Chronic pulmonary aspergillosis (CPA) is a usually incurable and progressive disease that causes significant lung function deterioration. It typically leads to death from respiratory failure, infection, or hemoptysis. Multiple underlying diseases are associated with CPA, including prior TB, nontuberculous mycobacterial infection, COPD, sarcoidosis, and allergic bronchopulmonary aspergillosis. Worldwide, the prevalence of CPA following TB has been estimated at about 1.2 million people. The disease is defined by the combination of at least one pulmonary cavity on thoracic imaging, with or without an aspergilloma, together with symptoms (usually weight loss, fatigue, cough, hemoptysis, and breathlessness) for >3 months, and serology (positive Aspergillus-precipitating IgG antibody in blood) or cultures or histology implicating Aspergillus species. Given the condition’s long-term nature and disabling symptoms, it is reasonable to anticipate an impact on physical, social, and psychological aspects of patients’ health status. To date, however, quantification of health status impairment in patients with CPA has not been undertaken. This is due, at least in part, to a lack of adequately validated scales that can be used in this population.

The St. George’s Respiratory Questionnaire (SGRQ) is a respiratory-specific, health-status measure that...
consists of three domains assessing the most common respiratory symptoms, activity status, and the perceived impact of respiratory illness on the patient’s daily life.7 The questionnaire has been well validated in COPD7-10 and asthma11 and also is used in assessing health status in several other respiratory illnesses, such as idiopathic pulmonary fibrosis,11 bronchiectasis,12 cystic fibrosis,13 and pulmonary TB.14 Moreover, the SGRQ has received wide acceptance and has been translated into in many different languages and validated in different cultures.15-17 However, to date, the scale has not been used, let alone validated, in assessing health status in patients with CPA. Therefore, we investigated the reliability and validity of the SGRQ in assessing health status in patients with CPA.

Materials and Methods

Study Population

Eighty-eight patients from the United Kingdom who had CPA and attended our tertiary referral clinic had their health status assessed as part of their routine clinic visit. Most were on antifungal therapy at the time of assessment. UK National Aspergillosis Centre criteria for banding CPA severity were used, with patients categorized as follows: band 1: ambulant and independent, no evidence of antifungal resistance, treatment with itraconazole capsules or no treatment; band 2: significant impairment of respiratory function (sufficient to impair activities of daily living, but ambulant) and/or failed or developed toxicity to itraconazole capsules and no evidence of azole antifungal resistance and/or evidence of mycobacterial disease; band 3: antifungalazole resistance documented and/or long-term nebulized or IV antibiotic treatment required (eg, bronchiectasis, Pseudomonas colonization) and/or wheelchair bound due to respiratory impairment and/or additional, severe, underlying diseases such as controlled HIV infection, or significant renal or hepatic dysfunction.18 The data were collected with the goal of establishing the usefulness and feasibility of adding a health-related quality-of-life measure to routine clinical assessment. Per UK National Research Ethics Service guidance, ethical approval or institutional review board approval is not required for this kind of work.

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The St. George’s Respiratory Questionnaire

The SGRQ measures respiratory disease–specific health status. It is a self-administered questionnaire developed by Jones19 and colleagues7,20 in 1991. The questionnaire has 50 items with 76 weighted responses that are subcategorized to three main aspects. The first eight items cover the respiratory symptoms and their frequency and severity; this is the symptom domain. The next 16 items concern limitation in activities due to shortness of breath; this is the activity domain. The last 26 items cover the consequent social and psychologic implications of the respiratory diseases; this is the impact domain. The scale is scored from 0 to 100, where the higher score indicates worse health status, and a difference or change of four points is considered clinically significant.8 The patients routinely completed the SGRQ every 3 months. To investigate test-retest SGRQ reliability, 17 clinically stable patients who had no exacerbation or other notable change in condition completed the questionnaire twice in 2 to 3 week intervals.

