A Study on Indirect and Intangible Costs for Patients with Knee Osteoarthritis in Singapore

Feng Xie, PhD,1 Julian Thumboo, FRCP (Edin),2 Kok-Yong Fong, FRCP (Edin),2 Ngai-Nung Lo, FRCS (Edin),3 Seng-Jin Yeo, FRCS (Edin),3 Kuang-Ying Yang, FRCS (Glasg),3 Shu-Chuen Li, PhD4

1Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada; 2Department of Medicine, National University of Singapore, Singapore; 3Orthopaedic Surgery, Singapore General Hospital, Republic of Singapore, Singapore; 4Discipline of Pharmacy & Experimental Pharmacology, School of Biomedical Sciences, University of Newcastle, Callaghan, NSW, Australia

ABSTRACT

Objectives: To estimate indirect costs through human capital approach and intangible costs through willingness-to-pay (WTP), and identify factors potentially affecting these costs in multiethnic Asian patients with knee osteoarthritis (OA).

Methods: Data were collected through face-to-face interviews among knee OA patients. Human capital approach was used to estimate indirect costs by multiplying: 1) days of absence from work because of OA, with average earnings per capita per day for working patients; or 2) productivity loss with the market price of housekeeping for retirees/homemakers. A closed-ended iterative bidding contingent valuation method was used to elicit willingness-to-pay for a hypothetical cure of OA as a proxy for intangible costs. Mann–Whitney U or Kruskal–Wallis H-tests were performed in univariate analyzes, and linear regression in multivariate analyzes.

Results: Indirect costs per year and intangible costs were estimated at US$1008 and US$1200, accounting for 2.8% and 3.3% of annual household income, respectively. The indirect costs were significantly higher for male or working patients, while intangible costs were higher for Chinese, working patients, with higher income, or worse global well-being.

Conclusion: This study demonstrated that eliciting indirect costs through human capital approach and intangible costs through WTP are acceptable and feasible in Asian patients with knee OA. Besides the direct costs, the indirect and intangible costs for the OA patients could be substantial.

Keywords: human capital approach, indirect costs, Intangible costs, knee, osteoarthritis, willingness-to-pay.

Introduction

Osteoarthritis (OA) is one of the commonest chronic diseases worldwide and imposes a substantial economic burden on patients. The costs of OA have been estimated to account for up to 1% to 2.5% of gross national product (GNP) in several Western, developed countries [1,2]. The only published cost of OA study in Asia estimated that the cost of OA accounted for 0.28% of GNP in Hong Kong [3]. The cost of OA is expected to remain increasing as the population ages [4–6]. This highlights the importance of quantifying the cost of OA for both health planning and resource allocation.

Cost of an illness is generally divided into three categories, namely direct, indirect, and intangible costs [7,8]. Direct costs include all resources associated with the provision of an intervention or treatment for an illness. As direct costs are easily and accurately identified and estimated [9], this cost component has been included in many cost of OA studies [9–15]. Of note, charges have been commonly used as a proxy for cost in these studies as costs are often regarded as sensitive and confidential.

Indirect costs refer to productivity loss incurred by an illness [7,8,16], and are very important in cost of illness studies as they can be substantial. For example, several studies have shown that estimated indirect costs were three times higher than direct costs and accounted for up to 80% of total costs in patients with OA [17,18]. Conversely, some other studies suggested that indirect costs were lower than direct costs in OA [3,19,20]. As far as methodology is concerned, most recently published studies used human capital approach, which broadly encompasses both paid and unpaid work (e.g., parenting or housekeeping) to estimate indirect costs of OA by using wage rate for absence from paid work or equivalent market price for unpaid productivity (i.e., productivity loss of homemakers) [3,14,15,18,19].

Intangible costs are defined as pain and sufferings of patients because of a disease, which are usually measured by using the reduction in quality of life [21,22].
Alternatively, one method of estimating the monetary value of intangible costs is contingent valuation method (CVM), a stated preference method based on the elicitation of levels of willingness to pay (WTP), which was first used in measuring intangible value of environmental improvements [23] and has increasingly been used in health-care economics [24–30]. Nevertheless, it remains controversial to value intangible costs in monetary terms as there is no real market existing. To date, only a few studies adopted this methodology in estimation of intangible costs in health [31–33].

Therefore, the objectives of this study are to estimate indirect costs through human capital approach and intangible costs through WTP, and identify factors potentially affecting these costs in multiethnic Asian patients with knee OA in Singapore.

