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Prevalence of Analgesic Prescriptions among Patients with Cancer in Japan: An Analysis of Health Insurance Claims Data

Takahiro Higashi[1], Tetsusuke Yoshimoto[2] & Motohiro Matoba[3]

[1] Department of Public Health/Health Policy, University of Tokyo, Tokyo, Japan

[2] Department of Palliative and Supportive Care, Social Insurance Chukyo Hospital, Nagoya, Japan

[3] Department of Palliative Medicine, National Cancer Center Hospital of Japan, Tokyo, Japan

Correspondence: Takahiro Higashi, University of Tokyo, Department of Public Health/Health Policy, Tokyo, Japan. Tel: 81-3-5841-3491. E-mail: higashi@m.u-tokyo.ac.jp

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Abstract

Objectives: To promote effective management of cancer pain as a nationwide health policy, it is necessary to monitor the performance of health care providers in managing pain in their patients. To plan a system that monitors the performance of pain management, the exact methods of measurement, including the range of target patients, and estimate the resources must be defined. Performance in pain management can be evaluated either in all patients with cancer or restricted to patients with cancer who are already taking analgesics. Restricting the target patient group to patients on analgesics may be more efficient but the extent of that efficiency remains uncertain.

Methods: Using insurance claims from eight employer-sponsored insurance companies, we analyzed data from patients (N = 2858) who had received anti-cancer treatment (ie, surgery, chemotherapy, and radiation therapy) for the five major cancers in Japan (ie, breast, colorectal, liver, lung, and stomach cancers).

Results: Overall, 22.9% of patients received some kind of analgesic prescription in the course of a month. Lung cancer patients were more likely to be prescribed analgesic prescriptions (any analgesics 34.8%; opioids 18.2%) than patients with the other four cancers. The observed percentage of patients who received analgesic prescriptions over the study period (ie, January 2005 to November 2009) decreased.

Conclusion: If we limit the target patient group to patients with cancer already on analgesics, we can reduce the number of persons to be contacted by about three-fourths, compared to assessing pain in all patients with cancer. Although we do not wish to ignore the problem of undetected pain among patients with cancer, beginning our systematic evaluation with patients with cancer already on analgesics may be a realistic option.

Keywords: analgesic prescription, pain management, performance measurement, cancer, opioid

1. Introduction

While pain is the most focused-on part of palliative care in cancer patients (Portenoy, 2011), management of pain is reportedly inadequate in many settings (Cleeland et al., 1994; Deandrea, Montanari, Moja, & Apolone, 2008; Okuyama et al., 2004; Uki, Mendoza, Cleeland, Nakamura, & Takeda, 1998). Few studies have examined the adequacy of pain management in cancer care in Japan (Okuyama et al., 2004; Uki, Mendoza, Cleeland, Nakamura, & Takeda, 1998). Even though cancer is the leading cause of death (Ministry of Health, 2010) in Japan, opioid consumption is relatively small compared to opioid consumption in other industrialized counties. According to a report by the International Narcotics Control Board, opioid consumption in Japan is the lowest among the G7 countries (The International Narcotics Control Board, 2010).

Concern over low opioid consumption in Japan has led policy makers to pay extra attention to pain control. The Cancer Control Act of 2007, which delegated comprehensive responsibility for cancer control to the Japanese government, specifically states that both national and local governments should "take measures to enable palliative care, such as pain control, from the early stages of cancer care processes" (Japan Law Data Archives, 2006). And The Basic Plan to Promote Cancer Control Programs established adequate pain control as a central agenda (Ministry of Health, 2007).

One way to foster adequate pain management in hospitals throughout Japan would be to establish a system to monitor their pain management programs. Measurement and feedback of hospital performance of pain management, preferably in comparison to other medical facilities, would motivate hospitals to improve their pain management (Hibbard, Stockard, & Tusler, 2003). Establishment of a pain management monitoring system would require that consistent methods be clearly defined to measure pain management in target patients and in the success/failure of treatment.

There are several ways to define the target patients who need pain management. The ideal way, which would be to include all patients with cancer who suffer from any kind of pain, would require a process of asking all patients with cancer (perhaps before definitive diagnoses are made) about their pain, since some patients may not have discussed their pain with their health providers. An alternative way may be to target only patients under some type of pain management or patients taking analgesic drugs. This way overlooks patients with pain not recognized by health providers, and thus fails to consider providers' ability or efforts to thoroughly detect patients' suffering. On the other hand, because this way does not rely on obtaining patients' reports, it provides a more defined range of target patients and saves the time and effort of interviewing individual patients about pain.

While the theoretical limitation associated with focusing on patients already being treated for pain is clear, an important unanswered question is: How much labor can we expect to save by limiting the number of target patients? We have found no studies in the literature that report the percentage of patients with cancer being treated for pain in Japan. Although surveys from other countries have reported their prevalence of pain (Breivik et al., 2009; van den Beuken-van Everdingen et al., 2007) and proportion of treatment for moderate to severe pain (Breivik et al., 2009), they have not focused on the frequency of prescribing pain medications associated with resource allocation for monitoring of pain management in hospitals. The purpose of this study was to gain insight into the current status and recent time trend of the use of pain medications in Japan. We analyzed a large database of insurance claims from multiple employer-sponsored insurance companies.

2. Methods

2.1 Dataset

2.1.1 The Health Insurance System in Japan

We analyzed insurance claims data sets from 8 employer-sponsored insurance companies. In Japan, all residents have health insurance from either their employment or their place of residence. Many large companies work with associated insurance companies (1435 insurance companies as of April 2012 (National Federation of Health Insurance Societies (Kenporen), 2012)). Relatively small companies who do not work with associated insurance company provide coverage through the Japan Health Insurance Association. Unemployed or retired persons and persons aged 75 years or older have coverage based on their place of residence from city or region-based insurance entities, respectively.

Health services are reimbursed on a fee-for-service basis according to a nationally defined fee schedule. The healthcare facilities submit claims every month for each patient. The claims list all the services and medications provided to patients in the facility as well as the diagnoses corresponding to those services and medications. For patients who receive drug prescriptions, claims for the medications are submitted by the pharmacy that has dispensed the prescription. These pharmacy claims also contain the names of the prescribing facilities, thus providing links to the prescribing claims.

2.1.2 Study Sample

For our study, eight insurance companies provided data from a total of 750 000 members consisting of the employees of affiliated companies and their dependents. Among them, three insurance companies provided claims from January 2005 to December 2009 and five provided claims from January 2008 to December 2009. The claims from these eight insurance companies included a total of 84652 patients with any type of cancer diagnosis, including tentative diagnoses. To avoid ambiguity of diagnosis on the insurance claims, we analyzed data on patients who had received anti-cancer treatment for the five major cancers in Japan, namely, breast, colorectal, stomach, lung, and liver cancers. Anti-cancer treatment included surgery, chemotherapy, hormone therapy, and radiation therapy. We excluded patients who had undergone only endoscopic treatment, because we suspected that cancer painmay not have been an issue for them.

2.2 Statistical Analyses

Analgesic drugs were classified according to the World Health Organization Pain Control Ladder (World Health Organization., 1996); non-steroidal anti-inflammatory drugs (NSAIDs) including acetaminophen, weak opioids (ie, codeine, dihydrocodeine, tramadol, and pentazocine), and strong opioids (ie, morphine, oxycodone, fentanyl,

pethidine, and buprenorphine). Low-dose aspirin (100mg/tablet) and the codeine contained in cold medicines were not regarded as painkillers. For each month during the study period, the proportion of patients with cancer who received each type of drugs was recorded.

The proportion of analgesic prescriptions were compared between patients' treatment phases (ie, after surgery, after chemotherapy, and after radiation) and primary cancer site. Definition of the treatment phase was based on the last anti-cancer therapy. For example, patients who received surgery followed by chemotherapy (at a later time) were considered to be "after surgery" for the period between surgery and chemotherapy, and "after chemotherapy" after the chemotherapy had been received. Primary cancer sites were determined on the basis of both the cancer treatment and diagnosis recorded on insurance claims. For those patients who had undergone surgery, including site-specific intervention (eg, radio frequency ablation therapy to the liver), the primary site of cancer was considered to be the target organ. For those patients who had received only systemic chemotherapy, where the target cancer had not been clearly established, or radiation therapy where the insurance reimbursement code was the same across different target sites, the diagnoses in the insurance claims were accepted as they had been recorded. The differences in the proportions were statistically tested using the chi-square tests.

The trend of prescribing analgesic drugs for cancer patients was described as the proportion of patient-prescribed analgesic drugs among the cancer patients who had used any health services during a given month. The person-month was the unit of analysis. The change in the trends was analyzed graphically. Also the beta coefficients to represent the trend was calculated using linear regression analyses where the percentage of analgesic prescriptions and the time variable were the dependent and independent variables, respectively, assuming the linearity of the relationship. Because the assumption of homoscedastic errors did not hold for some regression models, the robust standard errors were calculated with the White correction. No correlation between error terms and the independent variable was confirmed. All analyses were performed using Stata 11.2 (StataCorp LP, College Station, Texas).

3. Results

A total of 6656 patients had one of the five major cancers on the health insurance claims, among whom 2585 patients received treatment with surgery, chemotherapy, and/or radiotherapy during the study period, and thus were entered into the analyses. Patient characteristics are presented in Table 1. Average patient age was 53.4 years (Standard deviation: 10.6); 57.7% of patients were female. The most common cancer was breast cancer (n =923 [35.7%]), followed by colorectal cancer (n =615 [23.8%]) and stomach cancer (n =465 [18.0%]). The average duration of the observation period (ie, from first cancer treatment to last visit) was 33.8 months.

