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Health Locus of Control and Its Relationship with Quality of Life and Functioning in Multiple Sclerosis: Exploring the Mediating Role of Self-Efficacy

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Abstract: Background/Objectives: Health locus of control (LOC) refers to one's perceptions of who or what controls one's health. Recent evidence has found that chance LOC (CLOC) is associated with improved quality of life (QoL) in multiple sclerosis (MS). The purpose of the current study was to identify mediators and moderators of the LOC-QoL relationship in MS. **Methods:** For this study, 5266 participants with MS completed a questionnaire pack that included the Multidimensional Health Locus of Control Scale, the Unidimensional Self-Efficacy Scale for MS (USE-MS), and the World Health Organization Quality of Life Scale—BREF (WHOQoL-BREF). The relationship between LOC and QoL was examined within a structural equation model (SEM). **Results:** In the total sample, self-efficacy was found to fully mediate the relationship between LOC and QoL for both internal (ILOC) and CLOC orientations. Powerful others LOC (PLOC) had no association with QoL. The same results were found for the relationship of LOC to functioning. In the secondary progressive MS subgroup, the relationship between CLOC and QoL was only partially mediated by self-efficacy. **Conclusions:** LOC influences QoL through its impact on self-efficacy, one of several potentially mediating factors between LOC and QoL in MS. Disability did not moderate the associations of LOC, but moderation of the CLOC-QoL relationship by disease subtype was found. Psychological training to improve self-efficacy in MS may be particularly useful in those subgroups where LOC-QoL is largely mediated by self-efficacy.

Keywords: locus of control; quality of life; multiple sclerosis; disability; self-efficacy; TONiC study

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1. Introduction

Multiple sclerosis (MS) is an immune-driven neurological disease that has a profound impact on patients' quality of life (QoL). It has been reported that MS affects approximately 2.3 million people worldwide, and its prevalence is remarkably heterogeneous, varying from 50 to 300 patients per 100,000 inhabitants [1].

Health locus of control (LOC) refers to the individual's beliefs regarding control over health outcomes [2]. The construct is a mix of internal LOC (ILOC), external—powerful others LOC (PLOC), and external—chance LOC (CLOC) [3].

Early studies in MS [4] and other diseases [5,6] reported that an ILOC orientation, rather than PLOC or CLOC, was associated with improved QoL. However, a recent study

conducted in a large sample of patients with MS showed that CLOC was associated with improved QoL compared with other LOC orientations [7]. The authors postulated the following two reasons for this:

(1) The study controlled for level of disability as a confounding factor, thereby accounting for the fact that those with ILOC orientation had lower disability and short duration of disease;
(2) In conditions with heterogenous course and no cure, those who believe that their outcome is controlled by their own actions (ILOC) may engage in self-blame ("I must not be trying hard enough"); if they believe healthcare professionals determine the outcome (PLOC), they may feel resentful ("If they had only found the right drug for me. . ."); and belief in chance (CLOC) may lead to less psychological distress ("Everybody did their best but..."). Studies in cancer [8] and end-stage renal disease [9] have also found worse psychological outcomes related to ILOC. Another recent study found that in individuals with MS whose disability was comparatively more severe, higher CLOC beliefs correlated with improved QoL [10].

A systematic review of the relationship between LOC and MS concluded that this subject had been poorly explored; only one of the nine studies used a rigorous scientific method, and in general, sample sizes were small [11]. The author concluded that future studies should follow a randomized protocol, recruit large samples according to clearly defined inclusion/exclusion criteria, establish control groups, and use a solid conceptual framework.

The Wilson and Cleary model linking clinical variables with health-related QoL provides such a comprehensive framework [12]. This model defines health-related QoL as a product of four other clinical and biological health concepts; QoL is different to any preceding domain and is concerned with aspects of life satisfaction and wellbeing. In full, the model postulates a pathway from 'biological and physiological variables' → 'symptom status' → 'functional status' → 'perceived health' → 'health-related quality of life'. It has been shown that the characteristics of an individual, such as LOC and self-efficacy, can potentially influence QoL and its predictor variables. The Wilson and Cleary model also incorporates the later conceptual model represented by the International Classification of Functioning, Disability and Health (ICF) provided by the World Health Organisation [13].

There are many potential mediators in the LOC-QoL relationship in MS. A recent study in patients with acquired mobility impairment found that self-efficacy, which relates to a person's confidence in their ability to master a situation, fully mediated the relationship between LOC and life satisfaction [14]. Interestingly, the researchers found that 'movement disability' moderated the relationships between external LOC orientations and self-efficacy, in such a way that PLOC for low-disability patients was associated with reduced self-efficacy and PLOC increased self-efficacy in patients with more severe disability. The research group reasoned that in cases of disability, there was a necessity to rely on powerful others. While there is evidence that higher self-efficacy is associated with better QoL in MS [15,16], the role of self-efficacy has not been explored in the context of beliefs about locus of control.

