Longitudinal Analysis of Quality of Life for Stroke Survivors Using Latent Curve Models

Jun Hao Pan, BA; Xin Yuan Song, PhD; Sik Yum Lee, PhD; Timothy Kwok, MD

Background and Purpose—For the survivors, activities of daily living, handicap, and depression have a significant impact on health-related quality of life (HRQOL). How the dynamic changes of these variables relate to HRQOL over time in the subacute phase of stroke recovery has not been investigated. The objective of this study was to study longitudinal behaviors of HRQOL of the stroke survivors in relation to the changes in activities of daily living, handicap, and depression after stroke.

Methods—This was a prospective cohort study of first disabling patients with stroke. Subjects were interviewed at 3, 6, and 12 months after stroke for modified Barthel Index, London Handicap Scale, Geriatric Depression Scale, and the World Health Organization Quality of Life questionnaire (abbreviated Hong Kong version). A latent curve model was developed to analyze how the dynamic changes in activities of daily living, handicap, and depressive mood related to the changes in HRQOL.

Results—Two hundred forty-seven of 303 patients (82%) followed up at 3 months after stroke could complete the quality-of-life questionnaire. Their mean age was 68.8 years. The latent curve model analysis revealed that initial physical health HRQOL was independently associated with activities of daily living, handicap, and depression. The other 3 HRQOL domain scores were primarily associated with depression only. The rates of change in all 4 domains of HRQOL were significantly and inversely associated with rate of change in the Geriatric Depression Scale only.

Conclusion—Change in mood in the postacute phase of stroke recovery is the most significant determinant of change in HRQOL. More attention should be paid to the detection and management of poststroke depression.

Key Words: Bayesian approach ■ health-related quality of life ■ latent curve model ■ stroke

Stroke is a major health issue in the older population because it affects not only physical impairment, but also leads to disability,1 social nonparticipation (handicap),2 and depression.3 Such changes have a potentially far-reaching influence on health-related quality of life (HRQOL) of the stroke survivors. The impact of stroke on a patient is usually unanticipated and often devastating, requiring major adjustment in lifestyle and psychology of stroke survivors. Although patients have been found to maintain their functional status up to 1 year after inpatient stroke rehabilitation,4 cross-sectional studies of long-term stroke survivors have found poor HRQOL.5,6

The knowledge about the dynamic changes of HRQOL of stroke survivors and the associated factors of these changes is still growing. Ahlsio¨e et al7 found that although HRQOL was associated with greater disability, it failed to improve over time even when activities of daily living (ADL) function increased. There are some prospective data to suggest that psychosocial HRQOL improved between 3 and 16 months poststroke6,8 and remained stable afterward, but physical quality of life showed a decline.8 A more recent longitudinal study by our research group found that among Chinese stroke survivors, the environment and social interaction domains of HRQOL decreased during the first year after stroke, and depression had a more generalized adverse effect on HRQOL than basic functional disabilities.9 In the same study, it was observed that ADL, including instrumental ADL, remained stable, whereas occupation and orientation domains of handicap and depression deteriorated.10 These changes are indicative of the dynamic nature of psychosocial adjustment or maladjustment after stroke. To understand the relative importance of these interrelated factors in determining HRQOL in the first year after stroke, we constructed a dynamic latent curve model to study how the changes in HRQOL relate to the changes in ADL, handicap, and depression. The results would help steer the development of appropriate interventions to promote HRQOL of stroke survivors.

Methods

Participants
Hong Kong has a comprehensive and almost fully publicly funded hospital-based rehabilitative service for patients with stroke. The
setting of the study was in the Prince of Wales Hospital in Hong Kong, which is a regional university hospital with 1500 beds serving a population of 0.7 million people. Patients with acute stroke within 2 days of admission were identified and followed up at 3, 6, and 12 months poststroke. All patients included in the study were ethnic Chinese. Because this study aimed to study those with a first disabling stroke, patients were excluded if they had a moderate or severe premorbid handicap level (Rankin scale score ≥2).11 Those residing outside Hong Kong and those with a life expectancy less than 6 months, eg, with advanced cancer, were excluded. Written consent was obtained from the recruited subjects or their family caregivers (if the subjects were mentally incapable). The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong. The research assistants were fully trained in the administration of all questionnaires and were ensured to have satisfactory interrater reliability before data collection. Eighty percent of the follow-ups were performed by the same research assistants.