Table 1. Patient characteristics

Age		
<20	21	(0.8%)
20-39	243	(9.4%)
40-59	1619	(62.6%)
60-69	548	(21.2%)
>70	154	(6.0%)
Gender		
Female	1491	(57.7%)
Cancer site		
Breast	923	(35.7%)
Colorectal	615	(23.8%)
Liver	179	(6.6%)
Lung	412	(15.9%)
Stomach	465	(18.0%)
Treatment received		
Surgical Intervention	1586	(61.4%)
Chemotherapy	1629	(63.0%)
Radiation	594	(23.0%)

Tables 2 and 3 show the percentages of patients receiving analgesic prescriptions every month by treatment phase and by site of cancer, respectively. Overall, 22.9% of patients who used healthcare each month received analgesic prescriptions (Table 2). Analyses for each drug class revealed that NSAIDs or acetaminophen and opioids were prescribed in 19.8% and 9.1% of the patients, respectively. Strong and weak opioids were prescribed 6.2% and 4.0% of visits, respectively. When we separated patients by treatment received, patients after chemotherapy were most frequently prescribed analgesics (23.7%), while opioids were most frequently prescribed for patients after radiation therapy (9.8%). The analysis by site of cancer revealed that patients with lung cancer were more likely to receive analgesics (overall, 33.3%) than patients with other types of cancer (Table 3).

Table 2. Average proportion of analgesic prescriptions every month by treatment phase

	Overall	**After surgery**	**After chemotherapy**	**After radiation**	**P value**
Any analgesics	22.9%	21.4%	23.7%	22.8%	<0.001
ACA	1.9%	1.9%	2.2%	2.6%	<0.001
ACA/NSAIDs	19.8%	18.8%	20.7%	20.8%	<0.001
Opioid	9.1%	6.7%	9.4%	9.8%	<0.001
Weak opioid	4.0%	4.2%	3.8%	4.3%	0.16
Strong opioid	6.2%	3.6%	6.7%	6.5%	<0.001

Abbreviations: ACA acetaminophen; NSAID non-steroidal anti-inflammatory drug.

Table 3. Average proportion of analgesic prescriptions every month by site of cancer

	Breast	**Colorectal**	**Liver**	**Lung**	**Stomach**	**P value**
Any analgesics	20.0%	20.8%	23.8%	33.3%	17.1%	<0.001
ACA	1.9%	1.9%	2.5%	2.5%	1.9%	0.01
ACA/NSAIDs	18.4%	17.7%	19.9%	28.7%	14.4%	<0.001
Opioid	4.2%	8.9%	9.6%	17.6%	7.0%	<0.001
Weak opioid	2.1%	3.5%	7.0%	6.1%	2.8%	<0.001
Strong opioid	2.4%	6.6%	3.1%	13.2%	5.3%	<0.001

Abbreviations: ACA acetaminophen; NSAID non-steroidal anti-inflammatory drug.

Figure 1 shows a decrease in the percentage of patients who received analgesic prescriptions over the observation period (ie, January 2005 to November 2009). Table 4 shows that analgesic prescriptions decreased by 0.13% per month as calculated via regression analysis.

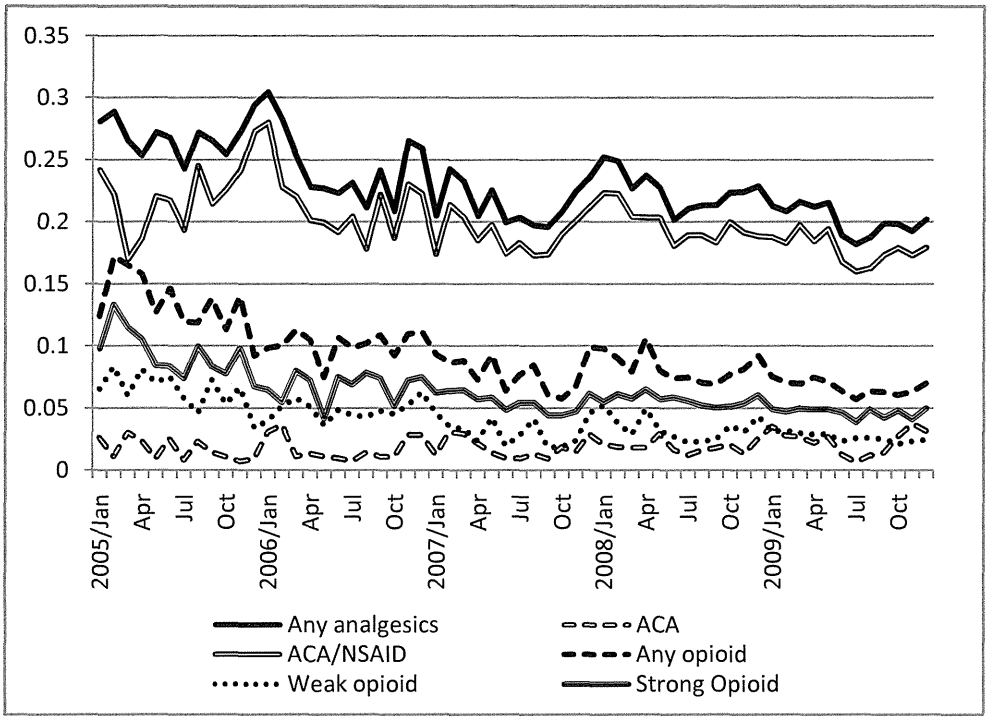

Figure 1. Trend of analgesic prescriptions over observation period

Table 4. Monthly decrease of proportion of analgesic prescriptions(linear regression analyses)

	Beta		(95% CI)	P value
Any analgesics	-0.13%	-0.15%	-0.11%	<0.001
ACA	0.01%	0.00%	0.02%	0.13
ACA/NSAIDs	-0.08%	-0.11%	-0.05%	<0.001
Opioid	-0.13%	-0.15%	-0.10%	<0.001
Weak opioid	-0.07%	-0.09%	-0.06%	<0.001
Strong opioid	-0.09%	-0.11%	-0.07%	<0.001

Abbreviations: ACA acetaminophen; NSAID non-steroidal anti-inflammatory drug.

4. Discussion

Our study, using health insurance claims data from employee-sponsored insurance companies, showed that about one fourth of the patients treated for the five major cancers in Japan received analgesic prescriptions. Since the patients counted in our study were in treatment, the true prevalence of pain that include patients with pain but not in treatment among these patients will be higher. Restricting our target group of patients to patients taking analgesic medications will facilitate selection of patients for evaluating the performance measurement of pain management. By selecting patients in treatment for this evaluation, we will be getting by with only one-fourth to one-fifth of the all the patients. In addition, restricting our target group to patients taking analgesic medication is likely to be more efficient for systematic evaluation purposes than identifying and assessing patients with pain from all patients with cancer.

It must be noted that our study neither implies that identifying patients with untreated pain is of little value nor does it advocate limiting target patients for the monitoring of pain management. Although the prevalence of pain among Japanese patients with cancer is unknown, the prevalence of analgesic prescriptions is much lower than prevalence of pain itself reported in other countries. One systematic review showed that about half of all diseases stages and a third of patients after curative treatment reported pain (van den Beuken-van Everdingen et al., 2007). A population-based survey from Europe and Israel showed that 74% of patients with cancer reported pain

(Breivik et al., 2009). Although the patients with cancer in our study were younger and in better condition than the average patient with cancer (Center for Cancer Control and Information Services, National Cancer Center, 2011), the gap between the prevalence of pain among patients with cancer and our finding that 22.9% of patients received analgesics may be an indication of the undertreatment of pain in Japan. This gap underscores the importance of detecting pain among cancer patients.

We need to implement better pain management for cancer pain nationwide. While we are not satisfied with a limited target patient group for assessment in planning a nationwide system, we understand that starting with a limited group is a realistic option. Uniform application of the assessment with clear definition is essential to encourage improvement. Even if we start small, we will eventually assess all patients with cancer who are experiencing pain and ensure that they have access to pain management and appropriate treatment.

In order to work toward a nationwide pain management system for cancer pain, we need to be cautiously aware of the nature of the data to be used and the findings on opioid consumption in Japan. The decreasing trend of patients receiving analgesic drugs in the observed data may be associated with the composition of patients in treatment phases shifted from acute-phase dominant to chronic follow-up phase dominant over time. Because we enrolled patients from the month in which they began cancer therapy and followed up later, patients under observation in the early years of the study period were usually enrolled right after the treatment, making them more likely to receive analgesic medications for pain that arose from the anti-cancer treatment (eg, wound pain after surgery, dermatitis after radiation therapy). In the later years of the study we observed patients both in regular follow-up and patients receiving acute treatment. Thus, a larger proportion of more stable patients in regular follow-up may have caused the overall proportion of analgesic prescriptions to decrease. Nonetheless, the decrease was not steep and therefore did not greatly influence our findings.

