

## Recent Non-Interventional Advances in Cancer Pain Among Singapore Patients

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### Abstract

**Introduction:** Pain is a common symptom in cancer patients, but very little information about the prevalence, severity, and treatment of pain in cancer patients in Singapore is available. Therefore, our prospective survey in the National Cancer Centre (NCC) outpatients is incorporated in this report. In addition, a review concerning the recent advances on non-interventional pain management in cancer treatment, which is relevant in the context, is discussed. **Materials and Methods:** For the prospective survey, a questionnaire was distributed for self-administration by patients while waiting for consultation at the NCC outpatient departments. Literature searches on advances in pain management were conducted, reviewed and discussed. **Results:** In the last decade, there have been advances in pain pharmacology ranging from wider therapeutic options and management approaches to novel delivery techniques. Acupuncture and massage therapy became increasingly popular among cancer patients. Some clinical trials of acupuncture show benefits in palliation of cancer pain. From the prospective survey, 41.2% of the responders reported pain in the past week, and only 70.8% talked to their doctors about their pain. One third of the patients received analgesics. Of these, 86.5% said that they were taking the prescribed medications, however, 37.4% admitted to having difficulties taking them. Non-drug methods were used by 25.4% of the patients. Medicated oil, cream or gel was used by 49.3%; only 2.6% reported use of Chinese herbs. **Conclusion:** Pain is a significant symptom in outpatients attending a cancer centre, affecting 41.2% of the patients. Although majority of patients who suffered from pain reported this to doctors, much more medical effort is needed to help patients to relieve their pain and proper complementary therapy could be considered.

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**Key words:** Cancer outpatients, Complementary therapies, Non-pharmacological pain treatments, Pain prevalence

### Introduction

Unrelieved pain is one of the most feared symptoms in cancer. As a result of pain, the quality of life of cancer patients is impaired. Since the first release of the World Health Organization (WHO) guidelines for the management of cancer pain,<sup>1</sup> in the past 2 to 3 decades, numerous studies have been reported with the aim to improve the quality of life of patients. Although the WHO guidelines for pain relief are effective, pain remains a problem among cancer patients. Among hospitalised cancer patients, pain was reported to be the most common symptom in overseas<sup>2,3</sup> as well as in Singapore context.<sup>4</sup> Among the outpatient and ambulatory cancer patients, the distress and problem of pain reported recently did not appear to be much better either.<sup>5-8</sup> Of note,

prevalence rates for pain reported could range from 20% to 80%.<sup>2,4,9</sup> This wide range can be due to the different stages of cancer, percentage of localised and metastatic diseases, cultural perception in pain, availability of pain management and method used to determine the rates of pain prevalence. Equally important are considerations for the cause of pain, whether the pain is due to non-compliance to the prescribed analgesics, or the reasons that drive such non-compliance.

Pain from cancer can arise from tumour invasion on surrounding tissue and bone or side effects from cancer treatments such as chemotherapy, radiotherapy and surgery.<sup>10</sup> The use of adjuvant analgesics for cancer pain has been reviewed recently.<sup>11</sup> Antidepressants, anticonvulsants,

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local anaesthetics, topical agents, steroids, bisphosphonates, and calcitonin are all adjuvants which have been shown to be effective in the management of cancer pain syndromes. This review examines recent advances on non-interventional pain management in cancer patients, covering both conventional pharmacotherapy and complementary approaches. Pain being unresolved through drug therapy is common experience for hospice patients. Therefore, more studies are needed to be done in this area, without discounting that complementary approaches towards cancer pain management may be beneficial.