Instruments
Outcome measures obtained from questionnaires included the modified Barthel Index (MBI) score,12 Geriatric Depression Scale (GDS) score,13 Chinese Mini-Mental State Examination score,14 World Health Organization Quality of Life measure (abbreviated Hong Kong version) scores,15 and the London Handicap Scale (LHS).16

Modified Barthel Index
Patients’ ADL were assessed through the MBI.12 It is a good measurement instrument in terms of reliability and validity and has been already applied in most studies of stroke as the measure of functional status. MBI has 10 items on ADL. The total score of 20 indicates full independence in ADL; a higher score represents a higher level of independence.

Geriatric Depression Scale
Poststroke depression was measured using the GDS. This scale has 15 items. The Hong Kong Chinese version has been validated locally.13 A score of 8 or more indicates depression.

Health-Related Quality-of-Life Measure
The World Health Organization Quality of Life measure is the shortened form of WHOQOL-100 translated into Cantonese Chinese.15 This version is a generic HRQOL instrument that comprises 24 items covering 4 domains: physical health, psychological health, social interaction, and environment. The stroke survivors are required to respond to the items on a 5-point Likert scale in which the categories range from “not at all” to “an extreme amount” (scores ranging from 1 to 5). The domain scores are converted by normogram to 100% score.

London Handicap Scale
Handicap is defined as the disadvantage brought on by impairment and disabilities experienced by an individual taking into account the influence of physical and psychological effects of a disease, the physical and social environment, and the effects of health service provisions.17 The most applied generic measure of handicap in stroke survivors is the LHS.16 LHS has been widely applied across different disease populations with the advantage of crosscultural validity and good reliability. It has been translated into Chinese and validated in Hong Kong.18 It consists of 6 questions measuring the levels of handicap (scores ranging from 1 to 6) in 6 dimensions, including mobility, independence, occupation, social integration, orientation, and economic self-sufficiency. Higher score indicates greater handicap. The stroke survivors are requested to mark the response that best describes their situations. The total score of all 6 domains was used to indicate overall handicap level.

Latent Curve Model
Latent curve models (LCMs) are popular longitudinal techniques in analyzing individual differences in the pattern of change. The pattern of change usually involves a random intercept and a random slope paired with each case to have a different trajectory over time. Recently, techniques of LCMs have been developed through the incorporation of many features of structural equation models.19,20

To facilitate the presentation, an unconditional linear LCM consisting of 4 repeated measures is briefly discussed. The basic LCM can be viewed as the following common factor analysis model:

\[ y = \Lambda \eta + \varepsilon \]

where \( y \) is a \( T \times 1 \) vector of repeated measures, \( \Lambda \) is a \( T \times m \) matrix of sequential known values of the growth curve records, \( \eta \) is a \( m \times 1 \) vector of latent growth factor, which contains scores on the \( m \) factors for a given individual, and \( \varepsilon \) is a \( T \times 1 \) vector of unique variances in \( y \). Equation (1) can be expressed in the following matrix form:

\[
\begin{pmatrix}
 y_1 \\
 y_2 \\
 y_3 \\
 y_4 \\
 y_5 \\
 y_6
\end{pmatrix}
= 
\begin{pmatrix}
 1 & t_1 \\
 1 & t_2 \\
 1 & t_3 \\
 1 & t_4 \\
 1 & t_5 \\
 1 & t_6
\end{pmatrix}
\begin{pmatrix}
 \eta_1 \\
 \eta_2 \\
 \eta_3 \\
 \eta_4 \\
 \eta_5 \\
 \eta_6
\end{pmatrix}
+ 
\begin{pmatrix}
 \varepsilon_1 \\
 \varepsilon_2 \\
 \varepsilon_3 \\
 \varepsilon_4 \\
 \varepsilon_5 \\
 \varepsilon_6
\end{pmatrix}
\]

