

# Validation of a comorbidity questionnaire in patients with neurological disorders

Nirosen Vijjaratnam ,<sup>1</sup> Shree Vadera,<sup>2</sup> Katharina Lefringhausen,<sup>3</sup> Christine Girges,<sup>1</sup> Anette Schrag<sup>1</sup>

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<sup>1</sup>Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK  
<sup>2</sup>Department of Medicine, Royal Free Hampstead NHS Trust, London, UK  
<sup>3</sup>Department of Psychology, Heriot-Watt University, Edinburgh, UK

**Correspondence to**  
Professor Anette Schrag;  
[a.schrag@ucl.ac.uk](mailto:a.schrag@ucl.ac.uk)

## ABSTRACT

**Rational** Several tools exist to assess comorbidities in neurological disorders, the most widely used being the Charlson Comorbidity Index (CCI), but it has several limitations. The Comorbidity and General Health Questionnaire (CGHQ) is a newly designed tool, which includes additional comorbidities associated with health-related quality of life (HR-QOL) and outcomes in neurological disorders.

**Aims and objectives** To assess the feasibility and validity of the CGHQ in patients with neurological disease.

**Method** Two hundred patients attending a general neurological clinic were invited to complete the CGHQ along with the EQ-5D-5L questionnaire. The CCI was simultaneously completed by the assessor. CGHQ comorbidity scores were compared with CCI, symptom burden and EQ-5D-5L scores.

**Results** The CGHQ captured 22 additional comorbidities not included on the CCI and more comorbidities were endorsed on the CGHQ. The CGHQ correlated weakly to moderately with CCI comorbidity scores. While both the CGHQ and CCI correlated negatively with the EQ-5D-5L Visual Analogue Scale, only the CGHQ correlated negatively with the EQ-5D-5L summary index. The CGHQ but not the CCI correlated strongly and positively with symptom burden scores.

**Conclusion** The CGHQ allows a more comprehensive assessment of comorbidities than the CCI and better correlates with patients' overall symptom burden and HR-QOL in neurological patients.

## BACKGROUND

Recognition of comorbidities is essential in clinical practice due to their impact on management decisions and health-related quality of life (HR-QOL).<sup>1</sup> In addition, assessment of comorbidities is important in evaluating patients' prognosis. Rating scales are an inexpensive and standardised method for measuring comorbidity and aid in management of patients with neurological conditions.<sup>2</sup> One of the most widely used clinician-completed measures is the Charlson Comorbidity

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There are a number of tools for the assessment of comorbidities, but existing tools do not account for a number comorbidities recognised to be of relevance for health-related quality of life and prognosis.

## WHAT THIS STUDY ADDS

⇒ The Comorbidity and General Health Questionnaire (CGHQ) is a newly designed tool, which measures comorbidities relevant to outcomes and health-related quality of life in neurological disorders. It captured 22 additional comorbidities and better correlated with health-related quality of life than the Charlson Comorbidity Index.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The CGHQ questionnaire could be included in clinical practice and clinical trials as a comprehensive and relevant assessment of comorbidities in patients with neurological disorders.

Index (CCI),<sup>3</sup> which predicts mortality in a range of neurological conditions.<sup>4-6</sup> The CCI is, however, limited to 16 potential comorbid diseases and does not directly assess comorbidities more recently shown to be associated with increased mortality or poor quality of life. It also does not assess other factors such as family history, polypharmacy or lifestyle factors that are known to be associated with a worse prognosis and quality of life. Furthermore, the scale was developed for use primarily in surgical settings and has not been updated substantially since its conception although modified weightings have been proposed.<sup>7 8</sup> The Comorbidity and General Health Questionnaire (CGHQ) was developed as a novel tool with the goal to assess better comorbidity burden in neurological diseases, incorporating additional comorbidities that have been shown to worsen HR-QOL.<sup>1 9</sup> Here, we