The impact of the insurance claims on our findings also warrants mention. First, the insurance companies that provided the data were employer-sponsored. As such, they exclusively enroll employees and employees' dependents. We suspect therefore that our target patient group tended to be younger than the average cancer patient. In fact, while the national statistics on the hospital-based cancer registries showed that most cancer patients to be in their 60s and 70s (Center for Cancer Control and Information Services & National Cancer Center, 2011), most of the patients with cancer in our studies were their 50s and 40s. Second, the accuracy of the diagnosis may be questionable. Since insurance claims place more emphasis on consistency between diagnoses and services provided than clinical accuracy, determining whether a diagnosis is tentative or final is difficult. Third, claims data do not describe the symptoms for which the drugs were prescribed. Therefore, we cannot determine whether NSAIDs were prescribed for pain, fever, or some other anti-inflammatory malady. Fourth, claims submitted to insurance companies lack information on services out of the fee-for-service reimbursement. In 2003 the Japanese health insurance system started paying per-diem based on predefined information from diagnosis-procedure groups in 82 participating hospitals. The number of participating hospitals gradually increased, and in 2011, a total of 1447 hospitals (19% of total) in Japan were participating (Bureau of Health Insurance, Ministry of Health, Labor, & Welfare, 2012). Most services and medications provided during hospitalization to these hospitals were not captured in regular insurance claims, increasing the likelihood of underestimating analgesic use during hospitalization. Fifth, we limited our analyses to the patients who received therapy for the five major cancers in Japan. By limiting the cancer type to the five major cancers, we could match the match the claim diagnoses with the treatment. This enabled us to exclude patients with a tentative diagnosis who turned out not to have cancer later or inactive diagnosis that was treated could remain on the claims even after treatments were over. However, in real clinical practice, the target for pain management should include all cancer types. We need to bear in mind that the results may have been different if we included all cancer types. Finally, since our data are derived from health insurance companies, the number of patients per hospital was small for many hospitals. Given that taking analgesic prescriptions in small denominators is not likely to produce stable results, we did not perform analyses at the level of individual providers.

5. Conclusion

Our study showed the prevalence of analgesic prescriptions among five major cancers in Japan. When planning for a system that monitors the performance of pain management, it is important to balance the resources used with the range of the target for the measurement. The frequency of analgesic prescription provided information for an evidence-based discussion on how to restrict or broaden the target population for monitoring using available resources. Even if we decide to begin systematic evaluation with a smaller target patient group (ie, patients already taking analgesics), we will do so keeping in mind that our ultimate goal is to provide pain relief to all patients with cancer in our country.

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References

Breivik, H., Cherny, N., Collett, B., de Conno, F., Filbet, M., Foubert, A. J., ... Dow, L. (2009). Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. *Ann Oncol, 20*, 1420-33. http://dx.doi.org/10.1093/annonc/mdp001

Bureau of Health Insurance, Ministry of Health, Labor, and Welfare, Japan. (2012). Overview of revision of fee-schedule 2012. Retrieved August 27, 2012, from http://www.mhlw.go.jp/bunya/iryouhoken/iryouhoken15/dl/h24_01-05.pdf

Center for Cancer Control and Information Services, National Cancer Center. (2011). Statistics of 2008 Cancer Cases from Hospital-based Cancer Registries in Japan. Retrieved August 18, 2012, from http://ganjoho.jp/professional/statistics/hosp_c_registry.html

Cleeland, C. S., Gonin, R., Hatfield, A. K., Edmonson, J. H., Blum, R. H., Stewart, J. A., & Pandya, K. J. (1994). Pain and its treatment in outpatients with metastatic cancer. *N Engl J Med, 330*, 592-6. http://dx.doi.org/10.1056/NEJM199403033300902

Deandrea, S., Montanari, M., Moja, L., &Apolone, G. (2008). Prevalence of undertreatment in cancer pain. A review of published literature. *Ann Oncol, 19*, 1985-91. http://dx.doi.org/10.1093/annonc/mdn419

Hibbard, J. H., Stockard, J., & Tusler, M. (2003). Does publicizing hospital performance stimulate quality improvement efforts? *Health Aff (Millwood), 22*, 84-94. http://dx.doi.org/10.1377/hlthaff.22.2.84

Japan Law Data Archives. (2006). Cancer Control Act. Retrieved August 8, 2012, from http://law.e-gov.go.jp/announce/H18HO098.html

Ministry of Health, Labor, and Welfare, Japan. (2007). Basic Plans to Promote Cancer Control Programs.

Ministry of Health, Labor, and Welfare, Japan. (2010). Vital statistics of Japan. Retrieved August 8, 2012, from http://www.mhlw.go.jp/toukei/list/dl/81-1a2.pdf

National Federation of Health Insurance Societies (Kenporen). (2012). About Kenporen. Retrieved August 9, 2012, from http://www.kenporen.com/outline/

Okuyama, T., Wang, X. S., Akechi, T., Mendoza, T. R., Hosaka, T., Cleeland, C. S., & Uchitomi, Y. (2004). Adequacy of cancer pain management in a Japanese Cancer Hospital. *Japan J Clin Oncol, 34*, 37-42. http://dx.doi.org/10.1093/jjco/hyh004

Portenoy, R. K. (2011). Treatment of cancer pain. *Lancet, 377*, 2236-47. http://dx.doi.org/10.1016/S0140-6736(11)60236-5

The International Narcotics Control Board. (2010). Report of the International Narcotics Control Board on the Availability of Internationally Controlled Drugs: Ensuring Adequate Access for Medical and Scientific Purposes. Retrieved August 8, 2012, from http://www.incb.org/pdf/annual-report/2010/en/supp/AR10_Supp_E.pdf

Uki, J., Mendoza, T., Cleeland, C. S., Nakamura, Y., & Takeda, F. (1998). A brief cancer pain assessment tool in Japanese: the utility of the Japanese Brief Pain Inventory--BPI-J. *J Pain Symptom Manage, 16*, 364-73. http://dx.doi.org/10.1016/S0885-3924(98)00098-0

van den Beuken-van Everdingen, M. H., de Rijke, J. M., Kessels, A. G., Schouten, H. C., van Kleef, M., & Patijn, J. (2007). Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Ann Oncol, 18*, 1437-49. http://dx.doi.org/10.1093/annonc/mdm056

World Health Organization. (1996). Cancer Pain Relief. Geneva, Switzerland: World Health Organization.

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Concordance of hospital-based cancer registry data with a clinicians' database for breast cancer

Mingji Zhang MD PhD,[1] Takahiro Higashi MD PhD,[2] Hiroshi Nishimoto MD,[3] Takayuki Kinoshita MD PhD[4] and Tomotaka Sobue MD PhD[5]

[1]Research Resident, [3]Section Head, [5]Head, Cancer Information Services and Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan
[2]Associate Professor, Cancer Information Services and Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center and Department of Public Health and Health Policy, University of Tokyo, Tokyo, Japan
[4]Chief, Breast Surgery Division, National Cancer Center Hospital, Tokyo, Japan

Keywords
breast cancer, clinicians' database, concordance of data, exchange information, hospital-based cancer registry

Correspondence
Dr Mingji Zhang
National Cancer Center
5-1-1 Tsukiji
Chuo-ku
Tokyo 104-0045
Japan
E-mail: mzhang@ncc.go.jp

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Abstract

Objective Reliable information is essential to both clinical and policy decision making. We aimed to shed lights on the similarity and differences between a hospital-based cancer registry with a clinicians' database for breast cancer by comparing the registered data on the same year.

Methods We performed a head-to-head comparison of breast cancer cases extracted from the hospital-based cancer registry and the clinicians' database maintained by the Division of Breast Surgery at the National Cancer Center Hospital in 2004.

Results The hospital-based cancer registry reported 827 cases of newly diagnosed breast cancer patients in 2004, while the clinicians' database contained 366 surgically treated cases from 2004. Of these, 276 cases overlapped. Presence or absence of treatment modality was discordant in 15% for radiation therapy, 19% for chemotherapy, and 24% for hormone therapy between the two data sets. Furthermore, the recorded disease pathology was discordant in 13% for pathology and 28% for staging, with 22% for T-stage, 7% for N-stage, 7% for M-stage.

Conclusions Although information contained in hospital-based cancer registry and clinicians' database are generally accurate, some important differences were revealed as a result of varying interpretations of clinical information. Analyses of these data sets must be made with attention to details such as eligible patients, registered treatment, and timing of registration.

Introduction

Effective cancer control policies require accurate information on epidemiology and practice patterns. Cancer registries can theoretically serve these purposes, but Japan has been delayed in establishing such systems with national coverage. Traditionally, two types of cancer registries have been developed: population-based and site-specific cancer registries. Population-based cancer registries, run by prefectural government health departments, aim to assess cancer incidence, while site-specific registries, managed by professional societies, focus more on collecting detailed clinical information [1]. Although both have more than 30 years of history, individual efforts are dependent on prefectures and cancer sites with no existent system that can provide a national picture of cancer incidence or practice patterns.

The Cancer Control Act [2] enacted in 2007 and the National Basic Cancer Plan mandate government promotion of cancer registries. To systematically enhance such activities, the government created a third system, hospital-based cancer registries, by mandating designated cancer centres to register all cancer cases diagnosed or treated at their facility. The items are standardized centrally and cover basic information including disease localization, clinical and pathological stages, and initial treatment provided. Data are collected by registrars trained by the Center for Cancer Control and Information Services at the National Cancer Center. Because standardized items are common for all types of cancer, the collected information lacks site-specific data such as types of surgery and names of chemotherapeutic drugs. However, when a facility participates in both registry schemes, basic information is collected twice: once by clinicians for site-specific

cancer registry and again by tumour registrars for hospital-based cancer registry. In the future, these two systems may be integrated within facilities for the sake of efficiency. In the meantime, however, the current situation provides a unique opportunity to confirm the accuracy of case identification and information in both databases (DBs). Knowledge of the difference and exchangeability of information is important because public agencies and the government tend to use hospital-based cancer registries, while clinicians use site-specific cancer registries to answer the same questions of outcome, survival, and patterns of care.

To understand the similarity and differences of the hospital-based cancer registry and site-specific cancer registry, we compared the hospital-based cancer registry with the clinicians' DB, which supplies data to a site-specific cancer registry at the National Cancer Center Hospital (NCCH), taking breast cancer cases as an example. The comparison provided basic information on exchangeability and differences between the two systems for future discussion of possible integration.

