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Patient Activation in Long-Term Conditions

A systematic review of the effectiveness of self-management interventions for improving patient activation using the short-form Patient Activation Measure and an empirical study of the variables associated with patient activation and self-management in Multiple Sclerosis.

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Doctorate in Clinical Psychology

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Lay Summary

This research portfolio has two chapters. The first chapter is a review of existing research and the second is a research study. People who live with an incurable illness may be more vulnerable to other health problems, feeling low in mood, and they may face social difficulties. Learning skills to manage health problems is called 'self-management.' The review of existing literature suggests that helping people to learn skills to manage their health problems, through 'self-management interventions,' has a positive effect on their confidence and ability to take control of their health problems. This is important because people who can take control of their own health often have a better quality of life. More research is needed to find out which types of self-management interventions might be most helpful for improving people's confidence in taking control of their own health.

The research study recruited 118 people living with Multiple Sclerosis (MS) to answer written questionnaires. The results of the study revealed that when people are aware of and act on their own personal values – that is, what is important to them - they might feel more confident about managing their health problems. Similarly, people who feel confident about the ways they manage their health might be more able to identify their personal values. It was also found that people with MS who feel confident and capable of managing their health problems are likely to do more to self-manage their condition (e.g. finding out information about MS, taking medication regularly and taking a break when tired). Our results also suggest that patients, who experience more empathy from their MS specialist nurse or doctor, might do more to self-manage their condition; however, it is also possible that when patients effectively self-manage, it improves the relationship they have with their clinician. Helping people with MS to recognise what is important in their life, and to take positive actions towards their values, may allow them to feel more confident in managing their condition. Additionally, interventions that aim to build self-management confidence and promote better patient-clinician relationships may help some patients to develop the ability to manage their MS successfully.

Full Thesis Abstract

Purpose: The systematic review explored whether self-management interventions improve patient activation in long-term conditions, and if any improvements are greater than the amount of change experienced by patients in usual care or active control conditions. It also aimed to determine if positive effects on activation are maintained at follow-up. The empirical study sought to explore relationships between patient activation, psychological factors (depression and valued living), perceived clinician empathy, perceived symptom severity, self-management and demographic variables. It also examined whether depression, valued living and perceived clinician empathy are unique predictors of activation, and if activation is a unique predictor of self-management for MS, when relevant confounding variables are controlled for.

Methods: For the systematic review, a comprehensive search of multiple electronic databases was conducted to identify intervention research reporting on patient activation outcomes, as measured by the short-form Patient Activation Measure (PAM-13), in people with long-term conditions. For the empirical study, a cross-sectional survey of 118 people with MS explored patient activation, MS symptom severity, valued living, depression, perceived clinician empathy, self-management for MS and demographic factors. Correlation and hierarchical regression analyses were employed to explore relationships between variables.

Results: Twenty-five studies were eligible for inclusion in the systematic review, reporting a wide range of long-term conditions. Twenty-one studies (10 RCTs; 1 non-randomised study; and 10 uncontrolled studies) found an improvement in patient activation at post-intervention. Nine studies reported a significantly greater improvement in activation in self-management conditions compared with usual care or an active control at post-intervention. In six out of eight studies, gains in patient activation were maintained in the intervention group at follow-up. However, in four of these six studies, patient activation in the control group also improved over time. Findings from the empirical study suggested that only valued living was a significant predictor of patient activation after controlling for demographic variables and MS symptom severity. Neither depression nor perceived clinician empathy significantly predicted activation. After controlling for valued living, depression and perceived clinician empathy, patient activation independently predicted 5.5% of variance in self-management for MS. Both activation and perceived clinician empathy were significant predictors of self-management for MS.

Conclusions: Self-management interventions improve patient activation in long-term conditions compared with usual care or active control. Patient activation gains appear to be maintained longer-term; however, the impact of self-management interventions on activation is unclear due to increases in activation in control groups over time. Valued living is associated with patient activation in MS, while patient activation and perceived clinician empathy are associated with MS self-management. Self-management interventions targeting valued living and the patient-clinician relationship may be effective for addressing low levels of activation in some patients with MS.

1. Systematic Review

The Effectiveness of Self-Management Interventions for Improving Patient Activation in Long-Term Conditions: A Systematic Review.

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Abstract

Purpose: To systematically review the evidence of the effectiveness of self-management interventions for improving patient activation, as measured by the short-form Patient Activation Measure (PAM-13); to determine if any improvements are greater than the amount of change experienced by patients in usual care or active control conditions; and to ascertain if patient activation gains are maintained at follow-up of 3 months or beyond.

Methods: A comprehensive search of multiple electronic databases was conducted between April and August 2017 (updated in December 2017) to identify intervention research reporting on patient activation outcomes, as measured by the PAM-13, in people with long-term conditions. Uncontrolled studies, together with randomised and non-randomised controlled trials, were included and evaluated against quality criteria developed for the specific purpose of the review. Authors of included studies were contacted in January 2018 to identify further published or unpublished literature.

Results: Twenty-five studies were eligible for inclusion in the systematic review, reporting on a wide range of physical conditions. Twenty-one studies (10 RCTs; 1 non-randomised study; and 10 uncontrolled studies) found an improvement in patient activation in self-management conditions at post-intervention. Nine studies reported a significantly greater improvement in patient activation in self-management conditions compared with usual care or active control groups at post-intervention. In six out of eight studies, gains in patient activation were maintained in the intervention group at follow-up. However, in four of these six studies, improved activation was also found in control groups at follow-up.

Conclusions: Compared with usual care or active control groups, self-management interventions improve patient activation in long-term conditions. Patient activation gains appear to be maintained longer-term in self-management conditions; however, the impact of self-management interventions on activation is unclear due to increases in activation in control groups over time.

1. Introduction

The effort to promote and prolong quality of life in long-term conditions (LTCs) within the context of increasing global life expectancy creates challenges for healthcare systems worldwide (Wang et al., 2016). According to the UK Global Burden of Disease Study (2010), the number of years lived with a disability is on the rise because of the increased prevalence of many chronic conditions with age (Murray et al., 2013). LTCs are defined as those that are not curable at present but may be managed, to some extent, by medication or other therapies (Department of Health [DoH], 2012). In England, approximately 15 million people live with a LTC, with care costs accounting for around 70% of the English health and social care budget (DoH, 2012). In Scotland, around 2 million people live with at least one LTC (The Scottish Government, 2009). The management of LTCs is typically dependent on the unique features of the specific condition; however, due to increased demand upon health care services, patient 'self-management' has gained increased prominence and is typically seen as a core component of contemporary models of care (Taylor et al., 2014).

What is self-management?

Barlow, Wright, Sheasby, Turner and Hainsworth (2002, p. 178) define self-management as "the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition." Self-management discourse is embedded in health guidelines, whereby the patient is encouraged to adopt an empowered, active role. The task of the healthcare professional is to share power and responsibility in the effort to promote patient autonomy, participation and decision-making in healthcare (Ellis et al., 2017). As a result, it is perhaps unsurprising that self-management is typically viewed in behavioural terms, where the DoH (2007) defines self-management of LTCs as the actions taken by individuals to support their own health and wellbeing. However, according to Barlow et al. (2002), effective self-management is dependent upon an individual's ability to self-monitor and flexibly bring about the cognitive, emotional and behavioural adjustments in order to preserve quality of life for as long as possible. It is widely accepted that self-management is more than adhering to treatment guidelines; it must also incorporate the psychological and social management of living with a chronic condition. The extent of psychological and social management required is dependent on the LTC, and subsequently what is necessary for effective self-management (Newman, Steed & Mulligan, 2004). For example, self-management of asthma might only entail using an

inhaler when required to prevent symptom exacerbations; whereas self-management for progressive MS may need medication adherence in the form of injections, behavioural changes, social and psychological coping strategies because of the extent and impact of symptoms on several areas of life.

Taylor et al. (2014) define a self-management intervention (SMI) as those that provide patients with education, training and support to develop knowledge, skills or psychological and social resources to undertake activities to manage a health condition. Taylor et al.'s (2014) proposed taxonomy of self-management components, to capture the range of self-management programmes offered across setting, disciplines, and diseases, comprises:

- Information provision;
- Psychological coping skills to help with adjustment;
- Specific action plans to support adherence to treatments;
- Practical assistance that is condition-specific (e.g. activities of daily living or training to enable self-management of specific tasks);
- Regular social or clinical support;
- Communication training;
- Guidance or advice on lifestyle alterations.

As well as differing on the basis of underlying health conditions, some studies have found that levels of engagement in self-management may vary in relation to age and gender (Blakemore et al., 2016; Bos-Touwen et al., 2015) and have a significant impact on the types of behaviour individuals engage with regarding their condition. For example, a man in his 70s with cardiovascular disease may take on a passive mentality of "do whatever the doctor decides to do." By contrast, a woman in her 40s with diabetes may wish to find out information about coping with diabetes via the internet and discussions with the diabetes nurse; she may also alter aspects of her lifestyle (e.g. making time for physical activity, paying attention to dietary sugar and wearing a pedometer to self-monitor) according to this advice. The aforementioned examples highlight the variability among individuals with LTCs concerning self-governance, monitoring and personal responsibility. It can be argued, therefore, that a patient's ability to engage in self-management behaviours is dependent on their knowledge, skill and confidence for managing their own health and healthcare, typically conceptualised as 'patient activation' (Hibbard, Stockard, Mahoney & Tusler, 2004).

Patient activation

The patient activation construct has emerged on a background of policy directions that aim to empower patients and improve the quality of care in LTCs (Wagner et al., 2001). The Chronic Care Model (see Wagner et al., 2001) is a framework that encapsulates the systemic components required to improve care in LTCs including patients, carers and healthcare teams. The model suggests that improving care requires interventions at each of the systemic levels, with interactions between informed patients and healthcare professionals as a key component leading to improved management of LTCs (Bodenheimer, Wagner & Grumbach, 2002). However, as highlighted by Hibbard, Mahoney, Stockard and Tusler (2007), the patient activation construct has historically been an underdeveloped aspect of the Chronic Illness Care Model, both in conceptual and empirical terms. The patient activation construct assimilates the closely related psychological constructs of self-efficacy (Lorig et al., 1996), locus of control (Wallston & Wallston, 1982) and readiness to change (Prochaska & DiClemente, 1986), but also comprises aspects of personal capability including communication skills, disease knowledge and attitudes regarding self-agency (Skolasky, MacKenzie, Riley & Wegener, 2009). While existing constructs traditionally assess specific psychological variables or behavioural outcomes; the development of the patient activation construct, and its measurement, sought to bring together both psychological and behaviour components thought to be involved in activation which can be applied transdiagnostically across illness groups for clinical and research purposes (Hibbard et al., 2004).

The patient activation construct captures beliefs and attitudes about acquiring and building skills, in addition to the actual implementation of self-management activities (Moore et al., 2016). It is a progressive process, whereby an individual who is more "activated" will demonstrate greater endorsement of the behaviours, attitudes and beliefs needed for illness self-management (Hibbard, Mahoney, Stockard & Tusler, 2005). The short-form Patient Activation Measure (PAM-13), the most widely used measure of this construct, is a 13-item self-report scale assessing skills, knowledge and confidence in illness self-management. Responses to items such as "*I am confident that I can follow through on medical treatments I need to do at home*" are rated from 'strongly disagree' to 'strongly agree.' Responses are converted to a 0-100 scale; with higher scores indicating greater levels of patient activation. The PAM-13 has demonstrated utility by linking activation levels to health outcomes, costs, and patients' experiences of care (Bodenheimer, Lorig, Holman, & Grumbach, 2002). According to the

authors of PAM-13 (Hibbard et al., 2005), there are four developmental increments in becoming a 'competent self-manager.' As individuals move through each stage, it is suggested that their autonomy and competence in self-management improves. The activation levels and basic descriptors are (Dixon, Hibbard & Tusler, 2009; Hibbard & Gilburt, 2014; Hibbard et al., 2007):

- Level 1: individuals play a passive role in their own health and are not actively involved in their healthcare provision. They may lack understanding of their role in their own healthcare and view self-management in terms of simple compliance.
    - *Example: The person who "just follows the doctor's orders," such as taking medication when they feel no benefit or have no knowledge of what their medication does. They may be forgetful and inconsistent in adherence.*

- Level 2: individuals may have a basic understanding of their health and healthcare needs but lack skills and / or confidence to manage their health effectively.
    - *Example: The person, who is increasingly aware of the importance of finding out about their condition and talks with others about their condition, but who may not be confident or skilled in carrying out actions to support their health (e.g. doing exercise inconsistently to manage weight).*

- Level 3: individuals have most of the facts about their health condition and are starting to take specific actions pertaining to managing their condition but may still lack some confidence and skills in managing their health.
    - *Example: The person who views their relationship with their healthcare provider as primarily a partnership, engages in multiple health-supporting behaviours to manage their health (e.g. lifestyle changes, taking medication), though may struggle in areas of self-monitoring and managing multiple behavioural changes to some degree.*

- Level 4: individuals are carrying out behaviours necessary to support their health and manage their condition; however, maintenance of these behaviours may be difficult in the face of life stressors. Individuals will view self-management in terms of being in control and responsive to changes when needed.
    - *Example: The person, who is engaging in various health-supporting behaviours to manage their own healthcare, recognises the impact of stress on their self-management and can effectively manage this impact via self-monitoring most of the time.*

Patient activation and positive health outcomes

There is evidence that individuals scoring highly on the PAM-13 are more likely to engage in health-supporting behaviours such as eating healthily and exercising regularly (Forbat, Cayless, Knighting, Cornwell & Kearney, 2009; Hibbard et al., 2007). Furthermore, individuals who score highly are significantly more likely to avoid health-limiting behaviours such as smoking and substance misuse (Greene & Hibbard, 2012).

Patients with LTCs who are more activated have also been found to be significantly more likely to adhere to treatment recommendations and self-monitor at home, prepare questions in advance of a medical appointment and seek information regarding their condition (Fowles, Terry, Hibbard, Bloom & Harvey, 2009; Hibbard, Greene & Tusler, 2009; Mosen et al., 2007). Moreover, the link between patient activation and health outcomes appears to be consistent across various health conditions, continents and diverse demographic backgrounds (Greene & Hibbard, 2012).

Several studies have shown that increases in patient activation positively correlate with health behaviours including the uptake of regular exercise, adherence with medication (Hibbard et al., 2007; Mosen et al., 2007), information seeking (Fowles et al., 2009), glucose testing, foot checks and eye examinations in diabetic patients (Rask et al., 2009; Remmers et al., 2009). Furthermore, low levels of self-reported activation have been found to predict hospital readmission within 30 days in patients with a range of physical health problems (Mitchell et al., 2014). These findings appear to suggest that the PAM-13 has predictive value in determining those likely to engage in self-management behaviours and, arguably, might be viewed as a transdiagnostic measure through which patient engagement in self-management can be captured.

Why examine patient activation as an outcome?

Patient activation is thought to be a modifiable construct (Hibbard et al., 2007) as evidenced by its increasing prominence as an outcome in a range of clinically important health indicators in studies evaluating the effectiveness of SMIs. Across many chronic conditions including heart failure, type II diabetes, and polyarthritis (Grønning, Skomsvoll, Rannestad & Steinsbekk, 2012; Lorig, Ritter, Villa & Armas, 2009; Shively et al., 2013) SMIs have been found to increase

patient activation, although these findings are not consistent across studies (Rygg, Rise, Grønning, & Steinsbekk., 2012; Ryvicker, Feldman, Chiu, & Gerber, 2013).

SMIs claim to 'activate' patients and improve engagement with self-management; however, Moore et al. (2016) suggest that the range and quality of outcome measures used to evaluate SMIs are highly variable. Some studies use disease-specific self-efficacy measures, others rely on patient self-report of specific behaviours, while others use quality of life measures. Furthermore, the variation between the quality and content of SMIs adds an additional complexity in making sense of this literature. Moore et al. (2016) recommended that, among others, data on patient activation should be gathered in evaluations of SMIs as measures such as the PAM-13 capture information on the array of knowledge, skills and beliefs a person needs to effectively self-manage their LTC.

In a review of the literature, Bolen et al. (2014) sought to evaluate the effectiveness of a range of patient activating interventions for adults with diabetes on several clinical outcomes including diabetes control. The results demonstrated these interventions safely and modestly improve diabetes control; however, an important methodological limitation of this review was that the authors did not examine the effectiveness of these interventions in improving patient activation as a possible mediator or moderator of change.

There is a need to review the current health literature in disease management to evaluate the effectiveness of SMIs for improving patient activation. While SMIs are heterogeneous in nature, reviewing the evidence for patient activation outcomes in this area has the potential to add to our understanding of the effectiveness of self-management interventions in line with current chronic care models, with potential benefits to patient quality of life.

1.1 Aims

We aimed to evaluate the available evidence regarding the effectiveness of SMIs in improving patient activation, as measured by the PAM-13, in adults with chronic physical health conditions. A secondary aim was to evaluate if any positive impact of SMIs on patient activation are maintained at 3 months follow-up or beyond.

2. Methods

2.1 Protocol

This review was registered on PROSPERO: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=72292, registration number CRD42017072292. Amendments to the protocol during the review are also available on this record.

2.2 Selection of studies for inclusion

Development of the study protocol and reporting was informed by the Centre for Reviews and Dissemination (CRD; 2009) and the PRIMSA recommendations (Moher, Liberati, Tetzlaff & Altman, 2009). The 'PICOS' method comprising: population, intervention, comparators, outcomes and study design, guided the eligibility criteria for studies as shown in Table 1.

Table 1. PICOS eligibility criteria for selection of studies.

	Inclusion criteria	Exclusion criteria
Population	• *Adults (≥16 years) living with a specified long-term physical health condition(s), in clinical and non-clinical settings. Studies may include individuals with mental health problems where physical health problems were documented in at least 70% of the total sample.*	• *Children and adolescents (<16 years), or adults without a long-term condition(s).*
Interventions	• *Self-management interventions delivered in any context or setting to increase patient activation as a primary or secondary outcome.*	• *Interventions considered insufficient for improving activation by review authors' subjective opinion.*
Comparators	• *No specifications set for comparative conditions (e.g., usual care, wait-list, active control).*	• *No exclusion criteria regarding comparators.*
Outcomes	• *Patient activation as measured by the short-form Patient Activation Measure (PAM-13);* • *Pre- and post-intervention or pre-intervention and follow-up data for PAM-13.*	• *No secondary outcomes.*
Studies & design	• *Randomised controlled trials; non-randomised trials and observational repeated-measures designs, including case series, conducted from January 2004 to present;* • *Published or unpublished research in any language.*	• *Small N designs* • *Studies with very underpowered intervention groups (n <9) due to their inability to appropriately address the review aims.*

2.3 Search strategy for identification of studies

Electronic database searches

The search strategy was developed in consultation with a senior university librarian experienced in systematic literature reviews. Initial searches were conducted between April and August 2017 and updated in December 2017. An initial search of Database of Abstracts of Reviews of Effects (DARE), Cochrane Database of Systematic Reviews (CDSR) and PROSPERO was carried out to investigate the scope of other reviews in this area and to ensure the research question had not previously been addressed.

The OVID gateway was used to search the following databases: EMBASE (1980 to August 2017), PsycINFO (1806 to August 2017), and OVID MEDLINE(R) (1946 to August 2017). EBSCO host was used to search CINAHL Plus and ProQuest was used to search Applied Social Sciences Index and Abstracts (ASSIA) (1987 to present). The following search terms were used: "patient activation" AND "self management" OR "self manag*" OR "self care" AND "chronic" OR "long term."

ProQuest Dissertations & Theses Global and the Electronic Theses Online Service (EThOS), accessed via the University of Edinburgh website, were also searched using the keyword "patient activation."

Other sources

Further to the database search strategy, manual searches were also conducted to capture potential additional papers in the literature missed by the search terms. All papers referenced in the originally identified studies and relevant reviews retrieved through database searches were examined. A Google Scholar search using the aforementioned search terms was performed, with the first ten pages reviewed for additional articles. Publications, which cited the included studies were also screened using Google Scholar. Finally, authors of eligible studies were contacted to identify any further studies which may have been missed or in progress.

2.4 Data collection and analysis

Selection of studies

The first author determined study eligibility for inclusion. Titles and abstracts of retrieved studies were reviewed in the initial stage of screening. Studies were retained for the inclusion at this stage if the title and/or abstract suggested that the study evaluated a self-management intervention. The full text of articles retained following title/abstract screening were subsequently reviewed against inclusion criteria. See Figure 1 for an overview of the search strategy and review stages.

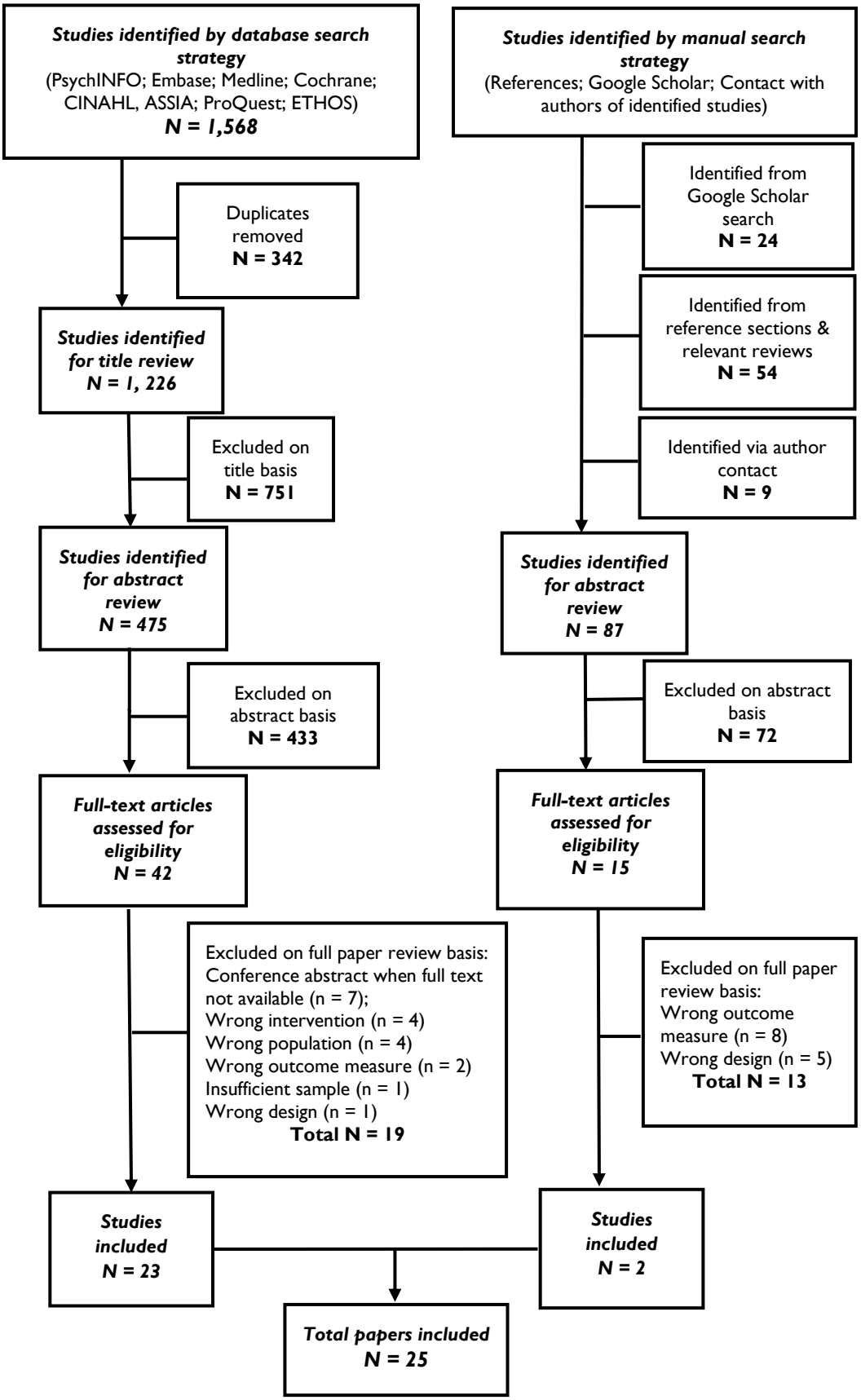

Figure 1. Flow chat of search strategies and results.