The loadings for \( \eta_i \), in relation to each of the repeated measures are fixed to 1.0 (the first column in \( \Lambda \)). That is, \( \eta_i \) equally influences all repeated measures across time. The loadings for \( \eta_i \), in relation to each of the repeated measures represent known times of measurement (\( t_i \), through \( t_T \)). The value of \( t_i \) is constrained to reflect the spacing between measurement occasions. Hence, in the LCMs, the factors can be interpreted as the initial status \( \eta_1 \) (random intercept) and rate of change \( \eta_2 \) (random slope). This 2-factor LCM is formulated so that the intercept factor serves as the starting point (initial status) for any change across time and the slope factor captures the rate of change of the trajectory over time.

The scaling of the slope can be specified by using either fixed values (eg, 0, 1, 2, 3) to represent a straight-line growth or unspecified values to allow estimation of an optimal pattern of change over measurement occasions. The equation for the latent growth factor \( \eta_i \) can be written as:

\[ \eta_i = \mu + B \eta + \delta \]

where \( \mu \) is a \( m \times 1 \) vector of the population averages of the latent individual growth factors, \( B \) is a \( m \times m \) matrix of coefficients expressing the structural relations between the \( \eta_i \) variables, and \( \delta \) is a \( m \times 1 \) vector of residuals. With the \( B \) matrix constrained to zero, Equation (3) becomes:

\[
\begin{pmatrix}
 \eta_1 \\
 \eta_2
\end{pmatrix}
= 
\begin{pmatrix}
 \mu_1 & \mu_2 \\
 \mu_2 & \mu_2
\end{pmatrix}
+ 
\begin{pmatrix}
 \delta_1 \\
 \delta_2
\end{pmatrix}
\]

A path diagram representing the model defined by Equations (2) and (4) is depicted in Figure 1. LCM is a useful tool for analyzing patterns of change and predictors of changes and the rich class of structural equation model techniques provide powerful tools for developing more useful LCMs for analyzing complex dynamic changes, for example, predictors may be specified in the models to account for the variation in the latent growth factor.

In this article, we extended the basic latent curve model to a more useful dynamic model as shown in Figure 2. Recognizing that MBI, LHS, and GDS could change over time, the model shown in Figure 2 was directed to assess how the changes in MBI, LHS, and GDS influenced the growth of each of the 4 HRQOL domains at 3 time points (model for physical health HRQOL was shown only).

Bayesian Approach
When coupled with powerful Markov chain Monte Carlo techniques, the Bayesian approach has been widely used in a variety of statistical models.21,22 In general, this approach has the following good features: 1) it is flexible to use useful prior information for achieving better results. In many practical problems, statisticians may have good prior information from some sources, for example, the knowl-
edge of experts and analyses of similar data and/or past data; and 2) the sampling-based Bayesian methods do not rely on asymptotic theory and give reliable statistical inference even with comparatively smaller sample sizes.

**Treatment of Missing Data**

In longitudinal studies, missing data are commonly encountered. For example, subjects can be missed at a particular measurement wave with the result that these subjects provide data at some, but not all, study time points. Alternatively, subjects who are assessed at a given study time point might only provide responses to a subset of the study variables, again resulting in incomplete data. Finally, subjects might drop out of the study or be lost to follow-up, thus providing no data beyond a specific point in time. In this study, most missing data belonged to the first 2 types of patterns. We deleted 4 subjects who dropped out at the follow-up study after baseline because these samples had little contribution in building the model. The subjects who could not complete the HRQOL questionnaires because of communication problems at the baseline were also deleted. The other dropout subjects were not significantly different from the followed-up subjects in age, sex, and MBI. Hence, the remaining missing data were treated as missing at random for brevity. The imputation of the missing data were included in our Bayesian analysis. Clearly, the effect of missing data was required to be taken into account for better statistical inference.

**Software WinBUGS**

All the analyses were performed using freely available WinBUGS (Windows version of Bayesian inference Using Gibbs Sampling) software, version 1.4. This software is able to produce reliable Bayesian statistics, including the Bayesian estimates and their SE estimates for a wide range of statistical models. The WinBUGS codes in conducting statistical analysis are presented in Table 5.