Methods

We extracted breast cancer cases from the hospital-based cancer registry and the clinicians' DB maintained by the Division of Breast Surgery in NCCH in 2004. Although the hospital-based cancer registry and clinicians' DB both collect breast cancer cases, they are independent data collection schemes with several differences.

Hospital-based cancer registry

For the hospital-based registry, information is collected by trained tumour registrars, who systematically extract cases based on pathology reports and other sources to register all cancer cases in the hospital according to the national standard. The unit of registration is the number of tumours. Thus, if one patient has two independent tumours (e.g. breast cancer and colon cancer, or two histologically different breast cancers), he/she is registered twice to represent both cancers. The index date is the date of initial diagnosis if the patient underwent definitive diagnostic test in the hospital or date of first visit to the facility if the patient was already definitively diagnosed with cancer before the first visit. The information collected is common to all cancer types, including cancer site, pathology, route of referral, presentation, clinical and pathological staging [based on the International Union Against Cancer (UICC) system], initial treatment provided in the hospital, and treatment outcomes. The registry does not collect information specific to individual cancers (e.g. hormone receptor status for breast cancer).

Cases were entered in the hospital-based cancer registry at approximately 6 months after diagnosis. Among the treatments provided, only initial therapy planned at diagnosis was documented.

Clinicians' database

In the clinicians' DB for breast cancer, practising physicians collect data in accordance with a template provided by the Japanese Society for Breast Cancer. Almost all patients surgically treated in the Division of Breast Surgery are included. The unit of registration is the patient, and the index date is the date of surgery in the hospital. Patients are registered each time they undergo an operation. Data recorded include clinical findings (e.g. cancer site, tumour size, stage), imaging findings (e.g. mammography, ultrasonography), pathology, complications, hormone receptor status, and specific therapeutic methods (e.g. types of surgery, regimen, dose of radiation, and chemotherapeutic dosage). Staging is assessed using Japanese General Rules for Clinical and Pathological Recording of Breast Cancer. The system differences between hospital-based cancer registry and site-specific cancer registry are summarized in Table 1.

Unlike in the hospital-based cancer registry, all provided therapies are registered in the clinicians' DB. No fixed timing is specified for data entry in the clinicians' DB, but it is presumed the information is updated continuously.

Analytic methods

We compared the concordance of case data registered in the hospital-based cancer registry versus the clinicians' DB. We also compared basic clinical information across overlapping cases, including clinical staging, the tumour-node-metastasis (TNM) classification, date of surgery, and presence or absence of radiation therapy, chemotherapy, and hormone therapy. For patients with discrepancies in documented information, we reviewed the medical record to determine accuracy of data and underlying reasons for the differences.

Results

Differences in registered subjects

The hospital-based cancer registry contained 827 cases diagnosed as breast cancer at the NCCH in 2004, while the

Table 1 Characteristics of the two types of cancer registries

	Hospital-based cancer registry	Site-specific cancer registry
Primary purpose	To assess current status of cancer care	To collect in-depth information for the advancement of clinical cancer management
Managing entity	Hospital	Academic society
Subjects	All diagnosed cancer patients at first visits to the hospital	Patients in major hospitals with cancers of specific sites
Data items	Diagnosis, initial treatment; follow-up 74 items	Variable by cancer site; 100–300 items
Data entry	Mainly tumour registrars	Clinician (physicians)
Problem	Lack of clinical details, especially site-specific information such as hormone status; shortage of tumour registrars	Incomplete follow-up; burden to clinicians

Table 2 Comparison of adjuvant therapy between hospital-based cancer registry and the clinicians' database

Hospital-based cancer registry		Clinicians' database							Concordance rate (%)
			Radiation therapy		Chemotherapy		Hormone therapy		
		All	Yes	No	Yes	No	Yes	No	
	All	276							
Radiation therapy	Yes		97	14					85
	No		13	138					
Chemotherapy	Yes				85	30			81
	No				5	139			
Hormone therapy	Yes						95	12	76
	No						32	123	

Yes: information present; no: information absent.

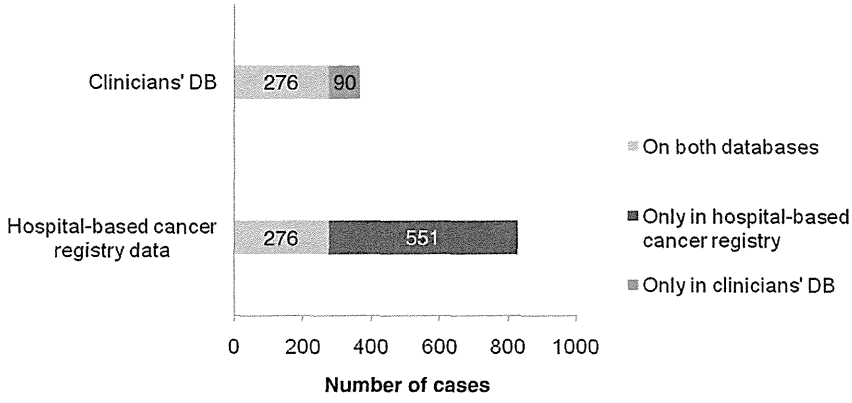

Figure 1 Comparison of subjects from the hospital-based cancer registry and clinicians' database (DB) in 2004.

clinicians' DB documented 366 cases who underwent breast cancer surgery in 2004. Among these, 276 cases were found in both DBs, 551 cases were registered only in the hospital-based cancer registry, and 90 cases were found only in the clinicians' DB (Fig. 1).

Among the 90 cases registered only in the clinicians' DB, the medical record was not available for one case. The other 89 cases were not in the hospital-based registry because they were diagnosed with breast cancer before 2004 and presented for repeat surgery in 2004.

In comparison, 551 cases were found only in the hospital-based cancer registry, among whom 85 later received surgery in 2005. Reasons for why these cases were not found in the clinicians' DB are detailed in Fig. 2.

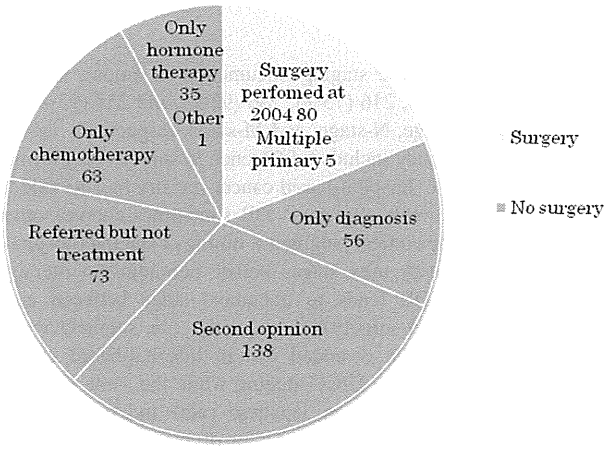

Figure 2 *Description of 551 cases only in the hospital-based cancer registry.*

Data concordance across overlapping cases

Treatment modality

Among 276 surgically treated patients, the date of surgery matched perfectly across the two DBs. Concordance rates of the presence of adjuvant therapies between the two DBs were also analysed (Table 2). Documentation on administration of radiation therapy was concordant in 235 cases (85%), chemotherapy in 224 (81%), and hormone therapy in 218 (76%). Among discrepant cases, the number of cases documented with receiving radiation therapy only in the hospital-based cancer registry (14) was similar to the number found only in the clinicians' DB (13). However, chemotherapy was logged more frequently in the hospital-based cancer registry (30 vs. 5) and hormone therapy was documented more frequently in the clinicians' DB (32 vs. 12).

Confirmation using the medical record revealed that reasons for the discordance included timing of registration, registration

Table 3 Reasons for discordance in adjuvant therapy between hospital-based cancer registry and clinicians' database

	Reason		
Adjuvant therapy	Timing of registration	Registration criteria	Human error
Radiation therapy			
14 (HD – yes, CD – no)	6 (43%)	0	8 (57%)
13 (HD – no, CD – yes)	2 (15%)	4 (31%)	7 (54%)
Chemotherapy			
30 (HD – yes, CD – no)	2 (7%)	3 (10%)	25 (83%)
5 (HD – no, CD – yes)	1 (20%)	3 (60%)	1 (20%)
Hormone therapy			
12 (HD – yes, CD – no)	3 (25%)	1 (8%)	8 (67%)
32 (HD – no, CD – yes)	17 (53%)	7 (22%)	8 (25%)

HD, hospital-based cancer registry database; CD, clinicians' database.

criteria, and human error (Table 3). For radiation therapy, the most frequent reasons for discrepancy, for both cases only in the hospital-based registry and only in the clinicians' DB were human errors (15 of 27 discrepant cases, 56%). For chemotherapy, the major reason for case only in the hospital-based cancer registry was human errors (25 cases, 83%), while the reason for case only in the clinicians' DB was most frequently different registration criteria (i.e. clinicians' DB register all treatments provided, three cases, 60%). For hormone therapy, human error again accounted for a majority of cases that were only in the hospital-based cancer registry (eight cases, 67%), while timing of registration accounted for cases being only in the clinicians' DB (17 cases, 53%).

Staging

Concordance in disease staging documentation among the 276 cases was 200 (72%), 216 (75%), 256 (93%), and 257 (93%) for clinical stage, T-stage, N-stage, and M-stage, respectively. Major causes for discrepancy included difference in sources of information for staging (i.e. hospital-based cancer registry has the rule to base on imaging, while clinicians' DB sometimes chooses other source based on the clinical judgment), timing of staging (hospital-based cancer registry uses stages before neo-adjuvant therapy, while clinicians' DB tends to document stage between neo-adjuvant therapy and surgery), staging rules (i.e. supraclavicular lymph-node metastasis is coded M0 in hospital-based cancer registry according to the UICC staging while the same situation is classified as M1a-stage in Japanese rule) and human error (Table 4). The most frequent reasons for disagreement are source of information for T-stage (17 cases, 42%), human error for N-stage (10 cases, 67%), and staging rule for M-stage (four cases, 67%).