Data extraction and management

The first author, using a data extraction form employed in a previous study by Chauhan, Morris and Ferreira (2016), performed data extraction for the current review. The data extraction form included the following information: author and publication date; study design; brief description of the intervention and control (if any); mean age; gender; sample; duration of the intervention and follow-up period.

For this review a coding frame based on the taxonomy developed by Taylor et al. (2014) was used to identify the components of each intervention to allow for decision-making around the complexity and suitability of the self-management approaches in the reviewed papers (see Appendix B). Each intervention was reviewed for its suitability for improving patient activation. The first author coded each intervention according to this coding frame and a second coder following detailed instructions validated the results. Any disagreements were resolved by discussion.

Assessment of methodological quality of included studies

In their current form, typical risk of bias tools or quality criteria were not felt to be appropriate for our research question. This issue was further compounded by the idiosyncratic nature of self-management interventions and the variation in methodological design of the included studies (e.g. RCTs and repeated-measures designs). Therefore, a set of quality criteria with the ability to assess studies for the current review were adapted from existing tools. The criteria developed for the purposes of this review can be viewed in Table 2 (see Appendix C for an operationalisation of the criteria).

All studies were assessed for quality by the first author and a second rater using the same quality criteria tool blindly assessed a randomly allocated proportion of studies (50%). The quality ratings were then crosschecked, and any discrepancies were resolved through discussion. Interrater reliability ranged between 0.85 and 1.00 across items.

The methodology checklist (Scottish Intercollegiate Guidelines Network [SIGN], 2012) was considered in relation to each criterion and the following ratings were employed: well covered (3 points), adequately addressed (2), poorly addressed (1), and not reported / not addressed (0). The highest overall score a study could receive was 39. A previous review

conducted by Pateraki and Morris (2017) utilised the quality classification system of ++, + or – based on guidelines by SIGN (2012). Studies were coded '++' where the overall rating was ≥75% (30-39); coded '+' where overall rating was ≥50% (20-29); and coded '-' where overall rating was <50% (0-19).

Table 2. Quality criteria for included studies.

Risk of bias quality criteria
1. Design: *Study design provides sufficient evidence that patient activation outcome is due to the intervention*
2. Recruitment: *Recruitment method and eligibility criteria were appropriate to ensure a representative and suitable sample*
3. Sample size: *Sample size (power) is sufficient for analysis relating to pre-and post- patient activation outcome*
4. Allocation bias: *Allocation process was appropriate to address allocation bias*
5. Equal groups: *Groups are comparable at baseline on key variables (i.e., patient activation, severity of condition, age, gender, education, where appropriate)*
6. Measure validity: *PAM-13 was appropriately administered and validated for use in sample population*
7. Follow-up: *Follow-up measure was administered to evaluate if effects are maintained long-term*
8. Intervention suitability: *Self-management intervention is suitable for increasing patient activation outcome*
9. Intervention delivery & assessment: *Delivery of the intervention was conducted and assessed appropriately*
10. Attrition (1): *Post-intervention attrition was low and/or comparable to control group*
11. Attrition (2): *Follow-up attrition was low and/or comparable to control group*
12. Analysis: *Analysis is appropriate for the review aims, measure or design and outcomes are appropriately reported*
13. Missing data: *Methods to address missing data are suitable*

3. Results

Figure 1 illustrates that 1,568 papers were initially identify through electronic database searches. The number of papers retained for review following each stage of the screening process and rationales for exclusion are detailed thereafter. Manual searches of the literature resulted in two further papers being identified as eligible for review.

3.1 Summary characteristics of included studies

In total, 25 studies satisfied inclusion criteria for review. Summary characteristics of included studies are detailed in Table 3. Of the 25 studies that met inclusion criteria, 13 studies were randomised controlled trials (RCTs). Of these, nine RCTs compared an SMI with usual care control; two RCTs compared an SMI with an alternative active control; and a further two RCTs compared an SMI with both treatment as usual and an active control. There were two non-randomised controlled studies, in which the control groups used were usual care and an alternative active control. The remaining 10 studies were uncontrolled repeated measures designs.

The SMIs were delivered in a variety of formats but could be classified as group/workshop interventions (11 studies), individual interventions (10 studies) and web-based interventions (four studies). The mean percentage of females in the intervention condition across studies was 57.22%, with a range of 0-100 percent. The duration of SMIs differed between formats; group and web-based SMIs typically lasted for six weeks (range: six to twelve weeks) compared with one-to-one SMIs which lasted approximately six months (range: one to twelve months). One-to-one SMIs appeared to offer the greatest intensity among the three intervention formats. Eight studies included follow-up periods of either three months (one study), six months (two studies), twelve months (four studies) or eighteen months (one study). All studies used the short-form Patient Activation Measure (PAM-13; Hibbard et al., 2005).

A summary of the methodological quality criteria ratings is provided in Figure 2. Areas of relative methodological strength across the literature were in the domains of measure validity within sample populations, intervention suitability and sample size. Areas of methodological weakness across studies were use of follow-up measures, attrition rates at follow-up and allocation bias.

3.2 Risk of bias and quality assessment

Risk of Bias and Quality Assessment ratings for each reviewed study are outlined in Table 4 and summarised in Figure 2. An independent co-rater also examined fourteen of the papers. Studies to be co-rated were selected via a randomly generated series of numbers by random.org. Agreement was reached on 156/182 ratings (i.e. 85.7%). In six ratings, disagreement of more than one point was found. These discrepancies were discussed, and agreement was reached by consensus. The criteria were then amended to improve clarity and consistency, where necessary.

Study design

Of the 13 RCTs, seven obtained the highest ratings (++) (Ehde et al., 2015; Grønning et al., 2012; Hibbard et al., 2007; Lorig et al., 2009; Lorig et al., 2010; Rygg et al., 2012; Shively et al., 2013). The remaining RCTs and both non-randomised trials were allocated an overall rating of (+) (Hibbard et al., 2009; Hochhalter, Song, Rush, Sklar, & Stevens, 2010; Maindal, Sandbæk, Kirkevold, & Lauritzen, 2011; Morrison et al., 2016; Ryvicker et al., 2013; Solomon, Wagner, & Goes, 2012; Titova et al., 2017; Young, Hertzog & Barnason, 2016). Of the 10 uncontrolled studies, seven were given a rating of (+) (Fløde, Iversen, Aarflot & Haltbakk, 2017; Kaltman et al., 2015; Kawi, Schuerman, Alpert, & Young, 2015; Kosmala-Anderson, Wallace, Turner & Bourne, 2014; Shah et al., 2015; Turner, Anderson, Wallace, & Kennedy-Williams, 2014; Turner, Anderson, Wallace, & Bourne, 2015). Three were allocated the poorest rating (-) (Crosby, Joffe, Peugh, Ware & Britto, 2017; Ledford, Ledford, & Childress, 2013; Wallace et al., 2009).

Power and sample representativeness

Sample sizes were generally adequate and in intervention conditions ranged from 16 to 1170 participants (4,280 intervention participants across 25 studies; *M*=171.2, *SD*=229.35). Good–to-moderate attrition rates for intervention conditions were found across studies, ranging between 0%-50 percent. The majority of studies utilised suitable analyses (n = 23) and addressed missing data appropriately (n = 18) to examine the effect of the intervention on patient activation. Post-hoc power analyses for pre-post results in each study's intervention groups were conducted. Using the G*power programme, a medium effect size was anticipated (d = 0.5 for t-test; f = 0.25 for ANOVA) and $\alpha = 0.05$. By this method, 19 of the

25 studies had a sample size sufficient to achieve power of ≥0.8. The remaining six studies had samples sufficient to achieve power of ≥0.6 to <.80.

Recruitment methods were generally adequate. Convenience sampling was evident throughout studies, though most specified eligibility criteria (e.g. physician confirmed diagnosis, presence of comorbidity or depression) which would allow for results that were reasonably representative and generalisable within the specified illness groups. Five studies had samples comprising clearly identified heterogeneous health conditions (Hibbard et al., 2007; Hibbard et al., 2009; Hochhalter et al., 2010; Solomon et al., 2010; Turner et al., 2015).

Table 3. Characteristics of included studies.

Year	Author	Design	Intervention and comparison	Mean Age (SD)	Sample Size (% female)	Patient Group	Duration	Follow-up
2017	**Crosby et al.**	Uncontrolled study	Chronic Disease Self-Management Program	18.7 (2.22)	22 (45.5)	Young adults with sickle cell disease	6 weekly 2.5 hr sessions	6 months
2017	**Fløde et al.**	Uncontrolled study	Diabetes self-management education programme	54 (12)	115 (47)	Adults with type II diabetes	12-15 hrs over 2/3 weeks	3 months
2017	**Titova et al.**	Non-randomised	Home-based self-management programme integrating disease education, e-learning, skill building & nursing support ***Vs. TAU***	73.6 (9.2) ***72.2 (9.4)***	91 (57.1) ***80 (57.5)***	Adults with COPD	6 months	None
2016	**Morrison et al.**	RCT	Interactive self-management website ***Vs. TAU***	44.6 (17) ***46.4 (14)***	25 (72) ***26 (77)***	Adults with uncontrolled asthma	12-week website usage period	None
2016	**Young et al.**	RCT	Self-management training in hospital & telephone reinforcement sessions ***Vs. TAU***	68.7 (11.8) ***71.8 (12.6)***	51 (62.9) ***49 (75.5)***	Adults with heart failure	1 x 1-1 training + telephone sessions for 12 weeks post-discharge	None
2015	**Ehde et al.**	RCT	Telephone-delivered self-management intervention ***Vs. Telephone-delivered MS education intervention***	51 (10.1) ***53.2 (10.0)***	75 (89.3) ***88 (85.2)***	Adults with MS	8 weekly 45-60min sessions ***As above***	12 months
2015	**Kaltman et al.**	Uncontrolled study	Behavioural activation and motivational interviewing sessions	49.7 (8.8)	18 (56)	Adults with type II diabetes and depression	6 weekly sessions + 2 monthly booster sessions	None
2015	**Kawi et al.**	Uncontrolled study	Online self-management program combined & physical activity	60.9	16 (100)	Adult females (50+) with knee osteoarthritis	6 weekly 2hr online self-management modules + 3x weekly exercise sessions for 10 weeks.	None

Year	Author	Design	Intervention and comparison	Mean Age (SD)	Sample Size (% female)	Patient Group	Duration	Follow-up
2015	**Shah et al.**	Uncontrolled study	Disease-specific educational classes + peer support groups + home-based monitoring + individualised exercise and nutritional goals	49.4 (12)	60 (68)	Adults with type II diabetes	1hr didactic group session + monthly home-based educational sessions for 6 months	None
2015	**Turner et al.**	Uncontrolled study	Disease self-management program	56.3 (14.6)	1170 (64)	Adults with mixed long-term conditions (diabetes, depression, skeletal pain, COPD)	7 weekly 3hr sessions	None
2014	**Turner et al.**	Uncontrolled study	Chronic Disease Self-Management Program tailored for COPD	68.3 (9.3)	205 (55.9)	Adults with COPD	7 weekly 3hr sessions	None
2014	**Kosmala-Anderson et al.**	Uncontrolled study	Diabetes self-management programme	62.3 (11.1)	285 (51.3)	Adults with type II diabetes	7 weekly 3hr sessions	None
2013	**Ledford et al.**	Uncontrolled study	Patient-physician communication coaching and education	59.8 (8.9)	128 (48.4)	Adults with type II diabetes	Brief 1-1 clinic appointment + tailored postcard reminder after 2 weeks + tailored letter reminder after 4 months	None
2013	**Ryvicker et al.**	RCT	Home Support Program ***Vs. Evidence-based recommendations to nurse and patient*** ***V.s TAU***	64.4 (11.1) ***65 (10.4)*** ***63.2 (10.9)***	188 (70.2) ***191 (64.9)*** ***208 (66.4)***	Adults with uncontrolled hypertension	12 months	None
2013	**Shively et al.**	RCT	Tailored activation sessions for self-management program ***Vs. TAU***	63.4 (9.10) ***68.9(11.73)***	43 (0) ***41 (2.4)***	Adults with CHF	6 sessions over 6 months	None

Year	Author	Design	Intervention and comparison	Mean Age (SD)	Sample Size (% female)	Patient Group	Duration	Follow-up
2012	**Grønning et al.**	RCT	Disease-specific educational and skills-based group plus tailored individual education session ***Vs. TAU***	58 (12) ***58 (11)***	71 (68) ***70 (70)***	Adults with chronic polyarthritis	3x 3hr group sessions fortnightly + 1 individual session	12 months
2012	**Rygg et al.**	RCT	Diabetes self-management program ***Vs. TAU***	66 (overall) 	73 (45 overall) ***73***	Adults with type II diabetes	15hrs over 3 sessions	12 months
2012	**Solomon et al.**	RCT	Access to personalised online portal with interactive health applications and educational modules ***Access to non-interactive health education website***	Range 25-64 	101 (50) ***100 (50)***	Adults with diabetes, asthma hypertension or 'other'	24hr access for 12 weeks	None
2011	**Maindal et al.**	RCT	Health-related action competence program ***Vs. TAU***	62.2 (6.9) ***61.2 (7.6)***	322 (47.2) ***187 (46)***	Adults with type II diabetes and dysglycaemia	2 x 1-1 counselling sessions + 8 group sessions = 18hrs over 3 months	None
2010	**Hochhalter et al.**	RCT	Skills-based patient-doctor communication workshop and health coaching ***Vs. Attentional control*** ***Vs. TAU***	76 (7) ***73 (6)*** ***73 (5)***	26 (65.4) ***27 (66.7)*** ***26 (65.4)***	Older adults with at least 2 chronic conditions (arthritis, lung disease, heart disease, diabetes, hypertension, depression, osteoporosis)	2hr workshop + 2x15min telephone coaching ***As above***	None
2010	**Lorig et al.**	RCT	Online diabetes self-management program ***Vs. TAU***	54.4 (10.6) ***54.2 (9.90)***	270 (71.1) ***491 (73.7)***	Adults with type II diabetes	6 weekly online sessions	18 months

Year	Author	Design	Intervention and comparison	Mean Age (SD)	Sample Size (% female)	Patient Group	Duration	Follow-up
2009	**Hibbard et al.**	Non-randomised	Tailored telephone coaching ***Vs. Telephone coaching as usual***	N/R ***N/R***	245 (N/R) ***112 (N/R)***	Adults with a primary diagnosis of asthma, COPD, CAD, CHF or diabetes	6 months	None
2009	**Lorig et al.**	RCT	Diabetes Self-Management Program ***Vs. TAU***	67.7 (11.9) ***65.4 (11.4)***	186 (62.4) ***159 (66.2)***	Adults with type II diabetes	6 weekly 2.5hr sessions	12 months
2009	**Wallace et al.**	Uncontrolled study	Diabetes education and brief behavioural change counselling sessions	56 (range 29-93)	250 (64.8)	Adults with type II diabetes	Initial 1-1 session + 2 telephone sessions over 1 month	None
2007	**Hibbard et al.**	RCT	Chronic Disease Self-Management Program ***Vs. TAU***	59.6 ***60***	244 (69) ***235 (69.6)***	Older adults with at least 1 chronic condition (diabetes, arthritis, hypertension, heart disease, COPD, hyperlipidaemia)	6 weekly 2.5 hr sessions	6 months

Abbreviations: CAD: coronary artery disease; CHF: chronic heart failure; COPD: chronic obstructive pulmonary disease; RCT: randomised controlled trial; TAU: treatment as usual

Table 4. Quality ratings of methodological ability to address review aims*.

	Design	Recruitment	Sample size	Allocation bias	Equal groups	Measure validity	Follow-up	Intervention suitability	Intervention delivery & assessment	Attrition (1)	Attrition (2)	Analysis	Missing data	Overall
Crosby et al. (2017)	Poorly addressed	Poorly addressed	Adequately addressed	Not reported / N/A	Not reported / N/A	Not reported / N/A	Well covered	Well covered	Not reported/ N/A	Adequately addressed	Not reported / N/A	Well covered	Not reported / N/A	**15 / 39 (-)**
Fløde et al. (2017)	Poorly addressed	Adequately addressed	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	Well covered	Poorly addressed	Well covered	Not reported / N/A	**22 / 39 (+)**
Titova et al. (2017)	Adequately addressed	Well covered	Well covered	Adequately addressed	Well covered	Well covered	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Adequately addressed	Adequately addressed	Not reported / N/A	**26 / 39 (+)**
Morrison et al. (2016)	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Adequately addressed	Not reported / N/A	Well covered	Well covered	**23 / 39 (+)**
Young et al. (2016)	Well covered	Adequately addressed	Well covered	Well covered	Adequately addressed	Well covered	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Well covered	**28 / 39 (+)**
Ehde et al. (2015)	Well covered	Well covered	Well covered	Well covered	Well covered	Well covered	Well covered	Well covered	Well covered	Well covered	Adequately addressed	Well covered	Well covered	**38 / 39 (++)**
Kaltman et al. (2015)	Poorly addressed	Adequately addressed	Poorly addressed	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Well covered	Well covered	Not reported / N/A	Adequately addressed	Well covered	**21 / 39 (+)**

* See Table 2 and Appendix C for details of quality criteria

	Design	Recruitment	Sample size	Allocation bias	Equal groups	Measure validity	Follow-up	Intervention suitability	Intervention delivery & assessment	Attrition (1)	Attrition (2)	Analysis	Missing data	Overall
Kawi et al. (2015)	Poorly addressed	Adequately addressed	Poorly addressed	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Adequately addressed	Well covered	Not reported / N/A	Well covered	Well covered	**21 / 39 (+)**
Shah et al. (2015)	Poorly addressed	Adequately addressed	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Well covered	Well covered	Not reported / N/A	Poorly addressed	Well covered	**22 / 39 (+)**
Turner et al. (2015)	Poorly addressed	Poorly addressed	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Well covered	Poorly addressed	Not reported / N/A	Well covered	Well covered	**21 / 39 (+)**
Turner et al. (2014)	Poorly addressed	Adequately addressed	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Well covered	Adequately addressed	Adequately addressed	Well covered	Well covered	**25 / 39 (+)**
Kosmala-Anderson et al. (2014)	Poorly addressed	Well covered	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Adequately addressed	Well covered	Not reported / N/A	Well covered	Well covered	**24 / 39 (+)**
Ledford et al. (2013)	Poorly addressed	Adequately addressed	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Adequately addressed	Adequately addressed	Adequately addressed	Not reported / N/A	Adequately addressed	Not reported / N/A	**17 / 39 (-)**
Ryvicker et al. (2013)	Well covered	Adequately addressed	Well covered	Well covered	Adequately addressed	Well covered	Not reported / N/A	Well covered	Adequately addressed	Well covered	Not reported/ N/A	Poorly addressed	Well covered	**28 / 39 (+)**
Shively et al. (2013)	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	Well covered	Well covered	Not reported / N/A	Well covered	Well covered	Well covered	Not reported / N/A	Well covered	Well covered	**30 / 39 (++)**

	Design	Recruitment	Sample size	Allocation bias	Equal groups	Measure validity	Follow-up	Intervention suitability	Intervention delivery & assessment	Attrition (1)	Attrition (2)	Analysis	Missing data	Overall
Grønning et al. (2012)	Well covered	Adequately addressed	Well covered	Adequately addressed	Well covered	Well covered	Well covered	Well covered	Not reported/ N/A	Well covered	Well covered	Well covered	Well covered	**34 / 39 (++)**
Rygg et al. (2012)	Well covered	Adequately addressed	Well covered	Adequately addressed	Well covered	Well covered	Well covered	Adequately addressed	Adequately addressed	Well covered	Well covered	Well covered	Well covered	**35 / 39 (++)**
Solomon et al. (2012)	Well covered	Adequately addressed	Well covered	Well covered	Well covered	Well covered	Not reported / N/A	Adequately addressed	Not reported/ N/A	Adequately addressed	Not reported / N/A	Adequately addressed	Poorly addressed	**24 / 39 (+)**
Maindal et al. (2011)	Well covered	Adequately addressed	Well covered	Adequately addressed	Well covered	Well covered	Not reported / N/A	Well covered	Adequately addressed	Adequately addressed	Not reported / N/A	Adequately addressed	Well covered	**28 / 39 (+)**
Hochhalter et al. (2010)	Well covered	Adequately addressed	Adequately addressed	Well covered	Well covered	Well covered	Not reported / N/A	Adequately addressed	Adequately addressed	Adequately addressed	Not reported / N/A	Well covered	Adequately addressed	**27 / 39 (+)**
Lorig et al. (2010)	Well covered	Adequately addressed	Well covered	Well covered	Well covered	Well covered	Well covered	Well covered	Adequately addressed	Well covered	Well covered	Adequately addressed	Well covered	**36 / 39 (++)**
Hibbard et al. (2009)	Adequately addressed	Adequately addressed	Well covered	Poorly addressed	Adequately addressed	Adequately addressed	Not reported / N/A	Adequately addressed	Poorly addressed	Poorly addressed	Not reported / N/A	Well covered	Adequately addressed	**21 / 39 (+)**
Lorig et al. (2009)	Well covered	Adequately addressed	Well covered	Adequately addressed	Well covered	Well covered	Well covered	Well covered	Well covered	Well covered	Adequately addressed	Well covered	Well covered	**36 / 39 (++)**

	Design	Recruitment	Sample size	Allocation bias	Equal groups	Measure validity	Follow-up	Intervention suitability	Intervention delivery & assessment	Attrition (1)	Attrition (2)	Analysis	Missing data	Overall
Wallace et al. (2009)	Poorly addressed	Adequately addressed	Well covered	Not reported / N/A	Not reported / N/A	Well covered	Not reported / N/A	Well covered	Adequately addressed	Well covered	Not reported / N/A	Adequately addressed	Not reported / N/A	**19 /39 (-)**
Hibbard et al. (2007)	Well covered	Adequately addressed	Well covered	Adequately addressed	Adequately addressed	Well covered	Well covered	Well covered	Adequately addressed	Well covered	Well covered	Adequately addressed	Not reported / N/A	**31 / 39 (++)**

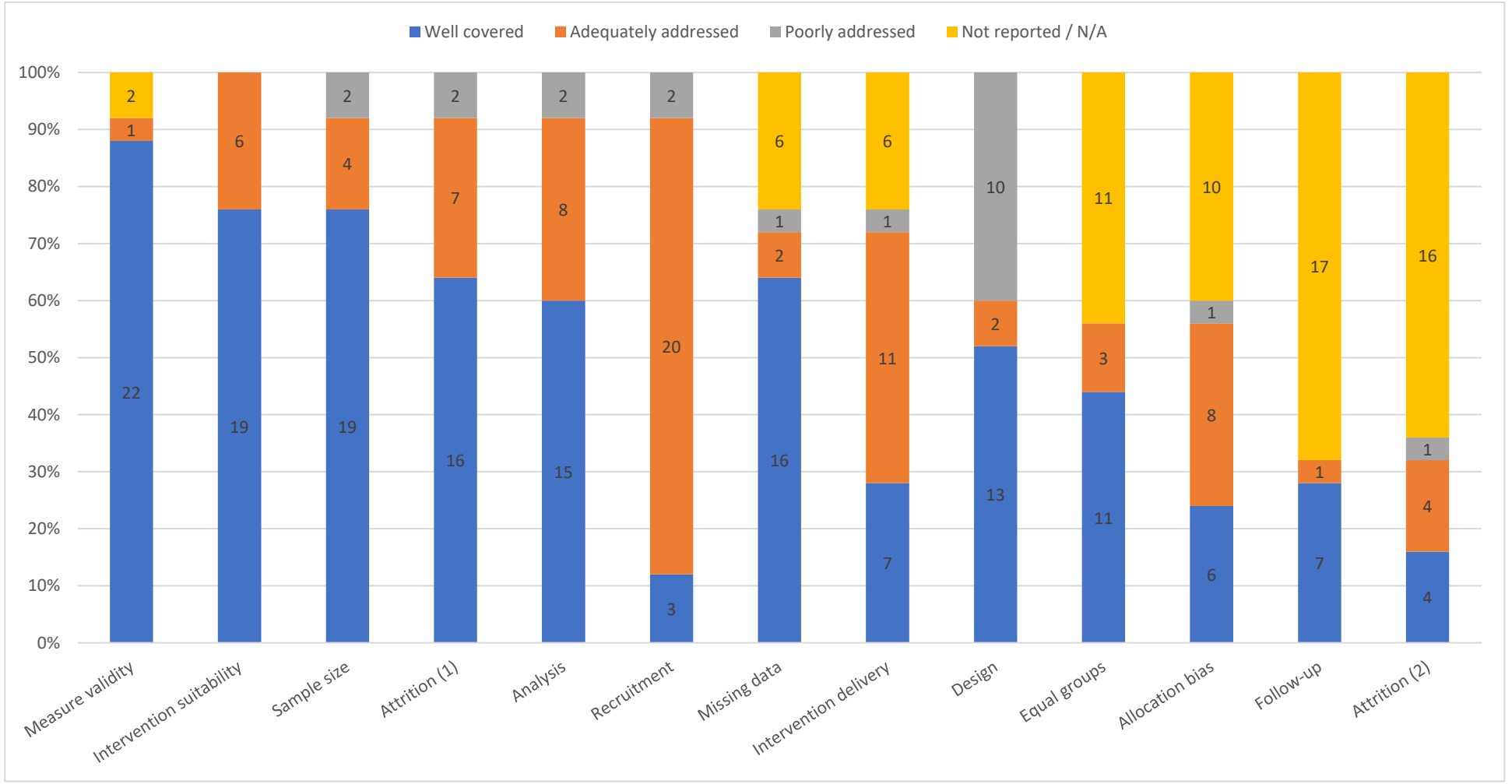

Figure 2. Summary of quality criteria ratings in order of relative methodological strengths across the literature.