So far, in Singapore, only one report on the study of pain in terminal cancer is available.<sup>12</sup> No information about the prevalence, severity, and treatment of pain in cancer outpatients in Singapore is available. With the advancement of cancer management, there is a need to review the problem of pain among cancer outpatients as more oncology treatments are available as an outpatient specialty. Therefore, given the paucity of report on the prevalence of pain in cancer outpatients in Singapore, in this review, we also incorporated a prospective survey conducted in the National Cancer Centre (NCC) to define the prevalence of pain in cancer outpatients in the Singapore context, and to document cancer pain management in Singapore. Lately, the American Cancer Society reported that more than half of the cancer survivors have used some form of complementary methods,<sup>13</sup> and interestingly, we found that some of our findings conducted previously had similar observations. In addition, there are considerable developments in interventional therapies in cancer pain to complement the conventional non-interventional pain management. This includes interventions such as celiac plexus neurolysis, intrathecal therapy and splanchnic blocks that serve to reduce opioid requirements and better manage the pain.<sup>14,15</sup> It is widely recognised that relief of cancer pain is a multimodal approach effort<sup>16</sup> and numerous clinical trials have been conducted to examine both the conventional non-interventional and interventional therapies to examine their effectiveness in improving quality of life while providing pain relief.<sup>17,18</sup>

## Materials and Methods

### Prospective Survey

A prospective survey was conducted in July 2002 in the 4 specialist oncology clinics located at the NCC building and therapeutic radiology centre of NCC located in Singapore General Hospital, over a period of 5 weekdays. The Ethics Committee approval was obtained from the NCC, Singapore. The survey form was given to every patient attending the specialist clinics. Patients were encouraged to fill it while waiting to see the doctor. Seven hundred

and thirty-one survey forms were accepted by patients at the clinics registration counters (Fig. 1). For patients who were unable to fill the questionnaire on their own, assistance was available, given by nurses and 2 third year Pharmacy students in the clinics over the period.

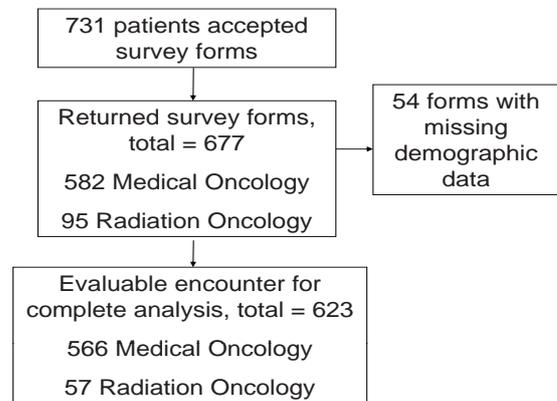


Fig. 1. Flow diagram of outpatient encounters over the survey period.

### Instrument

The questionnaire, entitled '3-minute survey' consisted of 22-items and was designed for self-administration by patients. It was available in both English and Chinese language. Twelve items required 'Yes' or 'No' responses including questions like (a) pain in the past week; (b) pain affecting quality of life such as pain duration, normal daily activities, appetite, sleep; (c) communicating pain incidence to their physician; (d) understanding of the prescribed pain medications. One item enquired the use of non-drug methods for pain relief such as acupuncture, rubbing oil, massage and total number of such medication taken in addition to pain medication. Following these items, the reasons for non-compliance were asked; 11 options were provided, one of which was reporting no-difficulty in taking the pain medication.

Demographic information was obtained by sticking the patients' label on the survey form when the forms were issued to those who agreed to participate in the survey. The questionnaire form was also used as an educational tool to create awareness that the pain can be controlled. This includes the proper understanding on pain, mode of administration of opioids, the common side effects of opioids and their management, common fears about opioids and the importance of medication compliance for effective pain relief.

The importance of pain in cancer patients is evidenced by a search in the PubMed database using the term 'pain'.

The search yielded over 468,500 hits, with over 57,700 reviews. When using keywords ‘pain, cancer’, over 60,400 hits were obtained. We also wanted to know how well our patients were being taken care of as compared to the overseas patients, and to better understand complementary therapies. Therefore, part of our survey aimed to capture the prevalence of patients using such therapies.