Using a Wilson and Cleary model framework, the current study explores the potential moderating and mediating relationships between LOC, self-efficacy, disability, and QoL according to data from a large-scale study of individuals with MS. Based on the current literature, we hypothesized the following:

(1) self-efficacy mediates the relationship between LOC and QoL and also the relationship between LOC and functioning (disability);
(2) the relationship between LOC and QoL is moderated by level of disability and MS subtype, in such a way that the level of disability or MS subtype changes the emphasis of LOC in relation to self-efficacy.

2. Materials and Methods

2.1. Sample

Participants were recruited into the Trajectories of Outcome in Neurological Conditions-MS (TONiC-MS) study. Eligibility criteria included adults with physician-verified MS (by McDonald criteria [17]) of any disease subtype and level of disability, providing they could give informed consent and complete the questionnaire packs (with the help of a scribe if necessary).

Data on disease subtype at the time of study entry were provided by clinicians involved in the patients' care and classified as relapsing-remitting (RRMS), primary progressive (PPMS), or secondary progressive (SPMS). Duration since diagnosis and Expanded Disability Status Scale (EDSS) band were obtained from medical records; higher bands indicated worse disability. Informed consent was obtained from all participants prior to enrolment.

Participants completed a baseline questionnaire pack including several patient-reported outcome measures (PROMs). The full data were further randomized into 'training' and 'validation' samples. Ethical approval was granted from the relevant research committees (reference 11/NW/0743).

2.2. Patient Reported Outcome Measures

1. World Health Organization Quality of Life Scale—BREF (WHOQoL-BREF), including 24 items covering 4 domains (physical, psychological, social relationships, and environment); a higher total score indicates higher QoL. Two stand-alone questions on QoL and satisfaction with health were not included. The total score from the 24 items, obtained via a bi-factor solution, was used in the current analysis [18,19];
2. Multidimensional Locus of Control Scale (MHLC) Form C, consisting of four domains representing internal (ILOC), powerful others—split into 'others' and 'doctors' but merged together in the current study (PLOC)—and chance (CLOC) [20]. Thus, each domain consisted of six items scored 1–6 (changed to 0–5), giving a domain score of 0–30, with a high score indicating greater emphasis on that domain;
3. Unidimensional Self-Efficacy Scale for MS (USE-MS), derived from a qualitative investigation of how patients with MS understand and express their self-efficacy though statements such as 'Despite my MS, I can do anything I set my mind to', containing 12 items scored 0–3, reflecting the patient's confidence in completing tasks and producing the desired outcomes [21];
4. World Health Organization Disability Assessment Schedule 2.0 (WHODAS-2.0) 32-item version, used in this analysis to report levels of functioning, omitting four items related to work. Higher scores indicate worse disability. This scale has been validated for MS [22,23].

All scales were transformed via Rasch analysis into interval level scales, through the use of previously published nomograms [7,19,21,23,24].

2.3. Analysis

After obtaining the appropriate descriptive statistics, the effect of LOC was examined within a structural equation model (SEM) framework, where it was considered as a variable on the causal paths to both QoL and functioning, mediated by self-efficacy. The results were consistent with the Wilson and Cleary model, with the characteristics of individuals being found to influence both functioning and QoL. Age and duration were also considered in the models. Various scales were included in the model as single-indicator latent variables, based on Rasch-transformed latent estimates [7,25]. Full details of the Rasch methodology applied are given in Appendix A.

The SEM was applied to the training samples and then, if appropriate, to a validation sample. Given the three latent and three exogenous variables, the minimum sample size for the models was 1258, with 0.8 power and 0.05 significance, together with an expected effect size of 0.1 [26]. Interpretation of path coefficients indicates that to be meaningful, a coefficient must be significant and have a value of at least 0.1 [27]. This latter requirement is particularly relevant to the current study, where each sample size exceeded 2500, giving sufficient power to detect very small effects. The various models were tested for moderation across disability and MS subtype. The significance level for the Wald test for invariance was set at 0.01.

3. Results

3.1. Descriptive

By the beginning of 2020, 5239 people with MS had returned baseline questionnaire responses, including responses to the MHLC questionnaire. Their mean age was 49.8 years (SD 11.9) and the mean duration of disease was 11.0 years (SD 9.6). Almost three-quarters (73.5%) were female. In total, 11.1% had primary progressive MS (PPMS), 66.9% had relapsing-remitting MS (RRMS), and 22.0% had secondary progressive MS (SPMS). Just over half (52.4%) had an EDDS score between 0 and 4, 36.5% had a score between 4.5 and 6.5, 6.4% between 7 and 7.5, and 4.7% between 8.0 and 9.5.

The mean Rasch-based estimate for ILOC was 11.8 (SD 5.0), PLOC 15.4 (SD 4.1), and CLOC 14.3 (SD 4.1). The kernel density estimates for each are shown in Figure 1. On each scale, indicators of LOC domain focus were defined by score above 15; their pattern is shown in Figure 2. Very few individuals with ILOC had only that focus, whereas almost a quarter (22%) of those with PLOC maintained a single focus.