**Results**

Between January and July 2002, there were 392 patients with stroke admitted to Prince of Wales Hospital. Of these, 303 (77%) were recruited and assessed in research clinic in Prince of Wales Hospital or at home at 3 months after stroke. Eighty-two patients were not eligible; 4 could not be contacted and 3 refused. The baseline characteristics of the recruited subjects were described elsewhere. Of these, 247 subjects (82%) could respond reliably to the HRQOL questionnaire. The characteristics of these subjects at baseline are shown in Table 1. The mean age was 68.8 years. The great majority were ischemic strokes: small artery thrombosis, 76; large artery thrombosis, 70; cardioembolism, 7; intracerebral hemorrhage, 7; and undetermined etiology, 76. According to the National Institutes of Health Stroke Scale score measured by trained nurses within 3 days of admission, 47 patients (19%), 157 patients (64%), and 43 patients (17%) had mild, moderate, and severe strokes, respectively. At 3 months after stroke, 138 (56%) patients achieved the maximum Barthel Index score of 20, indicating full independence in basic ADL. Eighty-four patients (34%) had raised GDS scores (8 or above) suggesting depression.
Two hundred forty-two subjects (98%) and 225 subjects (91%) were followed up at month 6 and month 12, respectively. The reasons for dropouts were death (N/H110056), moved (N/H110055), refusal (N/H110054), failed contact (N/H110053), in the hospital (N/H110052), and terminal illness (N/H110052). The subjects lost to follow-up were not significantly different from those followed up in age, sex, and MBI.

The descriptive statistics of the total scores for the outcome and explaining variables at the baseline (3 months after stroke) are shown in Table 2. The changes in scores of the 205 subjects who completed follow-up at months 6 and 12 are shown in Table 3. By conducting Wilcoxon signed rank test for the changes in functional status, mood, and HRQOL from 3 months to 12 months after stroke, we found that there was no significant change in the physical health domain of HRQOL and LHS scores, a significant ($P<0.05$) decrease in psychological social interaction and MBI scores, and a highly significant decrease ($P<0.001$) in environment HRQOL and GDS scores at both 6 and 12 months.

To better understand the relationships among HRQOL and MBI, LHS, GDS, we used the LCM to analyze the data by considering the 4 HRQOL domains separately, including physical health, psychological health, social interaction, and environment. The results of the analysis for the 4 HRQOL domains are shown in Table 4. As an example, the proposed model for physical health domain is shown in Figure 2, and the corresponding estimated structural equations, predicted by MBI, LHS, and GDS, were as follows:

$$
\eta_1 = -0.001 + 0.174\xi_1 + (-0.475)\xi_2 + (-0.310)\xi_3
$$

$$
\eta_2 = -0.013 + 0.280\xi_2 + (-0.312)\xi_4 + (-0.328)\xi_5
$$

where $\eta_1$=initial level of physical health domain and $\eta_2$=rate of change in physical health domain.

Therefore, initial physical health HRQOL was independently associated with ADL, handicap, and depression. The rate of change in physical health HRQOL was significantly and inversely associated with rate of change in GDS only.

The initial scores of the other 3 HRQOL domains were associated with depression only, except that psychological domain was marginally associated with ADL as well. Similar to physical health domain, the rates of change in these 3 HRQOL domains were associated with the rate of change in depression only.

To exclude the ceiling effect of MBI, the statistical analysis was repeated after excluding the 138 subjects with full MBI at baseline. This did not significantly alter the results given in Table 4.

