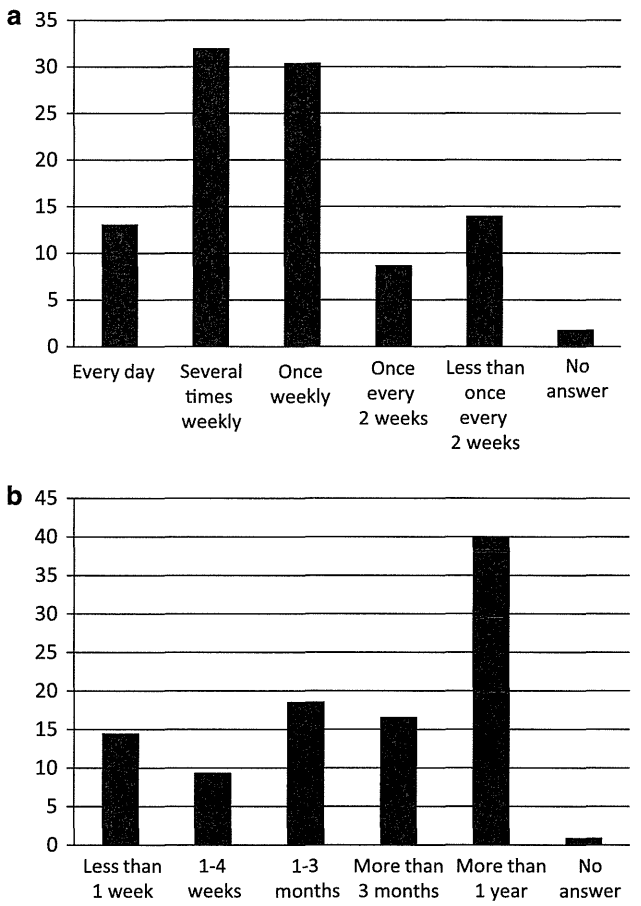


**Fig. 3** Frequency and duration of treatment for persistent chronic pain: treatment **a** frequency and **b** duration

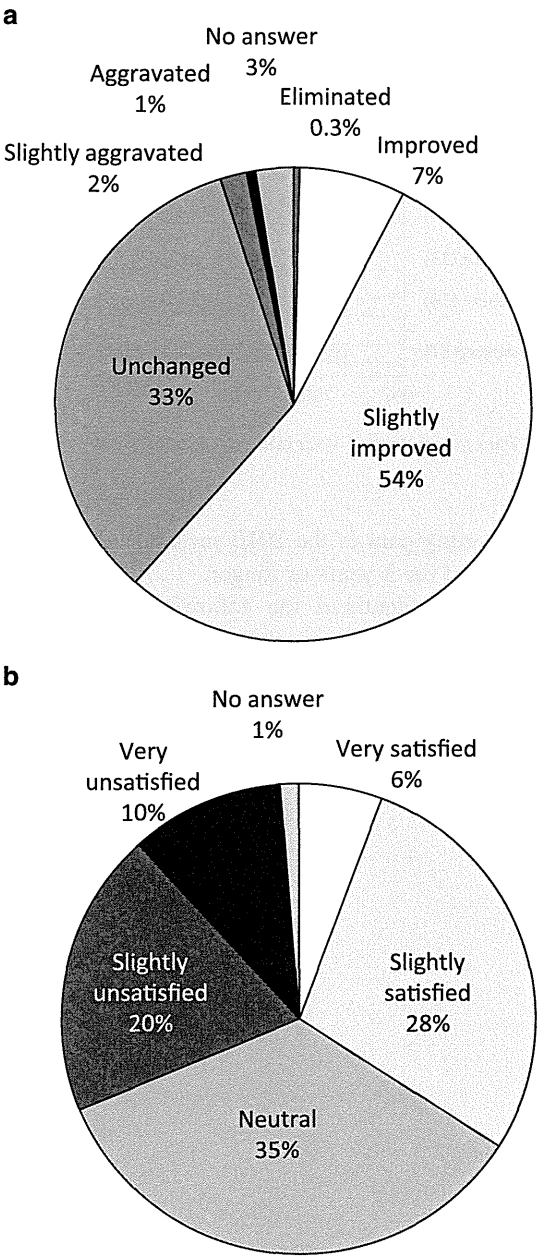


**Fig. 4** Initial treatment at a medical facility for chronic pain: **a** effectiveness and **b** patients' degree of satisfaction

were, "I thought I could take care of it myself" (24 %) and, "I didn't think treatment was necessary" (16 %), indicating inadequate recognition or knowledge of chronic pain. Another 24 % chose, "I didn't expect treatment to be effective," indicating a low expectation for successful treatment for chronic pain (Fig. 8). Approximately 40 % of the respondents with untreated chronic pain coped by using non-prescription drugs, health foods, or supplements, or tried to improve their diet or lifestyle.

## Discussion

### New development of chronic musculoskeletal pain

The incidence rate of new chronic musculoskeletal pain among those who did not have chronic pain the previous year was 11.1 %, and in actuality, 1 in 10 persons met the criteria for newly developed chronic pain. On the other hand, the prevalence rate of chronic pain calculated the previous fiscal year was 15.4 %, indicating that much of the chronic pain that met the criteria at that time resolved relatively quickly. Prevalence is generally calculated as prevalence rate = incidence rate × duration of illness; when the corresponding figures were inserted into the equation, the duration of chronic pain was 1.4 years. In other words, according to this calculation, chronic pain resolves in about a year and a half on average. However, this should be interpreted with caution, since it means that the pain no longer meets the criterion for chronic pain after about a year and a half, not that the pain has completely resolved. In addition, caution is required because 48 % of

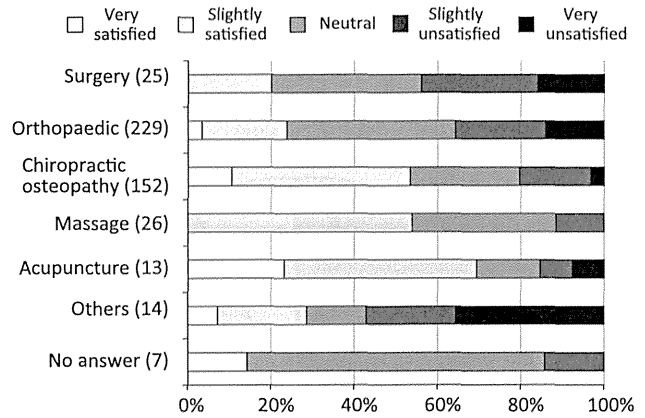


**Fig. 5** Patient satisfaction with initial treatment, by type of treatment facility

those reporting pain in the 2010 survey said that the pain had persisted for 3 years or longer.

This study identified the following risk factors for the new development of chronic pain: female gender, occupation (professional, managerial, clerical/specialist), a BMI ≥25, current use of alcohol, current use of cigarettes, and completing an education level of vocational school or higher. As many diseases are associated with low socioeconomic status [3], it is very interesting that chronic pain was instead associated with high socioeconomic status, including professional occupations, and higher levels of education. By occupation, managerial, professional, and technical work categories had the highest incidence. The lower back was the most frequently reported site of pain. Previous studies demonstrated that occupational factors, such as long periods of sedentary posture and psychological factors due to dissatisfaction with a work situation, a supervisor, or a dead-end job and boredom, appear to promote the development of new chronic pain [4, 5]. Furthermore, the recent studies demonstrated that the psychosocial factors play important roles in chronic musculoskeletal pain [6–8]. Because the limitation of the present study was that the psychosocial factors were not examined, further study should be performed to clarify the

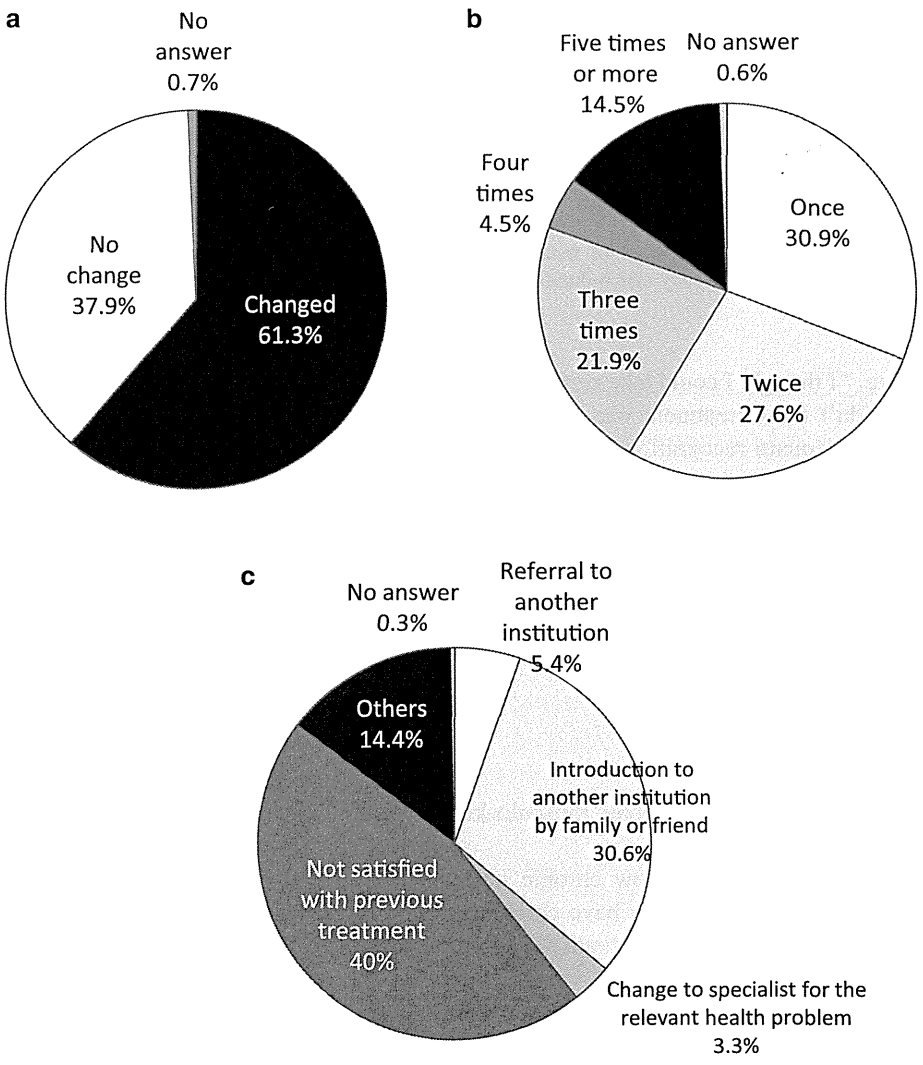


**Fig. 6** Circumstances of changes in treatment facility: **a** whether changed, **b** number of changes, and **c** reason for changing

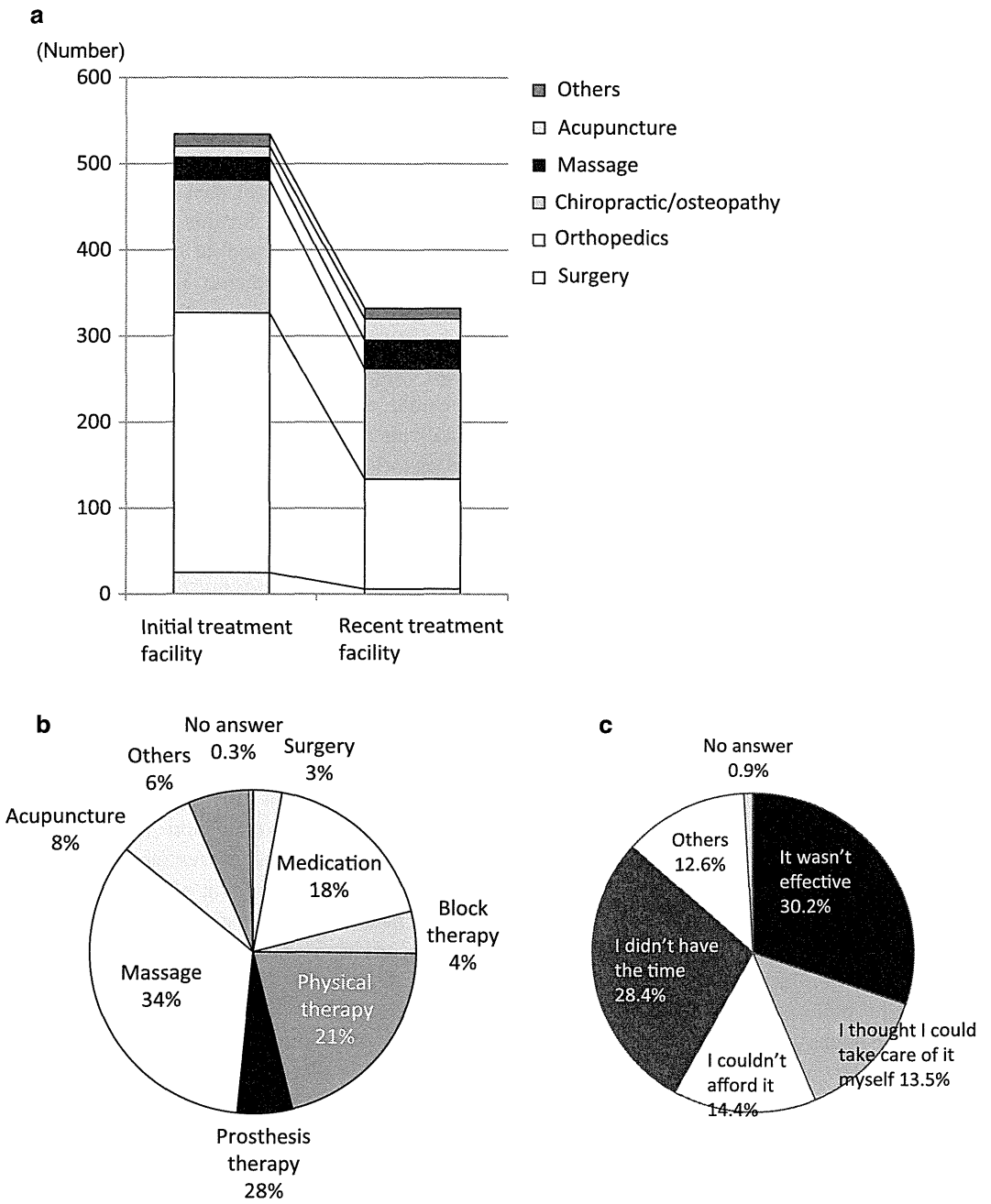


**Fig. 7** Details of changes in treatment facility: **a** initial and most-recent treatment facility, **b** type of most recent treatment, and **c** reason for discontinuing treatment

effects of these factors on the chronic musculoskeletal pain in the future. Taken together, consistent with the previous studies [9–12], the relationship between musculoskeletal pain and the identified factors such as female gender, high BMI and smoking may be explained in part by shared risk factors, both physical and psychosocial [13, 14]. The mechanism involved in the current identification of alcohol use as a risk factor for new development of chronic pain is unknown.