Randomizing the sample into 'training' and 'validation' groups revealed no significant differences between groups in terms of age, disease duration, gender, or disease subtype. There was no significant difference between groups in levels of ILOC or PLOC. CLOC was associated with a small significant difference (*t*-test 2.6033 (df 5237); $p = 0.009$), but with an effect size of 0.072, this difference was considered trivial.

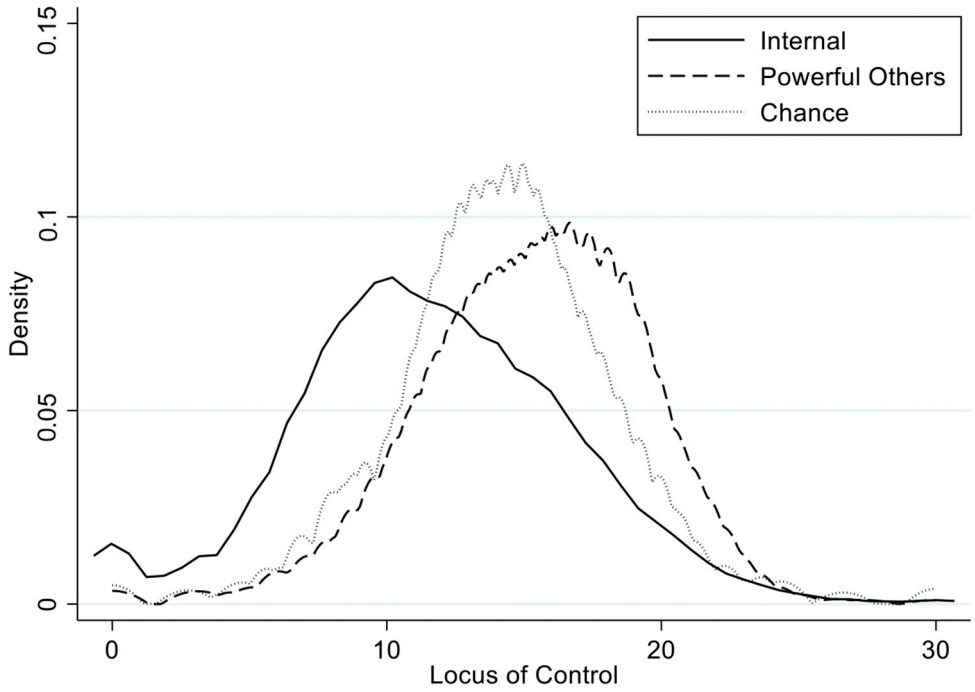

Figure 1. Kernel Density of Internal, Powerful Others, and Chance Locus of Control.

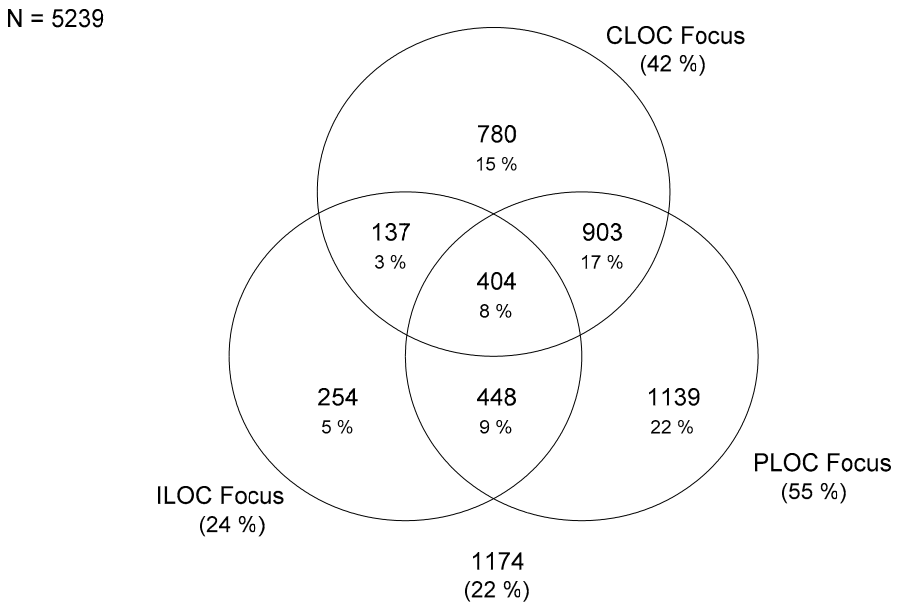

Figure 2. Distribution of LOC Types.

3.2. Structural Equation Models

The following set of models was used to test Hypotheses 1 and 2.