Interventions

Intervention components were identified based on the information available in each study and used to inform quality ratings. Nineteen studies appeared to provide a sufficiently detailed SMI to increase patient activation in terms of content, duration, intensity and professional input. Six studies were allocated a rating of 'adequate' for intervention suitability as they may have lacked the multiple components considered necessary for increasing activation. For example, disease-specific education or skills training/rehearsal of practical self-management tasks (see Appendix B) (Fløde et al., 2017; Hibbard et al., 2009; Hochhalter et al., 2013; Ledford et al., 2013; Rygg et al., 2012; Solomon et al., 2012). Two of these studies received a lower rating as replication would not have been feasible due to wider reporting issues within the papers. Three of the included studies provided minimum or no condition-related education (Hibbard et al., 2009; Hochhalter et al., 2010; Kawi et al., 2015).

Significant variation was observed in the training of intervention facilitators. This ranged from psychologists (e.g. Turner et al., 2015) to nurses, physiotherapists and dieticians (e.g. Maindal et al., 2011) to trained community health-workers (e.g. Shah et al., 2015). Intervention delivery and fidelity was adequately or well addressed in 18 of the 25 studies. Six studies reported no information regarding facilitators and procedure to assess adherence to the treatment protocol making replication difficult or impossible (Crosby et al., 2017; Grønning et al., 2012; Morrison et al., 2016; Solomon et al., 2012; Titova et al., 2017; Young et al., 2016). In the cases of Solomon et al. (2012) and Morrison et al. (2016), this quality criterion was not applicable as the interventions were purely web-based with no facilitator input.

Outcome measures and follow-up

Most studies provided either psychometric data for the PAM-13 in the included sample, where the alpha level was sufficient to be considered good, or psychometric properties within the study population had been provided elsewhere. In one study (Turner et al., 2014), psychometric data for the measure was not available for a specific condition (Chronic Obstructive Pulmonary Disease) but was rated 'well covered' as good psychometric data were available in similar populations, where there was good reason to believe they would apply to the population present in the study (e.g. lung disease). Only eight studies examined intervention effects ≥3 months beyond post-treatment, of which, six were RCTs (Ehde et al.,

2015; Grønning et al., 2012; Hibbard et al., 2007; Lorig et al., 2009; Lorig et al., 2010; Rygg et al., 2012).

Table 5. Summary of treatment effects for patient activation

Author & Year	Patient Activation-specific pre-post change	Effect size pre-to post-intervention (within subjects')	Effect size post-intervention (between subjects')	Pre-follow-up change
Controlled studies				
Morrison et al. (2016)	Significant increase in patient activation from baseline (Mean (SD) 65.7 (10.0)) to post-intervention (Mean (SD) 73.0 (13.9), $p<.001$) within intervention group. Significantly higher patient activation in intervention group compared with the control group at post-intervention (Estimated mean difference (95% CI) 7.72 (0.53 to 14.90), $p=.036$).	Hedges g =.60*	Hedges g =.47*	N/A
Young et al. (2016)	Significant increase in patient activation from baseline (Mean (SD) 57.3 (19.2)) to post-intervention (Mean (SD) 69.1 (16.7) $p<.001$) within intervention group. No significant differences between intervention and control group at post-intervention at .05 significance level ($p=.069$).	Hedges g =.65*	N/A	N/A
Ehde et al. (2015)	Significant increase in patient activation from baseline to post-intervention within intervention group (mean change score (95% CI) 9.1 (-10.3, -5.29) $p<.05$) and control group (mean change score (95% CI) 4.1 (-6.35, -1.98) $p<.05$). Significantly higher patient activation in intervention group compared with control group at post-intervention (mean change score (95% CI) 6.9 (-.92, -.23), $p<.05$).	Hedges g =.81*	Hedges g =.58*	Patient activation score maintained within intervention group but between-group differences no longer statistically significant at 12-month follow-up.
Ryvicker et al. (2013)	No significant change in patient activation relative to usual care.	N/A	N/A	N/A
Shively et al. (2013)	Significant increase in patient activation from baseline (Mean (SD) 61.3 (16.61)) to post-intervention (Mean (SD) 71.5 (17.43), $p<.001$) within intervention group. Significant increase in patient activation between groups (significant group x time interaction, $F=3.73$, $p=.03$). Significant group x activation level x time interaction ($F=3.89$, $p=.005$). Intervention group improved more over time compared with usual care with effects most clearly and strongly present for those moderately activated at baseline.	Hedges g =.59*	η_p^2 =.06	N/A

Author & Year	Patient Activation-specific pre-post change	Effect size pre-to post-intervention (within subjects')	Effect size post-intervention (between subjects')	Pre-follow-up change
Grønning et al. 2012	Significant increase in patient activation from baseline to post-intervention within intervention group (mean change score (95% CI) 3.07, (-6.2, 0.0), *p*=.05). Significantly higher patient activation in intervention group compared with control group at post-intervention (mean change score (95% CI) 5.98, (1.8, 10.2), *p*=.01).	Hedges g =.21*	Hedges g =.37*	Activation change maintained within intervention group after 12 months. Between group analyses for differences in patient activation approached significance at 12-month follow-up (mean change score (95% CI) 3.9 (-0.3, 8.0), *p*=.069)
Rygg et al. 2012	No statistically significant differences between intervention and control group found. Sub analyses found patients with poorest diabetes control in intervention group had significantly higher patient activation post-intervention compared with counterparts in control group (mean change score (95% CI) 10.2 (1.3, 19.2), *p*=.026).	N/A Sub analyses: Hedges g =.64*	N/A Sub analyses: Hedges g =.50*	No statistically significant differences between intervention and control group found.
Solomon et al. 2012	Significant increase in patient activation from pre- to post-intervention within intervention group (mean 5.967, SD 9.70, *t* (57) =4.683, *p*<.001). Significantly higher patient activation in intervention group compared with control group at post-intervention (*F* (1,123) =4.438, *p*=.04, *r*=.196). Sub analyses found significant difference in mean change over time for low, moderate and highest activated patients in intervention group (*F* (2, 55) =6.472, *p*=.003, *r*=.436). Post hoc analysis found significantly lower mean change in highest activated group, compared with moderately (mean difference (95% CI) –8.354 (–15.06, –1.64), *p*=.01, *d*=.45) and lowest activated group (mean difference (95% CI) –8.457 (–15.47, –1.45), *p*=.01, *d*=.45).	Hedges g =.42*	Hedges g =.18*	N/A
Maindal et al. 2011	Increase in patient activation in intervention group but results not statistically significant.	N/A	N/A	N/A
Hochhalter et al. (2010)	Significant increase in patient activation from baseline (Mean (SD) 57.1 (13.2)) to post-intervention (Mean (SD) 66.8 (18.5) *p*<.001) within intervention group.	Hedges g =.60*	N/A	N/A

Author & Year	Patient Activation-specific pre-post change	Effect size pre-to post-intervention (within subjects')	Effect size post-intervention (between subjects')	Pre-follow-up change
	No statistically significantly change in patient activation between groups over time.			
Lorig et al. (2010)	Significant increase in patient activation from baseline (Mean (SD) 64.9 (14.4)) to post-intervention (Mean (SD) 70.6 (14.4) $p<.001$) within intervention group. Significantly higher patient activation in intervention group Mean (SD) 70.6 (14.4)) compared with control group at post-intervention (Mean (SD) 68.13 (14.4), $p=.02$).	Hedges g =.40*	Hedges g =.17*	Intervention group showed significantly greater improvements in patient activation compared with usual care control ($p=.016$) at 18-month follow-up but result not significant following ITT analysis ($p=.052$).
Lorig et al. (2009)	Significant increase in patient activation from baseline (Mean (SD) 62.9 (17.8)) to post-intervention (Mean (SD) 67.4 (15.8), $p<.001$) within intervention group. Significantly higher patient activation in intervention group compared with control group at post-intervention (mean (SD) 4.52 (15.8) vs 1.75 (15.3), $p=.017$)	Hedges g =.27*	Hedges g =.17*	Intervention participants demonstrated continued improved patient activation at 12 months (mean change (SD) 4.30 (14.4), $p=.007$) compared with baseline but no comparison with control group.
Hibbard et al. (2007)	Significant increase in patient activation for both groups over time ($F=45.1$, $p<.001$). Significant increase in patient activation scores over time for Intervention group compared with control group ($F=13.44$, $p<.001$).	Not extractable	$\eta_p^2=.03$	Patient activation maintained in intervention group at 6-month follow-up but between-group differences no longer significant due to improvement in patient activation in control group at 6-month follow-up ($F=2.344$, $p=.127$).
Titova et al. (2017)	No statistically significant changes in patient activation within or between groups.	N/A	N/A	N/A
Hibbard et al. (2009)	From pre-to post-intervention, intervention group had 4.6-point gain in activation; control group had 2.6-point gain. Intervention group change in patient	Not extractable	Not extractable	N/A

Author & Year	Patient Activation-specific pre-post change	Effect size pre-to post-intervention (within subjects')	Effect size post-intervention (between subjects')	Pre-follow-up change
	activation was statistically significant (p<.001). No significant change in control group. Significantly higher patient activation in intervention group compared with control group at post-intervention (F=12.5, p<.01).			
Uncontrolled Studies				
Crosby et al. (2017)	Significant improvement in patient activation pre- (Mean (SD) 69.75 (13.17)) to post-intervention (Mean (SD) 75.36 (16.03), p=.03)	Hedges g =.38*	N/A	Results not sustained at 6-month follow-up (F=.911, p=.440,
Fløde et al. (2017)	Significant improvement in patient activation pre- (Mean (SD) 63.7 (15.3)) to post-intervention (Mean (SD) 70.1 (14.0) p<.001)	Hedges g =.43*	N/A	Results sustained at 3 months follow-up.
Kaltman et al. (2015)	Significant improvement in patient activation pre- to post-intervention (t=5.59, p=.001, d=1.32).	Hedges g =1.68*	N/A	N/A
Kawi et al. (2015)	Significant improvement in patient activation pre- to post-intervention (t (15) =4.45, p<.001).	Hedges g =.81*	N/A	N/A
Shah et al. (2015)	Patient activation found to be significantly higher post-intervention; 35 participants increased patient activation scores by one or more levels, 24 participants remained unchanged and 1 participant demonstrated lower patient activation. Findings were statistically significant (p<.001).	Not extractable	N/A	N/A
Turner et al. (2015)	Significant improvement in patient activation pre- (Mean (SD) 52.2 (12.4) to post-intervention (Mean (SD) 60.2 (15.8), p <.001, d=.65).	Hedges g =.57*	N/A	N/A
Turner et al. (2014)	Significant improvement in patient activation pre- to post-intervention (t=4.02 (104); p<.001; d=.36).	Hedges g =.36*	N/A	N/A
Kosmala-Anderson et al. (2014)	Significant improvement in patient activation pre- to post-intervention (t=7.06 (117), p<.001, d=.81).	Hedges g =.63*	N/A	N/A
Ledford et al. (2013)	Significant improvement in patient activation pre- (Mean (SD) 51.80 (11.78)) to post-intervention (Mean (SD) 77.39 (11.28)), p<.05.	Hedges g =2.21*	N/A	N/A

Author & Year	Patient Activation-specific pre-post change	Effect size pre-to post-intervention (within subjects')	Effect size post-intervention (between subjects')	Pre-follow-up change
Wallace et al. (2009)	Significant improvement in patient activation pre-post-intervention (*t*=6.32, *p*<.001, *d*=.42).	Hedges g =.40*	N/A	N/A

*Difference in post-intervention scores between intervention and control group; Effect size calculated with Lakens (2013) Version 3.2

Hedges g - a measure of effect size for use with t-test. Effect size estimates as follows: .2 (small); .5 (medium); .8 (large)

Partial η^2 - a measure of effect size for use in analysis of variance. Effect size estimates as follows: .01(small); .06 (medium); .14 (large)

3.3 Effects of self-management Interventions on patient activation

Within-group effects

The main findings and effect sizes related to the PAM-13 are found in Table 5. Out of 25, 21 studies reported a statistically significant increase in patient activation scores pre- to post-intervention in those receiving a self-management intervention, of which, six – all RCTs- were given the highest rating (++) for methodological quality (Ehde et al., 2015; Grønning et al., 2012; Lorig et al., 2009; Lorig et al., 2010; Shively et al., 2013; Young et al., 2016). Of the 21 studies which found a significant increase in activation, eight found a small-medium within-group effect size (Crosby et al., 2017; Fløde et al., 2017; Grønning et al., 2012; Lorig et al., 2009; Lorig et al., 2010; Solomon et al., 2012; Turner et al., 2014; Wallace et al., 2009). A further eight found medium-large effect sizes (Ehde et al., 2015; Hochhalter et al., 2010; Kawi et al., 2015; Kosmala-Anderson et al., 2014; Morrison et al., 2016; Shively et al., 2013; Turner et al., 2015; Young et al., 2016). Two found very large effect sizes (Kaltman et al., 2015; Ledford et al., 2013). Four studies reported no improvement within or between groups for patient activation (Maindal et al., 2010; Rygg et al., 2012; Ryvicker et al., 2013; Titova et al., 2017), of which, one study (Rygg et al., 2012) was allocated a rating of '++.'

Solomon et al. (2012) conducted exploratory analyses within the intervention group and found that increases in patient activation among 'highly activated' patients was significantly lower compared with 'moderately' and 'low' activated patients over time. In another study, although no significant increase in patient activation was found pre- to post-intervention within or between groups, sub-group analyses revealed participants with poorest diabetes control had significantly higher patient activation at post-intervention (Rygg et al., 2012).

SMI vs usual care

Twelve studies evaluated a SMI against a usual care control group, comprising of 11 RCTs and 1 non-randomised controlled study. Six RCTs found the SMI group to have significantly higher patient activation at post-treatment compared with usual care (Grønning et al., 2012; Hibbard et al., 2007; Lorig et al., 2009; Lorig et al., 2010; Morrison et al., 2016; Shively et al., 2013). Each of these six studies demonstrated small-to-medium between group-effect sizes (ranging from 0.17 to 0.47) and all, except one, were allocated the strongest rating (++) of methodological rigour. By comparison, six studies did not find significantly higher post-treatment differences between intervention and usual care groups and all, except one, were

given the second highest rating (+) of methodological quality (Hochhalter et al., 2010; Maindal et al., 2010; Ryvicker et al., 2013; Titova et al., 2017; Young et al., 2016). While Rygg et al. (2012) was allocated a higher methodological quality score of '++.'

SMI vs active control

Five studies evaluated the effects of a SMI against an active control. Four were RCTs and one was a non-randomised controlled study. Two RCTs found statistically significant differences between groups at post-intervention with results favouring the self-management condition (Ehde et al., 2015; Solomon et al., 2012). Methodological quality and effect sizes between the studies differed; Ehde et al. (2015) demonstrated a medium between-group effect (0.58) and was allocated an overall methodological bias rating of '++', while Solomon et al. (2012) found a much smaller between-group effect in their study (0.18) and received an overall methodological bias rating of '+.' One non-randomised controlled study, evaluated to be on the lower range of '+' for methodological rigour, also found a significant between-group difference, however, effect sizes were unable to be calculated (Hibbard et al., 2009). Two RCTs with a methodological quality rating of '+,' found no significant post-intervention changes in activation between the SMI and active control groups (Hochhalter et al., 2010; Ryvicker et al., 2013).

Effects at follow-up

Eight studies conducted follow-up analyses. Six studies, five of which received the highest methodological quality rating (++), reported that gains in patient activation within the intervention group were maintained at follow-up, as expected (Ehde et al., 2015; Grønning et al., 2012; Hibbard et al., 2007; Lorig et al., 2009; Lorig et al., 2010; Fløde et al., 2017). However, four of these studies also found that patient activation in the control groups improved at follow-up to the extent that they found no significant differences between the intervention group and comparison group at follow-up. One study reported that improvements in patient activation in the intervention group were not maintained at all at 6 months follow-up, although this study was of relatively poor methodological quality and received a rating of '-' (Crosby et al., 2017).

4. Discussion

This review aimed to evaluate the effectiveness of SMIs for improving patient activation in adults with long-term health conditions compared with other forms of active intervention or treatment as usual. A secondary aim was to evaluate if any positive effects on patient activation following intervention were maintained at follow-up.

4.1 Summary of results

The studies included in this review overall found a positive effect of SMIs on patient activation. In over half of the studies comparing a SMI with treatment as usual or an active control, the positive change in the SMI group was significantly greater than the change that occurred within the control group. The methodological ratings of the studies reporting significant between-group effects favouring SMIs were deemed overall better quality in contrast with studies that did not find significant between-group effects.

Relatively few studies had a follow-up period (n = 8). Out of those that did, the majority (n = 6) found that patient activation was maintained within the intervention group at follow-up. However, four of these studies also found improvements in the control groups over time, meaning that between-group differences (SMI vs. control) were no longer significantly different at follow up. Therefore, the impact of SMIs compared with control groups is somewhat uncertain. Nonetheless, patient activation gains in the self-management conditions were largely maintained at follow-up.

4.2 Quality of the evidence

The overall quality of the studies, with respect to their ability to address the review question, was adequate, with sampling, allocation method, intervention variability and inclusion of follow-up measures being areas of relative weakness. The representativeness of the populations in some of the included studies may be somewhat biased due to convenience sampling. In addition, the degree of variation between interventions makes it somewhat difficult to assess the internal validity of the results.

An important consideration are mechanisms of change associated with self-management. Whilst improved self-management ability is the aim of SMIs, one of the core processes to

facilitate this change are the beliefs and attitudinal changes towards acquiring specific skills in relation to the LTC (McAllister, Dunn, Payne, Davies & Todd, 2012). The process of measuring patient activation may also encourage reflection on these beliefs and attitudes, especially for those who may never have previously considered managing their health condition as an evolving 'skill.' Hence, the process of measurement by itself may have active therapeutic elements; this may explain increases in patient activation in some studies.

Most studies reported an increase in patient activation favouring the self-management intervention group. In studies that reported positive results, there were large variations among pre-post effect sizes. Varied effect sizes may suggest that, although interventions were well covered, some components (e.g. communication training/rehearsal with healthcare professionals) may be more effective for increasing activation. However, there is a notable lack of research in the literature comparing the effectiveness of different active components of SMIs. The view that some components of self-management may be more effective than others would appear to be supported by the finding that, across RCTs, effect sizes ranged from small (.21) (Grønning et al., 2012) to large (.81) (Ehde et al., 2015). Each of these studies were considered methodologically robust and all were rated 'well' in terms of intervention suitability for increasing patient activation. The variation may also suggest that intervention delivery, fidelity or heterogeneity of long-term health conditions are important factors affecting improvements in patient activation.

Relatedly, effect sizes could be considered in the context of heterogeneity among the intensity and format of interventions. On closer examination of the results, there would appear to be an overall trend towards larger effect sizes in the individualised treatments compared with group treatments. Individualised treatments are more likely to provide a greater intensity of professional input and be tailored towards individuals' self-management needs (Barlow et al., 2002), which may explain the larger impact on patient activation outcomes. It seems reasonable to expect that the greatest impact on patient activation would be evident in interventions providing a high degree of tailoring and professional input. Web-based interventions displayed a more consistent picture, with moderate effect sizes in the intervention group. While this is encouraging at a time where maximising staff time and resources is necessary, more studies evaluating web-based interventions in relation to patient activation are needed to determine the clinical significance of positive findings and maintenance of effects.

Given that the PAM-13 attempts to quantify change across four different levels of activation, scores should be interpreted with care. It is possible that some people, who showed no change in their activation scores, could have moved towards some meaningful shifts in specific self-management tasks but changes were subtle or in the process of contemplation. Another consideration of change scores on the PAM-13 is research suggesting that the relationship between behaviour and attitudes/beliefs is bidirectional rather than causal (De Leeuw, Engels, Vermulst & Scholte, 2008). For example, some individuals may have little confidence or belief in their ability to self-manage a health condition and, subsequently, demonstrate low activation scores. However, their confidence and beliefs are likely to be positively reinforced over time via repeated practice of self-management tasks and vice versa.

A high degree of sample bias may explain why no effect was found in some studies. For example, one study recruited hospitalised COPD patients with acute exacerbations (Titova et al., 2017). It was hypothesised by the authors that it may be unrealistic to expect clinically significant improvements in outcomes such as patient activation in older patients with high disease severity and diminished quality of life, irrespective of the intervention. Similarly, where the sample already has a relatively high proportion of participants with good levels of patient activation at baseline, there are likely to be 'ceiling effects' with less scope for improvement of this outcome, as was the case in the study by Rygg et al. (2012).

Several studies included in this review used participants from a range of illness groups, reflecting the transdiagnostic concept of patient activation. Encouragingly, most studies did not exclude potential participants with physical health comorbidities. This could be considered a strength as many patients with chronic conditions do experience comorbidity in real-life setting (Jones, 2010), improving the ecological validity of the results. Within the context of different health conditions, defining what patient activation 'looks like' is an important consideration (Ryvicker et al., 2013). For instance, individuals with asymptomatic conditions (e.g. hypertension) might view self-management as less essential and, therefore, may be less responsive to SMIs (Ryvicker et al., 2013). Heterogeneity among health conditions means that some self-management behaviours may be more important than others may across conditions. Considering this, further research should examine specific relationships between patient activation and self-management behaviours in specific health conditions.

A further issue is the extent to which the PAM-13 might overlap with measures of self-management. Although the scale does not measure a specific behaviour, several items of the

PAM-13 ask about existing engagement in self-management behaviours. Thus, the PAM-13 may correlate strongly with some measures of self-management. Consequently, patient activation may not be an entirely independent construct that can then be used to predict self-management. Whilst there may be some potential questions around conceptual overlap with patient activation and self-management, this issue does not appear to be portrayed in the extant literature and, perhaps, needs further attention. Nonetheless, it is important to balance current findings with the evidence linking patient activation with multiple positive health, social and economic outcomes (for review see Mukoro, 2012). In addition, one longitudinal study found that patient activation scores at baseline were associated with the uptake of cancer screening, obesity and smoking behaviour up to two years later; though more research is needed to determine a causal relationship between patient activation and self-management behaviours (Greene, Hibbard, Sacks, Overton & Parrotta, 2015).

Efforts to develop measurement tools to quantify patient engagement with self-management are to be applauded. From a theoretical perspective, further research in this area may enable us to delineate the fundamental mechanisms that facilitate self-managing behaviour and the working components of interventions that target these mechanisms (Jonkman et al., 2016). This could have useful implications for the design of contemporary self-management interventions.

4.3 Strengths and limitations of the review

To the authors' knowledge, this review is the first of its kind to assess patient activation, as measured by the PAM-13, as a clinical outcome. Traditionally, research trials and systematic reviews in disease-management have focused on changes to disease self-efficacy, biological markers, symptom burden, quality of life or adherence as key indicators of the effectiveness of SMIs. However, these indicators may be too heterogeneous across conditions. Global indicators of improvement, such as patient activation, are starting to be used for intervention evaluation in chronic health conditions (e.g. Moore et al., 2016). This is in line with policy and guidance from The Kings Fund and the Department of Health to support people to self-care and to deliver better services for people with LTCs (Coulter, Roberts & Dixon, 2013; DOH, 2006). In order to demonstrate the applicability and utility of patient activation as a transdiagnostic construct, the authors chose a narrative approach to data-synthesis and a meta-analysis was not performed in the current review due to the decision to include a diverse set of populations and interventions. The main limitation of this review is the degree

of heterogeneity among the studies reviewed in terms of both interventions and conditions. Consequently, the degree of confidence in results and findings should be interpreted in light of this variation. Nonetheless, it is unlikely that future studies further examining the conclusions of the present review would be free from heterogeneity.