We used the original Medical Research Council (MRC) dyspnea scale to assess shortness of breath. Although the MRC dyspnea scale was developed >50 years ago,21 it is still one of the most reliable, valid, and easily administered scales and has been used extensively in assessing breathlessness in respiratory studies. The patient selects one of five options, and every option correlates shortness of breath with a certain task magnitude starting from strenuous to light.22

We also used the Short Form-36 Health Survey (SF-36), which consists of eight domains: general health, physical functioning, role function, role emotional, bodily pain, vitality, social functioning, and mental health. In addition, two summary scores, a physical component summary (PCS) score and mental component summary (MCS) score, were calculated.23 This scale has been used in studying general health status in chronic respiratory illnesses such as asthma,24 bronchiectasis,12 and COPD.25

Lung function was also measured by a well-trained respiratory technician in our center at the same visit of the SGRQ completion or within 6 months. We obtained lung function measurement from the computerized database of our lung function laboratory for approximately 10% of the patients; this was done within a year from the SGRQ completion.

Additionally, the general health condition of every patient was graded by a physician in our referred center (grades: very poor, poor, fair, good, and very good). This was based on inspection of the medical record, taking into account key parameters such as main clinical manifestations (eg, shortness of breath, weight status, presence or absence of hemoptysis, fatigue, sputum production, and exercise tolerance), oxygen dependence, hospital admissions, comorbid conditions, and medications. Radiologic changes such as pericavitary thickening, pleural thickening, cavity size and number, and presence or absence of fungal ball also were assessed by the physician.

We used the Index of Multiple Deprivations to correlate SGRQ score with a range of socioeconomic factors. This index is a pooled score based on measures of income, education, housing, health, and crime for each postcode in England, as has been used in previous studies.26 To assess the impact of comorbidities, we used the Charlson Comorbidity Index and calculated the total scores as guided by Charlson et al.27

Statistical Analysis

Reliability of the SGRQ in CPA: We investigated the internal consistency of the SGRQ and each dimension using the Cronbach α coefficient28; a correlation ≥ 0.7 was assumed to indicate that questions within a dimension are likely to measure the same construct.29-31 We measured test-retest reliability using intraclass correlation coefficient (ICC) of the SGRQ and of each of its dimensions.
Validity of the SGRQ in CPA: To examine the convergent validity, total and dimensional scores of the SGRQ were correlated with the MRC dyspnea score, SF-36 PCS score, SF-36 MCS score, FEV\textsubscript{1}, FEV\textsubscript{1}/FVC, predicted, and FVC. The discriminating validity was also investigated using either the median of SGRQ total and activity dimension scores or mean of the SGRQ symptom and impact dimension between the CPA bands, MRC dyspnea grades, and the general health condition as judged by a respiratory physician.

Difference in medians of the nonparametric data (total SGRQ and activity dimension scores) between CPA severity bands. MRC dyspnea grades, and health-condition grades were examined using the Kruskal-Wallis test; analysis of variance was used to examine the difference in means of parametric data (SGRQ symptoms and impact dimension scores). Difference in medians of total SGRQ and activity dimension scores between CPA grades 1 vs 3 were investigated using the Mann-Whitney U test, and an equivalent, independent sample t test was used to examine difference in means of SGRQ symptoms and impact dimension scores.

The Pearson correlation coefficient was used to examine the correlation of symptom and impact domains with SF-36 PCS, SF-36 MCS, FEV\textsubscript{1}, and FVC. The Spearman correlation coefficient was used to examine the correlation of total SGRQ and activity scores with MRC dyspnea scores, SF-36 PCS score, SF-36 MCS score, FEV\textsubscript{1}, and FVC. The paired t test was used to compare the mean scores of the total and dimensional SGRQ scores at both visits. The association of CPA severity with impairment in health status was also investigated using linear and binary multivariate analysis. Data analysis was performed using SPSS version 15 (IBM Corp).

Results

Patients' Characteristics

Of 88 patients examined, 21 (23.9%), 51 (58%), and 16 (18.2%) had band 1, 2, and 3 CPA, respectively. Women made up 43.2% of the patient cohort and had slightly lower BMI, but less airway obstruction, than men. Other characteristics and demographic data of the study patients can be seen in Table 1.