3.2.1. Self-Efficacy as a Mediator Between LOC and QoL, and Between LOC and Functioning (Disability)

This model is illustrated in Figure 3, with ILOC → QoL as the focal relationship and including partial mediation by self-efficacy. This model (SEM1) performed adequately with the training sample and this level of performance was replicated (SEM2) in the validation sample (Table 1). All paths in both samples were found to be significant, but the coefficient of the direct path from ILOC to QoL was below 0.1 in both the training and validation samples. The direct, indirect, and total effects determined from the SEM2 validation sample are shown in Table 2. The total effect of ILOC upon QoL was largely driven by the indirect effect, supporting the suggestion that ILOC → QoL is fully mediated by self-efficacy. The total effect of self-efficacy upon QoL was calculated to be 6.7 times larger than that of ILOC.

Table 1. Statistical fitting for SEMs.

SEM	Focus	Type	χ^2	df	p	RMSEA	CFI	TLI
1	ILOC → QoL	Training	4.820	3	0.185	0.015	0.999	0.998
2	ILOC → QoL	Validation	3.690	3	0.297	0.009	1.000	0.999
3	PLOC → QoL	Training	2.123	1	0.145	0.021	1.00	0.996
4	CLOC → QoL	Training	6.480	3	0.090	0.021	0.998	0.996
5	CLOC → QoL	Validation	0.080	3	0.994	0.000	1.000	1.000
6	ILOC → Functioning	Training	1.238	1	0.266	0.032	1.00	0.999
7	ILOC → Functioning	Validation	3.606	1	0.058	0.010	0.999	0.990
8	PLOC → Functioning	Training	2.110	1	0.046	0.021	1.000	0.996
9	CLOC → Functioning	Training	0.103	1	0.749	0.000	1.000	1.000
10	CLOC → Functioning	Validation	0.026	1	0.873	0.000	1.000	1.000

Table 1. *Cont.*

SEM	Focus	Type	χ^2	df	*p*	RMSEA	CFI	TLI
11	ILOC → QoL	Training	13.47	6	0.036	0.031	0.997	0.991
12	ILOC → QoL	Validation	23.08	6	0.001	0.047	0.992	0.997
13	PLOC → QoL	Training	5.322	2	0.070	0.036	0.998	0.983
14	CLOC → QoL	Training	13.00	6	0.043	0.030	0.997	0.991
15	CLOC → QoL	Validation	24.91	6	0.000	0.049	0.991	0.974
16	ILOC → QoL	Training	11.12	9	0.268	0.016	0.999	0.998
17	ILOC → QoL	Validation	28.74	9	0.001	0.050	0.992	0.976
18	PLOC → QoL	Training	5.693	6	0.498	0.000	1.000	1.000
19	CLOC → QoL	Training	12.93	9	0.166	0.022	0.998	0.995
20	CLOC → QoL	Validation	27.4	9	0.001	0.049	0.992	0.977

SEM = structural equation model; RMSEA = root mean square error of approximation; CFI = comparative fit index; TLI = Tucker–Lewis index; ILOC = predominantly internal locus of control (LOC); PLOC = predominantly powerful others LOC; CLOC = predominantly chance LOC; QoL = quality of life.

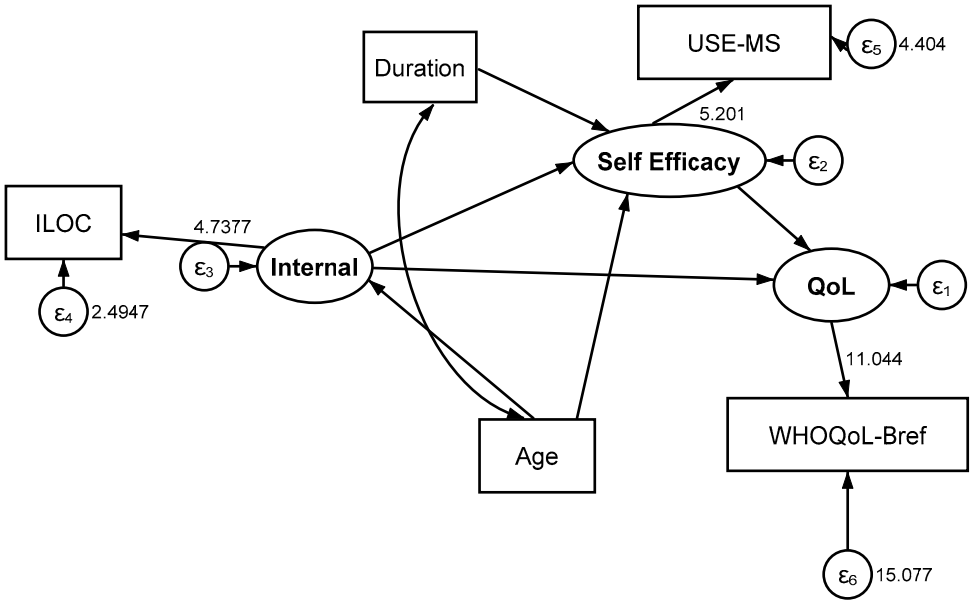

Figure 3. The relationship between internal locus of control and quality of life, partially mediated by self-efficacy; standardized effects. ILOC = predominantly internal locus of control; QoL = quality of life; WHOQoL-BREF = World Health Organization Quality of Life Scale—BREF; USE-MS = Unidimensional Self-Efficacy Scale for MS.