Pathology

Pathohistology was concordant between the two DBs in 239 (87%) cases (Table 5). The major reason for discrepancy lies in the different timings of pathological reports used for staging (15 cases, 43%) between the two data sets. When neo-adjuvant therapy was

Table 4 Comparison of staging between hospital-based cancer registry and clinicians' database and reasons for differences

		The reason for disagreement			
	Concordance rate	Source of information	Timing of staging	Staging criteria	Human error
Stage	200 (72%)				
T-stage	216 (78%)	17 (42%)	7 (28%)		16 (40%)
N-stage	256 (93%)		5 (33%)		10 (67%)
M-stage	257 (93%)			4 (67%)	2 (33%)

Table 5 Comparison of pathology between hospital-based cancer registry and clinicians' database

	Clinicians' database				
Hospital-based registry	Invasive	Non-invasive	Paget's disease	Missing	Total
Invasive	235	32	0	2	269
Non-invasive	3	3	0	0	6
Paget's disease	0	0	1	0	1
Total	238	35	1	2	276

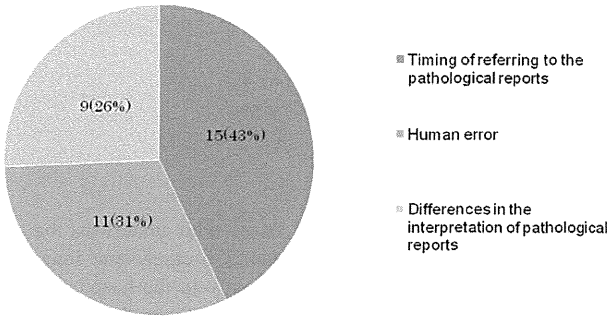

Figure 3 Major reasons for discrepancy in pathologies.

administered, the hospital-based cancer registry refers to pathological reports before neo-adjuvant therapy, while the clinicians' DB refers to pathological reports after neo-adjuvant therapy. In nine cases (26%), differences in the interpretation of pathological reports existed. For example, intraductal apocrine carcinoma is recorded as apocrine carcinoma in the hospital-based cancer registry but as non-invasive ductal carcinoma in the clinicians' DB. Eleven cases (31%) differed in the records as a result of human error (Fig. 3).

Discussion

This study revealed a moderate rate of concordance between hospital-based cancer registry data and the clinicians' DB for breast cancer. Differences in data for the same cases can be attributed to different registration timing, varying information sources, and human errors.

When differences in registered subjects are considered, it should be noted that the target subject differs between the hospital-based cancer registry and the clinicians' DB. While the former documents all diagnosed cancer patients seen at the NCCH, the latter focuses on patients who underwent surgery in the Division of Surgery. Capturing all cases is an important role of the hospital-based cancer registry as it supplies data to the population-based cancer registry. Therefore, more emphasis is given to finding all cases than to collecting detailed information on specific cancers, compared to the clinicians' DB. On the other hand, clinicians' DB has more emphasis on recording clinically detailed information. While the sample is limited to the patients in the Division, the DB has more than twice the items than the hospital-based cancer registry.

Data discrepancies were examined in the 276 cases contained in both data sets. The date of surgery matched perfectly, but substantial discordance was found in the administration of radiation therapy, chemotherapy, and hormone therapy. As the hospital-based cancer registry only documents initial therapy, adjuvant therapy not initially planned but added later based on surgical or pathological findings (i.e. those not initially planned) are not registered. This resulted in narrower coverage of information in the hospital-based cancer registry compared to that in the clinicians' DB, which contains all treatment provided in the facility. The timing of data entry is also different; while the hospital-based cancer registry waits 4 to 6 months after diagnosis to allow the initial therapy be completed [3], the clinicians' DB usually begins registering within 3 months of discharge from the NCCH, and updated when additional later on.

Care received in other hospitals may be underreported in both registry DBs [4,5]. Current cancer registry systems do not follow up patients who transfer care to other facilities. Similarly, the US National Cancer Institute study on Patterns of Care reported that the Surveillance, Epidemiology and End Results data on adjuvant therapy was also somewhat underreported [6–9]. To gain a comprehensive picture of patient care, a preferred approach may be integrating multiple data sources, including insurance claims.

Comparison of TNM stages also revealed the substantial discordance between the hospital-based cancer registry and the clinicians' DB, which may be attributed to different definition criteria. When neo-adjuvant therapy is provided, the hospital-based cancer registry documents the clinical stage prior to initiation of chemotherapy, while the clinicians' DB documents the cancer stage between chemotherapy and surgery. Furthermore, the preferred bases for staging (physical exams, ultrasonography, mammography) is precisely defined in the training of tumour registrars for the hospital-based cancer registry (i.e. use ultrasonography findings over other imaging studies and physical exams). In contrast, the clinicians' DB uses clinical judgment for staging rather than predefined rule. Similar mechanisms produced discordances in pathology documentation.

Given the differences between hospital-based cancer registry and site-specific cancer registry revealed in the study, a DB should be chosen according to the purpose of the analysis. The hospital-based cancer registry DB provides a large amount of detail on pathological types with ICD-O-3 coding, and covers both medical and surgical cases but lacks information specific to breast cancer, such as surgical method (breast conserving vs. mastectomy) and hormone receptor status. In contrast, the clinicians' DB provides detailed clinical information, but only contains surgical cases. Care must be taken when interpreting clinical stages with neo-adjuvant therapy because the clinicians' DB may document the pre-surgery staging as the clinical stage. It may be more appropriate to use the hospital-based cancer registry to analyse medical aspects of care or detailed pathology across cancers. However, surgery-related research questions appear to be better served by the clinicians' DB.

Our study has several limitations. First, all overlapping cases were proved to be surgical cases. If the clinicians' DB starts collecting data on medical cases, new sources of discrepancy may arise and warrant examination. Second, we only studied patients who were diagnosed with breast cancer in a highly specialized cancer hospital with many tumour registrars and breast surgeons, which may not be generalizable to other facilities. Our level of concordance may be overestimated in comparison to average Japanese cancer hospitals. Third, this study focused on patients diagnosed in 2004. Registry items and manuals are updated frequently. Also, the ability of tumour registrars may have improved. Progressive changes in the accuracy of DBs warrant evaluation.

In conclusion, our study found that data were generally accurate in both registries. However, important differences in the scope of registry, documented therapies, and timing of registration were highlighted, which may affect the results of research analyses. These data sets must be used with attention to the definition of collected items. As both data sets have characteristics unique to their purposes, integration of these two systems will require cautious standardization of items with collaboration from both sides.

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Conflict of interest

None to declare.

References

1. Japanese Association of Cancer Registries (2007) Handbook on Population-Based Cancer Registration in Japan, fifth revision, 2–3. Tokyo: Japanese Association of Cancer Registries.
2. Ministry of Health, Labour and Welfare (2006) *Cancer Control Act*. Available at: http://law.e-gov.go.jp/announce/H18HO098.html (last accessed 8 June 2010).
3. Center for Cancer Control and Information Services, National Cancer Center (2008) *Manual of Hospital-Based Cancer Registry*, 7–10.
4. Bickell, N. A. & Chassin, M. R. (2000) Determining the quality of breast cancer care: do tumor registries measure up? *Annals of Internal Medicine*, 132 (9), 705–710.
5. Warren, J. L. & Harlan, L. C. (2003) Can cancer registry data be used to study cancer treatment? *Medical Care*, 41 (9), 1003–1005.
6. Cress, R. D., Zaslavsky, A. M., West, D. W., Wolf, R. E., Felter, M. C. & Ayanian, J. Z. (2003) Completeness of information on adjuvant therapies for colorectal cancer in population-based cancer registries. *Medical Care*, 41 (9), 1006–1012.

7. Mariotto, A., Feuer, E. J., Harlan, L. C., Wun, L. M., Johnson, K. A. & Abrams, J. (2002) Trends in use of adjuvant multi-agent chemotherapy and tamoxifen for breast cancer in the United States: 1975–1999. *Journal of the National Cancer Institute*, 94 (21), 1626–1634.
8. Harlan, L. C., Clegg, L. X. & Warren, J. L. (2003) Chemotherapy in women with breast cancer. *Annals of Internal Medicine*, 139, 868.
9. Du, X. L., Key, C. R., Dickie, L., Darling, R., Delclos, G. L., Waller, K. & Zhang, D. (2006) Information on chemotherapy and hormone therapy from tumor registry had moderate agreement with chart reviews. *Journal of Clinical Epidemiology*, 59 (1), 53–60.

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Sex differences in the change in health-related quality of life associated with low back pain

Rei Ono · Takahiro Higashi · Osamu Takahashi · Yasuharu Tokuda · Takuro Shimbo · Hiroyoshi Endo · Shigeaki Hinohara · Tsuguya Fukui · Shunichi Fukuhara

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Abstract
Purpose To examine the sex differences in the impact of low back pain (LBP) on health-related quality of life among community-dwelling persons from a nationwide sample.
Methods Our analysis enrolled 2,358 participants from among 3,477 randomly selected subjects in Japan. The cumulative days each individual experienced LBP were prospectively measured over 1 month. The Physical Component Summary (PCS) and Mental Component Summary (MCS) in the Short Form 8-item Health Survey were evaluated before and after the study period. Sex differences in the impact of the cumulative number of LBP days on PCS and MCS scores were evaluated using linear regression analysis.
Results Among the 2,170 participants with complete data, the prevalence of LBP in women (32%) was higher than that in men (25%) during the study period. One-day increases in LBP days were associated with greater decreases in PCS scores among men than among women (−0.72 vs. −0.29, sex difference $P < 0.001$). In contrast, no relationship was noted between the number of LBP days and the change in MCS score for either sex after adjustment.
Conclusions Although a greater incidence of LBP was noted in women, health-related quality of life was more seriously affected in men with the same number of days with LBP in the month.