Methods

Patient Recruitment

Patients were recruited from the Departments of Rheumatology and Immunology and Orthopaedic Surgery in the Singapore General Hospital, a tertiary referral hospital in Singapore. Prior to the face-to-face interview, all patients were diagnosed with knee OA by their attending rheumatologist or orthopedic surgeon based on American College of Rheumatology classification criteria [34]. This was an Institutional Review Board-approved study and written informed consent was obtained for each patient.

Assessment of Demographic Characteristics

Patients were interviewed to obtain their demographic and socioeconomic information by using a structured data collection form. Patients were also asked to rate their global well-being on a 0 mm to 100 mm visual analog scale (VAS) anchored with worst imaginable health state at the lowest end and best imaginable health state at the highest end. After interview, each patient was asked whether they have any difficulty in understanding and answering these questions.

Estimation of Indirect Costs

The indirect costs were estimated using human capital approach. All patients were asked to estimate how many percent of productivity have been lost because of knee OA compared with the productivity before they had been diagnosed with OA. Additionally, working patients were asked to estimate the number of days of absence from work because of knee OA in the past year. As individual wage rates were not available and most of the patients who are still working are older (>50 years) for whom the difference in wage rate could be minimal, indirect costs for those who were working were thus calculated by multiplying the number of days of absence from work with average earnings per capita per day in Singapore between 1993 and 2003 (i.e., $139 per day, $1 = US$0.6) [35], and, for retirees/homemakers, by multiplying the percentage of productivity loss with current market price of housekeeping (i.e., $280 per month). Sensitivity analysis was performed to estimate highest indirect costs by using the highest average earnings per capita per day in Singapore between 1993 and 2003 (i.e., $144) [35], and the highest market price of housekeeping (i.e., $400), while the lowest indirect costs were calculated by using the lowest market price of housekeeping for both working and nonworking patients (i.e., $280 per month).

Estimation of Intangible Costs

To circumvent the difficulty to recruit a large number of knee OA patients in Singapore, we chose closed-ended iterative bidding CVM to elicit intangible costs as it can obtain specific amount of WTP and therefore needs a relatively small sample size [23]. In the process, patients were provided with an initial bid and asked whether they would like to pay this specified amount as one-time payment in addition to their current expenditures on treatment of OA for a hypothetical cure of knee OA (i.e., getting rid of all pain and suffering from the disease) with 100% effectiveness and without any side effects. If patients answered positively, then the amount was doubled. The procedure continued until patients expressed an unwillingness to pay the amount specified. Then the patients were further asked to specify the maximum amount they would like to pay between adjacent amounts to which they said “yes” and “no” in preceding questions. If patients answered negatively to initial bid specified, then the amount was halved until they expressed a WTP. Similarly, these patients were also further asked to indicate the maximum amount they would like to pay between adjacent amounts to which they said “no” and “yes” in preceding questions. To minimize the starting bid bias, patients were assigned at random to one of three different starting bids (i.e., $750, $1500, and $3000). As no empiric data were available, the choice of these three values was based on the annual report on earnings to represent low, middle, and high average monthly earnings in Singapore [36]. All costs were converted to 2005 Singapore dollars by applying 3% discount rate [23] and with equivalent US dollars in parenthesis. As noted, intangible costs were elicited using WTP, which are normally affected by income (i.e., ability to pay), we hypothesized that intangible costs will increase with higher income and be higher for Chinese patients who generally earn more than Malays and Indians in Singapore [35]. Additionally, higher indirect and intangible costs are assumed to be associated with higher productivity loss and worse global well-being of patients.
Statistical Analyses

Kolmogorov-Smirnov test demonstrated that the distributions of indirect and intangible costs were skewed. A series of nonparametric univariate analyses were therefore used. Mann-Whitney U-tests were performed to identify the effects of the dichotomous variables on indirect and intangible costs, while Kruskal-Wallis H-tests for polytomous variables. Separate multiple linear regression model was used to identify the effect of a pool of variables, including age, ethnicity, sex, working status, monthly household income, education, comorbidities, household size, productivity loss, and VAS score for global well-being, on the magnitude of indirect and intangible costs. All data were analyzed using STATA Intercooled v.8 (STATA Corporation, College Station, TX, 2003) with a significance level of 0.05, and all tests were two-tailed.