## Persistence of chronic musculoskeletal pain

The results showed that 45 % of the respondents who reported chronic pain in 2010 also reported chronic pain in 2011. It is possible that people who suffered from chronic pain through the entire period were more inclined to reply to the second questionnaire; thus, we cannot rule out the possibility that 45 % is an overestimation, even though the reply rate was 85 %. Multivariate analysis did not find any

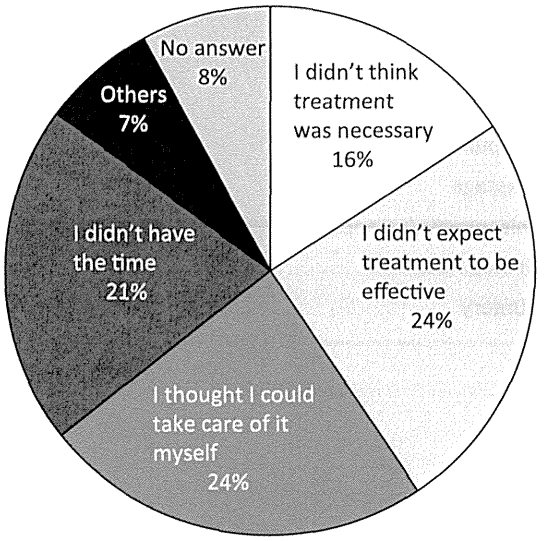


**Fig. 8** Reasons given for not seeking treatment for persistent chronic pain

associations between the persistence of chronic pain and basic attributes such as age and gender; the only associated factors were related to the pain itself. A pain severity VAS score of 7–8 was statistically significant. Although the odds ratio increased to 1.30 with the more severe pain reflected in VAS scores of 9–10, it did not reach statistical significance, perhaps because the sample size for this group was so small. The risk of chronic pain persisting a year later was twice as high among persons who had complained of constant pain compared to those who had reported a frequency of 2–3 times a week. The odds ratio for pain persistence was significantly higher for those who reported pain lasting 5 years or more. Based on these findings, those with constant, severe pain persisting 5 years or more appeared to be at the highest risk for the persistence of chronic pain 1 year later. These findings suggested that once the pathological condition of chronic musculoskeletal pain has been established, it could be quite difficult to relieve the chronic musculoskeletal pain. The risk of pain persisting was particularly high for those whose chief complaint was low back pain, compared to pain at other sites. Countermeasures to prevent chronic pain appear to be especially important for these high-risk populations.

## Problems in treating persons with persistent chronic pain and countermeasures

More than 8 out of 10 people with persistent chronic pain had a history of treatment, and while 3 of the 8 were still receiving treatment at the time of the survey, the other 5 had discontinued treatment despite the persistence of pain. Of those who had been treated for pain, 60 % were initially treated at a medical facility; these respondents reported a low degree of satisfaction even though 75 % had received frequent (daily or several times a week) treatment, and 40 % had been treated long-term (a year or more). Of particular note, results by type of treatment provider showed that respondents were less satisfied with treatment received at medical facilities than with folk medicine treatment. We thought that differences in pain severity might be responsible for this finding, but the average VAS scores of those treated at medical facilities and those treated with folk medicine were 6.0 and 5.7, respectively, and this difference was not statistically significant. Other factors might include a tendency toward unrealistically high expectations of medical facilities, and less communication and physical contact in comparison with folk medicine methods. Additional surveys will be necessary in order to verify these factors.

More than 60 % of the respondents with persistent chronic pain had changed their treatment facility; of these, approximately 60 % had changed once or twice. Surprisingly, 15 % of the respondents with persistent chronic pain changed 5 or more times, engaging in so-called "doctor shopping". A review of the initial and most-recent treatment facilities showed that approximately half of those initially examined in an orthopaedics department changed treatment facilities, but no major change was seen in those initially examined for folk medicine treatment. The results by type of treatment also showed that the use of massage and acupuncture/moxibustion increased, accounting for 42 % of the most-recent treatment types reported. This is consistent with the finding of a low degree of satisfaction with treatment at medical facilities. The recent nationwide survey of chronic pain sufferers in Japan also demonstrated they did not have a high degree of satisfaction with medical treatment [15].

The most common reason given for changing treatment providers or discontinuing treatment was, "because the treatment was ineffective", which reflects the inadequate effectiveness of the current treatments for chronic musculoskeletal pain. Nociceptive pain, neuropathic pain, and psychogenic pain are intermingled in chronic musculoskeletal system pain, and neuropathic pain is involved in chronic low back pain in particular [16]. Without an adequate grasp of the roles these factors play in the pathology of pain, treatment may fail because it is not appropriate for the patient. Furthermore, the recent studies demonstrated that the psychosocial factors play important roles in chronic musculoskeletal pain [13, 14]. Because the limitation of the present study was that the psychosocial factors were not examined, further study should be performed to clarify the effects of these factors on the chronic musculoskeletal pain in the future.

Many people with persistent chronic pain discontinued treatment. Others did not seek treatment, giving reasons

such as not having time, thinking they could take care of it themselves, not thinking they needed treatment, and so on. The majority of the respondents who were not treated for pain reported using non-prescription drugs to cope with the pain. Thus, poor recognition of the seriousness of chronic pain appears to be a problem. It is reported that chronic musculoskeletal pain takes a toll on both mental and physical health, and strongly impacts daily and social life [2]. However, it cannot be said that this state of affairs has been adequately conveyed to the Japanese public. We orthopedists, who specialize in treating the musculoskeletal system, have before us the important task of finding ways to reliably convey the importance of treating chronic pain, to both patients and the general public, through public awareness campaigns.

**Acknowledgments** This study was conducted as a 2011 Ministry of Health, Labour and Welfare Health Labour Sciences Research Grant for Comprehensive Research on Disability Health and Welfare (Survey study of chronic musculoskeletal pain).

**Conflict of interest** The authors declare that they have no conflict of interest.



## References

1. Annual Statistical Report of National Health Conditions. 2010/2011, Health and welfare statistics association, pp 72–3 (in Japanese).
2. Nakamura M, Nishiwaki Y, Ushida T, Toyama Y. Prevalence and characteristics of chronic musculoskeletal pain in Japan. J Orthop Sci. 2011;16:424–32.
3. Marmot MG. Understanding social inequalities in health. Perspect Biol Med. 2003;46:S9–23.
4. Ehrlich GE. Low back pain. Bull World Health Organ. 2003;81:671–6.
5. Kopec JA, Sayre EC. Work-related psychosocial factors and chronic pain: a prospective cohort study in Canadian workers. J Occup Environ Med. 2004;46:1263–71.
6. Matsudaira K, Palmer KT, Reading I, Hirai M, Yoshimura N, Coggon D. Prevalence and correlates of regional pain and associated disability in Japanese workers. Occup Environ Med. 2011;68:191–6.
7. Palmer KT, Reading I, Calnan M, Linaker C, Coggon D. Does knee pain in the community behave like a regional pain syndrome? Prospective cohort study of incidence and persistence. Ann Rheum Dis. 2007;66:1190–4.
8. Palmer KT, Reading I, Linaker C, Calnan M, Coggon D. Population based cohort study of incident and persistent arm pain: role of mental health, self-rated health and health beliefs. Pain. 2008;136:30–7.
9. Dodet P, Perrot S, Auvergne L, Hajj A, Simoneau G, Decleves X, Poitou C, Oppert JM, Peoc'h K, Mouly S, Bergmann JF, Lloret-Linares C. Sensory impairment in obese patients? Sensitivity and pain detection thresholds for electrical stimulation after surgery-induced weight loss, and comparison with a nonobese population. Clin J Pain. 2013;29:43–9.
10. Shiri R, Solovieva S, Husgafvel-Pursiainen K, Taimela S, Saarikoski LA, Huupponen R, Viikari J, Raitakari OT, Viikari-Juntura E. The association between obesity and the prevalence of low back pain in young adults: The Cardiovascular Risk in Young Finns Study. Am J Epidemiol. 2008;167:1110–9.
11. Adamson J, Ebrahim S, Dieppe P, Hunt K. Prevalence and risk factors for joint pain among men and women in the West of Scotland Twenty-07 study. Ann Rheum Dis. 2006;65:520–4.
12. Hakim AJ, Cherkas LF, Grahame R, Spector TD, MacGregor AJ. The genetic epidemiology of joint hypermobility: a population study of female twins. Arthritis Rheum. 2004;50:2640–4.
13. Matsudaira K, Konishi H, Miyoshi K, Isomura T, Takeshita K, Hara N, Yamada K, Machida H. Potential risk factors for new onset of back pain disability in Japanese workers: findings from the Japan epidemiological research of occupation-related back pain study. Spine. 2012;37:1324–12331.
14. Coggon D, Ntani G, Palmer KT, Felli VE, Harari R, Barrero LH, Felknor SA, Gimeno D, Cattrell A, Vargas-Prada S, Bonzini M, Solidaki E, Merisalu E, Habib RR, Sadeghian F, Masood Kadir M, Warnakulasuriya SS, Matsudaira K, Nyantumbu B, Sim MR, Harcombe H, Cox K, Marziale MH, Sarquis LM, Harari F, Freire R, Harari N, Monroy MV, Quintana LA, Rojas M, Salazar Vega EJ, Harris EC, Serra C, Martinez JM, Delclos G, Benavides FG, Carugno M, Ferrario MM, Pesatori AC, Chatzi L, Bitsios P, Kogevinas M, Oha K, Sirk T, Sadeghian A, Peiris-John RJ, Sathiakumar N, Wickremasinghe AR, Yoshimura N, Kelsall HL, Hoe VC, Urquhart DM, Derrett S, McBride D, Herbison P, Gray A. Patterns of multisite pain and associations with risk factors. Pain. 2013;154:1769–77.
15. Yabuki S, Ushida T, Takeshita K, Saura R, Ogawa S, Katsumata A, Hatanaka S. A nationwide survey of chronic pain sufferers in Japan. Clin Orthop. 2012;47:127–34 (in Japanese).
16. Freynhagen R, Baron R, Tölle T, Stemmler E, Gockel U, Stevens M, Maier C. Screening of neuropathic pain components in patients with chronic back pain associated with nerve root compression: a prospective observational pilot study (MIPORT). Curr Med Res Opin. 2006;22:529–37.

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RESEARCH Open Access

# The review of innovative integration of *Kampo* medicine and Western medicine as personalized medicine at the first multidisciplinary pain center in Japan

Young-Chang P Arai*, Hiromichi Yasui, Hideya Isai, Takashi Kawai, Makoto Nishihara, Jun Sato, Tatsunori Ikemoto, Sinsuke Inoue and Takahiro Ushida

**Abstract**

**Background:** The Japanese medical system is unique because it is the only country in the world where Western medicine and traditional Japanese medicine including *Kampo* medicine, traditional Japanese herbal medicine, are used in our daily clinical practice. Pain is essentially an interactive psychophysiological behavior pattern. Thus, an interdisciplinary approach is often recommended in providing appropriate therapeutic care for the patients suffering from chronic and intractable pain. In addition, we have been prescribing Kampo medicines in combination with Western medicines as personalized medicine in order to treat patients with chronic pain at our pain center. The aim of our study was to conduct a survey on the current use and the effect of Kampo medicines in our multidisciplinary pain center.