We found that neither SGRQ total nor dimensional score were affected by sex (Table 1). There was no statistically significant correlation between age and SGRQ dimensions and total scores. SGRQ total and activity dimension scores were slightly skewed and therefore presented as median and interquartile ranges (IQRs) as shown in Table 1; moreover, the median, IQR, and minimum and maximum ranges of SGRQ dimensions and total scores are also illustrated Figure 1.

Reliability of the SGRQ

Using Cronbach α for measuring internal consistency for the total score and each dimension (symptom, activity, and impact), we found α values of 0.94, 0.77, 0.91, 0.86, respectively. Total SGRQ had a highly statistically significant correlation with SGRQ symptoms, activity, and impact domains (0.64, 0.82, and 0.96, respectively). Symptoms domain had mild correlation with activity domain (0.41) and a moderate correlation with impact domain (0.61). However, a better correlation was seen between activity and impact domains (0.7) (P < .0001 for all these correlations). For test-retest reliability, the intraclass correlation coefficients for the total SGRQ and its dimensions (symptom, activity, and impact) were 0.97, 0.92, 0.94 and 0.95, respectively. There were small and statistically insignificant mean differences between scores at both completions as shown in Table 2, and the 95% limits of agreement of repeatability as shown in Bland-Altman plot (Fig 2).

Validity of the SGRQ

The SGRQ total and dimensional scores showed high convergent validity correlating with different objective and subjective measures in respiratory research. The MRC dyspnea score, SF-36 PCS score, and SF-36 PCM score had the highest correlation with total and dimensional SGRQ scores, as shown in Table 3. The maximum correlation was with both SF-36 scores and greater than the MRC dyspnea score (R\textsuperscript{2} = 0.5), suggesting that other important elements of ill health in these patients are being captured by the SGRQ.

Worse health status was associated with increasing severity of CPA; patients with severe CPA had worse health status than patients with mild or moderate disease. Moreover, the SGRQ showed significant discriminating ability in differentiating between all grades of shortness of breath. In addition, patients with more disease severity as justified by the respiratory physician scored consistently higher total and dimensional SGRQ scores, as can be seen in Table 4. This association between SGRQ total and dimensional scores with CPA severity bands was even better seen when plotted by band 1 vs bands 2 and 3 together (P = .007, .015, .004, and .002, respectively) as illustrated in Figure 3.

The Effect of Pulmonary and Extrapulmonary Comorbidities and Socioeconomic Factors on Health Status in CPA

We found more than nine pulmonary comorbidities in the sample. Thirty-three patients had COPD (38%), and 25 had bronchiectasis (28%) (e-Table 1). Using total SGRQ score as a dependent variable, multivariate linear regression analysis showed that only COPD had a significant association with impaired health status (β = 0.26, P = .03) after adjustment to TB, non-tuberculous Mycobacterium infection, asthma, allergic bronchopulmonary aspergillosis, bronchiectasis, pneumothorax, previous lung cancer, pneumonia, and sarcoidosis. When using the activity domain as the dependent variable, a similar finding was seen in which only COPD was significantly associated with impaired
This study addresses the validity and reliability of SGRQ in adequately assessing health status in patients with CPA. The SGRQ components and total scores achieved high internal consistency, and SGRQ components had good intercorrelation and correlated well with the total score. The questionnaire showed a high level of repeatability (demonstrated by high intraclass correlation, and minimal difference in the mean score of SGRQ components scores and total scores when completed again after 2 to 3 week interval. The total and dimensional SGRQ scores showed significant correlation with well-validated instruments widely used in respiratory research. The SGRQ had considerable discriminating ability, differentiating between different levels of disease severity, all grades of shortness of breath and health status (physician-rated). Activity ($\beta = 0.34; P = .003$). Using the symptoms domain, bronchiectasis and COPD showed a trend toward statistical significance and likewise, using the impact domain, only COPD trended toward significance. To further investigate this point, we compared the SGRQ total and dimensional scores of patients with CPA who had COPD (with or without bullae) vs those who did not have COPD. We found that although both groups had high SGRQ total and dimensional scores, the group who had underlying COPD (with or without bullae) had a higher SGRQ total and dimensional score as demonstrated in e-Table 2.

