Validation of a comorbidity questionnaire in patients with neurological disorders

Nirosen Vijiaratnam,1 Shree Vadera,2 Katharina Lefringhausen,3 Christine Girges,1 Anette Schrag1

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).1 In addition, assessment of comorbidities is essential in evaluating patients' prognosis. Rating scales are an inexpensive and standardised method for measuring comorbidity and aid in management of patients with neurological conditions.2 One of the most widely used clinician-completed measures is the Charlson Comorbidity Index (CCI).3 which predicts mortality in a range of neurological conditions.4–6 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.7 8 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.1 9 Here, we...
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. 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.

Table 1 Patient demographics

<table>
<thead>
<tr>
<th>N (%)</th>
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<tbody>
<tr>
<td>Total 200 (100)</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male 97 (48.5)</td>
</tr>
<tr>
<td>Female 103 (51.5)</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>≤40 63 (31.5)</td>
</tr>
<tr>
<td>41–50 23 (11.5)</td>
</tr>
<tr>
<td>51–60 41 (20.5)</td>
</tr>
<tr>
<td>61–70 32 (16.0)</td>
</tr>
<tr>
<td>71–80 29 (14.5)</td>
</tr>
<tr>
<td>≥80 12 (6.0)</td>
</tr>
<tr>
<td>Smoking status</td>
</tr>
<tr>
<td>Current smoker 45 (22.5)</td>
</tr>
<tr>
<td>Non-smoker 150 (75.0)</td>
</tr>
<tr>
<td>Missing data 5 (2.5)</td>
</tr>
<tr>
<td>Alcohol use</td>
</tr>
<tr>
<td>Current drinker 74 (37.0)</td>
</tr>
<tr>
<td>Non-drinker 119 (61.5)</td>
</tr>
<tr>
<td>Missing data 7 (3.5)</td>
</tr>
<tr>
<td>Family history</td>
</tr>
<tr>
<td>Dementia 25/199 (12.6)</td>
</tr>
<tr>
<td>Parkinson’s disease 17/199 (8.5)</td>
</tr>
<tr>
<td>Other neurological diseases 17/197 (8.6)</td>
</tr>
<tr>
<td>Heart disease 49/198 (24.7)</td>
</tr>
<tr>
<td>Osteoporosis/hip fractures 27/197 (13.7)</td>
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Assessments
Charlson Comorbidity Index
The CCI is a rater-completed scale developed by Dr Charlson in the late 1980s to predict perioperative complications. 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.

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. A summary index (SI) was derived from this using an online tool based on value sets for England. 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’.

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 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, 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. 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. Finally, in CCI4 comorbidities were not weighted (all scores equalled 1). Summary scores for the CGHQ were, CGHQ1:
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 ±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.
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 ≤40 years and the 61–70 years, 71–80 years and ≥80 years age groups.

| Table 3  | Symptom burden assessed by the CGHQ |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Symptom        | N (%)           | Symptom        | N (%)           | Symptom        | N (%)           | 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.

| Table 4  | Spearman’s rank correlations (r) for the CGHQ and CCI with symptom burden and EQ-5D-5L scores |
|-----------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Variables       | CGHQ1                           | CGHQ2                           | CGHQ3                           | CCI1                            | CCI2                            | CCI3                            | CCI4                            |
| CGHQ1           |                                  |                                  |                                  |                                 |                                 |                                 |                                 |
| CGHQ2           | $0.99^{**}$                      |                                  |                                  |                                 |                                 |                                 |                                 |
| CGHQ3           | $0.82^{**}$                      | $0.84^{**}$                      |                                  |                                 |                                 |                                 |                                 |
| CCI1            | $0.33^{**}$                      | $0.37^{**}$                      | $0.47^{**}$                      |                                 |                                 |                                 |                                 |
| CCI2            | $0.36^{**}$                      | $0.39^{**}$                      | $0.79^{**}$                      | $0.67^{**}$                      |                                 |                                 |                                 |
| CCI3            | $0.33^{**}$                      | $0.36^{**}$                      | $0.44^{**}$                      | $0.87^{**}$                      | $0.61^{**}$                      |                                 |                                 |
| CCI4            | $0.34^{**}$                      | $0.38^{**}$                      | $0.47^{**}$                      | $0.99^{**}$                      | $0.66^{**}$                      | $0.85^{**}$                      |                                 |
| Symptom burden  | $0.38^{**}$                      | $0.38^{**}$                      | $0.28^{**}$                      | $0.11$                           | $0.08$                           | $0.12$                           | $0.11$                           |
| EQ-5D-5L VAS    | $0.36^{**}$                      | $0.37^{**}$                      | $0.31^{**}$                      | $0.19^{*}$                       | $0.16^{*}$                       | $0.18^{*}$                       | $0.19^{**}$                      |
| EQ-5D SI        | $0.40^{**}$                      | $0.38^{**}$                      | $0.33^{**}$                      | $0.14$                           | $0.13$                           | $0.14$                           | $0.14$                           |

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 CGHQ between patients ≤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, influence management choices and are associated with poorer prognostic outcomes. 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.

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. 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.

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.

**Contributors** NV collected data, analysed data, prepared the initial manuscript and revised the manuscript. SV, KL and CG analysed data and revised the manuscript. AS designed the study, revised the manuscript and acts as guarantor.

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**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** We followed the UK Policy Framework for Health and Social Care Research decision tool on Defining Research which concluded that this research does not require a research ethics review. The study was carried out in accordance with relevant guidelines and regulations.

**Provenance and peer review** Not commissioned; internally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as online supplemental information.

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REFERENCES


Comorbidity and General health questionnaire

These questions apply to the past 12 months. Please answer these to the best of your knowledge.

Please indicate if you have had any of the following diagnoses (underline which one):

- Hypertension
- Diabetes mellitus (without – with end-organ damage)
- Hypothyroidism
- Obesity (BMI>30)
- High cholesterol
- Myocardial infarction (heart attack) or ischaemic heart disease
- Congestive Heart Failure
- Cardiac arrhythmias /atrial fibrillation
- Other heart disease
- Stroke or Cerebrovascular Disease
- Peripheral Vascular Disease
- Rheumatoid arthritis/Connective Tissue Disease
- (Osteo-) arthritis
- COPD/asthma/chronic lung disease
- Chronic Kidney Disease (moderate – severe)
- Chronic liver Disease (mild – moderate – severe)
- Chronic gastrointestinal disease (e.g. Crohn’s disease)
- Peptic Ulcer Disease
- Urinary system disorder
- Blood clotting disorder/deep vein thrombosis
- Fluid and electrolyte disorders
- Anemia
- Leukemia
- Malignant Lymphoma
- Solid tumor without metastasis
- Metastatic cancer
- Recurrent infections
- HIV
- Epilepsy
- Unexplained falls
- Parkinson’s
- Dementia
- Learning disability
- Other neurological disorder
- Depression
- Anxiety
- Alcohol problem
- Schizophrenia