**Methods:** Retrospective analysis was performed on 221 out of 487 patients suffering from chronic pain.

**Results:** The most frequent medical complaints for which Kampo medicines were prescribed were lower back/lower limb pain, neck/upper limb pain, various facial pains, headache/migraine, whiplash-associated disorder, and frozen shoulder. Kampo medicines were prescribed based on patient-centered Kampo diagnosis. Moreover, several Kampo medicines generally for the management of psychological symptoms were prescribed for about 70% of the patients. Pain improvement in the patients was categorized as follows: 26.3% with marked improvement, 12.7% with moderate improvement, 38.9% with some improvement, and 19.9% with no improvement.

**Conclusions:** Two thirds of the chronic pain patients with the use of Kampo medicines combined with Western medicine experienced further pain improvements.

**Keywords:** *Kampo* medicine, Multidisciplinary pain center, Chronic and intractable pain

## Overview

Traditional, complementary, and alternative therapies are widely used and researched in the USA and Europe [1,2]. One of the underlying reasons for this is to reduce the high costs of health care. There is a national health insurance system which enables everyone in Japan to receive advanced health care at a low cost. Another characteristic of the health insurance system in Japan is that patients can access Western and *Kampo* medical care at the same time in the same medical institution [1,2]. Kampo, or traditional Japanese herbal medicine based on traditional Chinese herbal medicine, has been used for the treatment of not only acute but also chronic pain in Japan [3]. The Ministry of Health, Labor and Welfare of Japan, approves the use of 148 Kampo preparations (traditional herbal medicines) [4]. Currently, most Kampo preparations are prescribed as extract formulations of high quality. Moreover, physicians who have studied Western medicine and Kampo medicine practice Western and Kampo medical care in their daily clinical practice.

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Pain is essentially an interactive psychophysiological behavior pattern, so an appreciation of the biopsychosocial model is essential for understanding and caring for patients with chronic pain. Thus, an interdisciplinary approach is often recommended and considered to be extremely relevant in providing appropriate therapeutic care for patients suffering from chronic and intractable pain [5]. Our center is the first multidisciplinary pain center established in Japan at July 2007. At our center, we have been prescribing Kampo extract formulations in combination with Western medicines in our daily clinical practice as an interdisciplinary approach in order to treat patients with chronic pain. However, to date, there have not been any reports on Kampo practice in multidisciplinary pain centers anywhere in the world because of the health insurance systems. We thus conducted a survey on the use of Kampo extract formulations and the effect of the formulations on patients with chronic pain in our multidisciplinary pain center.

## Methods

Retrospective analysis from August 2012 to July 2013 was performed on 487 patients suffering from chronic pain who visited the pain center of Aichi Medical University Hospital. All patients were referred from other hospitals to the pain center. Patients who were prescribed Kampo extract formulations were included.

After obtaining approval from the Ethics Committee of Aichi Medical University (a reference number, 13–097) and written informed consent, we routinely recorded demographics, symptoms, and course of pain in all patients. The intensity of pain was rated by the patients using a numerical rating scale (NRS) where 0 indicated no pain and 10 the greatest pain possible. All demographic and clinical data were extracted from medical records from August 2012 to March 2014 for the present study. In addition, patients were categorized as having marked improvement (≥60% improvement in NRS for pain compared to initial visit), moderate improvement (≥30% and <60% improvement in NRS compared to initial visit), some improvement (≥20% and <30% improvement in NRS compared to initial visit), and no improvement (<20% improvement in NRS compared to initial visit) depending on the state of pain improvement 6 months to 1 year after the initial visit. Moreover, patients who did not visit the hospital again even with an appointment for a follow-up visit and who visited the hospital for the purpose of receiving a second opinion were categorized separately.

## Results

We administered treatment after a medical conference attended by different types of professionals (anesthesiologists, orthopedists, psychiatrists, internists, dentists, nurses, physical therapists, and clinical psychotherapists). As required at the medical conference, we administered pharmacological (including Kampo medicine), physical, acupuncture, cognitive-behavioral, psychoanalytic, and psychological treatment. Kampo medicines were prescribed for 221 patients out of a total of 487 patients based on patient-centered Kampo diagnosis [3] while continuing Western medical care and the demographic characteristic data are presented in Table 1. Table 2 lists the most frequent medical complaints for which Kampo medicines were prescribed. Kampo medicines were prescribed to treat lower back/lower limb pain (36.6%, $n = 81$), neck/upper limb pain (13.1%, $n = 29$), various facial pains (13.1%, $n = 29$), headache/migraine (7.7%, $n = 17$), whiplash-associated disorder (5.9%, $n = 13$), and frozen shoulder (3.6%, $n = 8$). Pain improvement in all the patients who were prescribed Kampo medicines was categorized as follows: 26.3% with marked improvement, 12.7% with moderate improvement, 38.9% with some improvement, and 19.9% with no improvement. Table 3 shows Kampo therapy outcome of each complaint.

Table 4 lists the most frequently prescribed Kampo medicines for lower back/lower limb pain. We prescribed *Goshajinkigan* (22.2%, $n = 18$), *Shakuyakukanzoto* (17.3%, $n = 14$), *Yokukansan* (16.0%, $n = 13$), *Keishikajutsubuto* (14.8%, $n = 12$), *Hachimijiogan* (14.8%, $n = 12$), and *Juzentaihoto* (14.8%, $n = 12$) for the management of lower back/lower limb pain. Pain improvement in the patients who were prescribed Kampo medicines was categorized as follows (Table 3): 23.5% with marked improvement, 17.3% with moderate improvement, 23.5% with some improvement, and 28.4% with no improvement. In contrast, pain improvement in the patients who were not prescribed Kampo medicines ($n = 136$; median (range) of pain duration, 24 (3–320) months) was categorized as follows: 19.1% ($n = 26$) with marked improvement, 6.9% ($n = 9$) with moderate improvement, 12.5% ($n = 17$) with some improvement, and 25.0% ($n = 34$) with no improvement.

Table 4 lists the most frequently prescribed Kampo medicines for neck/upper limb pain. We prescribed *Keishibukuryogan* (34.5%, $n = 10$), Yokukansan (24.1%, $n = 7$), *Jidabokuippo* (17.3%, $n = 5$), *Tokishakuyakusa* (17.3%, $n = 5$), *Kamishoyosan* (13.8%, $n = 4$), *Kakkonto* (13.8%, $n = 4$), and *Kososan* (13.8%, $n = 4$) for the

**Table 1 Patient's characteristics**

| Patient's characteristics | Values |
|---|---|
| Age (years) | 57 [13–89] |
| Sex (M/F) | 79/142 |
| Weight (kg) | 56 [34–92] |
| Duration of pain (months) | 58 [3–400] |

Values are numbers or mean [range].

**Table 2 Most frequent medical complaints for which Kampo medicines were prescribed**

| Medical complaint | % (*n*) |
|---|---|
| Lower back/lower limb pain | 36.6 (81) |
| Neck/upper limb pain | 13.1 (29) |
| Various facial pains | 13.1 (29) |
| Headache/migraine | 7.7 (17) |
| Whiplash-associated disorder | 5.9 (13) |
| Frozen shoulder | 3.6 (8) |

management of neck/upper limb pain. Pain improvement in the patients who were prescribed Kampo medicines was categorized as follows (Table 3): 34.5% with marked improvement, 20.6% with moderate improvement, 13.7% with some improvement, and 17.2% with no improvement. In contrast, pain improvement in the patients who were not prescribed Kampo medicines ($n = 65$; median (range) of pain duration, 24 (3–168) months) was categorized as follows (Table 3): 20.0% ($n = 13$) with marked improvement, 9.2% ($n = 6$) with moderate improvement, 13.8% ($n = 9$) with some improvement, and 26.2% ($n = 17$) with no improvement.

Table 4 lists the most frequently prescribed Kampo medicines for various facial pains. We prescribed Kamishoyosan (44.8%, $n = 13$), Yokukansan (44.8%, $n = 13$), *Maobushisaishinto* (20.7%, $n = 6$), Keishibukuryogan (10.3%, $n = 3$), and *Goreisan* (10.3%, $n = 3$) for the management of various facial pains. Pain improvement in the patients was categorized as follows (Table 3): 34.5% with marked improvement, 17.2% with moderate improvement, 10.3% with some improvement, and 30.8% with no improvement.

Table 4 lists the most frequently prescribed Kampo medicines for headache/migraine. We prescribed Keishibukuryogan (29.4%, $n = 5$), Kamishoyosan (23.5%, $n = 4$), *Goshuyuto* (23.5%, $n = 4$), and Jidabokuippo (23.5%, $n = 4$) for the management of headache/migraine. Pain improvement in the patients who were prescribed Kampo medicines was categorized as follows (Table 3): 47.0% with marked improvement, 12.8% with some improvement, and 17.6% with no improvement. In contrast, pain improvement in the patients who were not prescribed Kampo medicines ($n = 20$; median (range) of pain duration, 42 (3–240) months) was categorized as follows: 25.0% ($n = 5$) with marked improvement, 10.0% ($n = 2$) with moderate improvement, 10.0% ($n = 2$) with some improvement, and 15.0% ($n = 3$) with no improvement.

Table 4 lists the most frequently prescribed Kampo medicines for whiplash-associated disorder. We prescribed Jidabokuippo (61.5%, $n = 8$), Keishibukuryogan (38.5%, $n = 5$), Tokishakuyakusa (23.1%, $n = 3$), Maobushisaishinto (15.4%, $n = 2$), and Yokukansan (15.4%, $n = 2$) for the management of whiplash-associated disorder. Pain improvement in the patients who were prescribed Kampo medicines was categorized as follows (Table 3): 30.8% with marked improvement, 15.4% with moderate improvement, 7.9% with some improvement, and 30.8% with no improvement. In contrast, pain improvement in the patients who were not prescribed Kampo medicines ($n = 12$; median (range) of pain duration, 18 (3–144) months) was categorized as follows: 8.3% ($n = 1$) with marked improvement, 16.7% ($n = 2$) with some improvement, and 33.5% ($n = 17$) with no improvement.

Table 4 lists the most frequently prescribed Kampo medicines for frozen shoulder. We prescribed *Nijutsuto* (87.5%, $n = 7$) and Keishikajutsubuto (37.5%, $n = 3$) for the management of frozen shoulder. Pain improvement in the patients was categorized as follows (Table 3): 88.9% with marked improvement and 11.1% with moderate improvement.

## Expert recommendations

Since the 1970s, great attention has been given to traditional, complementary, and alternative therapies around the world [1,2]. One of the reasons for the attention is the limited effectiveness of biomedicine for the treatment of chronic diseases. Based on the Japanese health insurance system, we can use Western medicine and traditional

**Table 3 Duration of pain and Kampo therapy outcome**

| | LB/LL pain | N/UL pain | Various facial pains | Headache/migraine | W-A disorder | Frozen shoulder |
|---|---|---|---|---|---|---|
| Duration of pain (months) | | | | | | |
| Median (range) | 30 (3–360) | 24 (3–360 ) | 24 (3–360) | 36 (3–360) | 12 (3–360) | 18 (3–36) |
| Improvement | % (*n*) | % (*n*) | % (*n*) | % (*n*) | % (*n*) | % (*n*) |
| Marked | 23.5 (19) | 34.5 (10) | 34.5 (10) | 47.0 (8) | 30.8 (4) | 88.9 (7) |
| Moderate | 17.3 (14) | 20.6 (6) | 17.2 (5) | 0.0(0) | 15.4 (2) | 11.1 (1) |
| Some | 23.5 (19) | 13.7 (61) | 10.3 (3) | 12.8 (2) | 7.9 (1) | 0.0 (0) |
| No | 28.4 (23) | 17.2 (5) | 30.8 (9) | 17.6 (3) | 30.8 (4) | 0.0 (0) |
| Dropouts | 4.8 (4) | 10.3(3) | 6.9 (2) | 23.5 (4) | 15.4 (2) | 0.0 (0) |

Of 221 new patients at Aichi Medical University Multidisciplinary Pain Center. LB/LL pain, lower back/lower limb pain; N/UL pain, neck/upper limb pain; W-A disorder, whiplash-associated disorder.