Moreover, using CPA bands (band 1 vs bands 2 and 3) as a dependent variable, binary regression analysis showed SGRQ total score only had a statistically significant association with CPA severity after correction for FEV$_1$, age, sex, and BMI (OR, 1.2; 95% CI, 1-1.1; $P = .05$). Moreover, when adding COPD comorbidity to the module, we found that only COPD comorbidity and SGRQ total score were independently associated with CPA bands (OR, 50.6; 95% CI, 2.9-878; $P = .007$) and (OR, 1.1; 95% CI, 1-1.14; $P = .027$), respectively. Additionally, considering the sample size, we replaced age and sex with aspergilloma, bronchiectasis, and pneumothorax and found that COPD comorbidity and SGRQ total score remained as the only two variables that independently associated with CPA bands (OR, 44.4; 95% CI, 2.7-742; $P = .008$) and (OR, 1.1; 95% CI, 1-1.12; $P = .028$), respectively.

Furthermore, using the Charlson comorbidities index, we found that comorbidities did not contribute to significant additional impairment of health status in CPA, as detailed in e-Appendix 1. We found no statistically significant association between socioeconomic status and SGRQ total and dimensional scores as detailed in e-Appendix 1.

### Discussion

This study addresses the validity and reliability of SGRQ in adequately assessing health status in patients with CPA. The SGRQ components and total scores achieved high internal consistency, and SGRQ components had good intercorrelation and correlated well with the total score. The questionnaire showed a high level of repeatability (demonstrated by high intraclass correlation, and minimal difference in the mean score of SGRQ components scores and total scores when completed again after 2 to 3 week interval. The total and dimensional SGRQ scores showed significant correlation with well-validated instruments widely used in respiratory research. The SGRQ had considerable discriminating ability, differentiating between different levels of disease severity, all grades of shortness of breath and health status (physician-rated).
eral studies used in assessing the validity of SGRQ in chronic pulmonary illnesses such as COPD and bronchiectasis.\textsuperscript{7,12}

CPA is a chronic respiratory illness that usually deteriorates progressively with a deleterious effect on different aspects of patients’ health. Both physical and social activities become limited, resulting in physical disability, isolation, and psychologic distress. Our demonstration of discriminant validity would suggest that the scale could be a valid and clinically useful tool to regularly assess and identify deterioration in health status of patients with CPA. A further clinical benefit of the SGRQ is that it can offer assessment of health status in general and in specific domains. Effective monitoring of health-status deterioration is crucial in CPA, since failure to proactively manage early deterioration may result in further lung damage and development of complications such as underlying comorbidities. However, COPD comorbidity significantly affected health status in patients with CPA.

In this study, the total SGRQ and its component scores (symptom, activity, and impact) also showed high internal consistency. A Cronbach’s value of $>0.7$ indicates good reliability of a scale.\textsuperscript{29} This strength of SGRQ structure was supported with a significant intercorrelation between components and even better correlation of components with total score, demonstrating that the scale measured different aspects of the same construct. We also observed the individual SGRQ components and total score showed a good correlation with the MRC dyspnea scale. The MRC dyspnea scale is a highly valid instrument that several studies used in assessing the validity of SGRQ in chronic pulmonary illnesses such as COPD and bronchiectasis.\textsuperscript{7,12}

Multivariate analysis showed that CPA severity was independently associated with impairment in health status after corrected for confounding factors such as underlying comorbidities. However, COPD comorbidity significantly affected health status in patients with CPA.

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<table>
<thead>
<tr>
<th>Domain</th>
<th>Score at First Completion</th>
<th>Score at Second Completion</th>
<th>Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms domain</td>
<td>55.7 (28.7)</td>
<td>56.8 (26.5)</td>
<td>1.1 (11.6)</td>
<td>.7</td>
</tr>
<tr>
<td>Activity domain</td>
<td>52.5 (31)</td>
<td>54.7 (32.4)</td>
<td>2.2 (10.6)</td>
<td>.4</td>
</tr>
<tr>
<td>Impact domain</td>
<td>43.1 (26.1)</td>
<td>43.1 (29)</td>
<td>0.05 (8.1)</td>
<td>.98</td>
</tr>
<tr>
<td>Total SGRQ score</td>
<td>47.5 (24.2)</td>
<td>48 (26.1)</td>
<td>0.5 (6.1)</td>
<td>.7</td>
</tr>
</tbody>
</table>

Data given as mean (SD) unless otherwise indicated. See Table 1 legend for expansion of abbreviation.