*Literature Search*

A full literature search up to 2011 July conducted in PubMed with keywords ‘pain in cancer patients, complementary,’ retrieved 292 articles, ‘recent advances on pain in cancer patients’ retrieved 146 articles, ‘acupuncture, cancer pain, randomized’ retrieved 57 articles. Over 500 papers from PubMed were retrieved and screened for the recent advances on pain in cancer patients, and relevant articles are cited and included in this review. Other keywords such as ‘chronic, acute, cancer pain, acupuncture, randomised, trials’ were also used.

**Results**

*Singapore Experience and Perspectives: A Prospective Survey of NCC Patients*

Of 731 survey forms accepted by the patients, 677 were returned (92.6% return rate, Fig. 1). Table 1 shows the demographic profile of patients. The responders have a mean age of 53.4 years. There were more females than

Table 1. Demographic Profile of Patients for Responders

	Overall Questionnaire, Responders (n = 623*)
<b>Gender</b>	
Male	192 (28.36%)
Female	431 (63.66%)
<b>Age</b>	
< 29 years	20 (3.21%)
30 to 44 years	125 (20.06%)
45 to 59 years	285 (45.75%)
60 to 74 years	161 (25.84%)
> 75 years	32 (5.14%)
<b>Race</b>	
Chinese	509 (81.70%)
Malay	60 (9.63%)
Indian	30 (4.82%)
Others	24 (3.85%)
<b>Language</b>	
Chinese	194 (31.14%)
English	429 (68.86%)

\*No demographic data available for 54 responder patients.

males (63.7% in responders).

*Prevalence of Pain and Prescription of Pain Medication*

Table 2 shows the prevalence of pain in patients classified by gender. Of the 279 patients (41.2% of 677 responders) who reported pain in the past week, 64.4% had pain lasting more than a week, 47.3% reported that normal daily activities were affected, 43.4% had appetite affected and 55.8% had sleep affected (Fig. 2). Among those who had pain in the past week, only 70.8% talked to their doctor about their pain. Generally, patients who suffered from pain in the past week have poorer quality of life as compared to the responders who had no pain. Out of 393 patients who reported no pain in the past week, 276 patients (40.8%) were “truly” pain free. They had not talked to their doctor about their pain and were not prescribed any pain medication.

Table 2. Prevalence of Pain in the Past Week, by Diagnosis and Gender

Diagnosis	Female %	Male %
Breast	42	0
Gastrointestinal tract (includes pancreas, liver, gallbladder and bile ducts)	34	45
Nasopharynx (includes head and neck)	43	40
Lung	69	50
Lymphoma	29	43
Urologic and gynaecologic	17	NA
Urologic and male genital	NA	47

Note: 86 cases (53 female, 33 male) with unconfirmed/benign diagnosis were excluded. NA: not applicable

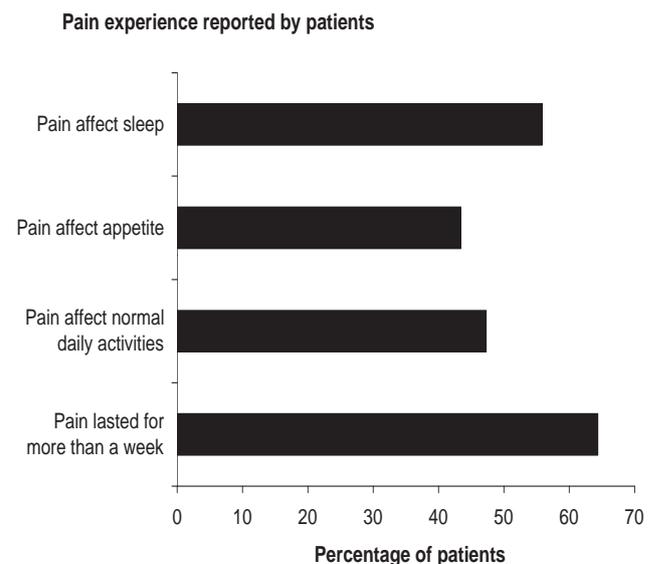


Fig. 2. Prevalence of pain experience.