**Table 1** Patient demographics

	N (%)
Total	200 (100)
Sex	
Male	97 (48.5)
Female	103 (51.5)
Age	
≤40	63 (31.5)
41–50	23 (11.5)
51–60	41 (20.5)
61–70	32 (16.0)
71–80	29 (14.5)
≥80	12 (6.0)
Smoking status	
Current smoker	45 (22.5)
Non-smoker	150 (75.0)
Missing data	5 (2.5)
Alcohol use	
Current drinker	74 (37.0)
Non-drinker	119 (61.5)
Missing data	7 (3.5)
Family history	
Dementia	25/199 (12.6)
Parkinson's disease	17/199 (8.5)
Other neurological diseases	17/197 (8.6)
Heart disease	49/198 (24.7)
Osteoporosis/hip fractures	27/197 (13.7)

aimed to explore the feasibility and validity of the CGHQ in a cohort of patients with neurological diseases.

## METHODS

Patients attending a general neurological clinic either for initial assessment and diagnosis or for follow-up of a previously diagnosed neurological condition were asked to complete a preclinic questionnaire before their outpatient consultation if no language or cognitive barrier was apparent. We aimed for a sample size of approximately 200 patients which previous studies have suggested as a fair size of scale validation.<sup>10</sup> Verbal consent was provided before completing the CGHQ and EQ-5D-5L. The CCI was completed by the clinician based on primary care physician referral letters that typically summarise all known health conditions to date. The analysis was based on a project registered as an audit at the Royal Free National Health Service Trust to assess the usefulness of a new clinical assessment method.

## Assessments

### Charlson Comorbidity Index

The CCI is a rater-completed scale developed by Dr Charlson in the late 1980s to predict perioperative complications.<sup>3</sup> This clinician-completed scale contains a list of 16 conditions with assigned weighting (1–6). The sum of the weights for each comorbidity, aside from the primary disease of interest, forms the Charlson index. The CCI has been shown to strongly predict mortality in a range of health conditions.<sup>6 11 12</sup>

### EQ-5D-5L

The EQ-5D-5L consists of two subsections: the EQ-5D-5L descriptive system and the Visual Analogue Scale (VAS). The descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Within each item, there are five possible outcomes: no problems, slight problems, moderate problems, severe problems and extreme problems. Participants are asked to indicate their health state by selecting the statement that most accurately represents their current health state. Each item is then given a digit from 1–5 based on the level selected by the participant. The digits for each of the five dimensions are combined to create a five-digit number that represents the participant's current health state.<sup>13</sup> A summary index (SI) was derived from this using an online tool based on value sets for England.<sup>14</sup> The VAS asks participants to mark their self-rated health on the day of completion on a vertical VAS from 0 to 100 with the endpoints labelled 'the worst health you can imagine' and 'the best health you can imagine'.<sup>13</sup>

### Comorbidity and General Health Questionnaire

The CGHQ is a patient-completed questionnaire which was developed with the aim of assessing comorbidities in patients with neurological conditions. Previously described key factors which influence multimorbidity<sup>15</sup> were used to guide the development of the CGHQ, and it drew on other existing comorbidity and prognostic tools (QRisk3, QRiskAdmissions, QMortality, Frax Fracture, JBS3, QCancer, QStroke or Qfrailty calculators). The questionnaire also included questions on occurrence of symptoms associated with neurological disorders<sup>16–18</sup>, the sum of which was used to calculate the symptom burden score. The CGHQ is attached in online supplemental appendix.

