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QUANTITATIVE METHODS SPECIAL SECTION

Modeling health-related quality of life in people recovering from stroke

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Abstract
Background The Wilson–Cleary (W–C) model of health-related quality of life (HRQL) has not been tested in stroke, and a better understanding of the components of HRQL during recovery would lead to a more integrated and person-centered approach to health management and outcome optimization for this vulnerable population.
Objective To enhance our understanding for how QOL emerges from the sequelae of stroke during the recovery period, the aim was to empirically test a biopsychosocial conceptual model of HRQL for people recovering from stroke.
Methods We present a multi-site longitudinal study of an inception cohort of 678 persons recruited at stroke onset and studied at key intervals over the first post-stroke year. As the most pronounced recovery after stroke occurs in the first 3 months, this time frame was chosen as the focus of this analysis. The measures for this study were chosen for their relevance to key constructs of stroke impact and for their optimal psychometric properties. Multiple measures for each of the W–C rubrics were available from instruments such as the Stroke Impact Scale, RAND-36, HUI, and EQ-5D, among others. A structural equation model (SEM) was fit using M*Plus*. To minimize potential bias arising from the missing data, multiple imputation was performed on the longitudinal data using SAS proc MI.
Results Of the 678 subjects who entered the cohort, 618 were interviewed at 1 month post-stroke and 533 at 3 months (486 and 454 had data at 6 and 12 months, respectively). A 3-month model with paths from biological factors to symptoms and symptoms to function fits well (CFI:0.966, RMSEA:0.044), though one model with paths from function to health perception did not (CFI:0.934, RMSEA:0.058). Allowing additional paths across non-adjacent rubrics improved fit considerably (CFI:0.962, RMSEA:0.044). A final model included emotional well-being under the

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symptom rubric (CFI:0.955, RMSEA:0.047). Including social support as an environmental factor had little impact on the model. Total variance in health perception explained was 76.3 %.

Conclusion These results emphasize that to optimize overall HRQL during the crucial first 3 months of recovery, interventions need to continue to focus on comorbid health conditions and on reducing stroke impairments. A function-only focus too soon in the recovery process may not produce the desired impact to optimize HRQL.

Keywords Stroke · Function · Disability · Health outcomes · Structural equation modeling

Introduction

There is a substantial literature describing the huge impact that stroke has on quality of life (QOL) and so why do we need yet another study? The important shift in health care thinking toward patient-centered care is now a strong motivator to understand the health components of QOL as these are under the influence of the health care system. In the context of stroke, a key period to understand these health components is during the time of peak recovery when health services are being delivered to enhance recovery with the ultimate goal of improving QOL. Knowing the drivers of QOL is an essential step in creating integrated models of care and developing a person-centered approach to health management. The existing literature has not gone far enough in delineating the interconnections between stroke sequelae and QOL.

The portrait of stroke impact which is most realistic arises from the studies of large numbers of individuals, entered at the time of stroke, and followed, as completely as possible, over time [1–14]. These studies have reported consistently that the aspects of physical function, positive mood, social support, and participation in social and community life are important. Several of these studies have produced regression models of contributors to health-related quality of life (HRQL) post-stroke. There are limitations to this approach [15]. The number of variables that can be studied at one time is constrained by sample size, and correlated variables cannot be studied in terms of their independent contribution. In addition, interactions with other variables measured at the same time are difficult to quantify.

A few studies have taken a more multivariate approach, with path models [16], latent curve models [17], and structural equation modeling (SEM) [18–22], but fall short of the aim of fully understanding HRQL post-stroke. All but four [17, 19, 22] were cross-sectional studies of survivors; sample sizes ranged from 61 [19] to 591 [8, 11]. Outcomes varied from participation restriction [19, 21, 23] to self-rated health [18], HRQL [22], and QOL [17, 20], and had a restricted set of explanatory variables, ranging from 3 to 12. While the International Classification of Function, Disability, and Health (ICF) was used in one study [19], no strong theoretical model was evident in the other studies.

Complicating the portrait is that, typically, there is confusion in the stroke literature about terminology such as function, HRQL, and QOL, which are often used interchangeably. The Wilson–Cleary (W–C) model of HRQL [24] is helpful in the context of stroke as it differentiates between these terms and identifies the components of HRQL, recognizing that HRQL may not be a primary concept but rather a constellation of complex and connected paths between and among biological and physiological parameters, symptoms, function, and health perception. These components, summarized as HRQL, link to QOL and are affected by personal and environmental factors. The W–C model has not been tested in stroke, and a better understanding of the components of HRQL during recovery from stroke would lead to a more integrated and person-centered approach to health management and outcome optimization for this vulnerable population at this crucial time in their lives.

Overall, the theoretical model outlines causal relationships between different patient outcomes to enhance understanding about the development of disability and its impact on HRQL. This understanding, in turn, will facilitate the targeting of interventions. While the model has been empirically tested in patients with a number of medical conditions [25–33], as well as in community-dwelling elderly samples [34], it has not been evaluated adequately in people with stroke.