### Table 1. Demographic and Clinical Characteristics of Stroke Subjects at 3 Months After Stroke*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No.</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤70</td>
<td>107</td>
<td>43.3</td>
</tr>
<tr>
<td>70–79</td>
<td>104</td>
<td>42.1</td>
</tr>
<tr>
<td>≥80</td>
<td>36</td>
<td>14.6</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>112</td>
<td>45.3</td>
</tr>
<tr>
<td>Male</td>
<td>135</td>
<td>54.7</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Old-age home</td>
<td>29</td>
<td>11.7</td>
</tr>
<tr>
<td>Own home</td>
<td>201</td>
<td>81.4</td>
</tr>
<tr>
<td>Lived alone</td>
<td>17</td>
<td>6.9</td>
</tr>
<tr>
<td>Martial status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>162</td>
<td>65.6</td>
</tr>
<tr>
<td>Widowed/single/divorced</td>
<td>85</td>
<td>34.4</td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3</td>
<td>71</td>
<td>28.7</td>
</tr>
<tr>
<td>≥3</td>
<td>176</td>
<td>71.3</td>
</tr>
<tr>
<td>Severity of stroke (NIHSS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (≤3)</td>
<td>47</td>
<td>19</td>
</tr>
<tr>
<td>Moderate (3–8)</td>
<td>157</td>
<td>63.6</td>
</tr>
<tr>
<td>Severe (&gt;8)</td>
<td>43</td>
<td>17.4</td>
</tr>
<tr>
<td>Level of ADL (MBI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent (20)</td>
<td>138</td>
<td>55.9</td>
</tr>
<tr>
<td>Partially dependent (15–19)</td>
<td>77</td>
<td>31.2</td>
</tr>
<tr>
<td>Dependent (&lt;15)</td>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>Cognitive function (MMSE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (≥20)</td>
<td>208</td>
<td>84.2</td>
</tr>
<tr>
<td>Impaired (&lt;20)</td>
<td>39</td>
<td>15.8</td>
</tr>
</tbody>
</table>

*Only those who could respond to the quality-of-life questionnaire were included; values were presented as no. and percentage.

NIHSS indicates National Institutes of Health Stroke Scale; MMSE, Mini-Mental State Examination.

Two hundred forty-two subjects (98%) and 225 subjects (91%) were followed up at month 6 and month 12, respectively. The reasons for dropouts were death (N=6), moved (N=5), refusal (N=4), failed contact (N=3), in the hospital (N=2), and terminal illness (N=2). The subjects lost to follow-up were not significantly different from those followed up in age, sex, and MBI.

The descriptive statistics of the total scores for the outcome and explaining variables at the baseline (3 months after stroke) are shown in Table 2. The changes in scores of the 205 subjects who completed follow-up at months 6 and 12 are shown in Table 3. By conducting Wilcoxon signed rank test for the changes in functional status, mood, and HRQOL from 3 months to 12 months after stroke, we found that there was no significant change in the physical health domain of HRQOL and LHS scores, a significant ($P<0.05$) decrease in psychological social interaction and MBI scores, and a highly significant decrease ($P<0.001$) in environment HRQOL and GDS scores at both 6 and 12 months.

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$$
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$$

$$
\eta_2 = -0.013 + 0.280\xi_2 + (-0.312)\xi_4 + (-0.328)\xi_5
$$

where $\eta_1$=initial level of physical health domain and $\eta_2$=rate of change in physical health domain.

Therefore, initial physical health HRQOL was independently associated with ADL, handicap, and depression. The rate of change in physical health HRQOL was significantly and inversely associated with rate of change in GDS only.

The initial scores of the other 3 HRQOL domains were associated with depression only, except that psychological domain was marginally associated with ADL as well. Similar to physical health domain, the rates of change in these 3 HRQOL domains were associated with the rate of change in depression only.

To exclude the ceiling effect of MBI, the statistical analysis was repeated after excluding the 138 subjects with full MBI at baseline. This did not significantly alter the results given in Table 4.

### Table 2. Descriptive Statistics of the Outcome and Explaining Variables of the 247 Patients With Stroke Measured at Baseline (3 months after stroke)

<table>
<thead>
<tr>
<th>Minimum</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (PHY)</td>
<td>6</td>
<td>44</td>
<td>56</td>
<td>69</td>
<td>88</td>
<td>56.30</td>
</tr>
<tr>
<td>QOL (PSY)</td>
<td>5</td>
<td>44</td>
<td>56</td>
<td>75</td>
<td>100</td>
<td>58.49</td>
</tr>
<tr>
<td>QOL (SO)</td>
<td>25</td>
<td>56</td>
<td>69</td>
<td>75</td>
<td>100</td>
<td>66.62</td>
</tr>
<tr>
<td>QOL (EN)</td>
<td>13</td>
<td>63</td>
<td>69</td>
<td>75</td>
<td>100</td>
<td>67.95</td>
</tr>
<tr>
<td>MBI</td>
<td>0</td>
<td>17</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>17.62</td>
</tr>
<tr>
<td>GDS</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>9</td>
<td>15</td>
<td>5.74</td>
</tr>
<tr>
<td>LHS</td>
<td>6</td>
<td>11</td>
<td>14</td>
<td>18</td>
<td>31</td>
<td>14.63</td>
</tr>
</tbody>
</table>