**Table 4 Most frequently prescribed Kampo medicines**

| Kampo medicine | % (*n*) | Ingredients (6, 8) |
|---|---|---|
| Lower back/Lower limb pain | | |
| Goshajinkigan | 22.2 (18) | Rehmannia, Cornus, Dioscorea, Alisma, Hoelen, Moutan, Cinnamon, Aconite, Achyranthes, Plantago Jukujio |
| Shakuyakukanzoto | 17.3 (14) | Glycyrrhizae radix, Peony, Liquorice |
| Yokukansan | 16.0 (13) | Tang-kuei, Gambir, Cnidium, Atractylodes, Holen, Bupleurum, Liquorice |
| Keishikajutsubuto | 14.8 (12) | Cinnamon, Hoelen, Moutan, Persica, Peony |
| Hachimijiogan | 14.8 (12) | Rehmannia, Cornus, Dioscorea, Alisma, Hoelen, Moutan, Cinnamon, Aconite |
| Juzentaihoto | 14.8 (12) | Ginseng, Astragalus, White atractylodes, Tang-kuei, Hoelen, Rehmannia, Cnidium, Peony, Cinnamon, Liquorice |
| Neck/Upper limb pain | | |
| Keishibukuryogan | 34.5 (10) | Cinnamon, Atractylodes, Aconite |
| Yokukansan | 24.1 (7) | Tang-kuei, Gambir, Cnidium, Atractylodes, Holen, Bupleurum, Liquorice |
| Jidabokuippo | 17.3 (5) | Cinnamon, Cnidium, Glycyrrhizae radix, Rhei rhizome, Quercus, Caryophylli, Nupharis rhizoma |
| Tokishakuyakusa | 17.3 (5) | Tang-kuei, Cnidium, Peony, Hoelen, Atractylodes, Alisma |
| Kamishoyosan | 13.8 (4) | Tang-kuei, Peony, Atractylodes, Hoelen, Bupleurum, Liquorice, Moutan, Gardenia, Ginger, Mentha |
| Kakkonto | 13.8 (4) | Pueraria, Ma-huang, Ginger, Jujube, Cinnamon, Peony, Liquorice |
| Kososan | 13.8 (4) | Cyperus, Perilla, Citrus, Ginger, Liquorice |
| Various facial pains | | |
| Kamishoyosan | 44.8 (13) | Tang-kuei, Peony, Atractylodes, Hoelen, Bupleurum, Liquorice, Moutan, Gardenia, Ginger, Mentha |
| Yokukansan | 44.8 (13) | Tang-kuei, Gambir, Cnidium, Atractylodes, Holen, Bupleurum, Liquorice |
| Maobushisaishinto | 20.7 (6) | Ma-huang, Asarum, Aconite |
| Keishibukuryogan | 10.3 (3) | Cinnamon, Atractylodes, Aconite |
| Goreisan | 10.3 (3) | Alisma, Polyporus, Hoelen, Atractylodes, Cinnamon |
| Headache/Migraine | | |
| Keishibukuryogan | 29.4 (5) | Cinnamon, Atractylodes, Aconite |
| Kamishoyosan | 23.5 (4) | Tang-kuei, Peony, Atractylodes, Hoelen, Bupleurum, Liquorice, Moutan, Gardenia, Ginger, Mentha |
| Goshuyuto | 23.5 (4) | Evodia, Ginseng, Ginger, Jujube |
| Jidabokuippo | 23.5 (4) | Cinnamon, Cnidium, Glycyrrhizae radix, Rhei rhizome, Quercus cortex, Caryophylli, Nupharis Rhizoma |
| Whiplash-associated disorder | | |
| Jidabokuippo | 61.5 (8) | Cinnamon, Cnidium, Glycyrrhizae radix, Rhei rhizome, Quercus cortex, Caryophylli, Nupharis Rhizoma |
| Keishibukuryogan | 38.5 (5) | Cinnamon, Atractylodes, Aconite |
| Tokishakuyakusan | 23.1 (3) | Tang-kuei, Cnidium, Peony, Hoelen, Atractylodes, Alisma |
| Maobushisaishinto | 15.4 (2) | Ma-huang, Asarum, Aconite |
| Yokukansan | 15.4 (2) | Tang-kuei, Gambir, Cnidium, Atractylodes, Holen, Bupleurum, Liquorice |
| Frozen shoulder | | |
| Nijutsuto | 87.5 (7) | White and blue atractylodes, Hoelen, Citrus, Arisaema, Cyperus, Scute, Clematis, Chianghuo, Pinellia, Liquorice, Ginger |
| Keishikajutsubuto | 37.5 (3) | Cinnamon, Hoelen, Moutan, Persica, Peony |

For lower back/lower limb pain, neck/upper limb pain, various facial pains, headache/migraine, whiplash-associated disorder, and frozen shoulder.

Japanese medicine including Kampo medicine in our daily clinical practice at the same time in the same medical institution [1,2,4]. Furthermore, Kampo has been used for the treatment of chronic pain in Japan from ancient times to the present [3,6,7].

The results of the present survey showed that Kampo medicines were prescribed to treat lower back/lower limb pain (36.6%, $n = 81$), neck/upper limb pain (13.1%, $n = 29$), various facial pains (13.1%, $n = 29$), headache/migraine (7.7%, $n = 17$), whiplash-associated disorder (5.9%, $n = 13$), and frozen shoulder (3.6%, $n = 8$). In fact, we had these cases in the same order in our center and Kampo medicines were prescribed when treatment with Western medicine alone was insufficient. And this survey shows that the use of Kampo medicines combined with Western medicine as an interdisciplinary approach provided some improvements for two thirds of these patients refractory to Western medicine alone.

Goshajinkigan, Shakuyakukanzoto, Yokukansan, Keishikajutsubuto, Hachimijiogan, and Juzentaihoto were the most frequently prescribed Kampo medicines for lower back/lower limb pain. Goshajinkigan, Shakuyakukanzoto, Keishikajutsubuto, and Hachimijiogan have been used since ancient times to treat melosalgia, low back pain, and numbness [8-11]. Yokukansan has been used to treat excitability, depression, and excessive muscle tension [8,9,12].

Keishibukuryogan, Yokukansan, Jidabokuippo, Tokishakuyakusa, Kamishoyosan, Kakkonto, and Kososan were the most frequently prescribed Kampo medicines for neck/upper limb pain. Keishibukuryogan, Yokukansan, Tokishakuyakusa, Kamishoyosan, Kakkonto, and Kososan have been used for the management of headache and chronic neck pain [8,9,13,14].

Kamishoyosan, Yokukansan, Maobushisaishinto, Keishibukuryogan, and Goreisan were the most frequently prescribed Kampo medicines for various facial pains. Keishibukuryogan, Kamishoyosan and Yokukansan have been prescribed to manage emotional distress, headache, and clenching or grinding of the teeth [8,9,12-14].

Keishibukuryogan, Kamishoyosan, Goshuyuto, and Jidabokuippo were the most frequently prescribed Kampo medicines for headache/migraine. Goshuyuto has been used since ancient times to treat a very severe headache accompanied by vomiting [8,9,15]. Moreover, Keishibukuryogan and Kamishoyosan have been prescribed for the treatment of emotional distress, a heavy feeling in the head and headache [8,9,13,14].

Jidabokuippo, Keishibukuryogan, Tokishakuyakusa, Maobushisaishinto, and Yokukansan were the most frequently prescribed Kampo medicines for whiplash-associated disorder. Jidabokuippo and Keishibukuryogan have been prescribed for the management of sprains and trauma or bruises [6,8,9,14].

Nijutsuto and Keishikajutsubuto were the most frequently prescribed Kampo medicines for frozen shoulder. Nijutsuto has been the first-line Kampo medicine for the treatment of frozen shoulder [8,9]. Keishikajutsubuto has been used to treat arthritis [9].

The interesting thing about the present survey is that we usually prescribed Yokukansan, Kamishoyosan, and Kososan, which have generally been prescribed for the management of psychological symptoms [3,12,13,16,17]. Yokukansan and Kamishoyosan have anxiolytic effects [12,13,17] and especially Yokukansan which is known to exert these effects via serotonin receptors [12]. Pain is essentially an interactive psychophysiological behavioral pattern [5]. Our previous study also showed that about 70% of patients were moderate to high psychopathological patients [3]. We thus postulated that Yokukansan, Kamishoyosan, and Kososan were used for psychopathological patients suffering from chronic pain at our center.

Since pain is an interactive psychophysiological behavioral pattern, it is important for medical staffs to recognize the biopsychosocial model when understanding and caring for patients with chronic pain. Thus, an interdisciplinary approach is often recommended and considered to be extremely relevant in providing appropriate therapeutic care for patients with chronic and intractable pain [5]. That is, inter-, multidisciplinary integrated approach is needed for patients with chronic and intractable pain as personalized medicine. Kampo has been used for the treatment of chronic pain in Japan from ancient times to the present [3,6,7]. Also, Kampo medicines have been prescribed based on patient-centered Kampo diagnosis. Thus, we postulate that Kampo could be part of personalized medicine. Accordingly, we have been prescribing Kampo extract formulations in combination with Western medicines in our daily clinical practice as personalized medicine in order to treat patients with chronic pain at our center. And we expect that the number of physicians who use Kampo in this way will increase soon.

There are merits and demerits for the clinical application of Kampo medicine, when compared with Western medicine. A lot of patients value Kampo medicine as a holistic, body harmonizing treatment and as a stimulant for self-healing without severe side effects [1]. In contrast, some patients suffering from chronic pain are likely to be so dependent and tend to be reluctant to receive the treatments based on its holistic, self-healing philosophy.

There are several limitations of the study. The present report is a retrospective and nonrandomized control analysis of Kampo treatment and thus lacks the reproducibility. Since we have to clarify the specific kind of pain for personalized approach and detailed points for multidisciplinary integration, we need prospective and comparative study that might be more appropriate to support predictive, preventive, personalized value, and the reproducibility of Kampo treatment, thereby obtaining solid evidence of Kampo medicine in personalized pain management algorithm.

## Conclusion

The retrospective analysis on 221 out of 487 patients suffering from chronic pain who visited the pain center of Aichi Medical University Hospital showed that the most frequent medical complaints for which Kampo medicines were prescribed were lower back/lower limb pain, neck/upper limb pain, various facial pains, headache/migraine, whiplash-associated disorder, and frozen shoulder. Two thirds of the chronic pain patients with the use of Kampo medicines combined with Western medicine experienced further pain improvements. Moreover, we usually used several Kampo medicines generally prescribed for the management of psychological symptoms.

**Competing interests**
The authors declare that they have no competing interests.

**Authors' contributions**
Y-CPA conceived of the study, participated in its study, and conducted all experiments. All authors conducted the acquisition of data. All authors helped to draft the manuscript. All authors read and approved the final manuscript.

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**References**

1. Hottenbacher L, Weißhuhn TE, Watanabe K, Seki T, Ostermann J, Witt CM: **Opinions on Kampo and reasons for using it–results from a cross-sectional survey in three Japanese clinics.** *BMC Complement Altern Med* 2013, **13**:108. doi:10.1186/1472-6882-13-108.
2. Moschik EC, Mercado C, Yoshino T, Matsuura K, Watanabe K: **Usage and attitudes of physicians in Japan concerning traditional Japanese medicine (kampo medicine): a descriptive evaluation of a representative questionnaire-based survey.** *Evid Based Complement Alternat Med* 2012, **2012**:139818. doi:10.1155/2012/139818.
3. Arai YC, Nishihara M, Inoue S, Makino I: **Kampo diagnostic procedure, Fuku shin, could be a useful diagnostic tool for psychopathological patients suffering from chronic pain.** *Evid Based Complement Alternat Med* 2013, **2013**:816216. doi:10.1155/2013/816216.
4. Yamakawa J, Motoo Y, Moriya J, Ogawa M, Uenishi H, Akazawa S, Sasagawa T, Nishio M, Kobayashi J: **Significance of Kampo, traditional Japanese medicine, in supportive care of cancer patients.** *Evid Based Complement Alternat Med* 2013, **2013**:746486. doi:10.1155/2013/746486.
5. Pergolizzi J, Ahlbeck K, Aldington D, Alon E, Coluzzi F, Dahan A, Huygen F, Kocot-Kępska M, Mangas AC, Mavrocordatos P, Morlion B, Müller-Schwefe G, Nicolaou A, Pérez Hernández C, Sichère P, Schäfer M, Varrassi G: **The development of chronic pain: physiological CHANGE necessitates a multidisciplinary approach to treatment.** *Curr Med Res Opin* 2013, **29**:1127–1135. doi:10.1185/03007995.2013.810615.
6. Hijikata Y, Miyamae Y, Takatsu H, Sentoh S: **Two kampo medicines, jidabokuippo and hachimijiogan alleviate sprains, bruises and arthritis.** *Evid Based Complement Alternat Med* 2007, **4**:463–467. doi:10.1093/ecam/nel105.
7. Kogure T, Tatsumi T, Shigeta T, Fujinaga H, Sato T, Niizawa A: **Effect of kampo medicine on pain and range of motion of osteoarthritis of the hip accompanied by acetabular dysplasia: case report and literature review.** *Integr Med Insights* 2011, **6**:13–17. doi:10.4137/IMI.S7884.
8. Otsuka K: *KAMPO-A Clinical Guide to Theory and Practice.* Edinburgh: Churchill Livingstone, Elsevier; 2010.
9. Shibata Y, Wu J: *KAMPO Treatment for Climacteric Disorders.* Brookline: Massachusetts, Paradigm Publications; 1997.
10. Suzuki Y, Goto K, Ishige A, Komatsu Y, Kamei J: **Antinociceptive effect of Gosha-jinki-gan, a Kampo medicine, in streptozotocin-induced diabetic mice.** *Jpn J Pharmacol* 1999, **79**:169–175.
11. Omiya Y, Suzuki Y, Yuzurihara M, Murata M, Aburada M, Kase Y, Takeda S: **Antinociceptive effect of shakuyakukanzoto, a Kampo medicine, in diabetic mice.** *J Pharmacol Sci* 2005, **99**:373–380.
12. Yamaguchi T, Tsujimatsu A, Kumamoto H, Izumi T, Ohmura Y, Yoshida T, Yoshioka M: **Anxiolytic effects of yokukansan, a traditional Japanese medicine, via serotonin 5-HT1A receptors on anxiety-related behaviors in rats experienced aversive stress.** *J Ethnopharmacol* 2012, **143**:533–539. doi:10.1016/j.jep.2012.07.007.
13. Hidaka T, Yonezawa R, Saito S: **Kami-shoyo-san, Kampo (Japanese traditional medicine), is effective for climacteric syndrome, especially in hormone-replacement-therapy-resistant patients who strongly complain of psychological symptoms.** *J Obstet Gynaecol Res* 2013, **39**:223–228. doi:10.1111/j.1447-0756.2012.01936.x.
14. Ogawa K, Kojima T, Matsumoto C, Kamegai S, Oyama T, Shibagaki Y, Muramoto H, Kawasaki T, Fujinaga H, Takahashi K, Hikiami H, Goto H, Kiga C, Koizumi K, Sakurai H, Shimada Y, Yamamoto M, Terasawa K, Takeda S, Saiki I: **Identification of a predictive biomarker for the beneficial effect of a Kampo (Japanese traditional) medicine keishibukuryogan in rheumatoid arthritis patients.** *Clin Biochem* 2007, **40**:1113–1121.
15. Odaguchi H, Wakasugi A, Ito H, Shoda H, Gono Y, Sakai F, Hanawa T: **The efficacy of goshuyuto, a typical Kampo (Japanese herbal medicine) formula, in preventing episodes of headache.** *Curr Med Res Opin* 2006, **22**:1587–1597.
16. Ito N, Yabe T, Nagai T, Oikawa T, Yamada H, Hanawa T: **A possible mechanism underlying an antidepressive-like effect of Kososan, a Kampo medicine, via the hypothalamic orexinergic system in the stress-induced depression-like model mice.** *Biol Pharm Bull* 2009, **32**:1716–1722.
17. Toriizuka K, Kamiki H, Ohmura NY, Fujii M, Hori Y, Fukumura M, Hirai Y, Isoda S, Nemoto Y, Ida Y: **Anxiolytic effect of Gardeniae Fructus-extract containing active ingredient from Kamishoyosan (KSS), a Japanese traditional Kampo medicine.** *Life Sci* 2005, **77**:3010–3020.