Overall, 200 patients (32.8%, 200/609) were prescribed pain medications. Of those who had pain in the past week, 59.9% were prescribed pain medications.

*The Number of Medication Taken*

Only 173 of the 200 (86.5%) patients with prescribed pain medications admitted to taking them while 12.6% patients reported not taking their prescribed medications. Of the 173 patients on prescribed pain medication, 67.1% were taking 1 pain medication, 22.0% had 2 pain medications, 4.1% had 3 pain medications, 6.9% had 4 or more pain medications. Over 70% of patients took at least 2 other medications, and 5% took more than 6 other medications in addition to their pain medication (Table 3).

*Possible Reasons for Non-compliance*

Out of 481 patients, 75.7% (n = 364) reported they did not have difficulties taking their medications as instructed. However, among 190 patients who were prescribed medication for pain, 37.4% reported difficulties taking medication as prescribed. Out of 9 reasons, the commonest top 5 problems were (Table 4): fear of side effects (15.3%); fear that pain medications will not work if the pain gets worse (14.7%); medicine too expensive (10.4%); swallowing difficulty (9.2%) and too many medications (7.4%).

*Prevalence of Patients Using Non-Drug Methods for Pain*

Non-drug methods were used by 25.4% of patients to help relieve their pain (Table 5). The commonest non-drug methods used were topical application (49.3%) and massage (35.5%). Only 2.6% reported use of Chinese medicinal herbs.

*Pain Management: Conventional Pharmacotherapy and Recent Advances*

**Conventional Pharmacotherapy:** The analgesic ladder from WHO describes 3 levels of pain and suggests combinations of different drugs based on the type and intensity of pain.<sup>1</sup> It provides a stepwise and systematic approach to managing cancer pain. Drugs to manage cancer pain include non-steroidal anti-inflammatory drugs (NSAIDs), weak opioids, strong opioids, and adjuvant analgesics. Table 6 details common drugs used in the management of cancer pain.

**Recent Advances:** In the last decade, there have been continuous advances in pain pharmacology. These include the development of cyclooxygenase-2 (COX-2) selective NSAIDs and transmucosal fentanyl citrate that provide new pharmacologic options for the treatment of cancer pain, topical anesthetic patch with antihyperalgesic properties

(lignocaine) and using drugs approved for other indications to treat pain (pregabalin, ketamine, bisphosphonates). Novel techniques and approaches to deliver pharmacological intervention include the use of pre-emptive analgesia, postoperative pain management with patient controlled analgesia and use of techniques such as intrathecal drug administration and epidural spinal cord stimulation. In addition, there is continued research on the role of the N-methyl-d-aspartate (NMDA) receptor and its antagonists that can augment analgesia and combat opioid resistance.<sup>19-22</sup>

**Opioid Switching:** Opioid switching is also becoming a more widespread therapeutic manoeuvre as more opioids have become available for use and knowledge about

Table 3. Number of Medication Use in Addition to Pain Medication

Including painkillers, how many different kinds of medicines are you taking altogether?	Number of Patients Responded (n = 446)
0 to 2	325 (72.87%)
3 to 5	99 (22.20%)
6 and above	22 (4.93%)

Table 4. Top Five Reasons for Non-Compliance to Pain Medication Use

Reasons
I am afraid of the side effects.
I am afraid the painkillers will not work if the pain gets worse.
My medicine is too expensive.
I have difficulty swallowing.
There is too much medicine to take.