Q1 indicates first quartile; Q3, third quartile; QOL, World Health Organization Quality of Life (abbreviated Hong Kong version); PHY, physical health; PSY, psychological; SO, social; EN, environmental.
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better statistical inference. This statistical approach has
dynamic manner. In addition, we used the Bayesian
related to the changes in all 4 HRQOL domains in a
survivors, whereas changes in basic functional status and
had the most significant effect on the HRQOL of stroke
of these interrelated variables in determining HRQOL was
all important predictors of HRQOL. The relative importance
For the stroke survivors, ADL, handicap, and depression are
Table 3. The Changes in Outcome and Explaining Variables at Months 6 and 12

<table>
<thead>
<tr>
<th></th>
<th>Change Between 6 Months and 3 Months</th>
<th></th>
<th>Change Between 12 Months and 3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum</td>
<td>Median</td>
<td>Maximum</td>
</tr>
<tr>
<td>QOL (PHY)</td>
<td>−50</td>
<td>0</td>
<td>(−7 to 6)</td>
</tr>
<tr>
<td>QOL (PSY)</td>
<td>−56</td>
<td>0</td>
<td>(−7 to 6)</td>
</tr>
<tr>
<td>QOL (SO)</td>
<td>−50</td>
<td>0</td>
<td>(−6 to 0)*</td>
</tr>
<tr>
<td>QOL (EN)</td>
<td>−38</td>
<td>0</td>
<td>(−12 to 0)†</td>
</tr>
<tr>
<td>MBI</td>
<td>−9</td>
<td>0</td>
<td>(0 to 0)*</td>
</tr>
<tr>
<td>GDS</td>
<td>−10</td>
<td>0</td>
<td>(−1 to 2)†</td>
</tr>
<tr>
<td>LHS</td>
<td>−8</td>
<td>0</td>
<td>(−1 to 1)</td>
</tr>
</tbody>
</table>

Note: The results were obtained based on 205 fully observed data across 3 time points. Values in parentheses are interquartile ranges. The P values were calculated in conducting Wilcoxon signed rank test.

*P<0.05.
†P<0.001.
QOL, World Health Organization Quality of Life (abbreviated Hong Kong version); PHY, physical health; PSY, psychological; SO, social; EN, environmental.

Discussion

For the stroke survivors, ADL, handicap, and depression are all important predictors of HRQOL. The relative importance of these interrelated variables in determining HRQOL was the subject of this study. The main finding of our analysis was that change in mood in the subacute phase of stroke recovery had the most significant effect on the HRQOL of stroke survivors, whereas changes in basic functional status and handicap had insignificant effects.

In this study, we used the LCM technique to examine how the changes in ADL, handicap, and depression were related to the changes in all 4 HRQOL domains in a dynamic manner. In addition, we used the Bayesian approach, which does not rely on asymptotic theory and gives reliable statistical inference even with small sample sizes and takes into account the effect of missing data for better statistical inference. This statistical approach has been applied to longitudinal studies about cocaine use by the University of California–Los Angeles Center for Advancing Longitudinal Drug Abuse Research.27,28 In these studies, the dynamic influences of various observed and latent variables such as formal treatment, depression, and family support on the dynamic change in cocaine use were analyzed. Incorporating latent class analysis29,30 and item response models31 in the current analysis represents further use of the proposed approach in longitudinal study of quality-of-life research.

Our subjects were representative of patients with stroke in Hong Kong where the great majority of patients with acute stroke are admitted to publicly funded hospitals. The rate of dropout was low and the subjects who dropped out were not significantly different from the followed-up subjects in age, sex, and MBI. Because the study started at month 3 and the subjects were restricted to those who could respond to the quality-of-life questionnaire, half of our subjects had full MBI scores at baseline. However, the results of the statistical analysis were not significantly altered after excluding the independent subjects.