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ORIGINAL ARTICLE

# The efficacy of a multidisciplinary group program for patients with refractory chronic pain

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**M Inoue, S Inoue, T Ikemoto, et al. The efficacy of a multidisciplinary group program for patients with refractory chronic pain. Pain Res Manag 2014;19(6):302-308.**

**BACKGROUND:** Chronic pain is a major problem because it can result in not only a reduction in activities of daily living and quality of life but also requires initiation of social assistance. Seeking only to eliminate pain itself would appear to be too narrow an objective, in addition to often being unachievable; therefore, a multifaceted, comprehensive approach with multiple objectives is needed.
**OBJECTIVE:** To describe the effects of a program (the 'Chronic Pain Class') offering cognitive behavioural therapy to small groups of individuals with refractory chronic pain in Japan. Exercise was an important feature of the program.
**METHODS:** A total of 46 patients who were experiencing treatment difficulties and decreased activity participated in the program. The programs were conducted in groups of five to seven patients who met weekly for nine weeks. Weekly sessions, which were approximately 2 h in duration, combined lectures with exercise. Several measures related to pain and physical function were administered at the beginning and the conclusion of the program.
**RESULTS:** Nine patients dropped out during the program. A number of measures (eg, pain intensity, disability, catastrophizing thoughts) showed significant improvements after intervention (P<0.002 after Bonferroni correction). Furthermore, most measures of physical function showed substantial improvement, especially seated forward bends, zig-zag walking, self-care and 6 min walk test (P<0.001).
**CONCLUSION:** The results of the present study provide evidence that a combination of cognitive behavioural therapy and exercise should be recommended to patients with refractory chronic pain.

**Key Words:** *Chronic pain; Cognitive behavioural; Disability; Multidisciplinary; Physical functioning*

## L'efficacité d'un programme multidisciplinaire de groupe pour les patients ayant des douleurs chroniques réfractaires

**HISTORIQUE :** La douleur chronique est un grave problème, car elle peut non seulement limiter les activités de la vie quotidienne et la qualité de vie, mais également entraîner de besoins d'aide sociale. L'objectif d'éliminer la douleur semblerait trop étroit, sans compter qu'il est souvent irréalisable. C'est pourquoi il faut plutôt adopter une approche polyvalente et détaillée, aux objectifs multiples.
**OBJECTIF :** Décrire les effets d'un programme (le « cours sur la douleur chronique ») qui propose une thérapie cognitivo-comportementale à de petits groupes de personnes du Japon souffrant de douleurs chroniques réfractaires. L'exercice était une caractéristique importante du programme.
**MÉTHODOLOGIE :** Au total, 46 patients qui éprouvaient des problèmes de traitement et qui faisaient moins d'activité physique qu'auparavant ont participé au programme. Ce programme était offert à des groupes de cinq à sept patients qui se rencontraient une fois par semaine pendant neuf semaines. Les séances hebdomadaires, d'une durée approximative de deux heures chacune, combinaient les conférences et l'exercice. Plusieurs mesures liées à la douleur et à la fonction physique étaient vérifiées au début et à la conclusion du programme.
**RÉSULTATS :** Neuf patients ont abandonné le programme. Plusieurs mesures (p. ex., intensité de la douleur, invalidité, pensées de catastrophisation) ont beaucoup diminué après l'intervention (P<0,002 après correction de Bonferroni). De plus, la plupart des mesures de la fonction physique se sont considérablement améliorées, notamment les flexions avant en position assise, la marche en zigzag, les soins personnels et le test de marche de 6 minutes (P<0,001).
**CONCLUSION :** D'après les résultats de la présente étude, il faudrait recommander une combinaison de thérapie cognitivo-comportementale et d'exercice aux patients souffrant de douleurs chroniques réfractaires.

Chronic pain reduces activities of daily living (ADL) and quality of life (QOL), is a burden not only on the patient but also on family members and others involved, and often severely limits family and social activities. Musculoskeletal pain is also a the major problems in Japan and its aging population because patients require assistance and may become bedridden. A national survey involving 10,000 individuals conducted by a research group from the Ministry of Health, Labour and Welfare revealed that 15.4% of the population experienced chronic musculoskeletal pain when chronic pain was defined as the presence of symptoms within the past month; persistent pain for at least six months; and a score of ≥5 on a visual analogue scale (VAS) (1). The survey also revealed a high frequency of lumbar, shoulder, neck and knee pain, low satisfaction with treatment and 'doctor shopping' in approximately one-half of the population. The findings suggest that chronic pain, which is often musculoskeletal in nature, not only reduces ADL and QOL, but also raises societal issues. Prolonged pain can result in sleep disorders, daytime sleepiness, decreased arousal, anxiety, depression, lack of appetite and decreased routine activity, occasionally causes withdrawal from society and otherwise disrupts daily activities (2). As a result, patients with chronic pain fall into a 'vicious cycle' in which these psychological and social factors complicate their condition. In these cases, satisfactory treatment outcomes may be unachievable using a uniform therapeutic approach seeking only to eliminate pain. Often, a multifaceted, comprehensive approach is needed (3-5). In particular, therapeutic approaches based on cognitive behavioural therapy under multiple academic disciplines (ie, multidisciplinary) are recommended.

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Cognitive behavioural therapy seeks to deepen the understanding of one's pain, and teach self-control and coping strategies to encourage behavioural modifications that enable the patient to better confront his or her pain and improve QOL. Treatment using multidisciplinary approaches began in the 1970s at the University of Washington School of Medicine (Seattle, Washington) (6) and was subsequently widely adopted in Western nations. The efficacy of group programs, one component of such approaches, has been widely reported (7,8). It is difficult, however, to conduct group programs profitably under Japan's health insurance system, and few medical institutions have the human resources necessary to operate such programs. Moreover, in Japan, multidisciplinary approaches consisting of cognitive behavioural therapy and exercise for chronic pain have not yet been reported and, therefore, it remains unclear whether these therapeutic strategies are applicable across a range of cultures and not only Western cultures.

In Japan, the Aichi Medical University Multidisciplinary Pain Center and Institute of Physical Fitness, Sports Science and Rehabilitation Center (Nagakute, Japan) began offering group programs for small groups with chronic pain, calling this program the 'Chronic Pain Class'. The program was established in reference to group programs performed in Western nations and has as its motto "Living a positive, active life in spite of pain". The program is an attempt at a multidisciplinary, all-personnel approach, including doctors and support staff, to improve ADL and QOL rather than an approach to directly treat pain. Therefore, in the present study we evaluated multiple outcome measures – not only measures related to pain, but also extensive physical functions. The present article summarizes our findings on the effects of the group program on patients with refractory chronic pain.

## METHODS

### Ethics committee

The present study received ethical approval from the Ethics Committee of Aichi Medical University (No.12-067).

### Subjects and informed consent

The present study included 46 participants (19 men and 27 women; mean [± SD] age 65.8±9.1 years) in the program and was offered from October 2011 to September 2013 (Table 1). All participants presented at the Pain Center of Aichi Medical University and were encouraged to participate in the program by their attending physician. Most participants were experiencing treatment difficulties and decreased activity or physical strength due to excessive inactivity caused by pain or difficulty dealing with pain. Patients who had experienced prolonged pain for >6 months were eligible to be enrolled in the program.

On presentation at the Pain Center, all patients were administered an assessment battery of standardized self-report measures, demographics, symptoms, history and duration of pain. Before consenting to the program, each participant was fully informed by the attending physician of course content, that the coursework would be performed safely, and that all personal information of the participants would be kept confidential.

The mean duration of pain was 8.6 years (range six months to 52 years). A high proportion of the participants had lumbar spinal diseases (eg, spinal canal stenosis, degenerative spondylosis). Twenty-two of the participants (48%) had undergone surgery of the spine or a leg joint. The most intense pain sites were the back in 19 patients (41%), legs in 17 patients (37%), and shoulders, arms and feet in three patients (7%) (Table 1).

**TABLE 1**
**Patients' demographic data and characteristics**

| Characteristic | n |
|---|---|
| Age, years | |
| 31–40 | 1 |
| 41–50 | 3 |
| 51–60 | 6 |
| 61–70 | 22 |
| 71–80 | 13 |
| 81–90 | 1 |
| Sex, n/n | |
| Male/female | 19/27 |
| Body mass index, kg/m$^2$ | |
| ≤20 | 9 |
| >20–25 | 23 |
| >25 | 14 |
| Duration of pain | |
| >6 months – 1 year | 8 |
| >1–3 years | 11 |
| >3–5 years | 6 |
| >5–10 years | 9 |
| >10 years | 12 |
| Disease type | |
| Lumbar spinal disease | 30 |
| Osteoarthritis | 4 |
| Ossification of posterior longitudinal ligament | 3 |
| Cervical spondylosis | 1 |
| Post-traumatic neck syndrome | 1 |
| Cervical myelopathy | 1 |
| Intramedullary thoracic spinal cord tumour | 1 |
| Spinal arteriovenous fistula | 1 |
| Cerebral infarction | 1 |
| Headache, nonspecific | 1 |
| Genital pain, nonspecific | 1 |
| Coccyalgia, nonspecific | 1 |
| Chief pain sites | |
| Back to lower back | 19 |
| Legs (thighs, lower legs) | 17 |
| Shoulders and arms | 3 |
| Feet | 3 |
| Neck | 2 |
| Head | 1 |
| Genitals | 1 |

### Program

All aspects of the program were performed on the fitness floor, in the pool and classrooms of the Institute of Physical Fitness, Sports Science and Rehabilitation of Aichi Medical University. Each group, which consisted of five to seven participants, met weekly (for approximately 2 h) for nine weeks. The program combined lectures with exercise. Pain measures and physical function were evaluated at the beginning and conclusion of the program (Table 2).

Before, during and after the program, personnel held conferences to share evaluations and the condition of each of the participants during the program, and to offer guidance under a common mission. At the start of the program, all participants underwent resting electrocardiography to allow a cardiologist to assess program eligibility.

**Evaluations:** A nurse interviewed each participant during the initial visit to the Pain Center. The interview consisted of questions about the history of the present illness, medical history, treatment and surgical history, social factors (academic background, occupation, income, family composition), lifestyle (exercise, hobbies, amount of spare time) as well as problems among family members, interpersonal relationships at the workplace and dissatisfaction with previous treatments. The interviews were designed to collect as much multifaceted patient information as possible on topics relevant to pain.