### Weighting approaches

Multiple methods were used to calculate summary scores. For CCI1, comorbidities were weighted according to the original scoring system of the CCI.<sup>3</sup> For CCI2, comorbidities were weighted according to the original scoring system with age group weights, where each decade over 40 adds 1 point to the total score obtained from the comorbidity index. In CCI3, comorbidities were weighted as suggested by Quan *et al* based on the HRs for mortality.<sup>19</sup> Finally, in CCI4 comorbidities were not weighted (all scores equalled 1). Summary scores for the CGHQ were, CGHQ1:

**Table 2** Prevalence of comorbidities on the CGHQ

Comorbidities new on the CGHQ			
Comorbidity	N (%)	Comorbidity	N (%)
Hypertension	37 (18.5)	Anaemia	16 (8.0)
Hypothyroidism	13 (6.5)	Recurrent infections	8 (4.0)
Obesity (BMI>30)	20 (10.0)	Epilepsy	28 (14.0)
Hypercholesterolaemia	42 (21.0)	Unexplained falls	12 (6.0)
Cardiac arrhythmias including atrial fibrillation	15 (7.5)	Parkinson's disease	10 (5.0)
Other heart disease	6 (3.0)	Learning disability	9 (4.5)
Osteoarthritis	27 (13.5)	Neurological disorder	12 (6.0)
Chronic GI disease	3 (1.5)	Depression	48 (24.0)
Urinary system disorder	9 (4.5)	Anxiety	51 (25.5)
Blood clotting disorder or deep vein thrombosis	8 (4.0)	Alcoholism	1 (0.5)
Fluid or electrolyte disorders	0 (0)	Schizophrenia	1 (0.5)
Comorbidities on the CGHQ and CCI			
Comorbidity	CGHQ N (%)	CCI N (%)	
Diabetes mellitus	20 (10.0)	27 (13.5)	
Congestive heart failure	3 (1.5)	5 (2.5)	
Peripheral vascular disease	0 (0)	2 (1.0)	
Chronic obstructive pulmonary disease	25 (12.5)	9 (4.5)	
Chronic liver disease	0 (0)	0 (0)	
Leukaemia	0 (0)	0 (0)	
HIV	0 (0)	0 (0)	
Myocardial infarction (or ischaemic heart disease)*	5 (2.5)	8 (4.0)	
Stroke†~	13 (6.5)	10 (5.0)	
(Rheumatoid arthritis* or) connective tissue disease	13 (6.5)	2 (3.08)	
Chronic kidney disease	1 (0.5)	1 (0.5)	
Peptic ulcer disease	1 (0.5)	0 (0)	
Malignant lymphoma	0 (0)	1 (0.5)	
Solid tumour with/without metastasis	3 (1.5)	6 (3.0)	
Dementia	2 (1.0)	1 (0.5)	
Hemiplegia	–	5 (2.5)	

~\*On the CCI: cerebrovascular disease.  
 †\*Only on the CGHQ.  
 BMI, body mass index; CCI, Charlson Comorbidity Index; CGHQ, Comorbidity and General Health Questionnaire; GI, gastrointestinal.

comorbidities overlapping with the CCI were weighted according to the Quan *et al* weighting; CGHQ2: the overlapping comorbidities were not weighted (all scores equalled 1); and CGHQ3: additional age group weights were added to overlapping comorbidities that were not weighted (scores equalled 1). For each CCI and CGHQ version, the sum of scores was used in further analyses.

### Statistical analysis

The Shapiro-Wilk normality test indicated that all variables were not normally distributed (CCI, CGHQ, CGHQ subscore, Symptom Burden, VAS and EQ-5D SI) ( $p < 0.01$ ). A closer inspection revealed that none of CGHQ versions showed a kurtosis level

above the acceptable threshold of  $\pm 2$ . We, therefore, conducted a Spearman's rank test to assess correlation between main variables with a  $p < 0.05$  to indicate statistical significance. Construct and convergent validity were assessed by examining correlation within and between the three CGHQ versions and within four CCI versions and between the CGHQ and CCI versions and EQ-5D-5L SI and symptom burden scores. Differences between males and females across the CCI and CGHQ scale versions were assessed using the Mann-Whitney U test. CCI and CGHQ differences across age groups were assessed with a one-way analysis of variance for scores without any weighting (CCI4 and CGHQ2) with Bonferroni post hoc tests

**Table 3** Symptom burden assessed by the CGHQ

Symptom	N (%)
Weight loss	12 (6.0)
Fatigue	82 (41.0)
Poor appetite	33 (16.5)
Poor sleep	85 (42.5)
Low mood	75 (37.5)
Constipation	41 (20.5)
Difficulty breathing	43 (21.5)
Visual impairment	23 (11.6)
Hearing impairment	8 (4.0)

CGHQ, Comorbidity and General Health Questionnaire.

applied thereafter with a significant difference at an alpha level of 0.01.

