretative Phenomenological Analysis

IPA is a critical realist methodology which comprises in-depth and rich interpretation of the accounts shared by individuals pertaining to a particular experience of significance, and which embraces the human quality of sense making (Forrester & Sullivan, 2018; Smith et al., 2009). It is an idiographic approach influenced by the philosophical and theoretical bases of both phenomenology and hermeneutics in its focus on aiming to understand the meaning of human experience and in interpreting the narrative of participants, who in turn are making sense of their own experience (Forrester & Sullivan, 2018; Smith et al., 2009).

IPA produces an account of lived experience in its own terms without existent theoretical preconceptions or frameworks (Brocki & Wearden, 2006; Reid et al., 2005) the interpretation being primarily based on a reading from *within* the transcript rather than importing a '*reading from without*' (Smith et al., 2009).

IPA is a method that enables the researcher to come as close to the participant's experience as possible, and in this case as close to the experience of being a participant in MS research as possible. This work aims to generate an interpretative phenomenological analysis of direct relevance, interest and value to those undertaking research involving pwMS in gaining an understanding and insight from the perspective of the participant and the significance of research participation to them.

Rationale for Employing IPA

Although IPA is recognised as having particular resonance for psychologists (Forrester & Sullivan, 2018; Smith et al., 2009) it is also regarded as an accessible methodology for those without such a background. IPA is chiefly concerned with experience of existential significance to the participant. Having a serious long-term incurable illness is of substantial consequence within the lives of the participants.

There are three key aspects of IPA that are of particular import to me: methodological credibility, epistemological alignment, and epistemological flexibility. In order for the target audience to take interest in and view this work as credible and worthy, they will need to have a degree of confidence in the methodology. IPA is an established and accepted methodology with increasing traction in the healthcare arena (Peat 2019; Biggerstaff & Thompson, 2008) which should facilitate the findings of this research being both accessible and acceptable to MS clinician-researchers and others involved in designing or implementing MS research. Clearly it is crucial that the choice of methodology is appropriate to do the job that it is employed it to do, and that it is epistemologically aligned. Whilst other methodologies, such as reflexive thematic analysis, could pass muster, IPA is for the many reasons further detailed in the methodology section is especially well suited for the aims of this particular study. IPA is a compelling approach to understanding lived experience and meaning of an important experience related to health (Smith et al., 2009). Being a flexible and inductive approach, it is especially suited to eliciting meaning from

hitherto unexplored territory (Smith et al., 2009) as is the case with this study. And finally, the epistemological flexibility of IPA allows me to tailor the approach to best represent the participant voice. We do not yet understand the existential significance of research participation in the lives of people with MS, but as illness is a natural topic for IPA inquiry (Smith, 2011) it follows that IPA is a fitting approach in order to explore this. This research brings together everything that I have experienced, everything I have learnt from research, everything that the coproductive collaborators, research participants, and pwMS have shared with me, have taught to me – these are woven into the fabric of the study, in its design, in its implementation and interpretation. The epistemological flexibility of IPA gifts to me the authorisation to build the study, with people with MS, for people with MS without feeling restricted or curtailed. IPA methodology, historical, theoretical and philosophical underpinnings together with its applicability in this setting will be further explicated in Chapter III.

Coproduction within this Study

Whilst the premise of the researcher and participant together coproducing or co-constructing the research findings is integral to IPA (Jeong & Othman, 2016), for this study a coproductive approach was further embraced to design and shape the research. The purpose of this was to draw on the experiential expertise of pwMS who have engaged in research in order to remediate my own limitations in not having direct experience of the phenomenon in question. Although coproduction is not a tightly defined construct its intent is consistently expressed as producing something jointly, collaborating and making joint decisions (Hickey et al., 2018). The way in this was enacted to enhance this study was in bringing together people with MS and who have participated in research to discuss, direct and shape the design and interview schedules for this study and to facilitate interpretation– this produced a study that was arguably significantly different to what would otherwise have been developed. This collaborative coproductive approach was positively acknowledged by the NHS Research Ethics Committee and has significantly developed the relevance and quality of this thesis which will be explicated further in later sections.

Thesis Structure

This chapter has established the background and rationale behind this thesis, explored the epistemological considerations, enunciated the stated aims, highlighted the unique contribution that this thesis will add to the field of research participation, and defined the relevance to clinical research practice.

Ensuing chapters include a review of the relevant literature, the methodological approach, study findings, discussion and conclusion. Chapter II (Literature Review) presents a summary of research participation literature, firstly providing a landscape overview before drilling down into qualitative explorations of research participation followed by a synthesis of literature pertinent to research participation for pwMS. The methodology, including an overview of the philosophical and theoretical background of IPA together with explanation of study conduct comprises Chapter III (Methodology). Chapter IV (Findings) starts with an idiographic summary of each of the individual participant analyses before presenting convergence and divergence in the cross-participant analysis. The penultimate chapter (Chapter V) discusses the findings in the context of the broader literature and the unique contribution that this thesis makes to extant knowledge of research participation. Chapter VI concludes this thesis by reiterating new knowledge presented in this thesis, further research requirements and the impact on clinical research practice. An alphabetised list of references cited within the thesis precedes the appendices, where study documentation incorporating ethical and institutional approvals together with the Participant Information Leaflet and Informed Consent documentation are included.

CHAPTER II

Literature Review

Introduction

This chapter provides a synthesis of the literature of direct relevance for this study; the aims of which are to understand the experience of and meaning for people with MS taking part in MS research. The strategy employed in identifying the literature included in this chapter is first described before presenting the literature under review. The purpose of this chapter is trifold; firstly, to provides a macro-overview of the field of research participant literature generally, secondly to provide a more focussed synthesis of qualitative experiential health research participation, and finally to underscore the paucity of literature that explores research participation specifically from the perspective of people living with multiple sclerosis (pwMS). The synthesis helps to both inform the study's design and also serves to illuminate the unique knowledge that this study will contribute to our understanding of MS research participation from the perspective of pwMS.

To assist with navigation within this chapter, it is divided into four sections; the search strategy followed by three literature review sections:

- **PART-A** – Literature Search Strategy
- **PART-B** – A panoramic overview of health research participation literature *per se*
- **PART-C** – A synthesis of qualitative experiential medical research participation studies
- **PART-D** – Published research participation experience specifically involving people with MS

PART-A

Literature Search Strategy

Databases Interrogated

Databases aligned with the aims of the research and bridging healthcare and social sciences (see Table 1) were interrogated using an iterative search process (Brettle & Grant, 2004). In Smith's (2011) evaluation of IPA's contribution to the literature, the authors utilised Web of Science, Medline and PsycInfo in order to identify IPA publications. Smith's rationale was that these cover most quality journals that publish IPA studies. For a broader and more robust search strategy to encompass the study of research participation itself, additional databases (CINAHL and SCOPUS) were also employed. Despite significant levels of overlap, unique publications were found in each database interrogated. EThOs (e-theses online service) was also included to search for unpublished academic literature.

Database	Scope of Database
SCOPUS	Elsevier database – large abstract and citation database of peer-reviewed literature - 22,800 titles from 5,000 + international publishers. Comprehensive representation of global research output in the fields of Social Science, Health Science, Physical Science & Life Science.
PUBMED	PubMed comprises over 29 million citations for biomedical literature from MEDLINE, life science journals, and online books – and include the fields of biomedicine and health, plus some of the life sciences, behavioral sciences, chemical sciences, and bioengineering. Content is largely but incompletely encompassed in Scopus. Used as a source and additionally to locate 'similar content' for key resources.
WEB of Science	A multidisciplinary research platform which enables simultaneous cross-searching of a range of citation indexes and databases
EThOs	Electronic theses on-line service. A British Library database of c. 500 000 doctoral theses. Interrogated to identify unpublished work aligned with the research aims.
CINAHL	CINAHL (the Cumulative Index to Nursing and Allied Health Literature) is the authoritative resource for nursing and allied health professionals, students, educators and researchers. The database provides indexing for 2,928 journals from the fields of nursing and allied health and contains more than one million records dating back to 1981.
PsycInfo	Covers the professional and academic literature in psychology and related disciplines, including medicine, psychiatry, nursing, sociology, pharmacology, physiology and linguistics.

Table 1: Databases Interrogated

Firstly, test searches were undertaken using MeSH and subject headings identified from known research participation literature. An iterative cycle of searching strategies yielded outputs that lacked both sensitivity and specificity. This limited specificity was due to crossover and general applicability of search terms associated with research participation *per se*. After several iterative cycles it was determined empirically that searching titles resulted in the most relevant balance of specificity and sensitivity. An example search term employed in SCOPUS is included below:

TITLE (study OR studies OR trial* OR research) AND TITLE (view OR attitude* OR experienc* OR perspective*) AND TITLE (participa* OR involve* OR subject OR enrol* OR ({tak* part} OR {took part})) AND TITLE-ABS-KEY (health OR illness OR disease OR clinical OR medical)

Equivalent search terms were developed for each database interrogated before merging and deduplicating the outputs within Endnote. However, this approach still resulted in broad corpus of literature requiring manual filtering. It became evident early within the exploratory searches that experiential exploration of MS research participation was, at best, limited. Manual filtering to remove out of scope literature was undertaken prior to a more tailored approach. After manual filtering in excess of 500 records of relevance were further reviewed and catalogued broadly by methodological approach, objectives and disease area. First titles, then abstracts and then full publication were reviewed where needed. This aim of this strategy was twofold, to understand and present an overview synthesis of the broader research participation literature, and further to specifically identify qualitative studies of lived experience of medical research participation. Simultaneously refined eligibility criteria (see table below) were applied to identify the more elusive literature that described or reported experiential aspects of medical or health related research participation from within the broader corpus. Publications within the more selective scope were then used to identify further literature of relevance by using the 'find similar' functionally in some databases and from working through cited references and 'cited by' – i.e. forwards and backwards citation searching. Additionally, hand searching of journals identified which were not included in the databases and additional database searching with revised terms was undertaken.

Inclusion and Exclusion Criteria

To ensure that relevant evidence was located, application of inclusion and exclusion criteria are recommended (Whittemore and Knafl, 2005) which also helps to improve and make transparent the process. Inclusion and exclusion criteria help focus the identification of appropriate literature to ensure that the results of the search are specific and relevant to the review aim. Examples of exclusion and inclusion criteria applied are listed in Table 2.

Health Research Participation Literature	
Inclusion Criteria	**Exclusion Criteria**
Evaluation of research participation by research participants Qualitative or quantitative Medical or clinical or health/illness research. Identifiable therapy area or healthcare setting, or health related. Abstract or full-text available in English	Not related to illness or health condition Primary research – i.e. not research of participation Non-English language Limited to clinician or professional perspective
Qualitative Experiential Research Participation Studies (medical, clinical or health/illness research)	
Included people with health condition enrolled in medical/clinical/health/illness research Qualitative methodology Experiential perspective	Not qualitative Not experiential • barriers or motivation only • hypothetical study scenarios • considered only facets of conduct versus experience such as informed consent processes, randomisation etc

Table 2: Inclusion and Exclusion Criteria

Literature searching was a distinctly non-linear process with iterative cycles of revised search strategies (Brettle & Grant, 2004), with extensive manual screening in addition to repeated forwards and backwards citation searching. The quest for research participation literature expressing the views of people with MS became an almost compulsive approach that was very much an art rather than a science! This complex, iterative and repetitive approach allowed a high level of confidence that extant directly relevant experiential research participation literature involving pwMS would be identified. For completeness searches of experiential enquiry of living with MS were also undertaken to understand if this literature extended to experience of MS research participation.

A Venn diagram is included below to visually represent the overarching landscape of literature of relevance to this thesis.

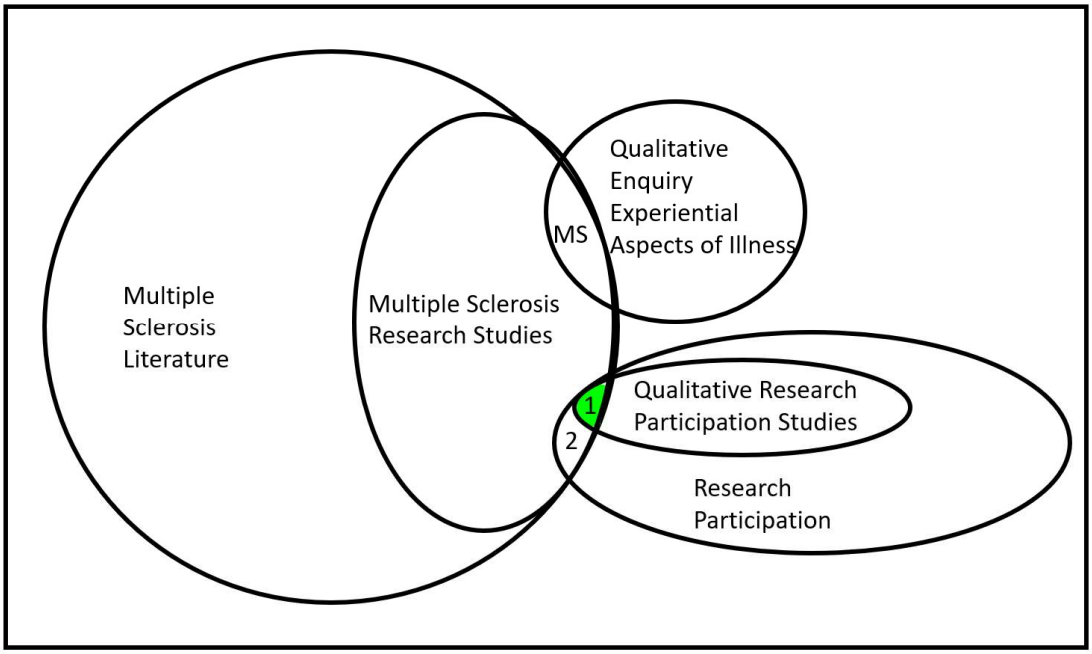


Diagram 2: MS, Research and Research Participation – Visual representation of Extant literature

PART-B

Research Participation Panorama

This section aims to provide a panorama of the landscape of literature pertaining to research participation more generally, providing important orientation in conducting and contextualising this research. Having appreciated the broader research participation landscape, PART-C then takes a more focussed view on the types of qualitative inquiry that specifically inform our understanding of medical or health research from the participants own standpoint. As proposed in the introduction, it is not that either qualitative or quantitative enquiry are somehow superior (Pope & Mays, 1995), each approach can be regarded as complementary. Qualitative studies have the ability to be receptive to the unexpected facets of human lived experience in a different way and to a different extent than with quantitative questionnaire-based studies (Madsen et al., 2000). And finally in PART D, pertinent literature specific to pwMS in the research participation arena is expounded.

Over 500 publications were located that explored some facet of research participation across a diverse range of health conditions. The most frequent investigation of research participation related to cancer studies, for example McGrath-Lone et al., (2016), Harrop et al., (2016), Morris and Schneider, (2010). Overall, approximately a third of the available research participation literature discussed cancer studies involving a range of approaches including both qualitative and quantitative methodologies. A considerable focus on quantitative generic research surveys (i.e. not aligned to any specific disease) was identified. (Almeida et al., 2007; Anderson et al., 2018; Henzlova et al., 1994; Kost et al., 2014; Shen et al., 2015), some of which are illustrated later in this section. Other research participation involving people with a diverse range of health conditions was represented to varying degrees. Explorations of participant experience in a range of mental health interventional studies were identified, including participants with depression (Andrighetti et al., 2017), schizophrenia (Grant, 2015; Taylor et al., 2010) or across multiple mental health conditions (Bibb & McFerran, 2017). Other conditions explored are listed in a rudimentary ranking of frequency of research participation literature; starting with HIV followed by acute or critical care medicine, genetics, pregnancy, sexual health, orphan diseases, respiratory medicine, gastroenterology, diabetes and rheumatological conditions. Even less frequent were studies

exploring research participation in people with sickle cell anaemia, people in perioperative research or those with ophthalmological disease. One of the least frequently identified research participation literature is the experience of people with neurological disease (Canvin & Jacoby, 2006; Kerrison et al., 2008; Maida et al., 2014; Namey & Beskow, 2011). Although there is a vast quantity of neurological clinical research published *per se,* research participation in neurological studies has been poorly represented equating to less than 1 in 50 of research participation literature.

The reasons for this limited exploration of neurological studies are not apparent and there is no evident correlation between this dearth and the prevalence of neurological conditions, nor the volume of research undertaken. Although published opinion seems to be lacking, according to Rog (2018, personal communication) it may be partially explained by the notion that traditionally neurology has been viewed as a specialty where judicious esoteric diagnoses have been made but where historically there have been limited therapeutic options, perhaps due to the complexities of the pathophysiology of the conditions themselves. Many neurological and neurodegenerative conditions still have very few disease modifying options. With the existence of few positive studies in many neurological conditions until recent years, it is likely that there has been less emphasis on assessing on the experience of neurological research participation to date. The extremely limited corpus of literature that related to research participation of pwMS is considered in the final section (D) within this chapter.

As highlighted above, a considerable focus on quantitative satisfaction surveys of research participation was evident in the literature. These quantitative research participation studies routinely employed surveys (Mathieu et al., 2012) or questionnaires (Henzlova et al., 1994) (validated or unvalidated) to measure various combinations of factors such as barriers or motivation towards trial participation (Maida et al., 2014), experience in terms of satisfaction with participation (Dayer et al., 2017) or with trial conduct including informed consent processes (Almeida et al., 2007), or willingness to repeat their research participation or to recommend participation to others (DasMahapatra et al., 2017). Across the studies, participants were generally approached by research or clinical staff, by post or by email. Results were generally expressed numerically either in tabulated form or utilising different chart types and participant quotes were rarely included. Survey participants

included those with specific health conditions (Maida et al., 2014), healthy volunteers, members of the general public, having been involved in clinical research or not, or could have participated in specific trials or have declined participation (Bevan et al., 1993). Trials of interest could be aligned with a particular geography, trial centre or condition, or hypothetical trial scenarios could be used to elicit responses (Gaudiano et al., 2016). In these quantitative approaches participant numbers were typically much larger than those in qualitative studies; ranging from tens (Au et al., 2015; Pflugeisen et al., 2016) to thousands (Henzlova et al., 1994; Kost et al., 2014) of participant responses. To exemplify such studies, and which typify those frequently encountered by those with a professional interest in clinical research, two quantitative participant experience studies are summarised below. Two further examples (DasMahapatra et al., 2017; Maida et al., 2014) which included pwMS, are discussed in PART-D.

An example of the aforementioned large-scale generic survey comes from the Center for Information and Study on Clinical Research Participation (CISCRP). CISCRP is a US-based non-profit organisation whose aim is to help inform the public, patients, medical or research communities and other stakeholders about clinical research. The objectives of this large survey study were to explore public and patient perceptions, motivations, and experiences of clinical research participation (Anderson et al., 2018). It was conducted online during 2017 and included responses from over 12 000 people of whom 18%, or 2200, had participated in a clinical trial. Findings, largely collected from multiple choice options, included motivation for participation, barriers to study enrolment, participation by race and ethnicity, experience and shortcomings associated with the informed consent process, negative impact on daily living, positive experiences and perceived value, benefit and positivity towards research *per se* (Anderson et al., 2018).

Another large-scale research satisfaction survey was conducted by a commercial clinical research organisation (Shen et al., 2015) which investigated similar domains to the CISCRP study. Questions included topics such as friendliness, helpfulness, skills and attitude of the study team, comfort of the waiting area, waiting times, likelihood of recommending the study team, appointment availability and overall satisfaction. Over one hundred thousand responses were collated over a number of years. Despite the vast size of the dataset, key conclusions were limited by the nature of the questions. Results indicated high levels of

satisfaction across all dimensions studied. Within a separately defined cohort additional questions were also included which sought to understand benefits of research. Overall, of most interest was the responses to the question that gauged study participant perceptions of their clinical research experience in terms of engagement in their own healthcare. This, however, was only sought in a much smaller subset of participants but all of whom (100%) responded that the clinical study improved the participants involvement and interest in their own healthcare. Although these large generic evaluations of research participation offer valuable insight, they cannot offer a rich interpretation of the meaning of participation to the individual.

And whilst this overview demonstrates the beginnings of a relevant incursion into the participant experience of research involvement it was evident at this stage that research participant experience expressed from the viewpoint of participants was relatively uncommon, and that research participation for people with neurological disease was particularly scant. Rarely was it evident *how* the patient participant feels, what the research *means*, how they made *sense* of the research, or whether there is a deeper significance.

PART-C

Qualitative Experiential Research Participation Studies

In undertaking this more focussed literature review I have borrowed some thinking from the grounded theory (GT) debate on the degree to which extant literature should be interrogated. The originator of GT (Glaser, 2005) deemed that exploration of existent literature was problematic and directed researchers to ignore the literature in order to avoid preconceptions; although current guidance is generally less radical advising preliminary reading to provide context for the study (Hallberg, 2010). Generally, the main aims of a literature review are to refine the research question, determine gaps in earlier research, to identify or ratify appropriate design, and data collection methods for the planned study. In considering these aims whilst simultaneously appreciating the inductive nature of IPA and the need to bracket (to be expounded more fully later) or to put aside preconceptions, I opted to consciously exclude interrogation of the findings from qualitative research participation literature at the review stage. [aside from a very small number of focussed publications that I felt required more in-depth understanding at this earlier stage in order to inform the research methodology]. The intent of this was to reduce onward bias in coproducing the interview guide, in conducting interviews and cocreating the narratives with participants, and subsequently in undertaking the analyses. My premise was simple, I could not unknow what I knew and so sought to not know. I did not wish to seek to, consciously or unconsciously, confirm what others had already found but to be wholly receptive to the individual participants in guiding the discussion topics of import to them (Smith & Nizza, 2022). Once all interviews and analyses had been completed then the literature in scope was revisited, the findings reviewed, synthesised and used to inform the discussion chapter. What follows here is an evaluation of the existent qualitative research participation literature considering scope, methodological approaches, conditions included and data collection methods.

Qualitative studies focussing on experiential aspects of participation in health or medical intervention studies are limited. Despite extensive search approaches less than forty examples of such studies were identified. Approximately half of these have been published in the last ten years, with the first example dating back to 1985 (Mattson et al., 1985). Aligned with the findings from the broader corpus of research participation literature, therapy areas of focus within in the qualitative experiential arena were more frequent for experience of oncology studies (Armstrong & Morris, 2010; Cohen et al., 2007; Cox, 2000; Harrop et al., 2016; Kvale et al., 2010; Madsen et al., 2007; Maloney et al., 2013; Nelson et al., 2013; Wootten et al., 2011; Yoder et al., 1997; Zaharoff & Cipra, 2018). Whilst some qualitative evaluations explored participant experience within multiple studies across a range of disease areas (Hussain-Gambles, 2004; Kerrison et al., 2008; Kost et al., 2011; Locock & Smith, 2011), only one was identified included pwMS (Kerrison et al., 2008), but which was not specific to MS. Other studies exploring trial experience of people specifically with neurological conditions were limited but included motor neuron disease (Bakker, 2016) and experience of a trial of acupuncture versus sham acupuncture in people with migraine (Paterson et al., 2008). People's experience of research in other conditions including cardiovascular disease (Dougherty et al., 1999; Mattson et al., 1985; van den Berg et al., 2017), diabetes (Lawton et al., 2003), benign prostate disease (Featherstone, 2003), intellectual disability associated with Prada Willi syndrome (McAllister et al., 2013), emergency care (Irani & Richmond, 2015; Tutton et al., 2018), rheumatoid arthritis (de Jorge et al., 2015) and surgery (Horwood et al., 2016) were also identified.

Unlike Signorell's recent review of methodological approaches in the evaluation of research participation experience (Signorell et al., 2021) studies involving mental health (Andrighetti et al., 2017; Carey et al., 2001; Grant, 2015; Read et al., 2020; Taylor et al., 2010), HIV (Liamputtong et al., 2015; Reynolds et al., 2013) and antenatal health (Harvey et al., 2018; Smyth et al., 2012) were within scope for this review. Signorell excluded studies which reported on participant experiences of clinical trials involving people with certain infective diseases, including malaria, tuberculosis, HIV and research participation in relation to mental illness was also excluded by the author. Signorelli argues that for such studies the focus is too specific in terms of disease orientation when discussing trial participation. However, this disease-specific nuanced experienced of trial participation is precisely the

strength that qualitative approaches, such as this current research can bring to light.
The sample sizes in the qualitative experiential research participation studies are generally, and expectedly small, ranging from three (McAllister et al., 2013) to over one hundred participants (Irani & Richmond, 2015; Reynolds et al., 2013) with the majority including less than 30 participants. In one case described as employing mixed methods (Signorell et al., 2021), over 1500 participants were included of whom 380 underwent a research participation interview (Mattson et al., 1985). Despite the qualitative aspect described in Mattson's study the findings presented have more resonance with a quantitative approach and lack the depth, richness or individual participant perspective or participant quotes that are often the hallmarks of qualitative enquiry. Of the qualitative research participation studies identified and included in this review, only one other study (Kost et al., 2011) failed to support their findings with excerpts from the participant narratives. Anchoring the findings in the participant words confers a richness and plausibility to the text (Nizza et al., 2021; Smith & Nizza, 2022); examples of which are included in the discussion section. It was interesting to observe clear trends both in the methodological approaches and means of data collection. Thematic analysis (including framework analysis) was selected as the analytical approach in most studies with only around a third utilising other approaches such as content analysis (Carey et al., 2001; Cox, 2000; Dougherty et al., 1999; Irani & Richmond, 2015), grounded theory (Andrighetti et al., 2017; de Jorge et al., 2015; Lawton et al., 2003; Locock & Smith, 2011; Madsen et al., 2007; Reynolds et al., 2013), discourse analysis (Armstrong & Morris, 2010) IPA (Harrop et al., 2016; Nelson et al., 2013) or other phenomenological approaches (Cohen et al., 2007; Kvale et al., 2010).

The approaches to data collection are especially interesting with the (in-depth) semi structured interview most widely employed in the studies explored within this review. A small number of studies employed focus groups either as the sole data collection (Kost et al., 2011; Reynolds et al., 2013; Zaharoff & Cipra, 2018) or in addition to other methods (Kerrison et al., 2008). Structured interviews (Yoder et al., 1997) or short response interviews (Irani & Richmond, 2015; Mattson et al., 1985) were also employed. Further, observations (Liamputtong et al., 2015) and questionnaires (Kerrison et al., 2008) were also used in isolated cases to supplement other data collection approaches. However, what constitutes an in depth semi-structured interview seemed to vary significantly. According to

Pope and Mays (1995) in-depth interviews are face-to-face conversations that do not use pre-set questions and are intended to explore a specific issue or topic (Pope & Mays, 1995). Similarly, the semi-structured interview is generally considered to comprise a loosely defined set of topics or questions but that is not rigid nor comprehensive (Bryman, 2016). For example, in IPA the interview guide is employed very flexibly during the participant interview as the participant directs the flow and topics of relevance to the experience under investigation (Smith et al., 2009; Smith, 2017). Some of the interview guides employed in the qualitative participant experience studies reviewed were unexpectedly structured or detailed (McAllister et al., 2013; Nelson et al., 2013; Paterson et al., 2008) sometimes comprising fifty or more specific questions (Grant, 2015; Hussain-Gambles, 2004) potentially leaving little room for the participant to guide the content.

The most challenging aspect to make sense of within this corpus of literature was the concept of *experience.* This challenge proved to be bidirectional in that when a trial purported to be considering, for example the motivation or barriers to research the findings related to motive to participate often included experiential aspects from trial participation versus decisional motivators. For example, Irani and colleagues sought to explore why people took part in emergency research (Irani & Richmond, 2015). The interviews were conducted 12 months after enrolment to the acute injury trial and whilst the aims were not experiential in nature it seems inevitable that participants having experienced the trial for 12 months that the responses will include or have been impacted by the time course and cannot purely reflect motivation to participate. The authors in this study acknowledge that the findings do not reflect the potential for temporal variation in perceptions of trial participation. Or conversely where the aims or objectives referred to experience this sometimes focussed on satisfaction or understanding of specific trial processes or trial conduct such as decision making, consent, randomisation, or treatment effect (Maloney et al., 2013; Nelson et al., 2013; Reynolds et al., 2013; Smyth et al., 2012) versus experiential aspects of significance or meaning. Further, studies nested or embedded within the research study or trial of interest (Harvey et al., 2018; Nelson et al., 2013; Read et al., 2020) sometimes appeared to be a qualitative extension of the primary research aims and represented a qualitative exploration within the trial rather than experiential aspects of participating in the trial. One example can be seen in Nelson's IPA exploration of

experiences of participants within a clinical trial comparing oral or intravenous treatments in metastatic breast cancer (Nelson et al., 2013). In Nelson's study the focus appears to be mostly anchored around treatment, symptoms and study practicalities albeit from a qualitative perspective. This distinction was by no means absolute and arguably represents the diversity within the qualitative health research participation literature.

Overall, the literature search for qualitative research participation studies identified very few studies that explored the in-depth experience of participants of research studies or trials and that applied the principles of IPA (Harrop et al., 2016; Nelson et al., 2013). Although these studies were not related to MS the authors approaches and considerations were anticipated to provide relevant insights for the design and conduct of the current study.

Harrop et al. (2016) embraced IPA to explore the experiences of ten participants with advanced lung cancer enrolled in a primary study to investigate the effects of low molecular weight heparin on survival. In parallel to the investigative treatment trial, participants were recruited to a study to evaluate their experience of participating in the primary research. Harrop's study was conducted using a contemporaneous longitudinal approach over a short timeframe, to minimise attrition. Participants underwent three interviews in eighteen weeks. The interviews focused around eight main topics: joining the trial, participating in the trial, treatment experiences and quality of life (QoL), symptom burden, management and QoL, experience of injecting, other health and trial experiences, and finally, end of study reflections. Findings from the broader research participation literature were generally reaffirmed, and although procedural understanding was found to be poor, participants experienced psychological, emotional and social benefits, with the overall experiences being regarded as generally highly positive. Interestingly, 'sense making' of participation differed between the interventional and control arms with participants in the treatment more likely to focus on possible treatment benefit whilst those in the control arm focused on personal fulfilment, positive attention and altruism.

Similarly, Nelson et al (2013) used an IPA methodology to explore experiences [with clinical trial related processes] of cancer patients' participation in a randomised controlled trial. The trial compared two bisphosphonate treatments in people with metastatic breast cancer. Interviews covered experiences and understanding of study treatment, the experience of

the delivery mechanisms (intravenous or oral), side effects and benefits, and quality of life issues. This exploration of trial participation primarily focused on trial processes, procedures, trial assessment and side effects. Results demonstrated that participants were overall satisfied with their randomised treatment, although most participants had an initial preference for oral treatment. Practical difficulties such as needle phobia, poor veins, difficulty with swallowing and gastric side effects, and effect on pain control were reported. Other practical considerations such as geographical location and distance to travel were evaluated but had little impact for participants. Participant understanding of trial processes, such as randomisation, and information about bisphosphonates were evaluated. It was determined that some participants showed limited understanding of certain aspects of the study. Factors influential to the decision to join the trial included altruism, treatment preference and clinical monitoring. This study had distinct foci on the trial procedures, understanding and treatment effects rather than significance or meaning or participation.

Learning from this section provided an appreciation of the existent gap in the literature regarding the experience of pwMS taking part in research, and also provided methodological guidance and pitfalls in the conduct of qualitative research participation studies.

PART-D

Multiple Sclerosis Specific Research Participation Literature

It seems remarkable that despite hundreds of thousands of publications that discuss multiple sclerosis, and a history of tens of thousands of MS research studies, that no qualitative studies dedicated to the experience of pwMS participants were identifiable from the extensive search strategy described in PART-A of this chapter.

Although some of the large-scale quantitative trial participation surveys are likely to have included pwMS this is only specifically highlighted in one such study (DasMahapatra et al., 2017) and one further quantitative study explored the willingness of pwMS to potentially enrol in MS research in a single centre study in Italy. Both of these quantitative research participation studies including pwMS are expounded below.

'*Peoplelikeme*' (PLM) is an online health information sharing website for patients which has over 200,000 members – there is particular engagement of people with certain neurological conditions including MS, Parkinson's Disease (PD) and Motor Neuron Disease (MND). Harnessing the broad international reach of PLM, DasMahapatra and colleagues invited over 1600 PLM members, who were registered as living with one of nine selected chronic health conditions, to take part in an online survey (DasMahapatra et al., 2017). With the other quantitative study on pwMS, Maida and colleagues took a different approach and explored research participation in terms of recruitment barriers from the perspective of pwMS in a single centre in Italy. Over four hundred consecutive pwMS outpatients were each asked to complete a questionnaire designed to elucidate reasons for and against research participation (Maida et al., 2014). With both studies around 350 pwMS provided responses. Both studies employed non-validated instruments and included asking pwMS to consider future participation from a hypothetical perspective. With DasMahapatra's online study, trial participation rates were amongst the highest for pwMS versus other conditions. Around 20% of pwMS responders had participated in an MS trial with most reporting being 'very' to 'extremely' satisfied with their participation although over a fifth withdrew before the study ended (DasMahapatra et al., 2017). The rate observed for trial participation in Maida's

single centre study was slightly higher at just over a quarter of those surveyed having participated in MS research previously, and over half expressed a willingness to participate in future. Those expressing a willingness to participate in future (hypothetical) research were more likely to be older, without children, have a diagnosis of secondary progressive MS and have participated in research previously (Maida et al., 2014). There was similarity between the two studies in terms of factors considered important to potential participants which included helping others, accessing treatment and enhanced specialist care, having a good relationship with the study team, the potential for side effects and having access to adequate information (DasMahapatra et al., 2017; Maida et al., 2014). Additional factors surveyed and deemed important in the online survey were the possibility of receiving placebo, time burden of participation, and confidentiality (DasMahapatra et al., 2017). In DasMahapatra's online survey people with PD or MS were more likely to endorse trials to other patients compared with people with the other long -term conditions included. The findings from each of the studies supported the notion that a significant majority of patients are not introduced to a trial opportunity (DasMahapatra et al., 2017; Maida et al., 2014). Further, DasMahapatra commented that clinic appointments for complex long-term conditions are often inadequate in duration to cover all aspects of clinical care let alone consideration of research opportunities (DasMahapatra et al., 2017). Whilst each of these quantitative studies provide some concordant and useful insight regarding research participation for pwMS, neither is designed to, nor can offer any enlightenment from an experiential perspective.

The only other study that considered research participation and which included (but again was not specific to) pwMS is this time a qualitative exploration of research participation published in 2008 (Kerrison et al., 2008). Kerrison's qualitative study was undertaken in the UK and involved ninety-five participants who shared their experiences through focus groups, or via a telephone interview or returned a questionnaire. The particular significance of Kerrison's study for this current research is that one of the primary studies included was a non-therapeutic MRI (magnetic resonance imaging) study involving 18 people with primary progressive MS (PPMS). Other participants were people with multiple myeloma, suspected lung cancer, overactive bladder, brain lesions or advance ovarian cancer taking part in studies aligned with their condition. Qualitative data collection methods for the pwMS

participants included different data collection methods; interviews (n=2) focus group discussions (n= 8) and questionnaires (n=8). The same topic guide was used for all data collection means and comprised three key areas of inquiry; how subjects became involved in the research, participants' views on the benefits of participation and what could have been done better. Results were analysed by means of subject content analysis. Limitations include the varied approach to data collection and the range of conditions and study types involved – the data and participant frame of reference are less homogeneous than routinely observed for qualitative participant experiential studies, as can be seen from the previous section comprising the synthesis of the literature in this area. Given the data collection methods, the methodological approach and the number of subjects included, this study does not aim to capture the depth or meaning that can be resultant of IPA. In general, Kerrison's findings are expressed in terms of benefits of research being regarded as additional care and health monitoring, access to information, and altruism, although this was tempered with the view that there is an expectation of mutual benefit in participation. Concordance with these findings was also seen in the overview of the research participation literature. Within the literature, there is a predilection to report the discomfort experienced by research participants (Naidoo et al., 2020). In line with Maslow's hierarchy of needs (Maslow, 2013), basic requirements and practical discomfort is important to people participating in research. In Kerrison's study, participant criticisms included a lack of attention to basic comforts, and critique of the study design, informed consent process and dissemination of results. In response to these findings Kerrison's recommendations for future research included remediation of these deficits including greater physical comfort for participants and increased opportunity for participants to be involved in the study design. Further, echoing themes expressed elsewhere in the literature, participants should have the access to and comment on the results. As a slightly bolder, but potentially more problematic suggestion, Kerrison proposed that communication between participants in the same trial should be facilitated, but which in practice could introduce the biases that quantitative trial designs strive so hard to minimise. Within Kerrison's study there are some findings that are specific to the participants in the MS study. Such examples include the suggestion for better ear protection during the MRI evaluation, and the wish for a warm drink after undertaking study procedures (Kerrison et al., 2008). In this same study, research conduct was criticised by participants with MS; questionnaires were conducted variably either before or after an

MRI. In other health scenarios this might be inconsequential, however for pwMS this could be impactful on the consistency of the results given the levels of fatigue experience by pwMS subsequent to an MRI (Kerrison et al., 2008). These findings could be meaningful as they illustrate the discomfort and concerns of research participants previously unknown to the researchers. This study highlights specific needs and considerations for research in differing health populations from the participant perspective.

MS Experiential Qualitative Studies

There exists a breadth of publications exploring different facets of life with MS via qualitative means offering increasing richness in our understanding of people with, or associated with, MS. This provided significant illumination and enrichment of my own knowledge, however this experiential representation of living with MS did not extend to the viewpoint of MS research participation. Areas of exploration in the lived experience of MS may be broadly clustered around several key domains; impact of MS on identity (Calsius et al., 2015; Irvine et al., 2009; Mozo-Dutton et al., 2012; Strickland et al., 2017; Willson et al., 2018), emotion (Anderson et al., 2020; Blundell Jones et al., 2014; Laing et al., 2020), dignity (Čáp et al., 2019; Žiaková et al., 2020), coping (Boland et al., 2012; Hunt et al., 2014; Reynolds & Prior, 2003; Stern & Goverover, 2018), physical aspects including sport and exercise (Adamson et al., 2018; Barlew et al., 2013; Borkoles et al., 2008; Sikes et al., 2019), treatments including both disease modifying treatment (Carey et al., 2021; Ceuninck van Capelle et al., 2017; Manzano et al., 2020; Miller, 2016; Miller & Jezewski, 2006; Miller et al., 2012; Van Reenen et al., 2019), and physical symptomatic management (Bulley et al., 2015; Renfrew et al., 2018) and a particular bolus in the sphere of impact on relationships either from the family (Boland et al., 2018; de Ceuninck van Capelle et al., 2016; Jonzon & Goodwin, 2012; Neate et al., 2018; Wawrziczny et al., 2019) or carer perspectives (Cheung & Hocking, 2004; Strickland et al., 2015).

It is of note that more than half of these qualitative MS analyses have been published during the period 2018 to 2022. The remaining half have been published in the preceding 15 years thus suggesting an increased application of qualitative methodology in chronicling the meaning and experiences of this lifelong cumulative degenerative condition. Despite this acceleration of in-depth qualitative exploration of life with MS, none of these focusses on the experience of taking part in an MS research study as a participant.

Arguably, the decision to take part in research of disease modifying treatments (DMT), either as an addition to or as an alternative to an established DMT, could be perceived to overlay an additional level of complexity that may encompass further unknown factors. Qualitative studies felt to be of relevance which explore DMT decision making for pwMS in the clinical setting are expounded below.