A comprehensive biopsychosocial model for HRQL for persons with stroke is needed to clarify the structure and relationships of variables that contribute to it. With this accomplished, opportunities and interventions to improve specific outcomes that reflect HRQL will be identified more easily.

To this end, a large cohort was assembled and followed over the first year post-stroke. The overall aim was to enhance our understanding for how QOL emerges from the sequelae of stroke during the recovery period to inform assessment and intervention. The specific objective was to empirically test a biopsychosocial conceptual model of HRQL for people with stroke. The first part of this objective was to evaluate a model of HRQL for persons with stroke during the early period post-stroke, at 3 months, for the purposes of estimating life's quality as people go through the recovery process. This period was selected because much recovery occurs within this time frame. This paper reports the results of testing the HRQL model at this time in the trajectory of stroke recovery.

Methods

Source of data

The data for this analysis came from a longitudinal study of HRQL involving 678 persons post-stroke recruited between 2003 and 2004, from 10 acute-care hospitals in Montreal QC, Toronto ON, and London ON, contributing 267, 301, and 110 subjects, respectively. The study has been described previously [35]. Measures of stroke impact were made at study entry and at 1, 3, 6, and 12 months post-stroke. Data came from the medical chart (at entry), from face-to-face interviews (at 1 month) and telephone interviews, subsequently. For people who could not respond for themselves, proxy responders were accepted. The project was approved by the Research Ethics Boards (REB) of each participating institution.

Overview of design

This cross-sectional analysis of data, at the key three-month post-stroke time point, aimed to explore the structure and relationships among variables falling under the rubrics of the W–C model (biology, symptoms, function, health perception, personal and environmental factors and quality of life) [24] and operationalized using SEM. SEM was chosen because it is designed for testing a priori hypothesized relationships among multiple correlated variables [15, 36, 37]. A defining feature of SEM is the use of latent variables that combine measured correlated variables into latent constructs by way of confirmatory factor analysis. The creation of latent variables reduces the measurement error inherent in constructs that are not directly measurable.

Subjects

Enrolled were people with first confirmed stroke, who spoke English or French, or who had "significant others" who were fluent in either of these languages, who provided written informed consent, and who did not have a serious comorbidity that was likely to dominate the pattern of care and result in serious health decline or death within the study period. Of the 678 subjects in the cohort, 618 were interviewed at 1 month post-stroke. Of the 600 subjects remaining at 3 months, 533 persons were interviewed (8 had died, 15 moved to long-term care, 1 moved out of the region, 18 could not be located, and 36 refused further participation).

Measures

The measures for this study were chosen for their relevance to key constructs of stroke impact and for their optimal psychometric properties. The constructs captured by these measures have been shown to be reliably ascertained over the telephone [38]. The measures are listed in Tables 1 and 2, according to their position along the conceptual framework of the W–C model; the scoring of each variable is also given.

Basic demographic and comorbidity information and that necessary to define severity of stroke and side of lesion were abstracted from the patient's medical chart by trained abstractors. Trained interviewers obtained information related to symptoms; to physical, psychological, cognitive, and social functioning; and to HRQL at each interview. At the 3-month interview, 133 of 533 persons required some proxy response.

Table 1 Description of the cohort on the W–C rubrics of personal, environmental, and biological and physiological factors

	N	Frequency or (mean)	Percent or [SD]
Personal characteristics of the individual			
Men/women	678	373/305	55.0/45.0
Age at stroke (years)	676	(67.3)	[14.8]
<45	–	63	9.3
45–64	–	204	30.2
65–84	–	345	51.0
≥85	–	64	9.5
Environmental characteristics			
Social resources[a]: 0(worst)–9(best)	464	(7.3)	[1.7]
Biological and physiological variables			
Side of lesion	654	–	–
Left/right/bilateral	–	293/325/36	44.7/49.5/5.5
Stroke severity[b]: 1.5(worst)–11.5(best)	667	(8.5)	[2.5]
Severe (0–5)	–	94	14.1
Moderate–high (5.5–9)	–	260	39.0
Moderate–low (9.5–10.5)	–	174	26.1
Mild (11–11.5)	–	139	20.8
Charlson Comorbidity Index[c]	677	(1.6)	[1.3]
0	–	138	20.4
1	–	235	34.7
2	–	168	24.8
3	–	80	11.8
4	–	38	5.6
5+	–	18	2.66

[a] Social resources: score with range from 0 (worst) to 9 (best) was created from questions 1,3,4,6–9 of the OARS Social Resource Scale [47, 48]

[b] Stroke severity measured using the CNS with range from 1.5(worst) to 11.5(best)

[c] Charlson Index [39]: higher indicates more comorbidity; hemiplegia, paraplegia, and dementia excluded

Table 2 Description of the cohort on the W–C rubrics of symptoms (impairments), function, and general health perception: observed and imputed values