## RESULTS

Two hundred participants completed the CGHQ. Ninety-seven (48.5%) patients were male. The mean age was 52.32 years (*SD* 19.29; range 18–91 years). Other patient demographics are summarised in [table 1](#). The CGHQ included 22 additional comorbidities to the CCI, all of which were endorsed by some patients. Commonly reported comorbidities not included on the CCI were anxiety (25.5%),

depression (24.0%), epilepsy (14.0%) and hypertension (18.5%). Conversely, the only item not covered on the CGHQ but on the CCI was hemiplegia, which was found in five patients on the CCI. This was, however, captured by the stroke and learning disability items on the CGHQ. More comorbidities were reported on the CGHQ and most comorbidities on the CCI were reported by patients on the CGHQ ([table 2](#)). Symptom burden reporting on the CGHQ is summarised in [table 3](#).

The three CGHQ versions correlated strongly ( $r=0.82$ – $0.99$ ) with each other and the CCI versions correlated moderately to strongly with each other ( $r=0.61$ – $0.99$ ). The CGHQ versions correlated weakly to moderately with all four CCI scales ( $r=0.33$ – $0.79$ ), indicating adequate construct validity.

There was a moderate negative correlation of the EQ-5D-5L VAS with the CGHQ versions and a weak negative correlation with the CCI versions. Only the CGHQ versions correlated significantly with the EQ-5D-5L SI. There was also a significant positive correlation of the CGHQ versions with symptom burden scores, but not with any of the CCI versions ([table 4](#)).

No significant differences between genders for any of the CCI and CGHQ scale versions were noted. Significant age group differences were, however, noted on the CCI4 between the  $\leq 40$  years and the 61–70 years, 71–80 years and  $\geq 80$  years age groups,

**Table 4** Spearman's rank correlations (n) for the CHGQ and CCI with symptom burden and EQ-5D-5L scores

Variables	CGHQ1	CGHQ2	CGHQ3	CCI1	CCI2	CCI3	CCI4
CGHQ1							
CGHQ2	<b>0.99**</b>						
	200						
CGHQ3	<b>0.82**</b>	<b>0.84**</b>					
	200	200					
CCI1	<b>0.33**</b>	<b>0.37**</b>	<b>0.47**</b>				
	200	200	200				
CCI2	<b>0.36**</b>	<b>0.39**</b>	<b>0.79**</b>	<b>0.67**</b>			
	200	200	200	200			
CCI3	<b>0.33**</b>	<b>0.36**</b>	<b>0.44**</b>	<b>0.87**</b>	<b>0.61**</b>		
	200	200	200	200	200		
CCI4	<b>0.34**</b>	<b>0.38**</b>	<b>0.47**</b>	<b>0.99**</b>	<b>0.66**</b>	<b>0.85**</b>	
	200	200	200	200	200	200	
Symptom burden	<b>0.38**</b>	<b>0.38**</b>	<b>0.28**</b>	0.11	0.08	0.12	0.11
	200	200	200	200	200	200	200
EQ-5D-5L VAS	<b>0.36**</b>	<b>0.37**</b>	<b>0.31**</b>	<b>0.19*</b>	<b>0.16*</b>	<b>0.18*</b>	<b>0.19**</b>
	193	193	193	193	193	193	193
EQ-5D SI	<b>0.40**</b>	<b>0.38**</b>	<b>0.33**</b>	0.14	0.13	0.14	0.14
	180	180	180	180	180	180	180

Note: In bold face: \*\* $p<0.001$ , \* $p<0.01$ ,  $p<0.05$ .