At baseline, i.e., the end of the third month after stroke, all the patients had completed rehabilitation in the hospital and returned to the community. This is consistent with local practice. At this stage of stroke recovery, our analysis suggested that ADL, handicap, and depression were all independently and significantly associated with the physical health domain of HRQOL. However, except that psychological HRQOL was marginally associated with ADL, the other

Table 4. Results of LCM Analysis for PHY, PSY, SO, and EN Domains of QOL

<table>
<thead>
<tr>
<th></th>
<th>Initial Level of ADLs (ξi)</th>
<th>Initial Level of Handicap (ξi)</th>
<th>Initial Level of Depression (ξi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial level of PHY</td>
<td>0.174* (0.069) [0.039, 0.307]</td>
<td>−0.475* (0.097) [−0.669, −0.290]</td>
<td>−0.310* (0.068) [−0.439, −0.177]</td>
</tr>
<tr>
<td>Initial level of PSY</td>
<td>0.167* (0.068) [0.034, 0.303]</td>
<td>−0.070 (0.095) [−0.193, 0.184]</td>
<td>0.782* (0.068) [−0.910, −0.647]</td>
</tr>
<tr>
<td>Initial level of SO</td>
<td>0.032 (0.096) [−0.166, 0.211]</td>
<td>0.088 (0.135) [−0.182, 0.350]</td>
<td>−0.511* (0.096) [−0.698, −0.330]</td>
</tr>
<tr>
<td>Initial level of EN</td>
<td>0.075 (0.081) [−0.084, 0.232]</td>
<td>−0.191 (0.114) [−0.431, 0.025]</td>
<td>−0.540* (0.081) [−0.700, −0.385]</td>
</tr>
</tbody>
</table>

Rate of Change of ADLs (ξi) Rate of Change of Handicap (ξi) Rate of Change of Depression (ξi)

Note: Values are coefficient estimates, SE estimates (given in parentheses), and 95% highest probability density (HPD) interval (given in brackets).
The estimates with asterisk are statistically significant because their associated HPD intervals do not include zero.
QOL indicates World Health Organization Quality of Life (abbreviated Hong Kong version); PHY, physical health; PSY, psychological; SO, social; EN, environmental.
Table 5. Appendix 1

model {
  for (i in 1:N) {
    # measurement models
    for (j in 1: P1) {
      y[j] ~ dnorm(mu[i], psi[j])
    }
    # for total domain score
    mu[i,1] <- eta[i,1] + mu[i,2] + mu[i,3] + 3.0*eta[i,2]
    # for MBI
    mu[i,4] <- -eta[i,1] + mu[i,5] + mu[i,6] + 3.0*eta[i,2]
    # for LHS
    mu[i,7] <- -eta[i,1] + mu[i,8] + mu[i,9] + 3.0*eta[i,2]
    # for GDS
    mu[i,10] <- -eta[i,1] + mu[i,11] + mu[i,12] + 3.0*eta[i,2]
    # structural equation
    x[i,1:6] <- dmnorm(u[i,1:6], phi[i,1:6,1:6])
    eta[i,1:2] <- dnorm(u[i,1:2], phi2[i,1:2,1:2])
    # end of i
    # priors on loadings and coefficients
    for (j in 1:P2) {
      bu[j] ~ dnorm(0, 5, 1, 0)
      gam[j] ~ dnorm(0, 0.5, 2)
      phi[i,j] ~ dgamma(9, 4.0)
      psi[j] ~ dgamma(9, 0.4)
    }
    phi[i,1:6,1:6] ~ dwish(R[i,1:6,1:6], 9)
    phi2[i,1:2,1:2] ~ dwish(R2[i,1:2,1:2], 4)
    } # end of model
  }

3 domains of HRQOL were significantly associated with depression only. For many clinicians and administrators, the outcome of stroke rehabilitation has often been measured by gain in functional status, and there is good evidence that stroke rehabilitation is effective in improving functional status.\textsuperscript{32} However, some trials of stroke rehabilitation have shown that functional gain is not necessarily associated with improvement in HRQOL.\textsuperscript{33,34} To promote HRQOL of patients with stroke, handicap and mood should therefore be included as important outcome indicators of stroke rehabilitation.\textsuperscript{35}

From month 3 to month 12, consistent with the literature,\textsuperscript{4} only a minority of subjects showed any change in functional status. This may explain why the changes in functional status were not significantly associated with changes in HRQOL. Depressive mood, on the other hand, was more changeable and, more importantly, related to the change in all 4 domains of HRQOL.