The following instruments were used to assess pain: a VAS for pain severity; the Pain Disability Assessment Scale (PDAS) for the degree of impact of pain-related disabilities on lifestyle; the Hospital Anxiety and Depression Scale (HADS) for assessing anxiety and depression (HADS

**TABLE 2**
**Summary of the group program**

| | Contents | Assigned medical personnel |
|---|---|---|
| Week 1 (2.5 h) | Opening ceremony | Doctor |
| | Assessments (measures of pain) | Doctor |
| | Assessments (physical function) | Physical therapist, trainer, nurse |
| | Floor exercise | Physical therapist |
| Week 2 (2 h) | Feedback (results of assessments) | Physical therapist |
| | Lecture (theory and treatment) | Doctor |
| | Floor exercise, aerobic exercise | Physical therapist, trainer |
| Week 3 (2 h) | Lecture (functional anatomy, tests) | Doctor |
| | Floor exercise, aerobic exercise | Physical therapist, trainer |
| | Water aerobics | Physical therapist |
| Week 4 (2 h) | Lecture (automatic thinking and pain awareness) | Doctor |
| | Floor exercise, aerobic exercise | Physical therapist, trainer |
| | Water aerobics | Physical therapist |
| Week 5 (2 h) | Lecture (cognitive reconstruction and sleep) | Doctor |
| | Floor exercise, aerobic exercise | Physical therapist, trainer |
| | Water aerobics | Physical therapist |
| Week 6 (2.5 h) | Lecture (dietary habits, nutrition) | Dietician |
| | Group meeting | Doctor |
| | Floor exercise, aerobic exercise | Physical therapist, trainer |
| | Water aerobics | Physical therapist |
| Week 7 (2 h) | Group meeting | Doctor |
| | Floor exercise, aerobic exercise | Physical therapist, trainer |
| | Water aerobics | Physical therapist |
| Week 8 (2.5 h) | Assessments (measures of pain) | Doctor |
| | Assessments (physical function) | Physical therapist, trainer, nurse |
| | Water aerobics | Physical therapist |
| Week 9 (2 h) | Feedback (results of assessments) | Physical therapist |
| | Home exercise instruction | Physical therapist |
| | Closing ceremony | Doctor |

Anxiety and HADS Depression); the Pain Catastrophizing Scale (PCS) for measuring catastrophizing due to pain; and the EuroQol 5 Dimension (EQ-5D) for assessing QOL. All of these measures were conducted using Japanese translations (9-13). The authors independently prepared and used a 38-question instrument referred to the 'Pain Test' to characterize patient understanding of lectures and awareness of pain. VAS scores were assessed for the patients in the supine, sitting and standing positions, and when moving. The patients were instructed to indicate, using an arrow, the intensity of pain in each of these positions on a 100 mm line, with 100 representing the worst pain and zero representing no pain. The PDAS is a scale for measuring lifestyle disabilities of chronic pain patients. Higher scores (on a scale of zero to 60 points) indicate greater degrees of lifestyle disability (10,14). The HADS is a scale for assessing two separate dimensions of anxiety and depression. Again, higher scores (zero to 21 points for anxiety and depression alike) indicate greater degrees of anxiety and depression (12,15,16). The PCS assesses catastrophizing (rumination, magnification and helplessness) about pain, with higher scores (zero to 52 points) indicating greater degrees of catastrophizing (13,17,18). The EQ-5D assesses (on a scale of zero to 1.0) the outcome on health-related aspects of QOL (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Zero indicates death and 1.0 indicates complete health (11,19).

The physical function assessment measured morphology (body weight, body fat percentage); flexibility (seated forward bends); all-body response time; balance (one-legged stand with eyes open); open-eyed, standing stabilometry (hereafter, 'distance of movement from the centre of gravity', 'area of movement from the centre of gravity'); muscular strength: isometric trunk flexion/extension strength, isometric knee flexion/extension strength; walking ability (time of 10 m zig-zag walk); daily activity ability (standing and sitting ability speed test); self-care ability test; and endurance (6 min walk distance [6MD]). Body weight and percentage of body fat were calculated with the impedance method using a body fat meter (TBF-102 Body Fat Analyzer, Tanita, Japan). Seated forward bends were analyzed by measuring the distance from the fingertips to the toes with the knees fully extended using a seated forward-bend measurement instrument (Takei Scientific Instruments, Japan). The results were expressed as positive numbers when the fingertips passed the toes and as negative numbers when the fingertips did not reach the toes. All-body reaction time was measured with an all-body reaction time meter (TKK 510b, Takei Scientific Instruments). The time from a light signal to jumping by the participant was measured and the mean of five attempts was calculated. For one-legged standing, each participant placed his/her hands on his/her hips, with eyes open, and raised one leg. Only one side was measured for a maximum of 180 s. Open-eyed, standing stabilometry was performed using a stabilometer (Win-Pod, Medicapteur, France). The distance of movement from the centre of gravity and area of movement from the centre of gravity were measured for 30 s with the participants standing still with their eyes open. Isometric trunk strength (standing) and knee strength (sitting) were measured using a muscle function analyzing and exercising device (Cybex Norm, Cybex International, USA). Maximum 5 s isometric strength was measured for both flexion and extension. The measurements were divided by body weight to calculate body weight ratios. To measure zig-zag walking, pylons were placed every 2 m along a 10 m walking course. The time required to speed walk around the outsides of the pylons and reach the finish line was measured (20). Standing/sitting ability is a measure of the ability to turn over in bed, stand and perform other similar activities. The time required to stand up from a supine position as quickly as possible and then sit down in a chair and stand up again was measured (20). Self-care ability is an overall measure of the ability to change clothing and perform similar activities. The participants were asked to grasp both ends of a length of rope, step across the rope, one leg after the other, while standing, pass the rope from behind them over their head, and return the rope to their front as quickly as possible. The time it took the participants to perform this series of motions was measured three consecutive times (20). For 6MD, the participants walked as far as possible for 6 min on a flat, 50 m course at the Institute of Physical Fitness, Sports Science and Rehabilitation, and the distance was measured (21).

**Lectures:** The lectures covered the theory of pain, functional anatomy, medical imaging examination and treatment for pain, acceptance and cognitive restructuring of pain, how to confront pain, coping skills, sleep, nutrition and control of activities (pacing). Each lecture was conducted by a doctor (orthopedic surgeon, psychiatrist or anesthesiologist), physical therapist or registered dietitian for approximately 30 min. Based on cognitive behavioural therapy, the lectures were designed to inform the participants about how to correct or eliminate excessive fear of pain, improper thinking for treating pain and anxiety caused by distorted cognition, as well as how to control activity levels using appropriate pacing. Group meetings were also held. The participants presented and discussed problems associated with and measures for model scenarios of chronic pain.

**Exercise:** A doctor (orthopedic surgeon), physiotherapist or trainer offered the participants group exercise sessions that consisted of relaxation, stretching, balance practice, muscle strength exercises and other floor exercises (30 min), aerobic exercise with an ergometer (10 min) and water-based exercise (30 min). Relaxation consisted of abdominal breathing with the participants laying supine with their eyes closed (22). The participants were instructed to place

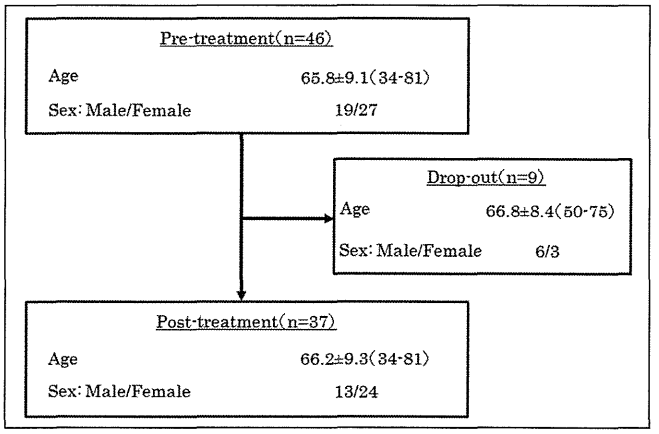


**Figure1)** *Participant distribution. Data presented as mean ± SD (range) or n/n. Nine participants dropped out during the program for specific reasons, while 37 participants completed the program.*

their hands on their bellies to confirm that their abdomens were moving. When stretching, the supine participants stretch the muscle groups in their shoulder girdles, lumbar area, hips, thighs and lower legs. Stretching consisted of self-performed static stretching with the muscle groups extended for 20 s each. Balance practice required the participants to get down on all fours, to raise an arm on one side and the leg on the opposite side and to remain upright on one knee and one hand. The participants engaged in muscular strengthening exercises to strengthen the trunk and leg muscle groups in the supine, sitting and standing positions, performing 10 repetitions under their own body weight. The participants were instructed to perform, at home, a selection of several of the exercises they were capable of completing in 15 min to 20 min. Exercise instruction was offered in relaxation areas within the facility in as quiet an environment as possible. The participants performed aerobic exercise for 10 min with an ergometer at a level of nine (very light) to 11 (fairly light) on the Borg Scale of Perceived Exertion, which is a subjective index of exercise strength (23). The load was gradually increased to accommodate the participants. Water aerobics, involving primarily walking as well as relaxation, stretching, muscular strengthening and balance practice, were conducted for 30 min.

### Record keeping and rules for participants

A record chart was given to each participant to enter weekly goals (specific and realistic goals for work, chores, hobbies/leisure activities and exercise), subjective levels of achievement, daily activities, home exercise and other activities. Each participant was also given a pedometer and asked to record the daily number of steps to assess activity levels. To prevent problems among participants as well as isolation, behaviour and language that refuted others or was competitive in any way about pain levels or number of operations was prohibited.

### Statistical analysis

Means and SDs were calculated for all values. The values of each measure before and after the program were analyzed using a paired *t* test in completed subjects (ie, subjects who completed the study); for subjects who did not complete the study, test parameters at baseline were compared with the completed group using the Mann-Whitney U test for analysis.

A significance level of $P<0.05$ was used for each outcome; however, multiple measures of outcomes had to be assessed to show the level of improvement of pain burden in completed subjects. Therefore, a Bonferroni-adjusted significance level of 0.002 was calculated to account for the increased possibility of a type I error ($\alpha=0.05$) for 25 hypothesized predictors. Cohen's d was also used to evaluate the magnitude of the effect size, calculated by standardized mean difference, with g>0.2 to 0.5 = small effect size, g>0.5 to 0.8 = medium effect size and g>0.8 = large effect size (24).

**TABLE 3**
**Changes in pain-related assessments at pretreatment and post-treatment**

| Variable | Pretreatment | Post-treatment | P | Cohen's d |
|---|---|---|---|---|
| VAS, mm | | | | |
| Supine | 32.0±25.5 | 21.2±23.5 | 0.004 | 0.473 |
| Sitting | 44.7±29.1 | 32.6±30.5 | 0.007 | 0.432 |
| Standing | 48.3±29.6 | 39.5±28.9 | 0.04 | 0.299 |
| Moving | 56.9±24.7 | 39.6±25.2 | <0.001* | 0.851 |
| PDAS | 25.0±8.5 | 19.1±8.8 | <0.001* | 0.714 |
| HADS | | | | |
| Anxiety | 7.4±3.7 | 6.6±3.5 | 0.03 | 0.329 |
| Depression | 8.1±2.9 | 6.1±3.4 | <0.001* | 0.668 |
| PCS | 32.2±11.1 | 25.7±11.7 | <0.001* | 0.673 |
| EQ-5D | 0.583±0.092 | 0.659±0.137 | 0.006 | 0.669 |
| Pain Test | 30.0±4.5 | 32.8±3.4 | <0.001* | 1.257 |

*Data presented as mean ± SD unless otherwise indicated. *Denotes statistical significance (P<0.002 after Bonferroni correction). Cohen's d Effect size based on the change score; EQ-5D EuroQol 5 Dimension; HADS Hospital Anxiety and Depression scale; PCS Pain Catastrophizing Scale; PDAS Pain Disability Assessment Scale; VAS Visual Analogue Scale*

## RESULTS

Nine participants dropped out during the program after developing a new disease, experiencing aggravated symptoms or for personal reasons, while 37 participants (13 men and 24 women; mean age 66.2±9.3 years) completed the program (Figure 1). Although the EQ-5D score (P=0.02) tended to be different between the noncompleted group and completed group, none of the parameters showed a significant difference between these two groups at baseline.

As presented in Table 3, a number of measures related to pain assessment showed a significant improvement after intervention (P<0.002 after Bonferroni correction). Pain intensity on moving and PDAS, HADS-Depression, PCS and Pain Test scores showed good to fair improvements with medium-level efficacy or higher (Cohen's d>0.5).

Furthermore, there were significant improvements in physical function assessments (Table 4). Satisfactory outcomes were observed in seated forward bends (Cohen's d=0.75), zig-zag walk (Cohen's d=0.60), self-care working ability (Cohen's d=1.06) and 6MD (Cohen's d=0.73). One-legged standing, stabilometry (distance of movement) and muscle strengths did not show a significant improvement or decline.

## DISCUSSION

Cognitive behavioural therapy for chronic pain patients involves the analysis of pain using a cognitive behavioural pain model that pain is not only influenced by its underlying pathophysiology, but also by an individual's cognition, affect and behaviour (25). The efficacy of cognitive behavioural therapy in chronic pain patients has been substantially investigated and reported on by researchers including Eccleston et al (26) and Henschke et al (4), who conducted meta-analyses. However, these strategies for chronic pain were not widely accepted in Japan. In the present study, we demonstrated the efficacy of this program in Japanese society, which has a different culture compared with other countries. Furthermore, the results implied that appropriate exercise combined with cognitive behavioural therapy are more effective for elderly patients than for the age groups studied in previous reports.