Van Reenen's (2019) examination of the decision-making process stresses that the choice to start a disease modifying medication is a decision that pwMS must makes themselves, with appropriate support of health care professionals, or important others in their support network. This premise is contradicted by a participant quote that indicates that the role of others in this-making process may dominate for some; 'Well *I'm not sure if I really had a choice at the time. …he [the neurologist] just said, like 'you need to start using medication now.' And I just accepted that*.' Similarly, Miller and Jezewski's phenomenological study (2006) makes some interesting observations in terms of the choice of DMT '*was sometimes made by the patient and other times by the care provider*'. In contrast, Van Capelle asserted that, whilst participants felt caught off-guard as the prospect of beginning lifelong treatment, each felt that they had been actively engaged in the decision-making process (Van Capelle 2017). The process of the treatment decision, including the option of no treatment, was considered as being a coproductive process in its own right in clinical practice, between the clinician and the MS patient (van Capelle et al., 2017). These observations accentuate the value and relevance of extrapolating this exploration to consider the possibility of an experiential treatment or potentially placebo in a clinical trial scenario for pwMS. Given the already unpredictable nature of the course of MS choosing whether to participate in research of an experimental treatment may add additional unknown complexities for pwMS.

Gaps and Insights from Research Participation Literature

This literature review has provided an overarching picture of the landscape in the broader corpus of research participation literature. A further in-depth interrogation of the more limited corpus of qualitative experiential research participation literature reveals a paucity in the viewpoint of people with neurological conditions, and specifically pwMS. Qualitative studies frequently included a more structured or topic specific approach than might be expected and thus potentially limiting the participant-centeredness or directedness of

findings. Methodological approaches employing IPA to understand participant experience were also surprisingly limited. Although IPA is not extensively drawn upon in exploring research participation, it is increasingly extensively employed to understand the lived experience of MS for the person living with (or caring for) pwMS. This provides further support for the study methodology selected as discussed later in this chapter. Further, whilst qualitative methods have been helpful in understanding the lived experience of having MS, and in taking treatment decisions associated with MS, the literature in this area does not extend to the experiences of taking part in MS research. Despite the vast volumes of MS related literature, the diversity of research participation literature only three studies in total were identified that included pwMS (DasMahapatra et al., 2017; Kerrison et al., 2008; Maida et al., 2014). Only one of those was specific to MS (Maida et al., 2014) which was a quantitative approach focused on recruitment, and only one took a qualitative experiential approach (Kerrison et al., 2008) but was not specific to pwMS. Kerrison's study did however affirm the need for disease specific considerations for research participation.

Whilst the literature to date that has provided highly valuable insight of research participation, it also serves to demonstrate the paucity of a richer discourse of the lived experience and in-depth meaning of research participation to those taking part. With so few studies that adequately illuminate the lived experience or meaning of taking part in research it seems clear that this is worthy of further exploration, particularly in the context of the otherwise heavily researched pwMS population. This study has the potential to provide a first qualitative incursion specifically into the world of pwMS taking part in MS research thus offering unique and impactful insight.

Chapter III

Research Methodology

Methodological Introduction

This chapter starts by setting out the aims and objectives of the research. IPA as a methodological approach is then explored, comprising a synopsis of the principles of IPA and its epistemological suitability to this research compared to other qualitative approaches. This is followed by a brief overview of the application of coproduction in research with relevance to this study. Further, quality aspects and worth are considered before moving on to describe the practical implementation, where the study schedule, data capture, data processing and analysis are explicated.

Research Aims

The aim of this research is to gain a rich understanding and to reveal meaning from accounts of people living with MS who have been taking part in MS research.

The further ambition is to enhance the awareness of MS clinician-researchers and others involved in the design and implementation of research involving pwMS.

It is evident from the in-depth literature review that whilst pwMS have extensively participated in research, the meaning and experience of research participation for pwMS as individuals has not previously been the focus of qualitative enquiry. This thesis therefore aims to contribute new knowledge that can be complementary to that arising from the traditional nomothetic approach. Findings can shine light on this hitherto underexplored area and potentially serve to enhance research communication, interaction and research practices going forward.

Methodology Outline

In order to orientate the reader a diagrammatic representation of the overall research approach is presented in Diagram 3 (page 38), and which will be expounded in greater detail throughout this chapter.

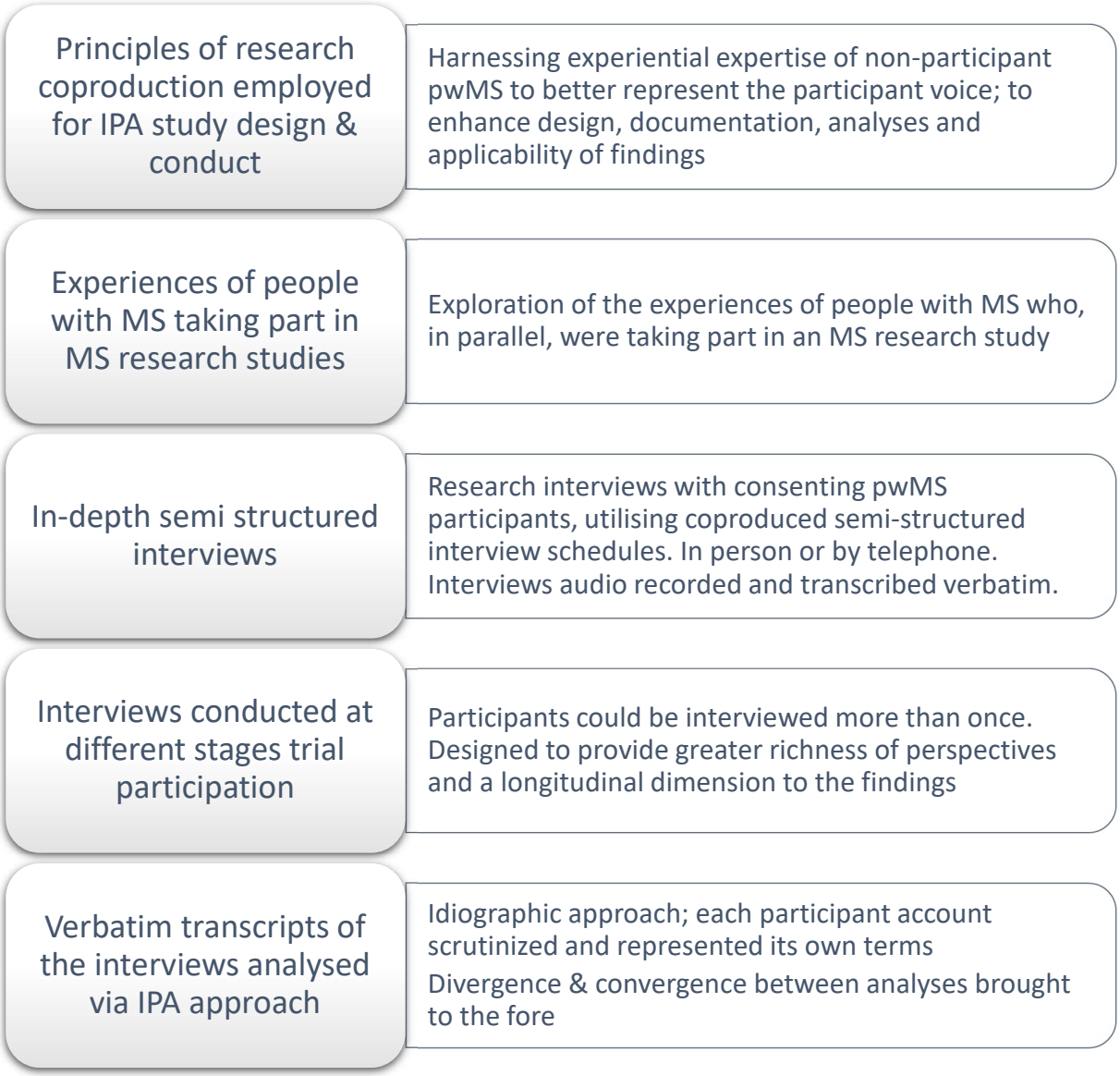


Diagram 3: Schematic Overview of Study Design

Interpretative Phenomenological Analysis

Introduction to IPA

Principles of interpretive phenomenological analysis comprise the framework for the study design, methodology, data collection and analysis. This section introduces IPA as a methodological approach, before moving on to examine the rationale for IPA as the appropriate approach for this study.

Although no written piece on IPA would be complete without acknowledging its historical and philosophical emergence, an exhaustive examination of the in-depth philosophical origins and complex theoretical deliberations around the evolution and application is outside of the scope of this thesis. It is, however, important to understand key tenets of IPA in order to define the essence of the IPA approach applied in this study.

IPA is a rapidly expanding qualitative methodological approach which is increasingly being embraced by those working in health sciences (Smith & Osborn, 2015). As an approach, IPA has both a relatively recent and distant historical course. Its inception as a defined qualitative approach came into being in the mid-1990s when it was first used as a distinctive research approach in health psychology by Smith (Shinebourne, 2011). Looking further back, IPA has at its roots in, and owes it genesis to three long established tenets of the philosophy of knowledge; phenomenology, hermeneutics and idiography (Eatough & Smith, 2008). IPA draws on each of these in order to inform its distinctive epistemological framework. IPA is often considered to be an approach rather than a tightly defined methodology (Larkin et al., 2006) and has what can be termed as epistemological flexibility (Larkin et al., 2006). Whilst the conduct of IPA needs to align with its underlying principles (phenomenological, idiographic, interpretative analysis of data from first-person accounts) the exact approach is open to embracing individual preference and variation, as described in Chapter I.

IPA explores how people make sense of their meaningful life experiences and their emotional response to that experience (Smith, 2011). IPA allows us to try and understand what it is like to walk in another person's shoes, accepting of the knowledge that this is never fully accessible nor completely achievable. (Forrester & Sullivan, 2018). In that respect it is a critical realist methodological approach (Fade, 2004) - it assumes that reality exists but access to that reality is always indirect (Forrester & Sullivan, 2018). Critical

realism proposes that our perception is partly contingent on beliefs and expectations thus acknowledging that there is always an intrinsic subjectivity in the generation of knowledge (Madill et al., 2000).

Phenomenology – 'Exploration of Experience'

Although epistemological, ontological and philosophical perspectives may differ, essentially the aim of all phenomenological research is the same, that is to explore lived experience (McConnell-Henry et al., 2009). Husserl, a mathematician, is acknowledged to be the father of phenomenology (McConnell-Henry et al., 2009) and is credited with first describing the study of experiences within the 'life-world', or lived experience (McConnell-Henry et al., 2009; Smith et al., 2009). IPA takes from phenomenology this focus on the aim to understand the meaning of human experience (Forrester & Sullivan, 2018) and seeks to illuminate on experiences of existential import *'as they are lived by an embodied socio-historical'* being (Eatough & Smith, 2008). This allows us to achieve close personal experience of elusive phenomenon (Smith, 2019).

Philosophers Sartre, Heidegger and Merleau-Ponty (Smith et al., 2009) each build upon Husserl's initial focus on the perception of experience, with their individual phenomenological and existential perspectives, by developing the view that people are immersed and rooted in an external world, where relationships to this world and others shape and define experience (Smith et al., 2009). This concept of inextricability is succinctly captured by Merleau-Ponty in Eatough and Smith (2008); *'Man is in the world, and only in the world does he know himself'*.

Heidegger, whose focus was deriving meaning from everyday human existence (Horrigan-Kelly et al., 2016) espoused an interpretative versus descriptive stance in IPA (McConnell-Henry et al., 2009) eschewing the presuppositionless approach to phenomenology that Husserl favoured. These opposing historical views lead to a certain ongoing tension and debate in how to express the phenomenological attitude and apply what is essentially a philosophical tenet into practice (Finlay, 2008). This deliberation between reduction and reflexivity in relation to the current study is articulated later in this section.

Whilst it inevitably the case that those conducting research will have a differing a perspective of the phenomenon to the experiential expert because their interpretation is

necessarily second order (Smith, 2019) the intent is to grasp the insider perspective as far as can be achieved. Further, it is important to remember that the focus of IPA is the *sense* that the person makes of their experience rather than the *nature* of the phenomenon itself (Eatough & Smith, 2008). Moreover, that the participants in IPA are recognised as the experiential expert of the phenomenon in question (Brocki & Wearden, 2006; Eatough & Smith, 2008).

When referring to *experience* in this context this relates to what can be defined as an experience of meaning rather than experience in general terms (Smith et al., 2009). Although *any* experience *can* be explored with IPA, its most relevant application is one that is of existential significance to the individual. What constitutes such an experience may be a major transition in life, the experience of illness or making an important decision (Smith et al., 2009). In this study, it is the experience and meaning of participating in MS research that is being explored. In conducting this study, an assumption is made that the experience of MS research participation has some degree of importance to the individual participant, but this assumptive stance will be bracketed (a topic considered later in some depth) or put aside in order not to influence participants during the semi structured interviews.

Hermeneutics

Hermeneutics is the theory of interpretation, and which was originally applied to biblical texts (Smith et al., 2009). IPA embraces hermeneutics from the perspective that humans are essentially sense-making creatures (Smith et al., 2009) or *'self-interpreting animals'* (Taylor & Charles, 1985). Humans are not passive perceivers of objective reality; this aligns with IPA in that the concept of an objective truth is dismissed (Gauci, 2019). Humans are constantly engaged in the interpreting of important life experiences (Gauci, 2019), formulating their own biographical stories that makes sense to them. People apply much reflective thought and emotion as they make sense of a significant event or experience. It is this making sense, finding meaning and understanding of the experience that is at the heart of IPA. IPA incorporates what is oft described as the double hermeneutic - the researcher is aiming to make sense of the participant making sense of their own experience. (Smith et al., 2009), albeit second order sense making.

This hermeneutic circle is a useful approach to considering context in terms of relationships between the part and the whole (Smith et al., 2009). IPA necessitates a dynamic, nonlinear,

and iterative approach to analysis (Eatough & Smith, 2008) involving moving back and forth between the part and whole in recursive cycles of interpretation.

As previously underlined, IPA has epistemological flexibility and a diversity of nuanced approaches are both legitimate, and encouraged (Smith et al., 2009). One such facet of this variability in stance is that of the application of the hermeneutics of empathy [in its own terms] or suspicion (Ricoeur, 1970; Smith et al., 2009). Smith (2009) asserts that IPA can stand a middle ground between both modes of hermeneutic engagement, that is by invoking a double hermeneutic of both empathy and of a degree of suspicion, each can contribute to a more comprehensive and layered interpretation (Eatough & Smith, 2008). However, it is important to note that the interpretive approach within IPA is derived from within the text itself, it does not rely upon *'borrowed hypotheses and theories'* from without the text (Reid et al., 2005). The findings *'must always be grounded in the meeting of the researcher and the text'* (Brocki & Wearden, 2006; Smith et al., 2009) but can generate relevant and novel analysis of important phenomenon within peoples lived experience (Reid et al., 2005).

The aforementioned biblical origins of hermeneutics bring about yet another debate within IPA; the Gadamer versus Schleiermacher debate (Smith et al., 2009). Gadamer asserts that in hermeneutics the focus is on making sense of the *text* specifically (or here this would be the interview transcripts) rather than of the author (here, participants). Schleiermacher however, defined interpretation in terms of being both grammatical (of the text) and psychological (of the author). Whilst Gadamer's approach may be prudent for historical texts of specific genre or linguistic complexity, Schleiermacher's more holistic view is considered by Smith (2009) to be more relevant to contemporary IPA. As IPA accounts are frequently generated at the behest of the researcher, this approach give rise to a more complete opportunity for a richer combined interpretation of the account and the person providing that account. This stance is propagated throughout this study with interview transcriptions conducted personally, thus enhancing the *connection* with, the feeling of *knowing* and *understanding* the participant. The participant's voice, tone and essence of what they are aiming to convey in the spoken word and non-verbal communication have considerable influence on the interpretation, versus looking only at the written transcripts in isolation. It is widely acknowledged that communication comprises an integration of both

verbal and non-verbal elements. Documenting of in-depth field notes during and following interviews, and during transcription further enhanced analysis of the participants narratives more completely. Other approaches intended to garner a more attuned and representative interpretation of the participants communication include coproductive involvement of experiential experts at the analysis stage (described in Chapter III).

During the interpretative process researchers talk of meaning that appears, or is revealed, that shines forth in the context of the lifeworld experience of the embodied socio-historical situated person (Eatough & Smith, 2008). Aligned with this concept of 'shining forth' Smith has proposed the notion of a gem; a gem being a nugget of enlightenment that can potentially represent the participant's understanding and meaning of their lifeworld in the context of the phenomenon (Eatough & Smith, 2008). It seems likely, guided by life experience, that a closer more complete connection with the participant *and* their formulated accounts is more likely to provide such illumination, and further, that the engagement of experiential expertise during analysis will additionally enhance the quality, rigor, and relevance of findings (Hemming et al., 2021). As a final note in this section, the first person use in the writings of IPA promulgates personal ownership (Smith, 2019), and thus the further recognition of role of the researcher-interpreter in the interpretative efforts.

Idiography – 'the Particular'

The third key strand of IPA theory concerns the idiographic nature of IPA, in that it is concerned with the individual, the particular case, in contrast to nomothetic approaches which pertain to large generalisable data sets at the population level (Forrester & Sullivan, 2018). The aim of IPA is to explore in detail and richness the accounts of each participant individually, appreciating their own experiences through case-by-case analysis. After the scrutiny and interpretation of individual cases it is then possible to look across cases for patterns of convergence and divergence and potentially, but tentatively, draw some generalisable inferences (Eatough & Smith, 2008; Tuffour, 2017; Nizza et al., 2021). Sample sizes tend to be small to allow richness and of interpretation and are generally from a tightly defined population (Smith et al., 2009).

Bracketing and Reflexivity

By employing the principles of IPA, the researcher must at times undertake quite intricate balancing acts (Larkin et al., 2006). The interplay between bracketing (or reduction) and reflexivity is one such poise where a palatable equilibrium must be reached between the epistemological stance of the researcher and Husserlian versus Heideggerian thinking. Reflexive practice is accepted as an integral part of the IPA research process which strives to identify and explicate the influence of the researcher on the analytical process and findings (Smith & Nizza, 2022). With IPA there must be tacit acceptance of the researcher's interpretative role (Brocki & Wearden, 2006) and necessitates that the researcher recognises, accepts, and actively evaluates their role as the means of interpretation. Reflexivity may be considered a key human quality (Biggerstaff & Thompson, 2008), and allows the researcher to acknowledge and reflect upon the researchers influence upon the data (Biggerstaff & Thompson, 2008). In Nagel's (1974) seminal writing on the experience of being a bat he poses the question *'what would be left of what it was like to be a bat if one removed the viewpoint of the bat?*' (Nagel, 1974). Crudely simplified, this could be taken to mean that there cannot be a view from nowhere (Biggerstaff & Thompson, 2008). Although this is somewhat of an oxymoron, it helps to frame the role that the researcher must inevitably hold in representing that viewpoint on behalf of the participant.

Given that IPA acknowledges the role of the researcher as the analytical instrument in the interpretative process, the notion of bracketing becomes somewhat contentious (Biggerstaff & Thompson, 2008). The concept of bracketing, as represented in the literature is controversial, ambiguous and much debated (Biggerstaff & Thompson, 2008; Tuffour, 2017). While Husserl asserted that it is necessary to put aside or bracket preconceived ideas in order to reveal the true essence of lived experience (McConnell-Henry et al., 2009), Tuffour (2017) asserts that IPA aligns more strongly with the hermeneutic approaches advocated by Heidegger, Merleau-Ponty and Sartre where reduction is rejected as impossible. Smith and colleagues (2009) appear to partially align with this notion in conferring lack of achievability or incompleteness of bracketing by describing the process as the 'attempt at bracketing' whilst simultaneously reaffirming that bracketing *'is seen by IPA as offering an important part of the research process'* (Smith et al., 2009). Further, that the relationship between the researcher and the data indicates the need for *'a more enlivened*

form of bracketing as both a cyclical process and which can only be partly achieved' (Smith et al., 2009). Whilst Smith *et al*'s (2009) earlier texts provide a focus on bracketing where researcher reflexivity may be inferred, interestingly both reflexivity and bracketing are each explicit in Smith and Nizza's more contemporaneous text on IPA (Smith & Nizza 2022).

Complexity arises further in that bracketing is defined and implemented in a multiplicity of different ways; there is no one accepted definition nor an accepted common understanding (Gearing, 2004). Bracketing represents a continuum of different approaches on which the researcher must locate themselves (Tufford & Newman, 2012). These differences in definition and application have led to the emergence of a proposed typology for bracketing, comprising six forms: ideal, descriptive, existential, analytic, reflexive, and pragmatic (Gearing, 2004). The absence of uniformity may therefore gift to qualitative researchers the ability to select the form of bracketing that is most appropriate for the research and researcher (Tufford & Newman, 2012). Further, Biggerstaff and Thompson (2008) assert that bracketing gives way to a more interpretative process as analysis proceeds. This leads into an additional complexity in the bracketing debate as there is a lack of consensus at to when or at what stage(s) that bracketing should be enacted. According to Ahern, Crotty (1996) describes bracketing as the approach by which the researcher attempts to avoid assumptions from defining the *'collection and construction of the data'* (Ahern, 1999). McNarry *et al* (2019) describe it as 'temporarily setting aside assumption'. Moreover, Smith seems to endorse this temporal premise by asserting the need for bracketing but indicating that there is time *after* the interview to allow those same preconceptions and foreknowledge to shape the subsequent interpretation (Smith et al., 2009). A further consideration arises from Hamill and Sinclair (2010) who suggest that the literature review be delayed until after data collection and analysis. In this way the data collection process and analysis are not shaped by existent literature and thereby that foreknowledge situated within extant literature is also bracketed (Chan et al., 2013).

These various arguments have led me to align with the concept that reflexivity and bracketing are not mutually exclusive but are *'fruits from the same tree'* (Ahern, 1999). At the very core of IPA is the attempt as far as possible to gain an insider perspective of the phenomenon being studied (Smith 2009), whilst acknowledging that the researcher is the primary analytical instrument (Fade, 2004). This is the balance of bracketing and reflexivity

that I have embraced in this study. For me there is a balance, an interplay between the Husserlian and Heideggerian dichotomy, and therefore congruent with Smith's direction, I stand the middle ground. Finlay (2008) describes the enactment of these complex interwoven processes as a '*dance'*; flipping between the attempt to bracket pre-understandings and conversely exploiting the same foreknowledge in the interpretative process (Finlay, 2008).

In order to achieve bracketing, a conscious approach is required which allows the researcher to be aware of and to recognise preconceptions, fore- understandings and perceptions that can influence the research process before they can be put aside. This in turn helps the researcher to be as fully receptive to the phenomenon as relayed by the participant as is possible (Chan et al., 2013). In this way bracketing itself is a reflexive process (Ahern, 1999).

Acknowledging the both the temporal debate and the incomplete nature of bracketing, within the current study bracketing was employed in generating the data, whilst reflexive thought informed the bracketing and continued throughout the analysis and writeup. Bracketing was therefore the reflexive process by which I consciously aspired to leave as much of myself out of the co-produced semi structured interview schedule, to set my opinions, assumptions and expectations aside during the interviews and to lay myself as open and receptive as possible to the participants experience as they relayed it to me. During this interaction I completely acknowledge that the participant is the experiential expert of the phenomenon in question (Brocki & Wearden, 2006; Eatough & Smith, 2008) and further, that the participant should be afforded significant influence on the direction of the interview (Brocki & Wearden, 2006).

I embraced reflexivity in a persistent effort to acknowledge, recognise and explicate my own role in the research and analysis. Reflexive thinking captured in field notes and a reflexive diary are expressed firstly in the reflexive discourse in Chapter I and within reflexive notes throughout the thesis. With this approach I aim to embed myself as an embodied socio-historical situated person within the research arena, to illuminate and make transparent the role of I, the researcher, in the process and to explicate some of the emergent dilemmas throughout the research journey.

Additionally, as described in Chapter II, I delayed the analytical review of findings from within the research participation literature until after the interpretative analyses so as to

bracket those finding from my foreknowledge. Only once the analyses were complete then the findings from existent research participation literature were interrogated and included within the discussion within this thesis. In adopting this position for bracketing and reflexivity I have found my own tempo in choreographing the dance that embraces both bracketing and reflexivity within this work.

Why IPA for this research study?

Having considered **what** IPA is, this section expounds the reasoning as to **why** IPA is suited to this work and examines the multiplicity of reasons why IPA is a befitting approach, versus other methodologies, to achieve the specific goals of the study in question. The rationale can be broadly categorised as follows; epistemological alignment, consideration of other methodological approaches, increasing use and acceptability of IPA in healthcare, resonance with clinical practice, including the patient-centeredness, complementary data generation (to the nomothetic approach) and future utility. Some of the topics touched upon in Chapter I are considered in greater depth here.

Epistemology

The study aims to reveal and illuminate meaning from the accounts of people with MS taking part in research for their condition. First and foremost, the *'choice of approach should be based upon the goals of the research'* (Johnson et al., 2004). The study aims are highly consistent with the inductive, experiential and interpretive approach of IPA.

From the exploration of the literature, as far as can be determined, there is no existent work published in the specific area of pwMS research participation lived experience. This further strengthens the argument as IPA is deemed particularly apt when the area is an '*unexplored territory where a theoretical pretext may be lacking'* (Reid et al., 2005; Smith & Osborn, 2003, 2003). IPA's suitability for exploring areas that are emotional, complex and emotionally laden such as illness is also well established (Smith & Osborn, 2015) and especially befitting for the longitudinal nature of the experience of illness (Brocki & Wearden, 2006). Living with multiple sclerosis is expectedly highly impactful and significant within peoples' lives and regarded as a fitting topic for IPA (Smith, 2011). Furthermore, within IPA, the participants are the *'primary experts'* (Brocki & Wearden, 2006) and should have a *'strong role in how the interview proceeds*' (Smith & Osborn, 2003). This study embraces the experiential expert status of the participant and further extends this ethos to

incorporate a coproductive approach to enhance the research quality and relevance. Although, as determined from the literature review, IPA has not been extensively applied in understanding research participation, IPA has been extensively employed to explore the lived experience of having MS, although this has not extended to having MS and taking part in research.

Other Methodological Approaches Evaluated

Smith and colleagues (Smith et al., 2009) assert that it is not a matter of selecting *'a tool for the job'* it a question of identifying *'what the job is'* which resonates with my understanding and approach. The epistemological position of the research aim guides the researcher towards the appropriate methodological approach. In this case, the person-centred experiential aims of the research are closely aligned to the principles of IPA. Once this connection was made it was extremely difficult to decouple the research from the IPA methodology or to consider other potential qualitative methodologies. However, for completeness, other qualitative methodologies including discourse analysis (DA) , grounded theory, cooperative enquiry and thematic analysis (TA) have consciously been evaluated in relation to the research question to ensure that IPA is an appropriate approach.

Numerous parallels have been drawn between IPA and grounded theory (Brocki & Wearden, 2006; Forrester & Sullivan, 2018) with both taking an inductivist approach; however, it is recognised that IPA is particularly relevant for understanding *personal experience* versus social processes (Brocki & Wearden, 2006). IPA allows greater granularity in the understanding of the lived experience of a small sample, and together with the opportunity to examine divergence and convergence between the participant accounts. (Smith et al., 2009). Grounded theory could be employed in this field, but I propose might be more suited to a less experiential intent (Smith et al., 2009), such as, for example, 'what factors influence people with MS in taking part in MS research?'

Discourse Analysis was discounted as this approach focuses on linguistic elements of how participants construct accounts of their experience which is not aligned with the research aims and could potentially find less resonance with clinical neurology researchers. Cooperative inquiry (Reason, 1999) was mooted as a viable alternative. The coproductive, and co-researcher elements applied here shares some of the features of cooperative

enquiry (Reason, 1999), however having a pre-defined research question is epistemologically misaligned with this methodology and so this was ruled out.

Thematic analysis (TA) is recognised as an alternative viable methodology aligned with the research aims. Although the theoretical groundings and the approach differ from IPA, it is possible to generate findings of depth and richness by employing reflexive or interpretative thematic analysis (Braun & Clarke, 2006), although TA lacks the idiographic approach of IPA. It has, however, been argued within the literature that TA is less informative in terms of clinical implications. Warwick and colleagues (Warwick et al., 2004) undertook a study exploring women's experience of chronic pelvic pain. The authors first conducted a thematic analysis of the narrative transcripts and then followed this with IPA of the same data set. They found that IPA revealed three major additional themes compared to TA and concluded that IPA offered a more enlightening and clinically relevant approach (Warwick et al., 2004). Whilst TA at the more interpretative end of the spectrum could have offered a valid alternative approach for this study (Braun & Clarke, 2006), the idiographic focus and established methodology within the healthcare arena favours IPA in this specific setting.

Increasing Use and Potential of IPA in Healthcare

IPA is increasingly being drawn upon by those in health sciences (Noon, 2018). IPA has been employed extensively in understanding the lived experience of illness (Smith, 2011) and has made a significant contribution in the health psychology arena (Shaw, 2011). This is evident from the increasing wealth of literature where IPA is applied in understanding illness and health care decisions (Brocki & Wearden, 2006). The fact that IPA is becoming increasingly accepted in the healthcare setting lends credibility to the chosen methodology (Biggerstaff & Thompson, 2008). This increasing use of IPA in the health setting has been evaluated in Smith's (Smith, 2011) appraisal of the contribution of IPA to literature. The number of IPA papers has steadily increased year on year (the majority arise from UK). In this evaluation Smith found that physical illness was the most frequent topic accounting for over one fifth of the IPA papers identified. Given that illness often has a significant impact on lives and lived experience, it is subsequently a natural topic for IPA enquiry (Smith, 2011). Qualitative research, and IPA in particular (Gauci, 2019) has a great deal to offer the medical profession in terms of its enrichment of knowledge and understanding of health or illness and the healthcare system (Kuper et al., 2008; Mays & Pope, 2000).

Qualitative paradigms can support the understanding of complex bio-psychosocial phenomena and consequently offers the potential for informing clinical practice (Biggerstaff & Thompson, 2008). IPA has the ability to bring to the fore, for example, the meaning and experience of being diagnosed with or living with a disease and can feasibly add meaningful value to health care professionals in numerous contexts. This experience-close approach is recognized to have potential utility for those authoring guidelines, in preventative medicine programmes, lifestyle choices and public health initiatives (Shaw, 2011). Echoing Shaw's thinking Gauci (2019) suggests that IPA research in the world of medicine could have bearing in a multiplicity of contexts, such as the doctor-patient relationship, healthcare communication, treatment adherence or multidisciplinary care teams (Gauci, 2019). Extrapolating these thoughts further, it could be expected that appropriately conducted IPA studies can potentially influence the shaping of further research, both qualitative and quantitative, and enhancing the research experience for participants with MS.

Resonance with clinical consultations

The entrenched nomothetic evidence-based approach in medical practice is perhaps understandable, as medical practices exists to support human life and health at the population level (Shaw, 2011). That being said, increasingly clinicians are starting to recognise that qualitative methods of enquiry may be more resonant with their own clinical and personal perspectives (Eakin, 2016) in terms of patient interactions (Biggerstaff & Thompson, 2008). The researcher-participant interaction in IPA can in many ways be viewed as being akin to traditional clinical practice in relation to HCP-patient relationship (Yardley, 2000). Further IPA may *speak to* those in health research because people have an innate interest in other people's accounts of illness, and the lived experience of others (Reid et al., 2005).

Accessibility

The output of IPA can be enormously powerful when it is conducted with the necessary care and commitment (Larkin et al., 2006). Although IPA is complex in its application, the outputs can be extremely accessible to the reader. IPA researchers have traditionalised the use of readily comprehendible language and straightforward terminology, rather than using language as a means to obfuscate understanding - a criticism levelled at some other qualitative approaches (Brocki & Wearden, 2006). This aspect is key as the intent with this

research is to bring across accessible participant-centred interpretations and subsequent learnings to the target audience, the MS clinical community, who are by nature more typically versed in nomothetic inquiry. It could be extrapolated that this target audience may have perhaps more limited experience, or more extreme, an uninformed opinion, of qualitative methodologies *per se* (Biggerstaff & Thompson, 2008). My intent is that by generating an accessible and plausible account of the experiences of pwMS who participate in traditional positivist research this may facilitate the MS clinical community to take meaning from the study's interpretive conclusions. This study is the first such qualitative inquiry of this nature, and therefore can make a significant contribution to the understanding of pwMS participating in research.

Complementary Enquiry

There is a progressive recognition of the *'constructed nature of illness'* (Brocki & Wearden, 2006) with researchers increasingly recognising the importance and value of understanding illness and treatment from the human perspective, and the meaning assigned to this by those with illness (Brocki & Wearden, 2006). Qualitative enquiry can provide an approach that is complementary and bring novel insights for health and disease (Yardley, 2000; Pope & Mays, 1995). Central to the intent of this current research study is the tenet that the IPA researcher can support the clinician-researcher *'to see how the case can shed light on the existing nomothetic research'* (Smith et al., 2009). IPA has the propensity to help healthcare professionals in understanding and contextualising findings from quantitative approaches (Gauci, 2019; Pope & Mays, 1995). This deepening of understanding of the person-centred experience may, in turn, serve to facilitate the defining of more relevant quantitative research questions by reducing potentially incorrect assumptions. (Brocki & Wearden, 2006; Johnson et al., 2004). The participants for this study originate as the subjects of nomothetic enquiry *'that construct people who never were and never could be'* (Datan et al., 1987). The findings of this study may therefore be of value in complementing and supplementing traditional quantitative enquiry in illuminating the lived experience and meaning of that research from a participant perspective.

Person-centredness

As has been established, IPA offers a genuinely complementary approach to traditional doctrines and which can bring additional insights into health and illness from a participant

centric perspective (Pope & Mays, 1995; Yardley, 2000). IPA is of particularly relevance to the medical field as Illness and healthcare issues are inherently of existential import to the service users or patients. (Gauci, 2019). This idiographic approach of IPA is therefore aligned with the NHS increased efforts to hear the voices of service user and is '*entirely congruent with the increase in patient centred research'* within the NHS (Brocki & Wearden, 2006; Reid et al., 2005).

Research is a significant activity for both NHS organisations and the majority of pharmaceutical companies. It therefore seems fitting that we should reach out and understand the meaning of research participation from this patient-centred perspective, aligned with patient-centred NHS Trust and Pharmaceutical company values.

In summary, IPA was selected as this current study is an exploration of participant experiences of being a research participant it investigates the participant experience with the intent of eliciting meaning in the examination of the interview accounts – this is consistent with the inductive and interpretive approach of IPA. It also aligns with areas of strength for IPA in terms of examining the lived experience of illness, plus significant and emotionally laden phenomenon. The idiographic approach has some parallels with the doctor-patient consultative relationship. Further the increasing utility of IPA within the healthcare arena, coupled with its ability to illuminate nomothetic research experience, strengthen its selection. The key rationale for selecting IPA over any other qualitative methodological approach is because it harmoniously aligns with the epistemology of the research aims in illuminating meaning in the individual experience of research participation.

Quality Considerations

A sizeable proportion of published qualitative, and in particular, IPA studies are considered to be conducted poorly (Tuffour, 2017). This may in part be owing to the misconception that IPA is easy to do (Shinebourne, 2011) – in truth it is easy to do… badly, but difficult to do well (Larkin et al., 2006). This perception of effortlessness may erroneously be partly due to its welcome accessibility to those without philosophical grounding (Shinebourne, 2011).

With IPA transparency is an important indicator of quality and therefore trustworthiness (Forrester & Sullivan, 2018) and given the expanding use of IPA in health research it is important that there are accepted approaches for evaluating its quality and trustworthiness

(Brocki & Wearden, 2006) and that this resonates with health researchers and clinicians. Traditional (positivist) research evaluation criteria such as representative samples and statistical analyses (which are particularly familiar to me) are deemed irrelevant for qualitative research (Brocki & Wearden, 2006; Yardley, 2000). So too the traditional premise of reproducibility is inappropriate as the concept of one objective truth is dismissed in IPA. Recognising that qualitative research is *'inherently valuable and immeasurably human'* (Soini et al., 2011) measures of quality need to befit this premise. The aim of quality measures in IPA are to ensure the *plausibility* and *integrity* of the final account that resonates with those with an interest in the research findings. In order to achieve this, reflexivity is explicit and verbatim excerpts from the transcripts are central to IPA. This transparency allows the reader to evaluate the interpretations made by the author (Brocki & Wearden, 2006).

Daly et al. (2007) set out to define specific criteria for assessing the contribution of qualitative studies in the medical field and a subsequent evidence hierarchy relevant to qualitative approaches. Daly's resultant cogitations designate generalisable studies at the apex of the hierarchy and single case studies relegated to a ponderous last-place status (Daly et al., 2007). Daly disparagingly cites an example of a qualitative case-study that brings to light the distress and impact of perceived soul-loss during caesarean childbirth (Rice & Lumley, 1994). It is complex and emotive case which crystallises the premise that in some scenarios physicians may regard the saving of a life as their consummate focus without being equipped with the necessary insight to acknowledge or respect individual or cultural perceptions. The implications on the individual may be disregarded with often significant impact, and so such case studies offer the opportunity for insight that can impact clinician attitudes and medical practice. Examples such as this bring to life the humanistic enlightenment that qualitative research can offer to clinicians. Daly appears to either disregard or fail to recognize that the example cited offers support for the exact opposite stance than intended.

Further, Yardley (2000) cautions against the aforementioned practice of qualitative methodology being evaluated against irrelevant criteria applied to traditional quantitative research by those who are unfamiliar or unsympathetic to the qualitative approach, and

thus who may fail to recognise the value in bringing *'fresh insight into health and illness'* that can be *'genuinely complementary*' to quantitative research.

Accepting that qualitative work, specifically IPA can make a meaningful contribution within the healthcare research environment, Smith's expert evaluation of IPA's contribution (Smith, 2011) summarises the contribution and quality of IPA in the literature. In this analysis, physical illness was the most frequent topic of IPA. Smith explains how lived experience is the *raison d'etre* of IPA. Given that illness often has a significant impact on lives and lived experience it is subsequently a natural topic for IPA enquiry. He evaluates the IPA papers that consider illness and categorises them in terms of quality by applying a set of defined criteria - of these 27 % were 'good', 55% achieved a status of 'acceptable' and 18% classified as 'unacceptable'. Smiths' evaluation echoes findings from the literature review conducted for this study - in that even where the methodology is described as IPA, some of the researchers appear interpret with only a small 'i' and as such is more of an exercise in cataloguing of themes and providing supportive quotes. More recently Nizza (2021) worked with colleagues, including IPA pioneer Smith, to publish updated guidance (Nizza et al., 2021) of how to evaluate and generate IPA research of sufficient quality. As this research has progressed from inception to implementation and interpretation, it has been continually evaluated against each Yardley's (2000) and Smith's (2011) and now Nizza's (2021) specific IPA criteria. Smiths and Yardley's criteria can be found in Appendix C and Nizza's framework forms the basis of the quality discussion in Chapter V.

Ascribing to the view that only those who live with MS can truly understand MS (Eskyte et al., 2019) and whilst aiming to get as close as possible to the insider perspective of the phenomenon of this inquiry (MS research participation for pwMS) a coproductive approach has been integrated into the design and implementation of this study. As with numerous other deliberations of relevance to IPAs epistemology, due consideration should also be ascribed to the challenges for researchers who can consider themselves as insiders who *do* share lived experience of the phenomenon in question. Whilst this insider insight is arguably highly relevant, it could also prove to be the proverbial double-edged sword. Firmly entrenched and personal views regarding the experience from the researchers own perspective would need to be bracketed as far as possible when entering the participants

own phenomenological world (Smith & Nizza, 2022) in order to be receptive of the participant's own meaning.

Following is a description of the approaches to further harness experiential expertise within the design and implementation of this research with the aim of enhancing the study's quality and applicability.

Coproduction

In fundamental terms, to coproduce is to make something together. Although coproduction is not a tightly defined construct and has no agreed definition (Boyle & Harris, 2009) it does embrace consistent and distinctive principles of collaboration and equal relationships.

Within this study coproduction has two philosophically related but separate applications. Firstly, the term has been widely used to signify the joint endeavors of the interviewer and interviewee to generate narrative outputs in qualitative research generally (Edwards & Holland, 2013; Kvale, 1996). Further, in IPA specifically it represents the complementary roles of the researcher and participant in the co-creation (Love et al., 2020) or co-construction of participants' meaning-making, where participants fulfil the role of co-researcher (Tuffour, 2017). Aligned with these descriptions the participants within this current study are regarded as co-creating or coproducing the narrative and meaning-making with the researcher during the participant interviews. This manifestation of coproduction is essentially inherent in the dynamic between the interviewer and the interviewee with an IPA approach.