Keywords Low back pain · Sex differences · SF-8 · PCS · MCS

Abbreviations

LBP	Low back pain
HRQOL	Health-related quality of life
HDS	Health Diary Study
SF-8	Medical Outcome Study Short Form 8-item Health Survey

R. Ono
Department of Community Health Sciences, Kobe University Graduate School of Health Sciences, 4-7-18 Tomogoka, Suma-ku, Kobe, Hyogo 654-0142, Japan

R. Ono (✉) · S. Fukuhara
Department of Epidemiology and Health Care Research, Graduate School of Medicine and Public Health, Kyoto University, Yoshida-Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan
e-mail: ono@phoenix.kobe-u.ac.jp

T. Higashi
Department of Public Health/Health Policy, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

O. Takahashi
Department of Internal Medicine, St. Luke's International Hospital, 9-1 Akashi-cho, Chuo-ku, Tokyo 104-8560, Japan

Y. Tokuda
Institute of Clinical Medicine, Graduate School of Comprehensive Human Sciences, University of Tsukuba, 1-1-1 Tennoudai, Tsukuba-shi, Ibaraki 305-8575, Japan

T. Shimbo
Research Institute, International Medical Center of Japan, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan

H. Endo
Department of International Affairs and Tropical Medicine, Tokyo Women's Medical University School of Medicine, 8-1 Kawata-cho, Shinjuku-ku, Tokyo 162-8666, Japan

S. Hinohara · T. Fukui
St. Luke's Life Science Institute, St. Luke's International Hospital, 10-1 Akashi-cho, Chuo-ku, Tokyo 104-0044, Japan

PCS Physical health component summary
MCS Mental health component summary
LOWESS Locally weighted scatter plot smoothing

Introduction

An important goal of healthcare is prolonging life while maintaining its quality. Although recent decades have seen an increase in the prevalence of chronic diseases, evaluation of the status of patients suffering from such conditions remains insufficient, in part due to the insensitivity of traditional outcome measures, such as mortality and morbidity. Among various proposed solutions, health-related quality of life (HRQOL) has recently gained recognition as a more sensitive, and thus more suitable, measure of chronic care outcome [1, 2].

Low back pain (LBP) is a major public health concern; there is a high prevalence of LBP in the general population, which creates an economic burden on society through increased utilization of health services [3–5] and, on a more individual level, causes poor physical health overall [6]. An analysis of eight datasets involving over 15,000 patients showed that the impact of musculoskeletal conditions on physical health in HRQOL was similar to or greater than that of other common chronic conditions, including cardiovascular conditions, cerebrovascular/neurological conditions, and visual impairment [1].

Researchers have recently reported sex differences in various aspects of LBP. Studies have shown that the prevalence of LBP is higher in women than in men, and women with LBP are more likely to seek care and to take sick leave than men [7–10]. Biological studies exploring the reasons for these phenomena have found that women tend to have lower pain thresholds and tolerance nociceptive stimuli than men [11, 12]. In contrast, some psychological studies have found men to have a greater increase in negative mood than women when exposed to the same degree of pain [13, 14]. These inconsistent findings make the overall influence of LBP on HRQOL uncertain.

Several studies have found that gender is related to HRQOL in subjects with LBP. Generally, these studies show that women with LBP have worse physical health scores than men with LBP [15]. Bingefors et al. [16] further examined the sex differences in the eight components of Short Form 36 and reported that women had worse physical function scores than men, while men tended to report worse in bodily pain and general health scores than women. Due to their cross-sectional design, however, these studies do not reveal information concerning the sex differences in the impact of LBP on HRQOL. Using the nationwide data of the Health Diary Study, in which the participants documented their daily health events and symptoms, we investigated the sex differences in HRQOL changes in response to LBP.

Materials and methods

Study sample

We used data obtained from the Health Diary Study (HDS), which aims to describe the frequency of health-related events, symptoms, and care-seeking behaviors in a nationwide sample of the Japanese population [17]. Study participants kept a health diary for 1 month during which they documented all health symptoms and related healthcare use every day between October 1 and 31, 2003, and completed pre- and post-diary questionnaires.

The HDS study was designed to represent the Japanese population based on a panel of 210,000 households registered with Japan Statistics & Research Co., Ltd. The sample process involved two steps: selecting persons willing to participate and then resampling the selected persons to represent the Japanese population. In the first step, the whole registered panel was stratified by residential area size (metropolitan areas, cities with 100,000 or more residents, cities under 100,000 residents, and rural areas), and a total of 5,387 households were randomly selected from these strata and contacted to assess their willingness to participate in the study. Of the 1,857 households that agreed to participate in the study, 1,464 households containing 3,852 individuals were resampled to attain a sample population structure representing the general Japanese population. By the end of the study, 3,477 participants (87.8%) from 1,286 households had completed the health diary and both pre- and post-diary questionnaires. Because this study focused on HRQOL associated with LBP, we limited our sample to persons aged between 18 and 75, for whom the HRQOL scale included in the study was designed [18]. We also excluded persons who were hospitalized during the survey period. The final sample included 2,358 individuals. The HDS protocol was approved by the Research Ethics Committee of the Kyoto University Graduate School of Medicine.

Variables

Cumulative number of LBP days

The cumulative number of LBP days was defined as the total number of days during the 1-month study period in which a participant documented in his or her diary "pain" or any other unusual feeling in either the back or lumbar region. The number of LBP days ranged from 0 to 31.

HRQOL

HRQOL was assessed using the Japanese version of the Medical Outcome Study Short Form 8-item Health Survey (SF-8), which is the short version of the SF-36 implemented through a self-administered survey. The SF-8 consists of eight items that represent the eight domains of the SF-36: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health [18, 19]. Using the differential weights assigned to each item, the SF-8 produces two summary scores: a physical health component summary (PCS) score and a mental health component summary (MCS) score. These scores were standardized based on the Japanese population in 2002. A score of 50 represented the mean for the Japanese general population, and a score of 10 was one standard deviation; lower scores indicate poorer HRQOL.

Statistical analysis

Differences in the baseline characteristics between men and women were examined using an unpaired t test and a χ^2 test. To examine the impact of the number of LBP days during the 1-month study period on HRQOL, we calculated the changes in PCS and MCS scores from the baseline (PCS_c and MCS_c, respectively) by subtracting the baseline SF-8 scores from the scores calculated after the 1-month study period. Negative values indicated a decline in HRQOL, while positive values indicated an increase.

We examined the relationship between the cumulative number of LBP days during the 1-month study period and differences in the changes in PCS and MCS scores between sexes using linear regression models. Before using linear regression models, we examined the linear relationship between PCS_c and MCS_c scores and the cumulative number of LBP days using a locally weighted scatter plot smoothing (LOWESS) curve, a technique for smoothing scattered values by fitting a weighted least-squares line into moving bands using nonparametric regression [20], and conducted linear regression analyses on the portion where linearity holds visually on the curve. We then examined the differences between men and women using the interaction terms of sex and cumulative number of LBP days in the regression models. The adjusted model included age, the number of baseline comorbidities (0, 1, ≥2), annual household income (<3,000,000 yen, 3,000,000–4,999,999 yen, 5,000,000–6,999,999 yen, 7,000,000–9,999,999 yen, 10,000,000–11,999,999 yen, and ≥12,000,000 yen), employment status (yes or no, with "yes" indicating a full-time or part-time job and "no" for any other response), and baseline PCS or MCS score as covariates [15, 16, 21]. We calculated individual comorbidities by counting the number of the following diseases that the person had: hypertension, diabetes mellitus, cerebrovascular disease, cardiovascular disease, lung disease, gastrointestinal disease, urinary disease, musculoskeletal disease, skin disease, mental disease, gynecological disease, cancer, and other diseases. All statistical analyses were conducted using Stata version 11.2 (Stata Corporation LP, College Station, TX, USA). An alpha level of 0.05 was set as the threshold to determine the statistical significance.

Results

Of the 2,358 subjects participating in the HDS, 8.0% ($n = 188$) were excluded due to missing annual household income data or an incomplete SF-8 questionnaire, leaving 2,170 subjects for the analysis. The excluded sample was, on average, older than the analysis sample (49.9 years old vs. 44.5 years old, $P < 0.01$) and contained a higher proportion of women (61.2% vs. 54.5%, $P = 0.08$).

Subject characteristics are described in Table 1. Women had lower scores than men for household income, employment status, baseline PCS, and baseline MCS. During the study period, 28.4% ($n = 617$) of the total sample experienced LBP at least once during the study period and were thus included in analysis. LBP was reported more frequently by women ($n = 373$, 31.5%) than by men ($n = 244$, 24.7%, $P < 0.01$). The average number of cumulative LBP days was 1.7 (SD: 4.8) for women and 1.3 (SD: 4.3) for men ($P = 0.04$). The average change in PCS and MCS scores was −1.1 (SD: 6.7) and 0.8 (SD: 6.7), respectively. Approximately one-third of the sample had more than one disease, and the most common baseline comorbidities were hypertension and musculoskeletal diseases.