Latent variable	Indicator scored 0 (worst) to 100 (best)	*N*	Observed Mean (SD)	Imputed Mean (SE)
Symptoms (impairments)				
Strength	SIS[a] (strength)	527	70.7 (26.1)	69.7 (1.0)
Continence	SIS 5f-g	529	94.0 (16.4)	92.7 (0.7)
Pain	RAND-36 (BP)	462	75.9 (27.7)	72.6 (1.4)
	HUI (pain)	500	85.0 (26.9)	83.5 (1.2)
Vitality	RAND-36 (VT)	461	51.1 (23.8)	49.5 (1.2)
Communication	SIS 4a-d	530	91.5 (17.3)	90.3 (0.7)
	HUI (speech)	504	96.9 (13.2)	
Vision	HUI (vision)	464	92.8 (13.3)	91.6 (0.6)
Memory	SIS (memory)	530	86.4 (19.2)	85.0 (0.8)
	HUI (cognition)	502	89.4 (20.0)	87.7 (0.8)
Emotional well-being				
	SIS (emotion)	522	79.8 (17.1)	78.9 (0.7)
	HUI (emotion)	481	90.9 (16.7)	88.7 (0.8)
	RAND-36 (MH)	460	74.6 (20.0)	72.1 (1.0)
Functioning				
Physical	SF-36 (PF)	464	52.8 (33.8)	50.3 (1.4)
	SIS 6a-i (mobility), SIS 7a-e (hand), SIS 5a-e,h,j (ADL) SIS 8d (participation)	530	72.4 (25.0)	70.8 (1.0)
	SIS (mobility)	530	75.2 (25.0)	73.8 (1.0)
	SIS (hand)	527	70.0 (34.7)	67.8 (1.3)
	HUI: average of self-care, ambulation, and dexterity	450	79.3 (28.6)	76.4 (1.1)
	HUI (ambulation)	492	75.7 (32.3)	73.1 (1.3)
	HUI (dexterity)	502	84.7 (27.4)	82.1 (1.1)
	HUI Mark 2 (self-care)	469	77.1 (41.1)	74.0 (1.6)
Social	RAND-36 (SF)	463	65.8 (32.6)	62.4 (1.3)
	SIS 8b (participation)	528	60.7 (39.3)	59.0 (1.5)
Role	Worst of RAND-36 RE and RP	464	38.3 (43.0)	35.9 (1.7)
	RAND-36 (RE)	462	70.0 (40.7)	65.8 (1.6)
	RAND-36 (RP)	464	40.5 (43.4)	38.9 (1.7)
Cognitive	MMSE	434	91.3 (12.0)	88.7 (0.7)
Health perceptions				
	EQ-5D VAS	450	72.1 (19.6)	70.3 (0.9)
	RAND-36 (GH)	458	64.4 (19.5)	62.9 (0.9)

Stroke Impact Scale (SIS), Health Utilities Index Mark 3 (HUI), Brief Version Mini-Mental State Examination (MMSE), Canadian Neurological Scale (CNS)

[a] Single-indicator latent variables were assigned a reliability of 90 %

Stroke severity was measured using the Canadian Neurological Scale (CNS) [39, 40]. It is scored from 1.5 (most severe) to 11.5 (least severe).

Comorbidity was documented by a combination of chart-abstraction and patient-reported data and quantified using the Charlson Index [41] with hemiplegia and dementia eliminated from the scoring algorithm. These, along with side of lesion, represent biological and physiological variables in the W–C model.

Variables and indicators of symptoms, functioning, and health perception were taken from subscales or questions in the Stroke Impact Scale (SIS) [42], RAND-36 [43], Health Utilities Inventory (HUI) [44], Brief Mini-Mental State Examination (MMSE) that is a measure of cognitive impairment adapted for scoring over the telephone [45, 46], and EuroQol (EQ-5D) [47, 48]. Information on social resources was obtained from the OARS Social Resource Scale [49, 50]. As symptom and function items were often found together in subscales from the above questionnaires, new subscales were created from individual items falling under the W–C rubrics. For example, an indicator of the physical function latent was created by combining items from the mobility, hand, activities of daily living, and participation subscales of the SIS.

Statistical methods

SEM [15, 36, 37], a methodology that encompasses factor analysis, path analysis, and regression, was used to test the W–C theoretical model against the observed data.

Mplus version 6.12 software was used for these analyses. SEM is an ideal method to test a priori hypotheses concerning relationships among constructs and variables. Latent and measured variables representing the W–C rubrics of biological factors, symptoms, functioning, health perception, emotional well-being, and personal and environmental factors were included, and pathways between them were used to calculate direct effects.

To minimize potential bias arising from the missing data, multiple imputation was performed [51–53] on the longitudinal data. This method was preferred over full information maximum likelihood (FIML) estimation as it can make use of information from all available time points, both before and after the index time point. It assumes that data are missing at random, but not completely at random, i.e., that while persons not interviewed might be those doing worse, they are missing at random among those who are doing worse. Five datasets were imputed using SAS 9.1 proc mi and Mplus used the 5 imputed datasets in the SEM analysis.