The second coproductive undertaking within this study is the inclusion of experiential experts during the design and analysis phases of the study. People with MS who have taken part in research previously, and who are not participants in this study were significantly involved in the study design, documentation, and during the analysis phase in generating the findings.

Within research, coproduction with collaborators can be involved at any stage of the research process, although this is seen occur less at the analysis stage (Hemming et al., 2021). Numerous benefits of a coproductive approach involving people with lived experience of the phenomenon under investigation in research design and implementation are highlighted within the literature (Hemming et al., 2021; Hughes & Duffy, 2018).

Specifically, involving people with relevant lived experience may also yield enhanced quality and effectiveness of the research (Brett et al., 2014; Szmukler et al., 2011; Williamson et al., 2010). Additionally, the coproductive approach may serve to help identify themes of greatest relevance in the particular context (Beer et al., 2005; Ross et al., 2005). Although few examples exist of coproductive involvement at the analysis stage, where this does occur, then it can be valuable in mitigating researcher misinterpretation (Rhodes et al., 2002; Staley, 2009) whilst providing additional dimensions with complementary or alternative viewpoints (Garfield et al., 2016; Hemming et al., 2021; Sweeney et al., 2013).

There are multiple overlapping definitions of coproduction within the literature (Hickey et al., 2018; Hughes & Duffy, 2018; SCIE, 2019). The essence of coproduction within this study largely aligns with published definitions captured in Table 3 (overleaf).

Defined Principles of Coproduction (SCIE, 2019)	Key Principles (Hickey et al., 2018)	Collaboration and coproduction (Hughes & Duffy, 2018)	Application of coproduction principles within this research study
Define people who use services as assets with skills	Respecting and valuing the knowledge of all those working together on the research – everyone is of equal importance	Members of the public with relevant lived experience	Involving the retrospective experience of people with MS to enhance the prospective research element in a similar cohort. Engaging people with MS to support the analysis and interpretation of research data
Break down the barriers between people who use services and professionals	Sharing of power – the research is jointly owned and people work together to achieve a joint understanding	Involved as members of the research team as researchers/co-authors or in ways where they contribute to key decisions regarding research processes and findings. It may also involve writing plain English (lay) summaries, contributing as co-authors and being part of a steering group..	The coproducers are all considered to be equal contributors, equal experts-the 'researcher' bringing viewpoints relevant to the research implementation and the equal partners each bringing their own individual value and experience
Build on people's existing capabilities	Including all perspectives and skills – make sure the research team includes all those who can make a contribution	Typically this includes people contributing to decisions such as the tools used, choice and wording of research questions, how data are analysed, how research findings are presented and how research might be implemented. This model is characterised by the reciprocal nature of the relationships and collaborative processes involved, even when participants undertake different roles based on their areas of expertise	
Include reciprocity (where people get something back for having done something for others) and mutuality (people working together to achieve their shared interests)	Reciprocity – everybody benefits from working together		The coproductive team members will be included on the publication should they wish to be so. It is hoped that they become involved as a meaningful activity which helps fulfil their interests, and benefit from engagement within the group.
Work with peer and personal support networks alongside professional networks	Building and maintaining relationships – an emphasis on relationships is key to sharing power. There needs to be joint understanding and consensus and clarity over roles and responsibilities. It is also important to value people and unlock their potential.	For collaboration to work and for decision making to be shared appropriately, sufficient training, supervision and support is provided.	As part of a project group they have the support of peers within the MS community, and from the researcher (and if expresses clinical concerns will be signposted to MS Nurses or primary care)

Table 3: Coproductive principles, and applicability to this research study

Reflexive Note: It was really important to me that the study employed principles of coproduction in its design, delivery and interpretation in recognition of the experiential expert nature of the participants, and the parallel ethos of the coproduced nature of the data in IPA. I had some internal conflicts… coproduction could only be enacted so far, as the study title and the methodology were already set. Given this, was I being fair to the coproductive team? Could this be called coproduction ? Further, my trepidation was that the coproductive team would guide the research in a direction that did not align with the academic requirement for a Professional Doctorate, that would misalign with the research intent. How could I enact coproduction with that in mind? I consciously bracketed these concerns prepared to cross that bridge when I came to it.

The NIHR widely supports and guides researchers to enhance public involvement in research. They have produced guidance documents on coproducing research (Hickey et al., 2018) and cite examples of where coproductive approaches been successfully enacted in practice. Coproduction in research is described as *'an approach in which researchers, practitioners and the public work together, sharing power and responsibility from the start to the end of the project, including the generation of knowledge'* (Hickey et al., 2018).

The value that public and patient (service user) involvement can bring is eloquently captured in the following quote from Professor Dame Sally Davies, ex-UK Government Chief Medical Officer; *'No matter how complicated the research, or how brilliant the researcher, patients and the public always offer unique, invaluable insights. Their advice when designing, implementing and evaluating research invariably makes studies more effective [and] more credible...' (Staley, 2009).*

Within this study *'coproduction is not just a word, it's not just a concept, it is a meeting of minds coming together to find shared solutions…* [it is]*a relationship where professionals and citizens share power to plan and deliver support together, recognising that both have vital contributions to make'* (SCIE, 2019).

This study harnessed experiential experts to enhance the quality, relevance and applicability of the study and its findings. Coproductive experiential experts collaboratively drove the study design, implementation plan and documentation content aligned with the study aims and methodology. Further, despite being hampered by SARS2-CoV19 restrictions the concept of coproduction continued into the analysis phase.

The coproductive experiential experts were pwMS who had previously participated in research and so were familiar with the frame of reference, MS research participation, for the planned IPA study. The coproductive experiential experts were identified by MS clinicians at the recruiting centre, via a local 'MS Treatment Centre' (non-NHS) and from coproductive experiential experts themselves. For clarity this cohort of pwMS coproductive experiential experts was separate from the participants within the study who were each concurrently involved in an MS clinical trial. An invitation describing the aims of the coproductive approach (included in the appendix) was provided to those considering becoming involved. Discussion groups were convened and conducted at the hospital and other locations as agreed by those involved, including cafés and experiential experts' homes, where preferred. Meetings lasted between 40 and 60 minutes. Groups varied in size from two to six attendees depending on availability. Membership of the coproductive group changed over time and continuity varied between individuals with tenure of between 1 and 4 meetings. Resultingly, those involved in the analysis phase were largely different individuals to those involved in the initial stages. During the initial series of meetings, the focus was on shaping the study design, ensuring that implementation was appropriate for the planned participants and in crafting the participant information. This was achieved through discussion between group members. My role vacillated between contributor and facilitator, drawing the discussion towards the pertinent topics and providing background information, where helpful. Discussions were often broad ranging with all attendees contributing differing experiences and perspectives. The group dynamic varied depending on the individuals present but an ethos of equals collaborating was fostered and maintained – there was a sense of peers working together to problem-solve.

During the analysis phase, fully anonymized and de-identified excerpts of the study participant interview transcripts and experiential statements were debated with non-participant coproductive experiential experts (this aspect is explicitly included in the information and consent for participants). The intent, as described was to either corroborate interpretation or extract further or alternative meaning. This approach enriched my interpretative efforts by increasing my foreknowledge and in turn the relevance and quality of the findings.

Implementation of the principles of coproduction is challenging in practice (Farr et al., 2021) and Farr's description of the premise of '*working toward*' coproduction resonates with my experience. The coproductive impact is explicated later in this and the subsequent chapters.

Echoing this same premise with the study participants within this study; where participants were interviewed more than once or where participants expressed an interest in the findings then their own experiential topics from their prior interviews were shared with them. The aim of this was again to harness experiential expertise and to provide alternative perspectives and / or authenticity to the findings.

Methods

The practical aspects of the study in terms of design, implementation, recruitment, data collection, analysis and ethical considerations are presented in this section. The methods employed have been shaped by a multiplicity of factors. Firstly, the literature review establishes this as the first inquiry of this nature with pwMS, as far as can be determined. This aligns with the premise of IPA's value in unexplored territory, in addition to IPA applicability to emotionally laden, experiential health related topics (Smith et al., 2009). Whilst IPA methodological literature (Smith et al., 2009) has influenced the overarching methods employed, coproductive expert experiential input has significantly shaped study practicalities, design, documentation and implementation.

Eligibility criteria

As the aim of this research is understand the lived experience and meaning of research participation for pwMS the eligibility criteria reflect this;

1. Adults with MS (over 18 years)
2. Taking part (or considering taking part) in an MS research study
    a. at any stage of the primary research study
        i. pre-consent
        ii. enrolled in the MS study – early or established
        iii. nearing study close
        iv. prematurely leaving the study for any reason
        v. following planned or unplanned study cessation
3. Able to speak English

Sample size

There is considerable debate in the literature regarding the number of interviews required for an IPA study for academic dissertations or doctoral theses. For IPA the premise of less is more (Hefferon & Gil-Rodriguez, 2011) is frequently encountered and Smith (Smith et al., 2009) suggests around 6 interviews for a Professional Doctorate. Rather that aiming to achieve saturation (Smith et al., 1999) the number of interviews is guided by the richness of the findings within those accounts. Once the research aims have been met and once a *'suitably persuasive story'* (Brocki & Wearden, 2006) has been told then the data is deemed

as sufficient. As explicated earlier, the intent within this study was to conduct between six and ten interviews with three to eight participants.

Participant Identification and Recruitment

Purposive sampling was employed in order to recruit a homogenous group of people who can provide insight into the specific experience of interest. Recruitment and participant interviews spanned approximately 24 months, which was extended due to the impact on recruitment of the SARS2-CoV19 global pandemic.

MS research practitioners and MS research investigators (neurologists) at the local MS centre identified and approached MS research participants with the ethics committee approved study invitation and Participant Information Leaflet. Those agreeable to considering participation in this IPA study could either:

a) Contact the researcher (contact details within the invitation letter) / or

b) Be contacted by the researcher **if** the invitee has opted for this approach and provided contact details

Potential participants were guided to take as much time as they needed in order to fully consider and to consult with friends or family whether or not to take part. Potential participants were offered a telephone call or face-to-face meeting to discuss the study. If happy to proceed, then the opportunity to complete the informed consent process was agreed. At this initial meeting participants were able to discuss further, ask questions, to delay or defer or to opt out entirely, without detriment or ill feeling. For face-to-face interactions refreshments were offered and travel costs reimbursed.

Data Collection

Aligned with the exploratory aim of the study and the selected methodological approach the data collection method is designed to be able to gather a rich first-person account of the phenomenon in question – the experiences of and meaning for pwMS taking part in research. Semi-structured interviews are widely considered as the most suitable means of generating an in-depth account with the participants and are the mostly widely employed data collection approach for an IPA study (Smith & Nizza, 2022). Although focus groups were contemplated during coproductive discussion, it was also mooted that this approach

could have impeded the idiographic intent of the study and could potentially stifle expression of disparate views, which is acknowledge in research participation literature (Irvine et al., 2009).

The longitudinal nature, the timing of interviews relative to the primary research together with the loosely structured interview schedules also arose from coproductive discourse between the researcher and non-participant experiential experts. Where possible, study participants were interviewed more than once to seek to understand the experience in greater depth and how participant experience and meaning may change over the time-course of the study, which aligns with some of the qualitative research participation studies in the literature review section (Cox et al., 2011; Harrop et al., 2016; Lawton et al., 2003). Participants could be at any stage of the primary MS study in which they were participating; at the start of their MS research journey, early or established within the study, nearing completion of the study, or in follow-up having recently completed their involvement.

Prior to the restrictions associated with the SAR2-CoV19 global pandemic, participant interviews were conducted face-to-face in the location of choice by the participant. Protocol amendments were subsequently submitted and approved permitting all participant interactions (from consent to interviews) to be conducted by phone, which has been approved by both university and NHS ethics committees. Ethical issues associated with location will be discussed later in the section.

Interview schedules

Aligned with an in-depth exploration of a phenomenon of import, interviews lasted between 40 and 80 minutes guided by the participant's discourse. Interviews were digitally recorded and transcribed verbatim by the researcher before undergoing an idiographic, inductive and iterative analytical process concordant with the IPA approach described by IPA pioneers Smith and colleagues (Smith et al., 2009).

Four semi-structured interview frameworks were coproduced with experiential experts to reflect the different stages of the primary study in which the pwMS participants were involved; see table 4). The interview framework was loosely structured and designed as a nominal guide to encourage participants to tell their stories freely, and in their own terms, without judgement or pressure, aligned with the participant led nature of the IPA interview

(Eatough & Smith, 2017; Nizza et al., 2021; Smith et al., 2009; Smith & Osborn, 2003; Smith & Nizza, 2022).

1) **During the decision-making period for the primary study (Pre-consenting for the primary MS study)** If you are comfortable to please can you tell me about your MS? Can you talk me through how you found out about the study? What do you think taking part in a research study might be like? What does the research study mean for you? What thought process did you go through in deciding whether or not to take part? Did you involve anyone else in the making the decision whether to proceed with the primary study, or not?
2) Prematurely leaving the primary study for any reason. Please talk me through what has happened since we last spoke? If participant became ineligible to continue with the primary study - How were you told that you would not be eligible (suitable) to continue with the study? Can you share with me how you felt when you found out (or decided) that you wouldn't be continuing with the study? Has your opinion of research changed? Has your view of your research doctor or nurse changed? Can you tell me in what ways it has been a positive or negative experience for you?
3) Early stages of the Primary Study/ Established in the study Please tell me about your experience so far of taking part in the study How is taking part in the study impacting on you? your family? Tell me about the positives and negatives? How do you feel about the study (& study staff)? If you can think back to what you said to me before you took part – is it what you were expecting? in what ways? Does taking part change how you feel about your MS? In what ways?
4) At the end or during the late stages of the primary study Please tell me about your experience of taking part in the study? How is taking part in the study impacting on you? your family? Tell me about any positives or negatives? How do you feel about the study (& study staff)? in what ways has this changed over time? If you can think back to what you said to me before you took part – is it what you were expecting? in what ways? Does taking part change how you feel about your MS? In what ways? How do you feel about the study coming to an end/ having ended?

Table 4: Coproduced Semi-structured Interview Guides

Field Notes

Aligned with the need for reflexivity in the enactment of an IPA approach, as expressed earlier in this chapter, I have captured field notes during, immediately following each interview, and on reflection of the content during the transcription process. These notes constituted situational context, thoughts, reflections, concerns and perceptions – essentially any detail that I considered could aid transparency and reflexivity in the interpretative process. These records were used to consciously work through, recognise, document and bracket preconceptions, and to best ensure that the interpretation is grounded in the collected data, accepting that this cannot be achieved completely. I intentionally and concurrently challenged and embraced the role of 'self' throughout the conduct and interpretation of the study, aligned with the principles of reflexivity (Brocki & Wearden, 2006). Similarly detailed notes were also captured during engagement with experiential experts at the analysis stage which were repeatedly accessed during analysis and writeup stages alongside all other sources (including audio recordings, transcripts, peri-analysis records, field notes).

Data Analysis

The interview outputs were analysed applying the principles of IPA. The basic premise in IPA is to move from the descriptive to the interpretative - *'IPA starts with but should go beyond standard thematic analysis'* (Brocki & Wearden, 2006). Notably, the exact approach is not prescriptive and different researchers have applied a range of techniques (Brocki & Wearden, 2006; Smith & Nizza 2022). As described earlier, Smith (2009) guides that the interpretation is based from within the text itself, not invoking pre-existing theoretical frameworks (Brocki & Wearden, 2006; Smith et al., 2009).

Although the process is described below in linear terms, in reality this belies the complexity of iterative engagement with each interview recording, the transcribed text and the essence of the interview itself, captured in audio recordings and detailed contemporaneous field notes and including engagement with coproductive experiential expert opinion. The analyses at each stage comprise iterative inductive rounds of interpretation.

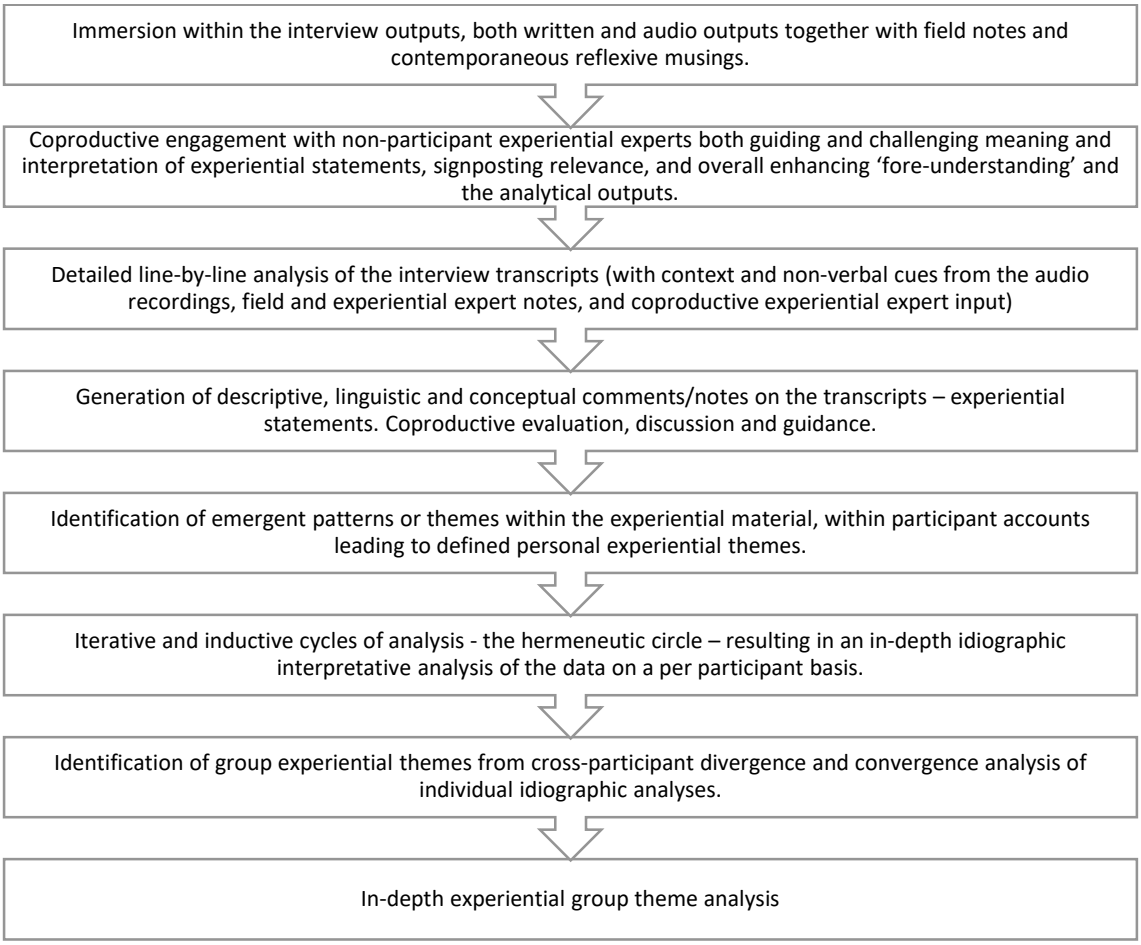


Diagram 4: Interpretative Analytical Process

During this analytical process care is taken to consciously recognise, explicate and bracket or counter my own emergent preconceptions during the identification of experiential topics and themes (Brocki & Wearden, 2006) as described in Chapter I, and within the Bracketing and Reflexivity Section earlier within this chapter. Coproductive discussion further supported recognition, identification and bracketing of discernable preconceptions and bias, whilst accepting my role as the analytical instrument with ever evolving fore-understanding as the series of analyses progressed.

Ethical Considerations

Research ethics refers to the moral principles guiding all aspects of research, from its inception through to completion and publication of results and beyond (Jonsson & Bouvy, 2018). For this study, in addition to a participant-centred approach throughout all stages of the research, ethical considerations have been incorporated into the ethics committee

applications and within the participant information. Coproductive input guided suitability of the information, practical aspects of taking part and mitigation of potential burden for participants.

Potential participants were only identified and approached by members of the direct care team or dedicated research team and were given the opportunity to discuss the study without providing their name or contact details. Those approached were completely at liberty to act or not act according to their preferences.

Participants were able to select the location of interviews for convenience and/or for privacy preferences. Participants were asked if they were comfortable speaking in the chosen location before continuing. The intent of this is both practical to enhance the coproductive nature of the narrative production in order to reflect the relationship of equals between the researcher and the participant. Only as many interviews were conducted as required to meet study objectives – all interviews conducted were included in the analyses.

Participant physical, psychological, and emotional needs have been paramount at all stages of the research. If a participant became upset by information they shared, this prompted a break in the interview with the option to cease the interview either temporarily or permanently. Further, participants could be signposted to appropriate professionals as required for medical or psychological support.

Strict confidentiality and privacy were maintained at all times for all study participants. No identifiable details of participants (or carers) were shared. All information, including transcripts and analyses were fully anonymised and de-identified. All data were held securely on password protected secure devices. Interview recordings were held as audio files on a password protected and encrypted digital voice recorder. Electronic documentation was accessible only by the researcher via a password protected laptop and secured file storage was protected by multi-factor authentication. Hard copy data, including printed anonymised de-identified transcripts, working analyses and participant consent forms, were stored in a locked cabinet to which only the researcher had access. Short written excerpts from interview transcripts shared with coproductive experiential experts in order to facilitate the interpretive process were fully anonymised and de-identified. All interview notes, recordings, transcripts and working documents will be destroyed after the project and ensuing publications have been completed. These measures and assurances

were described within the university and NHS ethics committee applications and within the participant information.

The PIL included the option for participants to have someone with them during the research interview if they wished. Jayne was accompanied by her husband Phil and they both actively engaged in the discussions. As their dialogue was so interwoven Phil also agreed for his input to be included in the analysis, essentially proving an emic perspective alongside Jayne's. Given the degree to which the dialogue was intertwined, on a practical level it would have been impossible to have excluded Phil's input from the transcript and subsequent analysis. Although Phil did not have MS, this approach felt appropriate because the research participation was described very much as a joint endeavour between Jayne and Phil, throughout the interview. This was not considered to be discordant with the ethical approval as being accompanied within the study was outline in the PIL, and Phil as a free-speaking individual willingly provided his perspective. In order to capture Phil's permission for his contribution to be specifically included he also provided written informed consent. Phil had been present during the informing discussion at the start of the meeting and had asked questions and sought clarification throughout the process and so was conversant with the aims and intent of the research.

Chapter IV

Findings

Introduction

This chapter starts with an overview of participant recruitment and challenges. Contextual consideration and reflexive observations of the participant semi-structured interviews are presented, before moving on to introduce the participant stories and personal-experiential-themes. A detailed examination of the group-experiential-themes across the full dataset is presented in terms of divergence and convergence, evidenced with idiographic excerpts from each participant interview. Findings are presented as tabulated and narrative syntheses.

Participant Recruitment

During the recruitment period approximately ten participants of MS research, identified by the MS clinical and research team at the recruiting centre, expressed initial willingness to take part in this study. Each potential participant was provided with the ethically approved study invitation and Participant Information. People approached with study literature had the option to provide contact details and permission to be contacted, to make contact directly with the researcher, or to take no action. Of the ten who expressed initial interest, four participants have proceeded to provide informed consent and to be interviewed, of these two participants have been interviewed twice (six interviews in total). Of the remaining potential participants, two made initial contact but subsequently conveyed that time constraints prevented further involvement. The remainder did not make contact nor provide contact details and no reasons were communicated for not wishing to proceed further.

The SARS-Cov-2 global pandemic has had significant impact on research in general. The clinicians who have helped recruit for this study have not been physically present at the research centre (hospital) for significant periods of time during the pandemic. Further, my observation is that under the additional challenges that a global pandemic brings, people are justifiably generally less willing to take part in discretionary activity. To remediate the impact of SARS-CoV-2 on study recruitment I submitted and received approval for a study

amendment to permit telephone consent and telephone interviews. Two interviews were conducted in person and the remaining four have been by telephone.

To protect participant identity and to avoid designating people as study numbers I have assigned each of the participants a pseudonym; Martha, Jayne (and Phil), Eve and Jude. Where the clinical care neurologist or research clinicians are referred to in the participant narratives they are designated as Dr Proctor, Dr Wells, Dr Fletcher, the neurologist' or the study nurse and 's/he' or 'they' are substituted for gender specific clinician pronouns.

The Analyses

The interpretive analysis comprised of rounds of phenomenological scrutiny (Forrester & Sullivan, 2018) and interpretative interrogation of the transcript, field notes and recorded interviews as described in the methods section. As previously indicated, I have invoked Schleiermacher's perspective as expressed by Smith (2009) in adopting a holistic approach. Non-verbal communication, demeanour and intonation gleaned from field notes and the audio recording each provide a richness, and necessary closeness to the participant's sense-making (Eatough & Smith, 2008) as far as I am able to achieve. Each source is revisited repeatedly during the analyses and write-up in order to ensure alignment with the original meaning conveyed by participants.

Each participant has their own unique experience of trial participation. IPA, as an idiographic approach, honours the individual lived experience but seeks convergence and divergence on an inter-participant basis. Whilst this approach necessarily enables focus on themes of greatest significance to the research question, it also creates a dualistic tension and can (and does) feel like a betrayal of the idiographic focus integral to IPA (Noon, 2018). I align with the premise that nuances and idiosyncrasies of each account could be lost if we 'go to early' with the prioritisation of overarching themes *across* rather than *within* individual analyses. IPA pioneers (Smith & Nizza, 2022; Smith & Shinebourne, 2012) suggest that it is preferable to start each participant analysis *'from scratch'* rather than utilise themes from the first transcript to shape the subsequent analyses. Accordingly, each participant narrative was analysed individually and independently of the others, deliberately bracketing findings from one analysis to another. Whilst the methodological approach to the analysis was consistently applied, the content, the idiographic context and individual experience of the

participants shaped the individual outputs. In adopting this approach, I clung to idiographic spirit for as long as possible within the analysis. Following this ethos to the fullest extent, I initially presented my analyses as a series of IPA case studies fully laden with the subtleties and nuanced tones of each participant voice before coalescing themes only at the last moment before moving into the discussion section. I contended that this most transparently represented the individual stories and experiences of the participants whilst fulfilling the cross-participant evaluation at the discussion stage. With academic reflection (and cognisant of word count restrictions) I revisited this approach, moving to present the findings as group-experiential-themes across the full dataset, whilst maintaining an idiographic emphasis. Once all interviews had been separately analysed and an interpretive analysis narrative constructed for each, only then personal-experiential-themes from each individual analysis were clustered to the cross-participant themes across the full dataset. This in turn provided a scaffold for the exploration of convergence and divergence across individual analyses.

Introduction to The Participants

This section starts with a tabulated overview (Table 5) of the four participants within this current study. This is followed by a summary of each of the individual participant analyses in order to help the reader first appreciate the ideographically grounded case studies, before moving on to the cross-participant evaluation; the aim of which is to compare participant experiences whilst retaining an idiographic focus in showing how each participant expresses commonality. Excerpts from participant narratives are reserved for the cross-participant analysis to retain flow and to avoid duplication. Judicious use of participant excerpts in the cross-participant-analysis (group-experiential-analysis) transparently tethers interpreted meaning to the relevant participant phrases.

Study Pseudonym^	MS Subtype	Interviews & medium	Age range	Ethnicity	Years since diagnosis / Years in Study
Martha	RRMS	1 – in person	35-44	White British	2 / 2
Jayne (& Phil*)	PPMS	2 – in person/ by phone	55-64	White British	2 / 4
Eve	RRMS	1 – by phone	45-54	White British	5 / 4
Jude	PPMS	2 – by phone	45-54	White British	13/ 0.5
RRMS = Relapsing Remitting Multiple Sclerosis; PPMS = Primary Progressive Multiple Sclerosis					
*Note1: Phil, Jayne's husband does not have MS and is not a participant of MS research - however he has been closely involved with Jayne's trial participation experience and consented to his essentially emic perspective being included as their narratives were closely intertwined.					
^Note 2: Each of the participants has been designated a text colour to differentiate between participant interview excerpts within the analyses. Key phrases in the interview excerpts are **emboldened**.					

Table 5: Participant Overview

Martha

The first interview took place in December 2019 at the clinical research facility within a local tertiary hospital. I had previously held a role within the research facility several years previously and so the context was very familiar to me. As the team knew me, Martha and I were left alone in the clinic room during the interview. This could potentially be less inhibitory for the Martha sharing her story. Further, my being trusted by the study team may have, in turn, helped the participant to build some trust in me. This would seem to be supported within the findings as she herself feels part of the team, which will be elaborated later.

Martha was receiving an intravenous infusion and would be *in situ* most of the day. Martha was in her mid to late forties and had been in the trial for almost two years. Martha was welcoming but was quite reserved which caused me some trepidation as the interview proceeded as I felt that I was struggling to build rapport. At times I reflected whether she might be sharing what she thought was expected rather than her actual beliefs.

During the interview, I feared that there was potential for the dialogue to not have appropriate richness or depth. For example, on exploring with her the decision to participate in the study she described it as a *'no brainer'* which I construed at the time to indicate that there was little significance of the study for her. Later, the meaning of this term, as I subsequently understood it to be, became apparent.

Reflexive Note: At that time my positivist thinking came to the fore; I had concern that the null hypothesis was true – that taking part in research is not a significant experience nor of particular meaning to this participant. I bracketed this fear and continued the interview.

Upon peeling back the layers of Martha's narrative, themes emerged during the phenomenological analysis which, during the cycles of interpretative analysis, translated into the significance for and meaning of trial participation for Martha.

The findings developed as four key strands (personal-experiential-themes) arising from multiple experiential topics. Several aspects represented precarious counterbalances and intricate dynamics between her status within the trial versus her status outside of the trial. In the spirit of IPA in moving between the whole and the part, these themes together appear to constitute the MS trial environment as a safe haven for Martha. The study environment is somewhere where she feels a sense of belonging, where she is in a fortunate position, having been deemed worthy of being fought for, and where in turn she can place her trust.

Personal-experiential- themes as presented in Table 6, are each represented in the final overarching analysis of the cross-participant themes.

Experiential Topics	Personal-experiential- themes
Deserving, being fought for in study, versus being cast aside in work	Worthiness
Part of the system, being no trouble	Belonging
Having better treatment than others	Privilege
Being able to rely on the doctor and the team, believing	Trust
Mourning the past, present impact and fear for the future	Defence against fear

Table 6: Personal Experiential Themes for Martha

Jayne (and Phil)

The first interview with Jayne was conducted in a café of Jayne's choosing (an option included in the participant information). The unfamiliarity of café setting caused me some advance angst; would there be tables available? Would there be space to write? Would it difficult for Jayne to share her story? Would it interrupt the flow of discussion? What if she became upset in a public place? My concerns about the venue, whilst not unfounded, manifested as different issues. I had arrived early and set myself up at a table near the door for easy access in case she had a level of disability that could impact her navigation through a busy cafe. The café was partially full; my concern about being overheard reverberated in my mind. The arranged time of meeting passed. Had they been and gone, like a failed blind date, or was that maybe her in the corner and I'd missed their arrival. I was on edge. My phone pinged; they were running late. Reassured I awaited their arrival with anticipation.

In the run up to the interview, Jayne's communication consistently employed the first-person plural and so I had come to expect that the second half of 'we' was Jayne's MS. I was looking forward to meeting them both. The actuality was that Jayne and her husband, Phil came as a package deal. From interview discussion they are both in their mid-fifties, speak with eloquence and come across as socially adept and jovial. The café they had chosen is a favourite of theirs and they had no such qualms about the setting – this was a trip out. Jayne and Phil are close, as well as being married (to each other) they are clearly good friends. The communication between them is full of banter and memories; they finish each other's sentences and frequently speak over and for each other. Because of this intertwined dialogue and their joint dynamic, the interview is with both Jayne and Phil, both of whom consented (in writing).

The ensuing interview dynamic was good; the sound quality was not. The interview felt appropriately on equal terms, that between the three of us we were coproducing the narrative. The café was full of lively chatter, coffee machine hissings and scraping of chairs. These distractions were accentuated on the audio recording and together with the entwined dialogue the transcription was challenging to produce. By the time I had a full and accurate transcript I had listened to the full audio interview multiple times and to each word or phrase, often obscured amongst the background clamour, repeatedly. Jayne and Phil's account was very much embedded in my head.

Reflexive Note: At this stage in the analyses, I learn that it is difficult to *not* make comparisons between the two interviews to date. I am consciously bracketing divergence and convergence in order to focus wholly on the trialogue between Jayne, Phil and myself, in its own right. For example, I noted that the term 'no brainer' had been used in the first two interviews, but pace and tone of the first two interviews were notably different. I resisted the temptation to draw early parallels. I retained an idiographic focus reserving exploration of similarities and differences across the full dataset until all interviews had been analysed separately.

In Jayne (and Phil's) case the experience of trial participation is multifaceted. Aside from Jayne having PPMS, they present their life as being largely uncomplicated and comfortable. Jayne had experienced a long lead-time of over ten years before receiving what was subsequently a not unexpected diagnosis. At the time of writing, there is currently no available disease modifying treatment (DMT) option for established primary progressive MS. The only 'treatment' choice they have been faced with following diagnosis is to either take part in a trial of a high-dose vitamin that Jayne has taken previously taken, and that they are both familiar with, or not.

Jayne expresses multiple layers of positivity. Akin to sedimentary rock, distinct seams emerged during analysis, representing different aspect of trial involvement meaning and experience. Some of these themes are closer to the surface, and more evident whereas others were exposed further into the interpretative process. These are rudimentarily ranked in the table below in order of their emergence in terms of their explicitness and tangibility within the narrative, rather than, necessarily, the degree of significance to the participant.

Experiential Topics	Personal-Experiential-Themes
Interest, adventure and advancing treatment	Altruistic satisfaction & fulfilment
Hope for therapeutic gain	Optimism
Being in the system, not being forgotten	Care
Doing something, being active in own care	Investment
Having a decision to make, striving for access	Empowerment

Table 7: Personal Experiential Themes for Jayne (and Phil)

It appeared to me that they both Jayne and Phil derive significant meaning from being a part of the MS study. Their gratification and feelings of altruism are partly contingent upon the

potential for benefit, low risk and lack of significant inconvenience. They also gain personal fulfilment from being involved on an intellectual level at the forefront of science. They enjoy the trial partly as it provides variety, and a surrogate role for Phil's previous role in society. Jayne expresses the hope to gain additional therapeutic benefit from the trial and they both have a sense of being in the system receiving additional care. This would stand them in good stead should Jayne's condition worsen, or other therapeutic options were to become available. Phil expresses his hope that the trial will give them access to her results in order to better understand the course of her decline, for him to make better sense of the future. Their involvement provides reassurance and helps to stave off fear and uncertainty of being left to fend for themselves whilst living with an incurable and untreatable progressive neurodegenerative condition. In the absence of other treatment choices, it was of significant import to Jayne to have the option for taking part in the study. Being in the study legitimises the treatment that she was already taking and allows her to feel empowered and invested in her own care. The trial was subsequently terminated prematurely, having failed to show measurable efficacy. I interviewed Jayne again following the cessation of the study which I analysed independently to the first.

It was at the start of Jayne's second interview (conducted by telephone) that I learnt that the trial that she had been part of had been terminated early several months previously.

Reflexive note: Admittedly I was frustrated that I had not had opportunity to speak with Jayne around the time of the trial termination. I resolved to bracket my disappointment from the discussion and to avoid supposition of how she might have felt at the time, and how the findings may have differed if the interview had been contemporaneous to the trial termination.

The first interview with Jayne has been together with Phil, her husband and who had provided an additional layer of insight whereas this time the interview was with Jayne alone.

Reflexive note: Jayne being alone on the call was aligned with my expectations, and neither did Jayne suggest that Phil joined, which would have been more practically difficult by phone. In retrospect I wonder if this was more purposeful on Jayne's part, and how Phil may have felt about not being included. At the start of the call Jayne closed the door as Phil was making a lot of noise. At the time of writing, I now reflect whether this was intentional to effect physical exclusion of Phil, despite his best efforts to make his presence known or whether Phil was simply busy and not interested in joining.

In the intervening period between the trial closing and the time of interview, it is expected that Jayne may have processed, reflected upon and made sense of her experience (Smith et al., 2009) of the trial ending. Given the time interval there may be less of a raw reaction at this later time-point. The interpretation will focus on the account that Jayne shares and will avoid speculation as to what the reaction might have been at the time.

Personal-experiential-themes of loss, relief and resignation were identified are exemplified in the analysis. In addition to multiple strata of loss, there are complex interplays between the different facets of Jayne's reaction to the study terminating; this is suggested by areas of inconsistency in her account. IPA is recognised for its strength in in illuminating ambiguity or tensions (Smith & Nizza, 2022). Variation between Jayne's two interviews support the premise of rationalisation contributing to her processing of the experience of the trials meaning and its subsequent termination.

Experiential Topics	Personal-experiential-themes
Disappointment, unfinished business, disempowered	Loss
Decision avoidance, balance of risk	Relief
Stoicism, rationalisation, pragmatism	Resignation

Table 8: Personal Experiential Themes after Trial Termination for Jayne

Eve

Eve opted for telephone consent and interview. I felt a good connection with her over the telephone. She is in her fifties, married, no longer works and lives close to me.

Reflexive note: Recognising that having close geographical proximity to Eve could give rise to assumptions on my part. I take care to evaluate my engagement with Eve and the analysis for any such bias – thus consciously seeking to, as far as possible, avoid or recognise and bracket any such beliefs that could influence my perceptions.

For Eve the MS treatment study came along at the time she needed a solution to her dire health situation, when she needed salvation from the MS ravaging her body.

Eve consistently expresses overwhelmingly positivity about the support that she received from the research team. She is willingly in their hands and seems to have abject faith in them. She feels rescued and subsequently nurtured by these gatekeepers of her care. Eve appears unerringly trusting that the research team has her best interests at heart and that they are invested in her personally. These plumes of commendation for the research team

belie some of the challenges that Eve faced along what was ultimately a solo journey. In what was an unexpected 'door-handle' conversation, as the interview was coming to a close, Eve shared her feeling of being unsated by the research in terms of her own individual journey, that her input, what she gave of herself was not fully reciprocated.

Eve's experience distils into two key but opposing personal-experiential-themes; she is 'in their hand's but ultimately alone on a 'solo journey'.

In contrast to other analyses but aligned with IPA's idiosyncratic approach, I felt that Eve's personal-experiential-themes are best captured as a rudimentary Venn diagram (Diagram 5) in an attempt to visualise and express the non-linear relationships between the personal-experiential-themes and experiential topics.

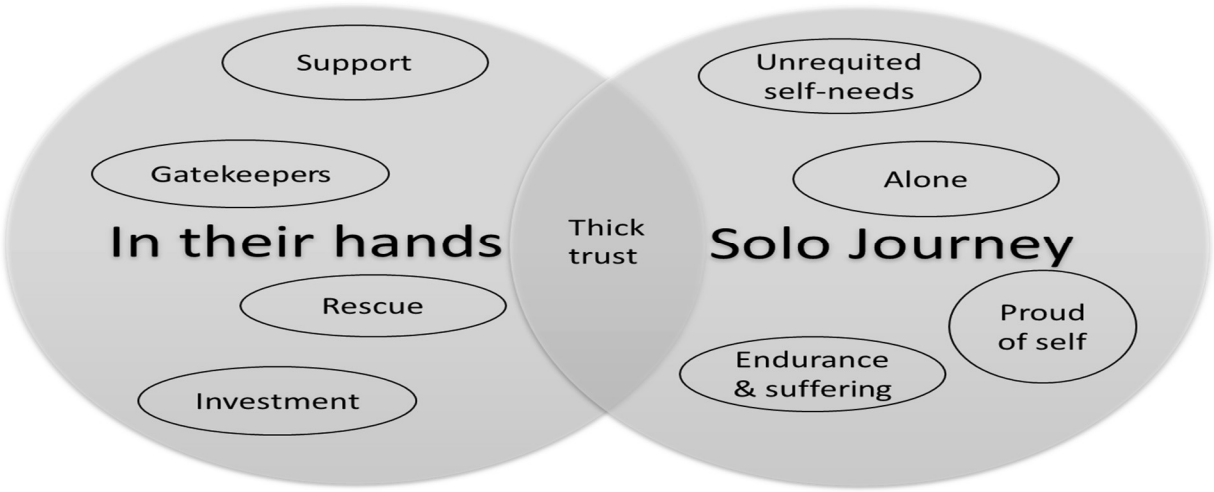


Diagram 5: Personal-Experiential-Themes for Eve

Reflexive Note: Eve's analysis has been the most difficult to accurately capture what I understand to be the meaning Eve conveyed during the interview. At times I felt that I lacked the (psychological) terminology that might more succinctly express and explain her perspective. Despite this limitation I have diligently striven to ensure that her meaning is expressed fully and accurately - as with all the interviews. There is the old adage 'never let the truth get in the way of a good story' (commonly attributed to Mark Twain, an American 19th century author) – here I taken the opposing stance in not letting a good story get in the way of the truth, as I understand it to be.