Results

Patient Characteristics

A convenient sample of 110 eligible patients were approached: 105 (response rate of 95.5%) agreed to participate in this study conducted from May to August of 2005, while five refused to participate in the study because they thought the questions were quite sensitive for them. All patients participated in this study indicated they do not have any problem in understanding these questions. Ninety-five patients (90.5%) answered these questions without difficulty compared with 10 patients with slight difficulty. Of note, when answering WTP questions, three patients (3.9%) would not like to pay for the reason that they do not have income to spend or their OA is very mild. Thus we considered the WTP from these three patients as true zero rather than protest zero, and included them in the data analysis [37,38]. As shown in Table 1, the majority of patients were female (76.2%), married (74.3%), ethnic Chinese (71.4%), retired or homemakers (80.0%), or with comorbidities (66.7%). These characteristics were similar to the general OA patients in Singapore, where there were 75.3% female, 83.6% Chinese, and 80.8% with comorbidities [39]. Near half of the patients had been diagnosed with knee OA for more than 5 years (46.7%), or with the monthly household income between $S$1000 to $S$2999 ($US$600 to $US$1799, 45.7%). The median productivity loss was 40.0%, while the median of the VAS score for global well-being was 70.0.

Indirect Costs

As the distribution of indirect and intangible costs were skewed, we used median rather than mean throughout the report. Indirect costs for each subgroup are listed in Table 2 and summarized below. Indirect costs for the cohort of patients in this study were $S$1680 ($US$1008) per year, which accounted for 2.8% of average annual household income [35]. Not surprisingly, the indirect costs borne by working patients were significantly higher than by patients who were retired or homemakers ($S$2086 vs. $S$1680 [US$1252 vs. US$1008], $P = 0.014$). As noted, no difference in indirect costs was observed among other variables in univariate analyses. Sensitivity analyses demonstrated that indirect costs ranged from $S$1344 to $S$2160 ($US$806 to US$1296), thus accounting for 2.3% to 3.6% of average annual household income, respectively.

Intangible Costs

Intangible costs were $S$2000 ($US$1200) for the cohort of patients in this study as shown in Table 2, which accounted for 3.3% of average annual household income [35]. The intangible costs for patients with a monthly household income above $S$3000 ($US$1800) were $S$3000 ($US$1800), compared with $S$1500 ($US$900) for those with the income below $S$1000 ($US$600), and $S$1700 ($US$1020) for those with the income between $S$1000 to $S$2999 ($US$600 to $US$900).

Table 1 Characteristics of patients (n = 105)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>63.6 (8.8)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>64.0 (14.0)</td>
</tr>
<tr>
<td>Female</td>
<td>80 (76.2)</td>
</tr>
<tr>
<td>Married</td>
<td>78 (74.3)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
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<tr>
<td>Chinese</td>
<td>75 (71.4)</td>
</tr>
<tr>
<td>Malay</td>
<td>15 (14.3)</td>
</tr>
<tr>
<td>Indian</td>
<td>15 (14.3)</td>
</tr>
<tr>
<td>Years of education</td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>30 (28.6)</td>
</tr>
<tr>
<td>1–6</td>
<td>33 (31.4)</td>
</tr>
<tr>
<td>7–10</td>
<td>32 (30.5)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>10 (9.5)</td>
</tr>
<tr>
<td>Retired/homemaker</td>
<td>84 (80.0)</td>
</tr>
<tr>
<td>Years with osteoarthritis</td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>9 (8.6)</td>
</tr>
<tr>
<td>2–3</td>
<td>22 (21.0)</td>
</tr>
<tr>
<td>4–5</td>
<td>25 (23.8)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>49 (46.7)</td>
</tr>
<tr>
<td>With comorbidities†</td>
<td></td>
</tr>
<tr>
<td>Household size</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>4.0 (2.0)</td>
</tr>
<tr>
<td>Monthly household income ($S$)</td>
<td></td>
</tr>
<tr>
<td>&lt;1000</td>
<td>29 (27.6)</td>
</tr>
<tr>
<td>1000–2999</td>
<td>48 (45.7)</td>
</tr>
<tr>
<td>3000–4999</td>
<td>16 (15.2)</td>
</tr>
<tr>
<td>&gt;5000</td>
<td>12 (11.4)</td>
</tr>
<tr>
<td>Productivity loss</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>40.0 (25.0)</td>
</tr>
<tr>
<td>VAS score for global well-being</td>
<td></td>
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<tr>
<td>Median (IQR)</td>
<td>70.0 (20.0)</td>
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</tbody>
</table>

†Self-reported comorbidities included hypertension (n = 46), diabetes (n = 41), high cholesterol (n = 15), cardiovascular diseases (n = 7), cancer (n = 5), heart disease (n = 5), asthma (n = 3), gastric ulcer (n = 2), rheumatoid arthritis (n = 2), cataract (n = 2), ocular disease (n = 1), thyroid nodules (n = 1), and skin disease (n = 1).