4.4 Implications for research and practice

Given the constraints on services as to what they can offer patients with LTCs, professionals may need to consider if in-service or locally developed SMIs are evidence-based, as well as how they might meaningfully evaluate effectiveness. Developing SMIs that aim to enhance patients' confidence, beliefs and attitudes towards acquiring self-management skills (i.e. patient activation) may result in effective self-management behaviours which maintain or, where possible, improve quality of life (Hibbard et al., 2004). The PAM-13 has good clinical utility as an outcome measure to evaluate the impact of SMIs, as activation outcomes have been linked to improved self-management and quality of life in a wide range of LTCs (Moore et al., 2016).

One of the limitations of the PAM-13 is the licensing cost for use in larger studies, a disadvantage if conducting large-scale RCTS. A free research license can be obtained for studies aiming to recruit no more than 250 participants. NHS England currently have an agreement to use the PAM-13 in an ongoing multi-site evaluation of services as part of their commitment to the 'Five Year Forward View' policy (NHS England, 2017). Combining PAM-13 with the collection of other information on self-management behaviours may enable researchers to capture the spectrum of change in areas impacted by SMIs. Given that improving this construct may be a precursor for self-management behaviour, a similar review evaluating the evidence of patient activation as a mechanism of change in SMIs may be useful. Such a review would strengthen the theory and evidence upon which new SMIs are devised for different conditions, as well as their successful implementation. Moreover, the current review has highlighted that a valuable contribution to the literature would be a review that attempts to quantify what changes in activation change may look like across conditions, both broadly and specifically. Finally, future research could seek to explore and target some of the factors that might predict patient activation in specific conditions to identify clinical populations at risk of poor self-management and, subsequently, poor health outcomes. Targeting modifiable factors that might affect patient activation could result in more efficacious self-management interventions.

4.5 Authors' conclusions

At present, there is currently evidence of a moderate-to-high quality that suggests that self-management interventions are effective for improving patient activation in long-term conditions compared with usual care or other active control groups. There is also preliminary evidence that positive effects on patient activation are maintained at follow-up of 3-months and beyond. Further randomised controlled studies evaluating self-management and control groups at follow-up are needed to strengthen the current evidence.

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II. Empirical Study

Patient Activation and Self-Management in Multiple Sclerosis: the role of Depression, Valued Living and Perceived Clinician Empathy.

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Abstract

Objectives: In long-term conditions, patient activation has an important influence on self-management and quality of life. Relatively little is known about the processes associated with patient activation in MS. The present study sought to explore relationships between patient activation, psychological factors (depression and valued living), perceived clinician empathy, perceived MS symptom severity, self-management and demographic variables. It also examined whether depression, valued living and perceived clinician empathy are unique predictors of activation, and if activation is a unique predictor of self-management for MS, when relevant confounding variables are controlled for.

Design: A cross-sectional design was used, recruiting 118 MS patients via a NHS outpatient setting.

Methods: Participants completed the short-form Patient Activation Measure, MS Impact Scale, Hospital Anxiety and Depression Scale, Engaged Living Scale, Consultation and Relational Empathy Measure, MS Self-Management Scale, together with demographic information. Correlations and hierarchical regression analyses were used to explore relationships between variables.

Results: After controlling for demographic variables and MS symptom severity, only valued living was a significant predictor of patient activation. Neither depression nor perceived clinician empathy were significant predictors. After controlling for valued living, depression and perceived clinician empathy, patient activation predicted 5.5% of variance in self-management for MS. Both activation and perceived clinician empathy were significant predictors of self-management.

Conclusions: Valued living is associated with patient activation in MS, while patient activation and perceived clinician empathy are associated with MS self-management. Self-management interventions, which target valued living and the patient-clinician relationship, may be effective for addressing low levels of activation in some patients with MS.

1. Introduction

Multiple Sclerosis (MS) is a progressive and disabling disease involving demyelination of the central nervous system, typically diagnosed between the age of 20-40 years old (Brück & Stadelmann, 2003). An estimated 127, 000 people live with MS in the UK (Mackenzie, Morant, Bloomfield, MacDonald & O'Riordan, 2014). The World Health Organisation (WHO, 2008) estimates a global prevalence of 30 per 100, 000, however the range is highly variable across continents. Europe is the continent with the highest estimated prevalence (80 per 100,000), with the highest rates in the world reported in Scotland (ranging from 145 to 193 per 100, 000) (Pugliatti, Sotgiu & Rosati, 2002). The condition affects men and women at a ratio of 2:3 (Thomas, Thomas, Hiller, Galvin, & Baker, 2009). People with MS can face a range of problems with mobility, fatigue, pain, cognition and sleep. Alongside physical complaints, MS is often associated with high rates of depression, distress, social and relationship difficulties and poor quality of life (Dennison, Moss-Morris, Yardley, Kirby & Chalder, 2013). At present, there is no known cure; therefore, treatment involves lifelong management of the disease and symptoms through medication, therapeutic support (e.g. physiotherapy) and lifestyle alterations.

In the context of growing demands on health care services, self-management is a promising approach to coping with symptoms associated with MS (Fraser et al., 2013). Self-management interventions (SMIs) aim to support people to develop the knowledge, practical skills and psychological resilience required to effectively manage the impact of an illness, and maintain quality of life (Barlow, Wright, Sheasby, Turner & Hainsworth, 2002). As interest in SMIs grows, it has become important to understand the mechanisms that lead individuals to become more engaged in managing their health. One psychological construct that has received growing attention in self-management concerns individuals' confidence, attitudes and beliefs around acquiring skills and performing self-management tasks, known as "patient activation" (Hibbard, Stockard, Mahoney, & Tusler, 2004).

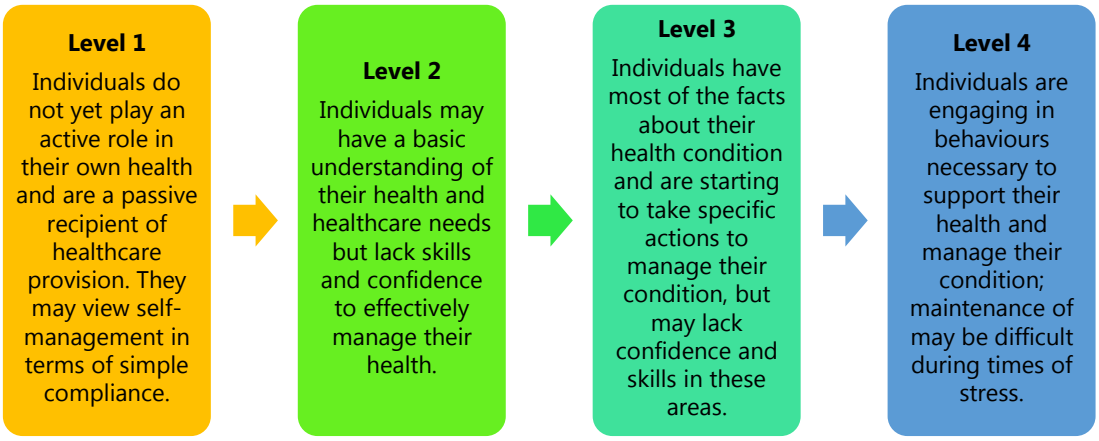
How is patient activation conceptualised and measured?

Patient activation is the extent to which an individual participates in his or her own care and illness management (Hibbard et al., 2004). The construct is suggested to reflect patients' knowledge of their condition, commitment to treatment routines, and openness with health professionals (Stepleman et al., 2010), and when these components interact, an individual is

more likely to be empowered, attuned and responsive towards their own self-care even in the face of challenges and limitations of their illness. The short-form Patient Activation Measure (PAM-13; Hibbard, Mahoney, Stockard, & Tusler, 2005), the most commonly used measure of activation, is a 13-item self-report scale assessing the extent to which individuals possess the skills, knowledge and confidence to self-manage. Responses to items such as "*I am confident that I can follow through on medical treatments I need to do at home*" are rated from 'strongly disagree' to 'strongly agree.' Scoring is converted to a scale of 0-100, where higher scores are indicative of higher levels of patient activation.

Activation is measured across four progressive levels (Hibbard et al., 2004). While formalised descriptors are available (see Figure 1: Hibbard et al., 2004), an example of low activation (level 1) might be the person who "just follows the doctor's advice," such as taking medication, though may be forgetful and inconsistent in adherence. At the opposite end of the continuum (level 4) are individuals who engage in various health-supporting behaviours to manage their own healthcare, recognise the impact of stress on their ability to self-manage and can effectively manage this impact via self-monitoring most of the time.

Figure 1. Descriptors of the 4-stage patient activation model (adapted from Hibbard et al., 2004)



The PAM-13 has been utilised to evaluate the outcome of interventions, across a range of settings and long-term conditions (LTCs) (Hibbard & Greene, 2013). There is evidence that scores on the PAM-13 are associated with positive health outcomes including reduced blood glucose, body mass index, cholesterol (Remmers et al., 2009; Rogvi, Tapager, Almdal, Schiøtz, & Willaing, 2012; Skolasky, Mackenzie, Wegener, & Riley, 2011) and health-promoting behaviours, for example, information seeking, self-management, and lifestyle changes (Hibbard et al., 2004; Hibbard et al., 2005; Hibbard, Mahoney, Stockard & Tusler, 2007). While NHS England policy has begun to support the use of PAM, robust evidence of its suitability and effectiveness in UK populations with LTCs has yet to develop and be circulated nationally (Roberts et al., 2016). Regarding the utility of the PAM-13 in a UK context, it is further highlighted that little is known about sociodemographic and clinical variables that may predict activation. One underpowered pilot study identified in the review by Roberts et al. (2016) explored patient activation and associated sociodemographic and clinical variables in a COPD population. It found no significant predictive relationships between gender, disease severity, COPD classification and patient activation, although, this conclusion may be explained by the small sample size (n = 40) and poor quality of the sample selection and recruitment, rather than the absence of any associations.

Evidence of patient activation as a predictor of self-management

There is evidence that the beliefs individuals hold in relation to their illness, appraisals of the challenges they face, and coping skills are all associated with levels of adjustment to their condition and wellbeing, and that these factors may act as a buffer against poor health outcomes (Dennison, Moss-Morris & Chalder, 2009). Lubetkin, Lu and Gold, (2010) found greater self-rated patient activation was related to better self-rated health among a general adult primary care population, while Goodworth et al. (2016) found a significant positive relationship between patient activation and outcomes of self-efficacy and quality of life in MS patients.

Moreover, interest in enhancing patient activation in chronic illness groups is growing as services strive to empower patients to take a more active stance in decisions and actions regarding their health. In a large trial involving 479 patients with a chronic illness randomly allocated to either a SMI or no intervention control group, positive change in patient activation was associated with greater uptake of health-promoting behaviours including regular exercise, stress management, and increased attention to dietary fat (Hibbard et al.,

2007). However, the authors found that the control group also improved on these outcomes and, as they did not control for potential confounding variables in their study (e.g. gender or disease severity), it is difficult to infer what factors may have influenced the differences between the groups. Several studies have demonstrated that symptom severity and gender are factors that may influence self-management (DiMatteo, Haskard, & Williams, 2007; Kerr et al., 2007; Manteuffel et al., 2014). A study by Rask et al. (2009) found that patient activation was positively correlated with disease-specific self-management activities including glucose testing, foot checks and eye examinations in diabetic patients. Whilst this is encouraging, most patients in this study were female, African-Americans and ceiling effects were observed as a large number of patients demonstrated high levels of activation at baseline; thus, the ability to generalise positive disease-specific outcomes from this study may be limited.

Most studies of the relationship between patient activation and self-management are cross-sectional, however, longitudinal studies examining whether patient activation predicts health behaviours have been reported (Greene, Hibbard, Sacks, Overton & Parrotta, 2015; Remmers et al., 2009). One study found that greater patient activation in diabetic patients was positively associated with future biomarkers of diabetes control (Remmers et al., 2009). A more recent study demonstrated that patient activation scores at baseline were associated with the uptake of cancer screening, obesity and smoking behaviour up to two years later (Greene et al., 2015). Although more longitudinal studies are needed, these findings indicate the possible value of patient activation in predicting health outcomes and the need to understand the factors that may put some patients at risk for lower levels of activation.

What variables might predict patient activation in MS?

Sociodemographic variables and depression

Research by Stærk (2015) supports the view that levels of activation observed in people with MS appear to be largely in line with levels of patient activation in other conditions (e.g. diabetes, cancer) as reported by Hibbard & Cunningham (2008). Goodworth et al. (2016) have suggested that the activation levels of MS patients could be affected by the unpredictability of MS relapse and progression, and that reliance on relationships with healthcare providers may differ somewhat from other LTCs. To date, only one study has explored potential predictors of patient activation in MS (Goodworth et al., 2016). This study found that patient activation was negatively associated with depression and positively

associated with quality of life and MS self-efficacy. It was also reported that education, perceived functioning, depression and MS self-efficacy were unique predictors and accounted for 35 percent of the variance associated with patient activation (Goodworth et al., 2016).

One surprising outcome of the study by Goodworth et al. (2016) was that, although a positive relationship was observed between activation and medication adherence in MS, the relationship did not reach significance as found in other studies (Bodenheimer, Wagner & Grumbach, 2002; Forbat, Cayless, Knighting, Cornwell, & Kearney, 2009). When exploring variables that may exert an influence over patient activation in MS; other variables need to be considered. One limitation of the study by Goodworth et al. (2016) is that the authors did not include a measure of self-management. Further studies should seek to examine if any relationship exists between patient activation and self-management in MS as, thus far, only a limited set of variables have been investigated in relation to patient activation in this condition.

Valued living

Acceptance and Commitment Therapy (ACT; see Hayes, Strosahl & Wilson, 1999 for full details) is an increasingly popular treatment for psychological problems in the context of LTCs. The aim of ACT is to coach individuals to work towards acceptance of personal struggles, orientate to their own values and take actions towards what is important to them – known as 'valued living' (Sheppard, Forsyth, Hickling & Bianchi, 2010). ACT entails the use of experiential exercises (e.g. defusion practice and identifying personal values), metaphors and behavioural principles (e.g. graded exposure) to facilitate emotion regulation and positive behavioural changes in accordance with personal values (Sheppard et al., 2010). Interest is growing regarding the role of valued living in LTCs. There is evidence that brief ACT interventions are successful for promoting symptom reduction and quality of life people with diabetes (Gregg, Callaghan, Hayes & Glenn-Lawson, 2007), epilepsy (Lundgren, Dahl & Hayes, 2008) and MS (Nordin & Rorsman, 2012). A study by Ferenbach, Gillanders and Harper (2011) found that ACT processes (i.e. cognitive fusion and acceptance) were stronger mediators of adjustment to MS than the content of cognitions (i.e. illness appraisals). Ferenbach et al. (2011) did not examine the role of valued living in adjustment to MS, but there is evidence that promoting valued living is important in the wider LTC literature. Lundgren et al. (2008) found evidence that valued living mediated seizure activity and quality of life outcomes in depressed epilepsy patients; while Ciarrochi, Fisher and Lane (2011) have shown that valued living was related to improved wellbeing and reduced distress in a sample of cancer patients. Such

studies provide preliminary evidence that valued living is meaningful for quality of life and management of adverse symptoms and, therefore, may be an important process in activation. As such, there would appear to be a reasonable basis on which to propose valued living may be associated with patient activation in an MS population.

The patient-clinician relationship

Effective patient-clinician communication is required for self-management processes, such as presenting to healthcare providers for routine care or adhering to treatment recommendations from professionals (Rieckmann et al., 2015). For example, Remington, Rodriguez, Logan, Williamson and Treadaway (2013) report that the quality of the therapeutic relationship is important in conditions like MS, and that there is greater adherence to treatment recommendations in those who perceive effective communication with their healthcare provider. Patient definitions of quality care suggest that empathy is a key factor underpinning perceptions of effective communication (Lewis, 1994). Empathy in clinical consultations involves the clinician's ability to convey an accurate understanding of the patient's perspective and feelings, and to respond helpfully to the needs of the patient (Mercer, Maxwell, Heaney & Watt, 2004). In some cases, clinicians may be the primary source of support for individuals with LTCs (Tang, Brown, Funnell & Anderson, 2008). It has been suggested by Mercer and Reynolds (2002) that clinician empathy improves patients' ability to understand their illness, enables patients to better-manage their health conditions and leads to better outcomes; however, there is a notable lack of research into the role of empathy in clinical outcomes. Further exploration of the role of empathy in the clinical encounter would be a meaningful component to consider in the context of patient activation in MS.

Summary

Collectively, research suggests that patient activation has an important influence on self-management for LTCs. However, relatively little is known about which processes are associated with activation in MS. Understanding the processes linked to effective self-management is especially important as MS clinicians rely on patients being self-directed and responsive to maintain and prolong good health status and quality of life. A study to explore relationships and investigate the predictive value of potentially modifiable variables related to activation in this population would be a useful expansion of the literature. Further clarifying these relationships could serve to identify which groups might be at risk for low activation,

what potential targets for treatment might be, and to better understand the value of and limitations of patient activation as a way of conceptualising and promoting self-management in MS.

1.1 Aims of the current study

The main aim was to (1) explore whether patient activation is related to psychological factors (depression and valued living), perceived clinician empathy, perceived MS symptom severity, MS self-management and demographic factors (age, gender and level of education), (2) examine whether psychological factors (depression and valued living) and perceived clinician empathy may predict patient activation when other relevant factors are controlled for and (3) examine whether patient activation may predict MS self-management when other confounding variables are controlled for.

Hypothesis 1: Patient activation will be negatively correlated with age, perceived symptom severity and depression; and positively associated with level of education, perceived clinician empathy, valued living and MS self-management.

Hypothesis 2: Psychological factors (depression, valued living) and perceived clinician empathy will be significant predictors of patient activation when other predictive demographic and clinical variables are controlled for.

Hypothesis 3: Patient activation will be a significant predictor of MS self-management when other predictive variables are controlled for.

2. Methods

2.1 Design

We employed a cross-sectional, questionnaire-based design to examine relationships between patient activation, perceived MS symptom severity, clinician empathy, depression, valued living, demographic information and self-management for MS.

The NHS South West Exeter Research Ethics Committee granted ethical approval and site-specific approval was obtained from the NHS Lothian Research and Development Department (See Appendices D and E).

2.2 Participants

Eligibility

Adults aged ≥18 years with a diagnosis of MS, according to ICD-10 criteria, given by a neurologist were eligible to participate. Those with cognitive impairment or insufficient understanding of the English language that would affect their ability to give informed consent and/or complete the study measures were excluded.

Recruitment

During the period of April to November 2017, a consecutive series of 153 participants attending the Anne Rowling Regenerative Neurology Clinic, Edinburgh, UK were invited to participate. One hundred and eighteen individuals returned the questionnaire packs (response rate = 77%) to the Anne Rowling Clinical Research Facility. Non-identifiable demographic information was collected to establish the characteristics of the sample.

2.3 Measures

Demographic Questionnaire: participants provided non-identifiable demographic data (age category, gender, level of education, MS type, length of diagnosis and use of Disease Modifying Therapies).

The Patient Activation Measure (PAM-13; Hibbard et al., 2005): contains 13 items assessing patient activation, that is, the skills, knowledge and confidence to manage an illness. Responses to items such as "*I am the person who is responsible for taking care of my health*" are rated from "strongly disagree" to "strongly agree." Scoring is converted to a scale of 0-100, where higher scores indicate higher levels of patient activation. The scale exhibits strong construct, convergent, discriminant and predictive validity and high internal reliability across several illness groups (Hibbard et al., 2005), including MS (α = .88) (Stepleman et al., 2010). Cronbach's alpha for the PAM-13 in the current study was .86.

The 'Physical' subscale of the Multiple Sclerosis Impact Scale (MSIS-29; Hobart, Lamping, Fitzpatrick, Riazi & Thompson, 2001): a 20-item self-report subscale measuring the severity of physical symptoms of MS. The MSIS-29 also comprises of one other 9-item subscale measuring 'psychological' symptoms of MS. For the current study, only the 'physical' subscale was used in analyses. Statements are rated on a 5-point Likert scale from 1 (not at all) to 5 (extremely) and pertain to the patient's experience of MS symptoms. Hobart et al. (2001) report the MSIS-29 physical subscale displays low floor and ceiling effects, good levels of variability and excellent test-retest reliability ($r \geq .87$) and internal consistency ($\alpha \geq .91$) in individuals with both relapsing-remitting and progressive types of MS. Cronbach's alpha for the MSIS-29 'physical' subscale in the current sample was .96.

The 'Valued Living' subscale of the Engaged Living Scale (ELS; Trompetter et al., 2013): a 10-item subscale assessing individuals' awareness and familiarity with their values, and the actions taken by the individual towards those values, as conceptualised by Acceptance and Commitment Therapy (ACT). The ELS contains one other 6-item subscale measuring 'life fulfilment.' Only the 'valued living' subscale was used in the analyses of the current study. Responses range from "completely disagree" to "completely agree" on a 5-point Likert scale, with higher scores indicative of greater engagement with values. The 'valued living' subscale of the ELS shows very good internal consistency (α = .87) and validity has been demonstrated by significant correlations with theoretically related process and outcome variables such as

psychological distress, mindfulness, and psychological flexibility (Trindade, Ferreira, Pinto-Gouveia & Nooren, 2016; Trompetter et al., 2013). Cronbach's alpha for the ELS 'valued living' subscale in the current sample was .87.

The 'Depression' subscale of the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983): a 7-item subscale measuring depressive symptomology. The HADS also contains another 7-item subscale assessing anxiety symptoms. Only the 'depression' subscale was used in analyses for the current study. Responses range from 0-21 and higher scores indicate greater levels of depression, with established cut-offs of 'normal' (0-7); 'mild' (8-10); 'moderate' (11-14); and 'severe' (15-21) (Stern, 2014). The 'depression' subscale of the HADS has acceptable reliability (α = .77) (Crawford, Henry, Crombie & Taylor, 2001). It has also been validated in previous research in MS (Honarmand & Feinstein, 2009; Spain, Tubridy, Kilpatrick, Adams & Holmes, 2007). Cronbach's alpha for the HADS 'depression' subscale in the current sample was .84.

The Consultation and Relational Empathy measure (CARE; Mercer et al., 2004): assesses perceptions of MS clinician communication and empathy in the consultation. The measure comprises 10 items such as "*how was the doctor at showing care and compassion*" rated on a 5-point Likert scale from 1 (poor) to 5 (excellent), with scores ranging from 10-50. Higher scores indicate greater perceived empathy. The measure has shown high internal reliability, with a Cronbach's alpha of .93 (Mercer et al*.,* 2004) and has demonstrated validity in both doctor and nursing consultations (α = .97) (Bikker, Fitzpatrick, Murphy & Mercer, 2015). Validation for use between different professional groups was a relevant consideration in the current study as both doctors and nursing staff lead MS consultations. Scores have also been found to be unrelated to age, gender, employment and self-reported general health (Bikker et al., 2015). Cronbach's alpha for the CARE in the current study was .97.

T*he Multiple Sclerosis Self-Management Scale Revised* (MSSM-R; Bishop & Frain, 2011): comprises 24 items assessing self-management knowledge and behaviours in adults with MS. Ratings are made on a scale from 1 (disagree completely) to 5 (agree completely), with higher scores indicating better self-management. The scale has been criticised for lacking possible additional self-management items relevant for MS (Ghahari, Khoshbin & Forwell, 2014); however, it is the only measure that attempts to quantify self-management in those with this condition. The measure has been used in a previous postal survey in MS, demonstrates high internal consistency (Cronbach's α = .85), satisfactory to good test-retest reliability,

moderate to high criterion validity for the factor structure against well-established measures, and moderate face validity (Ghahari et al., 2014; Wilski, Tasiemski & Kocur, 2015). Cronbach's alpha for the MSSM-R in the current sample was .82.