SEM has measurement and structural components. The measurement model uses factor analysis to define the relationships between the observed variables and unobserved latent variables, and this was the first step carried out in model development. Latent variables were scaled by fixing the loading of one of the observed variables to unity. While it is desirable to have multiple observed variables to reduce uncertainty in the latent variable, some latent variables could only be defined by a single observed variable, in which case they were assigned reliabilities of 90 %. We structured Tables 1 and 2 to present the results according to the measurement model.

To develop the SEM structural model for HRQL in stroke, we proceeded sequentially as hypothesized under the W–C model. The outline of our strategy follows the steps presented in the results Table 3. Our general strategy was to allow latent variables within the W–C rubrics to correlate and to apply paths across latent variables under different rubrics. Thus, biological variables were allowed to correlate with each other, symptom latent variables were allowed to correlate with other symptom latent variables, and function latent variables with other function latent variables. Initially, we allowed paths only across adjacent rubrics. Paths were applied across all possible pairs of latent variables within the pair of rubrics, but paths that were not statistically significant and not theoretically relevant were removed, i.e., each set of adjacent rubrics required paths, but not all pairs of latent variables were considered theoretically relevant. Paths across more distant rubrics were added later, based on the modification indices, and were retained when model fit was improved. Paths were applied from personal factors to all latent variables, though were kept only if significant or if needed to obtain convergence in any of the imputed datasets.

We first proceeded with fitting a model that included only physical or observable stroke sequelae as they are known to be affected by clinically identifiable biological or

Table 3 Model progression

Model	$\chi^{2,a}$	Degrees of freedom	RMSEA[b]	SRMR[c]	CFI[d]	TLI[d]
Biological factors (B) to symptoms (S) to function (F) to health perception (HP)						
1. B to S	73.4	52	0.025	0.023	0.988	0.977
2. B to S to F	301.3	130	0.044	0.033	0.966	0.946
2a. B to S to F, allowing path from B to F	292.3	129	0.043	0.032	0.967	0.948
3. B to S to F to HP	537.6	165	0.058	0.047	0.934	0.902
3a. B to S to F to HP, including B to F from (2a)	528.4	164	0.057	0.046	0.936	0.903
3b. B to S to F to HP, allowing B to F and HP, and S to HP	374.8	160	0.044	0.033	0.962	0.941
4. B to S to F to HP, with extra paths (3b) and emotion	527.5	213	0.047	0.034	0.955	0.932
5. B to S to F to HP, with extra paths and emotion (4) and selected paths from environmental factor	556.1	225	0.047	0.034	0.954	0.930

[a] χ^2 test of exact fit, using the Satorra-Bentler correction for non-normality, and associated degrees of freedom. None of the models reach the desired p value of greater than 0.05

[b] A measure of global close fit where values less than 0.05 represent good fit and values to 0.08 are considered reasonable

[c] A measure of badness of fit based on fitted residuals. Values less than 0.05 represent good fit and values to 0.10 reasonable

[d] CFI and TLI values greater than 0.95 are indicative of an acceptable fit, 0.97 of good fit. Both measure fit relative to an independence model, but the TLI includes a correction for model complexity

physiological abnormalities. As Wilson and Cleary present a debate as to how symptoms relating to emotional factors fit into their model, because there may be no clinically identifiable biological or physiological abnormalities associated with feelings such as depressed mood, we chose to fit the model first without this variable. However, in the context of stroke, there is biological evidence that side of lesion is associated with depression [54], and therefore, we confirmed that emotional well-being fit within the symptom rubric. As for the possibility that other stroke symptoms also contribute to feelings of depressed mood, this placement allows for correlations between these symptom sequelae, without inferring direction. The single environmental variable for social support was added last.

An assumption of SEM is multivariate normality. Many construct-specific measures, particularly those within the HUI, were not normally distributed, and non-normality was increased by splitting scales to create variables to load on symptom and functioning latent variables. Because of this, we used robust maximum likelihood estimation, which adjusts the standard errors. Model fit was examined first using the Satorra-Bentler scaled χ^2. However, as tests of exact fit invariably fail in large samples, measure of approximate fit was also considered: the root mean square error of approximation (RMSEA), the standardized root mean square residual (SRMR), the Comparative Fit Index (CFI), and the Tucker–Lewis, or non-normed fit index (TLI). Fit statistics were interpreted as summarized by Schermelleh-Engel et al. [55] (see footnote in results Table 3).

Results

Table 1 presents information on the cohort at baseline on variables under the personal, biological, and environmental rubrics of the W–C model. The mean age of the cohort at stroke onset was 67 years and 55 % were men. As this group consisted of stroke survivors who eventually returned to the community, the proportion of severe strokes was only 14 %.

Table 2 presents information on the cohort at 3 months post-stroke on variables under the symptoms, function, and health perception rubrics of the W–C model. Given are the means and standard deviations (SD) for the sample data as well as means and standard errors (SE) after imputation. All means are lowered with imputation, as would be expected if those doing worse are less likely to complete the interview.

Table 3 sets out the model progression. The strict interpretation of the W–C model is a progression from biological factors (B) to symptoms (S) to functioning (F) to health perception (HP).