The LOWESS curve between the cumulative number of LBP days and the changes in SF-8 revealed a change in the curve at approximately 15 days into the study period (Fig. 1). For men, the average change in PCS decreased linearly with the increasing cumulative number of LBP days. However, the scores in men experiencing LBP for approximately 15 days or more tended to increase as the number of days with LBP increased (Fig. 1a). For women, the average change in PCS was flat throughout the study period (Fig. 1b). In contrast, the MCS_c among men with less than 16 LBP days appeared to increase slightly as the number of LBP days increased, while the MCS_c among men with 16 or more cumulative LBP days decreased as the number of LBP days increased (Fig. 1c); no such relationship was observed in women (Fig. 1d). Because linearity was not visually confirmed in 58 subjects who had LBP for 16 or more days, these individuals were excluded from the analysis with regression models.

Table 1 Subject characteristics

	Total (n = 2,170)	Women (n = 1,183)	Men (n = 987)	P value
Age in years, mean (SD)	44.5 (15.2)	44.8 (15.5)	44.3 (14.7)	0.43
Cumulative days with LBP, mean (SD)	1.5 (4.6)	1.7 (4.8)	1.3 (4.3)	0.04
Comorbidities, number (%)				
0	1,518 (70.0)	806 (68.1)	712 (72.4)	0.11
1	442 (20.4)	252 (21.3)	190 (19.3)	
2+	210 (9.7)	125 (10.6)	85 (8.6)	
Annual household income, number (%)				
<3,000,000 yen	353 (16.3)	226 (19.1)	127 (12.9)	<0.01
3,000,000–4,999,999 yen	641 (29.5)	350 (29.6)	291 (29.5)	
5,000,000–6,999,999 yen	515 (23.7)	260 (22.0)	255 (25.8)	
7,000,000–9,999,999 yen	420 (19.4)	223 (18.9)	197 (20.0)	
10,000,000–11,999,999 yen	162 (7.5)	82 (6.9)	80 (8.1)	
≥12,000,000 yen	79 (3.6)	42 (3.6)	37 (3.8)	
Employment status, number (%)				
No	762 (35.1)	590 (49.9)	172 (17.4)	<0.01
Yes	1,408 (64.9)	593 (50.1)	815 (82.6)	
SF-8 (baseline), mean (SD)				
PCS	49.2 (6.5)	48.9 (6.6)	49.7 (6.4)	<0.01
MCS	48.0 (6.7)	47.7 (6.6)	48.4 (6.7)	0.01
PCS_c, mean (SD)	−1.1 (6.7)	−1.0 (6.6)	−1.3 (7.0)	0.32
MCS_c, mean (SD)	0.8 (6.7)	0.8 (6.6)	0.8 (6.8)	0.85

SD standard deviation, *PCS* physical component summary, *MCS* mental component summary, *LBP* low back pain

Table 2 shows the changes in PCS and MCS associated with a 1-day increase in the number of LBP days, as represented by the coefficients in the respective models with PCS_c and MCS_c in the unadjusted and adjusted models. In the unadjusted regression model for PCS_c, an increase in one LBP day was associated with a 0.51-point decrease in men's PCS scores ($P < 0.001$) versus a 0.04-point decrease in women's scores ($P = 0.70$), which is a statistically significant difference ($P < 0.001$). After adjusting for age, number of baseline comorbidities, annual household income, employment status, and baseline PCS score, an increase in one LBP day was associated with a 0.72-point decrease per day in men's scores ($P < 0.001$) versus a 0.29-point decrease in women's scores ($P < 0.001$), which is also statistically significant ($P < 0.001$).

In the unadjusted regression model for MCS_c, an increase in one LBP day was associated with a 0.27-point increase per day in MCS_c among men ($P = 0.008$) versus a 0.01-point decrease among women ($P = 0.87$), which is a statistically significant difference ($P = 0.03$). After adjusting for the above-mentioned covariates, an increase in one LBP day was associated with a 0.17-point increase per day in MCS_c among men ($P = 0.05$) versus a 0.02-point decrease among women ($P = 0.76$). However, this difference was not statistically significant ($P = 0.08$).

Discussion

In this study, we found that changes in HRQOL associated with an increased cumulative number of LBP days differed by gender. While PCS scores decreased more sharply in men than in women, the slope of change in MCS scores was not significantly different between both sexes after adjusting for age, the number of baseline comorbidities, annual household income, employment status, and baseline PCS/MCS scores. To our knowledge, this study is the first to prospectively examine the sex differences in the relationship between the number of LBP days and the change in HRQOL score. Our observation that men tend to suffer from more severe decreases in HRQOL than women with the same number of LBP days, which contrasts with previous findings, underscores the importance in accounting for the degree of LBP in examining sex difference in HRQOL.

Decreases in PCS scores noted in the present study were sharper in men than in women, indicating that men were more affected by LBP than women with respect to the physical domain of HRQOL. However, this finding appears to contradict previous work, such as those noted in the cross-sectional study by Salaffi et al. [15], which showed that women with LBP experienced worse physical health

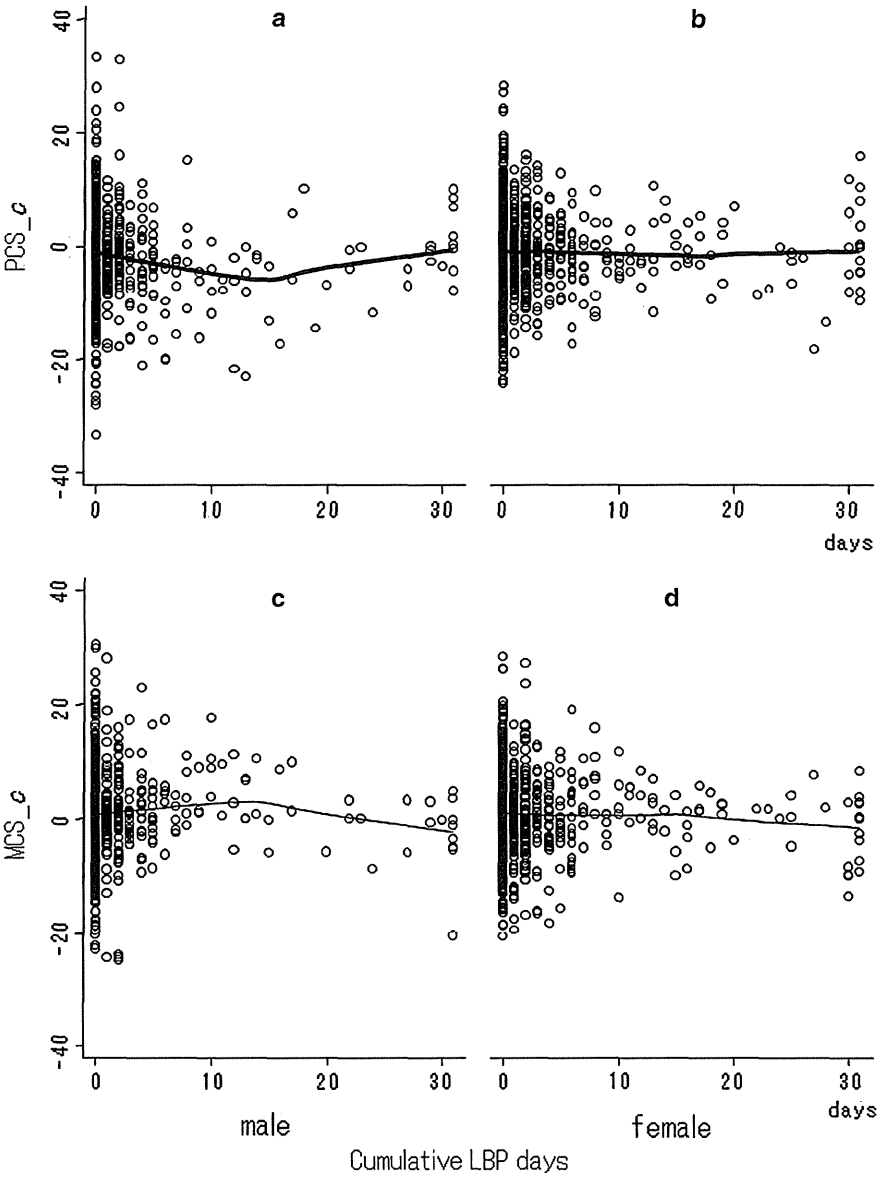

Fig. 1 Cumulative number of LBP days and differences in SF-8 summary score changes by gender. **a** Relationship between the cumulative number of LBP days and the change in PCS score in men. **b** Relationship between the cumulative number of LBP days and the change in PCS score in women. **c** Relationship between the cumulative number of LBP days and the change in MCS score in men. **d** Relationship between the cumulative number of LBP days and the change in MCS score in women

Table 2 Unadjusted and adjusted models of PCS_*c* and MCS_*c* from the cumulative number of LBP days in women and men

	Women			Men			Interaction
	Coefficient	95% CI		Coefficient	95% CI		
		Lower	Upper		Lower	Upper	
PCS							
Unadjusted	−0.04	−0.21	0.14	−0.51	−0.71	−0.31	<0.01
Adjusted	−0.29	−0.43	−0.14	−0.72	−0.89	−0.55	<0.01
MCS							
Unadjusted	−0.01	−0.19	0.16	0.27	0.07	0.47	0.03
Adjusted	−0.02	−0.16	0.12	0.17	0.004	0.33	0.08

PCS physical component summary, *MCS* mental component summary, *LBP* lower back pain, *CI* confidence interval

than men of similar socio-demographic levels and with similar comorbidities. This difference may be due to the fact that we counted the number of days with LBP, whereas Salaffi's study examined only the presence or absence of LBP. Interestingly, when we reanalyzed our data using only the presence or absence of LBP during the study period and ignoring LBP days, as was performed in Salaffi's study, we observed no sex differences in PCS (data not shown). These findings indicate the importance of considering the frequency of LBP when analyzing the effect of LBP on HRQOL.