Regarding PLOC → QoL, there was adequate fit in the training sample, with an extra relationship specified between disease duration and QoL. It was necessary to add additional paths from age and disease duration to QoL to achieve fit in the validation sample. However, both the direct and indirect paths for PLOC were non-significant (Table 2—SEM3).

Considering CLOC → QoL, both the training and validation samples used in the model were adequate. While the path from CLOC to self-efficacy was significant in the training sample, the magnitude was marginally below 0.1 [0.094] (SEM4). This was repeated in the validation sample, where the coefficients were smaller. It can thus be concluded that that there is only weak evidence to suggest that CLOC → QoL is mediated by self-efficacy. For SEM4, the direct, indirect, and total effects calculated using the training sample are

shown in Table 2, revealing that the total effect of CLOC was some nine times smaller than that of self-efficacy.

Table 2. Direct, Indirect, and Total effects in basic SEM models.

SEM	Dependent Variable	Sample and Variables	Direct Effect	Indirect Effect	Total Effect	% Variance Explained (R^2)
	QoL					
2		Self-efficacy	0.938	-	0.938	85.4
		ILOC	−0.069	0.213	0.140	
		Duration	-	−0.088	−0.088	
		Age	-	−0.068	−0.068	
3		Self-efficacy	0.992	-	0.922	85.0
		Duration	-	−0.094	−0.094	
		Age	-	−0.068	−0.068	
		PLOC	−0.011	0.018	0.008	
4		Self-efficacy	0.920	-	0.920	85.1
		Duration	-	−0.008	−0.008	
		CLOC	0.019	0.086	0.106	
		Age	-	−0.011	−0.011	
	Functioning					
7		Self-efficacy	−0.813		−0.813	71.4
		Duration	0.098	0.075	0.173	
		ILOC	0.021	−0.186	−0.165	
		Age	0.084	0.061	0.145	
10		Self-efficacy	−0.821	-	−0.821	71.6
		Duration	0.010	0.008	0.019	
		Age	0.007	0.005	0.012	
		CLOC	−0.039	−0.044	−0.083	

SEM = structural equation model; ILOC = predominantly internal locus of control (LOC); PLOC = predominantly powerful others LOC; CLOC = predominantly chance LOC; QoL = quality of life.

The model was re-specified with the focal relationship as ILOC → Functioning. Two additional paths were added, from age to functioning and from disease duration to functioning. The model was deemed to be adequate according to the training sample (SEM6), where ILOC → Functioning was fully mediated by self-efficacy, discounting a significant but non-meaningful direct pathway. The full mediation described by this model was confirmed in the validation sample, which revealed that the direct pathway was not significant. The direct, indirect, and total effects according to the validation sample are described in Table 2—SEM7.

Turning our attention to PLOC → Functioning, the model showed adequate fit in the training sample, but both PLOC paths were non-significant (SEM8). For CLOC → Functioning, the fit with the training sample (SEM9) was once again adequate. The pathway from CLOC to self-efficacy was significant, but that to functioning was not, indicating a fully mediated effect. These findings were supported by the validation sample; the direct and indirect effects are reported in Table 2—SEM10.

In summary, both ILOC and CLOC were found to have fully mediated effects upon QoL, albeit with a low coefficient for the latter. Regarding functioning, ILOC and CLOC were again associated with full mediation. PLOC had no significant paths to either QoL or functioning.

3.2.2. The Moderating Effect of Disability upon the LOC–Self-Efficacy–QoL Relationship

Disability, divided into EDSS 0–4 and ≥4.5, was added to the ILOC → QoL model as a moderator. For the training sample, the group-based model was found to be adequate (SEM11). ILOC was associated with full mediation at both levels of disability, and this effect was invariant, with no statistical differences in the estimated pathways across the levels of disability. The validation sample had a weak fit, although full mediation was retained at both levels of disability and the effect was once again invariant across the groups (SEM12). The direct, indirect, and total effects associated with EDSS 0–4 and EDSS ≥ 4.5 according to the training sample are shown in Appendix A, Table A1—SEM11a and SEM11b, respectively.

In the PLOC → QoL model, no significant path to self-efficacy or QoL was observed in either the training or validation samples, with only the former having marginal fit (SEM13). Additional paths were required to obtain a valid solution.

For CLOC → QoL, the training sample had adequate fit but the pathway from CLOC to self-efficacy in the EDSS 0–4 group was only marginally meaningful (0.094) (SEM14). These weak paths were invariant to group membership. The validation sample had less than adequate fit (SEM15) and the same weaknesses in path coefficients, including a non-significant pathway between CLOC and self-efficacy. The results revealed no variation associated with group membership. The direct, indirect, and total effects revealed through analysis of the training sample are shown in Appendix A, Table A1—SEM14a, SEM14b.