2.4 Procedure

Neurologists and specialist MS nurses in the Anne Rowling Clinical Research Facility approached potential participants about the study at the end of their consultation. Individuals expressing an interest in the study were invited to speak with a researcher in the facility (see Appendix F for study protocol). The researcher gave further details and provided people with packs containing a study information sheet (Appendix G), a study consent form (Appendix H), and the seven outcome measures (Appendix I). Contact details were requested to discuss participation after a 'cooling off' period and individuals were invited to take the packs home and consider whether they would like to complete the questionnaires and post them back to the researcher. A pre-paid envelope was included in the research pack. Consent to participate was provided by the return of the research questionnaires with or without the study consent form. Questionnaires and consent forms were separated upon return and marked with a unique identifier code.

2.5 Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows (Version 23) (IBM Corporation, 2015). Prior to statistical analysis, missing data and parametric assumptions were explored. Descriptive statistics for key variables were presented. T-tests were conducted to determine any differences between gender in relation to the outcome variables of patient activation and MS self-management. Correlational analyses were conducted for all key variables to ascertain relationships. For variables where relationships were significant, regression analyses were conducted with depression, perceived clinician empathy and valued living as independent variables, and patient activation and MS self-management as dependent variables. The data was examined to ensure no violation of regression assumptions including homoscedasticity, multicolinearity, linear relationships between predictor and outcome variables and normal distribution of residuals.

2.5.1 Power and sample size

Power analyses were conducted to determine the sample size required for the study. The relationships between valued living, clinician empathy and patient activation had not previously been studied; however, a previous study found a moderate correlation between depression and patient activation in MS patients (r = .43). Therefore, a medium effect size was anticipated. Using G*Power (version 3.0.10; Faul, Erdfelder, Buchner, & Lang, 2009) to detect a medium effect at .8 power at alpha level of .05, with seven independent variables (gender, age, level of education, MS symptom severity, depression, clinician empathy and valued living) and one dependent variable (patient activation), a sample size of 103 was required.

2.5.2 Missing data

Missing data items were analysed. Little's Missing Completely at Random (MCAR) Test indicated non-significance for all individual subscales and the entire dataset *(χ^2 (3488) = 3520.14, p = .35).* Expectation Maximisation (EM) was therefore employed to input missing data, in situations where ≤20 percent of data per case per subscale were missing. The EM method has a large body of empirical support and is reported to be superior to other imputation methods, as it requires a less stringent assumption about the missing data mechanism (Enders, 2011). Where >20 percent of data were missing per case per scale, the scale was excluded from analyses.

2.5.3 Tests of reliability

Cronbach's alpha tests of internal consistency were calculated for key variables and subscales. Values >.7 are generally considered to suggest adequate levels of reliability (Field, 2018). Within this study, reliability for all subscales and scales ranged from .82 (MSSM-R) to .97 (CARE), indicating good to excellent reliability.

2.5.4 Data analysis

Data were initially examined for outliers, levels of skewness and kurtosis. Histograms and box plots indicated some outliers in the data for PAM, CARE and MSIS-Physical scales. Outliers were corrected by the process of winsorizing which involves replacing extreme scores with a score 3 standard deviations from the mean, as recommended in Field (2018). On visual inspection, all variables were found to be reasonably normally distributed except

for the CARE scale and the MSIS-Physical subscale; however, Kolmogorov-Smirnov tests at $p > 0.05$ indicated a degree of non-normality (skewedness) in the PAM, CARE, MSIS-Physical and HADS-Depression scales. The Kolmogorov-Smirnov test has been criticised by some researchers for detecting significant results for small, unimportant effects in large samples (Field, 2018), however, in the current study converging evidence of non-normality was found in the distribution plots for two variables (CARE and MSIS-Physical). A bootstrapping procedure was, therefore, used in subsequent inferential analyses to correct for non-normality. Bootstrapping is a widely recognised statistical procedure to estimate statistical parameters (e.g. the population mean and its confidence interval) in samples indicating non-normality by way of resampling with replacement (Efron & Tibshirani, 1993; Field, 2018; Ong, 2014). Pearson correlations were calculated for all predictor variables to test for multicollinearity. All variables appeared to be appropriate for inclusion in further analyses as no extremely high correlations (0.9) were found.

2.5.5 Testing key hypotheses

Hypothesis 1: independent t-tests were used to test for gender differences in patient activation and MS self-management. Bootstrapped Pearson correlations based on 2000 samples were utilised to investigate the relationships among patient activation, MS self-management, psychological factors (depression and valued living), perceived clinician empathy, MS symptom severity, and demographic factors (age and level of education).

Hypothesis 2: hierarchical regression analyses using a bootstrapped estimation approach with 2000 samples was utilised to examine the predictive power of depression, clinician empathy and valued living in relation to patient activation when controlling for other potentially predictive demographic and clinical variables.

Hypothesis 3: a second hierarchical regression analyses was undertaken to examine the predictive power of patient activation in relation to MS self-management when controlling for other potentially predictive variables.

3. Results

3.1 Descriptive data

Demographic and clinical characteristics for the sample are presented in Table 1. A total of 118 questionnaire packs were returned with a response rate of 77 percent. Of the returned questionnaires, one participant returned completed questionnaires without demographic information; therefore, whilst the final sample was 118, demographic and clinical data for 117 participants are presented. Seventy-six individuals (65%) were female and 41 (35%) were male. For age category, the largest proportion of participants were between 45-54 years old (32.5%), followed by 35-44 years (25.6%). All participants except one indicated they were white Caucasian. College or vocational certificate was the level of education most commonly completed (30.8%), followed by high school (28.2%), then undergraduate degree (21.4%). Regarding MS type, 90 individuals (76.9%) had a diagnosis of relapsing-remitting MS, 18 (15.4%) had a diagnosis of secondary progressive MS and five (4.3%) had a diagnosis of primary progressive MS. Four individuals (3.4%) were uncertain of their MS type. The most commonly reported time category since diagnosis was between 1-5 years ago (30.8%), followed by 6-10 years ago (22.2%). Seventy-three (62.4%) individuals were taking Disease Modifying Therapies (DMT) for their MS and 44 (37.6%) were not. Table 2 presents overall sample means and standard deviations for key variables used in the study.

Table 1. MS sample demographic and clinical and characteristics

	n	**%**
Sample	117	100
Female	76	65
Age		
18-24 years	1	0.9
25-34 years	20	17.1
35-44 years	30	25.6
45-54 years	38	32.5
55-64 years	16	13.7
65+ years	12	10.3
Ethnicity		
White	116	99.1
Mixed race	1	0.9
Education		
High school	33	28.2
College / vocational certificate	36	30.8
Undergraduate degree	25	21.4
Masters level postgraduate degree	16	13.7
Doctoral/PhD level postgraduate degree	2	1.7
Other (not specified)	5	4.3
Type of MS		
Relapsing-remitting	90	77.6
Primary progressive	5	4.3
Secondary progressive	18	15.5
Uncertain	4	3.4
Time since diagnosis		
Less than 1 year	5	0.43
1-5 years	36	30.8
6-10 years	26	22.2
11-15 years	19	16.2
16-20 years	12	10.3
More than 20 years	18	15.4
Prefer not to say	1	0.9
Actively taking Disease Modifying Therapy		
Yes	73	62.4
No	44	37.6

Table 2. Descriptive statistics for key variables with comparative data

Scale	Scale Value Range	95% Confidence Interval		Mean (SD)	Comparative Data
		Upper	Lower		Mean (SD)
Patient Activation (PAM-13)	0 -100	57.05	61.38	59.24 (11.75)	63.18 (11.87)[a]
MS symptom severity (MSIS-29-physical subscale)	0 - 100	27.60	36.49	31.81 (23.69)	56.0 (27.0)[b]
Valued Living (ELS-Valued Living subscale)	10 - 50	36.24	38.50	37.34 (6.02)	No data available from MS sample[c]
Depression (HADS-depression subscale)	0 - 21	4.17	5.55	4.85 (3.67)	5.26 (SD 4.05)[d]
Perceived clinician empathy (CARE)	10 - 50	43.04	45.45	44.27 (6.62)	No data available from MS sample[e]
MS self-management (MSSM-R)	24 - 120	98.65	102.39	100.57 (10.42)	100.98 (11.59)[f]

CARE: Consultation and Relational Empathy measure; ELS: Engaged Living Scale; HADS: Hospital Anxiety and Depression Scale; MSIS: Multiple Sclerosis Impact Scale; MSSM-R: Multiple Sclerosis Self-Management Scale revised; PAM-13: Patient Activation Measure

[a] From Stepleman et al. (2010);
[b] From Jones et al. (2013);
[c] Chronic pain sample (*M* = 35.42, *SD* = 6.40) from Trompetter et al. (2013);
[d] From Honarmand & Feinstein (2009);
[e] Mixed LTCs sample (diabetes, coronary heart disease, chronic obstructive pulmonary disease) (M = 45.9, SD = 5.9) from Bikker et al. (2015);
[f] From Bishop & Frain (2011).

Means, standard deviations and 95% bias corrected, and accelerated confidence intervals based on 2000 bootstrap samples

3.2 Control variables

Two-tailed t-tests were conducted to compare gender scores for patient activation and MS self-management. Females scored significantly higher (M = 61.41, SD = 12.06) than males (M = 55.18, SD = 10.09; t (107) = 2.71, p = .004, two-tailed) for patient activation. The magnitude of the difference in the means (mean difference = -6.23, 95% *CI:* -2.06, -10.36) was moderate (Cohen's d = .56). No significant gender differences were observed for MS self-management. Significant gender differences found in relation to patient activation suggested that gender should be controlled for in hierarchical regression analyses where patient activation was the dependent variable.

3.2.1 Correlation analyses

The relationships between patient activation, age, education, MS symptom severity, depression, perceived clinician empathy, valued living and MS self-management were explored (see Table 3). As the preliminary Q-Q plots and Kolmogorov-Smirnov tests indicated potential non-normality in some of the variables (see section 2.5.4), all correlation analyses were bootstrapped. Statistically significant inverse relationships were found between patient activation and age (r = -.16, p = .05), MS symptom severity (r = -.46, p < .00) and depression (r = -.40, p < .00). Statistically significant positive relationships were observed between patient activation and level of education (r = .22, p = .01), perceived clinician empathy (r = .31, p < .00), valued living (r = .47, p < .00) and MS self-management (r = .43, p < .00). For MS self-management, statistically significant positive correlations were observed for clinician empathy (r = .44, p < .00) and valued living (r = .36, p < .00). The relationship between self-management and depression was not statistically significant, but approached significance (r = -.16, p = .06). According to Cohen (1988), the results overall suggest small to moderate correlations between variables, with all variables significantly correlated in the predicted directions. Significant relationships between patient activation and age, level of education and symptom severity suggested these variables should be controlled for in the subsequent hierarchical regression analyses where patient activation was the dependent variable (see Table 4). Likewise, variables demonstrating significant or near-significant relationships with MS self-management (depression, clinician empathy and valued living) were controlled for in the second regression analyses with MS self-management as the dependent variable (see Table 5).

Table 3. Pearson's correlation coefficients among patient activation, self-management and other key variables

	2 Age	**3** Level of Education	**4** MS Symptom Severity	**5** Clinician Empathy	**6** Valued Living	**7** Depression	**8** MS Self-Management
1. Patient Activation	-.16*	.22*	-.46**	.31**	.47**	-.40**	.43**
2. Age		-.24**	.20*	-.21*	.17*	.00	-.14
3. Level of Education			-.25**	.15	-.06	-.11	.06
4. MS Symptom Severity (physical)				-.31**	-.31**	.67**	-.07
5. Clinician Empathy					.25**	-.14	.44**
6. Valued Living						-.50**	.36**
7. Depression							-.16

Based on 2000 bootstrap samples

* Correlation is significant at 0.05 level (one-tailed); ** Correlation is significant at the 0.01 level (one-tailed)

3.3 Regression analyses

Separate hierarchical regression analyses were employed to assess the relative ability of depression, perceived clinician empathy and valued living measures (HADS-depression, CARE and ELS-Valued Living, respectively) to predict patient activation (PAM-13), and the ability of patient activation (PAM-13) to predict MS self-management (MSSM-R). Variables that demonstrated significant relationships with patient activation (gender, age, level of education and symptom severity) and MS self-management (depression, clinician empathy and valued living) in the bivariate analyses (see Table 3) were controlled for in the subsequent multivariate analyses. The two regression models are presented in Tables 4 and 5.

Predicting patient activation

In the first regression model, data met the assumption of independent errors (Durbin-Watson = 2.1) and multi-collinearity was not deemed to be a concern as tolerance scores ranged from .45 to .92 and variance inflation factor (VIF) scores from 1.08 to 2.20 (Pallant, 2016). Gender, age, level of education and MS symptom severity were entered at step 1, explaining 25% of the variance in patient activation. After entry of depression, perceived clinician empathy and valued living at step 2, the total variance explained by the model was 39%, F (7, 97) = 8.86, p < .00. Depression, perceived clinician empathy and valued living explained an additional 14% of the variance in patient activation after controlling for gender, age, level of education and symptom severity, R squared change = .14, F change (3, 97) = 7.39, p < .00. In the final model, only one of the variables was statistically significant, with valued living recording a higher beta value (beta = .37, p < .00) than depression (beta = -.04, p = .71) and perceived clinician empathy (beta = .07, p = .43). The positive co-efficient indicates that higher levels of valued living were associated with higher patient activation. Coefficients for all variables, including those with a non-significant contribution to the model, are presented in Table 4.

Predicting MS self-management

For the second regression analyses, data met the assumption of independent errors (Durbin-Watson = 2.2) and multi-collinearity was not deemed to be a concern as tolerance scores ranged from .63 to .94 and variance inflation factor (VIF) scores from 1.05 to 1.5. Depression, perceived clinician empathy and valued living were entered in step 1 and explained 27.5% of

the variance in MS self-management. After entry of patient activation at step 2, the total variance explained by the model was 33%, F (4, 106) = 13.03, p < .00. Patient activation explained an additional 5.5% of the variance in MS self-management after controlling for depression, perceived clinician empathy and valued living, R squared change = .06, F change (1, 106) = 8.70, p < .00. In the final model, two of the variables were statistically significant, with perceived clinician empathy recording a higher beta value (beta = .34, p < .00) than patient activation (beta = .28, p = .01). Higher levels of perceived clinician empathy and patient activation were both associated with greater MS self-management as indicated by positive coefficients. Coefficients for all variables are presented in Table 5.

Table 4. Summary of hierarchical regression to predict patient activation

Variable	B	95% CI Lower	95% CI Upper	Beta Standardised	t	P-Value	R	R^2	R^2_{change}
Step1							.50	.25	.25
Gender	3.79	-.61	8.13	.16	1.70	.07			
Age	-.57	-2.06	1.09	-.06	-.68	.51			
Level of Education	1.06	-.82	2.87	.10	1.09	.24			
MS Symptom Severity (physical)	-.19	-.27	-.11	-.38	-3.99	<.00**			
Step 2							.63	.39	.14
Gender	3.21	-.61	6.97	.13	1.54	.10			
Age	-1.37	-2.77	.21	-.15	-1.69	.08			
Level of Education	.91	-.78	2.45	.08	1.02	.28			
MS Symptom Severity (physical)	-.10	-.21	.02	-.21	-1.76	.07			
Depression	-.13	-.83	.47	-.04	-.35	.71			
Valued Living	.74	.39	1.13	.37	3.87	<.00**			
Clinician Empathy	.13	-.23	.46	.07	.81	.43			

Clinician empathy measured by the Consultation and Relational Empathy Measure (CARE); Depression measured by the Hospital Anxiety and Depression Scale (HADS); MS symptom severity measured by the Multiple Sclerosis Impact Scale (MSIS-29); Valued living measured by the Engaged Living Scale (ELS).
* Correlation is significant at 0.05 level; ** Correlation is significant at the 0.01 level
95% bias corrected, and accelerated confidence intervals based on 2000 bootstrap sample

Table 5. Summary of hierarchical regression to predict MS self-management

Variable	B	95% CI Lower	95% CI Upper	Beta Standardised	t	P-Value	R	R^2	R^2_{change}
Step1							.52	.27	.27
Valued Living	.46	.16	.78	.27	2.74	.01**			
Clinician Empathy	.63	.33	.94	.39	4.71	<.00**			
Depression	.03	-.48	.56	.01	.12	.89			
Step 2							.57	.33	.06
Valued Living	.29	-.02	.65	.17	1.71	.09			
Clinician Empathy	.53	.24	.84	.34	4.01	.00**			
Depression	.18	-.31	.69	.06	.69	.48			
Patient Activation	.25	.10	.42	.28	2.95	.01**			

Clinician empathy measured by the Consultation and Relational Empathy Measure (CARE); Depression measured by the Hospital Anxiety and Depression Scale (HADS); Patient activation measured by the Patient Activation Measure (PAM-13); Valued living measured by the Engaged Living Scale (ELS).
* Correlation is significant at 0.05 level; ** Correlation is significant at the 0.01 level
95% bias corrected, and accelerated confidence intervals based on 2000 bootstrap sample

4. Discussion

The current study had three aims: to explore the demographic, psychological and MS-related factors associated with patient activation; to determine the role of depression, valued living and perceived clinician empathy as relative predictors of patient activation; and to evaluate the extent to which patient activation is an independent predictor of MS self-management.

4.1 Summary of findings

Results from the current study provide insight into some of the factors that may influence patient activation and self-management in MS. Participants' level of activation and MS symptom severity were lower in the current study than reported in other MS studies (Ehde et al., 2015; Jones et al., 2013; Stepleman et al., 2015). Self-management for MS was consistent with that reported in a previous MS study by Bishop and Frain (2011). Depression symptoms were indicated in 23% of the current sample, which is comparable to the reported point prevalence of depression in 20-40% of people with MS in clinical settings (Schippling et al., 2016). Overall, scores from key variables suggest that the study sample was representative of a MS population. Self-reported MS symptom severity may have been lower in this sample due to the greater proportion of patients with relapsing-remitting than progressive MS. Rates of MS type in the current study are largely in line with figures reported elsewhere (Compston & Coles, 2008; Goodworth et al., 2016). Lower patient activation levels observed could potentially reflect greater representativeness in the current sample. Less representative samples are likely to have a greater bias towards better-educated participants, who in turn are likely to have higher activation (Hibbard et al., 2004). In the current study, demographic information suggests that around 60 percent of participants were educated to high school or college level. Moreover, the high response rate in the current study (77%) provides further evidence of sample representativeness.

Variables associated with patient activation

Greater activation was related to gender, higher education, valued living, perceived clinician empathy, and self-management. Women demonstrated higher activation scores than men in the current study. These findings are in line with previous research that suggests that activation is higher in individuals who are better educated and female (Bos-Touwen et al., 2015; Chubak et al., 2012; Goodworth et al., 2016; Rask et al., 2009). The negative

relationships observed between activation, age, depression and perceived severity of MS symptoms were also consistent with the results of previous research (Blakemore et al., 2016; Goodworth et al., 2016). Titova et al. (2017) has suggested that lower patient activation in older patients may be linked to higher disease severity with age. Cohort differences may also exist with older patients, as research suggests that older adults demonstrate a greater external locus of control and defer more to their healthcare provider to manage and oversee their health (Schneider et al., 2006). A significant positive relationship was observed between patient activation and self-management for MS in the current study (e.g. medication adherence; taking breaks when tired; and discussing symptoms/treatment decisions with MS clinicians). This finding is consistent with a body of research indicating a positive association between activation and self-management behaviours in the wider literature for LTCs (Hibbard et al., 2007; Marshall et al., 2013; Rask et al., 2009).

Predicting patient activation

Valued living was a significant predictor of patient activation after controlling for gender, age, level of education and MS symptom severity. This finding is consistent with previous research, which suggests that valued living may predict or mediate important health-related outcomes, such as psychological distress in cancer and seizure activity in epilepsy (Ciarrochi et al., 2011; Lundgren et al., 2008). Our findings indicate that being in contact with personal values and having the ability to take actions in line with these values is likely to promote positive adaptation when faced with adverse health conditions.

The finding that depression and perceived clinician empathy were not significant predictors in our study contrasts with previous research (Alexander, Hearld, Mittler & Harvey, 2012; Goodworth et al., 2016). In their study, Goodworth et al. (2016) found that depression did explain variance for patient activation in MS. However, their study utilised the Beck Depression Inventory, version 2 (BDI-II; Beck, Steer & Brown, 1996) to measure depression and, therefore, it may be that depression scores were overestimated in the Goodworth et al. (2016) study. The use of the BDI-II in physical illness populations has been criticised due to the inclusion of somatic items (e.g. fatigue) as it may inflate depression scores caused by symptoms inherent in the illness rather than depression (Moore, Moore & Shaw, 1998). Alexander et al. (2012) reported that, in individuals with multiple comorbid chronic conditions, greater perceived quality of relationship with clinicians was associated with higher levels of patient activation. Although participants perceived high levels of clinician empathy,

our conflicting result may indicate that MS individuals' activation levels could be less reliant on empathy within the patient-clinician relationship given the relatively infrequent contact with clinicians compared to some other health conditions. Additional aspects of the relationship, such as treatment goal-setting (Alexander et al., 2012) might be important to consider in relation to patient activation.

Predicting self-management

Patient activation was a unique predictor of self-management for MS in the current study. This study is the first to establish a relationship between activation and self-management in MS. Nevertheless, this finding is in line with previous research that has shown a significant positive relationship between patient activation and self-management behaviours in other LTCs such as exercising, medication adherence, managing stress and using self-management services (e.g. emotional support groups and health education classes) (Mosen et al., 2007). Our findings indicate that viewing oneself as having the knowledge, skills and confidence to take an active role in health management may promote the implementation of self-management behaviours when faced with MS.

Several studies have used the PAM-13 for predicting self-management behaviours (Greene et al., 2015; Marshall et al., 2013; Mosen et al., 2007) and, although the measure does not focus on specific behaviours, it may be that the PAM-13 is likely to predict variance in self-management as several items of the PAM-13 capture confidence in engaging with self-management behaviours. Whilst there may be some potential questions around conceptual overlap with PAM-13 and self-management measures, this study found that patient activation only demonstrated a medium correlation (.43) with MS self-management. Goodworth et al. (2016) reported a slightly larger association (.50) between patient activation and MS self-efficacy, possibly, because patient activation is more concerned with feelings of confidence and beliefs about one's ability to manage their own health rather than implementing specific self-management behaviours. Illness-specific self-management measures may capture elements of the patient activation construct; however, the strength of the inter-correlation in this study appears to indicate that self-management and patient activation are related but separate constructs.

We further explored this issue in the current study by examining the strongest correlations between items on the PAM-13 and MSSM-R to ascertain which items had the most potential

conceptual overlap. The three highest correlated items emerged with an r value ≥.40 (*r*=.40; *r*=.47; *r*=.47). These three items were then removed from the MSSM-R and a 'new' self-management measure variable was created for the purposes of data analysis. Cronbach's alpha for the 'new' measure was .71. Hierarchical regression analyses were re-run with the 'new' self-management measure as the outcome variable. Depression, clinician empathy and valued living were entered as predictors in step 1; and patient activation was entered as a predictor in step 2. After entry, and consistent with the final model presented in our results (see Table 5), patient activation remained statistically significant with higher levels of patient activation associated with greater MS self-management.

While there are related elements between patient activation and self-management, our view is that the PAM-13 captures additional information. As well as assessing knowledge, skills and confidence for self-management, it also appears to capture information about an individual's self-efficacy, resilience and locus of control regarding self-management tasks. On the other hand, patient activation as a conceptually distinct construct seems individually incapable of measuring specific clinically relevant information provided by multi-dimensional self-management tools. The issue of conceptual versus measurement overlap between patient activation and self-management remains largely unexplored but invites interesting reflections around the notion that measurement science and theory building coexist. Kelle (2015) has suggested that instruments designed to capture latent constructs, like patient activation and self-management, must account for and acknowledge the role of previous theoretical findings; similarly, theoretical knowledge can only be applied and tested with the use of valid and reliable measures.

Interestingly, perceived clinician empathy made a greater contribution to self-management than patient activation. MS patients may rely on the therapeutic relationship with their clinicians to 'check in', which may reinforce positive self-management behaviours (Alexander, Hearld & Mittler, 2014). Our finding perhaps indicates that a therapeutic alliance with healthcare providers has a buffering effect when patients are less activated. Further exploration of sub-components of the patient-clinician relationship to examine which aspects predict greater self-management in MS may be warranted.