Geriatric depression scale has been shown to have good agreement with clinical diagnosis of poststroke depression by psychiatrists.\textsuperscript{36} In this study, based on GDS, the prevalence rose from 35.7% at month 3 to 42.8% at month 12, the rates being similar as reported elsewhere.\textsuperscript{37} A prospective cohort study in Italy showed that most poststroke depression occurred in the first 3 months. Late onset of depression occurred occasionally and tended to be milder,\textsuperscript{38} but other studies have not found any difference between late- and early-onset depression in risk factor profiles.\textsuperscript{39}

Poststroke depression has a significant impact on healthcare utilization\textsuperscript{40} and mortality.\textsuperscript{41} The risk factors include female sex, severe disability, previous cerebrovascular or depressive episodes, and dysphasia.\textsuperscript{38,42} Meta-analyses of randomized trials found no convincing evidence that routine use of serotonin selective update inhibitors could resolve or prevent poststroke depression, but mood as reflected by depression scores was improved.\textsuperscript{39,43} Moreover, a care management program led by nurse managers, which included an initial counseling session, 2 monthly telephone follow-ups on depressive symptoms and drug compliance, and a medication algorithm, significantly increased the chance of remission with serotonin selective update inhibitor therapy in poststroke depression.\textsuperscript{44} Interestingly, sleep apnea, which is common among patients with stroke, has been associated with poststroke depression\textsuperscript{45} and nasal continuous positive airway pressure improves depression in such patients.\textsuperscript{46}

Family caregivers of more disabled patients with stroke are at high risk of depression themselves.\textsuperscript{47} Education and training has been shown to be effective in reducing perceived burden and depression in family caregivers.\textsuperscript{48} Interventions directed at depressed family caregivers may indirectly prevent depression in the patients with stroke, because depression in stroke survivors and their family caregivers is interrelated.\textsuperscript{47,49} It was unexpected that changes in handicap were not associated with changes in HRQOL. Increased participation in social and leisure activities has been identified to be an important perceived need by patients 1 to 3 years after stroke.\textsuperscript{50} For simplicity, we did not consider handicap in its separate domains. It is possible some domains of handicap do not significantly influence HRQOL. Handicap is also associated with mood.\textsuperscript{10} How handicap is perceived and reported may therefore be influenced by mood. Probably because of
this, changes in handicap were not independently associated with changes in HRQOL.

The strength of this study is the statistical model, which helped to delineate the relative contribution of functional status, handicap, and depression in the HRQOL of patients with stroke in a prospective manner. The limitation is that patients with stroke with significant cognitive impairment and those with aphasia were excluded from the study because of their inability to respond reliably to questionnaires. The HRQOL of these high-risk patients warrants separate studies.

What are the practical implications of our research findings on the provision of services to patients with stroke? Multidisciplinary rehabilitation is the mainstay of management of patients with stroke. There is evidence that organized stroke rehabilitation prevents mortality and promotes independence. However, after 3 months after stroke, the potential for further functional gain is limited. From then on, our data showed that the psychological sequelae of stroke are the major determinant of HRQOL. The current care services in the subacute phase of stroke recovery, ranging from nursing home and day care for the more disabled, day hospital rehabilitation for the moderately disabled, and outpatient clinic follow-up only for the mildly disabled, do not specifically address the problem of poststroke depression. It is well documented that postdepression is underdiagnosed and undertreated. It is a challenge to raise the awareness of this problem in these different care settings. Apart from drug treatment, there is a need to devise alternative strategies to manage poststroke depression for better quality of life of stroke survivors.

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