SD, standard deviation; IQR, interquartile range; VAS, visual analog scale.
to US$1799, \( P = 0.008 \)). The intangible costs were S$2900 (US$1740), S$1400 (US$840), and S$1500 (US$900) for Chinese, Malay, and Indian patients, respectively.

### Factors Influencing Indirect Costs

As shown in Table 3, the regression model with indirect costs as outcome variable demonstrated that sex and working status were the only two factors significantly affecting indirect costs (coefficient = 1685.0 and 2893.4, 95% confidence interval [95% CI] = 406.2–2963.8 and 1499.6–4287.2, \( P = 0.010 \) and 0.000, respectively). Notably, indirect costs were substantially higher, although not attaining statistical significance, for Malays compared with Chinese (coefficient = 1483.1, 95% CI = −93.3–3059.4, \( P = 0.065 \)).

### Factors Influencing Intangible Costs

In the regression model with intangible costs as outcome variable, income attained statistical significance as expected, which supports the validity of the WTP methodology [23]. In addition, both Malay and Indian patients incurred less intangible costs compared with Chinese patients (coefficient = −1557.2 and −1277.4, 95% CI = −2522.0 to −592.4 and −2247.5 to −307.2, \( P = 0.002 \) and 0.010, respectively). Working patients bore higher intangible costs than patients who were retired or homemakers (coefficient = 1100.5, 95% CI = 247.5–1953.6, \( P = 0.012 \)). Higher VAS score for global well-being was associated with less intangible costs (coefficient = −25.5, 95% CI = −50.1 to −0.9, \( P = 0.042 \)).

### Discussion

This study estimated indirect costs per year and intangible costs by using human capital approach and WTP technique, respectively, in patients with knee OA in Singapore. It demonstrates that these two methodologies are acceptable and feasible in this sociocultural
context. Moreover, the quantification of these two cost components has important implications in health-care delivery and planning. First, it can specifically contribute to better and comprehensive understanding of the economic burden of knee OA. This study confirmed that the economic burden incurred by knee OA would be substantial besides direct costs. Ignoring these two important cost components would therefore significantly underestimate the true burden of this chronic condition. Second, indirect and intangible costs of knee OA estimated in this study could be compared with the costs of other chronic conditions such as rheumatoid arthritis and hypertension [20]. This kind of comparison would provide useful information for governmental decision-makers in allocation of finite health resources. It is worth noting that to the best of our knowledge, this is one of the first studies to quantify intangible costs in monetary terms. As intangible costs were elicited using WTP, which can inversely be considered as a benefit from an effective health-care program for knee OA, it also helps pharmaceutical companies or health maintenance organizations to make a decision on developing a new treatment or health program for knee OA.

In this study, indirect costs of knee OA estimated in this study are comparable with those in other countries. The indirect costs estimated accounted for 2.3% (US$1175) of average annual household income in the United States [19,40], 3.0% (US$2040) in Canada [20,41], 4.0% (US$904) in Hong Kong [3], 4.7% (US$1981) in Italy [18,42]. Although certain variation in absolute magnitudes of indirect costs was observed across countries, relative magnitudes of indirect costs in terms of percentage of average annual household income were within the range of 2% to 5% across these countries. As the comparison is based on different studies applying the same methodology (i.e., human capital approach) among different populations across several continents (i.e., Europe, North America, and Asia), this finding implies that it might be viable to use this percentage range to quickly and approximately estimate indirect costs of OA in other countries around the world.

Nevertheless, it should be noted that another study also done in Canada [17] estimated that indirect costs accounted for 17.9% (US$1,497) of average annual household income. The main reason for the variation is that Gupta et al. used average monthly wage rate of US$1278 for professional homemakers, which is significantly higher than the wage rates used in other studies. The indirect costs will be increased to account for 18.6% of average annual household income if we use this wage rate in the estimation in our study.