Jude

Jude seems to express her experience of research participation openly with her opinions clearly conveyed. She uses repetition to reemphasise her beliefs and remains consistent throughout the interview.

Reflexive note: Jude seems open and free speaking; as a result I had a feeling of perhaps knowing her more than I do. I had to consciously remind myself that I do not know her, that I merely recognise something in her that resonates. I consciously take care to recognise and avoid assumptions.

I relish the pace of Jude's account - I engage with the recording and transcript with focus and awareness to ensure that her transmitted energy does not disguise other potentially veiled meaning. Aligned with the IPA premise of open interview questions and 'wandering together' (Eatough & Smith, 2017; Kvale & Brinkman, 2009) much of the interview is off topic for the study but clearly of great import to Jude. Germane themes are obvious during the first round of analysis and further intricacies become apparent as I pare back the layers of her account.

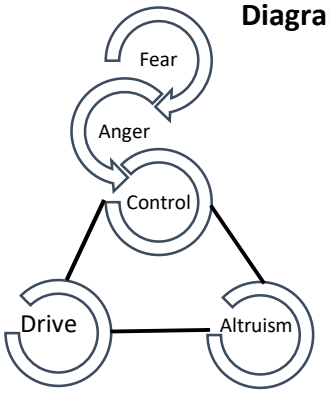
Reflexive note: Jude's meaning feels close to the surface; I find myself making an erroneous assumption that her energetic and fast-pace interview will require less extensive interpretive rounds in order to draw out the meaning, in contrast with the previous participant interview. Recognising this assumption, I ensure that I take the same painstaking methodical stepwise approach to the analysis.

Nobody puts baby in the corner

Significant emergent themes of Jude's experience of research participation were identified during analysis as control, drive and altruism, which are exemplified in the cross-participant

analysis. Within control are the subthemes of anger, fear and gaining or regaining control over the disease – Jude expresses how the trial makes her feel in particularly powerful terms. I use the term 'drive' to capture both determination and persistence – the former indicating intent and the latter, action. I again felt that Jude's personal experimental themes were best depicted in an idiographic representation as can be seen in Diagram 6.

Diagram 6: Personal Experiential Themes for Jude



Jude describes a lengthy campaign to identify and access a suitable trial. When she was finally offered an appropriate research opportunity the SARS-CoV-2 pandemic caused the study to be pushed out of her grasp at a time when she was feeling her condition decline due to the pandemic restrictions. Jude detests the disease that is threatening her independence. She is angry and fearful of where her disease might take her. Consequently, she is driven to take action in order to dominate her diseases. Jude feels empowered by being involved in the study; the trial is a mechanism to help effect some control over her condition both from a physical perspective (therapeutic efficacy) and from a psychological perspective (feeling of control). In the course of the interviews, Jude consistently expresses a philanthropic perspective; she repeatedly refers to the impact on other people during both interviews. She referred to others being impacted by chronic diseases, the effects of lockdown and the potential for wide-reaching therapeutic benefit resultant from the trial drug being tested.

I first meet Jude when she has recently started on the trial, and then again when she is more established within the trial. With the second interview the key themes of altruism, control and drive from the first interview re-emerge but with differing emphases shaped by her current lifeworld context. Jude was badly impacted by a viral influenza, and then contracted

SARS-CoV2 some months later. The initial viral infection led to a significant relapse on her right hand which thankfully resolved with oral steroid treatment. In this context, the trial as a means of providing her access to clinical care became particularly important. This unanticipated benefit for Jude provides a notable contrast with what Jude increasingly frames as unsatisfactory levels of clinical care that she has experienced previously. Jude's experience of this facet of trial participation expressed during her second interview contributes meaningful insight to the group-experiential-theme of 'Deriving Benefit (and harm)' and Human Connectedness. Jude's generous outlook is reemphasised and the importance of relationship with the study team starts to become significant for Jude. Additionally, I am also able to make an interesting observation that Jude has quickly normalised the trial as part of her self-representation when recording a workplace podcast to mark UK Disability Awareness week.

Cross-case (Group) Experiential Analysis

Having conducted meticulous analyses of each participant narrative in their own terms, through my lens as the analytic instrument aided by experiential expert copoductive input, I now proceed to consider convergence and divergence across the full dataset. The individuals involved in this study are each very distinct, with significant differences in their drivers, circumstances, expectations and experiences of research participation. Each individual account has been considered independently and in detail that respects the specific and personal contribution of each participant. These nuances and the subtleties validate, or rather, celebrate the idiographic approach inherent in IPA by portraying the person's ways of being in the world (Eatough & Smith, 2017). However, by comparing across individual analyses, it also exposes the different ways in which participants each experience the same phenomenon.

In order to visually illustrate convergence and divergence of experiential themes across the full data set I have grouped experiential themes of similar domains from the individual analyses and attributed the relative significance of each of these themes for each participant. As the personal experiential themes for each participant have been identified via an idiographic approach they do not map exactly between participants and so a 'best fit' approach is applied where similar domains are clustered to provide the group-experiential-themes. The ranking (from '+++' to '-') indicates the level of significance of that group-experiential-theme to the individual as determined from the idiographic analysis of the individual participant's account. The ranking ranges from '+++', indicating highly significant to the individual, to not significant or absent as represented by '-'.

The three group-experiential-themes are defined below:

1) Trial derived benefit or harm
2) Human connectedness

   and
3) Self

The group themes are then expounded below with thoughtful inclusion of participant excerpts. In this way the findings flow from trial→people→ self.

Group Experiential Themes	*Deriving Benefit (and harm) - TRIAL*				*Human Connectedness - PEOPLE*		*Self*			
Cross- participant Clusters	Clinical Impact	Control (psychological)	Enjoyment	Adverse effects / harm	Trust	Nurture	Isolation	Self-worth	Altruism	Activation/ Self Efficacy
Trial provides	Clinical Care, therapeutic benefit	Defence against fear, hope, optimism	Enjoyment, fulfilment,	Negative impact (side effects, psychological distress etc)	Trust, thick-trust, over-trust, gatekeeping	Belonging, support, nurture, cared for, rescued	Solo	Self worth, self-need worthiness Privileged, fortunate, proud	Altruistic satisfaction, helping others, scientific advancement	Empowered Action control Drive, Activation
Martha	++	++	-	+	+++	+++	-	+++	+	-
Jayne (& Phil)	+++	++	+++	+	+	++	-	+	+	+++
Eve	++	++	-	+++	+++	+++	+++	+++	+	-
Jude	+++	+++	-	+	++	+	+	-	+++	+++

***KEY**:* Relative significance of theme for each participant:
'+', '++' and '+++' = of low, medium and high significance to the individual participant, respectively
'-'= absent,

Table 9: Cross-Case / Group-Experiential Themes

GROUP-EXPERIENTIAL-THEME 1

Trial Derived Benefit and Harm

Participants within this study each emphasised a notion of general positivity associated with trial participation early within their narratives. This has the feel of the participant responding to their perceived anticipation of the interview intent. Whilst general positivity is a truism, on individual analysis this positivity encompasses different facets and meaning for each of the participants, as will be expounded within this section. This aligns the idiographic underpinnings of IPA whereby individual express the commonality of the experience in particular and different ways (Smith & Nizza, 2022).

Enjoyment

I understand from Jayne and Phil that they each derive a level of fulfilment and satisfaction, or enjoyment, from study participation that I did not directly detect within the accounts from the other participants. For others positivity seemed to have its base in other domains such as clinical benefit, hope, altruism, control, and relationship with the study team. Fulfilment and satisfaction align with the higher needs in Maslow's hierarchy described as self-actualisation; which encompasses personal growth, new knowledge, new experience and enjoyment (Maslow, 2013).

Jayne opens the topic of fulfilment with the customary statement of positivity of taking part in the research, which is a common opening statement and as described above has been understood to be associated with different meaning for each participant.

Jayne	*it's been really good and it's quite, its been quite positive. … it's generally it's been a positive experience*	*11:24*

Phil highlights numerous times, and Jayne concurs, that it is not a particularly burdensome study.

Phil	*Its not very onerous really is it, the study?*	*11:54*
Phil	*I do wonder whether your experience would be different if, if it was a more intrusive sort of research.,*	*33:54*
Jayne	*Probably*	*34:06*

Phil	*There must be some research, which is actually **quite tough** to do. And also **more onerous** in terms of timescales and things. I mean, once every three months to go to [local city] to be prodded by people. I guess **it's all right in it** ?*	*34:07*

Jayne's minimal response 'probably' in between Phil's emphatic description of the minimal impact could suggest that Jayne is slightly piqued that Phil is representing this aspect of her participation on her behalf.

Phil	*…as I say it's **not very intrusive** or **very onerous**.*	*51:10*

I understand from Phil's repetition that he feels that the low level of burden is an important aspect worthy of note which contributes to the level of satisfaction.

Jayne	*I have to take three, three things a day. **That's all**. three capsules a day.*	*13:12*
	It's not as if they take blood every time**, and you know…it's **just an hour	*48:10*

Jayne too acknowledges the low level of physical demands and minimal time commitment of the study. Whilst Jayne agrees with Phil's evaluation, she appears to be reclaiming the activity by staking her claim, that it is she that takes the study medication, and the blood taken is necessarily hers.

Mostly at the start of the trial related discussion but also reaffirmed later, Jayne and Phil each highlight their engagement with the study.

Phil	*… you're **on the edge** in the **beginning of something***	*15:12*
Jayne	*Yeah*	*15:15*
Phil	*that you **wanted to be part of** really*	*15:16*
Jayne	*…. it sounded like **quite interesting** and **quite exciting** to **be part of** research you know,*	*18.33*
Phil	*It's **very interesting***	*51:10*

Having clearly and repeatedly established the lack of physical burden, they express their relish in the interest the trial brings, the scientific intrigue and the sense of being part of medical advancement. They seem invigorated with their status of being within the trial.

Phil	*We've **asked about** them sort of like **the ongoing results** before they've **not published anything** yet.*	*19.37*

I understand from Jayne and Phil account that they feel more than passive receivers of the trial and enter into discussions with the clinician regarding availability of and publication of the trial results (in contrast to individual results).

In addition to appealing to their intellect it also provides them with a pastime and somewhere to be bringing a sense of purpose over and above their day-to-day routine

Jayne	*it's just every 3 months, off we go, … a day out, a day out in [local city]*	*52:20*
Phil	*We don't do much. We look forward to our days out*	*52: 32*

Whilst other participants each express positivity, none convey it in similar terms. As the analysis moves repeatedly between the part and the whole, Jayne and Phil's experience seems to be reflective of their lifeworld context both intrinsic to and extrinsic to the trial; low burden of the trial, lack of extrinsic complexities in terms of having time, opportunity and means of travel, and further, the opportunity for intellectual stimulation and interaction that fulfils a gap following retirement from roles that have societal status (discussed further in the third group theme). This is especially aligned with the premise of IPA's aims in understanding participants in the context of their own personal and social world (Smith et al., 2009).

Clinical impact

Whilst the desire for clinical impact from the trial treatment was identified in all of the participant narratives, it was expressed in contrasting ways throughout their respective accounts. Clinical impact, for the purposes of this study is being in *receipt* of perceived *physical* benefit related to health; therapeutic effect, clinical efficacy, clinical care and clinical assessments – related to the trial *per se*.

Increased medical oversight was clearly expressed by Jayne and Phil and also presented as especially meaningful in Jude's second interview. Within the clinical trial Jayne has four study visits per year, without the trial, Jayne would likely have only annual routine follow-up appointments with the neurologist.

Jayne	*yeah, and that's another thing. You know. **I'm having regular meetings**… It does feel as though they're sort of **keeping up with you**…*	*18.06*
Jayne	*…**instead of being looked at once a year I'm being looked at once every 3 months** … so.. and if there's a **problem** it would **show up quicker…***	*19.20*
Phil	*There's a feeling that we're **in the system**, probably, in a better way,*	*22.20*
Jayne	*Yes, yes*	*23.10*
Phil	***More so** than otherwise*	*24.07*
Jayne	*'Cause I mean, you know before … I **didn't really have much to do with anybody**. Once I was diagnosed, I had a physiotherapist came round for a few months, gave me some exercises and things like that, but apart from that, … I **didn't have contact** with anyone else.*	*26.17*

The additional assessments and evaluation of her condition within the context of the study seems to provide valuable reassurance to Jayne and Phil and to counteract the sense of abandonment outside of the trial. Previously Jayne has had contact with the physiotherapist, but which was short lived and dismissed as less meaningful as she was simply *given* exercises. They feel assured that if either Jayne's condition or treatment options change then they are in the system.

MS is a long-term neurodegenerative condition with no cure – it feels counterintuitive that the routine level of clinical care comprises infrequent follow-up, but the frequency is

directly proportional to the available interventions, and which are limited in primary progressive MS.

Jayne	***what would they <u>do</u> ??'***	*22.42*

Jayne recognises the limitations of available care and has dismissed the support of an MS nurse; the emphasis is on 'do' – there is nothing to be done.

Jayne's description of limited clinical interaction has resonance with Jude's narrative. For Jude the limited clinical intervention is a source of frustration as she repeatedly highlights the deficits in her pre-trial clinical care. During the first interview Jude had only recently started on the trial, but her reference to limited clinical care was a repeated presence in her dialogue. At this early stage she had already recognised that she'll be afforded increased clinical review within the study.

Jude	***And the fact that you're being seen more frequently***	*36.45*

During the first and second interview Jude has frequently lamented the limited time she has with her clinical neurologist to share 12 months of her health history. She has felt let down, and at times abandoned. The more frequent visits in the study counteract the limited resources she experiences in her clinical care. The impact of enhanced care really come to the fore during Jude's second interview. Having faced a disabling relapse following a viral infection Jude finds herself in need of medical attention which she approaches through the trial route rather than via her regular MS clinical care.

Jude	*So I **just rang**, cos [Study Nurse] had said to me, **'anything at all'**, and Dr Wells, **anything at all, any problems, just ring us**. So I phoned [Study Nurse] and I said , look I don't think it's a trial thing, or whether it was do with the flu….*	*1.44 (2)*

Jude seeking help via the research team resulted in a rapidly organised home-visit by a clinical MS nurse. On two other occasions during the interview Jude reiterates that Dr Wells advised for her to contact the study team in the event of any MS related issues; Jude seems to need this permission as justification for contacting the research team for help. Following this path Jude has received clinical care swiftly, efficiently and her relapse resolves with the

steroids prescribed for her. She outlines a stark contrast between her care in the trial with her prior experience of the routine clinical MS service.

Jude	*to actually sit down and **see a person**. Having **a face-to-face visit** is a lot more helpful. Now last week with me [sic] annual neurologist appointment and that was **just a five-minute phone call**.*	*26.05 IV2*
	*I was really upset because I feel **like I've just been left to rot** for eighteen months. Because I **couldn't get any help. I couldn't get any support.** I must have phoned and left messages for the MS nurses at least twelve times. Nobody phoning me back… **I don't ask for help unless I really need it. And the one time I wanted some help I couldn't get any***	*31.18*
	*Its just a **quick five minute** slot then s/he **cuts you short**. And it's like, right OK*	*41.25*

I understand from Jude's description and tone that seeing an actual person in the research setting serves to highlight the deficit in her usual care and that she is scandalised at the marked contrast between her research experience and her clinical care. The phrase 'left to rot' could be understood to mean that she feels discarded and parallels her clinical decline with decay. Jude feels disenfranchised by her limited contact and her dismissal at the close of the virtual appointment, particularly given that Jude describes herself as undemanding.

Jude appears to feel the need to justify that she did not join the trial for additional care, and that this aspect is a serendipitous but welcome unanticipated benefit.

Jude	***I didn't know that. I wasn't doing it for that**.*	*31.19*

Moreover, at Jude's recent study visit, the research clinician appears to validate her perception of her inadequate clinical care.

Jude	***I've been to the hospital last month**. And it was fine. But Dr. Wells is gonna order a ,[they] said I think we need to do another MRI scan, because I've **only ever had one at diagnosis**. So [they] said well I think what we need to do, given that you've **not had an MRI scan for 13 years**, we need to do another. So I'm waiting for that call. **You see I don't normally see Dr. Wells**.*	*24.47 (2)*

At her trial visit Dr Wells has highlighted that Jude has only ever undergone one MRI in her long history of MS, and given her recent relapse, a further scan is warranted. The inference

here is that she would not have been referred for this scan by her usual clinician and that the additional assessment is long overdue. She attributes the additional clinical assessment to now seeing a different clinician via the research team. I understand from Jude's description that she now regards her clinical care not just as scant, but as lacking now that the research visit has led her to now be assessed more fully.

In summary, within the trial setting she had ready and rapid access to face to face care. She has been listened to, supported, treated and received an additional scan (not a trial procedure) to assist with her clinical evaluation. It seems to me that Jude feels like she is finally receiving the treatment and care that her condition warrants but is reluctant to frame this directly. Whilst some or all of this may have occurred from the clinical service perspective it has been initiated and enacted through her trial involvements and she associates it as such. It is worth noting that '*regular review by an experienced neurologist'* is a defined aspect of the study in which Jude is enrolled.
(https://clinicaltrials.gov/ct2/show/nct03387670)

Therapeutic benefit

In terms of potential therapeutic benefit from the trial treatment, the findings indicate that whilst Jude understands the trial information, she concurrently harbours hope for potentially unachievable levels of clinical benefit. Eve and Martha each regard positive therapeutic impact as an expected outcome of the study treatment. This expectation is particularly prominent in Martha's account who recants numerically quantified expected efficacy levels from pre-trial discussions with the clinician. Whereas Jayne vacillates her view of therapeutic benefit adopting an alternative stance once the study had terminated as a result of demonstrated lack of efficacy across the trial.

Considering Jude's perspective first;

Jude	*this study is about slowing down progression. And if it means more time to be able to go out and buy shoes and walk about and to be able to get to the loo. So, cuz That's my worst fear Ermm then that's good. That thats good for me.*	*27.05*

I understand from Jude how important it is to her that this trial treatment might prolong the time that she has when she is able to continue normal activities such as shopping for shoes, but also key functions such as walking and going to the bathroom. She is driven by the need

to retain her independence and normality and fear of losing such fundamental aspects of life that are often taken for granted, which are further framed in the upcoming section.

Jude shares her hope that's she has been allocated to active drug rather than the placebo as she explains that it's a double-blind randomised trial.

Jude	*But in my mind at the moment, I'm just thinking, I have got **something that might make me better. …. And that I, that this is going to help to get me back to where I was pre-Covid***	*30.82*

Although Jude knows that the treatment is being assessed for its efficacy in slowing progression (that it reduces the pace of worsening but doesn't improve existent symptoms) she harbours what might be regarded as unrealistic hope that it can return her to an improved state of health.

During Jude's second interview her expression of hope of therapeutic benefit from the experimental drug is heightened as she attributes changes in her urine smell and output with the possibility of being randomised to active treatment. She has sought signs of symptom improvement since starting the trial treatment but assigns the lack of a therapeutic effect to the health issues that she has experienced over the previous months. Whilst Jude is aware and accepting of the significant chance that she is receiving placebo she remains optimistic for clinical impact.

Further exploring the concept of therapeutic benefit, Martha appreciates she has received treatment via the trial that would not otherwise be accessible to her.

Martha	*but it **wasn't on the NHS** at the time and he just said it's something that got a **better success rate to prevent any more lesions** than anything that was actually out at the time.* *Because it had a **90, 95 percent success** of preventing any more lesions*	*02:47*
Martha	*.. it's been tried in other countries, and it's been passed and y'know it's got good results. So. It's **better than some of the options**. I'd say it's **ridiculous**, some of the success rate I suppose of some of the **mainstream** medications…*	*09:44*

The research clinician has outlined the expected clinical impact of the drug, from a nomothetic perspective, and which Martha is able to recall in detail. My impression is that Martha interprets that this will translate into the individual impact for her. Martha recants

its regulatory status in other countries as further support for the drug and contrasts the anticipated level of success with other treatments. The precision with which she recalls this indicates the importance of the effectiveness of the trial drug to Martha

In the same way as Jude, Martha seems to be evaluating how her symptoms proceed throughout the course of the study

Martha	*I feel that some of my symptoms have worsened but I **haven't had any additional symptoms.***	*10:33*
Martha	*So that's a **good thing** I suppose*	*10:38*
Researcher	*How do you feel that this this trial is helping?*	
Martha	***I haven't had any more symptoms** from what I have from the beginning, I say and I suffer with back pain and tension headaches and I have numbness, started on my right side, I have got some on my left foot as well now. But I'm not you know, **nothing's really got significantly worse**. Just a **little bit** because I didn't really know until they were doing a test on my feet. That's when **they realised**.*	*10:46*
	*Like I say I **haven't had any relapses***	*18:37*

Martha expresses confidence in the ability of the trial drug to stave off physical decline. She describes her grip as worsening and the additional sensory loss in her foot. Although her symptoms may be progressing, it is important to Martha that she can retain belief that the trial medication is having the level of positive effect the research clinician described to her.

Martha	*I think the study was five years. But even if, they said even if this didn't go on the NHS, **if it worked for me, I'd be on it. It'd be my treatment***	*14.09*
Martha	*So mmm **I'd be on this for as l.., for ever**.*	*14.19*

Furthermore, Martha has received reassurance that even if the study treatment is not made more widely available (on the NHS) that she will remain on the same treatment in perpetuity. This confers to Martha a sense of security and certainty in contrast to having a condition which has a highly uncertain course.

Eve too links her participation with anticipated clinical benefit, which hinges on her dire health situation that brough her to being offered study participation. As soon as Eve starts to talk about the research study she is transported back to describe in detail the time of her presenting symptoms (loss of left sided vision and left sided numbness).

Eve	*somebody came to me and said, **we're thinking it could be MS**. And that was **like a bolt out of the blue***	*9.45*

Eve talks quickly and candidly about her evolving symptoms, her time on a stroke ward, and the shock of receiving the MS diagnosis. The disease continued to progress rapidly, and Eve's health continued to decline at a terrifying rate; severe relapses temporarily take away her vision and, at times, her ability to walk or use her hands. Frightened at the speed and severity of her decline, Eve paints a vivid picture of just how desperate her health situation was. The MS treatment that she had initially been prescribed was not working well for her and was accompanied by troublesome ('*horrific'*) side effects.

Eve	*And he asked **how would I feel about going on a trial drug**?*	*11.23*

Around nine months after diagnosis she was offered trial participation by the MS Neurologist – the feeling of this being a seminal moment for Eve was manifest in her intonation.

Eve	*Well, **why wouldn't I**, you know …. I've **nothing really to lose at that point***	*11.40*

Eve	***for a long time, I just didn't, I just didn't know what was wrong with me, …so now, I know what I've got, how do I deal with it? How do I manage this**?*	*29.11*

Akin to Martha and Jayne's term 'no brainer', but grounded in different lifeworld context, there almost is no decision to be made, she needs urgent intervention. Following the trauma of not knowing what was wrong with her, to her relief at having a diagnosis, the study seemed to be a part of the answer to her question *'how do I deal with it?*'. This notion of dealing with the MS would seem to encompass both the physical treatment, but also the psychological impact of the disease (revisited at other points in the analysis).

Eve	*I mean the **health benefits obviously**, now I went through **from being in a really bad place with it to you know so much better now.** So **obviously, that is number one, isn't it?***	*39.16*

Eve recognises and almost takes for granted the expected health benefits of the trial. Later in the analysis it will be seen that the health benefit is not necessarily as clear as might be expected from her statement here.

Although initially Jayne's explanation of research participation focussed on the sense of satisfaction and of having nothing to lose in taking part in research, it also became clear that she was hoping for therapeutic benefit.

Jayne	*… when I started this study, I didn't really feel as though anything had changed. So [frequent interruptions from spouse] hopefully I'm on the ermm I'm on* ***placebo*** *you know, I don't know. I mean, I've been on the, the actual biotin for six months, and I still* ***don't feel much different*** *so maybe it's just…*	*21:32*
Phil	*but, then* ***maybe that's a good thing***	*22:58*
Jayne	*Mm well I'm* ***not worse particularly****, maybe a little bit, not much. So at the very least, if it's* ***slowed things down*** *that's fine by me.* ***I'd go for that.***	*23:23*

Jayne was initially randomised to either placebo or active treatment, and then switched to open label active treatment six months ago. Jayne reframes her perceived lack of impact of the randomised trial treatment by expressing her hope that she was allocated placebo. Now that she's receiving open-label biotin she allows herself to believe that given her condition has worsened only slightly that the treatment is slowing her progression. It is not just that she has *'nothing to lose' (16.04)* by taking part, but feels that she does have something to gain in terms of positive impact on her MS.

Jayne	*They've extended because it's sort of showing* ***good results****.*	*10:23*
	the results were ***good, promising****.*	*20:01*

She discusses her belief in the efficacy by highlighting that the study was extended with an open label period as the results had been encouraging. Pre-trial the clinician had been equally enthusiastic about the potential of the yet unproven treatment as can be understood from the excerpt below.

Jayne	*Well, I think even before we joined it, it was* ***looking good*** *from Dr Proctor's point of view. He said that it was* ***looking very good***	*35:23*

Jayne expresses a high degree of confidence in the expected effectiveness of the trial treatment. The findings suggest that she does not wish to face the possibility that her belief in the treatment is unfounded and clings to the hope that her health decline will be slowed. During Jayne's second interview once the trial has stopped, she reappraises the treatment's effect.

Jayne	*… as far as anybody* ***knew it was all looking reasonably, …, reasonably hopeful that something might come of it.***	*1.37*

Although Jayne seems to have accepted and made sense of the study's termination, she expresses her feeling of loss of the expected potential for the study to have made a positive difference to her health. Jayne is perhaps understating her feelings of the study ending and is able to present a positive reframe.

Jayne	*I can't say I was altogether surprised.* ***Because I hadn't really noticed any improvement****. …,* ***I wasn't thinking ooh this has really worked****. Ermm that is really disappointing,* ***which probably would have been worse if I if I'd been thinking oh, this is very promising. And then they stopped it.***	*4.29*
Jayne	*They did actually say that* ***I'd been on the biotin***	*5.02*
Jayne	*I cant remember when that was but* ***I was quite disappointed with that because I though ooooh, I haven't noticed any difference****, so you know. So. He he*	*5.39*

Jayne described that the trial ending was less impactful, less important to her as she hadn't felt a benefit of the active treatment and therefore the end was almost expected. In summary, the treatment was not working so it was essentially no loss to her. Rationalisation is a typical often subconscious approach to justify something that is difficult to accept or to make it seem 'not so bad after all' or 'is for the best'. This is a frequently employed self-defence mechanism (AQR.org.uk). Rationalisation is a repeated concept throughout Jayne's second interview in relation to the trial stopping unexpectedly

Psychological Benefits

This part of the analysis seeks to explicate the psychological perspective or non-physical positive impact of trial participation. Domains identified in the initial analyses, such as fear, hope and taking control are considered here.

Comparing the findings highlighted a degree of concordance between Martha and Jude in terms of the fear they hold for the future, and their strategies to defend against this. From the prior section, Eve expressed the traumatic effects of her condition and the salvage offered by the trial, whereas Jayne displayed a relatively phlegmatic demeanour although sometimes using humour or laughter to deflect attention from more difficult emotions.

To understand why the trial might be considered part of Martha's defence against her fear of the disease, it is necessary to understand her lifeworld by appreciating just how much the disease has devastated Martha's life and continues to affect her every day. She knows that her condition is only going to worsen, and she must protect herself as far as she can against this. Martha laments the past as she explains how much her life has been ravaged by the disease

Martha	*I don't work anymore. I found it too much of a struggle.*	*03:37*
Martha	*I think it's affected me a lot physically.*	*20:57*
Martha	*Because I mmm I used to cycle everywhere and used to go the gym three times a week. And I carried on trying but because of the dizzy spells and I had a pain in my upper right leg. I just couldn't do it anymore; now, mostly because like I say I was always on my feet.*	*20:59*

MS has caused Martha to stop working and to cease physical leisure pursuits of cycling and frequent gym attendance. Martha had once been very active, but the impact of the MS meant that she can only partake of light therapeutic exercise. Employment is widely acknowledged for its importance in providing a sense of personal and professional identity (Gini, 1998) and so the impact on Martha of MS leading to the end of her career is expectedly very significant to her. I understand from Martha's interview that she mourns the person that she once was. Despite the difficulties Martha gives the impression that she strives hard to carry on and to do her best in the circumstances.

Martha	*It's all I can do really.*	*11:33*
Martha	*… you have to keep going*	*11:36*

Moreover, Martha indicated that she was acutely aware that her condition will deteriorate further over time. During the interview, Martha came across as resigned and accepting of her fate, but her account also indicated that she is afraid of the anticipated progressive worsening of her health. Given what she has lost already, she expresses fear at what her future life may comprise. Despite Martha's treatment being guaranteed, her future is precarious.

Martha	*… but I just don't want to be on morphine where I'm having injections. **Where does it stop**…*	

Although she is referring specifically to morphine to manage pain this is indicative of escalating treatments to manage progressively worse symptoms. During the interview, her fear is palpable as her voice trembles at the rhetorical question she poses '*where does it stop'*; for Martha there is no end to this

I understand from Martha that trial participation is part of her strategy to mitigate her fear.

Martha	*I say it's **one of those diseases that's just got to deteriorate in time**. And I understand that. **So I've got to try and do as much as I can now to prolong it.***	*21.04*
Researcher	*Being in this study is part of that?*	
Martha	***Definitely***	*21.53*

Although she appears to hold dread for what her future may hold, she describes how she feels empowered to act. By being in the study, the findings indicate that she is taking action against her disease and maximising the time she has before what she regards as inevitable decline. This is a particularly interesting and powerful strand of Martha's experience of research participation. I recognise this hitherto veiled quality in Martha. At times throughout the interview, Martha seemed to exhibit a degree of dependence on others or of being a victim. In contrast here she comes across, despite or maybe because she is understandably fearful, as self-motivated and quietly determined.

Similarly , to understand the importance trial participation to Jude it is first necessary to understand Jude's attitude towards her MS.

Jude	***this is a god awful disease***	*4.17 & 34.28*
	It's a god awful crappy disease	*20.47*
	I'm telling it that you are not controlling me	*23.00*
	I'm managing IT, rather than IT managing me	
	It's been defining me and I hate it	*32.56*
	Its life changing, it can be very life changing	*34.28*

Jude describes the MS almost as a sentient being. Her disease is a *thing* to be hated – she appeared to be angry at having MS, and she is outraged at what MS does to her. She seems to be defiant towards the disease and constantly defending herself against this evil entity.

Jude	*the **last couple months, to some extent it has managed me**. … I've had to think , right! **Well, you've run that battle today, mate, But I'm still in the war***	*23.30*

Although she describes this as a constant, battle she recognises that circumstances (the SARS-CoV-2 pandemic) have allowed it (the MS) to take some victories against her as continues her fight.

Jude	*…**it has been horrendous. It's just been horrendous**. It has been for everyone, **but for people with chronic diseases it's just been awful, because you've literally just been left***	*45.24*
	And that has made me very angry…angry at the situation.	*45.57*

As a result, Jude expressed a lot of anger at the Covid situation and the resultant impact of the lockdown on her health, the health of others, and the delay in her being able to join the trial. She describes how she feels repeatedly let down and experiences a sense of being abandoned, '*just being left*', which compounds her resentment.

During the interview and analysis, I understand Jude's anger to be an expression of her fear, with her terror permeating her description of her recent decline and her future potential deterioration.

Jude	***I've declined***	*7.00, 7.17, 7.53, 8.40, 9.56*	
	I feel vulnerable now		*8.30*
	I felt more vulnerable		*8.40*

In the interview, Jude describes her alarm at how the disease is impacting her over time. Her distress seems evident, fear palpable, as she repeatedly reiterates how her disease has worsened in recent months and how she now feels at risk. Further to this, during her second interview Jude emphasises this fear in her description of her reaction to additional loss of physical function as she experiences a disabling relapse of her right hand.

Jude	*I can honestly say that I was **the most frightened that I ever have been**.*	*5.15 (2)*
	*–That week for me was the **most frightening week** in the 13 years of having this disease. It was, **it was awful**.*	*29.06 (2)*

This description serves to reemphasise the primeval fear of sporadically but increasingly losing control over her own body, and which appears to drive her to act.

Jude	*I want to deal with it myself. I do everything that I can for myself to keep myself well.*	*11.30*
	And if I've got to be proactive. I'm a proactive person… I've got to be for my own peace of mind. And for myself, be positive, and be doing something about it.	*23.15*

To assuage this fear, the findings suggested that Jude needs to feel in control of *it*, and strives against *it* defining her. She needs to believe that she's done everything possible to stave off her disease, with no future regrets. She is highly motivated to meet the challenge of dominating her disease – the fear of not doing so repeatedly breaks through during the interview.

Jude	*And I want to be I feel as though (weeps) - I'm getting a bit tearful then*	*20.09*
	I think it's a god awful crappy disease. (weeps)	*20.47*
	If I can help, if I can help stop it. (weeps)	*20.59*

As we speak the emotion is just below the surface and she weeps as she tries to describe why the study is so important to her. At this point Jude is too distressed to continue on this topic [we take a break, I offer support, and suggest that we cease the interview. Jude expresses her wish to proceed with a different topic before returning to this topic later]. When we revisit the topic later (with Jude's permission) Jude reiterates that's she's afraid of how her future might look with this progressive neurodegenerative disease. This phrase, below, captures the essence of Jude's angst for her future.

Jude	*It's thinking about where the disease could take me,*	*39.05*

Jude recognises the importance for her psychological health to feel invested in the management of her condition by taking positive action.

Jude	*… it's about taking back control for me. … I've not just been a pushover and I've not just I've not just sat back and let it rule me.*	*24.08*

For Jude trial participation seemed to be a key aspect of her defence strategy against her dread of her possible future. Refusing to be dominated by the condition, the trial is a tangible aspect of her armoury in taking back control – not allowing ***it*** to define her. She fights ***it*** all the way. Nobody, no thing is telling Jude what to do.

Findings from Jayne's second interview reinforce the findings from her first interview in terms of taking action.

Jude	*My kids and my husband they think its really good that I'm doing it because they understand. They live with me and they understand how the disease impacts me. …**They see it having a positive impact** mentally on me*	*32.44*
	*[husband] think, he thinks mentally. It's made me, **it gives me something to focus on. I'm not letting it ride roughshod over me. I'm trying to do something about it in a positive way**.*	*35.10*
	*It just makes me feel for me mentally. Yeah, **I'm doing something about it**.*	*49.11*
	I want to try and do something about 'it'**. And that's the only way I can do something about 'it'. **And I'm telling 'it' in me [sic] mind , I'm telling 'it', you're not going to win.	*49.37*

Jude intertwines parts of her vehemence in her fight against *it* with her altruistic intent which is considered later. The key benefit for Jude is to feel that she is taking direct action to effect control. Being psychologically poised to tackle the disease is, from her repeated reference to this, an important strategy for Jude and the trial is an important facet of this defence mechanism. I ask Jude to explain how now being on the trial makes her feel – her response is incredibly powerful.

Jude	***Empowered. Empowered***	*25.05*
	*So yeah, **I feel empowered now because I'm part of something***	*42.47*

Jude seems able to draw strength from being a part of the trial. I understand this in two possible ways – on an individual level acting against her disease and simultaneously as part of the wider campaign to help defeat the condition. This reading aligns with her hope for self-benefit concurrently with her desire to help others. Jude's description leads me to understand that under the auspices of the trial she feels less alone, less abandoned.

The anxiousness that Jude exhibits in relation to her future is in marked contrast to Jayne and Phil's portrayal who seem to express a greater degree of acceptance and represent themselves as being more phlegmatic about their collective future. Although Jayne and Phil's reaction appears less fervent, the premise of taking measures against the disease remains significant.

Phil	*Makes you feel as so you are **doing SOMETHING**, I think*	*12.37*

Jayne	*But it was a really,* ***it was real actual relief when I heard I was going to be on. I would have been really disappointed, I think if I hadn't been.***	*13:40*

From Jayne and Phil's interview, it is Phil who first makes direct reference to having a degree of control. This is then reinforced by Jayne's relief at securing a place on the trial. My understanding of Phil's comment is that he is not prepared to be a passive bystander of the neurodegeneration that is slowly ravaging his wife, companion and friend.

The study is in fact the only potential disease-modifying treatment option open to them following diagnosis, albeit an unproven experimental intervention. They are invested in the management of Jayne's MS by actually doing something, by taking action. Although there is little than can be done for PPMS, they are taking all steps possible; participation in the trial, exercise and vitamin D supplements as recommended by the neurologist. During Jayne's second interview conducted after the trial had been terminated due to a lack of efficacy, Jayne's narrative suggests now that the absence of taking action or control is meaningful to her.

Jayne	*It's like Well, that's it there's noth.. you know, there', there's not, there's nothing yet but yeah, it was* ***it was a good feeling to be feeling you were doing something that there was something that you could do, you know, that might have might have a beneficial effect****. Yeah. And now that once that went Yeah, I suppose that was part of the disappointment. Really.* ***Oh, that's it, then. There is no more hope.*** *he* *But I mean, yeah.* ***Thinking that ooooh there's something that might make a difference., that's good. And once they say, Well, no, it's not, until the next thing comes along,*** *I suppose.mmmm.* ***It is disappointing****.*	*23.55*

The trial having ceased, Jayne now faces the absence of being able to act directly against her disease. Jayne laughs seemingly to dispel the seriousness her feeling of hope being dispelled, but whilst remaining optimistic that another opportunity will present itself which reinforces the value that she assigns to taking action.

The premise of control is less inherent within Eve's account, and which does not come to the fore in the idiographic analytical process. I surmise that because other themes are significantly more meaningful for Eve that other aspects may take precedence in her account. Having considered the physical and psychological positive attributes of trial participation, harm as a consequence of trial participation is explored next.

Harm

Harm is conventional nomenclature representing the antithesis of benefit in clinical and trial related outcomes, and which encompasses both physical and psychological components. The World Health Organization defines harm in healthcare as *'an incident that results in harm to a patient such as impairment of structure or* function *of the body and/or any deleterious effect arising there from or associated with plans or actions taken during the provision of healthcare, rather than an underlying disease or injury, and may be physical, social or psychological [e.g., disease, injury, suffering, disability and death]*' (Panagioti et al., 2019).

Within this study harm expressed by participants is manifest mostly as physical suffering or psychological distress associated with the trial processes, the trial ending or the trial drug. Typically, harm associated with a clinical trial might be thought of in terms of adverse effects of the experimental treatment. All participants within this study refer to side effects associated with the trial drug. From Jaynes's perspective the trial treatment is without any possibility of side effects. Martha explicitly denies experiencing any side effects, whereas Jude attributes side effects to active treatment and therefore as a positive. Eve suffers significantly from the effect of the trial treatment but does not associate it with the research.