The initial model (Model 1) relates biological factors to symptoms (with personal factors included in all models). This model fits very well, with RMSEA and SRMR well below 0.05 and the CFI and TLI both greater than 0.97. Although the Satorra-Bentler χ^2 was statistically significant, in this and all subsequent models, suggesting poor fit, this was offset by the very large sample size and low ratio of the χ^2 to its degrees of freedom (1.4).

Subsequent models retained paths from simpler models and added paths to adjacent rubrics (Models 2 and 3) and then across non-adjacent rubrics (Models 2a, 3a, and 3b).

Model 2 added paths from symptom to function latent variables. Fit remained acceptable, although somewhat lower: RMSEA was 0.044, SRMR was 0.033, and the CFI and TLI were 0.966 and 0.946, respectively. When the strongest path from biology to functioning identified from the modification indices (specifically, from bilateral stroke to role functioning) was added (Model 2a), there was little change in the model fit.

A strict interpretation of the Wilson–Cleary model was not a good fit for health perception (Model 3), and the inclusion of the additional path from biology to function identified in Model 2a again had little impact (Model 3a, RMSEA:0.057 and SRMR 0046 but CFI:0.936 and TLI:0.903). Fit only was improved after the addition of direct paths over non-contiguous levels: to health perception from biology (comorbidity) and from symptoms (paths from pain, vitality, and memory), as well as to function (role) from biology (side of lesion) (Model 3b: RMSEA:0.044, SRMR 0.033, CFI:0.962, TLI:0.941).

The role of emotional well-being was then considered. By treating emotional well-being as a symptom, allowing it to receive paths from biological factors and personal factors, correlate with other symptoms, and explain functioning and health perception, we obtained a model with an acceptable fit (Model 4: RMSEA:0.047, SRMR 0.034 and CFI:0.955, though TLI:0.932).

A single environmental factor, social resources, was added to create model 5, the final model. In the W–C model, environmental factors are theorized to impact on all rubrics after biological variables. In the context of stroke, we would not expect direct effects of an environmental factor on symptoms other than emotional well-being but we allowed direct effects to function (physical, social, and role) over and above indirect effects through emotional well-being; fit changed little. Total explained variance in health perception was 76.3 %.

Figure 1 presents an overview of this final model, and the values for the direct effects are given in Table 4. In Table 4, variables, whether latent or observed, are set under the appropriate W–C rubric; columns on the right provide the estimate of direct effect with its standard error, along with a standardized version of the effect (standardized beta: SB) for

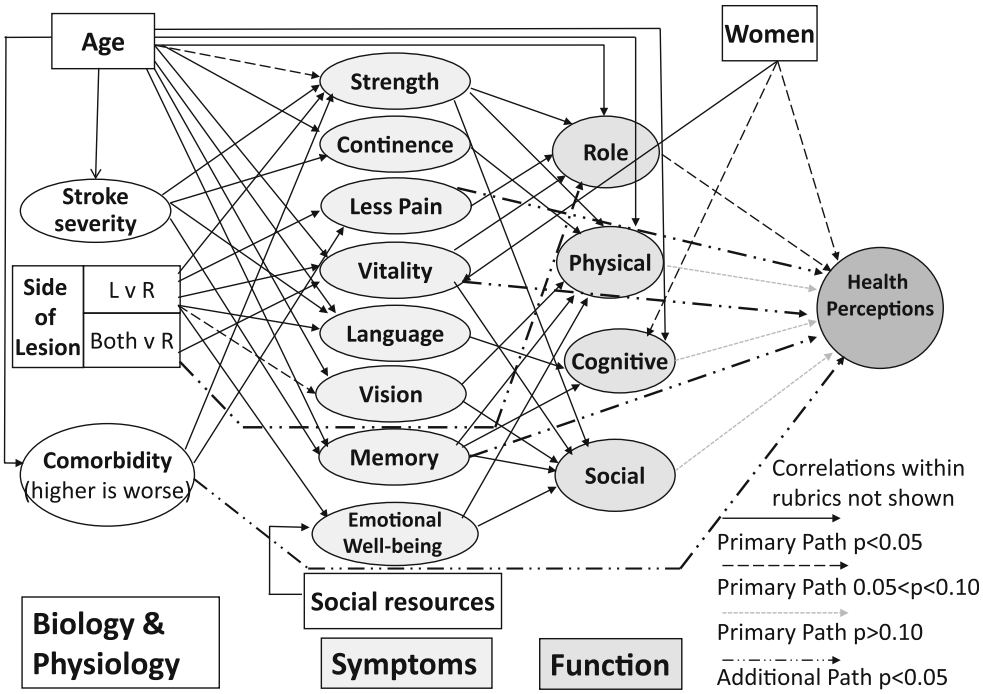

Fig. 1 Final SEM model for stroke based on the Wilson–Cleary theoretical model. While all latent variables within rubrics were allowed to correlate, thesecorrelations are not shown