Our results regarding MCS changes were inconclusive given their slight increase in conjunction with LBP days among men and the nonsignificant sex differences observed. Previous studies reported a tendency for LBP to affect physical health rather than the psychological dimensions of HRQOL [16]. Other studies that examined the recovery of HRQOL after surgery for back, knee, and hip problems have shown that while patients' physical health improved relatively quickly, mental health recovered over a longer period of time [22, 23]. Therefore, more dramatic changes in MCS may have appeared after the completion of our study.

Our finding that men experience a sharper decrease in HRQOL than women who report the same number of days with LBP indicates that a given amount of pain affects the HRQOL of men more seriously than that of women. We hypothesize that psychosocial factors associated with LBP, such as mood disturbance and anxiety, may play a role in this phenomenon. Affleck et al. [13] reported that men were more likely than women to experience an increase in negative mood the day after a painful day. Similarly, Keefe et al. [14] reported that men were more likely than women to experience an increase in negative mood and a decrease in positive mood the morning after an evening of increased pain. Edwards et al. [24] reported that anxiety was associated with increased pain severity and interference by pain in male patients but found no association in female patients. Robinson et al. [25] reported significantly stronger relationships between pain-related anxiety and LBP in men than in women. Taken together, these previous findings suggest that men experience more anxiety and greater mood disturbance than women for the same number of days of LBP, in turn contributing to the reduced physical HRQOL. Although mental health scores as assessed in the present study did not appear to capture this temporary psychological change, future studies may further explore the mechanisms behind this sex difference.

Several limitations of the present study warrant mention. First, our sample was selected from people registered with a market research company, and many households refused to participate in the initial random sampling. Therefore, our sample population may differ in certain respects from the general population. Nevertheless, because most resampled households ultimately agreed to participate in the study, we feel that we were able to sufficiently maintain internal validity. Second, a number of variables known to be related to gender, such as educational attainment, were not controlled for. As such, the sex differences in these variables may have confounded our findings. Third, our analysis used data that were limited to pain frequency and lacked information on pain intensity, while both factors can influence HRQOL [26]. However, because pain intensity and frequency are positively related [27], we believe that our analysis of pain frequency can, to a certain degree, capture the level of pain intensity. Finally, as linearity in regression analyses did not visually hold for the small number of subjects with 16 or more cumulative number of LBP days, we excluded these subjects. Future studies may need to include responses from subjects who experience 16 or more days of LBP.

In conclusion, we identified sex differences in the relationship between the cumulative number of LBP days and physical, but not mental, health status. Although a greater prevalence of LBP was noted in women, quality of life was more seriously affected in men for the same number of days with LBP. These results underscore the complexity of the impact of LBP on HRQOL, and future studies in this area should, in particular, take into consideration duration of LBP and not simply its presence or absence while also accounting for sex differences.

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References

1. Sprangers, M. A., de Regt, E. B., Andries, F., van Agt, H. M., Bijl, R. V., de Boer, J. B., et al. (2000). Which chronic conditions are associated with better or poorer quality of life? *Journal of Clinical Epidemiology, 53*(9), 895–907.
2. Alonso, J., Ferrer, M., Gandek, B., Ware, J. E., Jr., Aaronson, N. K., Mosconi, P., et al. (2004). Health-related quality of life associated with chronic conditions in eight countries: results from the International Quality of Life Assessment (IQOLA) Project. *Quality of Life Research, 13*(2), 283–298.
3. Hart, L. G., Deyo, R. A., & Cherkin, D. C. (1995). Physician office visits for low back pain. *Spine, 20*(1), 11–19.
4. Walker, B. F., Muller, R., & Grant, W. D. (2003). Low back pain in Australian adults: The economic burden. *Asia-Pacific Journal of Public Health, 15*(2), 79–87.
5. Maniadakis, N., & Gray, A. (2000). The economic burden of back pain in the UK. *Pain, 84*(1), 95–103.
6. Fanuele, J. C., Birkmeyer, N. J., Abdu, W. A., Tosteson, T. D., & Weinstein, J. N. (2000). The impact of spinal problems on the health status of patients: Have we underestimated the effect? *Spine, 25*(12), 1509–1514.
7. Veerapen, K., Wigley, R. D., & Valkenburg, H. (2007). Musculoskeletal pain in Malaysia: A COPCORD survey. *Journal of Rheumatology, 34*(1), 207–213.
8. Chenot, J. F., Becker, A., Leonhardt, C., Keller, S., Donner-Banzhoff, N., Hildebrandt, J., et al. (2008). Sex differences in

presentation, course, and management of low back pain in primary care. *Clinical Journal of Pain, 24*(7), 578–584.
9. Linton, S. J., Hellsing, A. L., & Halldén, K. (1998). A population-based study of spinal pain among 35–45-year-old individuals. Prevalence, sick leave, and health care use. *Spine, 23*(13), 1457–1463.
10. Müllersdorf, M., & Söderback, I. (2000). The actual state of the effects, treatment and incidence of disabling pain in a gender perspective—A Swedish study. *Disability and Rehabilitation, 22*(18), 840–854.
11. Wise, E. A., Price, D. D., Myers, C. D., Heft, M. W., & Robinson, M. E. (2002). Gender role expectations of pain: relationship to experimental pain perception. *Pain, 96*(3), 335–342.
12. Riley, J. L., 3rd, Robinson, M. E., Wise, E. A., Myers, C. D., & Fillingim, R. B. (1998). Sex differences in the perception of noxious experimental stimuli: A meta-analysis. *Pain, 74*(2–3), 181–187.
13. Affleck, G., Tennen, H., Keefe, F. J., Lefebvre, J. C., Kashikar-Zuck, S., Wright, K., et al. (1999). Everyday life with osteoarthritis or rheumatoid arthritis: Independent effects of disease and gender on daily pain, mood, and coping. *Pain, 83*(3), 601–609.
14. Keefe, F. J., Affleck, G., France, C. R., Emery, C. F., Waters, S., Caldwell, D. S., et al. (2004). Gender differences in pain, coping, and mood in individuals having osteoarthritic knee pain: A within-day analysis. *Pain, 110*(3), 571–577.
15. Salaffi, F., De Angelis, R., Stancati, A., Grassi, W., & MArche Pain Prevalence INvestigation Group (MAPPING) study. (2005). Health-related quality of life in multiple musculoskeletal conditions: a cross-sectional population based epidemiological study. II. The MAPPING study. *Clinical and Experimental Rheumatology, 23*(6), 829–839.
16. Bingefors, K., & Isacson, D. (2004). Epidemiology, co-morbidity, and impact on health-related quality of life of self-reported headache and musculoskeletal pain–a gender perspective. *European Journal of Pain, 8*(5), 435–450.
17. Fukui, T., Rhaman, M., Takahashi, O., Saito, M., Shinbo, T., Endo, H., et al. (2005). The ecology of medical care in Japan. *JMAJ, 48*, 163–167.
18. Fukuhara, S., & Suzukamo, Y. (2004). *SF-8 Japanese version manual*. Kyoto: NPO Health Medicine Evaluation Research Organization.
19. Ware, J. E., Kosinski, M., Dewey, J. E., & Gandek, B. (2001). *How to score and interpret single-item health status measures: A manual for users of the SF-8 health survey*. Lincoln, (RI): QualityMetric Incorporated.
20. Diggle, P. J., Heagerty, P., Liang, K. Y., & Zeger, S. L. (2002). Exploring longitudinal data. In P. J. Diggle, P. Heagerty, K. Y. Liang, & S. Zeger (Eds.), *Analysis of longitudinal data, 2nd edn* (pp. 33–53). Oxford: Oxford University Press.
21. Pereira, C. C., Palta, M., Mullahy, J., & Fryback, D. G. (2011). Race and preference-based health-related quality of life measures in the United States. *Quality of Life Research, 20*(6), 969–978.
22. Rampersaud, Y. R., Ravi, B., Lewis, S. J., Stas, V., Barron, R., Davey, R., et al. (2008). Assessment of health-related quality of life after surgical treatment of focal symptomatic spinal stenosis compared with osteoarthritis of the hip or knee. *The Spine Journal, 8*(2), 296–304.
23. Bachmeier, C. J., March, L. M., Cross, M. J., Lapsley, H. M., Tribe, K. L., Courtenay, B. G., et al. (2001). A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. *Osteoarthritis Cartilage, 9*(2), 137–146.
24. Edwards, R., Augustson, E. M., & Fillingim, R. (2000). Sex-specific effects of pain-related anxiety on adjustment to chronic pain. *Clinical Journal of Pain, 16*(1), 46–53.
25. Robinson, M. E., Dannecker, E. A., George, S. Z., Otis, J., Atchison, J. W., & Fillingim, R. B. (2005). Sex differences in the associations among psychological factors and pain report: A novel psychophysical study of patients with chronic low back pain. *J Pain, 6*(7), 463–470.
26. Skevington, S. M. (1998). Investigating the relationship between pain and discomfort and quality of life, using the WHOQOL. *Pain, 76*(3), 395–406.
27. Heymans, M. W., van Buuren, S., Knol, D. L., Anema, J. R., van Mechelen, W., & de Vet, H. C. (2010). The prognosis of chronic low back pain is determined by changes in pain and disability in the initial period. *The Spine Journal, 10*(10), 847–856.