For Martha it is the lack of adverse effects compared to other treatments that other people endure that is of particular significance.

Martha	*the **others** [drugs] have quite **significant side effects***	*02:58*
	*And **I haven't had any side effects** from it.*	*03:12*
	*, as I've said **I haven't had any side effects**., it's been fine*	*06:43*
	*a lot of the **other medications** that are for MS have got quite **severe, nasty side effects.** And so **obviously, I don't suffer from any side effects**. I don't know about anybody else*	*09:20*

The lack of side effects for the trial treatment compared to the terrible effects of other drugs is the message that Martha seems to recall from the pre-trial information. Although Martha has experienced several adverse symptoms – any of which could be associated with her MS, or with the drug or equally completely unrelated. Her description, repetition and the use of the word 'obviously' leads me to understand she does not consider that she has

or could experience adverse sequelae. I am not suggesting that the research clinician had not fully explained the potential for unexpected or severe side effects as part of the informed consent process, but that over time this is how Martha has processed and made sense of the safety aspects of the study (the double hermeneutic).

Similarly, Jayne is resolute that the drug treatment within her trial cannot be associated with side effects.

Jayne	*it's there's nothing, there's **no side effects** or anything like that. Because I had actually been taking biotin and I know so I knew that, you know, there's **no problem with it**. It's **not like a drug** with **side effects** or you know **possible dangers** really or anything like that*	*14.40*

The investigation medicinal product (IMP) has the same chemical constitution as a known micronutrient, however it is being tested as a MS disease modifying treatment (DMT) at significantly higher doses than would be taken as a nutritional supplement. Because it is classified as a vitamin it has positive associations. It is considered, at worst, as nourishing but essentially benign. At the substantially higher dose employed in the study, it is not yet known if it has clinically meaningful efficacy, nor if there are safety or tolerability issues which could pose a serious health risk. Clinical equipoise is fundamental to research; the purpose of the research is to fully characterise those effects- good *or* bad. It appears from the interview that Jayne lacks personal equipoise in relation to the efficacy and safety of investigational treatment. Further Jayne ascribes a similar stance to the clinician. From Jayne's perspective both her and the researcher-clinician hold a firm belief in the (unproven) benefit of the treatment, and moreover that Jayne eschews any possibility of adverse effects.

On the other hand, Jude's experience and view of side effects is contrary to the other participants. During Jude's second interview she describes what she considers to be some benign side effects. When Jude increased her study drug dose, as mentioned previously, she noticed more frequent urination and a change in how her urine smells. This leads Jude to harbour a belief that she is on the active medication and so these possible side-effects for Jude are a positive.

Eve indicated that she found some of the trial procedures to be burdensome. At different points Eve talks about '*going through*' with aspects of the trial which indicates her sense of

having to endure the study procedures; and which contrasts with the positivity she mostly portrays. Further Eve also experienced an unexpected and severe reaction to her first trial infusion.

Eve	*I think the very **first infusion** I had was a **bit of a shock**.*	*17.15*
	*And err following day, I mean, I couldn't even keep sip of water down**. I was so sick…. And it took me a few weeks to kind of get over it.***	*17.47*
	*for about three weeks afterwards **I don't feel well after being on the drug - but that has nothing to do with the research**.*	*32.42*

Eve describes the sudden and impactful side effects which she acknowledged to be as a result of the trial infusion. However, she seems clear in her own mind that it was unrelated to the research. Eve appears to rationalise her involvement in the study by disassociating the negative effects of the trial infusion from her positive perception of the trial experience– it appears as if she is unwilling to acknowledge any downside of the trial, although she has clearly suffered at times along the way.

Additionally, the study drug, as an expected manifestation of its mode of action, significantly compromises Eve's immune system at the time of a global viral pandemic.

Eve	*…this viruses coming over and**, and I asked the nurses at the time, - am I doing the right thing?***	*18.07*
	having my immune system… depleted just as this is potentially coming over?	
	*…how you gonna lock yourself away for six months. **And basically, that was what I did**. You know, once **we** realised that*	

Eve indicates that she is aware of the potential risks to her and seeks guidance from the research team, before subsequently needing to shield for six months as a result of the immunosuppression. Further into the study, and into the pandemic Eve again questioned whether to go through with a further dose of the immune suppressing infusion.

Eve	*Then when we went back in August, again, we had the conversation about **is it really safe? but they were happy for me** to go through it. … So I had it again, … but then things kind of got worse.*	*18.21*

Of the four participants in this interpretative study, I consider Eve to have been the most negatively impacted by her trial involvement, in physical terms. However, Eve's interview dialogue came across as buoyant and unfalteringly positive in describing the overall

experience of trial participation, until the final minutes of the interview, which will be discussed later

Jayne indicates a level of psychological impact with the following excerpt suggesting that that the timing of medication had played on her mind.

Jayne	*I did notice that when I stopped doing it, I noticed that I wasn't looking at the clock all the time. And counting how long since I've last eaten and that sort of thing.*	*11.14*

During the Jayne must adhere to quite precise timing of her trial medication. During the second interview, after the trial had ceased, the timing of trial treatment relative to food was, in retrospect, identified as a nuisance and source of slight anxiety for Jayne.

Jayne	*I mean, initially, it took a bit of getting used to but I'd really **I'd got into the habit, the swing of it.***	*12.55 [INT2]*

However, during the first interview, and on reflection in the second interview, Jayne had been extremely engaged with the process and the intellectual challenge of problem solving the timing of the trial treatment during the study. She described in detail the intricacies of the timings she had put in place, with a sense of pride and achievement. It is interesting to note that her experience shifts with context. It would seem that a degree of rationalisation has occurred with Jayne redefining some study experiences once the study had ended.

Jude also attributes a level of psychological distress in understanding the premise of randomisation but not knowing her assignment.

Jude	*I'm **trying to believe** that I have got the **actual drug and not the placebo***	*30.23*

In addition to the angst that Jude relayed at the prospect of receiving placebo Jude also describes an additional source of anguish as part of the study assessments.

Jude	*Yes, I've had to do the questionnaire. And I must admit, I find I found them **a bit scary.** You know, like, **do you need assistance to have a wash? Do you need assistance to get dressed and I thought, god, no I don't but I don't want to be there,, I don't want to go to that place… It's scary**. When I actually see it in black and white, and somebody is asking me a question.. **It takes me to a place where I don't want to go…***	*44.20*

In responding to trial questionnaires about her levels of dependence for basic daily activities Jude feels forced to face the prospect of her potential future decline. This questioning necessitates her facing what could be her future reality and loss of independence. This could be seen to fuel her ever present fear, despite the positivity of trial involvement and effecting control.

Impact of Trial Cessation

Whereas Martha and Eve are both on treatment that is scheduled to continue regardless of trial involvement, Jude is very conscious that her trial could cease.

Jude	*So what I've been told is, they're going to look at the results, the will we'll be looking at the results of that. And if they feel there isn't any kind of positives about it or is not a big enough. Not a big enough percentage to say it's a success. They will pull* ***the trial, right, but they would also pull me as well.*** *They're not going to leave other patients on it for another six months. Okay. And I understand that there are other trials****. So if that does happen, I'll try something else.***	*29.27*

Again, Jude exhibits palpable distress at the prospect of this opportunity for taking control being removed should the trial not show positive results. I understand that Jude does not want to dwell on the possibility that the trial that she has fought so hard to be a part of could end. This fear seems quickly denied consideration as she talks of going into an alternative trial in the event the current study ends.

Whilst Jude expresses her fear the possibility of the trial ending, Jayne experienced her trial being terminated unexpectedly. This seems to lead to some mixed feelings, sometimes at odds to her first interview (including her view of the drug efficacy, and the timing of medication as explicated earlier).

Jayne	*They were a lovely lot. So… But* ***I don't particularly miss having to go****.*	*18.47*

Despite enjoying the experience of participation on multiple levels (identified within her first interview) and having great appreciation for the study team she claims not to mind ceasing attendance – this was largely attributed to the threat of the pandemic.

Jayne	***all the different things you had to do each time you went, were all mapped out*** *and all that sort of thing. So it was it was* ***all looking relatively positive. And then all of a sudden,…***	*24.43*

But equally Jayne seems to miss the planned activity that she had found satisfaction in and as a result feels let down. I conclude that Jayne feels slightly shocked at her trial having ended abruptly and there seems to be a sense of unfinished business. Further, Jayne employs the word 'disappointment' or 'disappointing' over twenty times in her post trial interview this repetition seeming to signify her sense of loss.

From Eve's description of her reaching the end of the trial indicates a more pronounced reaction. She seems distraught at the prospect of losing the nurturing relationship of the study team.

Eve	*Err* ***very sad, very sad*** *[emotional weeping] to be honest. So sad because err. . But I will be continuing my treatment on the NHS at the same hospital. So you know, if* ***they've promised that****, if I'm going in,* ***they'll either pop over and see me, or they said you know, I can always just pop in and just say Hi****….. And we just sort of left it that we've got. They've got my contact details. I've got theirs….,* ***that bridge hasn't sort of completely been taken down - its still there. So Yeah, it's, it's just moving on isn't it really…***	*24.43*

As Eve's research journey comes to an end her fear at the prospect of losing the connection that has been so vital for her seems very impactful. She is bereft. Her emotion breaks through as she explains that the ties have not been severed completely and that she and the team will remain in contact. She tries to be stoic ('*just moving on'*) but she is seemingly not prepared to move forward without the comfort of knowing that they are still there for her, that she is still connected. For Eve the relationship with the study team comes across as being exceptionally important to her, and which is explored in the next group theme.

GROUP-EXPERIENTIAL-THEME 2

Human Connectedness

The second group-experiential-theme of human connectedness relates to participant relationships with the study-team. This theme arose from individual participant personal-experiential-themes encompassing the relevance of human interaction to the participants (as opposed to trial procedural consequences). Domains discussed include trust, nurture, belonging and isolation.

Trust

Trust is variably defined in the literature, most often it is explained in terms of a confident expectation regarding another's behaviour (Barbalet, 2009). Trust is a key tenet in both healthcare and research which includes both confidence in and reliance upon the clinician (Ward, 2018). Within this group-experiential-theme Eve appears to experience the most significant intensity of trust, alongside her sense of nurture. Martha's account also suggests that she appears to experience a powerful sense of trust and belonging.

In contrast, although Jayne and Phil enjoy the scientific intrigue and the research engagement with the investigator as described in the previous section, they express far less in terms of connectedness with the research team. Jude had only been in the study for a short time with one subsequent trial visit by the time of her second interview. Despite this Jude shares one of the most poignant notions across all of the narratives. Jude succinctly captures her connection with and trust in the research investigator.

Jude	***He …makes… me… feel …safe***	*27.04 (2)*

The fact that she states that the MS research clinician makes her feels protected denotes a thick trust, and that in contrast she has not felt secure previously. This is a powerful message delivered with monosyllabic emphasis. There could be many reasons for this feeling of safety, for example; the research clinician may have greater time to undertake a full assessment under the auspices of the study (the notion of expert follow-up is integral to the study description), the research assessment being face to face, the trial representing an opportunity for a 're-baselining', the fact that the investigator is required to be an experienced MS-specific clinician, an improved dynamic between Jude and the research clinician or simply just a question of chance.

Within Martha's account one of the most potent examples of her seemingly unquestioning trust relates to her decision to participate. At the start of this chapter, I aired my concern that at the time of the interview, it initially appeared that taking part in the study was a decision of little consequence for Martha.

Martha	*So it was a bit of a **no brainer** really*	*3.11*

The term '*no brainer'* does not, as I had initially understood, represent a lack of significance but eloquently signifies the completeness of the trust that causes the decision to be almost no decision at all. Having examined this response in the context of the trust that Martha has placed in her doctor it seems that beneath this unassuming response is the complex culmination of unerring trust in the doctor who has diagnosed her. Martha's representation of the decision-making process has over time undergone a degree of her own analysis and sense making and so it is her current interpretation of that process that is being examined in this work, although necessarily from a second order perspective.

Interestingly Jayne uses exactly the same phrase ('*no brainer'*) within her account in describing her decision to take part in the research – although for Jayne the origins might be regarded differently; self-derived reasoning, perceived study benefits and the fact that trial participation is the only option open to Jayne seem to be behind Jayne's decision to take part.

As described earlier in this chapter, Martha has confident recall of the information that she was provided with by the study doctor two years ago (in terms of efficacy and side effects). Martha repeatedly references this information giving the impression that this justifies her trust, as her recollection of what the clinician-researcher described is aligned with how her experience has unfolded. The trust that Martha exhibits is also reflected in her attitude to the sharing of study results.

Researcher	*Do you see, do you get to see the results?*	
Martha	*No. No, I don't**. I presume** I would if I asked.*	*08:00*
	*they say, you know, Dr Fletcher has **signed everything off** and **said it's fine**. So.. So I haven't been told, but I **presume** I would if I got a lesion or anything.*	*08:04*
	*No, as I say I've asked before, say, no **everything's fine** So no additional lesions or anything. it's going smoothly so far.*	*08:22*

I interpret Martha's narrative to indicate that she unconditionally accepts that the research team have her best interests at heart, in contrast to her work-place relationships. She feels reassured and links the 'signed off' with positive endorsement of her health. This is a presumptive stance, trusting rather than knowing that something of significance to her health would be shared with her.

Similarly, Eve was left to assume that her results were fine after a study assessment such as a scan as can be seen below.

Eve	*I go for you know an MRI scan - **and if you don't hear anything, then I just assume everything's fine.***	*43.03*

On the other hand, Jayne knew, by asking, that results would not be shared with her but trusted that anything of significance would be acted upon

Jayne	*No, **no we don't know anything**. I presume, I did ask at the beginning. **Presumably** if there was something , **if something turned up, showed up they would react to it***	*30.54*

The premise of trust is further echoed and amplified in Eve's account. It seems that throughout the analysis that Eve feels such support and has such deep trust of the team that she is able to divest some of her responsibility of battling to control the MS to these trustees of her care. Eve exhibits thick trust, a level of trust often reserved for family members.

Eve	***I wasn't actually testing the drug itself**, because the drug was already out there and being used for other things*	*11.40*
	*But that **they were testing it for MS**. So that helped, sort of in my mind*	
	*I was quite happy **to go along with it really**.*	*14.45*

Seemingly, by her own admission, Eve doesn't understand all aspects of the study, for example she didn't understand that the drug is under investigation and had incorrectly understood that it is used for other conditions. My understanding of this is that regardless of her limited knowledge, she is happy to follow their recommendations due to the trust she has for the team. When Eve demonstrates an awareness of the potential risk of immunosuppression during the SARS-CoV-2 global pandemic she questions whether she is doing the right thing.

Eve	*…this viruses coming over and,* ***and I asked the nurses at the time, - am I doing the right thing*** *having my immune system… depleted just as this is potentially coming over?* *…at that point, we still didn't realise quite what COVID was, would mean, and* ***we had a bit of a laugh about it****. And the nurses were saying, you know,* ***laughing*** *Oh, yeah, you know, how you* ***gonna lock yourself away*** *for six months.* ***And basically, that was what I did****. You know, once* ***we*** *realised that*	*18.07*

Eve describes the humour that she and the nurses find in the situation, laughing about the worse-case scenario of having to lock herself away for a half a year due to the immunosuppression caused by the trial drug. The use of 'I' and 'we' is interesting here – the impact is on her but the recognition of the issue as it came to light was collective.

As Eve describes it, the team's response could potentially be interpreted as somewhat glib and dismissive. However, Eve seems completely accepting of and trusting of their advice. Her concerns are seemingly assuaged by *faith* in their advice rather than reasoned argument. Eve justifies their advice to her that '*we*' didn't quite realise the impact, that is that it was justifiable and reasonable advice. Whether it was or it wasn't– Eve trusts their guidance.

Eve	*Then when we went back in August, again, we had the conversation about* ***is it really safe? but they were happy for me*** *to go through it. Well, alright, then, you know, I'm going to trust,* ***I trusted their decision****. So I had it again, … but then things kind of got worse. f*	*18.21*

Eve again questioned whether to go through with a further dose of the immune suppressing infusion during the pandemic. She viewed it as *their* choice to make; she did not have need of an informed decision, to have belief in them was sufficient.

Reflexive note: it is important to be cognisant that this is Eve's own interpretation – it is not possible to know from her account what the basis or background of this advice might be. There may have been multidisciplinary decision making, evaluating the risk-benefit ratio, or discussions with the sponsor company, analysis of her bloods, the course of her disease or a well-reasoned and coherent argument from the consultant – Eve may only be aware of the tip of the iceberg and not aware (or potentially not interested) in the basis of the advice.

Eve	*. I mean, the weird thing is, **there's still are lot of things that kind of confused me a bit**, but **it's just that knowing that they've got your back covered***	*22.22*

Eve's narrative reinforces the strength of her thick-trust by confessing that there were many aspects of the trial that she did not understand but she was secure in the knowledge that that the team were protecting her. Despite describing herself as confused she is at ease with her seemingly limited level of knowledge and completely comfortable with divesting some of her decision making to the research team. In the circumstances described above this level of thick-trust could be regarded as over-trust and frames her isolation, as discussed at the end of this section.

Reflexive note: I am repeatedly questioning if she is right to lay such faith and responsibility in these people – she accepts their every word and feels soothed and reassured. This is not how I operate - does that influence my view of the situation? I have re-reviewed the analysis to reduce any bias resultant from my views, but accepting that as the interpretative instrument my frame of reference is my own.

Nurture & Belonging

Again, both Eve and Martha's accounts have concordance in their sense of nurture under the auspices of the trial. Eve from the perspective of being in their hands, supported and invested in, and for Martha the feeling of being nourished with a sense of belonging and feeling of kinship within the safe-haven of the research team.

Eve	*it was him **who got me on to it**, so. **He's been with me right the way throughout.***	*34.13*

Eve acknowledges the MS neurologist as the key protagonist for trial participation– he was the one that *'got [her] onto it'* and has been there '*with*' her throughout. Eve seems to attribute a degree of privilege in being offered the study and being supported by the consultant throughout. This premise of continuity of having a relationship appears important for Eve.

Reflexive Note: Through the interpretative process I understand that Eve feels that the research team are heavily invested in her - that they are always '*there for'* her, that the consultant has been '*with'* her throughout. I propose that it is very important to Eve to feel this level of support and involvement in what is ultimately her own journey. I am questioning whether this 'thick trust' is warranted and whether I am right to question this.

Where does justified trust in medical and clinical support become over-trust? Here I have to remind myself that I am interpreting Eve's own interpretation of her experience – the double hermeneutic.

Eve	*So **from that point onwards**, everybody, you know, there's been **so much help. All my questions have always been answered. I've never felt like I've been pushed to one side***	*10.03*
	because they were so kind** and I think **because they explained everything so well**. I felt there was **such a lot of support** that **I was quite happy to go along with it really.	*14.45*

Eve frames the above as the reason for taking part, *because* of the quality of the care and the feeling of being supported. I view this as trifold, firstly Eve feels that she is repaying their kindness and support by being amenable to participate, secondly, she is taking part in order to benefit from their kindness and support, and finally that Eve has developed unquestioning trust and is therefore content to proceed on their say so.

Eve	*they, you know, they, they took the time, they explained it to me and how they would **be there for me**, just if there were any bad effects, or if I had any adverse reaction to it. So yeah, and then that was it.*	*15.40*

This particular phrase where she talks of the research team being 'there for me' supports the premise of her relying on the team, is repeated multiple times through the course of the interview.

Eve	***there for me**.*	*15.40, 17.51, 20.13, 22.09, 31.58, 41.07*

This reiteration indicates the significance and importance to Eve, and the value she assigns to the feeling of being cared for and being championed, of knowing there is always someone she can turn to. Eve feels understood, known, and, as with Jude and Martha, feels safe in their hands.

Eve	*… **I cannot praise them highly enough**. I think if they if I hadn't have had the **support** and, from, and I think that was the **that was the biggest thing**, the **amount of support** I've had from them, and **knowing that they'll always be there for me.** I think if it hadn't been for that, **I wouldn't have gone through this as well as I have..***	*22.09*

During the majority of the interview Eve's expresses unwavering belief in the support and care from the study team which helps to carry her through difficult times - this is of key importance for Eve.

Martha too experiences a sense of nurture and belonging. Whilst there are numerous complementary definitions of belongingness in the literature (Levett-Jones & Lathlean, 2008), the most widely known is perhaps that of Maslow (1943) who defined belonging as the human need to be accepted, recognised, valued and appreciated by a group of other people (Maslow, 2013) – this definition resonates with Martha's trial experience as I understand it to be.

Martha introduces her difficult work situation quite early in the conversation when we are exploring how the trial fits in with her daily life

Researcher	*And how does that [the trial assessments] fit in with your day to day life?*	*3:34*
Martha	*I found it [work] too much of a* ***struggle****…*	*3:37*
	Because ***I suffer*** *with backpain and dizzy spells with headaches. I've got numbness down my right- side so it made it pretty dangerous.*	
	It seems like I'm going to be ***pushed aside*** *and just…*	*4:37*
	They're trying to ***get rid of me****.*	
	There's ***not a lot I can do*** *because I haven't had anything in writing. So it's* ***quite difficult***	*5:32*

Martha explains that that her complex health issues prevent her from working and that she had become perceived to be a hazard in the workplace. She suggests that she is not valued by her employers, either in terms of the work she can no longer do, nor in the guise of a severance payment. In this troubling work scenario, she feels that there is no one championing her, and she feels disenfranchised.

Reflexive Note: Initially I did not recognise that this was of direct relevance to Martha's research participation and the research question, but in the context of the whole narrative this hardship provides an important backdrop. This echoes the premise of moving back and forth between the part and the whole, and in regarding participants as socio-historically situated persons, and exemplifies the interpretative nature of IPA.

It became increasingly apparent that the interplay between involvement in the study and the exogenous psychosocial aspects of her life are critical to understanding the meaning of

study participation; this is an interplay between her external life and trial inclusion that arises several times across the different facets of her participation.

In contrast to the workplaces, her complex health issues in the context of the MS trial are expected, commonplace and intrinsically linked to her reason for being involved in the study. Rather than be something that casts her aside, it is her illness that legitimises her involvement in the study; she and her MS are valued.

Martha	*he wanted to get me on this study…*	*1:46*
	I got diagnosed and Dr Fletcher wanted me on this on this err research He said he was fighting for me to get on it.	*20:15*
	I was on the second one coming on this so…I was number two	*22:39*

In this scenario she is worthy of support, deserving of the investigator's attention and intervention. It feels that is important for her to emphasise that someone is advocating for her. The fact that she was only the second person on the study, and that she reemphasizes this early participation demonstrates what she perceives as the doctor's urgent battle to have Martha participate in this study. Feeling cherished and championed in the study is in sharp contrast to her being cast aside in her working life.

The ensuing sense of kinship with the research team and her sense of fitting in (and being no trouble) suffuse her narrative.

Martha	*Oh they are lovely, everybody's been so lovely, so friendly*	*7:01*
	Everyone is so nice.	
Researcher	*Does that make a big difference?*	*7:06*
Martha	*Yeah, of course it does. Especially when you're spending so much time here when you're coming in for so many appointments. Y'know. It's nice to see familiar faces. …, it does make a difference.*	*7:07*

Martha starts by indicating how familiar she is with the team and that she is *always* there, like a piece of the furniture. Martha seems to find comfort and reassurance being within the same familiar team. Martha reemphasises her level of connectedness and insider status by sharing in an almost conspiratorial nature an aspect of the study that she should be blinded to.

Martha	***It's supposed to be in a tent up*** *That's* ***not supposed to be, I'm not supposed to know*** *that I'm on this shorter one but the tent they put up was always falling down. Multi-millions on the err thing, and then a pound tent that just didn't cover it. Ha*	*15:03*

Her clandestine view of this is expressed in her demeanour and intonation during the interview. Martha is possibly reflecting what has been said to her by the team having been taken into their confidence reaffirming her sense of belonging. However, Martha does not take her sense of belonging for granted and is keen to maintain this dynamic.

Martha	*I just read my book and* ***let them get on*** *with the paperwork, … we chat in between, but yeah.* ***I just let them*** *get what they need to do.*	*07:42*

And on being asked what she wanted for her lunch by the research nurse.

Martha	*No,* ***anything that's going's*** *fine with me…*	*09:01*

My understanding of this aspect of Martha's narrative is that she reciprocates their acceptance of her into the fold with her complaisance – she does not wish to be seen as a burden. By being so amenable there is no reason for her insider status to be challenged, she is below the radar and readily accommodated rewarding their acceptance of her with her obliging attitude. Martha proudly shared that her daughter is a nurse; feasibly this could enhance her sense of kinship with the research nurse team and also shape how she interacts with them.

Although seemingly trivial, the response about her lunch is particularly interesting to me. Martha is at the research facility for a full day, in a windowless room connected to an infusion. It might be expected that lunch would be a welcome distraction, a pleasure even. I draw parallels to travel by air; the meal option is a universally welcome interruption to the restrictive tedium, and despite generally not being *haute cuisine*, is a source of focus, choice and discussion – it is virtually ritualised. Her drive to not be seen as needy, not to be bothersome in order to secure her sense of togetherness comes across as almost martyr-like at times.

In isolation, this could potentially indicate alternative meaning for Martha; that she feels repressed or disempowered in the research domain (or off her food). However, by moving back and forth between the individual phrases in the context of the full transcript, together with Martha's demeanour, I would contend that the former postulate is representative of

the significance for Martha. In order to secure her belongingness Martha is willing to trade physiological preferences for her psychological needs.

Isolation

The third strand of this connectedness theme considers the antithesis, isolation. In examining the findings across that participant accounts the premise of abandonment (or equivalent domains such as neglect, rejection or being forgotten), comes through aligned with different ideographically determined personal-experiential-themes for each participant. It has become apparent that trial participation counteracting feelings of abandonment is an important premise in its own right for people with MS taking part in research. Jude felt extremely isolated prior to her study involvement and although Jayne and Phil seem to exhibit profound togetherness, they expressed a fear of being isolated without the attention afforded by the study. Martha could potentially have felt isolated given her work situation but as discussed previously has found a sense of being cherished and belonging within the safe-haven of the study team. Ironically, despite Eve's meaningful sense of being cherished by the research team, there are times where she seems overwhelmingly alone; she panics at the irreversibility of the treatment, additionally she had to self-isolate because of the trial treatment, she experienced unexpected severe adverse sequelae of treatment, and further her family do not fully understand her condition or the impact of the trial on her. And finally, at the end of the study, she felt uninformed about how the study treatment had impacted her disease.

Regardless of the level of support that Eve relishes from the study team, when it comes to the realities of the study impact Eve is essentially alone on a solo journey. Eve's concern regarding her impending experimental treatment sets the scene for this concept.

Eve	*And then **it became real**. And I think I've had a little sort of **mini panic** because of that, because I thought Oh, God, you know, **this is an infusion. It's not, it's not a tablet** where I was, you know, took a tablet and I don't have to take it again. This is like I take, you know, a day's worth of an infusion going in me? . **How do you get it out? If anything goes wrong sort of thing.***	*15.33*

Eve had a significant wait before she became eligible for the study. Whilst she was awaiting the green light the trial treatment was an abstract concept, not something she needed to consider. Now that it's becoming a realty the idea of something being pumped into her body that this is irreversible seems daunting, especially compared to her previous treatment in tablet form. I consider it healthy for Eve to be questioning her participation and demonstrating her awareness of the potential risks. The team readily assuage her concerns with the promise of support.

Eve	*they, you know, they,* ***they took the time, they explained it to me*** *and how* ***they would be there for me, just if there were any bad effects****, or* ***if I had any adverse reaction*** *to it. So yeah, and* ***then that was it****.*	*16.00*

The team are cheering her on from the side-lines but the consequences are in practical terms hers alone. Eve, trusting of their investment in her, is soothed by their explanation and reiteration of their support and so proceeds with the study, and the consequences.

Eve	***I had to go through*** *sort of MRI scans and blood tests*	*12.13*

At different points of the interview Eve expresses her sense of having to endure the study procedures, the side effects and self-isolation (as explicated in the harm section). Whilst supported, it was a solo journey with Eve bearing the burden.

Eve	*but* ***they were happy for me to go through it.*** *…* ***So I had it again, … but then things kind of got worse****.*	*18.30*

When it comes to repeating the infusion and the physical isolation Eve is again reassured by the team, whom she appears to trust implicitly. This essence of being alone on her path, but championed and encouraged, also appears manifest in her description of how she depicts her family support.

Eve	*The family. I mean, we're only a small family, but everybody* ***was really supportive of my decision to go through this,***	*16.40*

Eve doesn't talk about her family to a great extent throughout the interview. From the above excerpt it seems that Eve felt that the family were aligned with her decision but, as I understand it, had not been involved in coming to that decision. Describing the family here as small serves to emphasise that their involvement was limited. She indicates that she felt

that they were they were behind her but did not fully appreciate what she was going through.

Eve	*That's the **hard part, nobody would understand**. That's the, it's the sort of you know the swan scenario, isn't it? Sailing along paddling but like crazy underneath... So it's very, **very difficult for people to understand**. So you go in for a day, **and they just, the family, have been totally supportive, but its is very difficult for them to actually understand. how tiring it is** how, you know Yes, **you do feel sick afterwards** and erm. It's just finding a way that explains to people **actually how it makes you feel off afterwards**, you know **going through it** go through all that was **the worst part for me**.*	*36.10*

Eve seems to find the premise of the impact of MS not being understood to be very challenging which exacerbates her feeling of being alone. The family were caring but Eve felt that they did not recognise or relate to the tiredness and sickness that resulted from the trial treatment. Not being understood leaves Eve feeling isolated which she regards as the most difficult aspect of MS and of the trial. This is an interesting finding – to Eve the support from the research team appears to be the most important aspect of trial participation. Even this can only partly counter her sense of isolation at not being understood, and of bearing the consequences of the trial. Despite these challenges, Eve seems pragmatic and recognises that nobody else can be in her shoes

Eve	*I think that you know, **nobody can explain to you what's actually having it, what it's going to be like for you***	*17.15*

Reflexive note: Eve appears very balanced and accepting of how her solo experience unfolded. And yet earlier she shared the fact that the nurses were laughing with her , at what subsequently became a reality in her need to shield for many months. Is Eve, albeit not overtly or consciously, sharing the less supportive or less-informed side of her care . Or is Eve's pragmatism simply resultant of her intense trust in them. I vacillate this point and ultimately conclude that it is the latter.

In contrast to the main essence of her narrative, with Eve feeling invested in, below Eve provides a glimpse of understanding the research from a different standpoint, framing her separateness.

Eve	*They [research team] **were doing it for them as much as they were doing it for me.***	*23.32*
Eve	***just a fish in their ocean***	*48.20*

> *…Because I still really , you know, err I am a little bit* ***in the dark as to how , what things are and how it's affected me.***

Eve recognises that the researchers have a broader aim, that from their perspective that she is not the focus of the research. This final aspect of her sense of isolation revisits the doorhandle conversation, that she shares just as the interview was drawing to a close. In line with IPA's acknowledgment that people think about themselves and their place in the world, Eve poignantly expresses her aloneness as being *'just a fish in their ocean'.* Despite being in the trial for four years she did not have a clear understanding of how the treatment has impacted her individually – this aloneness is in marked contrast to the sense of nurture and trust that she expresses so vividly.

GROUP EXPERIENTIAL THEME 3

'Self' aspects of trial participation

Having examined trial derived benefits and harm, human connectedness, the third and final group-experiential-theme relates to aspects of self in trial participation including activation (or self-efficacy), altruism and summation of self-worth

Altruism

Altruism is a much-explored facet of trial participation (Godskesen et al., 2015) and is often cited as a key motivator in taking part in research. In research participation, altruism can be described as the willingness to help others and to contribute towards the advancement of medical knowledge (McCann et al., 2010).

Although all participants made some reference to altruistic pride or satisfaction, it was often linked to self-benefit, or to a lack of challenge or of adverse consequences of their own participation. Despite Jude's anger, her deep hate of her condition, and the challenges of accessing the study, she expressed a consistent desire to benefit others in addition to herself. Jude draws upon the importance of helping others regularly throughout her interviews – this comes across as earnest, and not conditional on ease of participation; indeed, Jude would go to any lengths to participate as could be seen in her willingness to travel to London for the study albeit for her own benefit too. For the other participants altruism was expressed but emerged with seemingly less conviction.

About a quarter way through the interview Martha describes her pride in the potential benefit to others

Martha	*I suppose I'm quite proud of the fact that I'm in part of the study? Because obviously its gonna benefit other people*	*08:50*

Here Martha's expression of her gratification at helping others by being in the study does not fully resonate as her actual beliefs. This is indicated by her using the term 'suppose', her questioning intonation in her comment (from the recording and field notes)

Martha	*Well, it's nice to be able to do something that will help other people, because obviously like I say a lot of the other medications that are for MS have got quite severe, nasty side effects. And so obviously, I don't suffer from any side effects. I don't know about anybody else, but it's*	*09:20*

	nice to be able to partake in something that will help other people. So, you know, it's a good thing.	

Martha further attests to the altruism of her taking part directly coupled with the relative disadvantages of other treatments for other people, where they experience 'severe' and 'nasty' effects whilst Martha is free from side effects. The benefitting of others is a bonus that she acknowledges but her own benefit, and the lack of negative impact is of significant importance to her.

For Jayne and Phil's case it is necessary to consider altruism in the context of their acknowledged ease of trial participation.

Jayne	*Well, I mean, it's been, it's been **really good** and it's quite, its been **quite positive.** You know, I mean, it's, it's not, it's **not a major hassle**. Really. Honestly, I have I have transport **so am all right**.... getting there and back. So that's not that's **not a problem**. They've always been **very friendly** and **helpful** and **kind** and, you know, it's generally it's been a **positive experience***	*11:24*

This frames from the outset that her involvement is largely pleasant and straightforward from a practical perspective, that she doesn't have particular barriers to overcome. The lack of difficulty or negative sequelae appear important, and allow Phil and Jayne to enjoy the feeling of giving something back, of philanthropic or altruistic motivation, without major consequence.

Phil	*Yeah. It's not, mmm Its **not very onerous** really is it, the study?*	*11:54*

As elucidated earlier Phil has repeatedly drawn attention to the ease of study participation , and that this partially contributes to the overall level of satisfaction

Jayne	*because I thought well I've got **nothing to lose**, it would be **really good to be able to contribute***	*16:04*

Throughout the trialogue, Jayne and Phil describe trial participation in terms of both benefits to themselves and as helping other. I would describe their desire to assist others as genuine, but it is within the context of the lack of perceived risk and difficulty. This is a drug that Jayne is already very familiar with, it is not an onerous study, and they are enjoying being a part of the research.

Jayne	*Well, yeah. I mean, **at the very worst**, it will make **no difference** to anybody. It's not going to make people worse, it's **not something that is going to harm people**, so, **I don't see there's anything to lose** really.* *Yeah, I mean, if nobody was prepared to step up then nothing would ever change. If I can do something. You know. **I don't see why not** really*	*29:37* *30:07*

Jayne perceives that there is no reason not to help others, indicating that her altruism is a serendipitous aside, an additional bonus factor, rather than a driver. This premise is manifest throughout the interview.

Similarly, Eve seemingly finds satisfaction in potentially benefitting others.

Eve	*Oh, yeah. Massively, massively, you know, (exhales) its it's just just this sort of makes it feel that **there's a point to it all, basically, you know, it's not just about making me feel better.** You know, there is actually a more, a **bigger point to all of this, a bigger you know reason for doing it.** So yeah, I'm a lot happier that, so it would have been a shame to **have gone through it**. And then they say, Oh, no, it's not. It's, they're not gonna release it or. **I would have been very, very disappointed then.** So Yeah. It's**, it's come to a good conclusion**. (Laughs.)*	*12.13*

Eve	*feel that being on the study has actually **helped get it out there on the NHS**, because it wasn't available before.* *So from my point of view, I think I feel like it's been **completely worthwhile, worth doing** you know, if it means other people now, it's just available for everyone... on the NHS **for other people. I'm hoping that I paid played a bit of a part in that …*** *…**So that that helps as well**.*	*25.34*

Eve feels good that she been part of the process of the treatment being made available, that she has contributed to helping other people like herself. She is invested in the study and it is important to her that it was a successful outcome. She is able to view the research from a different standpoint and see the wider value. I feel that this this sentiment helps her to justify the difficult journey and the challenges that she has endured.

Eve	*Um, I think I mean, it was like I say**, I was fortunate** that I've **not had to worry about work** for, me **children are all grown** so I've **not had to worry about looking after children**. So I think if if, if people were dealing with that, I could understand that being a negative, **I was fortunate I didn't**.*	*32.15*

Again, although altruism is not a key driver to Eve's participation, as with Martha and Jayne, she appears to relish in the wider good, which in turn helps her to find the challenges more palatable. She also recognises that she is fortuitous in not having complexities that would have made her participation more difficult from a practical perspective.

Of all the participants within this study Jude appears to exhibit the most consistent altruistic intent.

Jude	***If I can help if I can help stop it***	*20.59*
	I just feel that I owe it to me, and ***other people who might get this disease to find something to make it better.***	*22.57*
	if I can just be part of something that helps. That looks at ways that we can stop future generations getting this disease or if we get it, there's a way that we can control it and stop it getting so bad, then I've been part of that	*24.08*
	I want to help, I want to help the medics, I want to help anybody. … I want to do, do something positive, to help and if it doesn't help me it might help, help future generations not have to go through it.	*34.28*

Jude seems to exhibit a natural inclination to extend the feeling of injustice and of hope for benefit to others. Jude naturally desires therapeutic benefit from the trial, but she also feels part of something that is fighting this awful condition to aid doctors to help future generations, even if it does not help her.

Jude	*Yeah, I think that's a shame, really, because* ***there might be other people out there who would be willing to be part of a trial. but What if nobody came back to them*** *?. They just, they would, they just think oh, well, they're not interested. And* ***that's not fair.***	*37.48*

Similarly, Jude recognises that not everyone might be as persistent as she has needed to be in gaining access to the STAT2 trial. Consequently, she laments the injustice that others may miss the opportunity of trial participation.

Jude	***This could something amazing that helps people, helps people as well as helping me and I think the MS live I think it's just a I don't think you quite realised just how many people in the world have the disease***	*42.07*

Jude recognises the potentially wide impact the study could have given the prevalence of MS, again not just considering her own perspective. Across the two interviews Jude appears consistently philanthropic in her outlook repeatedly referring to the impact on other people

This benevolent attitude is further evidenced in Jude recording a workplace podcast in recognition of UK Disability Awareness week.

Jude	*I've never made a secret of it… And so I recorded a podcast about MS*	*15.34*

Jude has repeatedly asserted during the interview that she does not keep her MS secret. With the podcast she is taking firmer stand by publicly disclosing (in the work setting) her personal experience of her disability. This contrasts slightly with her first interview where she indicated that she chose not to proactively share her disease in the workplace. Jude has lived with the diagnosis and impact of MS for thirteen years, although it does not define her (Jude's own phrase), it is arguably a part of who she is. In recording the podcast Jude chooses to share aspects of MS that are very personal to her and extremely impactful on her life such as the importance of the location of the toilet, discrimination she has experienced and physical limitations. Jude reference to her trial participation during the podcast would seem to signify its meaning to her. In sharing this, it seems that the trial is now a part of her MS identity alongside physical and psychosocial factors of import.

Activation

The other key theme with the 'self' group-experiential-theme is activation (or self-efficacy). The NHS describes patient activation as an individual's own skill confidence and knowledge in managing their own health and health care (Hibbard & Gilburt, 2014). Whilst both Martha and Eve were introduced to the concept of study participation by the clinician who then proceeded to facilitate their enrolment, Jayne and Jude each had to actively pursue study participation for themselves.

Jayne and Phil describe their experience of having to be proactive to ensure their eligibility and enrolment. Further, Jude had to take the initiative to identify and orchestrate her own participation in a campaign that lasted several years.