In contrast, intangible costs were generally measured using reduction in quality of life [21,22]. As few studies are using WTP to quantify intangible costs, it is difficult to make a systematic comparison. In the very few published studies which quantified these costs in monetary terms, CVM was also used to elicit WTP as a proxy for intangible costs. The intangible costs accounted for 3.0% (US$1387) of average annual household income for sharp-related injuries in the United States [31], and 0.42% (US$193 per year) for urinary storage symptoms in the UK [33]. Additionally, several observations in estimating intangible costs are worth noting. First, the starting bid bias is known as one of the major limitations when applying closed-ended iterative bidding CVM in eliciting WTP [37]. Nevertheless, the influence is not statistically significant in this study, although there is a slightly increased intangible costs (i.e., WTP) associated with larger starting bid (Table 2). Second, intangible costs for the patients with better health status (i.e., higher VAS scores for global well-being) were less than the costs for those with worse health status. We expected that

| Table 3  Multiple linear regression analyses for indirect and intangible costs |
|---------------------------------|-------------------------------|
| **Dependent variables**         | **Indirect costs**           | **Intangible costs**        |
| **Coefficients (95% CI)**       | **Coefficients (95% CI)**    | **Coefficients (95% CI)**   |
| **P**                           | **P**                         | **P**                       |
| Age (per year)                  | 6.92 (−56.37, 70.21)          | 10.63 (−28.11, 49.36)       | 0.387 |
| Malay*                          | 1483.05 (−93.30, 3059.39)     | −1557.17 (−2521.95, −592.40) | 0.002 |
| India*                          | 680.88 (−904.26, 2326.02)     | −1277.36 (−2247.50, −307.20) | 0.010 |
| Malen                          | 1685.00 (406.18, 2963.82)     | −407.91 (−1190.59, 374.76)  | 0.303 |
| Working patients†               | 2893.38 (1499.58, 4287.18)    | 1100.51 (247.46, 1953.56)   | 0.012 |
| Income (per dollar)             | 0.07 (0.19, 0.34)             | 0.28 (0.12, 0.44)           | 0.001 |
| Education (per year)            | −79.78 (−178.27, 18.81)       | 55.69 (−4.65, 116.03)       | 0.070 |
| With comorbidities‡             | 241.64 (−874.76, 1358.03)     | −383.05 (−1066.32, 300.22)  | 0.268 |
| Household size (per person)     | −285.49 (−650.75, 79.78)      | −88.23 (−311.78, 135.32)    | 0.435 |
| Productivity loss (per percentage) | 28.90 (−1.75, 59.56)         | 13.00 (−5.76, 31.76)        | 0.172 |
| VAS score for global wellbeing (per unit, range, 0–100) | 22.66 (−17.54, 62.87) | −25.31 (−50.12, −0.90) | 0.042 |

*The reference group is Chinese.†The reference group are retirees and homemakers.‡The reference group is without comorbidity.

95% CI, 95% confidence interval; VAS, visual analog scale.
both the productivity loss because of knee OA and
global well-being should be associated with intangible
costs. Nevertheless, a significant relationship between
productivity loss and intangible costs was not observed
in this study. As most of the patients (70 of 105) were
diagnosed with comorbidities, it might be very difficult
for them to distinguish the pain and sufferings from
OA and other diseases. Therefore, intangible costs
might be overestimated in this study, as the costs could
not be exclusively attributable to knee OA. This issue
might be addressed by comparing the intangible costs
incurred by knee OA patients with the control patient
group without the disease [11]. As noted, the substi-
tional ethnic differences in intangible costs persisted
with adjustment for other demographic variables. This
observation might be explained by the tradition that
Chinese patients thought arthritis is a natural process
for the elderly, which make them reluctant to see a
doctor at the early stage of the disease (personal com-
munications with patients). Thus, most Chinese
patients seen in the hospital were quite severe and
consequently bore higher intangible costs.

One of the major limitations of this study is that the
productivity loss incurred by family members or car-
egivers was not assessed, as most of the patients in this
study reported that they did not recall such informa-
tion at all. Thus, the magnitude of indirect costs esti-
ated in this study could be considered as at a lower end
of the spectrum. A suggestion for further refine-
ment would be to include the indirect costs borne by
the caregivers in future study [16]. Additionally, the
number of days of absence was estimated based on
the recall of patients, which might not be accurate.
Nevertheless, the clinicians were also approached to
obtain more accurate estimation. Second, the impact
of comorbidities on cost estimation was not assessed
in this study, which will limit the comprehensive evalua-
tion of the economic burden of OA on patients with
comorbidities compared with those without any
comorbidity. Finally, because of the limitation in number of patients with other types of OA, we cannot
recruit these patients in this study. Nevertheless, it is
worth noting that estimating indirect and intangible
costs for other types of OA is necessary, which can
contribute to comprehensive evaluation of the eco-

In conclusion, this study demonstrated that eliciting
indirect costs through the human capital approach and
intangible costs through the WTP are acceptable and
feasible in Asian patients with knee OA. Our study
also estimated that indirect and intangible costs for
the patients with knee OA could be substantial.

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