![Figure 2](http://journal.publications.chestnet.org)
hemoptysis, which may otherwise have been preventable or amenable to treatment. Moreover, this association between CPA severity and SGRQ scores suggests that the SGRQ could serve in assessing health status in clinical trials, measuring response of CPA to medical or surgical intervention from the patient’s perspective. In other chronic respiratory diseases, such as COPD, it has been documented that a four-point change in SGRQ scores represents the minimum clinically significant difference. However, future studies are needed to determine the equivalent value in CPA.

SGRQ scores showed only modest correlation with impairment in lung function, which accords with previous studies in other chronic progressive pulmonary diseases, such as COPD and bronchiectasis (e-Appendix 1). As with patients with bronchiectasis and pulmonary TB, SGRQ scores in this cohort were not affected by sex difference, supporting the stability of SGRQ in assessing health status in CPA.

This study showed that COPD was the most common and effective underlying comorbidity with CPA. Since both CPA and COPD are chronic, progressive, inflammatory, pulmonary diseases, a possibility of an existing interaction between these two diseases can be suggested. Perhaps “synergistic” destruction of pulmonary tissue and inflammation would contribute to the high SGRQ score of those who had both diseases. Further investigation of the management of such cases may be warranted. This finding should be further investigated in a longitudinal cohort study. Moreover, another interesting observation was that the SGRQ total score maintained its association with CPA severity even after being adjusted to several possible cofounders, including COPD and other underlying chronic pulmonary diseases. This shows that health-status impairment in CPA is independently related to CPA severity, but can be exaggerated by the presence of other coexisting pulmonary diseases.

We found no statistically significant association between socioeconomic status and SGRQ total and dimensional scores (e-Appendix 1). This is consistent with findings in other chronic progressive pulmonary diseases in which socioeconomic factors did not correlate with SGRQ score, as shown by Stahl and colleagues.

Table 3—Correlations Between Total and Dimensional SGRQ Scores and the Physiologic and Outcomes Measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Symptom Domain</th>
<th>Activity Domain</th>
<th>Impact Domain</th>
<th>Total SGRQ Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC dyspnea score</td>
<td>0.39⁺</td>
<td>0.49⁺</td>
<td>0.46⁺</td>
<td>0.51⁺</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>-0.5⁻</td>
<td>-0.60⁻</td>
<td>-0.72⁻</td>
<td>-0.7⁻</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>-0.42⁻</td>
<td>-0.4⁻</td>
<td>-0.65⁻</td>
<td>-0.64⁻</td>
</tr>
<tr>
<td>FEV₁</td>
<td>-0.37⁻</td>
<td>-0.36⁻</td>
<td>-0.2</td>
<td>-0.23⁻</td>
</tr>
<tr>
<td>FEV₁ % predicted</td>
<td>-0.3⁻</td>
<td>-0.29⁻</td>
<td>-0.16</td>
<td>-0.22</td>
</tr>
<tr>
<td>FVC</td>
<td>-0.2⁻</td>
<td>-0.19</td>
<td>-0.2</td>
<td>-0.22</td>
</tr>
</tbody>
</table>

MCS = mental component summary; MRC = Medical Research Council; PCS = physical component summary; SF-36 = Short Form-36 Health Survey. See Table 1 legend for expansion of other abbreviations.

⁺P < .001.
⁻P < .01.
⁻⁺P < .05.