Jayne	*It took a **while to actually get accepted** on it in the end because we were, it was quite near the end of the acceptance period. There was a it was a **bit dodgy** whether*	*12:45*
Phil	*you **Almost didn't make it**. did you?*	*13.04*
Jayne	*No, because I had to stop taking the biotin I was already taking.*	*13:21*
Phil	*they'd **missed you off** a list or something? Because, I … something **something had happened**. I don't know what it was. But then **I rang up**.*	*13:40*

In this context, Jayne and Phil are empowered in *having* a decision to make, and the fight to enact that decision. There was a possibility that they would miss study enrolment and it was their own motivation, or activation, that ensured their involvement.

Jayne	*But it was a really, **it was real actual relief when I heard I was going to be on. I would have been really disappointed, I think if I hadn't been.***	*13:40*

The importance and meaning of participation is demonstrated by the efforts they both made to follow through, and subsequently be accepted on to the study. Jayne was greatly relieved to have been accepted on to the study and they were cognisant that this was the only treatment option open to them following diagnosis which drove their determination to not allow the opportunity to slip through their fingers.

Jude's crusade for trial participation was somewhat lengthier and more tortuous than Jayne and Phil's experience. The drive that Jude exhibits to take action against her disease is one of the most notable aspects of her account. Jude's tenacity is motivated by the prior themes of fear and the need to take control over the impact of her disease on her life and on her future. Jude's journey to trial participation can be seen in Diagram 7.

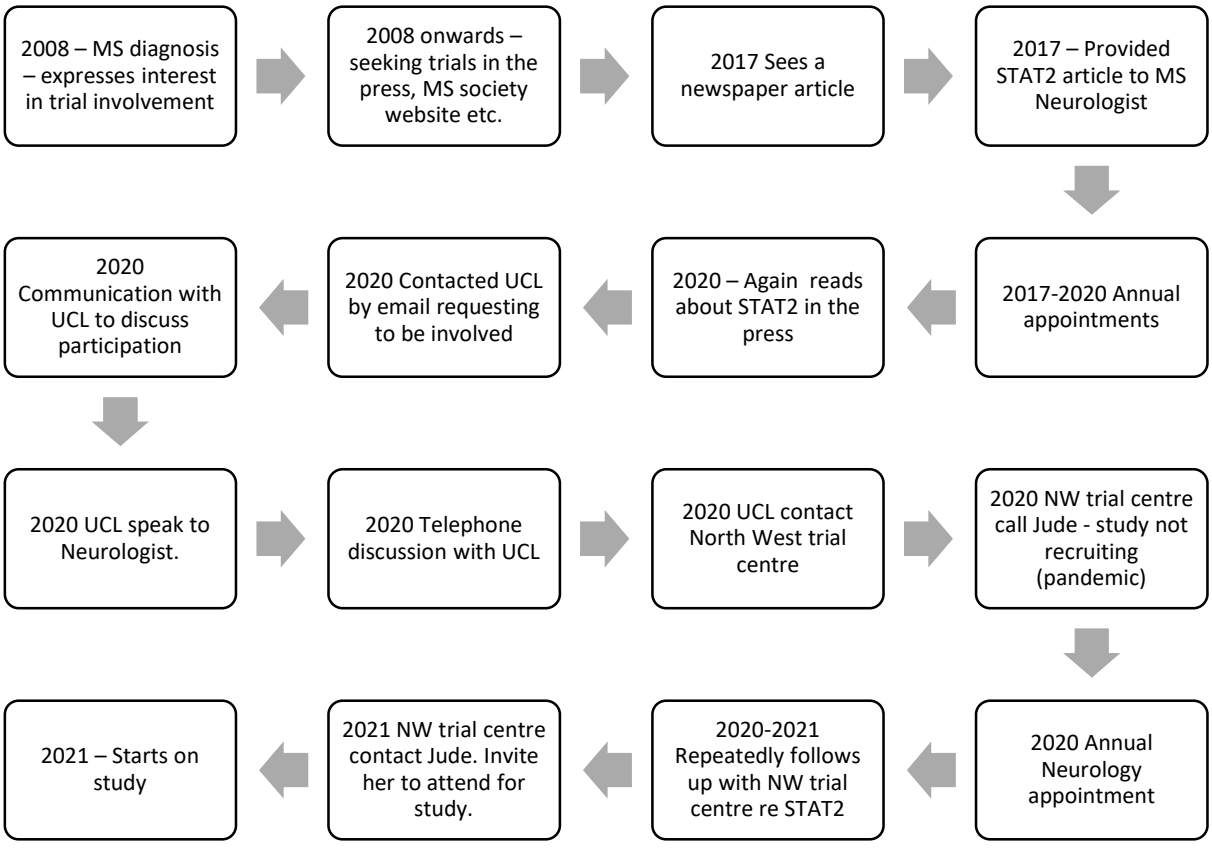


Diagram 7: Jude's Persistent Journey

Jude's journey towards trial participation originates in 2008 when Jude receives her diagnosis of primary progressive MS.

Jude	*And **from the get off, I did say to the neurologist, look, this is a god awful disease. And if there's anything, anything at all, research, you know, drug trials, anything like that. I would like to be involved. And I think he wrote on my file at that point.***	*4.17*

Jude advises the Neurologist of her keenness to be involved in research, which is then documented in her notes. She is anguished and expresses a sense of urgency to take action against this '*god awful disease*'.

From that point onwards Jude takes it upon herself in proactively seeking suitable trials in the press, on MS websites. Identifying a study that she could be eligible for she describes how she presents a newspaper cutting to her neurologist and repeatedly, but fruitlessly, raises her wish to take part in research during her annual appointments.

Per the NHS constitution, the NHS pledges to inform patients of studies they may be eligible more. Here Jude is reversing the role and letting her NHS consultant know of a study she could be eligible for.

Jude	*Perhaps **[the neurologist] doesn't know about it.** Ermm You know, **s/he doesn't know about all the trials, … Is it because s/he doesn't know, or is it because time constraints? Because I know after five minutes, you know, you literally get five minutes to talk about 12 months.***	*18.52*

Jude questions whether the fact that her neurologist is not specifically an MS neurologist and so may be less familiar with the trials, or whether its due to the brevity of the clinical appointments. Either way Jude appears frustrated by the lack of progress in her quest for taking part in a study.

Jude is again alerted to the study from a newspaper article and takes matters into her own hands by contacting the lead centre in London. The study team at UCL facilitate her involvement liaising with the Northwest trial centre, the hospital where her neurologist is based, just a few miles from her hometown. When the study, at last, looks to be a realistic proposition, she learns that recruitment is on hold due to the SARS2-CoV19 pandemic.

Jude	***I got a call from [the NW trial centre] … they weren't seeing patients**. So there has been a delay.*	*7.35*

Jude's disappointment and frustration is tangible as she described this. Jude continues to contact the trial centre and finally, in 2021 as the lockdown lifts, the Northwest trial centre finally contacts Jude to invite her to come in for the study.

At the time of the first interview Jude had started study treatment one week previously. It has seemingly been a tortuous journey and Jude has shown tremendous drive which evidences the importance of study participation for Jude.

Additional aspects of self

The impact on MS on identity and self are topics that have been extensively explored and published (Irvine et al., 2009; Mozo-Dutton et al., 2012). Numerous aspects of the importance of self, associated with trial participation, are embedded within and across the themes considered within this chapter. This final segment of this chapter brings these together to complete this study's findings.

Themes of worthiness and self-need appeared particularly pertinent for Martha and for Eve. Martha mourned her past self and had lost aspects of her identity when she could no longer work, as discussed earlier. Being championed by the study investigator, and her acceptance within the research setting gave her a sense of worth and privilege. Worthiness is a constituent of esteem, which can be defined in terms the attitudinal evaluation and respect a person receives in terms of their merit or value as a person. (Taormina & Gao, 2013). As relevant within the discussion around human connectedness, Martha felt lacking in worth from being cast aside at work, whereas in contrast she felt her worth validated by being fought for by the clinician (*he said he was fighting for me to get on it. 20.15).*

Her sense of being in a privileged situation through trial participation is recognisable from her tone and narrative. Privilege can be considered to encompass five core aspects; firstly as a special advantage that is not commonplace, that it is granted rather than earned, relating to a preferential status or rank, which benefits of the recipient to the exclusion of others and finally that it may be outside of the experiencer's awareness (Black & Stone, 2005). In Martha's lifeworld (separate to the research context) her disease sets her apart and as different from the average person. Within the clinical research setting these symptoms are unremarkable, expected and accepted, and so are essentially neutral in terms of her difference. The research treatment with its *'better success rate [9.44]]*' and absence of side effects (as perceived by Martha) provides Martha with something that sets her apart, in a positive sense, from others with MS, rather than from others *without* MS. She is privileged versus others unable to access the treatment as its *'not on the NHS [2.47]*'. People with MS on mainstream treatments have options that Martha describes as *'ridiculous [9.44]*' and have not been singled out for her superior life-long treatment. Feeling fortunate and deemed worthy of being fought for, Martha inadvertently portrays an air of self-satisfaction.

In contrast to the problematic and stressful aspects of her life this is one area where she is on the winning team.

Eve also seems to attribute a degree of privilege in being offered the study and being supported by the consultant throughout, as explicated earlier (human connectedness)

In a similar vein Jayne and Phil felt a certain level of importance at being involved in research, and particularly for Phil this appeared to fulfil a need that he had lost since retiring from work, and public office as a magistrate.

Jayne	***Makes you feel a little bit important.***	*29.40 IV 2*

Researcher	*Are you pushed for time or are you OK?*	
Jayne	***no no no, we're fine***	*46:10*
Phil	*We're* ***never pushed for time***	*46:21*
Jayne	*No not really,* ***noo.***	*47:03*
Phil	***Ever since we've retired***	*47:15*

Phil has been a magistrate and has worked in various professional roles; he has much to say on a broad range of topics. Phil, now retired, is in practice a carer for his wife who will inevitably decline over the coming years.

Phil highlights that he thinks that *'it is important to keep contact… Or you can lose touch; you just need that personal…' (41.08)*

Phil's sounds wistful and taken together with his other comments appears to reflect his mourning of times past where he perhaps felt greater level of social standing or social interconnectedness. This study fills a gap for Phil, it seemingly provides intellectual stimulation, an opportunity for peer-to-peer dialogue with professionals and a feeling of import. More so than for Jayne, this trial appears to provide Phil with an alternative role and purpose.

Eve's doorhandle revelation in the final minutes of the interview has been described in connection to trust and connectedness / isolation. This troubling disclosure of unfulfilled individual self needs arose in response to the ubiquitous 'is there anything else you wanted to say?' Eve had surprised me with a troubling revelation of her unsated self needs

Eve	*… they're **constantly sending me information about the clinical trial**. erm you know, **if it there were any changes on clinical trial, it's give me an update…. ,** but **I know I probably only had to ask**, but , ha, it's**, if you did ask then they will tell me. Yeah, no, no, no, you're doing really well, and everything's fine.** And - but actually, but **what do my scans show,** what, what does that **what does that blood test mean**?*	*44.32*

Whilst Eve received updates on the trial, Eve is frustrated that her own individual results* and progress were not shared with her. On asking about her clinical progress Eve receives only platitudes Eve repeats these same tenets multiple times which accentuates her dissatisfaction at this aspect of her experience.

**Note - Depending on the study design study outcomes may have been 'blinded' to reduce in-trial bias. If that was the case then that could have been explained.*

More than simply having access to and understanding her trial assessment results; Eve is left not knowing how the trial treatment has impacted her MS.

Eve	*You know, this, this is how **you've**, you know, we feel the drugs worked and **this is how it's worked for you**.*	*42.53*
	*, **this is how it stops the progress of your MS**. It there was anything like that, then that was that would have been useful.*	*48.04*

Eve spends some time on this topic explaining what she would have liked to have learned about her individual clinical progress within the trial, what her results showed, how the trial drug has impacted her MS.

Eve	*Because I still really , you know, err I am a little bit **in the dark as to how , what things are and how it's affected me.***	*49.14*

Despite earlier stating that the health benefits are '*obvious*', after four years on the trial she remains unclear if or how the trial treatment may have impacted her health. During the interview Eve has continually extolled the benefits of her study experience, mostly driven by her sense of nurture, nevertheless this is a very significant deficit for her. As soon as she finishes framing this deficit she immediately reverts to the overarching positivity of participation and her admiration for the team as if she feels guilty for having shared a negative aspect.

Reflexive note: I find this revelation startling. Eve is very undemanding and phlegmatic in her description of her experience and so the significance of this statement was not initially apparent. I admit to feeling disappointed for her.

Eve perceives a marked mismatch in her information needs and the information provision. There are multiple reasons why this is the case for Eve – the results may not have been able to be shared, she may not have expressed her need for information as clearly as she believes, she may have received information but not understood fully;at numerous points she confesses her limited understanding of some aspects of the study *'(a lot of it was a little bit over my head, and I don't have a medical background [45.30])* the study team may have assumed or misjudged what Eve needed to know, her perception may have changed over time. Whatever the reason for the mismatch it is important that clinician researchers are aware and can mitigate this deficit.

Summary Findings

Each participant in this study was, in turn a participant in an MS interventional clinical trial of an investigational medicinal product. The individual analyses of each participant account(s) of their trial participation led to an idiographic portrait of that person's unique experiences of taking part in the MS trial in which they were enrolled, as represented in the first part of this chapter. When comparing across personal experiential themes, there were multiple similarities and differences between individual analyses. Where 'like-domains' were clustered to provide cross participant or group-experiential-themes of benefit and harm, human connectedness and self, it remained the case that each of the participants experienced a particular phenomenon or theme to different extents (Table 9) or in differing ways. Trial participation was expressed by all in positive terms, but which focussed on different beneficial aspects for each of those involved. It seemed to be the case that lifeworld context influenced participation experience. For example, Jayne (and Phil) who appeared phlegmatic and accepting of Jayne's MS, expressed enjoyment and scientific intrigue that was effectively absent from other accounts. Findings also suggested that Phil found that the sense of import might fulfil some aspect of societal engagement reminiscent of prior social standing.

The experience of actual or possible physical adverse effects from trial treatment was commented on by each participant but could be understood to had varying degrees of significance for each as will be further explored in the discussion. All participants valued the premise of additional care and the potential for therapeutic benefit which was linked to hope or regaining control by or staving off further neurological decline. Within each account there were elements that indicated some degree of misunderstanding of the trial intent, assessments or of anticipated benefits which is discussed in more detail in the next chapter. From participant accounts it could be considered that trust was especially impactful for Martha, Jude and Eve which resulted in a sense of safety, belonging and of nurture. The trial environment seemed to represent a safe-haven for Martha in contrast to her health-condition setting her apart in her employment situation. Whereas Jude also felt safe and trusting of her care under the auspices of the trial, and which could be understood to be in the context of her experience of clinical care which she expressed as being lacking. Eve's level of trust and the value she assigned to the support from the research team seemed to

eclipse some other factors of trial participation to the extent that Eve, although dissatisfied with and lacking understanding of the effect of the trial treatment, expressed faith in the level of investment by the team in her wellbeing. Trust and power in the doctor patient relationship are each explored in the discussion chapter.

Whilst two participants drove participation themselves (Jayne and Jude), the two other participants (Martha and Eve) appeared to have the impression that their trial enrolment was driven by their clinician (who was the trial investigator), but which was not problematic for them. Altruism was expressed as a source of satisfaction by all participants, but which was in each case contingent on lack of complexities in taking part or expressed against a background of anticipated benefit. Both activation (or self-efficacy) and altruism are considered in greater detail in the discussion chapter. The findings represented here are discussed in Chapter V in the context of extant research participation literature and that of other domains relevant to the experiential themes identified.

Chapter V

Discussion

Introduction

This chapter opens with an evaluation of quality considerations, research scope and constraints (or boundaries). It then moves on to discuss the findings in the context of extant literature, thereby illuminating the unique contribution that his thesis contributes to existing knowledge. Human experience is multi-ontological and multidimensional, and appreciating that the participants within this study are not exclusively participants of research but people with a fear-inducing, challenging and unpredictable long-term health condition navigating the UK health system, relevant literature explored within this discussion spans a range of domains to best contextualise the findings. Literature appropriated for this discussion draws upon the experience of having MS or other long-term conditions, interactions and relationships within the healthcare and research arena, DMT decision making (in the clinical setting), as well as research participation specific works across different health conditions and experimental treatments. Aligned with the idiographic participant-focused nature of this thesis, where appropriate, the discussion employs participant quotes from published qualitative research participation literature. This approach seeks to exemplify both commonality and variance between participant idiographic accounts within the findings of this study and other literature describing research participation in terms of and phraseology, experience and meaning.

Quality Considerations

Firstly, IPA is considered an appropriate methodology for enquiry of this nature, as explicated earlier within this thesis. Previously unexplored, health-related, emotionally laden topics are particularly suited to IPA, and further IPA is increasingly gaining traction in healthcare research because of these qualities (Biggerstaff & Thompson, 2008; Eatough & Smith, 2017; Smith et al., 2009; Smith & Nizza, 2022).

As described in Chapter III, quality standards for qualitative work (Yardley, 2000) and IPA specifically (Nizza et al., 2021; Smith, 2011) have been incorporated and revisited throughout the design implementation and outputs for this study. The more recent

contemporary understanding of quality considerations in IPA (Nizza et al., 2021) is employed here as the appropriate platform for this aspect of the discussion. The co-authors of this article, Nizza, Farr and Smith, advocate four markers of appropriate IPA quality, summarised in Table 10. Each of these will be considered in turn with exemplified with study specific considerations that demonstrate the alignment with quality indicators.

Quality indicator	Brief description
Constructing a compelling, unfolding narrative	The analysis tells a persuasive and coherent story. The narrative is built cumulatively through an unfolding analytic dialogue between carefully selected and interpreted extracts from participants.
Developing a vigorous experiential and/or existential account	Focus on the important experiential and/or existential meaning of participants' accounts gives depth to the analysis.
Close analytic reading of participants' words	Thorough analysis and interpretation of quoted material within the narrative helps give meaning to the data and the experience it describes.
Attending to convergence and divergence	Idiographic depth and systematic comparison between participants creates a dynamic interweaving of patterns of similarity and individual idiosyncrasy.

Table 10: Quality Indicators for IPA (Nizza et al 2021)

Constructing a compelling, unfolding narrative

Participant narratives were appropriately coproduced between the participant and the researcher during semi-structured interviews where topics of import were led by the interviewees. The researcher prompted or guided discussion only to bring the discussion back *towards* the experiential phenomenon in question, while being cognisant that aspects of import were often intertwined with narrative that may, prior to analysis, feel less closely related to the focus of the research. Interviews were therefore relatively long with a median duration of over 60 minutes. Participants appeared to speak candidly and openly during the interviews, although the first interview felt more restrained which may reflect researcher inexperience or participant qualities, or a combination thereof. Moreover, appreciating that that only those people who live with MS can truly understand what MS means (Eskyte et al., 2019), the semi-structured interview questions and the study design was coproduced between the researcher and experiential experts. People with MS who had participated in MS research previously and who were not participants within this study shaped, guided and coproduced the interview framework, schedules and study documentation, across a number of meetings convened for that purpose. This approach was well received by and specifically praised by the designated NHS ethics committee

appraising the study. Coproduction at the design stages harnessed experiential expertise to bring greater relevance, applicability, and openness to the interview guide thus enhancing the quality.

Developing a vigorous experiential and/or existential account

The focus of the findings were the experiential aspects of research participation as drawn out from the participant narratives. Experiential notions were grouped into three master experiential themes deriving benefit and harm, human connectedness and self. In turn these included notions that seemed of existential import to participants such as hope and taking (back) control, being activated, deriving altruistic satisfaction, deriving a sense of belonging and feeling safe. Practical aspects of trial participation often surveyed in evaluating the experience of trial participation were not explored.

Whilst some phenomenological aspects were more apparent, or closer to the surface others emerged upon layered analysis applying the hermeneutic circle to derive further meaning; and aligned with the concept of 'gems' and 'suggested gems' requiring greater depth of analysis (Eatough & Smith, 2017). Analysis was, expectedly, not a linear process but was dynamic and iterative – moving back and forth between the part and the whole. Within this study the whole, inspired by Schleiermacher's holistic ethos as described by Smith (Smith et al., 2009), as described in the methodology chapter - entailed repeated revisiting of interview transcripts, recordings and fieldnotes thus taking into account intonation, pauses and non-verbal cues. The aim was to ensure that the findings most closely aligned with the meaning with its manifold layers and as expressed by the participant, as understood by the analytical instrument, the researcher.

Close analytic reading of participants' words

Some concepts were manifest in the accounts of one participant but more deeply buried in others. One example that illustrates this concept is described here; the premise of feeling secure for Jude was explicitly expressed ('he makes me feel safe') whereas for Martha it required deliberations between the part and the whole, her trial experience and her lifeworld context. This allowed the understanding of the trial environment as a safe- haven for Martha to be drawn from her narrative. The safe-haven idea encompassed feelings of being worthy and of being fought for, in contrast to being cast aside in her employment. Further the trial being something that that situates her as being 'normal' in the context of

the research (i.e. having MS). Moreover, Martha expresses notions that can be interpreted as her feeling privileged versus others that have MS, by receiving the care and superior interventional treatment within the trial versus other pwMS outside of the trial who have to tolerate '*ridiculous'* treatments. Extensive inclusion of verbatim excerpts from participant accounts tethers the interpretation to the words used by the participant.

Again, in order to enrich the interpretative process, pwMS who had research experience provided experiential expert insight and contextual 'insider' knowledge. This was enacted by discussing participant narrative excerpts (per the ethically approved study design) moving between individual words, phrases or paragraphs. Frequently this aligned with the researcher phenomenological interpretation but often brought new additional perceptions or, rarely, generated a *de novo* understanding or an opposing view. Each new steer contributed to researcher's evolving and shifting fore-understandings (Eatough & Smith, 2017) and enriched the interpretative process. In short, coproduction interpretative phase helped me, the researcher, to be more '*in the shoes'* (Pietkiewicz & Smith, 2014) of the participant.

Attending to convergence and divergence

The final strand of Nizza's quality indicators is that of integrating convergence and divergence whilst maintaining idiographic depth. Within the current study this has been achieved by generating separately analysed case studies for each participant with each case examined on its own terms. As the study progressed findings from each interview were consciously bracketed or put aside at all stages to reduce bias during interviews, and during interpretation and write-up – thus consciously ensuring receptivity to the idiosyncratic nuances of each participant. This approach maintained an idiographic focus before seeking convergence and divergence across the full data set comprising four separate participant analyses. At this stage the careful attendance to convergence and divergence led to the generation of cross-participant experiential group themes. Convergence and divergence between participants, and with published literature is then further considered within the second part of this chapter.

Further Considerations

This thesis has fulfilled its stated aims in revealing experiential meaning from the accounts of pwMS taking part in research. As with all studies there are constraints or boundaries which should be acknowledged, and which may have a bearing on future research.

Firstly, aligned with the principles of IPA, insights generated from interpretive qualitative research is coproduced between the researcher and the participant. The synergistic output of that connection at that particular moment in time may be understood in different ways. The findings represent one truth resultant of the particular frame of reference through the lens of the analytic instrument, the researcher (aided by experiential experts). Taking this into consideration, the study findings should be regarded as stimulating and challenging concepts rather than one definitive truth. The participants narratives and perceived meaning are represented transparently in their own terms, without importing extrinsic theories (Eatough & Smith, 2017). Furthermore, IPA also recognises that interviewer characteristics can impact participant responses. As far as possible this is addressed through bracketing of preconceptions and reflexive processes whilst acknowledging that in qualitative methodologies researcher bias can never be fully eliminated (Eatough & Smith, 2017). Furthermore, IPA was originally developed and employed within the field of psychology (Shinebourne, 2011). At times, and as expressed elsewhere, I have felt that had I had the grounding of those trained in the human psyche, that might have allowed me to more succinctly capture particular notions. I do however consider that I have received and understood the participant's meaning and transparently represented their own distinct voices through my particular lens.

A deliberately small sample size is entirely concordant with the idiographic approach and depth of an IPA study, and three interviews (or more) is considered sufficiently rich for a doctoral level study (Smith & Osborn, 2003). Given the qualitative nature of this study generalisability was not a focus of this study. However, some important messages and new insights from pwMS taking part in MS trials can be seen within the interpretation of accounts from this small cohort.

Further, research has highlighted the tendency for people to recreate autobiographical memories in order to form a coherent and favourable view of their self in the moment (Wilson & Ross, 2003). Participant recall-bias and interpretation or sensemaking is

therefore also expected to be inherent in responses provided (Smith et al., 2009) and is aanticipated element of the double hermeneutic. Additionally, it is important to consider the potential influence of selection bias. This study employed purposeful sampling and all participants that made contact received consistent communication. It is not possible to determine if or how potential recruitment bias at the recruiting centre might have influenced which trial participants were approached by the recruiting centre, nor what may have influenced participants themselves to agree to participate. For example, it is possible that participants approached are those with a deeper interaction with the study team or were selected for particular qualities such as positivity. Whilst it was not a specific requirement of the study parameters, all participants within this study were participants in an interventional clinical trial of an investigational medicinal product (CTIMP) for MS. This can be regarded as a positive aspect in terms of the homogeneity of the cohort; it would however also be of interest to compare the experience of those taking part in CTIMP versus the experience of taking part in different types of MS research.

An additional factor to consider is the stage of the primary research - participants within this study had a range of tenure within the primary study, per the research design (early, established, study close and terminated prematurely). This diversity provided an additional perspective and richness to the data. It proved not to be possible to recruit a participant who was considering trial participation but who had yet to join the study which would have provided further perspectives. Two of the four participants were interviewed twice which gave a longitudinal perspective thus providing greater insight as to how trial participation experiences changes over time – a greater degree of longitudinal separation is likely to yield additional findings. Whilst it is worthwhile considering such constraints, it would not have been possible to have included all potential permutations for an IPA study of this nature in a hitherto unexplored phenomenon.

The clinical course of MS and its prognosis in any individual depends on a multiplicity of factors such as age, gender, type and frequency of relapse, lesion load on MRI scan and extent of spinal cord involvement (Scolding et al., 2015). It is reasonable to envisage that the subtype of MS, the trial interventions, and the expectations for the trial could influence the participant's experience of the trial. Within this study participants all had a diagnosis of relapsing remitting or primary progressive MS. Whilst these two subtypes account for

almost all cases at diagnosis, most people with RRMS will go on to develop secondary progressive MS, which is therefore the second most common subtype. People with SPMS were not represented within this small study, possibly resultant of the trials ongoing at the recruiting centre during the recruitment period for the current study. It would be interesting to explore if the MS subtype influences the participant experience of trial participant, or whether other factors, such as lifeworld context, are more impactful.

In the relapsing remitting form of MS, a gender ratio around 3:1 of female to male diagnosis exists (Orton et al., 2006). Further, it is recognised that men and women living with a chronic illness tend to employ different coping and acceptance strategies (Pakenham & Fleming, 2011) with women more likely to adopt a combination of varied coping strategies (Endler et al., 2001). Within this study all participants were white British females between the ages of 35-64. Phil, the only male interviewed provided an emic view of his and Jayne's joint trial experience but was himself not a participant of an MS research study.

It is also to be noted that a multitude of other participant attributes may influence particular facets of experience. For example, educational attainment is determined to be the most powerful predictor of levels of patient activation in those living with chronic disease (Van Do et al., 2015) however, within this study educational attainment of participants was not determined and so the impact of this factor on findings cannot be evaluated.

As with every research study, dissertation or thesis generated in this particularly challenging temporal zone, the impact of the SARS2-CoV19 has to be recognised. Within the study the original intent was that all interviews would be conducted in person. This proved to be impossible due to SAR2-CoV19 restrictions and so interviews were mostly conducted by telephone, with only the first two interviews being in person. It is possible that the method of data collection by telephone may have impacted participant responses. My initial concern was that interviews by telephone may restrict the ability to develop rapport. However, inquiry has indicated that telephone interviews can be effective in qualitative research (Sturges & Hanrahan, 2004) and participants can be more willing to share sensitive information (Novick, 2008). Further the detailed descriptions and the length of the interviews (30 -80mins) indicate that the telephone interviews provided appropriately rich and detailed data.

Study Findings in Context of Existent Literature

A far as can be determined this is the first study that explicitly brings forth the previously unheard voices and perspectives of participants in MS clinical studies of investigational medicinal products. The interpretative phenomenological approach has realised the intricacies of research participation experience for pwMS in the context of their own lifeworld. Findings discussed within this thesis have resonance with studies that have explored research participation for people with different health conditions, and which are exemplified throughout this discussion. However, this thesis has shed new light onto the world of the pwMS and their particular experience of being a participant in the clinical trial context, which will be drawn out throughout this discursive incursion.

To help orientate the reader the structure of this section is broadly aligned with the cross-case or group-experiential themes within the findings chapter; trial derived benefit and harm, human connectedness, and finally, self with a focus on activation /self-efficacy and altruism. Additional concepts from the literature are drawn into the discussion to further contextualise and explicate participant meaning described in the findings.

Trial Derived Benefits and Harm

As illuminated in the findings section, trial involvement was understood to represent a means of taking control (psychological) and to gain therapeutic (physical) benefit, as well as a source of enjoyment or fulfilment for one participant. Amongst the participants harm was manifest as facing fears of future self, side-effects and the experience of a trial ceasing prematurely. Psychological and physical benefits of trial participation, and trial induced harm for pwMS in the context of relevant published are explored below.

Psychosocial Implications of MS

Considering the disease profile of MS it is unsurprising that pwMS experience lower quality of life and are more likely to report clinically significant psychological issues including increased levels of depression and anxiety. Developing or being diagnosed with MS is resultant in feelings of insecurity, loss, and grief (Dennison et al., 2016; Finlay, 2003; Strickland et al., 2017).

Psychological adjustment to MS is seen to be lower than for other chronic conditions such as inflammatory bowel disease, rheumatoid arthritis, spinal injury and muscular dystrophy (Pakenham & Fleming, 2011). This is believed to be attributable to the unpredictability of the course of the disease, lack of a cure, the neurological basis and because onset is often during an individual's reproductive years (Motl et al., 2009). Anxiety is an inherent aspect of living with a chronic incurable disease (Audrey, 1988). People with chronic disease frequently experience a feeling of lack of control over their condition and that can result in feelings of short- or long-term powerlessness, which can be defined as *'the inability to have agency in one's own life'* (Fitzgerald Miller, 2000). Further unpredictability, such as with MS, can exacerbate feelings of powerlessness (Bakker, 2016; Fitzgerald Miller, 2000).

Central to anxiety is fear, particularly for people suffering from chronic diseases, such as cancer and MS (Herschbach et al., 2005; Khatibi et al., 2020). Furthermore, anger is often a secondary response caused by underlying uncertainty, concern and fear (Gautam, 2021; Van Reenen et al., 2019). It is no surprise therefore that it is estimated that between 16 and 57% of people with MS suffer from anxiety (Butler et al., 2019). A thematic analysis exploring anxiety in pwMS (Butler et al., 2019) illuminated many concepts that resonate

with findings from this study; concern about the future impact of lives, coping with the uncertainty of MS and effecting control over the disease.

Van Reenen found that pwMS often felt and urgency or compulsion to take action by starting medication, and that this drive is often exacerbated by the uncertainty and fear of both physical and mental deterioration (Van Reenen et al., 2019). Similarly, the author describes the commitment for pwMS to do everything within their power, to regain control or to influence the course of their MS and their lives (Van Reenen et al., 2019). Further, that the taking of oral medication is associated with trying to maintain familiar or normal life (Van Reenen et al., 2019). Extending this premise further, an IPA of pwMS DMT clinical decision-making describes the role of DMT initiation providing a sense of regaining control and eliciting hope in the face of the fear of decline (Carey et al., 2021) with participants feeling empowered in tackling the disease.

These tenets resonate with the experiences of pwMS within this current study, as understood through the analytic process, where the premise of taking action was regarded as important for participants. The association of tablet or oral medication being a more normal or less risky treatment was recognised in Eve's account as she panicked at the prospect of an infusion in contrast to her prior oral medication. The notion of taking control to counteract powerlessness by '*doing something'* was enunciated by participants and seen to be enacted through taking part in the MS treatment study. Jude, particularly, expressed views that seemed to be aligned with the literature with hope for a better future, taking back control from the disease and feeling empowered by taking part in the study, and for Eve the trial was a means of firefighting acute decline. Further, the term *'no brainer'* employed by two of the participants in connection with taking part in their MS study also suggests that there is almost no choice or decision to be made, that they felt compelled to act. This is intensified by the research scenarios described within the study, whereby two of the participants have no licensed treatment options available to them and so the trial is the only potential treatment option (albeit experimental) open to them. Equally, for the other two participants the trial provides access to a treatment that is only available in the trial setting, although other treatments would be available outside of the trial in the clinical setting.

Carey (2021) also identified the maintaining of normality as important to patients as a motivation for initiating a DMT. The premise of normality comes through most impactfully for Jude who is afraid of where the disease might take her and cites shopping for shoes and being able to go to the bathrooms as the normalcy that she strives to maintain resultant of trial treatment. Van Reenen (2019) also illuminated the notion of pwMS hoping to feel an effect of the medication (in the clinical setting) but that often this physical feedback is lacking. This is potentially even more complex in the trial setting where participants are aware of the possibility of receiving either inactive placebo or an unproven active treatment. Jayne had hoped that (prior to open label active treatment) that she had been assigned to placebo in order to explain the lack of physical beneficial effects. Conversely Jude expressed anxiety that she could have been randomised to placebo but expressed views that indicated her desperation to take action against the disease. Jude subsequently perceived physical feedback in the guise of possible side effects which she interpreted as indicating her assignment to active treatment.

Specifically, reference in qualitative research participation literature also support this premise of taking action as a means of taking control and counteracting powerlessness. For example, findings from studies involving people with chemotherapy induced nausea (Hughes et al., 2013), cardiac symptoms (van den Berg et al., 2017) and rheumatoid arthritis (de Jorge et al., 2015) each support the notion that participation in clinical trials can offer a meaningful opportunity to counteract powerlessness by helping to effect or regain a level of control. In Hughes' qualitative study exploring participant experience of a randomised trial comparing acupressure treatment versus sham treatment for chemotherapy induced nausea, the authors exemplified the notion of the trial offering the opportunity to regain control with a participant quote; *'I felt because I think part of having cancer is you lose control, and I am quite, the sort of person that likes to be in control and this is enabling me a little bit of control back'* (Hughes et al., 2013). Or as Jude eloquently expressed, to feel *'empowered'* by taking action.

Hope Associated with Trial participation

Hope in the health or trial setting can be described *'as a positive, future-oriented emotional state, which manifests as a desire for a particular healthcare outcome'* (Hallowell et al., 2016). In one study exploring hope in people with MS (Soundy et al., 2012) participants were able to confront their disease through extrinsic hopes including medicine, faith, the development or retaining aspects of life of import, or gaining a sense of purpose in life again. Participants needed to reflect on their losses such as social roles, leisure activities, employment or their identity and found such losses hard to accept. Chronic conditions such as MS are recognised to affect identity or relationships with self (Carey et al., 2021). Within Soundy's aforementioned study, participants (pwMS), individuals frequently needed to re-establish a sense of purpose or to find a new direction. Participants expressed hope of life being restored to a pre-diagnosis status; this aligned with Jude's hope for regaining her prior health status which is explored further within this chapter. Further, clinical trials were specifically called out as a means of retaining generating hope through action (Soundy et al., 2012) where one participant specifically made reference to a trial as their only source of hope. Trial participation as an important means of finding or maintaining hope is highlighted in several explorations of research participant (Harrop et al., 2016; Kohara & Inoue, 2010; Soundy et al., 2012; Sulmasy et al., 2010; Todd et al., 2009). Examples included in the literature include the premise of hope for patients who have no other treatment options open to them (Cox et al., 2011), or where hope may be dashed by not being ascribed the hoped-for treatment (Cooper et al., 2017). In the current study both Jayne and Jude have no options for DMTs outwith a trial scenario whereas both Martha and Eve are eligible for other treatments, but the investigational drug they received within the study was only accessible via the study at the time they started on the trial.

Aligned with existent participation and MS experiential literature, hope is a meaningful premise to people with long term or incurable conditions. Within this study hope for therapeutic benefit or therapeutic optimism was expressed by each of the participants and is a key aspect of trial participation. The first participant (Martha) had very high expectations of clinical benefit whereas the second participant (Jayne) initially seemed to have almost neutral expectations as she had been taking the trial treatment at a much lower dose prior to the trial, but upon detailed analysis it became more apparent that she

harboured hopes of therapeutic impact. Eve, entering the trial from a dire health situation and taking a licensed DMT with terrible side-effects, did not ascribe much narrative to therapeutic benefit. Jude maintained what might be described as an overly optimistic hope for therapeutic benefit which she held concurrently, but in contrast, with a good understanding of the trial design. Hope within this study, however, could be seen to distil into two interconnected themes, the hope for a therapeutic effect or what might be termed therapeutic optimism (Hallowell et al., 2016) as described above, but also the related and less tangible additional *feeling* of hopefulness, which is a sense of positivity associated with the possibility of a good outcome (Kwong, 2020). Literature in research participation largely seems to consider hope and feelings of hopefulness as the same concept which potentially warrants further exploration. Where hope is unrealistic then principles of therapeutic misunderstanding and unrealistic optimism, as discussed later in this section, need to be considered.

Other positive aspects for research participants illuminated in the findings section included access to treatment and to HCPs, enhanced and additional clinical care, and increased surveillance; each of these are repeated theme in trial participation literature (Bishop et al., 2012; Harrop et al., 2016; Kerrison et al., 2008; Lawton et al., 2003; Maida et al., 2014; Unger et al., 2016) although this domain was reported less positively in a trial participation satisfaction survey conducted in the 1990s (Verheggen et al., 1998). A pwMS participant in Kerrison's research participation study exemplifies the importance of this; '*Initially I got the chance to speak to the researchers conducting the research. They showed me the scans and explained things to me, how the research was progressing. GP said you are getting a free brain scan every three months. Getting information from the horse's mouth about your condition'* (Kerrison et al., 2008).

Within the current study, the benefit of enhanced care was very evident from Jude's account who had described feeling '*abandoned'* and resentful of time-restricted annual appointments in the clinical setting. Jayne too valued the increased interaction and additional investigations such as the MRI scanning. Martha commented on the frequency of her appointments, but which also seemed to be linked to her sense of belonging. Eve too felt that the trial setting provided greater continuity in care providers, more intensive interaction and more ability for building a relationship with the research team versus a

clinical team. Jude particularly values a renewed interest in her condition with face-to-face consultations and clinical care accessed rapidly via the research team.

Excerpts from participant experiences in a cardiovascular study in Russia, explored via an inductive constant comparative method, echo Jude's experience of being able to make contact regarding non-trial health concerns; '*I can call any time and ask a question about any of my diseases, even unrelated to the research study'* and '*I like that in any moment, if I need anything, medical help will be provided to me'* (Zvonareva & Engel, 2014).

The next two participant excerpts from Harrop and Lawton's participant experience studies respectively, are each similar to the way in which Jayne also termed this enhanced oversight facet of trial participation, as can be appreciated within the findings chapter; '*Well, I think being part of the trial, you're looked at better than if I wasn't on the trial. You know, you're being watched more, you know, and so, and because you see the research nurse. Otherwise, you are living on your own and you never see anyone. At least they are keep[ing] tabs on you'* (Harrop et al., 2016). And again, this additional reassurance is valued by a participant with a long-term health condition enrolled in a research study; *'Also, you're — how can I put it? You felt happy because the tests that you've had made you feel that you wouldn't have had them if you didn't come to the centre. You wouldn't have had an MOT every three or four months. It does give you a lovely cushion to know that, whatever, they are going to pick something up, even if it's not diabetic related, which I found very good'* (Lawton et al., 2003). Even where a participant finds that they are receiving placebo the enhanced holistic benefit of trial participation in terms of increased medical oversight is recognised to be of value from a participant perspective (Bishop et al., 2012).