3.2.3. The Moderating Effect of Disease Subtype on the LOC–Self-Efficacy–QoL Relationship

With disease subtypes defined as PPMS, RRMS, and SPMS, the model fit in the ILOC → QoL training sample was adequate (SEM16). The effect of ILOC was fully mediated and invariant across all three groups. The fit of the validation sample, with only weak replication, indicated that the influence of ILOC on QoL was fully mediated by self-efficacy in PPMS and RRMS but partially mediated in SPMS (SEM17). The direct, indirect, and total effects according to the training sample are shown in Appendix A, Table A1—SEM16a–16c.

Regarding PLOC → QoL, an adequate fit was achieved in the training sample (SEM18). The path from PLOC to self-efficacy was not significant for PPMS or RRMS, while it was significant for SPMS. However, this could not be validated.

In the analysis of CLOC → QoL, the training sample provided an adequate fit (SEM19). CLOC was partially mediated in both PPMS and RRMS, while in the SPMS subtype CLOC had only a direct but not significant effect. This model also showed variability in their paths to self-efficacy that was associated with both age and duration of disease; for example, neither of the progressive subtypes showed a significant relationship between disease duration and self-efficacy, but RRMS did. There was only weak support from the validation sample (SEM20). The direct and indirect effects of CLOC across disease subtype (according to the training sample) are shown in Appendix A, Table A1—SEM19a–19c.

In summary, the influence of LOC on QoL was largely mediated through self-efficacy. Where a satisfactory model was achieved, the pathways from ILOC and CLOC to QoL were not affected by the level of disability, but both ILOC and CLOC were associated with differences in the moderating effect of disease subtype, notably for SPMS. PLOC was associated with no significant effects across any of the models.

Regarding Hypotheses 1 and 2, the following conclusions can be stated:

(1) 'Self-efficacy mediates the relationship between LOC and QoL, and between LOC and functioning (disability)'—this hypothesis is supported for both ILOC and CLOC, but not for PLOC.

(2) 'The above mediating relationship between and QoL is moderated by the level of disability and the MS subtype, in such a way that the level of disability or the MS subtype can change the emphasis of the LOC in relation to self-efficacy'—All models showed invariance with regard to disability; however, in relation to the disease subtype, the results for ILOC and CLOC varied and were influenced by variable pathways in SPMS. As such, this hypothesis is supported for the MS subtype but not for disability.

4. Discussion

Variable levels of LOC were found in the data, with ILOC showing a lower median than either PLOC or CLOC. ILOC also had a lower sole focus than the others, mostly sharing its focus with other LOC domains. The SEM results acquired in the current study support the hypothesis that the effects of ILOC and CLOC upon QoL are (fully) mediated by self-efficacy. Likewise, a full-mediation model was found to apply for both ILOC and CLOC with regard to functioning. No evidence was found to support either the direct or indirect effects of PLOC upon self-efficacy, QoL, or functioning. Therefore, this study provided no evidence to support the suggestion that PLOC increased self-efficacy in MS patients with higher levels of disability, as was found in relation to movement disabilities [14].

In general, the models used in the current study did not indicate a moderating influence on the examined pathways, except for the influence of disease subtype on ILOC and CLOC in relation to QoL. Specifically, the mediating effect of self-efficacy between LOC and QoL was weaker in SPMS compared with the other subtypes. In the current study, progressive subtypes, particularly SPMS, were associated with lower self-efficacy. This may have been reflected in the strength of its ability to mediate, leaving room for a direct effect of ILOC. Also, in this subpopulation, it is likely that other personal factors play a greater mediating role.

The differences found in the current study compared with previous studies [10] may be a function of the measures used to assess QoL. The Wilson and Cleary model separates QoL from functioning, the latter being only one influence upon QoL. The MSQoL-54 used in previous work is predominately a measure of symptoms (impairments) and functioning (activity limitation and participation) [28]. In this respect, the findings from the current study on LOC → Functioning may allow closer comparison.

An earlier taxonomy of personality suggested that self-esteem, LOC, generalized self-efficacy, and neuroticism contribute to a broad personality trait termed 'core self-evaluation' [29]. The authors hypothesized that this broad trait relates to motivation and performance, and this was supported by three separate studies. Furthermore, when the core traits were considered as one nomological network, they proved to be more consistent predictors of behavior than when used in isolation. This provides an important context to the current study findings, as it may be that self-efficacy downregulates the effects of LOC upon QoL.

Other mediators have been observed with respect to QoL in MS. One study that used a disease-specific QoL measure to examine risk factors and protective factors relating to QoL in MS found that resilience increased QoL [30]. In another study, depression accounted for the majority of a fatigue–QoL relationship when modelled as a mediator [31].

Coping strategies and self-blame are two other important factors to consider. One study that investigated coping as a moderator reported that self-blame predicted worse mental health-related QoL (HRQoL) [32]. As suggested in a previous study, higher

levels of QoL seen in those with MS and a CLOC preference may be partly due to reduced self-blame in these individuals compared with others who rely more on internal forces or other people to control their health outcomes [7].