comparison purposes. Only effects significant at $p < 0.10$ and other paths retained for theoretical reasons are included. We do not present those paths retained only to reach convergence across all imputed datasets. Age is measured in years. Other variables, except for comorbidity, are scored with higher scores indicating less disability (including stroke severity and pain, despite the labels). As latent variables are scaled on one of their indicator (observed) variables, symptom, function, and health perception latent variables are all scaled 0–100. As expected, the degree of comorbidity as well as many symptoms and functions increase with age, most notably vision, which shows a difference of −0.227 units across subgroups that differ by one additional year of age (SB: −0.257), similarly, memory (SB: −0.180 by year). Vitality is lower in women than men (SB: −0.163). Emotional health was higher in those with more social resources (SB: +0.563). Less severe strokes (higher CNS stroke severity scores) are associated with better scores in strength, continence, language, and memory. Greater language difficulty was found for people with lesions to the left side of the brain (SB: −0.139). Strength has a strong association with physical function (SB: +0.653), although it also impacts favorably on social and role function (SB +0.360 and + 0.256, respectively). Functions were not strongly associated with health perception; the contribution of role function was small (SB: + 0.114, $0.05 < p < 0.10$) and those of physical, cognitive, and social function non-significant. Rather, we found better health perception was driven by less comorbidity (SB: −0.113) and less pain (SB:0.347), better memory (SB:0.193), and more vitality (SB:0.371). Figure 2 presents a redrawn W–C model based on the paths observed in this study.

Discussion

We modeled HRQL using the framework of the W–C model, in a sample of people with stroke originally drawn from an inception cohort but who were community dwelling at the time of measurement, 3 months post-stroke onset. In the context of stroke, an inception cohort is invaluable, even when the analyses may be cross-sectional, because the biases from including only a survivor group are minimized. Many of the relationships uncovered in a survivor cohort may not be the same in an inception cohort.

We found that the strict interpretation of the W–C model holds well from biology to function (through symptoms); however, we did not find support for a strong link from function to health perception, but rather from comorbidity (biology rubric) and symptoms to health perception. We have redrawn the W–C model reflecting the paths from this sample of persons with stroke in Fig. 2. We did not have data to model to overall QOL and hence our paths ended at health perception. Because the sample was community dwelling, there were some paradoxical findings, namely that older persons had milder strokes. This is compatible with stroke as only functional older persons with stroke could return and remain at home.

The observation that only role function, and not physical or cognitive function, linked to health perception is

Table 4 Direct effects between latent variables forming the Wilson–Cleary model of HRQL for stroke

Personal	Environmental	Biology	Symptoms	Function	Health perception	Direct effect	SE	Standardized (STDYX)
Age		Severity				0.015	0.007	0.092
Age		Comorbidity				0.020	0.003	0.241
Age			Strength			−0.103[a]	0.056	−0.063
Age			Continence			−0.144	0.041	−0.139
Age			Vitality			−0.184	0.059	−0.116
Age			Language			−0.096	0.039	−0.087
Age			Vision			−0.227	0.033	−0.257
Age			Memory			−0.218	0.044	−0.180
Age				Role		0.187	0.085	0.074
Age				Physical		−0.164	0.041	−0.097
Age				Cognitive		−0.132	0.026	−0.150
F versus M			Vitality			−7.703	1.709	−0.163
F versus M				Cognitive		1.599[a]	0.948	0.060
F versus M					Health P	1.842[a]	1.092	0.059
	Social R		Emotional			6.124	0.479	0.563
	Social R			Physical		−0.564[b]	0.422	−0.040
	Social R			Social		−0.671[b]	0.714	−0.042
	Social R			Role		−0.788[b]	0.994	−0.038
		Severity	Strength			4.224	0.397	0.414
		Severity	Continence			0.855	0.268	0.134
		Severity	Language			1.308	0.333	0.190
		Severity	Memory			1.083	0.282	0.145
		Comorbidity	Strength			−1.530	0.665	−0.078
		Comorbidity	Pain			−1.954	0.830	−0.098
		Comorbidity			Health P	−1.402	0.582	−0.113
		Left versus right	Strength			4.985	1.660	0.101
		Left versus right	Pain			4.863	2.091	0.097
		Left versus right	Vitality			5.934	2.333	0.125
		Left versus right	Language			−4.594	0.982	−0.139
		Left versus right	Vision			1.700[a]	0.959	0.065
		Left versus right	Emotional			5.665	1.282	0.144
		Bilateral versus R	Vitality			−6.721	3.372	−0.065
		Bilateral versus R		Role		−15.881	5.045	−0.096
			Strength	Role		0.395	0.058	0.256
			Strength	Physical		0.672	0.031	0.653
			Strength	Social		0.426	0.047	0.360
			Continence	Physical		0.239	0.050	0.146
			Pain	Role		0.167	0.071	0.110
			Pain		Health P	0.217	0.045	0.347
			Vitality	Role		0.561	0.107	0.352
			Vitality	Social		0.232	0.081	0.189
			Vitality		Health P	0.243	0.052	0.371
			Language	Cognitive		0.277	0.101	0.346
			Vision	Physical		0.203	0.064	0.105
			Vision	Social		0.265	0.081	0.120
			Memory	Physical		0.121	0.054	0.086
			Memory	Cognitive		0.266	0.085	0.363
			Memory	Social		0.300	0.088	0.186