Depression was not a significant predictor of self-management in our study, which seems unexpected given that previous research has shown that depressed individuals are less likely to attend and engage with self-management programmes (Cassidy, Turnball, Gardani &

Kirkwood, 2014; Hadgkiss et al., 2015). Valued living was not a significant predictor of self-management for MS when patient activation was added to the regression model. Thus, may suggest that valued living and patient activation may have some shared variance in relation to predicting self-management for MS.

4.2 Methodological considerations

This study was the first to explore the relative role of depression, valued living and clinician empathy as predictors of patient activation, and to establish an association between patient activation and self-management for MS. The use of the PAM-13, which is currently the only measure to capture this construct, allowed for the possibility of assessing patient engagement from a transdiagnostic perspective that is comparable across different health conditions. Goodworth et al. (2016) attempted to ascertain some of the modifiable variables associated with patient activation in MS and suggested that addressing depression may be a key treatment target. The present study investigated two unexplored variables to identify further areas of intervention for people at risk of lower levels of activation and poorer self-management. The study was sufficiently powered and validated measures with robust psychometric properties were utilised, most of which had been previously demonstrated in an MS population. The sample was recruited from one NHS site in Scotland and while this might introduce a degree of bias, the high response rate (77%) and participant demographic characteristics suggest the sample is broadly representative of a UK MS population. The method for data collection may have created further bias whereby individuals with greater functional disability were unable to participate, however, the high response rate in this study is encouraging.

It would be valuable to integrate self-report measures with direct measures of MS self-management such as medication adherence and lifestyle behaviour. This endeavour may require creative methods of measurement but would be an important addition to enhance validity of future studies. The cross-sectional design prevents causal inference; therefore, future research could entail experimental studies explicitly manipulating and testing causal links between variables. Finally, the present study also highlights a need for longitudinal research to increase confidence in findings and explore new ideas. One potentially interesting and valuable area of future research would be longitudinal studies that follow patient activation in the context of disease progression (i.e. transition from relapsing-remitting to progressive MS diagnosis).

4.3 Clinical implications

Whilst causality cannot be inferred from these results, our findings have important implications for clinicians working with individuals with MS. Clinicians largely depend on patients' own management of seeking help when required, making lifestyle alterations and adhering to therapeutic recommendations. Patients with low activation are less likely to play an active role in staying healthy, present to health services when required and adhere to treatment recommendations (Hibbard & Gilburt, 2014). Our finding that perceived clinician empathy might predict better self-management of MS recognises the key role of clinicians' in supporting and reinforcing adaptive behaviours. Clinicians could assess constructs like valued living and perceived empathy and target interventions to promote these processes in an effort to improve activation and self-management in people with MS. Clinical consultations or interventions to activate patients might be more successful when linked to the patient's values, particularly those around physical self-care, self-direction and social relationships. Measures that assess value-consistent behaviour in various life domains (e.g. physical self-care, recreation), may be clinically useful as part of consultations to identify individuals who might be at risk for lower activation and are in need of support.

There is growing evidence that value-consistent behaviour can be enhanced with interventions like Acceptance and Commitment Therapy which aim to improve quality of life and functioning by cultivating patients' acceptance of difficult, and sometimes unchangeable, circumstances and commitments to personally held values (Wersebe et al., 2017). ACT has been shown to increase valued living and reduce psychological distress in MS (Gillanders & Gillanders, 2014; Nordin & Rorsman, 2012), but it may also promote meaningful change with regard to activating patients to engage in self-management activities. In accordance with government strategies (NHS England, 2016) for the management of long-term conditions that call for "healthcare professionals to abandon traditional ways of thinking" (Coulter, Roberts & Dixon, 2013, p. 1), it could be argued that increased knowledge about the role of other ACT-related constructs in relation to activation for self-management may provide an alternative way to conceptualise difficulties associated with MS.

4.4 Conclusions

The current study expands the existing literature by demonstrating that valued living is associated with patient activation when gender, age, education and symptom severity are

controlled for in an MS population. It further established that patient activation and perceived clinician empathy are associated with MS self-management when depression and valued living are controlled for. The findings suggest that self-management interventions, which integrate components to enhance valued living and the patient-clinician relationship, may be effective for addressing low levels of patient activation and enhancing self-management behaviours in some people living with MS.

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Appendices

Appendix A: Author Publication Guidelines

British Journal of Health Psychology

The aim of the British Journal of Health Psychology is to provide a forum for high quality research relating to health and illness. The scope of the journal includes all areas of health psychology as outlined in the Journal Overview.

The types of paper invited are:

• Papers reporting original empirical investigations, using either quantitative or qualitative methods, including reports of interventions in clinical and non-clinical populations;

• Theoretical papers which report analyses on established theories in health psychology;

• We particularly welcome review papers, which should aim to provide systematic overviews, evaluations and interpretations of research in a given field of health psychology; and

• Methodological papers dealing with methodological issues of particular relevance to health psychology.

Authors who are interested in submitting papers that do not fit into these categories are advised to contact the editors who would be very happy to discuss the potential submission.

All papers published in The British Journal of Health Psychology are eligible for Panel A: Psychology, Psychiatry and Neuroscience in the Research Excellence Framework (REF).

1. Circulation

The circulation of the Journal is worldwide. Papers are invited and encouraged from authors throughout the world.

2. Length

Papers describing quantitative research (including reviews with quantitative analyses) should be no more than 5000 words (excluding the abstract, reference list, tables and figures). Papers describing qualitative research (including reviews with qualitative analyses) should be no more than 6000 words (including quotes, whether in the text or in tables, but excluding the abstract, tables, figures and references). The Editors retain discretion to publish papers beyond this length in cases where the clear and concise expression of the scientific content requires greater length.

3. Editorial policy

The Journal receives a large volume of papers to review each year, and in order to make the process as efficient as possible for authors and editors alike, all papers are initially examined by the Editors to ascertain whether the article is suitable for full peer review. In order to qualify for full review, papers must meet the following criteria:

• The content of the paper falls within the scope of the Journal

• The methods and/or sample size are appropriate for the questions being addressed

• Research with student populations is appropriately justified

• The word count is within the stated limit for the Journal (i.e. 5000 words, or 6,000 words for qualitative papers)

4. Submission and reviewing

All manuscripts must be submitted via Editorial Manager. The Journal operates a policy of anonymous (double blind) peer review. We also operate a triage process in which submissions that are out of scope or otherwise inappropriate will be rejected by the editors without external peer review to avoid unnecessary delays. Before submitting, please read the terms and conditions of submission and the declaration of competing interests. You may also like to use the Submission Checklist to help your prepare your paper.

5. Manuscript requirements

• Contributions must be typed in double spacing with wide margins. All sheets must be numbered.

• Manuscripts should be preceded by a title page which includes a full list of authors and their affiliations, as well as the corresponding author's contact details. You may like to use this template. When entering the author names into Editorial Manager, the corresponding author will be asked to provide a CRediT contributor role to classify the role that each author played in creating the manuscript. Please see the Project CRediT website for a list of roles.

• For articles containing original scientific research, a structured abstract of up to 250 words should be included with the headings: Objectives, Design, Methods, Results, and Conclusions. Review articles should use these headings: Purpose, Methods, Results, and Conclusions. As the abstract is often the most widely visible part of your paper, it is important that it conveys succinctly all the most important features of your study. You can save words by writing short, direct sentences. Helpful hints about writing the conclusions to abstracts can be found here.

• Statement of Contribution: All authors are required to provide a clear summary of ‘what is already known on this subject?’ and ‘what does this study add?’ Authors should identify existing research knowledge relating to the specific research question and give a summary of the new knowledge added by your study. Under each of these headings, please provide 2-3 (maximum) clear outcome statements (not process statements of what the paper does); the statements for 'what does this study add?' should be presented as bullet points of no more than 100 characters each. The Statement of Contribution should be a separate file.

• Conflict of interest statement: We are now including a brief conflict of interest statement at the end of each accepted manuscript. You will be asked to provide information to generate this statement during the submission process.

• The main document must be anonymous. Please do not mention the authors’ names or affiliations (including in the Method section) and always refer to any previous work in the third person.

• Tables should be typed in double spacing, each on a separate page with a self-explanatory title. Tables should be comprehensible without reference to the text. They should be placed at the end of the manuscript but they must be mentioned in the text.

• Figures can be included at the end of the document or attached as separate files, carefully labelled in initial capital/lower case lettering with symbols in a form consistent with text use. Unnecessary background patterns, lines and shading should be avoided. Captions should be listed on a separate sheet. The resolution of digital images must be at least 300 dpi. All figures must be mentioned in the text.

• For reference citations, please use APA style. Particular care should be taken to ensure that references are accurate and complete. Give all journal titles in full and provide doi numbers where possible for journal articles. For example:

Author, A., Author, B., & Author, C. (1995). *Title of book.* City, Country: Publisher. Author, A. (2013). Title of journal article. *Name of journal, 1,* 1-16. Doi: 10.1111/bjep.12031

• SI units must be used for all measurements, rounded off to practical values if appropriate, with the imperial equivalent in parentheses.

• In normal circumstances, effect size should be incorporated.

• Authors are requested to avoid the use of sexist language.

• Authors are responsible for acquiring written permission to publish lengthy quotations, illustrations, etc. for which they do not own copyright. For guidelines on editorial style, please consult the APA Publication Manual published by the American Psychological Association.

• Manuscripts describing clinical trials are encouraged to submit in accordance with the CONSORT statement on reporting randomised controlled trials.

• Manuscripts reporting systematic reviews and meta-analyses are encouraged to submit in accordance with the PRISMA statement.

• Manuscripts reporting interventions are encouraged to describe them in accordance with the TIDieR checklist.

6. Supporting information

Supporting Information can be a useful way for an author to include important but ancillary information with the online version of an article. Examples of Supporting Information include appendices, additional tables, data sets, figures, movie files, audio clips, and other related nonessential multimedia files. Supporting Information should be cited within the article text, and a descriptive legend should be included. Please indicate clearly on submission which material is for online only publication. It is published as supplied by the author, and a proof is not made available prior to publication; for these reasons, authors should provide any Supporting Information in the desired final format.

For further information on recommended file types and requirements for submission, please visit the Supporting Information page on Author Services.

7. OnlineOpen

OnlineOpen is available to authors of primary research articles who wish to make their article available to non-subscribers on publication, or whose funding agency requires grantees to archive the final version of their article. With OnlineOpen, the author, the author's funding agency, or the author's institution pays a fee to ensure that the article is made available to non-subscribers upon publication via Wiley Online Library, as well as deposited in the funding agency's preferred archive. A full list of terms and conditions is available on Wiley Online Library.

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Prior to acceptance there is no requirement to inform an Editorial Office that you intend to publish your paper OnlineOpen if you do not wish to. All OnlineOpen articles are treated in the same way as any other article. They go through the journal's standard peer-review process and will be accepted or rejected based on their own merit.

8. Author Services

Author Services enables authors to track their article – once it has been accepted – through the production process to publication online and in print. Authors can check the status of their articles online and choose to receive automated e-mails at key stages of production. The author will receive an e-mail with a unique link that enables them to register and have their article automatically added to the system. You can then access Kudos through Author Services, which will help you to increase the impact of your research. Visit Author Services for more details on online production tracking and for a wealth of resources including FAQs and tips on article preparation, submission and more.

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10. Colour illustrations

Colour illustrations can be accepted for publication online. These would be reproduced in greyscale in the print version. If authors would like these figures to be reproduced in colour in print at their expense they should request this by completing a Colour Work Agreement form upon acceptance of the paper.

11. Pre-submission English-language editing

Authors for whom English is a second language may choose to have their manuscript professionally edited before submission to improve the English. A list of independent suppliers of editing services can be found in Author Services. All services are paid for and arranged by the author, and use of one of these services does not guarantee acceptance or preference for publication.

12. The Later Stages

The corresponding author will receive an email alert containing a link to a web site. The proof can be downloaded as a PDF (portable document format) file from this site. Acrobat Reader will be required in order to read this file. This software can be downloaded (free of charge) from Adobe's web site. This will enable the file to be opened, read on screen and annotated direct in the PDF. Corrections can also be supplied by hard copy if preferred. Further instructions will be sent with the proof. Excessive changes made by the author in the proofs, excluding typesetting errors, will be charged separately.

13. Early View

British Journal of Health Psychology is covered by the Early View service on Wiley Online Library. Early View articles are complete full-text articles published online in advance of their publication in a printed issue. Articles are therefore available as soon as they are ready, rather than having to wait for the next scheduled print issue. Early View articles are complete and final. They have been fully reviewed, revised and edited for publication, and the authors' final corrections have been incorporated. Because they are in final form, no changes can be made after online publication. The nature of Early View articles means that they do not yet have volume, issue or page numbers, so they cannot be cited in the traditional way. They are cited using their Digital Object Identifier (DOI) with no volume and issue or pagination information. E.g. Jones, A.B. (2010). Human rights Issues. *Journal of Human Rights*. Advance online publication. doi:10.1111/j.1467-9299.2010.00300.x

Further information about the process of peer review and production can be found in this document. What happens to my paper? Appeals are handled according to the procedure recommended by COPE.

Appendix B: Taxonomy of Self-Management Components for Coding Studies

TAXONOMY	ELABORATION	EXAMPLES FROM STUDIES INCLUDED IN THIS REVIEW (*DELIVERED DIRECTLY TO PATIENTS)*
1. EDUCATION ABOUT CONDITION AND MANAGEMENT	--	• Explanation of cardiovascular risk and dysglacaemia; symptoms, physiology, causes and treatment. • 3-week patient education programme, covering living with diabetes, epidemiology, basic knowledge, complications, improving metabolic control, measuring blood glucose, diet and physical activity (diabetes)
2. INFORMATION ABOUT AVAILABLE RESOURCES	Including: • financial benefits • social support • charitable organisations	• Advice on accessing community resources (chronic poly-arthritis)
3. PROVISION OF/AGREEMENT ON SPECIFIC ACTION PLANS AND/OR RESCUE MEDICATION	Definition: • a personalised action plan should be tailored to the person, enabling people to recognise when symptoms are worse and setting out actions to be taken when control deteriorates	• Use of behavioural change problem-solving care plan or contract where patient sets up a plan for a difficult time, discuss and adjust plan with HP as appropriate (chronic heart failure)
4. REGULAR CLINICAL REVIEW	--	• External regular review (chronic poly-arthritis)
5. MONITORING OF CONDITION WITH FEEDBACK TO THE PATIENT	Including: • feedback from clinician • feedback from technology • self-evaluation	• Weekly testing and review of A1C level and opportunity to discuss A1C value with community health reps following education classes, who gave personalised feedback / recommendations to patients (diabetes) • Remote monitoring system to provide timely alerts and feedback from health professional in response to worrisome responses to a question or vital signs being outside pre-set limits (chronic heart failure)
6. PRACTICAL SUPPORT WITH ADHERENCE (MEDICATION OR BEHAVIOURAL)	Including: • medicine reviews • dosette boxes • prompts • reminder checklists	• Biweekly telephone calls by nurse to review patient's blood pressure log and medication adherence (hypertension) • Weekly reminder emails to patients to facilitate adherence to complete online self-management modules for 6 weeks (osteoarthritis) • 'Buddy' system to increase compliance with exercise participation (diabetes)

TAXONOMY	ELABORATION	EXAMPLES FROM STUDIES INCLUDED IN THIS REVIEW (*DELIVERED DIRECTLY TO PATIENTS)*
7. PROVISION OF EQUIPMENT	--	• Remote monitoring device provided to record weight, heart rate and blood pressure daily (chronic heart failure) • All intervention group participants were provided with a pedometer free of charge to record levels of physical activity daily (diabetes)
8. SAFETY NETTING	Including: • specialist telephone advice • out of hours advice	• Availability of electronic messaging with healthcare professional in addition to access to patient portal.
9. TRAINING/REHEARSAL TO COMMUNICATE WITH HEALTH PROFESSIONALS	--	• Patients taught skills via group-based activities around 'Making the most of consultations with health professionals' and 'Preparing for clinical consultations' (COPD) • 'Talking with healthcare providers' covered as part of self-management program (sickle cell disease)
10. TRAINING/REHEARSAL FOR ACTIVITIES OF DAILY LIVING	--	• Training in balancing life with long-term condition
11. TRAINING/REHEARSAL FOR PRACTICAL SELF-MANAGEMENT ACTIVITIES	--	• Training in measuring blood glucose (diabetes) • Training in monitoring blood pressure (hypertension)
12. TRAINING/REHEARSAL FOR PSYCHOLOGICAL STRATEGIES	Including: • problem-solving • action planning • goal-setting • reframing • distraction • relaxation • cognitive restructuring	• Personal goals aimed at improving self-management of disease (sickle cell disease) • Patients taught techniques to deal with frustration, fatigue, pain and isolation (mixed health conditions) • Mindfulness practice, relaxation training and handling unhelpful emotions (COPD)
13. SOCIAL SUPPORT	Including: • Befriending • peer support • peer mentoring • group socialising	• Encouraging participants to interact and to assess their own and their peers' progress towards managing their condition by sharing ideas, advice and support with each other

TAXONOMY	ELABORATION	EXAMPLES FROM STUDIES INCLUDED IN THIS REVIEW (*DELIVERED DIRECTLY TO PATIENTS)*
14. LIFESTYLE ADVICE AND SUPPORT	Including: • Diet • Physical activity • smoking cessation	• Participant walking groups organised and assisted by health care providers as part of intervention • Nutritionist providing information to enhance physical activity and dietary intake.

Appendix C: Quality Criteria and Assessment of Bias Tool

Do self-management interventions improve Patient Activation in long term conditions?

Study Author(s):

_____

Year: _____

QC1. Does the study design provide sufficient evidence that Patient Activation outcomes are due to the intervention?	
Well-covered	Randomised controlled trial (RCT)
Adequately addressed	Non-randomised controlled trial / multiple baseline
Poorly addressed	Repeated measures design / uncontrolled trial
Not reported / Not applicable	Single case experimental design / case study with pre-post quantified data
QC2. Are the recruitment method and inclusion/ exclusion criteria appropriate to ensure a representative sample that can be generalised?	
Well-covered	Representative recruitment procedure (e.g. random sampling) applied to reduce selection bias and appropriate sample eligibility criteria are applied to address the review aims (e.g. a homogenous sample of individuals with the same, defined long-term health condition requiring clear and specific self-management behaviours).
Adequately addressed	Convenience recruitment procedure applied, but appropriate attempts have been made to address sample representativeness or participants' inclusion criteria are only adequately appropriate to address the review aims (e.g. a heterogeneous sample of individuals with mixed long-term health conditions requiring a variety of self-management behaviours).
Poorly addressed	Convenience recruitment procedure without sufficient attempts to reduce bias in sample selection or participants inappropriate to address the review aims (e.g., heterogeneous sample of individuals with defined but mixed long-term conditions not restricted to physical health requiring a variety self-management behaviours).
Not reported / Not applicable	Recruitment method poorly described & unclear eligibility criteria or participant characteristics (e.g., a sample of individuals with long-term conditions which are not specified).
QC3. Is sample size (power) sufficient for analysis relating to pre and post Patient Activation outcome measure?	
Well-covered	Number of participants who completed both pre-and post-measures in the intervention group is sufficient to achieve power of at least 0.8, where a medium effect size is anticipated, and alpha is 0.5.
Adequately addressed	Number of participants who completed both pre-and post-measures in the intervention group is sufficient to achieve power of at least 0.7, where a medium effect size is anticipated, and alpha is 0.5.
Poorly addressed	Number of participants who completed pre-and post-measures in the intervention group is sufficient to achieve power of less than 0.7, where a medium effect size is anticipated, and alpha is 0.5.

Not reported / Not applicable	Sample size not reported / known
QC4. Is the allocation appropriate to address allocation bias?	
Well-covered	Appropriate process of allocation to treatment groups is applied to address bias and investigator(s) and / or participants are blinded (e.g. random allocation method used).
Adequately addressed	Only adequate process of allocation to groups is used to address bias (e.g. poor randomisation method used or investigator(s) and / or participants are not blinded).
Poorly addressed	Control group is not randomised.
Not reported / Not applicable	No control group used.
QC5. Are groups comparable at baseline on key variables? *	
Well-covered	The treatment and control groups are comparable at baseline or sufficient attempts have been made to statistically control for the differences.
Adequately addressed	The treatment and control groups only adequately comparable at baseline or only adequate attempts have been made to control for differences.
Poorly addressed	The treatment and control groups are not comparable at baseline or no attempt has been made to address the differences or control group is used.
Not reported / Not applicable	No control group is used.
*Note	Key baseline variables include: Patient Activation; severity of health condition; age; gender; and education, where applicable.
QC6. The Patient Activation Measure is appropriately administered and validated for use in sample population(s) or similar?	
Well-covered	Good reliability and / or validity properties are reported (≥0.8) in the study population(s) or similar population(s), with good reason to believe they would apply to the current study population (e.g. where the level and type of self-management required is similar between long-term conditions).
Adequately addressed	Adequate reliability and / or validity properties reported (≥0.5 and <0.8) in the study population(s) or similar population(s), with good reason to believe they would apply to the current study population (e.g. where the level and type of self-management required is similar between long-term conditions).
Poorly addressed	Poor psychometric properties reported (<0.5) in the study population(s) or similar population(s).
Not reported / Not applicable	Psychometric properties are not known in the study population(s).
QC7. Follow-up PAM is administered to evaluate if effects are maintained long-term?	
Well-covered	Long-term (≥6 months) post-intervention follow-up scores available for PAM measure.
Adequately addressed	Short-term (≥3 and <6 months) post-intervention follow-up scores available for PAM measure.

Poorly addressed	Post-intervention follow-up of <3 months duration.
Not reported / Not applicable	No post-intervention follow-up data available for PAM.
QC8. The self-management intervention is suitable for increasing Patient Activation in the context of long-term conditions? *	
Well-covered	A sufficiently detailed self-management intervention is used, and this seems appropriate to increase Patient Activation (number of sessions, content* and level of input).
Adequately addressed	An adequately detailed self-management intervention is used, or this seems only partially appropriate to improve Patient Activation (number of sessions, content* and level of input).
Poorly addressed	The self-management intervention is not sufficient to ensure validity or is not adequate to increase Patient Activation (number of sessions, content* and level of input).
Not reported / Not applicable	Intervention is not described and details not available.
*Note	A sufficient self-management intervention should include the provision of education plus at least two additional components based on the taxonomy of self-management support components by Taylor et al. (2014). Other consideration of suitability includes whether the intervention is standardised or is locally developed.
QC9. Is the delivery of the intervention conducted and assessed appropriately?	
Well-covered	The treatment is conducted by health professionals and / or peer facilitators who have received suitable training in the intervention. Accurate and consistent application of the intervention is also suitably measured (e.g. via supervision or independent rating of audio/video tapes).
Adequately addressed	The treatment is peer-led or conducted by health professionals who have received adequate training in the intervention. Accurate and consistent application of the intervention may or may NOT be adequately measured but biased (e.g. self- or participant-rated).
Poorly addressed	The treatment is not conducted by suitably trained individuals and no appropriate measurement of accurate and consistent application of the intervention is used.
Not reported / Not applicable	No information about the facilitators' background / training or procedure to access fidelity available.
QC10. Attrition at post-intervention* is low and / or comparable to control group?	
Well-covered	Attrition from the study is low (≤30%) and, if applicable, approximately equal across treatment and control group (e.g. ≤10%).
Adequately addressed	Attrition from the study is moderate (>30-49%) or, if applicable, less than 30% but with moderately unequal dropout rates across treatment and control group (e.g. >11-19%).
Poorly addressed	Attrition from the study is poor (≥50%) and, if applicable, with substantially unequal dropout rates across treatment and control group (e.g. ≥20%).
Not reported / Not applicable	Attrition rates at post intervention are not reported or considered.
*Note	Attrition refers to non-completion of the Patient Activation Measure at post-intervention.