This study highlights the importance of self-efficacy as a mediator between LOC and QoL in MS. Self-efficacy can be improved with certain psychological techniques, both in general and specifically in cases of MS. For example, self-care training provided by nurses has been shown to improve self-efficacy in MS [33]. Based on the findings of the current study, such techniques would be useful for those who believe that internal forces or fate control their health outcomes, but they may be less useful for those who consider such outcomes to rely on other people. For the latter group, other mediators in the LOC-QoL relationship (such as resilience, depression, coping, and self-blame) should be explored so that psychological interventions can be deployed in an individualized manner.

4.1. Limitations and Strengths

There are many ways in which LOC can be operationalized in this type of analysis, and the presented results therefore reflect the operationalization of the current study. The use of the Wilson and Cleary model predicates the separation of functioning to QoL, and comparison with other studies that have used the former as an endpoint may thus be difficult. Furthermore, the adopted model included a simplification of the pathway, while it did not include the wide range of symptoms such as fatigue or cognitive effects that may play an important role in the pathway. The interpretation of the fit of the SEM may be considered by some to be strict. Nevertheless, we relied on a non-significant χ^2 as the primary indicator of whether or not the covariance matrix implied by the model was sufficiently close to the sample covariance matrix for the differences reasonably to be considered as having been due to sampling error [34]. Acknowledging that the sample sizes in the current study were relatively large, the ancillary fit statistics are also reported; in all cases, these were acceptable. The model LOC → Functioning is relatively weak, relying as it does on a single degree of freedom.

The current study's approach also has several strengths. These include the model's consistency with the theoretical Wilson and Cleary framework, the large sample size, and the use of Rasch analysis to deliver estimates of interval levels for the SEM. Finally, the training and validation samples strengthened the results through cross-validation.

4.2. Future Work

A myriad of potential mediators may affect the LOC-QoL relationship in MS, and some of these are discussed above. Any model specifying these mediators should measure them within a clear conceptual framework in order to facilitate comparisons between studies. The concept of self-efficacy as part of a broad personality trait ('core self-evaluation') might be a fruitful area to explore. Such an approach might also consider the concept of self-management [35].

5. Conclusions

In conclusion, the relationships between ILOC/CLOC and QoL were shown to be fully mediated by self-efficacy, while no such relationship was found for PLOC. There is no evidence to support moderation of LOC → QoL pathways according to the patient's level of disability, but MS subtype did moderate the relationships between ILOC/CLOC, self-efficacy, and QoL, indicating that mediators other than self-efficacy play a more important role in SPMS.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in this study.

Data Availability Statement: The datasets presented in this article are not readily available due to reasons of confidentiality and because the study is ongoing. Requests to access the datasets should be directed to Carolyn Young.

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Appendix A

Methods of Rasch Analysis

Data from each (sub)scale were tested against the requirements of the Rasch measurement model [24]. Briefly, these requirements included (i) unidimensionality, (ii) monotonicity, (iii) homogeneity, (iv) local independence, and (v) group invariance [36,37]. Whichever set of items are added together to provide the score, they should satisfy all of the requirements, as follows: (i) they should measure one thing (domain/construct/trait); (ii) the probability of a positive response to an item (or in the case of polytomous items, the transition from one response category to the next) should increase along with the underlying trait, as should the total score [38]; (iii) the same hierarchical ordering of items should hold for each level (or grouping) of the score [39]; (iv) items should be conditionally independent of one another [40]; and (v) the response to items across different groups such as age or gender should be the same, conditional on the total score—this is referred to as (the absence of) differential item functioning (DIF) [37].

Each requirement was tested. A *t*-test was used to determine whether two separate groups of items would deliver significantly different estimates, following the procedure described by Smith [41]. The hierarchical ordering of items across the scale was determined through a Chi-square test of fit based on grouped scores. Monotonicity was evaluated through inspecting the ordering of item categories. Conditional item dependence was determined though the correlation of residuals; pairwise correlations should not exceed 0.2 above the average residual [42]. Where clusters of locally dependent items were found, consideration was given to grouping these into 'super items' or testlets (simply adding them together to make one larger item, the latter based on a priori defined groups) to absorb the local dependency [43]. RUMM2030 software provided a bi-factor equivalent solution retaining a specified proportion of the variance. In the reporting of this "explained common variance (ECV)" a value less than 0.7 is indicative of requiring a multidimensional model, a value above 0.9 requires a unidimensional model, and the grey area in between is

undetermined, requiring further evidence [44]. Consequently, an ECV value of 0.9 or above was considered acceptable in the current analysis. Where possible, when two parallel forms are created from either a subscale structure if this is present, or from the pattern of local dependency in the item set, a latent correlation ≥ 0.9 is required. This is consistent with the reliability required for individual use [45]. Consequently, valid parallel forms require both their latent correlation to be $\geq$0.9 and their ECV to be $\geq$0.9.