A further positive aspect of trial participation identified within this study is that of scientific intrigue which equates to findings located within research participation literature, albeit to a less evident frequency. The pwMS participants in Kerrison's study held the science of the study in high regard and were excited by scientific and medical progress; *'Fantastic machine. Let me look at the scan. Very expensive'* and *'they are excited about what they do and it comes across'* and *'I feel that the doctor at the hospital feels that they are getting somewhere, and that's very exciting'* (Kerrison et al., 2008). The next quote resonates most closely with Jayne (and Phil's) account where there was enjoyment in meaningful activity. This benefit may be very significant for those with serious conditions whose activity and

feeling of worth may be impacted by their health limitations; '*Yeah, yeah, I mean, it's something to do, you know; it's good fun, it breaks things up. Life gets a bit boring when you are stuck like this, you know'* (Harrop et al., 2016). The next excerpt below is from a person with Motor Neuron Disease (MND) whose participation in study is being evaluated in a qualitative exploration. Like MS, MND is neurological, degenerative, and incurable but the path of the disease is generally far quicker and always fatal. Disease modifying options are extremely limited in availability and effectiveness. In this context the meaning and value of study participation to the individual is especially poignant; '*Participating gives me a sense of usefulness. It makes the disease less useless'* (Bakker, 2016). These examples contextualise the value and meaning that participants, including pwMS within this current study, assign to research participation in terms of physical and psychological benefits.

Harm Derived from Study Participation

A relatively recent review by Naidoo (2020) synthesised the negative aspects or burden of trial participation across a broad corpus of research participation in different therapy areas (Naidoo et al., 2020). This thematic synthesis contained significant crossover with the participation literature cited for this thesis although none of the studies evaluated in the review included pwMS. It is an important piece of work in that it brings the recent experience of trial participation, albeit with a focus on negative aspects or burdens, to the fore in current literature. While some of the adverse impacts identified by Naidoo have a degree of resonance with finding in this study, many did not. Individual findings within the Naidoo study depend on the original study objectives; some findings were interpretative in nature whilst others were more practical in nature than explored within the current study. For example, Naidoo et al (2020) highlighted participant burden in committing to the study requirements whereas participants within the current study appeared very willing to accept trial requirements. Further, Naidoo highlighted participant fear of being the proverbial guinea pig which again was not evident in the current study. Neither was the premise that participants harboured concern that trial activities were enacted in furtherance of the researcher's career. Although Eve suggested that the researchers were doing the study for themselves as much as her, there was no indication that she attributed this to career progression. Naidoo highlights the notion of participants being overwhelmed with trial information; whilst Eve alluded to a surplus of trial information she did not seem to indicate

that this was stressful but rather she would have preferred more individualised outputs. In contrast to Naidoo's findings, Eve did not appear embarrassed to admit her limited understanding; Eve described her confusion at many aspects of the trial but indicated that her trust of the team appeared to assuage her needs. Additionally, Naidoo highlighted that participants can feel intimidated within the trial scenario however in contrast to this, participants within this study seemed to feel very comfortable, experiencing a sense of nurture and belonging. Anger at placebo intervention and wasting of the participants' time with placebo intervention, injustice or psychological distress at randomisation were each identified by Naidoo as troublesome for participants but which had only nominal concordance with the current study where Jude was fearful at the premise of receiving placebo but not the premise randomisation itself. Whereas Jayne had suggested that she had hoped to be on the placebo arm as she had not felt a benefit of treatment. According to Naidoo, some participants in a cancer trial had found the requirement to record nausea and vomiting symptoms had served to worsen their symptoms. This reaction to responding to study assessments echoes with Jude's negative experience at facing her potential future decline through responding to study questionnaires. Naidoo also raises practical burdens of trial participation such as demands on time, researchers not taking scheduling preferences into account, the inconvenience of travelling in rush-hour traffic and cost of participation, whereas practical aspects such as these were not articulated in the current study. Its divergence from the current study is not unexpected given the review's objectives. Further, participants within the current study hail from one research centre and were free to express any aspect of trial participation of import to them individualy, aligned with the participant directed interviews within IPA approaches. Whilst some negative experential aspects did emerge from partipant narratives, as represented in the findings chapter, this was not a key focus of participant's narratives with this thesis.

The next topic, therapeutic misunderstanding has significant representation within the Naidoo (2020) review in addition to the wider literature. Its relevance in connection to the current study is drawn out in the following section.

Therapeutic Misunderstanding

Participant expectations during a study can rest on their understanding of benefit, harm or the focus of trial procedures. In the current study concepts of therapeutic misunderstanding

were drawn from different themes across the group-experiential themes as will be elaborated below. Therapeutic misunderstanding is seemingly a common phenomenon (Appelbaum et al., 2004; Canvin & Jacoby, 2006; Joffe, 2006; Lidz et al., 2015; Lidz & Appelbaum, 2014; Lidz et al., 2004; Morán-Sánchez et al., 2019; Naidoo et al., 2020; Warner et al., 2003). Although definitions vary across the literature, therapeutic misunderstanding can broadly be subdivided into three similar but potentially ethically separate strands; therapeutic ***misconception***, therapeutic ***misestimation*** and unrealistic therapeutic ***optimism*** (Horng & Grady, 2003).

Therapeutic misconception broadly reflects the research participant's failure to understand the distinction between the clinical research and clinical care in terms of therapeutic intent, individualized care or perception of risk (Lidz et al., 2004). It operates when participants believe that *each aspect* of the research study is designed to benefit the participant directly. Although research participants may benefit therapeutically from the research, the aim of the study is to generate generalisable data, rather than provide individualised care (Henderson et al., 2007; Horng & Grady, 2003). However, it is important to appreciate that therapeutic misconception does not necessarily reflect inadequate information sharing by the research team nor participant ineptitude but can instead arise from differing frames of reference; the investigator from an interventional efficacy (and safety) perspective and the participant's from a personal health viewpoint (Lidz et al., 2015).

Although some consider that underestimation of possible risk and overestimation of therapeutic benefit from an experimental intervention falls within the definition of therapeutic misconception (Lidz et al., 2004) Horng, however, assigns participant overestimates of potential benefit, underestimates risk of harm, or both, to therapeutic misestimation. And designates therapeutic optimism at the participant hoping or expecting the best possible outcome for themselves (Horng & Grady, 2003). Further, Jansen (2020) defines the concept of *unrealistic* optimism (in clinical research) as a potentially problematic bias whereby study participants hold the belief that they are more likely to experience positive effects and/or less likely to experience adverse consequences than others. This is considered potentially problematic as such bias impedes the rational understanding of the benefits and risks associated with trial participation (Jansen, 2020).

Regardless of these nuanced definitions, therapeutic misunderstanding is commonly cited in association with research participation in the literature, and examples identified from research participation studies closely align with findings from within the current MS research participation study. One example from a study specifically evaluating therapeutic misconception in South Africa gave rise to clear examples of a lack of understanding and unrealistic expectations; *'very little risks as it is at phase 3. The fact that I'm now in phase 3 means that I am progressing well. The treatment is working'* (Malan & Moodley, 2016).

Similarly therapeutic misconception was rife in a malaria study in Bangladesh where participants believed that the trial was for the benefit of individual patients whereas the objective was purely to provide information to inform public health policy. The misconception is typified in the following excerpt; *'I understand that I will get treatment and I will recover, by the grace of Allah. They told me many things but I didn't understand everything'* (Das et al., 2014).

Similarly, in the UK, in the SANAD epilepsy study where patients were randomised between different licensed antiepileptic drugs, patients repeatedly misunderstood the premise of the trial. Some participants believed that, despite the process of randomisation, treatment would be individualised; *'[Consultant] said he put all the information he had about me, he would put it all in the computer, and then the computer would choose what the computer thought was the best drug for me'* (Canvin & Jacoby, 2006).

Within this current study examples of therapeutic misunderstanding are frequent and rippled throughout the group-experiential-themes, and sometimes conflicting within accounts. One of the most prominent examples was Jayne's apparent conviction that the investigational treatment within her study was devoid of any possibility of side effects. This was based on the notion that at doses several orders of magnitude lower that is a taken as a vitamin, and that she had been taking it pre-trial at these lower doses she did not experience any adverse effects and so extrapolated this to the trial setting. Martha also seemed to hold exceptionally high expectations of her treatment efficacy together with firm belief in the absence of possible side effects.

Clinical trials frequently require investigations such as lumbar punctures, blood samples, imaging, or biopsies that assess trial outcomes but that may have no benefit to the participant (Miller & Brody, 2003). The results of such assessments may not be shared with

the research clinician to maintain blinding and reduce bias. Even where there is potential therapeutic benefit from the investigational medicinal product under evaluation the overarching goals of the trial are not tailored personal clinical care, but instead the acquisition of scientific knowledge for general application (Brody, 2012). From the findings within this thesis the misbelief that trial participants should be or would be provided with the results of potentially blinded trial-specific assessment can also be regarded as therapeutic misconception. Martha and Eve could each be seen to be conflating trial specific results with assessments for their own clinical benefit and whilst Jayne understood that results were not routinely shared, she had assumed that meaningful results would be shared if warranted.

Eve in fact demonstrates awareness and acceptance that the triallists were gathering information from her for the purposes of the study rather than for her individual needs. Her ensuing frustration directed towards the deficit in individual results is reflective of the nature of the trial as a scientific experiment generating generalisable data rather than individualised personal care, and her own frame of reference. Information needs are influenced or activated by the context and situation of an individual including physical, psychological and social dimensions. Patient or participant information provision should focus on the patient's unique needs and not the professional agenda. In short, information provision needs are heterogenous, change with time and should be holistically focused (Ormandy, 2011).

The following quote reverberates with Eve's account in the current study, in that information needs were unmet. *'I would like to know if they have discovered anything new, in understandable language'* (Kerrison et al., 2008). As seen in the findings, Eve had expressed frustration that she received study level but not individually tailored progress. In contrast, given that Kerrison's study related to non-interventional pathophysiological research in pwMS, this appears to be more aligned with scientific advancement than the individual journey. The premise of 'understandable language' aligns with the findings for Eve as she referred to her limited comprehension of study information and lack of medical background at several timepoints in her interview.

Patients with health conditions tend to overestimate treatment benefits (Heesen et al., 2017) and underestimate treatment risks (Reen et al., 2017). This overestimation of benefit

was evident in the accounts of each Jude, Jayne and Martha. Jude description of the trial in which she was enrolled demonstrated good understanding of the research aims. In parallel however, she illuminated her unrealistic hope of being returned to previous state of health despite her clear understanding that the active treatment (should she be on active treatment) could, at best, only slow the rate of progression and not effect improvement.

On the balance of evidence, it is a fine-line that separates therapeutic optimism, mis-estimation (Malan & Moodley, 2016) and unrealistic optimism. However, we should temper judgement by recognising that people generally do have an optimistic predisposition, and that '*self-deception is [regarded as] a valuable personal coping tool'* (Smith & Longo, 2012). A hopeful state of mind does not pose an ethical dilemma in clinical research, but moreover, evidence supports the notion that people with dispositional optimism (the 'glass half-full' perspective on life) are overall more healthy than others that do not (Jansen, 2011).

Research within the NHS continuum of care?

It appears that the NHS itself may promote therapeutic misconception. The NHS frequently frames research as part of the continuum of care and provides justification for research being promoted as an integral part of clinical care (Peveler, 2020). The UK NIHR makes a bold statement that *'increasing the integration of research and care is key to the future, and the best way to deliver patient care'* (NIHR, 2021). Data from clinical research's positive impact on clinical outcomes are interpreted to provide further motivation to incorporate research into standard clinical practice (Downing et al., 2017). Further oncology clinical guidelines frequently advocate a trial as a preferred ***treatment*** *option* (Gennari et al., 2021; Gradishar et al., 2021).

Ethical concern related to therapeutic misunderstanding, together with the seemingly opposing push to embed trials in clinical care might lead to the conclusion that research participation in a clinical environment is not a healthy activity. Rather than seeing menace in the shadows, multiple studies on research impact have demonstrated the wider benefits of research activity. Interventional clinical research activity in UK NHS hospitals is associated with an improvement in the quality of care and reduced levels of mortality. (Jonker et al., 2020). Data gathered from disease-specific studies [ovarian cancer, coronary artery disease, and colorectal cancer] supports enhanced survival for patients treated at those hospitals with higher research activity (Downing et al., 2017). This echoes prior

findings that the more research active Trusts exhibited improved mortality outcomes following acute admissions, and that such trusts appear to have key differences in composition than those that are less research active (Ozdemir et al., 2015).

Although research activity involves only a very small proportion of total patients this is deemed to have a positive, but indirect, effect on performance on staff and the Trust and which is measurable at the patient level and within Quality Commission (CQC) ratings (Jonker et al., 2020). This indirect beneficial influence is considered to be driven by superior quality of information provision to patients, greater confidence in the treating physicians, enhanced staff teamwork, and an overall higher quality of inpatient experience. Whilst evidence behind the objective benefits of trial participation on an NHS Trust or on *a population* level are increasingly recognised, it takes theses such as this one to provide idiographic awareness from an experiential perspective for individuals actually taking part in research.

Reflexive Note: Hearing the accounts of participants, and in linking this with the literature regarding therapeutic misunderstanding has caused me to question afresh my previous view of trials as part of the continuum of care with the UK healthcare system. I have consistently subscribed to the standpoint that trials provide a valid treatment option, with potential access to treatments that might not otherwise be available whilst be cognisant of the position of equipoise – and that NHS trusts who are research active have better outcomes. I have experienced a sea-change viewing trials versus clinical care through an ethical lens rather than a therapeutic lens and significantly shaped by the findings of this study, whilst retaining a high regard and allegiance for trials within the healthcare system for the reasons cited above.

Adverse Effects / Side Effects

Within Carey's IPA of (clinical) DMT decision making, participants expressed concern at initiating a DMT in connection with perceived efficacy versus the perceived risk (Carey et al., 2021). Furthermore, Jayne and Eve both considered that oral therapies were less hazardous than infusions or injections which appears to be a commonly held belief with preference for oral therapies over injection or infusion therapies consistently represented in the literature (Visser et al., 2020). This seems to draw parallels with Eve's pre-infusion panic in advance of her first trial infusion where she laments the irreversibility of an infusion versus a perceived lesser adverse impact of a pill, which although sounds rational is not necessarily the case – for example certain cytotoxic oral cancer drugs have been repurposed for MS treatment.

Adverse effects associated with medicinal products are extensively explored in clinical literature, including MS treatments. Whereas qualitative research participation literature expends surprisingly little focus on participant experience of the side effects of experimental investigational products (Harrop et al., 2016; Naidoo et al., 2020). Within the current study the attitude towards possible side effects of experimental treatments, even amongst four participants, is diverse and somewhat unexpected from my own perspective. One participant (Jayne) denies the possibility of side effects, one participant (Martha) repeatedly reaffirms her experienced absence of side effects, one finds comfort in experiencing side effects that she attributes to active treatment (Jude), and one experienced severe side effect to the trial infusion (Eve) but disassociates it from the research. Each participant has their own reasons for their specific view on the likelihood or existence of possible side effects. Jayne signified that her treatment was devoid of possible side effects because of its origin as a micronutrient or vitamin (when used as doses many orders of magnitude lower). The experimental treatment within Jayne's study was eventually shown to lack efficacy and, unbeknown to Jayne at the time of interview, was shown to exhibit potential for deleterious health consequences from interference of laboratory tests (Cree et al., 2020).

The following excerpt helps to frame individual context for the significance of side effects. This participant (in a Crohn's disease study) appears to have shifted their perspective from being in a position of evaluating risks and benefits to now being situated where they feel that the potential for benefit outweighs any potential risk; '*In the past, it was …… I was more, shall I say, I was more critical of treatments and I'd weigh it up. Now, I just think I've got nothing to lose so the process is pretty easy, you know, it's, let's give it a go, let's give it a go and I'll put up with the side effect'* (Cooper et al., 2017). The language used here also echoes language employed by participants (Jayne and Eve) in the current study who also felt that they had *'nothing to lose'.*

Human Connectedness

Nurture and Feeling Safe

The premise of human connectedness was interpreted as being of particular import to participants within this study. For Eve this connectivity and sense of nurture and trust was of such significance that it appeared to eclipse other, potentially positive and negative aspects, of trial participation. Whereas for Martha it was the safe-haven of the research environment that seemed significant and where she felt a sense of belonging. In Harrop's IPA study of participant experience in a randomised controlled trial in people with advanced cancer (Harrop et al., 2016) one of the participants framed the importance of the relationship with the study team, which has concordance with Martha's sense of belonging; *'…it's like home from home. It's, there's no 'oh you're the patient, we're the experts'* (Harrop et al., 2016). Further, participant experience explored during a grounded theory study of people taking part on a long-term diabetes study in the UK, demonstrated the value of human connectedness with the research team where participants described '*a sense of bereavement'* (Lawton et al., 2003) when the trial came to close. This emotive response was closely echoed in findings of this current IPA, where Eve's description as she wept suggested that she too was bereft at the prospect of losing her relationship with the study team, as explicated in the findings section.

The next topic of significance within the Human Connectedness group-experiential-theme is that of trust and of trusting from the research participation perspective.

Trust

In the clinical trial arena both trust and mistrust are multifaceted. Participants' level of trust for research *per se*, the pharmaceutical industry and for the (clinical) staff involved in research is extensively represented in the literature. The world of research today has been shaped by historical mistrust. Mistrust associated with clinical trials include the premise of mistreatment, being taken advantage of, mistrust of randomization, being used as a guinea pig, stigmatisation, and unintended consequences such as side effects (Smirnoff et al., 2018). Further, levels of mistrust of trial activities are seen to be more prevalent in minority groups (Clark et al., 2019). The infamous Tuskegee syphilis study is extensively acknowledged as a reason to mistrust research particularly given the heinous and sustained deception and mistreatment of people involved in the study (Scharff et al., 2010). Although

a justifiable factor, racial differences in mistrust of the medical establishment is likely rooted in deeper historical and personal experiences (Brandon et al., 2005).

Furthermore, the Vioxx debacle, and in the UK, the notorious Northwick Park catastrophe are good examples of incidents that significantly damaged public and professional confidence in pharmaceutical trials. The pharmaceutical company who developed Vioxx deliberatively obscured data regarding cardiovascular sequelae of the drug, and further, conducted studies that would knowingly fail to detect such risks (Krumholz et al., 2007). With the Northwick Park incident six men who were administered a trial monoclonal antibody soon developed catastrophic multisystem failure as an unanticipated but direct result of the investigational product (Goodyear, 2006). Whilst lack of trust is frequently cited as a significant barrier to trial participation (Williamson & Bigman, 2018) propensity to participate is influenced if the request is made by a trusted individual (Research!America, 2017), particularly physicians (Clark et al., 2019).

Doctor-patient or Investigator-Participant Relationship

Various models exist to describe the doctor patient-relationship; from essentially contractual or service provision to the other extreme, the paternalistic fiduciary model with its inherent power imbalance (Bending, 2015). Bending favours a middle ground trust-based relationship to more accurately capture the nature and nuances of the contemporary interaction. In the trust-model doctors offer advice that is not only evidence-based and competent but that also that is aligned with the patient's best interests [including disclosure of any conflicts of interest] (Bending, 2015). The author goes on to discuss the blurring of boundaries between research and clinical care especially where clinicians wear two hats – of treating physician and research investigator. This is relevant to the current study as the research investigators are the clinical neurologists for two of the participants, or from within the same department for the other two participants. This particular premise of conflating research and clinical care correlates with therapeutic misunderstanding. Within the research arena, to be worthy of participant trust, research investigators must first themselves have full awareness of differences between clinical research and clinical care, and be prepared to expressly communicate this to potential research participants (Miller & Brody, 2003).

In the UK, when members of the public are asked to assign levels of trust in various professions and occupations, the medical profession consistently garners the highest ranking (McDonald, 2014). Doctors are regarded as something more than technical experts in being seen as honourable (McDonald, 2014). Some patients have a tendency to quickly develop strong trust in their doctors, regarding them as almost godlike in terms of both their abilities and their allegiance to patients – such beliefs in many cases could constitute over-trust (Hill & O'Hara, 2006). The archetypal thick-trust is typical of the trust within families where blind-trust is often at play.

Reflexive Note: From my own experience within a clinical research environment within the NHS here I find myself questioning if all doctors or clinician-researchers in all situations can be deemed to neatly fulfil one model or another, or whether each clinician or indeed each doctor-patient or researcher-participant relationship may lean toward one model or another depending on the circumstances and needs of the participant

Some researcher-participant relationships might resonate more with a fiduciary model, whether driven by the attitudes of the patient (or participant) or by the clinician – this would appear to be the case in the present study. Some participants from this present study seemingly exhibited thick-trust and who had a preference to relinquish their decision making, or power, to the research team. This premise is echoed again later when reviewing the literature on the power dynamic.

In contrast to general findings of mistrust that pervades the clinical trial literature, but aligned with the high level of trust in physicians, participants in this study seemed to exhibit intense levels of trust in the clinician-investigator and research team. This thick trust became apparent in the accounts of both Martha and, to an even greater extent, Eve. With thick-trust the individual cannot countenance betrayal, wrongdoing of fault within the trusted relationship and would attribute negative experience to extrinsic or external factors, or further, negative traits may be reframed as positive (Hill & O'Hara, 2006). This has particular resonance with Eve's account. Eve confesses to not understanding the trial, to being confused and feeling in the dark at the end of the study. Eve has been content to turn her care over to the research physician and team as part of a ritual of trust that has assisted her psychologically in her time of need. It is often regarded that the sicker a patient is then

the more vulnerable that they are and the greater trust that the patient, or in this case participant experiences. Eve was extremely unwell at the time of being offered trial participation, which could help to explain the deep level of trust she appeared to invest in the researcher and their team. There is absolutely no suggestion of misfeasance on the part of the research team, but either way Eve does not attribute the abovementioned perceived shortcoming to the team. Her faith in the team has meant that she has not felt the need to have a detailed understanding. Even when Eve feels let down by the lack of sharing of her own personal trial journey, she is quick to point out that it is herself to blame by not asking (despite repeatedly asking) or because the research team are under too much time pressure to accommodate her needs. Almost before drawing breath, Eve reemphasises her belief in the team as if she feels guilty as sharing a criticism of the experience. Whilst this could give rise to some cause for ethical scrutiny it is to be remembered that this type of thick trust, or potentially over-trust is not uncommon and may even be associated with health benefits. Patients who have strong trust in their doctors are more likely to provide honest relevant personal information, agree to and stick with recommended treatment or intervention (Thom et al., 1999), and feasibly more likely to experience positive health benefits from the trusting relationship itself as the physician themselves act as a placebo (Hall, 2002).

Across trial participation experiential literature of qualitative design, trust is a frequent element of participant accounts (Tutton et al., 2018) including minority ethnic communities in the UK (Hussain-Gambles, 2004). The premise of trust shaping research experience is validated in an exploration of experience in study of participant experience in those with irritable bowel syndrome (Bishop et al., 2012). One participant, despite accepting and understanding the premise of a placebo arm, could not countenance that he might be receiving placebo because he felt so cared for by and trusting of the research practitioner. On subsequently finding that he had been allocated to placebo he described the meaningful positivity of study participation, despite having received the placebo intervention throughout the study.

Similarly in a drug trial comparing two treatment strategies for women with uncomplicated urinary tract infection in primary care in a qualitative interview study using summarising content analysis, the authors describe trust whereby a participant expresses her faith in the clinician; *'I have trust in my doctor. I feel in good hands. …I had no concerns that they would*

try anything or that something bad would happen to me (Bleidorn et al., 2015). This aligns with the trial providing a safe-haven, which emerged within the findings for Jude, Martha and Eve in the current study. Further, in an interpretative phenomenological study of lived experience of a wound dressing trial in an emergency setting in the UK the authors identified trust in the research team and clinicians a powerful and consistent theme. In this study participants were vulnerable owing to the physical and emotional impact of injury. Participants felt dependent on and trusting of the research clinicians to act in their best interests and not cause harm (Tutton et al., 2018) which again resonated with accounts within this study of being rescued or saved from a dire health situation and participants feeling able to trust their best interests would be maintained. Trust and power are inexorably linked in relationships within clinical and research settings and so the power dynamic in healthcare and clinical research is considered next.

The Power Dynamic

Any literature search relating to 'power' and 'clinical trials' inevitably yields discourse of complex statistical calculations; add in the search term 'dynamic' and the output is transferred to adaptable trial designs! Despite these search frustrations, researcher-participant power dynamics in qualitative research have been extensively deliberated within the literature (Anyan, 2013; Dowling, 2005; Karnieli-Miller et al., 2009). Within the positivistic world view, the participant-investigator (researcher) relationship in the healthcare context is often considered more closely related to the concept the clinical doctor patient relationship (Karnieli-Miller et al., 2009). It is this relational concept that is expounded below, particularly given that the research investigators are either the same or close colleagues of their routine clinical doctor, and which would seem to hold true from findings within this study.

Power, including social power (or the ability to influence) is an inescapable premise in all relational interactions (Goodyear-Smith & Buetow, 2001). Similar to the trust models described earlier, within the literature the power dynamic in doctor-patient relationship can be grouped into three archetypal clusters (Shutzberg, 2021). At one end of the spectrum is the paternalistic extreme where the power resides wholly with the physician (parent-child relationship). The second is the physician as partner, or adult- adult relationship where power is more equally distributed between the parties. At the other far extreme is the idea

of the patient-consumer, as the sole decisionmaker, retains the power with the clinician acting merely as technical service supplier or information provider (Goodyear-Smith & Buetow, 2001; Shutzberg, 2021).

The middle ground of mutual power more closely aligns with the NHS long-term commitment to employ shared decision-making, and a positive shift in power as a fundamental part of integrating personalised care in our UK Health System (NHS SDM 2019). Equality of power is uncommon in any individual interface and even where doctors do fully inform patients, are respectful of their preferences, and enact the ethos of shared decision making the nature of the relationship means that the balance of power is generally weighted towards the physician (Goodyear-Smith & Buetow, 2001). Mutual power and shared decision-making enables people with health conditions to take a joint collaborative stance with clinicians in agreeing on a plan of action that each concur is safe, efficacious and ethically appropriate (Goodyear-Smith & Buetow, 2001). The NHS stance on shared-decision making echoes the above premise enact '*a process in which clinicians and individuals work together to select tests, treatments, management or support packages, based on evidence and the individual's informed preferences'* (NHS SDM 2019*).* This approach ensures that personal preferences are incorporated into the decision which in turn leads to enhanced adherence to the agreed treatment strategy and consequently improved outcomes (Stacey et al., 2017). Generally, people who feel in control of their own health and are actively invested in health-related decision-making exhibit significantly improved clinical outcomes (Anderson et al., 1995). Further, perceived control is positively linked to well-being and negatively related to psychological distress such as anxiety and depression (Endler et al., 2001).

NHS Shared Decision Making

Importantly, the NHS shared decision-making guide does qualify its position that patients should be as involved in the decision making *'as they would wish'* (NHS SDM 2019). There are people who do wish to delegate their decision-making to their clinicians with the recognised adage *'doctor I'm in your hands'*. Doing so is not, as it might initially appear, paternalistic, indeed the converse is true; McKinstry asserts that by declining to enable the patient to divest their decision-making could be construed as *taking* that same decisional control from the patient (McKinstry, 1992).

Akin to the power-dynamic concept in coproductive study design with members of the public (Green & Johns, 2019), equal power does not equate to equal knowledge. Patients ***are*** the experiential experts in their own condition, their bodies, preferences and lifeworld. Clinicians expectedly have medical expertise, and thus each party exercises correspondingly important but differing sources of power (Goodyear-Smith & Buetow, 2001). In short, having equality in power does not necessarily equate to research investigators and participants having the same role in decision making.

It is evident from the literature that both patients and physicians are at different points on a continuum representing the power dynamic. This reverberates with the findings of this study where there appears to be a differential between the experiences of some patients and probably, according to participant narratives, the stance of some clinicians. Eve is prepared to divest decision making seemingly willingly shifting the balance of power to the research team. She openly shares that she does not understand much of the trial information and indicates that this in untroubling to her and at various points she describes situations where 'they' were happy for her to proceed with trial interventions, shifting the decisional power away from herself. Jude experiences a degree of powerlessness with her clinical care whereby she reclaims power taking matters into her own hands to secure trial involvement. Although at this point it should be recalled that there is an increasing hermeneutic separation between either me as the author or you the reader and the research team; we are each experiencing the phenomena second or thirdhand. We are thus further displaced from the manifold interpreted views of the clinicians who have not had the opportunity to speak for themselves, as the participant has.

Shared Decision Making – DMT Initiation

Some experiential aspects of research participation involving investigational DMTs share consonance with the corpus of literature representing initiation of a disease modifying therapy for pwMS as discussed in the literature review chapter. Although the population represented in the current MS DMT literature relates to clinical decision making, and almost exclusively pwRRMS (Carey et al., 2021; Reen et al., 2021; Van Reenen et al., 2019) the current study includes both relapsing remitting and progressive forms of MS. The concept of decision making for pwMS in relation to DMT choice has been increasingly chronicled in recent years within the literature (Carey et al., 2021; Eskyte et al., 2019; Manzano et al.,

2020; Van Reenen et al., 2019). Compared to DMT decision making in the clinical setting, the trial situation is arguably more complex with possibility of placebo treatment in some studies, trial related therapeutic misunderstanding and the premise of the trial derived benefits over and above any disease modifying intervention. These, and concordant aspects of trust, taking control against the disease and maintaining normality have been considered in relevant sections within this chapter.

Research into patients' decision preferences indicates that most people with MS prefer an active role in treatment decisions and advocate shared decision-making and informed choice (Heesen et al., 2004). Although a substantial proportion may prefer a passive role in decision-making, while very few would choose entirely autonomous decision-making (Deber and Kraetschmer, 2007). However, preferences may vary by nationality, age, level of education, familiarity with the condition and a multitude of other factors (Cameron et al., 2019; Deber et al., 2007). Of particular interest, in Carey's DMT decision making IPA (2021) the author suggests that participants *'desired greater steer from healthcare professionals in making their DMT decision'* (Carey et al., 2021). As explicated earlier, from the current study it seemed to be the case that participants perceived an influential lead from the clinician-researcher for Martha, Eve, and to a lesser extent, Jayne taking part in the research. Jude appeared to have had very little steer and drove participation and access to the trial herself. Further Carey shares numerous themes regarding DMT decision making that have resonance with themes and notions within this current study included elsewhere. As with Carey's work, participants expressed negative emotion in relation to the MS in terms of the shock of diagnosis or the impact of the disease on future health as a driver to take action, and again, discussed elsewhere in this chapter. One aspect of the current research participation study that lacks concordance with Carey's IPA of DMT decision making is the desire for participants to consult with peer pwMS in the selection of DMT. Here, only one of the participants in this IPA expressed a desire to convene with other pwMS the others each eschewed such interaction.

Eskyte's critical interpretative synthesis of DMT decision making suggested that neurologists often play a dominant role in the process of selecting a DMT and pwMS either take the clinician's advice into account or directly accept the proposed treatment option (Eskyte et al., 2019). Similarly, in Van Reenen's IPA study of clinical DMT decision-making one

participant quote indicated the influence of the neurologist in taking treatment, as explicated in the literature review section. This influence is echoed in this current study in the accounts of Eve and Martha where it sounded like the neurologist had a significant role in the trial participation decision; again being cognisant that this represents their own interpretation over time (the double hermeneutic).

Self

Activation / Self-Efficacy

Linked to the previous ideas of control by taking action and following on from shared decision making are the interrelated concepts of self-efficacy and patient activation, defined below.

Hibbard's Patient Activation Definition (Hibbard & Gilburt, 2014)	**Bandura's Self Efficacy Definition (Bandura, 2014)**
An individual's knowledge, skill, and confidence for managing their health and health care.	People's beliefs about their capabilities to produce designated levels of performance that exercise influence over events that affect their lives.

Table 11: Definitions of Activation and Self Efficacy

As well as being a *'measure of a person's knowledge, skills and confidence to manage their own health and wellbeing'* patient activation is regarded as *'a core enabler for supporting self-management and personalising care'* (NHS-England, 2018). People with higher levels of activation tend to have better outcomes than those with lower levels of activation, who are less likely successfully be involved in their own health management (NHS-England, 2018). Patient activation is a behavioural concept which draws upon Social Cognitive Self-Efficacy Theory as first described by Bandura (Bandura, 1977). It has been said that patients with low activation *'live without the sense of hope and resourcefulness that many of us take for granted'* (O'Shea, 2014).

In comparing these two constructs, patient activation is specific to health it applies more to the individual than a specific behaviour, whereas Bandura's self-efficacy has application beyond health and applies to specific actions. Further, measures of activation include self-efficacy items (Hibbard & Gilburt, 2014). Given the overlap (Goodworth et al., 2016), contextual similarity (Hamilton & Li, 2020) and significant intercorrelation (Goodworth et al., 2016; Van Do et al., 2015; Young et al., 2016; Young et al., 2017) between these constructs, for the purpose of this thesis, they are considered in parallel.

A substantial corpus of literature exists concerning the relationship between self-efficacy and health in MS, including health promoting behaviours, adjustment, and adherence to medical regimens (Eccles & Simpson, 2011; Mohr et al., 2001; Riazi et al., 2004; Schmitt et

al., 2014) physical, and social functioning (Amtmann et al., 2012), Quality of life (Motl et al., 2009) and health related quality of life (Motl et al., 2013). Additionally, Schmitt (2014) found that self-efficacy plays '*a significant role in individual adjustment to MS across multiple areas of functional outcome, beyond that which is accounted for by disease related variables and symptoms of depression'* (Schmitt et al., 2014). It has also been shown that the subjective importance of participation in everyday activities and situations is closely linked to levels of self-efficacy (Yorkston et al., 2008). Further, self-efficacy has been demonstrated to be a key mediator for continuation of employment in pwMS (Ford et al., 2019). And recently, self-efficacy has been affirmed as being one of the dominant mediating factors between symptoms, disability, perceived health and QoL in pwMS (Young et al., 2021). These represent some examples of the work executed to date exploring the key importance of self-efficacy in pwMS, where self-acceptance, self-efficacy and adaptive coping seemed to provide participants with positive perspectives (Kassie et al., 2021). Similarly, patient activation, as a modifiable attribute, is regarded as being of key import in pwMS taking control over their own disease (Feys et al., 2016; Soelberg Sorensen et al., 2019).

However, within the bolus of literature considering self-efficacy or activation in MS or other long term health conditions there is an absence of identifiable exploration of either of these interrelated concepts directly related to trial participation (in contrast to exploring within the context of a trial setting (Young et al., 2017). Although the current study did not set out to explore activation or self-efficacy, I propose a potential relationship between these constructs and research participation for some MS trial participants. High levels of either self-efficacy or patient activation may be an important driver for some in identifying and securing access to a trial. Further trial participation itself may fulfil aspects of these concepts by being an outlet or means of expressing activation or self-efficacy personal attributes; that is in having the capability to exercise influence over or to be a core enabler in their health management. In drawing this conclusion, I am interpreting the drive exhibited by some of the participants (Jayne and Jude) within this study to identify, pursue and secure trial access as meeting (measurable) aspects of self-efficacy or activation. This encompasses activation domains such as taking action, having confidence and knowledge to take action and staying the course under stress (Hibbard et al., 2004) and similar domains in

various MS self-efficacy instruments of independence, worries, personal control and social confidence (Rigby et al., 2003; Young et al., 2012). This hitherto unexplored topic would merit further appraisal, potentially within a more quantitative evaluation utilising existent activation and self-efficacy instruments.

Altruism

Altruism is widely regarded and frequently cited as a key *motivational* factor in accepting research opportunities (Balfour et al., 2010; Chin et al., 2016; Godskesen et al., 2015; Verghese et al., 2020). Definitions of altruism vary across the literature but routinely include the premise of voluntary action to benefit others that does not benefit nor reward the actioner (Steinberg, 2010).

Opinion of the role of altruism in clinical trials within the literature is divided. Emmanuel and Patterson express the view that altruism can be the only legitimate justification for choosing to undergo randomisation of treatment within a trial setting (Emanuel & Patterson, 1998). Within the clinical trial arena pure altruism can exist but altruistic intent is often conflated with a degree of anticipated self-benefit or at least an absence of harm or inconvenience. Altruism of this variety is termed weak altruism (Canvin & Jacoby, 2006) or conditional altruism (McCann et al., 2010) each of which denote an element of self-interest. Weak altruism was originally coined to describe a trial scenario where patients consent to participate in a trial only because they perceive no difference between treatments and so regard no disadvantage to taking part. In evaluating the SANAD epilepsy study the term was extended to include the premise of participants being willing to help others but only where they could also help themselves (Canvin & Jacoby, 2006). More latterly the term 'conditional altruism' was adopted to succinctly capture the inclination to benefit others but where participation also hinges on the notion that taking part will provide some individual benefit, without significant disadvantage to self (McCann et al., 2010). Lawton and colleagues (2019) go a step further by introducing a new concept *'the altruselfish agenda'* coined to capture the premise that altruism and self-interest are often inextricably entwined (Lawton et al., 2019).

The notions of weak, or conditional altruism as opposed to pure-altruism were manifest within the account of participants in this study. Each of the four participants expressed positivity in the benefitting of others because of their participation, to a greater or lesser

extent. None participated for purely altruistic reasons as each expressed hope or expectation of therapeutic benefit or lack of barriers. Jude consistently expressed philanthropic intent whilst openly counterbalancing this with self-benefit. Phil made repeated reference to the lack of burden of the trial in which his wife, Jayne was involved, and she summarised that there's no reason to not help others, which correlates with the concept of weak or conditional altruism. Eve has had the most challenging experience of trial participation and so the concept of her part in benefitting the wider MS community in the drug being made available on the NHS seems to represent a source of validation of her participation. The positive outcome of the trial appeared important to Eve's feeling of altruism whereas Jayne acknowledged that positive or negative outcomes of a trial are similarly important. Eve also references the lack of practical complexities, such as child-care or work, which facilitated her involvement in the study. Martha proudly acknowledged the benefit to others but counters this with her own positive experiences and lack of harm.

Within the research participation literature, altruism is one of the most extolled motivations for trial participation in different disease areas. The following excerpts from participation literature resonates with the experiences with the current study as it represents feelings of positivity and validation at contributing to medical advancement; '*I think taking part in the trial is quite, it makes you feel better actually because it is a useful tool and it's going to be of use for other people in the future……Yes because it makes you feel better doesn't it if you feel you are contributing something*' (Hughes et al., 2013).

The below findings from participant experiences within a cancer trial have concordance with Jayne's insight that a negative outcome also advances medical science*; 'no trial ever has a negative, negativity. It always has a positive; there's always something positive that comes out of it, even if it is only to say, 'We don't want to go up that route''* (Harrop et al., 2016). In the context of trial participation experience, altruism can and should be regarded as something more than a theoretical motivational factor towards trial participation. It can be viewed as a positive coping mechanism for patients enrolled in a clinical trial (Sanders et al., 2013). From this study and the corpus of literature on this topic, positive feelings of altruism are often counterbalanced or contingent on self-benefit or an absence of harm or inconvenience. Altruism may be viewed as providing feelings of worth, value and pride, as well as justification for difficult trial experiences. Within this study the level of altruism is

succinctly captured by the term conditional altruism as coined by McCann and colleagues (McCann et al., 2010).

New Knowledge and Implication for Clinical Research Practice

The study utilised a coproductive approach with pwMS experiential experts during the study design and crafting of the study documentation. Further the coproductive approach was extended into the analysis phase which is an approach that is rarely adopted (Hemming et al., 2021). The study aims were unique as the experience of pwMS taking part in research has, as far as can be determined, not explicitly been the topic of qualitative enquiry previously, as discussed in Chapter II. The methodology employed, which is particularly suited to hitherto unexplored territory (Smith et al., 2009), allowed the complexity and intricacy of the meaning and significance of trial participation for pwMS to be drawn out. These rich and significant findings have been represented ideographically whilst illuminating how participants experience similar themes in differing ways. Expectedly there was some concordance with findings from other qualitative exploration of research participation in other health conditions, but this is the first time the voices of pwMS have been heard in this way. Additionally, this thesis brings new concepts to the fore for pwMS in terms of, for example, the extent of therapeutic misunderstanding for pwMS in the trial setting and the potential bidirectional relationship between self-efficacy (or patient activation) and MS trial participation for some participants. There appeared to be a notable interaction between the participant's lifeworld context and their experience of the study or meaning derived from the study. Human connectedness was a key concept for participants in the trial setting where a sense of nurture, belonging and trust were of particular significance to participants. The concept of trust encompassed both positive and concerning aspects where thick-trust potentially contributed to therapeutic misunderstanding. The notions of therapeutic optimism, hope and gaining or taking back control through trial participation, as understood from the accounts of the participants was especially powerful. Altruism in this setting was seen largely to be conditional or contingent on anticipated benefit, lack of harm or life-world complexity, but was an important source of satisfaction for participants experience during their trial involvement.