CCI, Charlson Comorbidity Index; CGHQ, Comorbidity and General Health Questionnaire; SI, Summary Index; VAS, Visual Analogue Scale.

and on the CGHQ2 between patients  $\leq 40$  years and 61-70 years after Bonferroni correction with a  $p < 0.01$ .

## DISCUSSION

We were able to demonstrate that the CGHQ, a novel questionnaire assessing comorbidities, largely provided the information collected in the widely used CCI as well as additional relevant information on comorbidities relevant to HR-QOL. We demonstrated construct validity using a variety of different scoring methods. Moreover, the CGHQ had considerably stronger correlation with symptom burden and health-related quality of life than any versions of the CCI.

Comorbidities and symptom burden can have a detrimental effect on quality of life,<sup>1</sup> influence management choices and are associated with poorer prognostic outcomes.<sup>20</sup> A comprehensive and standardised routine assessment can therefore assist clinical management. While the CCI captures 16 comorbidities and no other patient factors, the CGHQ examines 38 comorbidities as well as symptom burden and provides the opportunity to assess medication history and family history, thus casting a wider net and gaining deeper insight into multiple aspects of patients' health. Despite this, the majority of participants completed all items on the questionnaire, suggesting it is comprehensive but not overwhelming. As a self-completed questionnaire, a concern was the CGHQ potentially missing diagnoses patients do not report. However, we found that more diagnoses were reported and only a minority of diagnoses listed in medical records were not reported by patients, in keeping with previous studies showing a higher rate of comorbidities on self-completed questionnaires than administrative approaches.<sup>21</sup> The list of additional conditions elicited in this survey included mental health diagnoses which have a significant prevalence in neurological conditions and substantial functional impacts.<sup>22</sup>

In both the CCI and CGHQ, no significant gender differences were noted, but some differences between older age groups and the youngest age group were noted. Interestingly, although multimorbidity has been proven to be highly prevalent in older people compared with younger-aged or middle-aged groups, in a study in over 1.5 million participants more than half of people with multimorbidity and almost two-thirds of those with physical-mental health comorbidity were less than 65 years old. The same study showed a strong correlation between socioeconomic depravity and multimorbidity, although a weaker correlation than that between age and multimorbidity.<sup>23</sup> Larger studies exploring this as well as examining the CGHQ across different ethnicity and socioeconomic backgrounds in patients with neurological conditions may, therefore, be of interest considering low socioeconomic status is associated with a variety of neurological diseases.<sup>24-26</sup>

We envisage future CGHQ use in both clinical and research settings but several limitations of the current

study need to be acknowledged and some overcome. First, the study was carried out in neurology outpatient clinics and may not apply in the same way to inpatients or other patient populations. Modified versions of the CCI now exist and future studies comparing them to the CGHQ in neurological cohorts would also be important. Further studies are required to examine acceptability of the instrument and its usefulness in different neurological conditions as well as its ability to predict mortality in longitudinal studies, which is a key goal for comorbidity questionnaires.

In conclusion, our data suggest that the CGHQ, a novel comorbidity index specific to neurological disease, is a comprehensive and useful instrument for the assessment of comorbidities in a cross-sectional sample of general neurological patients. While clinical management cannot rely solely on self-report, the CGHQ assesses a broad range of comorbidities and multiple aspects of patient health and allows for structured assessment of comorbidities relevant to prognosis and subjective HR-QOL. Longitudinal analysis in larger cohorts and across different patient populations will be needed to assess its acceptability, performance and predictive value but our findings suggest this may be a promising tool for assessment of comorbidities and prognostication in patients with neurological disorders.

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## ORCID iD

Nirosen Vijjaratnam <http://orcid.org/0000-0002-9671-0212>

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