Table 4 continued

Personal	Environmental	Biology	Symptoms	Function	Health perception	Direct effect	SE	Standardized (STDYX)
			Memory		Health P	0.168	0.080	0.193
			Emotional	Role		0.181[b]	0.150	0.094
			Emotional	Physical		0.146	0.068	0.113
			Emotional	Cognitive		−0.043[b]	0.042	−0.065
			Emotional	Social		0.388	0.101	0.261
				Role	Health P	0.047[a]	0.025	0.114
				Physical	Health P	0.008[b]	0.045	0.012
				Cognitive	Health P	0.021[b]	0.061	0.018
				Social	Health P	0.050[b]	0.058	0.093

All variables except for comorbidity are scored with higher scores being better

[a] $0.05 < p < 0.10$. All other associations are $p < 0.05$ unless otherwise indicated

[b] $p > 0.10$

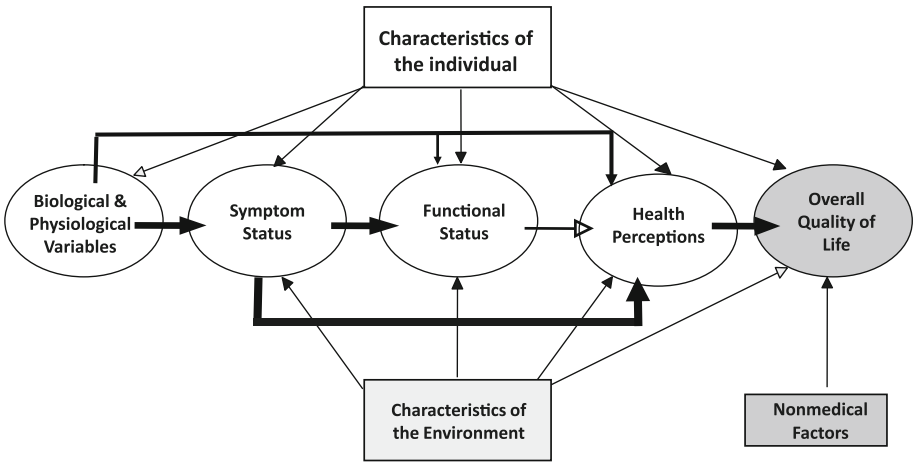

Fig. 2 Redrawn Wilson–Cleary model of HRQL for stroke

intriguing. First, this supports that physical and cognitive function may be different from role function even though the W–C model places these all at the same level. This is also consistent with stroke recovery, as the impact of physical function on role participation and other downstream outcomes wanes over time as there is very little observable improvement in physical function past 3 months and people learn to get on with their life with their existing impairments and limitations. Therefore, there is much room for improvement in role function, as what people do with their impairment becomes more important to health and quality of life in chronic stroke than what their actual impairment is; there is also room for great variation across people as success in "getting on with one's life" is individually determined. As this was a community-dwelling stroke survivor cohort, those whose stroke impairments were so severe as to make living in the community unsupportable were excluded from the cohort from inception.

Whether these relationships would hold for other health conditions is a topic for future research. Outcomes are more similar across health conditions than they are different, but the pathways to these common outcomes will differ depending on the specific impairments and their unique impact on downstream effects. Stroke, as it affects the brain and then virtually all domains of function, and because it has a sudden onset, is an excellent model to uncover key relationships, which may or may not hold across other conditions.

The World Health Organization's biopsychosocial model within the framework of the ICF [56] distinguishes conceptually between activity and participation (role), and earlier research by our team has shown that participation is a strong and independent predictor of physical and mental health and of global QOL [3].

In our model, comorbidity (biology rubric) and symptoms are linked to health perception but, as this was a cross-sectional model, it may be that health perception and

the biological representation of health measured by comorbidity and symptoms are related under a rubric of health. Health could be a latent variable made up of clinical variables (health status) and how the patient feels. Under this thinking, health would include not only measured variables for biological health but also patient-reported outcomes (PROs). There is some literature indicating that self-perceived health is mediated by an (unmeasured) inflammatory response to an illness or injury and distinguishes between people with the same biological profile but differing levels of health perception [57–60].

Merging both biology and patient perception under a health rubric may harmonize efforts to impact on patients' lives across different disciplines. In stroke, this harmonization is evident because there is little that can be done after the fact to improve the biological damage (tPA notwithstanding [61]), leaving the health of people with stroke in the hands of different types of health professionals [62]. However, many other health conditions (cancer for example) are more dominated by the biology, leaving less room for other professions working downstream to improve the path to better function and QOL [63].