Whilst the findings in their own right offer meaningful new knowledge and illuminate the significance and complexity of trial participation for pwMS, this thesis offers insight that can translate into important developments in clinical research practice. Findings can help clinicians and others involved in designing, implementing, or recruiting to MS research to recognise their necessarily different frames of reference. By standing in the shoes of pwMS research participants researchers can appreciate the meaning of trial involvement through the lens of the participant, albeit indirectly. Enhanced awareness may serve to increase the priority placed on identifying appropriate research opportunities for those that may derive benefit from participation from physical and psychological perspectives. The insight offered here also has the potential to help researchers avoid the hazards of ethically worrisome therapeutic misunderstanding through adoption of enhanced communication and by addressing participant information needs. And further, to appreciate the potential for over-trust and potential inadvertent imbalances in the power dynamic in terms of shared decision making in the trial setting. Moreover, findings presented here need to be shared the pwMS community and those who may be considering or proceed to take part in MS research. The aim would be to help offer insight, increased transparency, and a deeper understanding of participation from those who have shared their experience here. This approach could help pwMS to understand the value and significance of participation whilst avoiding some of the pitfalls of therapeutic misunderstanding, over trust and unmet information needs.

The next and final chapter concludes this thesis in summarising findings, the unique contribution to the current body of knowledge, further research needs, and the potential for impact on clinical research practices going forward.

Chapter VI

Conclusions

Introduction

This chapter concludes the thesis by restating the research aims and summarising the key findings aligned with the study objectives. A reflection on the value and contribution of unique knowledge generated by this research is included to help contextualise the potential impact of this work. Finally, this chapter will consider how these findings may be applied in practice and identify areas where further research is needed.

Background

This study has involved in-depth idiographic experiential analysis (applying the principles of IPA) of six interviews with four pwMS who have participated in MS research trials. The study set out to explore this hitherto uncharted territory; the experiences and meaning of MS research participation for pwMS. The literature review revealed that research participation for pwMS has not explicitly been the subject of qualitative or experiential enquiry previously. This thesis therefore provides new knowledge and greater insight into understanding the experiences of pwMS taking part in MS research.

IPA, as explicated previously, is particularly suited to health-related experiences, unexplored domains, and where the experience is emotionally laden. Hence the use of IPA methodology has enabled the importance and meaning of research participation for participants with MS to be drawn out from an idiographic perspective, and for cross participant similarities and differences to be explored.

Findings

Whilst the role of clinical trials in this context is to generate population level generalisable data, turning the periscope towards the participant and their lifeworld from an idiographic perspective, the impact of such research on an individual level is significantly meaningful and should be recognised as such. This thesis has provided a unique lens into the world of the pwMS and their experience of being a participant in the clinical trial context.

Although there were similarities across the idiographic analyses within this relatively homogeneous sample, each participant exhibited their own nuanced perspective and

meaning of taking part in research. This thesis demonstrated that each idiosyncratic experiential narrative is shaped by a multiplicity of influencing factors such as the type of research, their own attitude to their MS, their anticipated future self, lifeworld context, and study expectations including their understanding and their own processing of the trial meaning.

The parallels identified across the participant experiential themes led to the identification of three group-experiential themes; trial derived benefit and harm, human connectedness, and self as described in the findings. These key themes have then been considered within the context of existent participant experience literature and other published domains of relevance such as trust and power, hope, activation/self-efficacy, altruism, DMT clinical decision making and therapeutic misconception. Whilst the review of literature before, during and after the data analysis, identified concordance with other published literature in the field of research into research participation, none specifically examines the experiences of pwMS in a clinical trial setting. Published research participation literature across different research scenarios and health conditions identified similar domains of importance to participants as identified within this thesis. These included valuing additional care, expressing therapeutic optimism and misconception, the importance of trust, concepts of altruism, of taking control by action, and of hope. Contextualising the themes within extant literature further highlighted the unique contribution that these findings provide. For example, self-efficacy in the context of MS research participation, the potential extent of therapeutic misconception for pwMS in the research setting, or parallels between clinical DMT decision making and the decision to take part in a trial of an investigational medicinal product for pwMS, have not previously been considered.

Within this study, the concept of finding hope and of taking or regaining control has been especially striking within the analyses, as has the premise of trust, belonging and of feeling safe for pwMS participating in research trials. This thesis highlights that the importance of human connectedness to pwMS trial participants should not be underestimated, particularly given that pwMS are more likely to experience social isolation. Despite being a fear-laden life-altering degenerative condition some pwMS may have only brief annual clinical appointments, and which more latterly have been virtual. Whilst virtual appointments were necessarily the case during the global pandemic restrictions and recognising the increasing

pressure under which the NHS and clinicians operate, such practices appear to be continuing. The trial scenario from the perspective of pwMS, as seen within the findings, may be perceived to offer more face-to-face interaction, enhanced care in addition to experiencing a sense of nurture, belonging and feeling safe.

Therapeutic misunderstanding encompasses the conflation of clinical care and trial processes, or unfounded expectations of investigational treatment. As discussed in the literature and expressed in the discussion, therapeutic misunderstanding appeared prevalent with the participants here despite an appropriate informed consent process. This could result from the difference in frames of reference from researchers versus that of the research participant perspective. Equally it is interesting to note that participants were able to concurrently hold conflicting views of the potential impact of investigational trial treatments; on one hand being able to express accurate understanding of study information whilst in parallel describing contradictory and unfounded or unrealistic expectations of the experimental treatment.

Although the ethical basis of research is distinct from that of clinical practice it seems that these were conflated at multiple junctures, not only as expressed by participants but in stated aims of the NHS to embed research within clinical care and treatment, as described in the discussion. Given the NHS ethos and the crossover between MS clinicians and research investigators, this thesis has identified that there is a blurring of boundaries that can contribute to therapeutic misconception. Further, the premise of equipoise for both the clinician and participant was represented in participant accounts as sometimes lacking, although it must be remembered that this is the perception of the participant having made sense of their own experiences over time – the double hermeneutic. However, despite the ethical challenges, it is important not to 'throw the baby out with the bathwater' by acknowledging that NHS trusts that do embed research into their strategic direction do tend to fare better and have improved patient outcomes. And vitally, as indicated in the findings, research participants in this study expressed significant positivity and described benefit across a number of domains from participating in MS research.

Significantly, the findings suggested that self-efficacy or activation was a key aspect of the drive to take part in a study for Jayne and Jude. Trial participation may be considered as a means of an individual fulfilling or expressing personal attributes associated with

activation/self-efficacy, particularly where options to take action might be more limited from a clinical perspective. Further the application of methods to enhance self-efficacy is considered to have profoundly positive effects on a range of parameters for pwMS and this could potentially extend to trial participation - research exploring the association of self-efficacy (or activation) and trial participation would seem warranted.

Although, within research participation literature, altruism is commonly expressed as a *motivation* for research participation, this thesis indicates that positive feelings associated with helping other or advancing science were experienced by participants during the study, but that self-benefit was also openly expressed, and which aligns with the premise of conditional altruism.

This thesis has established that contextual factors of people's everyday lives and realities are potentially more important for some than clinical need in the context of research participation experience. This suggests that research-clinicians should be cognisant that in offering a clinical trial of an investigation medicinal product they are, from the frame of reference of the pwMS participant, proffering something altogether more complex and entangled with participant lifeworld context, psychosocial positionality and expectations. From the perspective of a potential participant, a trial is potentially an opportunity to take action in order to gain or regain control, to experience a sense of hopefulness, to regain societal value, experience altruistic satisfaction, to gain a sense of belonging, to build trusting relationships to the extent that decision making might be partially divested, to be cossetted within a safe haven, to potentially gain therapeutic benefit and enhanced clinical care or simply to enjoy the experience.

Impact on Clinical Research Practice

Although the findings are from a small number of participants, in the context of the wider literature some tentative inferences may be drawn that can help to guide research practice going forward. This thesis highlights the import of understanding the lived experience of pwMS in taking part in research in the context of their own individual lifeworld. Arguably, credence should be assigned to the experiential aspects of the research journey of pwMS, and that clinicians conducting research should be cognisant how study related decisions, including the decision to proceed, are understood by participants. This thesis revealed that

research participation provided different benefit to participants. Overall participating in MS research can provide meaningful psychological and physiological advantages, and so, where appropriate, opportunities to take part in studies should be made accessible for those eligible.

The unique contribution that this thesis offers can help clinicians in avoiding unwittingly influencing pwMS participants and further in guiding participants to make more fully informed and ethically sound decisions throughout the research – and not solely at the start of the process, as has been the focus of much prior research. Research clinicians should also take steps to minimise aspects of therapeutic misunderstanding, accepting that therapeutic optimism is not ethically flawed. Further, thick trust can be a powerful motivator for participant action, not just in joining the trial but throughout the research experience. Further, this thesis has highlighted that terminology employed throughout the trial should be appropriately clear to remind participants of the unproven nature of the research carefully counterbalanced to avoid destroying ethically sound hope. Despite researchers presenting relevant information, this is not necessarily understood, absorbed, nor desired by the participant. This thesis also suggests that those involved in leading MS research should further take into consideration the ongoing information needs of participants. This includes research clinicians first being clear in the demarcation of research and clinical practice, and communicating this unambiguously for the benefit of participants, to be deserving of their trust. Wherever possible, and if desired by participants, study assessment results should be made available to participants either during the study, or as the study concludes to provide a research journey that is understood by and individualised for the participant. Potentially could this be worked into trial protocols to provide an individual summary when trial unblinding permits. Given the electronic nature of study databases this could take the form of an automated report of individual study progress contextualised by members of the research team for the individual.

Furthermore, the findings have direct relevance for pwMS outside of the trial setting. Sharing pertinent findings from this thesis with the pwMS community via appropriate patient-oriented forums would serve to enhance understanding and transparency around MS research. As such, this new knowledge can help pwMS to have greater awareness of trial participation experience to further inform the decisional processes in taking part in and

continuing in research. And further, to appreciate how trial participation may benefit pwMS but also to avoid some of the pitfalls of therapeutic misunderstanding, unfulfilled information needs and their role in shared decision-making.

Further Research

This thesis presents the first incursion into explicitly exploring the experiences of and meaning for pwMS taking part in MS trials and as such is intended as the *beginning* of the journey to better understand research participation from the perspective of pwMS. The findings in this thesis indicate that further exploration of pwMS participant interpretations and is warranted in order to generate a corpus of knowledge in order to tailor research design, information and participant experience accordingly. As discussed earlier in this conclusion, further exploration of self-efficacy in relation to research participation should be undertaken. It is also important to explore how different people with different subtypes of MS, diverse experiences of MS, and the numerous experimental interventions influence the research participation experience; and ultimately to maximise the potential benefit of research to pwMS.

Summation

To conclude, this thesis provides a unique insight into the significant impact of trial participation for individuals with MS, from an idiographic perspective across the themes of trial derived benefit and harm, human connectedness and self. New understandings gained from this research and the ideas presented in this thesis are of direct relevance and interest to MS clinicians and others involved in designing or implementing research with pwMS. Such individuals can increase their awareness of participant understanding, experience and needs from a psychosocial lifeworld perspective in contrast to considering only the scientific generalisable intent of research. Despite ethical and information caveats, researchers should allow participant to enjoy the benefits that a trial may afford, provided that ethical considerations, such as clear communication and principles of equipoise are appropriately fulfilled. Further research in this area is warranted to understand those topics highlighted to help provide more detail and depth that can support future research practitioners.

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Appendices

Appendix A - Ethics & Institutional Approval Documentation

University of Salford Ethics Committee

University of Salford MANCHESTER

Research, Enterprise and Engagement
Ethical Approval Panel

Doctoral & Research Support
Research and Knowledge Exchange,
Room 827, Maxwell Building,
University of Salford,
Manchester
M5 4WT

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www.salford.ac.uk

10 June 2019

Dear Lorraine,

RE: ETHICS APPLICATION HSR1819-063 – 'An interpretative phenomenological analysis of the experiences of people with Multiple Sclerosis (pwMS) taking part in MS research studies.'

Based on the information that you have provided, I am pleased to inform you that your application HSR1819-063 has been approved to go forward to NRES (HRA).

Once you have received it, please submit a copy of the NRES (HRA) approval letter to Health-ResearchEthics@salford.ac.uk so that it can be placed on your application file.

If there are any changes to the project and/or its methodology, then please inform the Health Research Ethics Support team as soon as possible.

Yours sincerely,

[redacted]
Chair of the Research Ethics Panel

University of Salford MANCHESTER

Amendment Notification Form

Title of Project:		
'An interpretative phenomenological analysis of the experiences of people with Multiple Sclerosis (pwMS) taking part in MS research studies		
Name of Lead Applicant:	**School:**	
Lorraine M Trainor	Health & Society	
Are you the original Principal Investigator (PI) for this study?		Yes
If you have selected 'NO', please explain why you are applying for the amendment:		
Date original approval obtained:	**Reference No:**	**Externally funded project?**
10/06/2019	HSR1819-063	Yes

Please outline the proposed changes to the project. *NB. If the changes require any amendments to the PIS, Consent Form(s) or recruitment material, then please submit these with this form highlighting where the changes have been made:*

It is proposed that telephone communication may be utilised for this project going forward – both to complete and document the informed consent process and to undertake the participant interviews.
The informed consent process would be documented based on verbal consent recorded by phone. Potential participants would still receive the written invitation, participant information leaflet (PIL) and consent form prior to giving consent, and would have opportunity to review/ consider and decide prior to consenting.

Interviews would be conducted by phone, and recorded, at a pre-arranged time to suit the participant.

When the time comes that face to face contact is permitted and appropriate, participants would have the option to proceed either with telephone contact or face to face per their own preference.

Please say whether the proposed changes present any new ethical issues or changes to ethical issues that were identified in the original ethics review, and provide details of how these will be addressed:

In place of written informed consent there will be an option to record verbal consent
IC documentation will be completed to reflect the verbal process transparently – all such documentation will be retailed per standard practices.

Version 3.0 – Nov 2018

Amendment Approved:	**YES**	***Date of Approval:***	**18/06/2020**

Chair's Signature:

Once completed you should submit this form and any additional documentation to the relevant Ethics Panel that reviewed the original proposal:

School of Health & Society	Health-ResearchEthics@Salford.ac.uk
School of Health Sciences	
School of Built Environment	S&T-ResearchEthics@salford.ac.uk
School of Environment & Life Sciences	
School of Computing Science and Engineering	
Salford Business School	SBS-ResearchEthics@salford.ac.uk
School of Arts & Media	A&M-ResearchEthics@salford.ac.uk

Version 3.0 – Nov 2018

University of Salford MANCHESTER

Amendment Notification Form

Title of Project:		
'An interpretative phenomenological analysis of the experiences of people with Multiple Sclerosis (pwMS) taking part in MS research studies.'		
Name of Lead Applicant:	**School:**	
Lorraine M Trainor	Health & Society	
Are you the original Principal Investigator (PI) for this study?		Yes
If you have selected 'NO', please explain why you are applying for the amendment:		
Date original approval obtained:	**Reference No:**	**Externally funded project?**
10/06/2019	HSR1819-063 –	Yes
Please outline the proposed changes to the project. *NB. If the changes require any amendments to the PIS, Consent Form(s) or recruitment material, then please submit these with this form highlighting where the changes have been made:*		
To extend the recruitment and interview period to 31-12-21 (due to Covid 19 delays and associated impact on recruitment/ interview availability etc)		
Please say whether the proposed changes present any new ethical issues or changes to ethical issues that were identified in the original ethics review, and provide details of how these will be addressed:		
None perceived		

Amendment Approved:	**YES**	***Date of Approval:***	**16/09/2020**

Chair's Signature:

Version 3.0 – Nov 2018

NHS
Health Research Authority

South Central – Berkshire Research Ethics Committee

Whitefriars
Level 3, Block B
Lewin's Mead
Bristol
BS1 2NT

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

04 August 2019

[redacted]

Dear Ms Trainor

Study title:	**An interpretative phenomenological analysis (IPA) of the experiences of people with multiple sclerosis (pwMS) taking part in MS research**
REC reference:	**19/SC/0424**
Protocol number:	**N/A**
IRAS project ID:	**267148**

The Proportionate Review Sub-committee of the Berkshire Research Ethics Committee reviewed the above application in correspondance.

Ethical opinion

On behalf of the Committee, the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

The PR S-C would like to extend its congratulations and acknowledge this excellent application which was a pleasure to read. The grasp and appropriate use of IPA was particularly pleasing. The PIS is well written and engages well with participants at a personal level, it is gracious with no coercion. Engagement with people with MS is excellent - going well beyond typical PPI. They have been involved in all stages of the study and will continue to be so as members of the expert steering group with a key role in validating interview transcripts. The proposal is well written and easy to follow as a result of the helpful flowcharts. Thank you for this application.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Number	Condition
1)	Add to the PIS 'this study has been reviewed by South Central Berkshire Research Ethics Committee and has been given a favourable opinion'

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

It is a condition of the REC favourable opinion that all clinical trials are registered on a publicly accessible database. For this purpose, clinical trials are defined as the first four project categories in IRAS project filter question 2. For clinical trials of investigational medicinal products (CTIMPs), other than adult phase I trials, registration is a legal requirement.

Registration should take place as early as possible and within six weeks of recruiting the first research participant at the latest. Failure to register is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

As set out in the UK Policy Framework, research sponsors are responsible for making information about research publicly available before it starts e.g. by registering the research project on a publicly accessible register. Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

You should notify the REC of the registration details. We routinely audit applications for compliance with these conditions.

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion").

NHS
Health Research Authority

Approved documents

The documents reviewed and approved were:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		16 July 2018
Interview schedules or topic guides for participants	v2.0	17 March 2019
IRAS Application Form [IRAS_Form_19072019]		19 July 2019
IRAS Application Form XML file [IRAS_Form_19072019]		19 July 2019
IRAS Checklist XML [Checklist_19072019]		19 July 2019
Letters of invitation to participant [MS IPA INVITE]	V2.0	17 March 2019
Organisation Information Document		02 July 2019
Participant consent form [MS IPA ICS]	v2.0	17 March 2019
Participant information sheet (PIS) [PIL]	v2.0	17 March 2019
Research protocol or project proposal [MS IPA study proposal]	V1	13 June 2019
Summary CV for Chief Investigator (CI) [CI CV]		
Summary CV for student		13 June 2019
Summary CV for supervisor (student research)		12 June 2019
Summary CV for supervisor (student research)		13 June 2019

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

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 Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at:

Health Research Authority

https://www.hra.nhs.uk/planning-and-improving-research/learning/

With the Committee's best wishes for the success of this project.

19/SC/0424	Please quote this number on all correspondence

Yours sincerely

[redacted]
HRA Approvals Manager

On behalf of

[redacted]
Chair

Email: nrescommittee.southcentral-berkshire@nhs.net

Enclosures: List of names and professions of members who took part in the review

"After ethical review – guidance for researchers"

Copy to: [redacted], (Sponsor Contact)

NHS
Health Research Authority

Attendance at PRS Sub-Committee of the REC meeting in correspondence

Committee Members:

Name	*Profession*	*Present*
[redacted]	Retired Social Scientist	Yes
	Retired Corporate Lawyer	Yes
	Senior Research Support Associate	Yes

Also in attendance:

Name	*Position (or reason for attending)*
[redacted]	Approvals Manager

Health Research Authority Approval Letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Ms Lorraine Trainor
16 Wellington Road
Timperley
Altrincham
WA15 7RE

Email: hra.approval@nhs.net
HCRW.approvals@wales.nhs.uk

22 August 2019

Dear Ms Trainor

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**An interpretative phenomenological analysis (IPA) of the experiences of people with multiple sclerosis (pwMS) taking part in MS research**
IRAS project ID:	**267148**
Protocol number:	**N/A**
REC reference:	**19/SC/0424**
Sponsor	**University of Salford**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Northern Care Alliance – Research & Development Letter of Access – (initial)

Research & Innovation

NHS
Northern Care Alliance
NHS Group

Research and Innovation Department
Summerfield House, 1st Floor
Salford Royal NHS Foundation Trust
544 Eccles New Road
Salford M5 5AP
25th October 2019

Ms L Trainor
Post Graduate Student Researcher
University of Salford
The Crescent
Salford M5 4WT

Dear Ms Trainor

Letter of Access for Research: IRAS 267148 / S19NEURO15

This letter should be presented to the organisation before you commence your research at the site. The participating organisation is: **Salford Royal NHS Foundation Trust.**

In accepting this letter, each participating organisation confirms your right of access to conduct research through their organisation for the purpose and on the terms and conditions set out below. This right of access commences on 28th October 2019 and ends on 30th September 2020 unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from Salford Royal NHS Foundation Trust. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving confirmation from the individual organisation(s) of their agreement to conduct the research.

The information supplied about your role in research at the organisation(s) has been reviewed and you do not require an honorary research contract with the organisation(s). We are satisfied that such pre-engagement checks as we consider necessary have been carried out. Evidence of checks should be available on request to the organisation(s).

You are considered to be a legal visitor to the organisations premises. You are not entitled to any form of payment or access to other benefits provided by the organisation(s) or this organisation to employees and this letter does not give rise to any other relationship between you and the organisation(s), in particular that of an employee.

While undertaking research through the organisation(s) you will remain accountable to your substantive employer but you are required to follow the reasonable instructions of the organisation(s) or those instructions given on their behalf in relation to the terms of this right of access.

Saving lives, Improving lives

Northern Care Alliance – Research & Development Letter of Access – (renewal)

Research & Innovation

NHS
Northern Care Alliance
NHS Group

Research and Innovation Department
Summerfield House, 1st Floor
Salford Royal NHS Foundation Trust
544 Eccles New Road
Salford
Manchester
M5 5AP

Date: 28/09/2020

Lorraine Trainor
Post Graduate Student Researcher
University of Salford
The Crescent
Salford M5 4WT

Dear Lorraine,

Letter of Access for Research: IRAS 267148 / S19NEURO15

This letter should be presented to the participating organisation before you commence your research at that site.
The participating organisation is: **Salford Royal NHS Foundation Trust.**

In accepting this letter, the participating organisation confirms your right of access to conduct research through their organisation for the purpose and on the terms and conditions set out below. This right of access commences on **01.10.2020** and ends on **30.09.2021** unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from Salford Royal NHS Foundation Trust. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from the R&I office giving confirmation from the participating organisation of their agreement to conduct the research.

The information supplied about your role in research at the participating organisation has been reviewed and you do not require an honorary research contract with the organisation. We are satisfied that such pre-engagement checks as we consider necessary have been carried out. Evidence of checks should be available on request to Salford Royal NHS Foundation Trust.

You are considered to be a legal visitor to the participating organisations premises. You are not entitled to any form of payment or access to other benefits provided by the organisation to employees and this letter does not give rise to any other relationship between you and Salford Royal NHS Foundation Trust, in particular that of an employee.

Saving lives, Improving lives

IRAS 267148 Confirmation of Capacity and Capability at Salford Royal NHS Foundation Trust

Dear Sponsor Representative,

IRAS reference:	**267148**
R&I reference:	**S19NEURO15**
Study title:	**An interpretative phenomenological analysis (IPA) of the experiences of people with multiple sclerosis (pwMS) taking part in MS research**
Study Short Title:	**Lived experience of multiple sclerosis (MS) research participation**
PI:	**D Rog**
Site:	**Salford Royal**
NIHR:	**No**
Delivery Reportable to DoH:	**No**
Funding source:	**Non-commercial**
Date site selected:	**24th August 2019**
Number of calendar days to recruit 1st participant:	**65 calendar days**
Target date for first participant recruited:	**2nd November 2019**
Target as confirmed in the Organisation Information Document:	**3 - 8**

This email confirms that Salford Royal NHS Foundation Trust has the capacity and capability to deliver the above referenced study. Please find attached our agreed Organisation Information Document as confirmation. Also attached is the HRA approval letter dated 22nd August 2019. The documents highlighted on this letter have been reviewed and approved at Salford.

We agree to start this on a date to be agreed when you as sponsor give the green light to begin. Once agreed, please confirm the site activation date to all in this email.

Dear Sponsor Representative – please send any study amendments to SalfordRDamendments@srft.nhs.uk to ensure prompt review.

Appendix B

Study Documentation

Coproductive Invitation

Invitation

MS Research Project Group

Hello

We are doing some research into the experiences of people with MS taking part in research studies.

As you have previously taken part in an MS research study I would like to invite you to be part of a small group to help shape this research project.

The aim is to form a small project group of people with MS who would be happy to contribute to the research - not as participants or trial subjects but rather to provide some guidance towards how the study might be run, given your experience with prior MS studies.

It's completely up to you if it's something you might wish to do - and you are very welcome to contact me to discuss before deciding, either by phone or e-mail.

It's quite informal and the group would only meet a few times per year, but your knowledge and experience could help to improve the research study - and I hope it will be an interesting and rewarding activity in which to be involved.

Travel expenses (or taxis) and refreshments will be provided and we would do our best to accommodate any other specific or individual requirements that might enable you to contribute.

Thank you for considering.

My name - Lorraine Trainor ('the researcher')
My contact number - 07595 204244
The project e-mail address-MSResearch.ProjectGroup@gmail.com

Study Invitation Letter for Potential Participants

A Study Exploring the Experiences of People with MS (pwMS) Taking Part in MS Research

Hello

We'd like to invite you to take part in our research study.

Joining the study is entirely up to you. Before you decide we would like you to understand why the research is being done and what it would involve for you.

The attached leaflet, called the Participant Information Leaflet (PIL) tells you all about the study and what is involved if you take part.

If you decide you might be interested in taking part then the lead researcher will go through this information sheet with you, to help you decide whether or not you would like to take part and answer any questions you may have.

We'd suggest this should take around 10-20 minutes. Please feel free to talk to others such as family or friends, about the study if you would like to.

What next?– if you are interested in taking part or discussing further then there are two ways of making contact:.

1) *Either you can contact me on 07966 804557 or email me on msresearch.projectgroup@Gmail.com*

OR

2) *I can contact you if you provide your phone number and/or email on the slip in the attached prepaid envelope.*

You are very welcome to contact me for an informal chat and to ask any questions without making any commitment to take part.

Thank you for considering

Best wishes

The Researcher: Lorraine Trainor

Phone 07966 804557

msresearch.projectgroup@Gmail.com

Study Title : A Study to Explore the Experiences of people with MS taking part in MS Research

Invitation

I would like to invite you to take part in a research study which involves interviews.

Before you decide, you need to understand why the research is being done and what it would involve for you.

Please take time to read the following information carefully.

Please ask questions if anything you read is not clear or you would like more information.

Take as much time as you need and speak to friends or family before you decide whether or not to take part.

The study involves being interviewed and sharing your experiences of taking part in MS research. You might be interviewed up to four time, or maybe just once, it depends at what stage of the main study you are at. Interviews can be conducted by phone or in person..

Further information and contact details

For general information about research you may wish to look on the internet, if you have access - One example of a site that talks about research is :
https://www.nihr.ac.uk/

Details of other UK organisations that may be helpful:

MS Trust :
https://www.mstrust.org.uk/
0800 032 38 39

MS Society :
https://www.mssociety.org.uk/
0808 800 8000

The researcher contact details are
Lorraine M Trainor
07966 804557
MSresearch.projectgroup@gmail.com

You can also speak to your MS Nurse, MS Doctor, or one of the research team for the main MS study, if that would be helpful to you.

What is the purpose of the study?

The purpose of this study is to understand the meaning of the lived experience of taking part in a research study for people with MS.

As far as we can tell this hasn't been explored in depth before and we are keen to understand more about your experience of research participation.

It is hoped that this may help researchers to have a better understanding & to improve the experience of people like you in future research being undertaken

Why have I been invited to take part in this study?

You have been invited because you are an adult (over 18) who has MS, and because you are either taking part in MS research (an MS study or MS trial) or you are currently considering taking part in MS research.

Your MS doctor or MS Nurse, or one of the research team has identified you as someone potentially suitable for this interview study alongside the MS study that you are considering or have been enrolled in.

There may be up to 8 people involved in this interview study.

Do I have to take part in this interview study?

***No** - it is completely up to you to decide if you would like to take part or not.*

Your MS doctor and MS Nurse do not mind if you decide to take part or decide not to and this will not affect the care you receive and will not affect your involvement in the main MS study

After reading this information, having had time to consider, discuss and ask questions, if you decide to take part we will then ask you to sign a consent form to show that you have agreed to take part.

You are free to withdraw at any time, without giving a reason (and again this will not affect the care you receive nor your involvement in the main MS study).

If you do decide to withdraw at any stage then we would not contact you again, but if you have already been interviewed then the fully anonymised and deidentified information from the interview will still form part of the results – but nobody else will know that this has come from you .(The reason for this is that it may be difficult to separate & remove your data if it has already been analysed and included in the results along with data from other participants.)

What will happen to me if I take part?

We will arrange with you suitable times and places for you to be interviewed, up to a maximum of 4 times over the course of a year.

The interview will be very informal – it's an opportunity for you to share your experience of the main MS study and what it means to you.

You do not have to discuss anything that you do not feel comfortable sharing.

There will be some questions to help guide the interview, but you can talk about whatever is important to you relating to taking part in MS research (an MS study or an MS trial)

The interviews will be more like a chat and can be as long or short as you like – on average they may last around 40 minutes – but you can stop at any time or take a break.

You can choose how and where you want to be interviewed – at the hospital, or in your own home, or maybe at a favourite café if you are happy to speak in a public place, or if you prefer, by phone.

Depending on the stage you are at in the main MS study you could be interviewed up to 4 different times, but you can decide to stop or skip an interview at any time.

During the interview the interviewer will prompt you to share your experience by asking some broad questions, but you can decide not to answer the questions and to share what you feel is important instead.

There are no right or wrong answers and you cannot be judged by what you have said.
Anything that you say will be completely anonymised and de-identified – this means that there will be no identifiable data, nor any 'clues' that would mean that someone could work out who it is.

The interviewer will take some notes whilst you talk and will audio-record the interview (sound only – only the interviewer will have access to these recordings and they will not be heard by anyone else). The interview content will then be transcribed (written down) and different issues or topics will be looked at within what you have shared.

If you would like to the interviewer/researcher can share the topic or themes that they have found in what you have shared during your interviews.

The researcher will study what you have shared and look for meaning and aspects that are important for you and others who are taking part in research – this research technique is called Interpretative Phenomenological Analysis – it really just means looking in depth and looking for meaning in your experience.

We would hope that you might enjoy taking part and sharing your thoughts about taking part in research, but it may not be for everyone.

Expenses and payments?

Any reasonable travel costs or parking costs will be paid – this includes the cost of taxis if required to travel to the interviews.

Refreshments – snack food (cakes, sandwiches, biscuits or fruit) and hot or cold soft drinks will be available, and we will do our best to accommodate any dietary restrictions.

What are the possible benefits or disadvantages and risks of taking part?

Possible Disadvantages and Risks :

The study doesn't involve any medicines, or tests or procedures and so the risks of taking part are very low.

It is up to you to decide what you wish to share in the interviews, but it is possible that you may become upset when you talk about some aspects that are important to you – if this happens we can pause or stop the interview or move on to a different topic.

If you do become very upset then we can stop the interview and we can put you in contact with someone to offer you the necessary support.

You would be giving up some of your time to take part but we can work around times that are best for you.

Possible Benefits :

There is no direct benefit of taking part but you may enjoy having the opportunity to share your experiences of research participation.

The information we get from the study may help to increase the understanding of the experiences of people with MS taking part in research studies and may improve the future research.

But what if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researcher who will do their best to answer your questions.
Lorraine M Trainor 07966804557 MSresearch.projectgroup@gmail.com

If you remain unhappy and wish to complain formally you can do this by contacting the Research Supervisor Dr [redacted] Senior Lecturer / Research Lead (Health Directorate), School of Health & Society, Mary Seacole Building, Frederick Road Campus, University of Salford, Salford, M6 6PU [redacted]

If the matter is still not resolved, please forward your concerns to Professor [redacted] Chair of the Health Research Ethical Approval Panel, Room MS1.91, Mary Seacole Building, Frederick Road Campus, University of Salford, Salford, M6 6PU. Tel: 0161 295 2778. [redacted]

Will my taking part in the study be kept confidential?

Yes, your taking part will be kept completely confidential - your involvement will not be shared with anyone else.

When we talk about data we mean any information about you such as your name, or address, or details of your health etc, or anything that you share with us during the interview

It is important that you understand and are comfortable about how data are collected and stored and that you are comfortable and confident that your privacy will be maintained.

The interviewer/researcher may gather some identifiable information and personal information if you choose to share No identifiable details will be shared with anyone else. All information and outputs will be fully anonymised and de-identified – this means that there will be nothing to link it to you and no 'clues' that anyone could identify you.

All data will be held securely on a password protected computer or a secure storage area on university computers - any paper copies will be in a locked cabinet and only the researcher will ever have access.

All interview notes, recordings and transcripts will be destroyed after the project has been successfully written-up, or 3 years after the end of the project, whichever is the sooner.

Some of what you say may be shared with other people who are helping with the research – but this would just be short written sections with no identifiable details – the reason for this is that we want to make sure that we understand what your research experience means to you and it is helpful to have the input of others to do this.

Some short sections (excerpts or quotes) may be used when the study is written up or published in a journal – but again no one will note that this has come from you – you can ask to see this before it is published, and we'd be very happy to share it with you

Your interview information (transcript) and anything you share will be given a code name unrelated to you – this will be gender neutral and have absolutely no link to your actual name or any identifiable details.

If you do agree to take part, the consent form will contain the following sentence – and by signing the consent form you will be agreeing to this 'I am aware that if I reveal anything related to criminal activity and/or something that is harmful to self or other, the researcher will have to share that information with the appropriate authorities.'

Can I have someone with me when I take part in study ?

Yes, that's absolutely no problem, as long as you are comfortable having them there during the interviews/ discussions.

What will happen if I don't carry on with the study?

You can withdraw from the study at any time, that's no problem – you need to be aware though that the data collected up to your withdrawal will remain part of the study – this is because it would be difficult to separate anonymised data that has been merged with data from other participants.*

**By data we mean the written down version of the discussion we had when we interviewed you.*

What will happen to the results of the research study?

The results of this study will be incorporated into and academic thesis (essentially a long essay!) and may also be published in a multiple sclerosis professional journal.
None of your personal nor identifiable details will be included but we may include some quotes from what you have said.

Who is organising or sponsoring the research?

The study is sponsored by the University of Salford. Lorraine Trainor is the researcher - contact details are on page 4.

And Finally, …

Whether you decide to take part or not – THANK YOU for reading this leaflet and for considering – we wish you all the best

This study has been reviewed by South Central Berkshire Research Ethics Committee and has been given a favourable opinion.

Participant Informed Consent Form

IRAS Project ID: **267148**¶

Centre : Salford Royal Hospital¶

Study Number: MS IPA 2019¶

Participant Identification Number for this trial: _____¶

CONSENT FORM¶

- *Title of Project: A Study to Explore the Experiences of people with MS taking part in MS Research*¶
- ¶

Name of Researcher: Lorraine M Trainor Phone 07966 804557¶

Please initial box ¶

1. I confirm that I have read the information sheet dated 14th June 2020 (version 3.1) 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 without giving any reason, without my medical care or legal rights being affected.¶ ☐

¶

3. I understand that if I do withdraw, the data I have given up to that point will be used in the research.¶ ☐

¶

4. I am aware that if I reveal anything related to criminal activity and/or something that is harmful to self or other, the researcher will have to share that information with the appropriate authorities.¶ ☐

¶

¶

5. I agree to take part in the above study by being interviewed and for this to be audio-recorded.¶ ☐

¶

¶

_____ _____ _____¶

Name of Participant Date Signature¶

¶

¶

_____ _____ _____¶

Name of Person taking consent Date Signature¶

¶

¶

14JUN20-V3.1¶

When completed: 1 for participant; 1 for researcher site file; 1 to be kept in medical notes.¶

Appendix C

Quality Measures & Guides

What makes a good IPA paper?

(Smith, 2011)

The paper should have a clear focus. Papers providing detail of a particular aspect rather than a broad reconnaissance are more likely to be of high quality. This focus may be determined at the outset or emerge during analysis. This focus is apparent in many of the good IPA papers illustrated, for example, Chapman et al. (2007) examine the impact of one particular technology in heart disease. Turner et al. (2002) sample one specific group of ex-professional sports players.

The paper will have strong data. Most IPA is derived from interviews and this means that, for the most part, getting good data requires doing good interviewing. This is a particular skill that must not be underestimated. The quality of the interview data obtained sets a cap on how good a paper can subsequently be. Examples of good data are given in many of the summaries of good papers presented earlier. High-quality data is integral to the success of these papers.

The paper should be rigorous. One should aim to give some measure of prevalence for a theme and the corpus should be well represented in the analysis. Extracts should be selected to give some indication of convergence and divergence, representativeness and variability. This way the reader gets to see the breadth and depth of the theme. For papers with small sample sizes (1_3), each theme should be supported with extracts from each participant. For papers with sample sizes of 4_8, in general, extracts from half the participants should be provided as evidence. For larger sample sizes, researchers should give illustrations from at least three or four participants per theme and provide some indication of how prevalence of a theme is determined. The two papers on chronic fatigue syndrome by Dickson et al. (2007, 2008) have, for IPA, a relatively large sample size. Their persuasiveness is enhanced by careful articulation of measures of prevalence. The overall corpus should also be proportionately sampled. In other words, the evidence base, when assessed in the round, should not be drawn from just a small proportion of participants.

Sufficient space must be given to the elaboration of each theme. In certain circumstances it may well be better to present a subset of the emergent themes so there is room to do justice to each, rather than presenting all themes but doing so superficially. The French et al. (2005) paper on patient explanations for heart attack is enhanced by having an extended and elaborate account of one of the emergent themes.

The analysis should be interpretative not just descriptive. An interpretative commentary should follow each of the extracts presented. The author is thereby showing the ways extracts are contributing to the unfurling theme. In order to do this the researcher is engaging in the double hermeneutic: trying to make sense of the participant and trying to make sense of their experience. For further discussion on pushing interpretation deeper, see Smith (2004).

The analysis should be pointing to both convergence and divergence. Where an IPA study reports data from more than one participant, there should be a skillful demonstration of both patterns of similarity among participants as well as the uniqueness of the individual experience. The unfolding

narrative for a theme thus provides a careful interpretative analysis of how participants manifest the same theme in particular and different ways. This nuanced capturing of similarity and difference, convergence and divergence is the hallmark of good IPA work.

The paper needs to be carefully written. Good qualitative work always requires good writing. The reader will feel engaged by a well-wrought, sustained narrative. As a result, he/she will consider they have learned in detail about the participants' experience of the phenomenon under investigation. Have a look at some of the papers rated good in this review to see what good writing looks like.

Characteristics of Good Qualitative Research

Essential qualities are shown in bold, with examples of the form each can take shown in below each heading (Yardley, 2000).

Sensitivity to context

Theoretical; relevant literature; empirical data; sociocultural setting; participants' perspectives; ethical issues.

Commitment and rigour

In-depth engagement with topic; methodological competence skill; thorough data collection; depth/breadth of analysis.

Transparency and coherence

Clarity and power of description/argument; transparent methods and data presentation; fit between theory and method: reflexivity.

Impact and importance

Theoretical (enriching understanding); socio-cultural; practical (for community, policy makers, health workers).