Group invariance (DIF) was tested through ANOVA of residuals for age, gender, duration since diagnosis, education level, whether or not the patient was self-employed or employed, and whether they worked full-time or part-time. Where DIF was identified it was tested through comparison of individual estimates from split and unsplit solutions, to identify whether it was 'substantive' [46]. Where the differences were significant (according to the paired *t*-test), the results are reported as an effect size where a value higher than 0.1 is considered to represent substantive DIF. In such cases, the scale works in different ways according to the contextual factor under consideration, and these results are reported separately.

A hierarchical approach was adopted to determine the fit of the data to the model's existing scales, with level 1 as the priority (Table A2). All the aspects listed above had to be met. Where a level 5 solution was unavailable, item deletion was considered (level 6). If this failed, level 7 was utilized to test whether the scale satisfied ordinal scaling; if not, level 8 indicated failure.

Table A1. Moderated models: Direct, Indirect, and Total Effects.

Model	Dependent Variable/Moderator	Sample and Variables	Direct Effect	Indirect Effect	Total Effect	% Variance Explained (R^2)
SEM11a	QoL					
	EDSS 0–4	Self-efficacy	0.953		0.953	85.1
		ILOC	−0.057	0.124	0.067	
		Duration		−0.005	−0.005	
		Age		−0.005	−0.005	
SEM11b	QoL					
	EDSS 4.5+	Self-efficacy	0.888	-	0.888	83.6
		ILOC	−0.090	0.152	0.063	
		Duration	-	0.001	0.001	
		Age	-	0.010	0.010	
SEM14a	QoL					
	EDSS 0–4	Self-efficacy	0.945	-	0.945	85.0
		CLOC	0.003	0.089	0.092	
		Duration	-	−0.005	−0.005	
		Age	-	−0.005	−0.005	
SEM14b	QoL					
	EDSS 4.5+	Self-efficacy	0.858	-	0.858	82.0
		CLOC	0.034	0.032	0.066	
		Duration	-	0.001	−0.002	
		Age	-	0.009	0.009	
SEM16a	QoL					
	PPMS	Self-efficacy	0.975	-	0.975	88.4

Table A1. *Cont.*

Model	Dependent Variable/Moderator	Sample and Variables	Direct Effect	Indirect Effect	Total Effect	% Variance Explained (R^2)
		ILOC	−0.080	0.152	0.073	
		Age	-	0.009	0.009	
		Duration	-	−0.000	−0.000	
SEM16b	QoL					
	RRMS	Self-efficacy	0.955		0.955	87.0
		ILOC	−0.071	0.162	0.090	
		Age	-	−0.004	−0.004	
		Duration	-	−0.011	−0.011	
SEM16c	QoL					
	SPMS	Self-efficacy	0.817	-	0.817	81.1
		ILOC	−0.064	0.164	0.099	
		Age	-	0.007	0.007	
		Duration	-	0.002	0.002	
SEM19a	QoL					
	PPMS	Self-efficacy	0.952	-	0.952	87.1
		CLOC	−0.017	0.121	0.104	
		Age	-	0.009	0.009	
		Duration	-	−0.000	−0.000	
SEM19b	QoL					
	RRMS	Self-efficacy	0.944	-	0.944	86.6
		CLOC	0.008	0.088	0.096	
		Age	-	−0.004	−0.004	
		Duration	-	−0.011	−0.011	
SEM19c	QoL					
	SPMS	Self-efficacy	0.791	-	0.791	81.4
		CLOC	0.070	0.036	0.107	
		Age	-	0.007	0.007	
		Duration	-	0.002	0.002	

SEM = structural equation model; EDSS = expanded disability status scale; PPMS = primary progressive multiple sclerosis (MS); RRMS = relapsing-remitting MS; SPMS = secondary progressive MS; ILOC = predominantly internal locus of control (LOC); CLOC = predominantly chance LOC; QoL = quality of life.

Table A2. Strategies to determine the fit of the data to the model.

Level	Nature	Adjustments	Reporting		
			Chi-Square	ECV $\geq$0.9	Latent Correlation $\geq$0.9
1	Item-based	None	Interaction	No	No
2	Item-based	Clusters for local item dependency	Interaction	Yes	No
3	Domain-based	On existing sub-scales > 2	Interaction	Yes	No
4	Parallel form	On existing sub-scales $\leq$ 2 or 2 local dependency patterns or conceptual groups	Conditional	Yes	Yes
5	Parallel form	On alternative items	Conditional	Yes	Yes

Table A2. *Cont.*

Level	Nature	Adjustments	Reporting		
			Chi-Square	ECV ≥0.9	Latent Correlation ≥0.9
6	Item deletion	On all original items Repeat Levels 1–5	Interaction	No	No
7	Mokken scaling	on items if unidimensional. Loevinger's coefficient H ≥ 0.4—moderate	No	No	No
8	Fail	No valid ordinal scale	No	No	No

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