QC11. Attrition at follow-up* is low and / or comparable to control group?	
Well-covered	Attrition from the study is low (≤30%) and, if applicable, approximately equal across treatment and control group (e.g. ≤10%).
Adequately addressed	Attrition from the study is moderate (>30-49%) or, if applicable, less than 30% but with moderately unequal dropout rates across treatment and control group (e.g. >11-19%).
Poorly addressed	Attrition from the study is poor (≥50%) and, if applicable, with substantially unequal dropout rates across treatment and control group (e.g. ≥20%).
Not reported / Not applicable	Attrition rates at follow-up are not reported or considered.
*Note	If applicable, attrition refers to non-completion of the Patient Activation Measure at the longest follow-up period within the study.
QC12. Analysis is appropriate for the review aims, measure and study design (e.g. adjusted for potential confounders*) and outcomes are appropriately reported?	
Well-covered	An appropriate statistical analysis is conducted (excl. missing data analysis) and the outcomes are appropriately reported, AND potential confounders are clearly specified and controlled for, where applicable.
Adequately addressed	An adequately appropriate statistical analysis is conducted (excl. missing data analysis) and the outcomes are only adequately reported. Baseline differences between groups are specified and controlled for.
Poorly addressed	Inappropriate or poorly conducted statistical analysis is used or the outcomes are poorly reported. Potential confounders are not considered or controlled for.
Not reported / Not applicable	Statistical analysis not carried out or reported OR potential confounders are not considered.
*Note	Potential confounders related to the Patient Activation construct include baseline differences in age, education and PAM scores.
QC13. Is the method to address missing data suitable?	
Well-covered	No missing data or intention to treat analysis / appropriate alternative (e.g. maximum likelihood, if missing data are likely to be random) is used.
Adequately addressed	Modified ITT is mentioned with an acceptable explanation for the modification.
Poorly addressed	Missing data are poorly addressed
Not reported / Not applicable	No missing data analyses are reported or there is a lack of clarity regarding the method used.

Appendix D: Research and Ethics Committee (IRAS) Approval Letter

Health Research Authority
South West - Exeter Research Ethics Committee
Whitefriars
Level 3
Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 0207 104 8043

06 January 2017

Ms Laura Alexander
Department of Clinical Neurosciences
Western General Hospital
Crewe Road, Edinburgh
EH4 2XU

Dear Ms Alexander

Study title: **Patient Activation in Multiple Sclerosis: the role of depression, value-based living and perceived clinician empathy.**

REC reference: **16/SW/0330**
IRAS project ID: **213383**

Thank you for your letter of the 21st December 2016, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion
On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of the favourable opinion

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

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission 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 Approval (England)/ NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

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

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.
There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

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).

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" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Covering letter on headed paper [Response Letter to REC]	version 1	10 December 2016
Covering letter on headed paper [REC response letter 2]	N/A	21 December 2016
GP/consultant information sheets or letters [GP Letter informing of participation]	version 3	20 December 2016
GP/consultant information sheets or letters [MS Clinician Information Letter]	version 2	20 December 2016
IRAS Checklist XML [Checklist_09112016]		09 November 2016
IRAS Checklist XML [Checklist_16122016]		16 December 2016
IRAS Checklist XML [Checklist_21122016]		21 December 2016
Letters of invitation to participant [Participant cover / invitation letter]	version 1	07 November 2016
Letters of invitation to participant [Participant Cover Letter]	version 2	20 December 2016
Non-validated questionnaire [Demographic Questionnaire]	version 1	14 October 2016
Non-validated questionnaire [Demographic Questionnaire]	version 2	20 December 2016
Other [Guidance notes for completing questionnaires]	version 1	14 October 2016
Other [Guidance sheet for Participants Completing Questionnaires]	version 2	20 December 2016
Other [Participant Thank You Letter]	version 2	20 December 2016
Other [Permission to Contact Form]	version 1	01 December 2016
Participant consent form [Participant Consent Form]	version 3	20 December 2016
Participant information sheet (PIS) [Participant Information Sheet]	version 3	20 December 2016
REC Application Form [REC_Form_09112016]		09 November 2016
Research protocol or project proposal [Study Protocol]	version 2	20 December 2016
Summary CV for Chief Investigator (CI) [CV for CI]	Version 1	11 October 2016
Summary CV for supervisor (student research) [CV for supervisor]	version 1	08 November 2016
Validated questionnaire [Patient Activation Measure]	version 2	20 December 2016
Validated questionnaire [Multiple Sclerosis Impact Scale]	version 2	20 December 2016
Validated questionnaire [Engaged Living Scale]	version 2	20 December 2016
Validated questionnaire [CARE Measure]	version 2	20 December 2016

Validated questionnaire [Hospital Anxiety and Depression Scale]	Version 2	20 December 2016
Validated questionnaire [Multiple Sclerosis Self-Management Scale]	version 2	20 December 2016

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.

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

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

Feedback

You are invited to give your view of the service that you have received from the Research Ethics Service 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

We are pleased to welcome researchers and R & D staff at our RES Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

16/SW/0330	**Please quote this number on all correspondence**

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

Yours sincerely,

Pp Bywater

Mrs Joan Ramsay Vice - Chair

Email: nrescommittee.southwest-exeter@nhs.net

Enclosures: *"After ethical review – guidance for researchers"*

Copy to: *Ms Charlotte Smith*

Mr Gavin Robertson, NHS Lothian Research & Development Office

Appendix E: NHS Lothian Research and Development Approval Letter

University Hospitals Division

NHS Lothian

Queen's Medical Research Institute
47 Little France Crescent, Edinburgh, EH16 4TJ

FM/CF/approval

6 January 2017

Research & Development
Room El .12

Mrs Shuna Colville

University of Edinburgh
Anne Rowling Regenerative neurology Clinic
Chancellor's Building
49 Little France Crescent
Edinburgh
EH16 4SB

Tel: 0131 242 3330
Email:
accord@nhslothian.scot.nhs.uk
Director: Professor David E Newby

Dear Mrs Colville

Lothian R&D Project No: 2016/0321	REC No: 16/SW/0330
Title of Research: Patient Activation in Multiple Sclerosis: the role of depression, value-based living and perceived clinician empathy.	
Participant Information Sheet: Version 3.0, dated 20 December 2016	Consent Form: Version 3.0, 20 December 2016
Protocol: Version 2.0, dated 20 December 2016	

I am pleased to inform you this letter provides Site Specific approval for NHS Lothian for the above study and you may proceed with your research, subject to the conditions below.

Please note that the NHS Lothian R&D Office must be informed of any changes to the study such as amendments to the protocol, funding, recruitment, personnel or resource input required of NHS Lothian.

Substantial amendments to the protocol will require approval from the ethics committee which approved your study and the MHRA where applicable.

Please keep this office informed of the following study information:

1. Date you are ready to begin recruitment, date of the recruitment of the first participant and the quarterly recruitment figures thereafter.
2. Date the final participant is recruited and the final recruitment figures.
3. Date your study / trial is completed within NHS Lothian.

I wish you every success with your study.

Yours sincerely

Fiona McArdle.

Ms Fiona McArdle

Deputy R&D Director

CC: Mrs Laura Alexander, University of Edinburgh

Appendix F: Study Protocol

THE UNIVERSITY of EDINBURGH

Study Protocol

Patient Self-Management in Multiple Sclerosis: the role of depression, value-based living and perceived clinician empathy.

Protocol Authors

Laura Alexander

Dr Paul Morris

Dr David Gillespie

LIST OF ABBREVIATIONS

ACCORD	Academic and Clinical Central Office for Research & Development - Joint office for University of Edinburgh and NHS Lothian
ACT	Acceptance and Commitment Therapy
ARRNC	Anne Rowling Regenerative Neurology Clinic
CARE Measure	Consultations and Relational Empathy Measure
ELS	Engaged Living Scale
HADS	Hospital Anxiety and Depression Scale
ICD-10	International Classification of Diseases - 10
LTC(s)	Long Term Condition(s)
MS	Multiple Sclerosis
MSIS-29	Multiple Sclerosis Impact Scale - 29
MSSM-R	Multiple Sclerosis Self-Management Scale - Revised
PA	Patient Activation
PAM	Patient Activation Measure
PwMS	Persons with Multiple Sclerosis
QoL	Quality of Life
VBL	Value-Based Living

SUMMARY

Multiple Sclerosis (MS) is a complex, unpredictable illness and self-management is a key treatment component. Research shows that Patient Activation, the willingness and capacity of a person to take on the role of self-managing their health, is a key concept of effective self-management and health outcomes. However, levels of Patient Activation in those with long-term conditions can vary. Little research has explored Patient Activation in those affected by MS. Exploring levels of Patient Activation and factors that may influence patient self-management is of value as it can help to identify patient needs in relation to self-management early on and may allow for preparatory or additional support to be provided in order to allow them to gain benefit.

Reasons that individuals may experience low Patient Activation levels may include; the type of MS they have; feeling low in mood; and personal demographic variables like age, gender and level of education. Several variables remain underexplored but seem important to Patient Activation levels including: the severity of symptoms as experienced by the person (regardless of MS type); feeling detached from personal values (often called "value-based living"); and the quality of relationship quality the individual experiences with their healthcare professional (often called "clinician empathy"). The main research question is: do depression, value-based living and clinician empathy explain the variance in Patient Activation levels, over and above patient demographic variables and MS symptom severity?

The design of the study means that participants will answer a set of questionnaires once only. The study will run for 10 months and recruit those attending the Anne Rowling Regenerative Neurology Clinic with a diagnosis of relapsing-remitting or progressive types of MS. Individuals will be informed about the study by a researcher and invited to ask questions. They will be invited to take the information sheet, consent form and questionnaires home to consider. A researcher will contact individuals by phone within one week of being given this information to find out if they wish to take part or not. If individuals would like to take part, they will be invited to complete and return the questionnaires to the clinic by free-post. The questionnaires will ask about factors thought to be important in predicting Patient Activation levels and will take around 30 minutes to complete. Participant data collected will be unidentifiable and used in statistical analysis to address the research questions. Results of the study will be available by Spring/Summer 2018. All participants will be offered a summary of the findings if they are interested. This study is an academic, non-profit piece of work being done as part of completion of the Doctorate in Clinical Psychology at the University of Edinburgh.

1. BACKGROUND

Patient Activation and review of the literature

Interest in patients' self-management of their healthcare is growing as services strive to enhance person-centred approaches and improve quality of life (QoL). Patient Activation (PA) is a key concept which refers to a person's willingness and capacity to take on the role of managing their own health and health care (Hibbard et al., 2004). The Patient Activation Measure (PAM-13; Hibbard et al., 2005) is a measurement scale of Patient Activation asking about patient rated knowledge and beliefs about their condition, confidence in treatment regimens and self-efficacy (Stepleman et al., 2010). The outcome score places an individual at one of four levels of activation, from least activated (1) to most activated (4); the four levels of activation are:

- Level 1: Disengaged and overwhelmed
- Level 2: Becoming aware, but still struggling
- Level 3: Taking action
- Level 4: Maintaining behaviours and pushing further

Research highlights that PA is associated with positive changes in health behaviours, treatment adherence, health outcomes and cost-efficiency related to illness-management (Bodenheimer et al., 2002; Forbat et al., 2009; Hibbard et al., 2007 Hibbard & Greene, 2013).

Individuals with long-term conditions (LTCs) reporting depressive symptomology unsurprisingly report lower levels of PA compared with the general population (Hibbard & Cunningham, 2008; Lester et al., 2007; Nijman et al., 2014; Rijken et al., 2014). PA is typically measured via self-report which may not accord with actual behaviour; although, several studies have shown that increases in PA positively correlate with behaviour such as the uptake of regular exercise and compliance with medication in various health populations, including diabetes and cancer patients (Hibbard et al., 2007; Mosen et al., 2007). These findings provide some evidence that PA may have predictive value in determining those likely to engage in self-management and, for that reason, collecting additional data on outcomes akin to self-management and / or quality of life in illness is clinically useful (NHS England, 2016).

To date, two US studies have explored PA in MS (Goodworth et al., 2016; Stepleman et al., 2010). MS is "a chronic, inflammatory, demyelinating disease of the central nervous system" typically diagnosed between 20-40 years of age (Brück & Stadelmann, 2003). Treatment involves lifelong management of the disease and symptoms through medication, lifestyle changes, physiotherapy and ongoing contact with services. Self-management is therefore considered a key component of MS care (Bishop & Frain, 2011). The levels of PA observed in people with MS (PwMS) in the US appear to be largely in line with levels of PA in other LTCs (e.g. diabetes, cancer) according to Hibbard & Cunningham (2008). One difference was that a majority of MS patients scored within a range indicating PA level 3, unlike other chronic disease groups with a majority scoring PA level 4 (Stepleman et al., 2010). The authors suggest the differences may be attributable to the unpredictability of MS symptom relapses and reliance on relationships with healthcare providers which may differ somewhat from other LTCs.

Variables associated with PA in MS

Stepleman, Goodworth and colleagues also found significant negative correlations between PA and depression, and significant positive relationships between PA and outcomes of psychological wellbeing. Additionally, PA was greater in employed, higher-educated participants, similar to findings from papers exploring other LTCs. One surprising outcome was that a positive relationship was observed between PA and medication adherence in PwMS but the relationship did not reach the levels of significance expected in accordance with the wider literature (Bodenheimer et al., 2002; Forbat et al., 2009). Goodworth et al. (2016) have published figures suggesting demographic variables, MS-related variables, depression, QoL and self-efficacy account for approximately 35 percent of the variance in PA.

Psychological variables associated with PA

The literature surrounding patient self-management and QoL in MS conveys the importance of processes aiming to promote positive experiences for patients both inside and outside of the clinic. With the increasing popularity of Acceptance and Commitment Therapy (ACT; see Hayes et al., 1999 for full details) in the treatment of psychological difficulties in LTCs, interest is growing around the role of value-based living (VBL) in psychological outcomes. VBL is defined as the extent to which a person is living in accordance with personally-valued aspects of life and has received relatively less attention than other constructs related to ACT (Wilson et al., 2010). Lundgren et al. (2008) found evidence that VBL mediated seizure activity and QoL outcomes in depressed epilepsy patients; while Ciarrochi et al. (2011) has shown that VBL was related to improved outcomes on measures of wellbeing and distress in a sample of cancer patients. In PwMS, ACT processes have been shown to be stronger mediators of psychological outcomes, compared with Cognitive Behaviour Therapy processes, although no measure of VBL was included (Ferenbach, 2011). Despite limited studies, the above papers provide preliminary evidence that VBL is meaningful in relation to QoL and illness management in LTCs. As such, there would appear to be a reasonable basis on which to propose VBL may be an important factor in relation to PA in PwMS.

Clinician variables associated with PA

Within the clinic, the patient-clinician relationship may be another key aspect of patients' willingness to participate in autonomous illness management processes, such as presenting to healthcare providers for routine or acute care or following treatment plans agreed with professionals. There is recognition that an effective, empathic and mutually respectful patient-clinician relationship is a vital component of establishing patient engagement in healthcare and treatment (Rieckmann et al. 2015). Remington et al. (2013) reports that "patients who believe they have a high-quality relationship with their clinician are more likely to follow treatment recommendations" and that the longevity of the therapeutic relationship is especially important in LTCs like MS. Positive patient perceptions of communication and partnerships with their clinician is shown to increase patient confidence in healthcare processes and is an independent predictor of patient satisfaction with the clinical encounter (Little et al., 2001; von Puckler, 2013). It is therefore further hypothesised that the therapeutic relationship between MS patients and clinicians would also be a meaningful component to consider in the context of PA and self-management behaviours in MS.

The role of VBL on depression and symptom severity

Relatedly, the wider, more pernicious impact of depression in MS has been observed in poorer outcomes relating to physical health and illness management, with lifetime prevalence rates of around 50% for depression compared with an estimated 10–15% in the general population (Schubert & Foliart, 1993; Siegert & Abernethy, 2005). Evidence suggests that depression has a stronger association with patient-reported symptom severity than biological markers of disease progression (Chwastiak et al. 2002; Mohr e*t al.,* 2001); while DiMatteo et al. (2000) has noted that depressed patients are more likely to be non-adherent to treatment recommendations than their non-depressed counterparts. The direction of the association between depression and severity of symptoms in MS is unclear but is likely to affect engagement with positive, meaningful experiences linked with quality of life (Devins & Binik, 1996). Therefore, there appears to a precedent for examining the role of VBL in depression and anxiety, beyond MS symptom severity, in PwMS in order to understand how improvements in QoL may be facilitated.

1.1 RATIONALE FOR STUDY

PA is particularly relevant in illnesses which are long-term and progressive. Unsurprisingly, researchers have tried to understand PA by focusing in on groups of people categorised by their particular long-term conditions, including cancer, diabetes and heart disease. To date, people affected by MS have received little attention in relation to understanding PA in an outpatient sample of PwMS in the UK.

To better understand who is most likely to experience low levels of PA, a number of researchers have attempted to identify predictor variables. Current understanding defines predictor variables as baseline variables accounting for better or worse outcomes regardless of the condition. Whilst there seems to be a large number of variables relating to biological, psychological and social factors in predicting levels of PA, a relatively limited number of variables have been explored in those with MS including, biological characteristics (e.g. MS type), depression and sociodemographic variables (e.g. age, gender and level of education). It is proposed that exploring factors that are predictive of PA levels can inform interventions which can improve patient self-management and enhance health outcomes and quality of life in those with MS. This is important as patient disengagement in illness is costly to both the individual and health and public services. Further, if individuals are not receiving the support they need to allow them to better self-manage, this can impact on those around them (e.g. families, carers and support systems).

There are potentially important variables that have not been examined. This study will focus on some of these underexplored variables including, MS symptom severity, value-based living and clinician empathy. The predictive value of less explored variables in PA levels over and above better known variables will be analysed.

Alongside the research mentioned above, a number of studies have also explored the link between PA and the uptake of health-promoting behaviours such as exercise, diet and adherence to medication. Few, if any, studies have attempted to link PA levels with the uptake of self-management behaviours in PwMS. This is possibly due to a lack of quality methods of measuring self-management in MS and the limitations of self-report measures. Nevertheless,

it would be a valuable contribution to the limited literature in this area as it is unclear how PA levels translate into self-management behaviours specific to MS. This study will also explore whether PA levels are associated with patients' own reports of their engagement in self-management behaviours associated with MS.

Finally, the wider impact of depression in MS has been shown to relate to poorer outcomes in physical health. Research has shown that those affected by MS who are depressed experience their symptoms as more severe than those who are not depressed. The reason for this is unclear but may be related to experiencing less positive or meaningful experiences in life as a result of pain or low mood. Value-based living may be a useful factor to examine in relation to mood and anxiety in PwMS, more so than MS symptom severity. Further, VBL may act as a moderator variable in the relationship between depression and symptom severity. Moderators influence the magnitude of the relationship between two variables and, potentially, identify subgroups of people who are more or less likely to experience change. It is, therefore, lastly proposed that this study should examine the role of value-based living in depression and anxiety and whether value-based living is a moderator variable where there is a relationship between depression and severity of MS symptoms.

The proposed hypotheses for this study are:

1. Depression, value-based living and clinician empathy will significantly predict Patient Activation levels over and above patient demographic variables and MS symptom severity.

2. Higher Patient Activation will be linked to greater uptake of self-management behaviours associated with MS.

3. Value-based living and clinician empathy will significantly predict depression and anxiety over patient demographic variables and MS symptom severity.

4. Value-based living will moderate the relationship between MS symptom severity and depression.

2. STUDY OBJECTIVES

Primary Objectives

The primary objective of this study to address the research question:

1. Are depression, value-based living and clinician empathy significantly predictive of Patient Activation over and above patient demographic variables and MS symptom severity?

2. Is higher Patient Activation linked to greater uptake of self-management behaviours associated with MS?

3. Are value-based living and clinician empathy significantly predictive of depression or anxiety over and above patient demographic variables and MS symptom severity?

4. Does value-based living moderate the relationship between MS symptom severity and depression?

Secondary Objective

The secondary research objectives of this study are to address the following research question:

To explore what levels of Patient Activation are present in an outpatient group of MS patients in the UK.

3. STUDY DESIGN

It is anticipated that this study will run for approximately 10 months in a single-site using a cross-sectional sample of patients attending outpatient appointments at the Anne Rowling Regenerative Neurology Clinic (ARRNC), Edinburgh Royal Infirmary in NHS Lothian. The data will then be examined using multiple hierarchical regressions, correlation and moderation analyses to address the research questions. Participants will be asked for some demographic information (e.g. age, gender, level of education). The case for collecting sociodemographic data in the current study is indicated by previous papers which have established these variables account for around 10% of the variance in Patient Activation levels (Goodworth et al., 2016). They will also be asked to complete six self-report questionnaires (detailed below) measuring: Patient Activation; MS symptom severity; value-based living; depression; the patient-clinician relationship; and MS self-management behaviours. The six self-report measures are:

Outcome measures

1. *The Patient Activation Measure – 13 (PAM-13; Hibbard* et al*., 2005)*

The PAM-13 is a 13-item self-report instrument assessing patient skill, knowledge and confidence in self-management of their illness. Responses to items such as "I am confident that I can follow through on medical treatments I need to do at home" are rated from "strongly disagree" to "strongly agree." Scoring is converted to a scale of 0-100, where higher scores illustrate higher levels of Patient Activation.

The scale exhibits good psychometric properties, demonstrating high internal reliability (α = .88). Dimensions measuring preventative, consumeristic and disease self-management behaviours are strongly associated with activation scores, suggesting strong construct validity (Hibbard et al., 2004; Hibbard et al., 2005). A recent study has validated the PAM-13 in an MS clinic sample (Stepleman et al., 2010). Results suggest the measure demonstrates good Rasch person reliability (α = .83), Rasch item reliability (α = .98) and comparable internal reliability coefficient for MS populations (α = .88). Strong construct validity is reported as with the previous papers, indicating that the scale is a robust and suitable measure for use with the MS population. The brevity of the scale also has considerable utility in clinical settings.

2. *The Multiple Sclerosis Impact Scale (MSIS-29; Hobart* et al*. 2001)*

The MSIS-29 is a self-report measure of MS symptoms with two subscales measuring severity of physical and psychological symptoms of the disease. The current study will use only the physical subscale of the MSIS-29 as Ferenbach (2011) reports that the psychological subscale may demonstrate some theoretical overlap with outcome measures of psychological distress. The strong psychometric properties outlined below suggest the sole use of the physical subscale in the current study is suitable. Statements are rated on a 5-point Likert scale (1 = not at all to 5 = extremely) and pertain to the patients' experience of MS symptoms. The measure was developed from original 129 items generated from interviews with MS patients and allows for a disease-specific measurement of symptom impact as captured by the patients' perspective; this is not offered by other existing scales (Hobart et al., 2001).

Hobart et al. (2001) report the MSIS-29 physical subscale displays low floor and ceiling effects, good levels of variability and excellent test-retest reliability ($r \geq 0.87$) and internal consistency ($\alpha \geq 0.91$) among a random sample of individuals with relapsing-remitting and progressive types of MS. The physical scale is responsive to symptom change (effect size g = .82). Hobart et al. (2005) have found the MSIS-29 physical scale to be more sensitive to detecting change in physical MS symptoms, compared with various well-established scales like the Short-Form Health Survey (SF-36; Ware et al*.,* 1992) and the Expanded Disability Status Scale (EDSS; Kurtzke, 1983) over time (see Costelloe et al., 2007 for details).

3. *The Engaged Living Scale (ELS; Trompetter* et al*., 2013)*

The ELS measures the extent to which a person is engaged in committed action towards their values and relates to the valued living aspect of the ACT model. It is a 16-item self-assessment tool rated on a 5-point Likert scale (1 = not at all to 5 = totally agree) and total scores range from 16 to 80, with higher scores demonstrating better engagement in value-based living. Statements include: "I have values that give my life meaning." The ELS consists of two subscales measuring valued living and life fulfilment.

Trompetter et al. (2013) have evaluated the psychometric properties of the scale in a non-clinical sample and a clinical sample consisting of chronic pain patients undergoing an online ACT intervention. The two subscales and total scale of the ELS demonstrate good to excellent internal consistency (Valued Living and Life Fulfilment α = .86; Total Scale α = .90). The outcomes on the ELS show positive correlations with related theoretical process variables from the ACT model (mindfulness and acceptance) and outcome variables in mental health (pain interference in daily life, anxiety, depression and psychological wellbeing) (Trompetter et al., 2013). Moreover, this paper found the clinical sample to score lower on this scale, suggesting greater discrepancy between values and behaviour compared with a normative population. It is felt that the ELS is a suitable measure for engagement in value-based living for this project given its brevity and the chronic pain sample used in psychometric evaluation of the paper may not be too dissimilar to the sample included here.