Han et al. [18], in a prevalent stroke sample ($n = 591$), used SEM to link comorbidity, functional disability, and depressive symptomatology to self-rated health. Their overall purpose was to identify whether depressive symptomatology was a third fundamental component, along with physical disease (based on the number of comorbid conditions and medications) and functional disability(ADL and IADL impairments), contributing to self-rated health in this population. They did not follow the strict W–C model and modeled function to symptoms (here of depression) because in the context of stroke, it would be reasonable to assume that in some people, the depressive symptoms arose because of the functional loss.

Wilson and Cleary stated it was not clear where mental or emotional health belonged in their continuum. We included emotional health as a symptom, based on the questions included in the three scales that formed our latent variable, allowed it to correlate with other symptoms, and modeled paths to function. We found that people with lesions involving the right hemisphere had lower values on measures representing emotional health, compatible with the literature [54]. Thus, at least some of the emotional symptoms come from the lesion itself and not only function.

SEM does not determine how to draw the paths, it provides a fit based on the model provided. It requires further qualitative and quantitative inquiry to justify the direction of the paths, which might be time varying, particularly in the context of stroke, which has a sudden onset and a slow recovery.

Although our models fit well based on the RMSEA, SRMR, and CFI, the TLI dropped below 0.95. The TLI would have fared worse than the other fit indices due to the penalty applied for model complexity. In order to ensure all five imputed datasets reach convergence, some paths that would otherwise have been dropped needed to be retained, deflating the value of the TLI. However, we interpreted these fit statistics based on the overview by Schermelleh-Engel et al. [55], although other studies have applied less stringent criteria [28, 30]. Furthermore, the models did not meet the exact fit criteria of the χ^2 test. While a statistically significant χ^2 value is not surprising given the large sample size, there may be residual conceptual problems with the model. Although we tested the W–C model, stroke outcomes research is influenced strongly by the ICF model. There is considerable conceptual and operational overlap between the two models [64]. However, the two models differ in where variables in the cognitive domain are located. In the ICF model, a failed item on a test of cognition such as getting the day of the week incorrect would indicate an impairment of orientation. Missing appointments would be the consequence of the impairment and would fit under activity limitation in the ICF. In the W–C interpretation, symptoms are what people complain of. The questions about memory are from measures that ask the patient whether they have noticed that they miss appointments, thus a symptom. The value on a cognitive test shows the "function" associated with the symptoms that they cannot name the day of the week correctly. Placing the cognitive test as a "symptom" would clearly be incorrect. Placing it under "biology" would not be appropriate either because the biological data for cognitive impairment would need to come from neuroimaging. Because we were following the W–C model, we placed variables in the cognitive domain using this model. Wilson and Cleary do comment that they are not sure where various aspects of mental health belong on the path from biology to QOL. This should be the subject of further qualitative and quantitative inquiry.

There are a number of limitations to our approach. The measurement strategy did not include any direct measures of stroke impairment or stroke impact such as gait speed or manual dexterity. All associations between continuous variables were modeled as linear. Only one time point was modeled and the directionality of the links cannot be proven. There was missing data because of dropouts and missing items on measures. Our choice of using only five imputations would have reduced our power somewhat: a simulation by Graham et al. [65] found that with a missing information proportion of 30 %, using 5 imputations reduced power to 93 % of optimal based on 100 imputations. However, a strength and a unique feature of this study is that a cross-sectional SEM model was tested within a longitudinal study of an inception cohort, permitting the use of previous and subsequent information to

manage the missing data. Although FIML is available to deal with the missing data in SEM analysis, we chose to perform multiple imputation. We made this decision because within-subject correlation is stronger than cross-sectional, between-subject correlation. Multiple imputation provides an estimate of the value had the person been assessed, along with a degree of uncertainty derived from multiple reasonable estimates. Multiple imputation assumes data are missing at random, though not necessarily completely at random [51, 52], minimizes bias from ignoring missing, and increases power. QOL studies have taken a variety of approaches for the missing data, from FIML [25] to excluding missing data [22, 28, 30, 34, 66]. In an SEM of perceived health in patients with left ventricular dysfunction, only 146 of 318 subjects were included, though it was noted that those included had less severe disease than the 172 who were left out because of the missing data. Excluding missing data is likely to introduce bias and certainly affects generalizability and power.

Although the sample size of this study was large, it was not large enough to warrant a split sample for model validation. However, future analyses will include validation of this model at other time points of the dataset.

The W–C model has not been tested in stroke previously, and a better understanding of the components of HRQL during recovery from stroke is important in the development of a more integrated and person-centered approach to health management and outcome optimization for this vulnerable population at this crucial time in their lives. The findings of a strong link from comorbidity (biology rubric) and symptoms (impairments) to health perception, but not for function to health perception, suggest that to optimize overall HRQL during the first 3 months post-stroke, interventions need to focus on comorbid health conditions and on reducing stroke impairments rather than shifting too soon to a function-based approach. Sullivan et al. [19] also concluded from their SEM model in stroke that these linkages can inform treatment and policy and emphasized as well that stroke impairments are important contributors to participation, acting through function.

This information is important for the planning of health services as rehabilitation services, which focus on reducing stroke impairments but have often ceased long before three months, potentially reducing the opportunity for people recovering from stroke to optimize HRQL.

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