Significant improvements from before to after the program were observed in several measures of pain, including the VAS (moving), PDAS, HADS-Depression, PCS and Pain Test. The distorted perception that chronic pain patients have of pain leads to greater fear of pain and reinjury from activity as well as depression, other psychiatric and

**TABLE 4**
**Changes in physical function before and after treatment**

| Variable | Pretreatment | Post-treatment | P | Cohen's d |
|---|---|---|---|---|
| Weight, kg | 57.8±11.0 | 57.4±11.5 | 0.02 | 0.333 |
| Body fat, % | 25.8±8.7 | 25.8±8.9 | 0.49 | 0.001 |
| Seated forward bends, cm | 1.9±12.7 | 5.0±11.5 | <0.001* | 0.750 |
| All body reaction time, s | 0.484±0.136 | 0.451±0.108 | 0.04 | 0.310 |
| One-legged stand with eyes open, s | 47.1±50.1 | 54.0±61.7 | 0.12 | 0.196 |
| Stabilometry, standing with eyes open | | | | |
| Distance of movement of centre of gravity, mm | 321.2±104.6 | 340.6±113.2 | 0.21 | 0.200 |
| Area of movement of centre of gravity, $mm^2$ | 257.7±154.1 | 212.4±119.2 | 0.01 | 0.379 |
| Muscle strength, isometric, Nm/kg | | | | |
| Knee flexion | 0.48±0.19 | 0.46±0.17 | 0.21 | 0.166 |
| Knee extension | 1.54±0.48 | 1.53±0.41 | 0.36 | 0.047 |
| Trunk flexion | 1.23±0.50 | 1.27±0.47 | 0.24 | 0.115 |
| Trunk extension | 1.65±0.73 | 1.66±0.71 | 0.47 | 0.021 |
| Zig-zag walking test, s | 9.3±4.1 | 8.3±3.1 | <0.001* | 0.593 |
| Standing/sitting ability test, s | 9.1±5.0 | 7.4±2.7 | 0.002 | 0.535 |
| Self-care working ability test, s | 8.6±2.6 | 6.6±1.6 | <0.001* | 1.057 |
| 6 min walk distance, m | 461±134 | 519±159 | <0.001* | 0.728 |

*Data presented as mean ± SD unless otherwise indicated. *Denotes statistical significance (P<0.002 after Bonferroni correction) Cohen's d Effect size based on the change score*

psychological conditions and excessive inactivity. In the present study, 35 (95%), 17 (46%) and 23 (62%) participants exhibited PDAS and HADS anxiety and depression scores above predefined cut-off points (10, eight and eight points, respectively) (10,16), which indicates that many experienced substantial pain-induced disabilities, anxiety and depression. Studies of intervention factors involved with cognitive behavioural therapy for chronic pain patients revealed that improvements in catastrophizing, pain coping skills, confronting pain and attention to pain are important variables for improving disabilities and mood (27-29). Several studies have also investigated the relationship of catastrophizing to pain intensity and degree of disability (30,31) and found that catastrophizing has a greater impact on disability than actual physical function (32). Others found that improvements in catastrophizing precede improvements in disabilities (33,34). Additionally, a significant improvement in scores on the Pain Test, which assessed understanding of the lectures and awareness of pain, indicates that learning coping skills and how to confront pain reduces catastrophizing thoughts and improves disabilities, anxiety and depression. Gradually achieving treatment goals helps patients feel more competent while promoting treatment and preventing recurrence (35,36). The program improved self-efficacy by providing specific, achievable weekly goals, by requiring participants to document their subjective degree of achievement of these goals, and teaching the participants how to achieve their short-term goals without aggravated pain. In the program, these changes in awareness improved QOL by encouraging the participants to increase their activity level, resume hobbies and leisure activities, and actively deepen their relationship with society.

Assessments of physical function revealed significant improvements in seated forward bends, zig-zag walking, self-care ability and 6MD. The increased pain caused by repeated exercise causes chronic pain patients to develop a strong fear of exercise ('kinesiophobia') (37). Excessive inactivity results in decreased activity, often leading to decreased fitness. Muscle tightness and shortening caused by persistent pain as well as joint deformation, postural abnormalities, muscle and soft tissue scarring and fibrosis caused by aging, and other dysfunctions occur concurrently, complicating the state of the patients and triggering new pain. Before this program, many participants had these conditions, thereby exhibiting a marked decrease in physical function (below-average measures for their sex and age). Exercise instruction must involve not only a local approach for the site of pain, but also a whole-body approach including posture and endurance. Additionally, the load applied must be carefully selected to avoid inducing pain during exercise whenever possible. We incorporated low-impact floor exercises (eg, relaxation, stretching, muscle strengthening exercises, balance training), aerobic exercise and water aerobics in the program with a relatively low load level of nine to 11 on the Borg Scale (23).

Seated forward bends assess the flexibility of the lumbar area and backs of the thighs (38). Self-care ability is impacted by the range of shoulder abduction and extension and the extensibility of the lumbar muscle group. The relaxation component of the floor exercises is believed to reduce muscle tightness, and the stretching component is believed to improve muscle blood flow and extensibility of the lumbar muscle group (39), thereby affecting improvements in seated forward bends and self-care ability. Another factor likely to be contributing to the improvement is the extended range of joint motion due to buoyancy and the reduced muscle tightness due to the warm water temperature during water aerobics (40).

Abe et al (41) reported a correlation between zig-zag walking speed and the thickness of the quadriceps and strength of knee extension. The muscle-strengthening exercises of the program were low impact, involving primarily the trunk and legs, with body weight serving as the load on a track or water resistance serving as the load in the water to avoid aggravation of pain. Although the assessments did not reveal an increase in maximal isometric knee or trunk strength, heavy loads (≥60% of maximal muscular strength) must be used continuously for at least nine weeks (two to three times per week) to increase the maximum muscular strength of elderly individuals (42). Previous studies have also indicated that, although low-impact muscle-strengthening exercises improved maximal trunk and leg strength, these studies lasted from six months to one or more years (43). Achieving improved maximum muscular strength during the nine-week duration of this program would not have been feasible. However, despite no change in muscle strength of the quadriceps, intervention of the program resulted in an improvement in walking performance in subjects, which may be a result of improvement in psychophysical interaction (eg, improvement in kinesiophobia).

All-body reaction time, a measure of agility, tended to improve. Contributing factors likely include neurological activation (visual information transmission, cerebral information processing) and better contraction rates of trunk and leg muscle groups (44).

In stabilometry, the distance of movement from the centre of gravity indicates the distance moved by the centre of the projected pressure, and the area of movement from the centre of gravity indicates the area moved by the centre of the projected pressure. Although these

are measures of balance, the distance of movement from the centre of gravity did not significantly change, while the area of movement from the centre of gravity somewhat decreased in this program. This is likely due to the fact that participants began balance practice on a track on all fours, a position that did not cause anxiety about falling, and the position of the practice was gradually shifted to a standing position, thereby avoiding excessive muscle tightness and, as a result, effectively improving balance. Moreover, while in the water, the participants experienced the postures and movements that they could not achieve on a track, thereby improving not only proprioceptors and joint receptors of muscles for maintaining posture but also the function of nerves and muscles through the stimulation of posture-maintaining muscle groups of the trunk, legs and many other organs (45,46). These improvements also may have improved balance. The results of the 6MD test, a simple and convenient measure of respiratory and cardiovascular exercise tolerance, improved by approximately 60 m. Ergometers, which were used in this program, provide better overall cardiorespiratory function and overall endurance as well as the neuromuscular re-education for walking, as evidenced by muscle activation similar to that achieved with walking (47,48). Walking exercise in the water improves cardiorespiratory and fitness function due to water pressure and increased energy expenditure per work performed (49,50), both of which we postulate may have contributed to better 6MD results.

The program was offered in a group format, which features group dynamics that give participants an incentive to achieve goals and lessen the sense of isolation and alienation. At the beginning of the program, however, some participants were competitive about the degree of their pain and the number of times they had had surgery, and interfered with one another. Such interpersonal problems may result in dropouts. Thus, we implemented rules prohibiting these actions. No participant subsequently dropped out due to interpersonal problems.

Supine and sitting VAS scores indicated signs of improvement and, moreover, moving VAS scores improved significantly, although the approach did not directly address pain itself, as shown in several studies (51,52). The techniques for controlling and managing pain instructed by our lectures improved psychiatric and psychological function, and exercise improved physical function. The features of the group program likely further promoted therapy, thereby alleviating pain as a consequence.

Although we demonstrated that novel features in the 'Chronic Pain Class' based on cognitive behavioural therapy were applicable to Japanese society, there were four major limitations to the present study. First, as described in the 'Subjects' and 'Methods' sections, subjects in the present study were encouraged to participate in the program by their attending physician; therefore, there may have been a selection bias. Second, the multiple measures only applied for patients who agreed to this program without using any subjects as a control; and third, these results are based on a small sample size (n=37). Finally, at the baseline level, although the results did not reveal significant differences in test parameters between completed subjects and noncompleted subjects, the aspect of QOL may be different. This result may indicate that it is more difficult to complete this program for patients with a lower QOL score than for subjects with a high QOL score. Thus, we cannot adequately evaluate the efficacy of 'Chronic Pain Class' according to type of patient with chronic pain. Therefore, we must offer this program to a larger population of patients with refractory chronic pain in future research studies and compare the results against other conventional treatments for chronic pain in Japan.

## CONCLUSIONS

We evaluated the efficacy of a nine-week multidisciplinary group program based on cognitive behavioural therapy for chronic pain patients. Significant improvements in pain intensity on moving, depression, disability, catastrophizing thoughts, flexibility, ADL, walking and endurance following the program suggest that the program was effective.

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**DISCLOSURES:** The authors have no conflicts of interest to declare.

## REFERENCES

1. Nakamura M, Nishiwaki Y, Ushida T, Toyama Y. Prevalence and characteristics of chronic musculoskeletal pain in Japan. J Orthop Sci 2011;16:1-9.
2. Meyer-Rosberg K, Kvarnström A, Kinnman E, Gordh T, Nordfors LO, Kristofferson A. Peripheral neuropathic pain – a multidimensional burden for patients. Eur J Pain 2001;5:379-89.
3. Flor H, Fydrich T, Turk DC. Efficacy of multidisciplinary pain treatment centers: A meta-analytic review. Pain 1992;49:221-30.
4. Henschke N, Ostelo RW, van Tulder MW, et al. Behavioural treatment for chronic low-back pain. Cochrane Database Syst Rev 2010;(7):CD002014.
5. Inoue S, Ushida T, Inoue M. Clinical characteristics and multidisciplinary management of chronic musculoskeletal pain. Brain Nerve 2012;64:1287-97. (Japanese)
6. Fordyce WE. Behavioral Methods in Chronic Pain and Illness. St Louis: CV Mosby, 1976.
7. Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. Pain 1999;80:1-13.
8. Scascighini L, Toma V, Dober-Spielmann S, Sprott H. Multidisciplinary treatment for chronic pain: A systematic review of interventions and outcomes. Rheumatology (Oxford) 2008;47:670-8.
9. Arai YC, Nishihara M, Inoue S, Makino I. Kampo diagnostic procedure, Fuku shin, could be a useful diagnostic tool for psychopathological patients suffering from chronic pain. Evid Based Complement Alternat Med 2013;2013:816216.
10. Arimura T, Komiyama H, Hosoi M. Pain disability assessment scale: A simplified scale for clinical use. Jpn J Behav Ther 1997;23:7-15. (Japanese)
11. Japanese EuroQol Translation Team. The development of the Japanese EuroQol instrument. J Health Care Soc 1997;8:109-23. (Japanese)
12. Kitamura T. The Hospital Anxiety and Depression Scale. Arch Psychiatr Diagn Clin Eval 1993;4:371-2. (Japanese)
13. Matsuoka H, Sakano Y. Assessment of cognitive aspect of pain: Development, reliability, and validation of Japanese version of Pain Catastrophizing Scale. Jpn J Psychosom Med 2007;47:95-102. (Japanese)
14. Yamashiro K, Arimura T, Iwaki R, Jensen MP, Kubo C, Hosoi M. A multidimensional measure of pain interference: Reliability and validity of the pain disability assessment scale. Clin J Pain 2011;27:338-43
15. Matsudaira T, Igarashi H, Kikuchi H, et al. Factor structure of the Hospital Anxiety and Depression Scale in Japanese psychiatric outpatient and student populations. Health Qual Life Outcomes 2009;7:42.
16. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361-70.
17. Osman A, Barrios FX, Gutierrez PM, Kopper BA, Merrifield T, Grittmann L. The Pain Catastrophizing Scale: Further psychometric evaluation with adult samples. J Behav Med 2000;23:351-65.
18. Sullivan MJ, Bishop SR. The pain catastrophizing scale. Development and validation. Psychol Assess 1995;7:524-32.
19. Dolan P. Modeling valuations for EuroQol health states. Med Care 1997;35:1095-108.
20. Nagamatsu T, Oida Y, Kitabatake Y, et al. A 6-year cohort study on relationship between functional fitness and impairment of ADL in community-dwelling older persons. J Epidemiol 2003;13:142-8.

21. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. Guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-17.
22. Otis JD. Managing Chronic Pain: A Cognitive-Behavioral Therapy Approach. Oxford: Oxford University Press, 2007.
23. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377-81.
24. Cohen J. Statistical Power Analysis for the Behavioral Sciences. Hillsdale: Lawrence Erlbaum Associates, 1988.
25. Keefe FJ. Cognitive behavioral control of arthritis pain. Med Clin North AM 1997;81:277-90.
26. Eccleston C, Williams AC, Morley S. Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst Rev 2009;CD007407
27. Jensen MP, Turner JA, Romano JM. Changes after multidisciplinary pain treatment in patient pain belief and coping are associated with concurrent changes in patient functioning. Pain 2007;131:38-47.
28. Moss-Morris R, Humphrey K, Johnson MH, Petrie KJ. Patients' perceptions of their pain condition across a multidisciplinary pain management program: Do they change and if so does it matter? Clin J Pain 2007;23:558-64.
29. Wessels T, van Tulder M, Sigl T, Ewert T, Limm H, Stucki G. What predicts outcome in non-operative treatments of chronic low back pain? A systematic review. Eur Spine J 2006 Nov;15:1633-44.
30. Sorbi MJ, Peters ML, Kruise DA, et al. Electronic momentary assessment in chronic pain I: Psychological pain intensity. Clin J Pain 2006;22:55-66.
31. Sorbi MJ, Peters ML, Kruise DA, et al. Electronic momentary assessment in chronic pain II: Pain and psychological pain responses as predictors of pain disability. Clin J Pain 2006;22:67-81.
32. Severeijns R, Vlaeyen JW, van den Hout MA, Weber WE. Pain catastrophizing predicts pain intensity, disability, and psychological distress independent of the level of physical impairment. Clin J Pain 2001;17:165-72.
33. Burns JW, Kubilus A, Bruehl S, Harden RN, Lofland K. Do changes in cognitive factors influence outcome following multidisciplinary treatment for chronic pain? A cross-lagged panel analysis. J Consult Clin Psychol 2003;71:81-91.
34. Spinhoven P, TerKuile M, Kole-Snijders AM, Hutten Mansfeld M, Den Ouden DJ, Vlaeyen JW. Catastrophizing and internal pain control as mediators of outcome in the multidisciplinary treatment of chronic low back pain. Eur J Pain 2004;8:211-9.
35. Bandura A. Self-efficacy: Toward a unifying theory of behavioral change. Psychol Rev 1977;84:191-215.
36. Deci EL, Ryan RM. The support of autonomy and the control of behavior. J Pers Soc Psychol 1987;53:1024-37.
37. Todd D. Kinesiophobia: The relationship between chronic pain and fear-induced disability. Forensic Examiner 1998;7:14-20.
38. Battie MC, Bigos SJ, Fisher LD, et al. The role of spinal flexibility in back pain complaints within industry. Spine 1990;15:768-73.
39. Weppler CH, Magnusson SP. Increasing muscle extensibility: A matter of increasing length or modifying sensation? Phys Ther 2010;90:438-49.
40. Dundar U, Solak O, Yigit I, Evcik D, Kavuncu V. Clinical effectiveness of aquatic exercise to treat chronic low back pain: A randomized controlled trial. Spine 2009;34:1436-40.
41. Abe T, Ogawa M, Loenneke JP, Thiebaud RS, Loftin M, Mitsukawa N. Relationship between site-specific loss of thigh muscle and gait performance in women: The HIREGASAKI study. Arch Gerontol Geriatr 2012;55:e21-5.
42. Campbell WW, Joseph LJ, Davey SL, Cyr-Campbell D, Anderson RA, Evans WJ. Effects of resistance training and chromium picolinate on body composition and skeletal muscle in older men. J Appl Physiol 1999;86:29-39.
43. Yamauchi J, Nakayama S, Ishii N. Effects of bodyweight-based exercise training on muscle functions of leg multi-joint movement in elderly individuals. Geriatr Gerontol Int 2009;9:262-9.
44. Bergmark A. Stability of the lumbar spine. A study in mechanical engineering. Acta Orthop Scand Suppl 1989;230:1-54.
45. Simmons V, Hansen PD. Effectiveness of water exercise on postural mobility in the well elderly: An experimental study on balance enhancement. J Gerontol A Biol Sci Med Sci 1996;51:233-8.
46. Tokuno CD, Carpenter MG, Thorstensson A, Garland SJ, Cresswell AG. Control of the triceps surae during the postural sway of quiet standing. Acta Physiol 2007;3:229-36.
47. Christensen LO, Johannsen P, Sinkjaer T, Petersen N, Pyndt HS, Nielsen JB. Cerebral activation during bicycle movements in man. Exp Brain Res 2000;135:66-72.
48. Ericson MO, Nisell R, Arborelius UP, Ekholm J. Muscular activity during ergometer cycling. Scand J Rehabil Med 1985;17:53-61.
49. Costill DL. Energy requirements during exercise in water. J Sports Med Phys Fitness 1971;11:87-92.
50. Takeshima N, Rogers ME, Watanabe E, et al. Water-based exercise improves health-related aspects of fitness in older women. Med Sci Sports Exerc 2002;34:544-51.
51. Basler HD, Jäkle C, Kröner-Herwig B. Incorporation of cognitive-behavioral treatment into the medical care of chronic low back patients: A controlled randomized study in German pain treatment centers. Patient Educ Couns 1997;31:113-24.
52. Fedoroff IC, Blackwell E, Speed B. Evaluation of group and individual change in a multidisciplinary pain management program. Clin J Pain 2014;30:399-408.

# Alexithymia Is Associated with Greater Risk of Chronic Pain and Negative Affect and with Lower Life Satisfaction in a General Population: The Hisayama Study

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## Abstract

***Introduction:*** Chronic pain is a significant health problem worldwide, with a prevalence in the general population of approximately 40%. Alexithymia — the personality trait of having difficulties with emotional awareness and self-regulation — has been reported to contribute to an increased risk of several chronic diseases and health conditions, and limited research indicates a potential role for alexithymia in the development and maintenance of chronic pain. However, no study has yet examined the associations between alexithymia and chronic pain in the general population.

***Methods:*** We administered measures assessing alexithymia, pain, disability, anxiety, depression, and life satisfaction to 927 adults in Hisayama, Japan. We classified the participants into four groups (low-normal alexithymia, middle-normal alexithymia, high-normal alexithymia, and alexithymic) based on their responses to the alexithymia measure. We calculated the risk estimates for the criterion measures by a logistic regression analysis.

***Results:*** Controlling for demographic variables, the odds ratio (OR) for having chronic pain was significantly higher in the high-normal (OR: 1.49, 95% CI: 1.07–2.09) and alexithymic groups (OR: 2.56, 95% CI: 1.47–4.45) compared to the low-normal group. Approximately 40% of the participants belonged to these two high-risk groups. In the subanalyses of the 439 participants with chronic pain, the levels of pain intensity, disability, depression, and anxiety were significantly increased and the degree of life satisfaction was decreased with elevating alexithymia categories.

***Conclusions:*** The findings demonstrate that, in the general population, higher levels of alexithymia are associated with a higher risk of having chronic pain. The early identification and treatment of alexithymia and negative affect may be beneficial in preventing chronic pain and reducing the clinical and economic burdens of chronic pain. Further research is needed to determine if this association is due to a causal effect of alexithymia on the prevalence and severity of chronic pain.

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## Introduction

Chronic pain is a common problem, with prevalence estimates at approximately 40% of the general population [1,2]. The impact of pain on economies is enormous. For example, the cost of back pain alone is equivalent to more than one-fifth of one country's total health expenditure and to 1.5% of the annual gross domestic product of the UK [3]. In addition to its economic impact, chronic pain is arguably one of the health care issues with the greatest negative impact on quality of life.

Chronic pain is known to have significant biological, psychological, and social causes and consequences [4–6], and thus adequate pain assessments and treatments should address all of these factors. In order to expand the potential targets of pain treatment and therefore help minimize the prevalence of the

negative impacts of chronic pain, research is needed to identify the biopsychosocial factors that are most consistently associated with pain and pain-related outcomes.

A potential factor that may contribute to the development and maintenance of chronic pain is alexithymia [7,8]. Alexithymia is the label used to describe a personality trait associated with an inability to regulate negative affect [9]. The term is derived from Greek, and literally means "a lack of words for feelings" [10]. Alexithymia is a disturbance of both cognitive and affective functioning characterized by difficulty in recognizing or describing one's emotions. The most common measure of alexithymia is the 20-item Toronto Alexithymia Scale (TAS-20) [11]. The TAS-20 assesses three components of alexithymia: (1) difficulty identifying feelings (DIF); (2) difficulty describing feelings (DDF); and (3) externally-oriented thinking (EOT).

In our previous research, we found a measure of alexithymia to be positively associated with pain intensity and interference, and negatively associated with vitality in a sample of individuals with neuromuscular disease and chronic pain [12]. We also found evidence that the effects of alexithymia on pain may be mediated by negative affect [13]. Additionally, research in pain populations by our group and others has identified the TAS-20 DIF scale as the most consistent factor associated with chronic pain and pain-related dysfunction [7,14,15]. However, the studies addressing the relationship between alexithymia and chronic pain to date have used participants who are not necessarily representative of the population (e.g., patients, transit workers, and students), which limits the generalizability of extant findings. To our knowledge, there are no studies examining the role that alexithymia might play in comprehensive chronic pain in a general population.

To elucidate this association, we performed a population-based cross-sectional survey in a Japanese community. We hypothesized that (1) the measure of alexithymia is associated with chronic pain, (2) this association is mediated by negative affect, and (3) the DIF domain of alexithymia is associated with criterion measures stronger than the other components of alexithymia. Our planned analyses regarding the associations between alexithymia and measures of additional pain-related outcomes (specifically, pain intensity, depression, anxiety, disability, and life satisfaction) were considered exploratory, as these associations have not yet been tested in prior research.

## Methods

### 1. Study participants

The Hisayama Study is an ongoing, long-term cohort study examining cardiovascular disease and its risk factors in Hisayama, a suburban town adjoining Fukuoka City, a metropolitan area in southern Japan. Full community surveys of the health status of residents aged 40 and older have been repeated every five years since 1961 [16]. Data for the present study were taken from responses to questions regarding pain and psychological functioning included in the whole survey administered in 2010.

Among 2,223 residents aged 40 and older who participated in the health survey, a total of 1,027 residents (participation rate: 46%) consented to participate in these questions of the 2010 whole survey. Of these, 66 had missing data and 34 did not complete the questionnaires, leaving a final sample of 927 participants (326 men and 601 women) (Fig. S1). This study was approved by the Kyushu University Institutional Review Board for Clinical Research. Written informed consent was obtained from all participants.

### 2. Measures

**2.1. Alexithymia.** Alexithymia was assessed for each participant using the 20-item Toronto Alexithymia Scale (TAS-20), which is the most psychometrically valid measurement of alexithymia [11]. As mentioned above, the TAS-20 consists of 20 statements that reflect three domains of alexithymia: (1) DIF; (2) DDF; and (3) EOT. Each item is rated on a 5-point Likert scale, with 1 = "strongly disagree" and 5 = "strongly agree."

We classified the participants as alexithymic (TAS-20 score >60) or non-alexithymic (TAS-20 score ≤60) based on their total TAS-20 scores according to previous studies [9], and subsequently classified the non-alexithymic group into three subgroups: low-normal alexithymia (score <44), middle-normal alexithymia (score 44–50) and high-normal alexithymia (score 51–60) based on their tertile values. In addition to the tertile values in this study, a total score of 51–60 has been defined as "borderline alexithymia" or "possible alexithymia" in some studies [17]. We also divided the TAS-20 subscale scores of the three domains into quartiles, as there are no published cutoffs for classifying individuals into alexithymic groups for the TAS-20 subscales. The Japanese version of the TAS-20 has been shown to be both reliable and valid [18].

**2.2. Assessment of presence of acute and chronic pain.** The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" and also explains that "Pain is always subjective." The definition of 'chronic' pain based on duration has not been clearly established, but 3 or 6 months or more is generally used [19,20]. According to this definition, we defined chronic pain as having any subjective pain for more than 6 months.

As part of the Hisayama Study health survey, the participants were asked to indicate whether they experienced any pain and how long the pain has lasted. Those who reported <6 months of pain and those with pain that had been experienced for 6 months or longer were classified as having acute (i.e., recent onset) and chronic pain, respectively. For complementary information, the participants with pain were asked to select their primary pain site using the IASP site categories [19]: 1 = head and face, 2 = neck, 3 = shoulder and arms, 4 = chest, 5 = back, 6 = stomach, 7 = low back, 8 = legs, 9 = pelvic and genital area, 10 = pain at more than one site.

**2.3. Pain intensity.** The participants were asked to rate the average intensity of their pain in the past week on a 100-mm visual analogue scale (VAS). Anchors were "No pain" (0 mm) and "Pain as bad as it could be (100 mm)." A great deal of evidence supports the reliability and validity of the VAS as a measure of pain intensity [21].

**2.4. Disability.** Participants were asked to rate their average disability in the past week on a 100-mm VAS. Anchors were "No disability" (0 mm) and "Disability as bad as it could be (100 mm) [22]."

**2.5. Life satisfaction.** Participants were asked to rate their global life satisfaction on a 100-mm VAS. Anchors were "Feeling no life satisfaction at all" (0 mm) and "Feeling life satisfaction as good as it could be (100 mm) [23]."

**2.6. Negative affect.** Negative affect was measured with the depression and anxiety scales of a Japanese version of the Symptom Checklist 90-revised (SCL-90-R). SCL-90-R scales have established validity and reliability [24].

**2.7. Demographic/descriptive variables and covariates.** Age, sex, marital status, educational level, and economic status are factors that could potentially influence both