4. *The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983)*

The HADS is widely used in both clinical and research settings (Herrmann, 1997). It is a brief 14-item measuring anxiety and depression. The two subscales can be summed to give a total score of psychological distress. In the current study, both subscales will be used; depression scores will be included for the main analysis and anxiety scores will be included for exploratory analysis. The HADS has good psychometric properties. In a large (N = 1792) UK sample (Crawford et al., 2001), the anxiety and depression subscales were found to have α values of .82 and .77 respectively, with the total score yielding a value of .86. The correlation between the subscales was found to be moderate in magnitude (r = .53).

Being a brief measure, the HADS has a low item burden, and is easy to complete. Hence, it was considered suitable for use in this study. It has been used previous research with PwMS (Spain et al., 2007; Vaughan et al., 2003), including research validating the HADS for use with PwMS (Honarmand & Feinstein, 2009). Results of reliability and validity in the HADS are shown to be unaffected by cognitive impairment in MS (Gold et al., 2003).

5. *The Consultation and Relational Empathy Measure (CARE; Mercer* et al*., 2004)*

The CARE Measure is a patient-reported assessment of doctors' communication and empathy in the consultation and takes around 5-10 minutes to complete. The items included are theoretically grounded in the concept of empathy in the clinical context (see Mercer et al., 2004 for full details). It consists of ten items asking about the ability of the doctor to understand and respond to patient concerns (e.g. "How was the doctor at showing care and compassion?"). It is rated on a 5-point Likert scale (1 = poor to 5 = excellent), with scores ranging from 10 to 50. Higher scores indicate higher perceived empathy. The measure demonstrates high internal reliability, with a Cronbach's alpha of .93 and has strong correlations with established measures of empathy such as the Reynolds Empathy Scale (r = .84) and the Barrett-Lennard Empathy Subscale (r = .85).

This measure was selected for the current study as it has demonstrated validity in both doctor and nursing consultations and has a similarly high internal consistency (α = .97; see Bikker et al., 2015). Validation among professionals is considered important in the current study given both doctors and nursing staff lead consultations in MS clinics. Additionally, a variety of patient demographics and symptom presentations are observed in the MS population suggesting the need for a measure which can produce a score that is unaffected by patient characteristics. Bikker et al. (2015) has found scores from the measure to be unrelated to age, gender, employment, self-reported general health and language spoken. Patient reports also suggest that the brevity and relevance of the measure are endorsed across various sociodemographic groups (Mercer et al., 2005).

6. *The Multiple Sclerosis Self-Management Scale-Revised (MSSM-R; Bishop & Frain, 2011)*

The multidimensional measure comprises of 24 items assessing self-management knowledge and behaviors in adults with MS. The scale factors include: relationship/communication with health professionals; treatment-related barriers and adherence; social supports; knowledge and information about MS; and health maintenance behaviours. Ratings are made on a frequency-based scale from 1 (disagree completely) to 5 (agree completely), with higher scores indicating better self-management. One notable criticism of the scale is outlined by Ghahari et al. (2014) suggesting the MSSM-R may lack additional self-management items relevant for MS; however, it is currently the only measure that especially addresses self-management among those with MS. An MS-specific measure was felt to be important for the current study.
The authors cite good internal consistency (Cronbach's α = .85) for the overall scale in a postal survey of patients reporting all types of MS. Wilski et al. (2015) have subsequently reported a higher reliability figure (Cronbach's α = .90) in their study. Four factors are shown to demonstrate reliability coefficients above .70, and one (health maintenance behaviours) was found to be .59, below acceptable guidelines (Nunnally, 1978). For this reason, Bishop & Frain (2011) recommend the use of the composite scale in research. Further psychometric evaluation has shown the MSSM-R demonstrates satisfactory to good test-retest reliability, moderate to high criterion validity for the factor structure against well-established measures, and moderate face validity (see Ghahari *et a*l., 2014 for full details).

Procedure

Data for this study will be collected from adults attending the ARRNC. The ARRNC manager will be a primary point of contact and will inform MS clinicians about the study by providing an information sheet outlining the purpose of the research.

MS clinicians will inform the researcher of potential participants attending that day who meet the study inclusion / exclusion criteria from their clinic list. The principal research or a research assistant will be present in the ARRNC 2 days per week to recruit. The researchers will approach those potential participants during their attendance at the ARRNC and explain verbally the purpose of the study and that participation is entirely voluntary. Potential participants will also be given an information sheet and the opportunity to ask any questions at this point. This will ordinarily happen in the waiting area before or after appointments. Alternatively, MS clinicians will introduce the study and provide an information sheet to potential participants during appointments.

If initially interested, participant contact details will be requested for the researchers to make contact with the potential participant no less than 24 hours and within 1 week of being introduced to the study. Potential participants will be invited to take home a research pack containing: the participant information sheet, a consent form, the questionnaires and a return stamped envelope. To ensure responses remain anonymous, measures will have a unique identifier. At this point, potential participants will be informed that taking a research pack home does not imply consent and they may choose not to participate even if they accept a research pack.

If the individual agrees to take part, they will be invited to complete the questionnaires at home and return to the ARRNC via post. Some participants may prefer to complete the questionnaires in the waiting area and return the research pack in person. If the individual does not wish to participate, they will be thanked for their consideration and their details removed from the study list to ensure they are not contacted again regarding the same study

Duration of participant involvement

The recruitment phase of the study is expected to last for approximately 10 months; anticipated to start in December 2016. Early termination of the recruitment period will be considered if the desired sample size of 120 participants is achieved. The last contact by the principal researcher is expected to be in June 2018 to provide a summary of the findings to participants following completion of the thesis. Therefore, the maximum time a participant will be involved in the study will be 19 months (if recruitment occurs in the first month) and the minimum time involved in the study will be 9 months (if recruitment occurs in the final month).

4. STUDY POPULATION

Number of participants

The current study aims to recruit, on average, 12 MS patients per month to obtain a desired sample size of 120 participants. The recruitment period allocated for this study will be 10 months which will be monitored and reviewed regularly to identify risks of under-recruiting quickly.

Inclusion criteria

- Participants will be aged 18 years or over.
- Participants will have a diagnosis of either relapsing-remitting or progressive types of MS according to ICD-10 criteria, with the diagnosis given by a Neurologist.

Exclusion criteria

- Individuals who have not experienced an MS-related disability or impairment for 12 months or more.
- Individuals with significantly impaired intellectual or cognitive functioning (e.g. diagnosis of a moderate-severe learning disability or dementia) or severe mental health problems that may impede their ability to provide informed consent, understand or complete questionnaires.
- Individuals, who are unable to provide informed consent, understand or complete questionnaires due to poor proficiency in the English language. The questionnaires used in this study have been standardised in the English language and translating these documents will affect the psychometric properties of the questionnaires. This will significantly impact on the reliability and validity of the study results.

Identifying participants

Potential participants will always be initially identified by MS clinicians (Neurologists and Specialist MS Nurses) conducting outpatient clinics in the ARRNC. If individuals meet inclusion criteria for the study, they will be approach in person and provided with a verbal explanation of the purpose of the study and an information sheet upon contact with the principal researcher, research assistant or MS clinician. Contact details will be requested from potential participants and permission sought to contact them by telephone within 1 week and always 24 hours following introduction to the study. They will then be invited to complete a consent form if they are interested in participating in the study.

Consenting participants

Once appropriate candidates for the study have been identified by MS clinicians, they will be approached by the principal researcher, research assistant or MS clinician about the study while they are in the ARRNC. A verbal explanation of the study will be provided and potential participants will be invited to read over the participant information sheet. They will also have the opportunity to ask any questions they might have regarding the study. A request will be made for the contact details of potential participants' and permission to contact them with 1 week and always 24 hours after being given this information. This is for the purposes of finding out whether they would like to take part or not following the "cooling off" period. This will allow

potential participants to consider their thoughts and questions before making a decision about participation. Upon making contact, the researcher will invite any additional questions about the study from potential participants prior to seeking their consent. All potential participants will be told they have the right to refuse or withdraw consent to take part in the study at any time. Participants who give consent will be asked to return their signed consent form with the completed questionnaires via post or in person to the ARRNC. A consent form will be provided in the research pack taken home by potential participants to allow them to consider the full parameters of what they are consenting to.

5. STATISTICS AND DATA ANALYSIS

Sample size calculation

Regression, moderation and correlational analyses will be used in this study. The statistical software G*Power 3 (Faul et al., 2009; available from: http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3) was used to obtain an a priori sample size for the analysis requiring the highest number of participants in the current study. The sample size calculated for the multiple hierarchical regression analysis thereby provides sufficient power to run the other proposed analyses in this study.

The calculation is based on conventional guidance assuming a medium effect size (Cohen, 1988), a power level of .80 and an alpha level of .05 (Sink & Stroh, 2006). The result indicated a minimum sample size of 85 is required to run the proposed multiple hierarchical regression analyses; with four predictor variables entered first (age, gender, level of education and MS symptom severity), followed by another three predictors (depression, patient-clinician relationship and value-based living) hypothesised to be important within the current study. However, a paper by Green (1991) presents sample size calculations by Cohen (1988), based on the same assumptions above, which indicates a sample of 108 would be desirable for a multiple regression with seven predictor variables to achieve a medium effect size. However, to have sufficient power to detect a more clinically meaningful effect size, this study will seek to recruit 120 participants to ensure, as far as possible, that the aims of the project can be sufficiently addressed.

Discussions with clinicians at the ARRNC suggest that those affected by MS are a motivated participant group, with an estimated 40 per cent response rate to postal surveys. Higher postal response rates have been cited in UK studies by the MS Society (available at: https://www.mssociety.org.uk/ms-resources/lottery-treatment-and-care-technical-report) and by Manouchehrinia et al. (2015) with response rates of 44% and 54%, respectively. Further, Nakash et al. (2006) report that postal responses can be improved in health populations by offering telephone reminders.

Clinicians at the ARRNC have provided the following information which suggests obtaining a sample size of 120 over a 10-month recruitment period is a viable aim:

- Approximately 2000 patients, receiving ongoing input, are held on the MS service database in Lothian.
- Between 15-18 patients attend clinics per day, with clinics operating 5 days per week. An estimated 300-360 patients are seen per month.
- The majority of patients attend appointments at the MS clinic once or twice per year.
- It is estimated that approximately 70% (250 patients) attending per month will meet the inclusion criteria for the current study.
- Three clinicians (2 specialist MS nurses and a Neurologist) in Lothian have reported confidence in obtaining a sample size of 120 participants in the proposed recruitment period with the data collection method outlined.

Although recruitment difficulties are not anticipated in NHS Lothian, ethical approval would be sought to recruit from another NHS site at a later point in the event that difficulties arise (e.g. attrition rates being unexpectedly high). A pre-emptive step has been taken by approaching NHS Greater Glasgow and Clyde and NHS Fife to ask if they would be willing to assist with

recruitment in the event of under-recruiting in Lothian. The initial IRAS application seeks to recruit from a single site (NHS Lothian) in the first instance.

Proposed analyses

Primary research questions:

1. Are depression, value-based living and clinician empathy significantly predictive of Patient Activation levels over and above patient demographic variables and MS symptom severity?

To address primary research question 1, hierarchical multiple regression analysis will be used. Data screening, prior to analysis, will examine whether the assumptions of the regression are met. These include: missing data; normality, linearity and homoscedasticity of residuals; curvilinearity; heterogeneous variance; and influence of outliers (Tabachnick & Fidell, 2014). To examine the variance explained by depression, value-based living and the patient-clinician relationship, over and above patient demographic factors and MS symptom severity, the measure of self-reported Patient Activation will be fixed as the dependent variable. Age, gender, level of education and MS symptom severity will be entered in the initial step. Depression, value-based living and the patient-clinician relationship will then be entered in the second step to examine changes in the variance in Patient Activation.

2. Is Patient Activation linked to MS-specific self-management behaviours?

Primary research question number 2 will be explored through a correlation analysis examining the association between Patient Activation and self-management behaviours associated with MS. Previous data screening, will examine whether the required assumptions of the regression are met.

3. Are value-based living and clinician empathy significantly predictive of depression or anxiety over and above patient demographic variables and MS symptom severity?

Primary research question number 3 will be addressed using two separate hierarchical multiple regression analyses. Previous data screening, will examine whether the required assumptions of the regression are met. Predictive values of value-based living and clinician empathy over and above patient demographic factors and MS symptom severity, will be examined by fixing depression as a dependent outcome variable in one analysis and anxiety as a dependent outcome variable in a second analysis. Age, gender, level of education and MS symptom severity will be entered in the initial step in both analyses. Value-based living and the patient-clinician relationship will then be entered in the second step of both analyses to examine changes in the variance in both depression and anxiety.

4. Does value-based living moderate the relationship between symptom severity and depression?

Primary research question number 4 will be addressed using moderation analysis. For testing moderation, several papers recommend moderated regression analysis to examine interaction effects (Cohen & Cohen, 1983). Value-based living will be examined as a moderator of depression and MS symptom severity. Depression and value-based living will be entered in the first step of the regression analysis. In the second step, the interaction terms between depression and value-based living will be entered. A significant increase in the variance of

patient-reported MS symptom severity following the second step of the regression analysis will indicate a moderating effect of value-based living (Cohen & Cohen, 1983; Kleinbaum et al., 1988).

Secondary research question:

What levels of Patient Activation are present in an outpatient group of MS patients in the UK?

To address the secondary research question, descriptive statistics will be used to demonstrate the range of patient demographic information and Patient Activation levels in the sample.

6. REPORTING PUBLICATION AND NOTIFICATION OF RESULTS

The results of the study will be written up in a thesis format and submitted to the Doctorate of Clinical Psychology at the University of Edinburgh. The format of the thesis will include both a systematic review and a journal article. It is the intention of the principal researcher to submit both for publication to a journal relevant to clinical and health psychology. The results of the study will also be presented within NHS Lothian MS services. Where participants have indicated they wish to receive a written summary of the findings from the study, these will be sent to individuals via post. A summary of the findings and the final journal article will also be made available to the MS Society for dissemination of the findings to the wider population of those affected by MS.

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APPENDIX 1: GLOSSARY OF TERMS FOR REFERENCE

ACCEPTANCE and COMMITMENT THERAPY – A psychological intervention that uses acceptance and mindfulness strategies and a commitment to changing behaviour to help a person adapt to and cope with changing circumstances or demands in their life.

ANNE ROWLING REGENERATIVE NEUROLOGY CLINIC – A charitable research facility of the University of Edinburgh which specialises in neurological conditions like Multiple Sclerosis.

CLINICIAN EMPATHY - The extent to which a patient feels listened to and understood by their healthcare professional during the clinical consultation process.

DEMOGRAPHIC VARIABLES – Characteristics of a population of people such as age, gender and level of education.

DEPRESSION - A group of symptoms that include: low mood or negative emotion that lasts for a period of two weeks or longer which is present in most situations; feelings of worthlessness; loss of enjoyment in previously enjoyed activities; low energy and motivation; sleep and appetite disturbances (including over/under eating or sleeping); poor concentration and memory; and lowered sex drive. This list is not exhaustive of the symptoms experienced.

INTERNATIONAL CLASSIFICATION OF DISEASES -10 (ICD-10) – A list of medical classifications of physical and mental disease and codes published by the World Health Organisation which includes symptoms and treatments.

LONG TERM CONDITIONS - A condition that cannot be cured with current medical knowledge but can be managed with medication and other therapies. Examples of Long Term Conditions are diabetes, heart disease and MS.

MULTIPLE SCLEROSIS (MS) - A chronic disease which gets worse over time. It involves damage to the sheaths of nerve cells in the brain and spinal cord. Symptoms can include numbness, severe fatigue, pain, mobility problems and impairment of speech and of muscular coordination. This list is not exhaustive of symptoms experienced.

MS TYPE – Those affected by MS can be diagnosed with “relapsing-remitting” or “progressive” types of MS. With relapsing remitting MS, people have “attacks” of symptoms which then fade away either partially or completely. Around 85 per cent of people with MS are diagnosed with this relapsing-remitting MS. Secondary progressive MS comes after a diagnosis of relapsing-remitting MS and is thought to be a result of a build-up of damage to nerve cells by “attacks.” Primary progressive MS is rarer and affects about 10 to 15 per cent of people diagnosed with MS. Symptoms gradually get worse over time, rather than appearing as “sudden attacks.”

PATIENT ACTIVATION - The willingness and capacity of a person to take on the responsibility of self-managing their own health. It is measured by the Patient Activation Measure (PAM-13) which asks about a person’s knowledge, beliefs, confidence and self-efficacy in relation to managing a health condition. Resulting scores on the PAM-13 places people on one of four levels of activation. Levels range from: Level 1: Disengaged and overwhelmed; Level 2: Becoming aware, but still struggling; Level 3: Taking action; Level 4: Maintaining behaviours and pushing further.

QUALITY OF LIFE - The standard of health, comfort, and happiness experienced by an individual or group.

SYMPTOM SEVERITY - How severe a physical symptom feels in terms of intensity, sensation or duration.

VALUE-BASED LIVING - The extent to which a person is engaged with living in line with their personally held values. Values differ from person to person, as do the levels of importance people place on their values. Self-assessment of value-based living is completely subjective.

VARIANCE - The variation of a characteristic in a population (e.g. levels of height will vary within a population).

Appendix G: Study Information Sheet

THE UNIVERSITY of EDINBURGH

NHS Lothian

Participant Information Sheet and Consent Form
Patient Self-Management in Multiple Sclerosis: the role of depression, value-based living and perceived clinician empathy.

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?
The purpose of the study is to investigate patient self-management in people with Multiple Sclerosis, also known as 'Patient Activation', and the factors which may influence this. 'Patient Activation' reflects the willingness of a person to self-manage their health condition, as well as their ability to do so. This is important for effective self-management and better health. Studying patient self-management is important to better identify the needs of people with MS in relation to self-managing their illness and to understand what additional support is needed. This study hopes to recruit 120 people to fulfil the purpose of this research.

Why have I been asked to take part?
You have been asked to take part as you have been previously diagnosed with Multiple Sclerosis (MS) and attend the Anne Rowling Regenerative Neurology Clinic to see an MS clinician.

Do I have to take part?
No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive, or your legal rights.

What will happen if I take part?
Your involvement in the study will take around 30 minutes in total. You will be asked for some demographic information and provided with six questionnaires to complete asking about: 'Patient Activation'; self-management activities related to MS; MS symptoms; mood; the relationship you have with your MS clinician; and value-based living.

If you think you might like to take part, you will have the opportunity to ask further questions. We will provide you with a research pack containing a consent form and the questionnaires. You will be given additional time to think about taking part and we will ask for your contact details and permission to contact you within 1 week and always at least 24 hours after being given this information. This is to find out your decision and remind you to return the consent form and questionnaires if you still wish to take part. You have the right to change your mind

about participating in the study or withdraw at any time. If you decide you no longer wish to take part or you decide to withdraw from the study, this will not affect you or the care you receive at the clinic in any way.

What are the possible benefits of taking part?
You may not directly benefit from taking part in this study, although the findings may be useful or interesting to you. It is hoped that the results from this study will inform on the future healthcare of other patients. It is hoped that in the longer term, MS services developing patient-centred approaches to the care and management of patients will benefit from the results of this research.

What are the possible disadvantages and risks of taking part?
It is not thought that there are many disadvantages, however, we recognise there might be a burden of time (30 minutes on average). In addition, completing the questionnaire asking about your mood may highlight some concerns for individuals around their own mood and wellbeing. If you feel concerned about your mood or you think you might need some support, please speak to your GP or an MS clinician to discuss this further.

Will my taking part in the study be kept confidential?
Information will be collected by questionnaires. All information which is collected about you during the course of the research will be kept strictly confidential and any information about you which leaves the clinic will have your name, address and other identifiable information removed so that you cannot be recognised. The researchers may need access to some of the data in your medical records to carry out this research.

To ensure that the study is being run correctly, we will ask your consent for responsible representatives from the Sponsor (University of Edinburgh) and NHS Lothian to access your medical records and data collected during the study, where it is relevant to you taking part in this research. The Sponsor is responsible for overall management of the study and providing insurance and indemnity. With your consent we will inform your GP that you are taking part.

Will my information be shared?
For the purposes of making improvements to their questionnaires, some organisations ask that data from their questionnaires is sent back to them. Before the data is sent back it is made completely unidentifiable.

Unidentifiable questionnaire responses will be shared with Insignia Health LLC who hold the exclusive rights to the Patient Activation Measure (PAM), one of the questionnaires you would be asked to complete. Participant's identity and personal information will not be shared with Insignia Health LLC.

Insignia Health will not alter your data, share it with other parties, or publish results. They will only use unidentifiable data to continually improve the Patient Activation Measure (PAM) and its guidelines for use.

What happens when the study is finished?
At the end of the study we will analyse the data collected and the results will be written up as a research report. Personal data collected during the study will be disposed of securely within 12 months after the study has ended.

Unidentifiable research data (data from which no individuals could be identified) will be archived and stored at the University of Edinburgh, where it will be used to assist publication of results from the project and to facilitate relevant secondary uses which the project team deem would enable additional public benefit.

What will happen to the results of the study?

The study will be written up in the format of a thesis and submitted to the University of Edinburgh for scientific review. It is intended that a paper will be submitted for publication to a scientific journal in the field of clinical and health psychology. You will not be identifiable in any published results. A summary of the findings from the study will be made available to participants who indicate they would like to receive this. This summary would be sent to participants by post.

Who is organising the research and why?
This study is being done in fulfilment of the requirements of the Clinical Psychology Doctoral Training Programme at the University of Edinburgh. It is an academic, non-profit piece of work but may receive some financial support from the University of Edinburgh and NHS Lothian.

Who has reviewed the study?
The study proposal has been reviewed by NHS South West Exeter Research Ethics Committee. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. A favourable ethical opinion has been obtained from NHS South West Exeter REC. NHS management approval has also been obtained.

Can I speak to someone after I have taken part?
You may wish to ask further questions about the study or reflect on your experience of answering the questionnaires after taking part. If you would like to discuss anything after participating, you can contact the researcher on the telephone number provided below. The researcher will ask you what you would like to discuss and focus on addressing your questions, thoughts or issues raised in relation to the study.

If the researcher has any further concerns about you following the discussion, they would share this information with your direct clinical care team within the MS service. They may also contact your GP if necessary; however, we would always try to speak to you about this first.

If you would like to discuss anything about the study before or after taking part, please contact:
Laura Alexander, Trainee Clinical Psychologist / NHS Lothian
School of Health in Social Science,
Doorway 6, Medical Quad, Teviot Place
Edinburgh
EH8 9AG
Tel: 07979 375799 Email: s1578313@sms.ed.ac.uk

If you would like to discuss this study with someone independent of the study please contact:
Azucena Guzman, Lecturer in Health and Ageing, University of Edinburgh
Room 2.10, Doorway 6, Medical Quad, Teviot Place
Edinburgh
EH8 9AG
Tel: 0131 651 5162 Email: Azucena.Guzman@ed.ac.uk

If you wish to make a complaint about the study please contact NHS Lothian:
NHS Lothian Complaints Team
2nd Floor, Waverley Gate, 2 - 4 Waterloo Place
Edinburgh
EH1 3EG
Tel: 0131 536 3370 Email: feedback@nhslothian.scot.nhs.uk.

Thank you for taking the time to read this information sheet.

Appendix H: Study Consent Form

THE UNIVERSITY of EDINBURGH

NHS Lothian

CONSENT FORM
Patient Self-Management Study

Participant ID: ☐

Laura Alexander, Trainee Clinical Psychologist / NHS Lothian
School of Health in Social Science, Doorway 6, Medical Quad, Teviot Place
Edinburgh, EH8 9AG
Tel: 07979 375799 ***Email: s1578313@sms.ed.ac.uk***

Please initial box

1. I confirm that I have read and understand the information sheet (version no. 3, date 20/12/2016) for the above study and have had the opportunity to consider the information and ask questions. ☐

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 relevant sections of my medical notes and data collected during the study may be looked at by individuals from the regulatory authorities and from the Sponsor(s) (NHS Lothian and the University of Edinburgh) or from the/other NHS Board(s) where it is relevant to my taking part in this research. I give permission for those individuals to have access to my records. ☐

4. I agree to my unidentifiable data being shared with Insignia Health LLC for the purposes of ongoing improvements to the Patient Activation Measure. ☐

5. I agree to my General Practitioner being informed of my participation in this study and being contacted should concerns about my wellbeing arise. ☐

6. I would like to receive a summary copy of the study results by post. ☐

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

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature