In this study we hypothesised that anxiety/depression, one of five dimensions in the health-related quality of life (HRQoL) measurement tool EQ-5D, could predict outcome after total hip replacement surgery.

Pre-operative and one-year post-operative data from the Swedish Hip Arthroplasty Register, including 6158 patients with primary osteoarthritis of the hip, were analysed. In order to examine the association between anxiety and outcome with respect to pain and satisfaction an analysis of covariance was used.

The pre-operative EQ-5D anxiety/depression dimension was a strong predictor for pain relief and patient satisfaction (p < 0.001).

Orthopaedic surgeons involved in the care of patients eligible for total hip replacement surgery should be aware that mental health may influence post-operative pain and HRQoL. An appropriate assessment of mental health may enable a modification in the way these patients are managed in order to optimise the outcome after joint replacement surgery.

Between 8% and 10% of patients have persistent symptoms after undergoing total hip replacement (THR). The presence of co-morbidity results in poorer outcomes, as measured by both disease-specific and generic assessment tools. However, attempts to predict the outcome of joint replacement surgery, in order to identify poor responders, have not identified specific factors responsible for the poor results.

In order to optimise cost-effectiveness, expensive and/or frequent healthcare interventions should be reserved for patients who gain substantial benefit. Attempts should also be made to measure not only the direct medical costs, but the community costs (e.g. home-help service, transportation service for the disabled) and the indirect costs (e.g. productivity loss).

Patient-related factors have gained increased acceptance in assessing the outcome of joint replacement surgery. Currently, the Swedish Hip Arthroplasty Register assesses patient satisfaction, pain relief and health-related quality of life (HRQoL), using the EuroQol System (EQ-5D). In this study we used subjects in the Swedish registry to examine the hypothesis that anxiety/depression (one of the five dimensions of the EQ-5D) is a significant variable in predicting satisfaction and pain relief after THR. Furthermore, we examined whether pronounced anxiety/depression causes an increase in pain, as measured on a visual analogue scale (VAS).

Patients and Methods
The Swedish Hip Arthroplasty Register, begun in 1979, provides prospective observational nationwide data. The rapid growth of new surgical techniques, and of implant technology, warrants a continuous and objective monitoring of results in order to improve outcomes. In order to increase the utility of the register, a standardised protocol, including patient-reported outcome parameters, was introduced stepwise in Sweden from 2002. All patients complete a questionnaire pre-operatively and at one year post-operatively containing ten items, including Charnley’s functional categories (A, B, and C), a VAS for no pain (0) to unbearable pain (100), disease-specific questions, and a generic EQ-5D measurement; the intention is to repeat these measurements at six and ten years post-operatively. The EQ-5D is a HRQoL instrument that evaluates patients in five dimensions, namely mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three levels of severity (1, no problems, 2, moderate problems and 3, severe problems) generating 243 possible combinations of response. The EQ-5D can be presented as a health profile or as a global health index with a weighted total value (British tariff used) for HRQoL; the minimum value is -0.594 and the maximum 1.0. The Charnley category allows...
for the correction of scores because of different co-morbidity burdens. As a complement to the follow-up instrument, a VAS for satisfaction (satisfied (0) to dissatisfied (100), disease-specific question) was added. The questionnaire is posted to the patient at one, six and ten years after operation. The general response rate to the Swedish register after one reminder is 92%.7,8,10,11

**Patients.** The study thus includes 6158 patients from 37 different hospitals, who underwent THR because of primary osteoarthritis and who had completed the questionnaires both pre-operatively and one year post-operatively, between 1 January 2002 and 31 May 2005. A subgroup of 481 patients in the Western Region of Sweden, with complete data on cost was selected for health economic analysis.

In a post hoc analysis we identified patients who reported pre-operative anxiety/depression and one year post-operatively to examine whether they were different from those who reported no anxiety/depression pre- and/or post-operatively. In this analysis it was decided that patients reporting persisting anxiety/depression in the fifth dimension of the EQ-5D questionnaire constituted a ‘persistent anxiety’ group (i.e. moderate or severe anxiety/depression pre-operatively and moderate or severe anxiety/depression at follow-up). Conversely, patients reporting other combinations constituted a ‘remaining’ group.

**Health economic methods.** Cost-utility analysis is a form of cost-effectiveness evaluation that combines utility measurements, such as the HRQoL score with survival and cost data. In the case of THR, the incremental cost of the operation is compared with the benefits, measured by the improvement in HRQoL scores. Non-surgical treatment is considered the alternative intervention. One frequently used utility measure is the quality-adjusted life-year (QALY). The cost per QALY gained can be computed as an independent measurement that allows cost-effectiveness comparisons of interventions in different medical fields.10 Utility values range between 0 (dead) and 1 (full health) (i.e. EQ-5D index 0.0 to 1.0). When the EQ-5D index is used for cost-utility analysis, all negative values are set to 0.0. The difference in EQ-5D index pre- and one year post-operatively was calculated to generate the QALYs gained at one year. In this model, the hypothetical non-treatment alternative is set to the pre-operative baseline level, even though osteoarthritis is often progressive. For cost calculations, we used cost per patient databases. Individual cost per patient values consider only the total sum of direct medical costs during the hospital stay in conjunction with the operation, collected from hospital databases. Cost-utility is then computed in this simple model by dividing the cost of the operation with the QALYs gained at one year, without discounting.

**Statistical methods.** The association between the five EQ-5D dimensions, Charnley categories, gender, age as independent variables and the VAS results (pain and satisfaction) as dependent variables was analysed using analysis of covariance (ANCOVA). The pain VAS was regarded as a nominal scale and the change calculated as a percentage. Two-tailed probability values less than 0.05 represented a significant difference. SPSS 14.0 (SPSS Inc., Chicago, Illinois) was used for all statistical analyses. The results are presented as the mean and SD.

Differences between groups concerning baseline scores and the scores one year post-operatively were tested by either a paired t-test or non-parametric tests as appropriate.

**Results**

**Pre-operative.** The pre-operative mean age of the cohort was 69 years (27 to 96, 57% women) and the distribution in Charnley categories was A (44%), B (14%) and C (42%). The 3597 patients classified in Charnley categories A and B reported lower mean values for pain (VAS 60, SD 16.2) and a higher mean pre-operative EQ-5D score (0.43, SD 0.31) compared to group C patients (n = 2561; VAS 64, SD 16; EQ-5D 0.34, SD 0.32) (p < 0.001, Mann-Whitney U test). Patients (n = 198) who reported severe anxiety/depression also reported worse pre-operative pain than all other patients (VAS 71, SD 17) (p < 0.001, Mann-Whitney U test). A larger proportion of women (49%) than men (35%) reported pre-operative anxiety/depression.

**Post-operative.** Patients with co-morbidity (Charnley category C) had a significantly worse outcome with regard to pain relief, satisfaction and EQ-5D scores than did patients in Charnley categories A or B (p < 0.001, Mann-Whitney U test). Women had worse outcome scores than men in satisfaction and EQ-5D index (p < 0.001, Mann-Whitney U test). The mean values gained in pain and EQ-5D scores are shown in Table I. The improvement in pain scores was similar in all groups. The patients with a pre-operative anxiety/depression score of 2 or 3 had an increase in their EQ-5D score one year post-operatively (p < 0.001, Mann-Whitney U test).

**Anxiety/depression and outcome.** Adjusting for all dimensions of EQ-5D pre-operatively, Charnley category, age and gender, multivariate linear regression analysis showed that the degree of pain relief and satisfaction one year after surgery were related to pre-operative anxiety/depression in the fifth EQ-5D dimension and reduction of the Charnley category. As shown in Figures 1 and 2, patients in Charnley category C reported an adjusted mean 5.6 VAS units (SE 0.53) in satisfaction and an adjusted mean 8.2 percentage points (SE 0.82) less pain reduction than patients in categories A and B (p < 0.001, ANCOVA). Patients with any pre-operative anxiety/depression reported an adjusted mean 4.0 VAS units (SE 0.55) lower in satisfaction and had 4.4 percentage points (adjusted mean SE 0.84) less pain reduction than patients who did not report anxiety/depression pre-operatively (ANCOVA, p < 0.001). The satisfaction outcome for women was 2.2 VAS units (adjusted mean SE 0.53) lower than for men (ANCOVA, p < 0.001), but there was no significant difference in the percentage of the pain reduction in the analysis of covariance (p < 0.79).

**Post-hoc analysis.** The possible combinations and number of patients with respect to pre- and post-operative anxiety/depression in VAS units are shown in Table II. Patients with
Persistant anxiety/depression (1043 patients) were among the group with the poorest outcome for pain relief and patient satisfaction (Table II).

Analysis of covariance (adjusting for age, gender and co-morbidity) showed that persisting moderate or severe problems in any of the EQ-5D dimensions were related to inferior results in the VAS for satisfaction and the degree of pain reduction, with the exception of the mobility dimension (ANCOVA, p < 0.001). This analysis strengthened the relationship between anxiety/depression and a poor outcome.

The number of patients who improved among the ‘persistent anxiety’ and ‘remaining’ patients was calculated with respect to the other four EQ-5D dimensions (mobility, self-care, usual activities and pain/discomfort) and to the gain in EQ-5D index. As shown in Table III, considerably more remaining patients improved than did persistent anxiety/depression ones. It is of particular interest that only 24% of the patients in the persistent anxiety/depression group improved in the mobility dimension, compared to 59% in the remaining group.

### Table I. Mean values for pain (visual analogue score, VAS) and EQ-5D index pre-operatively and mean values for pain (VAS), pain relief, EQ-5D index and gain in EQ-5D index one year after surgery for different patient cohorts and subdivided into groups with or without anxiety/depression

<table>
<thead>
<tr>
<th>Group</th>
<th>Anxiety/depression pre-operatively</th>
<th>Number</th>
<th>Pain pre-operatively Mean (SD)</th>
<th>Pain post-operatively Mean</th>
<th>Pain relief Mean</th>
<th>Satisfaction Mean (SD)</th>
<th>EQ-5D index pre-operatively Mean</th>
<th>EQ-5D index post-operatively Mean</th>
<th>EQ-5D index improvement in mean</th>
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<tr>
<td>All</td>
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<td>1</td>
<td>3530</td>
<td>59 (16)</td>
<td>13</td>
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<td>15 (19)</td>
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<td>2 + 3</td>
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<td>65 (15)</td>
<td>17</td>
<td>-49</td>
<td>20 (22)</td>
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<td>0.71</td>
</tr>
<tr>
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<td></td>
<td>1 to 3</td>
<td>2652</td>
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<td>13</td>
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<td>15 (19)</td>
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</tr>
<tr>
<td>Women</td>
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<td>3506</td>
<td>64 (16)</td>
<td>15</td>
<td>-49</td>
<td>19 (22)</td>
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<tr>
<td>Charnley</td>
<td></td>
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<td>11</td>
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<td>13 (17)</td>
<td>0.51</td>
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<tr>
<td>Charnley</td>
<td></td>
<td>C</td>
<td>1236</td>
<td>65 (15)</td>
<td>14</td>
<td>-51</td>
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<tr>
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<td>1</td>
<td>1726</td>
<td>57 (16)</td>
<td>12</td>
<td>-45</td>
<td>14 (18)</td>
<td>0.52</td>
<td>0.83</td>
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<tr>
<td>Women</td>
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<td>2 + 3</td>
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<td>63 (16)</td>
<td>16</td>
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<td>18 (20)</td>
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<tr>
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<td></td>
<td>1</td>
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<td>13</td>
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<td>17 (20)</td>
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<tr>
<td>Women</td>
<td></td>
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<td>1702</td>
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<td>21 (23)</td>
<td>0.25</td>
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<tr>
<td>All</td>
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<td>14</td>
<td>-48</td>
<td>17 (21)</td>
<td>0.39</td>
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</table>
Health economic results. Cost-utility in the subgroup of 481 patients was calculated (412 in the ‘remaining’ group and 69 in the ‘persistent’ group). The mean cost per patient in the remaining group was 95 200 Swedish kronor (US$ 13 500) and the mean improvement in adjusted EQ-5D index (QALYs gained) was 0.38 (SD 0.31), generating a cost per gained QALY of 248 000 Swedish kronor (US$ 35 100). On the other hand, cost per patient in the persistent anxiety group was 98 900 Swedish kronor (US$ 14 000). As the mean QALYs gained was 0.26 (SD 0.19), the cost per QALY gained was 383 000 Swedish kronor (US$ 54 300), which is 55% more than for the remaining group. The difference in QALYs gained between these groups was significant (paired t-test, p = 0.032)

Discussion
Satisfaction, pain relief and improvement of HRQoL are the main patient-reported outcomes of primary joint replacement in osteoarthritis. This study confirms that two previously identified factors influenced outcome following THR surgery. Co-morbidity, assessed by the Charnley classification, portends a worse outcome, and outcome scores for women are lower than those for men as measured by pain, satisfaction and HRQoL scores.15-18 However, we also demonstrated that a factor previously poorly understood in hip surgery, pre-operative anxiety/depression, may explain persistent discomfort after THR. In fact, the pre-operative EQ-5D dimension of anxiety/depression was among the strongest predictors of pain relief and satisfaction after surgery. This is, surprisingly, in contrast to the pre-operative radiographic severity and function, which are not related to outcome.3-5 The finding that satisfaction and HRQoL scores at one year seem to be influenced by pre-operative anxiety/depression could potentially help improve the results of THR surgery.

In a study predicting outcome after knee replacement surgery, the SF-36 mental health scale was negatively related to the WOMAC outcome scores at one and two years after surgery.21 The authors claimed that studies which examine psychometric variables more specifically are needed for interventions aimed at improving HRQoL in patients with diseases that include chronic pain.

Pain is the main indication for THR in patients with osteoarthritis. However, the mechanisms behind pain in osteoarthritis are still unknown. The relationship between pain caused by osteoarthritis and anxiety/depression is complex,22 and factors that determine an individual’s pain experience need to be identified.23 In this study, patients with the most pronounced anxiety/depression reported the highest pre-operative VAS scores for pain. This suggests that anxiety/depression may increase pain, making decisions about the indications for surgery difficult. We do not suggest that patients with anxiety/depression should be denied THR. Perhaps the focus of initial treatment in these patients should be upon their mental state.
In the current healthcare economy, with its financial limitations, cost-utility analyses highlight outcome in order to enable the optimal allocation of resources. THR surgery is cost effective compared to other medical treatments. However, patients with poor outcomes will compromise the cost-effectiveness of the surgery, as demonstrated in this study and it is of importance to identify poor responders and to adjust the pre-operative treatment for this group.

An interesting finding in this study was that patients with persisting anxiety showed poor improvements in their EQ-5D mobility dimension. This could be a form of kinesiophobia associated with anxiety. There is growing evidence that pain-related fear as a dimension of anxiety may be more disabling than pain itself, at least for patients with back pain. This suggests that improved individual information regarding expectations after THR may facilitate training and physical activity, and positively influence the outcome.

In this study, 60% of the patients with pre-operative anxiety/depression did not report anxiety at their one-year follow-up. This has a great effect on the EQ-5D index. In an attempt to separate patients with nervous excitement or unease, more likely because of the operation, from those with persisting anxiety, we constructed a persistent anxiety group and compared this group with the remaining patients. This post hoc analysis revealed that the mean increase in EQ-5D index scores was lower in the group with persisting anxiety. Nevertheless, the relationship between anxiety/depression and the outcome of THR surgery needs to be confirmed by prospective studies using specific and sensitive psychometric measurements.

The strength of this study is in the large number of patients collected from a nationwide, prospective, observational database. Consequently, performance bias, which can occur if patients are recruited from selected surgeons and centres, is avoided.

Orthopaedic surgeons involved in the care of patients eligible for THR surgery should be alert to the fact that mental health may influence the pain experience and HRQoL outcome. An appropriate assessment of mental health may enable the management of those patients to be modified, in order to optimise their outcome after joint replacement surgery.

This study was an analysis of the databases in the Swedish Hip Arthroplasty Register, which was founded by the Swedish Board of Health and Welfare, the Swedish Association of Local Authorities and Regions and the County Council of the Western Region of Sweden. No commercial funding is related to this article. The Swedish Hip Arthroplasty Register continuously collects prospective, observational data regarding all total hip replacement surgery in Sweden. The Register holds a general approval from the Local Ethical Vetting Board in Göteborg (decision 5 067-02).

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References