Table 4—The SGRQ Total and Domains Scores Defined According to CPA Bands, MRC Dyspnea Grades, and Clinical Assessment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Symptom</th>
<th>Activity</th>
<th>Impact</th>
<th>Total SGRQ Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPA bands</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Band 1</td>
<td>56 (24.7)</td>
<td>66.2 (35.4-92.5)</td>
<td>40.5 (25.2)</td>
<td>56.6 (29.9-68.7)</td>
</tr>
<tr>
<td>Band 2</td>
<td>71.2 (20.1)</td>
<td>85 (66.2-93.3)</td>
<td>56.8 (19.9)</td>
<td>70.3 (53.1-77.3)</td>
</tr>
<tr>
<td>Band 3</td>
<td>65.2 (22.5)</td>
<td>92.5 (79.7-98.1)</td>
<td>59.1 (21.3)</td>
<td>69.1 (62.7-79.9)</td>
</tr>
<tr>
<td>P value</td>
<td>.034</td>
<td>.016</td>
<td>.009</td>
<td>.014</td>
</tr>
<tr>
<td>MRC dyspnea grades</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>12.4</td>
<td>11.5</td>
<td>7.8</td>
<td>9.6</td>
</tr>
<tr>
<td>Grade 2</td>
<td>50.8 (32.1)</td>
<td>66.2 (16.4-76.1)</td>
<td>35 (26.3)</td>
<td>51.2 (17.6-62.3)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>66.8 (19.7)</td>
<td>74.1 (59.9-89.5)</td>
<td>51.9 (18.8)</td>
<td>62.4 (46.3-71.8)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>69.5 (18.6)</td>
<td>92.5 (54.3-100)</td>
<td>62.7 (21.5)</td>
<td>75.9 (63.8-82.8)</td>
</tr>
<tr>
<td>Grade 5</td>
<td>76 (25.5)</td>
<td>92.5 (89.4-100)</td>
<td>62.2 (19.7)</td>
<td>75.9 (65.1-84.3)</td>
</tr>
<tr>
<td>P value</td>
<td>.036</td>
<td>.001</td>
<td>.011</td>
<td>.007</td>
</tr>
<tr>
<td>Respiratory physician rating</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very poor</td>
<td>70.2 (26.5)</td>
<td>65 (53.3-75.5)</td>
<td>87.7 (17.1)</td>
<td>74.5 (64.3-84.5)</td>
</tr>
<tr>
<td>Poor</td>
<td>71.2 (16.6)</td>
<td>57 (30.5-69.3)</td>
<td>81.5 (15.4)</td>
<td>66 (61.8-75.3)</td>
</tr>
<tr>
<td>Fair</td>
<td>64.8 (18.4)</td>
<td>57.5 (41.5-69)</td>
<td>75.4 (24.1)</td>
<td>67 (54.3-73.8)</td>
</tr>
<tr>
<td>Good</td>
<td>63.9 (22.1)</td>
<td>46.5 (35.5-59.3)</td>
<td>65.3 (25.2)</td>
<td>55 (43.3-66.8)</td>
</tr>
<tr>
<td>Very good</td>
<td>40.8 (18.5)</td>
<td>17.5 (12.3-22.8)</td>
<td>26 (17.3)</td>
<td>21.5 (18.5-35.3)</td>
</tr>
<tr>
<td>P value</td>
<td>.005</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Data presented as mean (SD), except Activity and Total SGRQ Score, which are given as median (IQR). See Table 1 and 3 legends for expansion of abbreviations.

*Data from 58 patients.
larger studies are required to replicate these findings and to examine other potential factors that would effectively influence health status in CPA. Indeed, studies are required to investigate the association of health-status impairment with socioeconomic conditions, frequency and severity of exacerbations, and the duration of exacerbation burden on health status after recovery.

Conclusions

The SGRQ showed significant reliability and validity in examining health status in patients with CPA. This suggests that SGRQ would provide CPA studies with valid assessment of health status and identify meaningful differences in routine clinical practice.

Acknowledgments

Author contributions: Dr Al-shair is guarantor of the manuscript and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Dr Al-shair: contributed to study design, data collection and analysis, and writing the manuscript, and served as principal author.

Dr Atherton: contributed to study design and data collection and entry and revision of the manuscript.

Ms Kennedy: contributed to data collection and revision of the manuscript.

Ms Powell: contributed to data collection and revision of the manuscript.
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