Table 5. Non-Drug Methods for Pain Relief Reported by Patients

Non-drug Means for Pain Relief	n	%
Medicated oil, cream or gel	75	49.3
Massage	54	35.5
Reflexology	4	2.6
Physiotherapy	1	0.7
Acupuncture	3	2.0
Chinese herbs	4	2.6
Medicated plasters	3	2.0
Aromatherapy	3	2.0
Hot water bottle	2	1.3
Meditation	2	1.3
Magna block	1	0.7
Total	152	100.0

Table 6. Common Drugs Used in Cancer Pain Management<sup>25,26</sup>

Drugs and Mechanism	Dosing	Specific Notes
<b>ACETAMINOPHEN</b>		
Not fully elucidated, believed to inhibit the synthesis of prostaglandins in the central nervous system and work peripherally to block pain impulse generation.	(PO) 325 to 1000 mg every 4 to 6 h. Max. dose 4 g/day.	Indicated for mild cancer pain.  Useful adjunct to NSAIDs, opioids and other adjuvant analgesics.
<b>NSAIDs</b>		
Inhibits cyclooxygenase enzymes, which results in decreased formation of peripheral and central prostaglandins precursors.		Indicated for mild to moderate pain, including cancer-related bone pain.  NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including fatal myocardial infarction and stroke.
<b>Celecoxib*</b>	(PO) 200 mg daily or 100 mg every 12 h. Max. dose 400 mg/day.	
<b>Diclofenac</b>	(PO) 50 mg every 8 h. Max. dose 150 mg/day.	NSAIDs may increase risk of gastrointestinal irritation, inflammation, ulceration, bleeding, and perforation.
<b>Ibuprofen</b>	(PO) 400 mg every 4 to 6 h. Max. dose 3200 mg/day.	Use the lowest dose possible, and taking each dose with/immediately after food.
<b>Indomethacin</b>	(PO) 25 to 50 mg every 8 to 12 h. Max. dose 150 mg/day.	Use with caution in elderly.
<b>Ketorolac</b>	(IV/IM) 15 to 30 mg every 6 h. Max. 5 days.	
<b>Mefenamic acid</b>	(PO) 250 mg every 6 h. Max. dose 1000 mg/day.	
<b>Meloxicam</b>	(PO) 7.5 to 15 mg every 24 h. Max. dose 15 mg/day.	
<b>Naproxen</b>	(PO) 250 mg every 8 h or 500 mg every 12 h (naproxen base). Max. dose 1000 mg/day.  (PO) 275 mg every 8 h or 550 mg every 12 h (naproxen sodium). Max. dose 1100 mg/day.	
<b>Sulindac</b>	(PO) 150 to 200 mg every 12 h. Max. dose 400 mg/day.	
<b>OPIOIDS</b>		
Binds to opiate receptors in the central nervous system, causing inhibition of ascending pain pathways, altering the perception of and response to pain.		Drug of choice for moderate to severe pain.  No clinically relevant ceiling effect to analgesia. Dose increases until analgesia is achieved or until unacceptable side effects.
<b>Codeine</b>	(PO) 15 to 60 mg every 4 to 6 h. (IM) 15 to 60 mg every 4 to 6 h.	Extended or sustained release dosage forms should not be crushed or chewed.
<b>Tramadol</b>	Immediate release formulation: (PO) 50 to 100 mg every 4 to 6 h. Max. dose 400 mg/day.  Extended release formulation: (PO) 100 mg once daily. Max. dose 300 mg/day.	Use with caution in elderly.

Table 6. (con't) Common Drugs Used in Cancer Pain Management<sup>25,26</sup>

Drugs and Mechanism	Dosing	Specific Notes
<b>Morphine</b>	Doses and dosage intervals should be titrated to pain relief/prevention. (PO) 5 to 30 mg every 3 to 4 h. (IM) 5 to 10 mg every 3 to 4 h. (IV) 1 to 2.5 mg every 5 min as needed. (SR) 15 to 30 mg every 12 h (may need to be every 8 h in some patients.) Rectal 10 to 20 mg every 4 h.	
<b>Oxycodone</b>	(PO) 5 to 10 mg every 4 to 6 h. Controlled release 10 to 20 mg every 12 h.	
<b>Fentanyl</b>	(IV) 25 to 50 mcg/h. (IM) 50 to 100 mcg every 1 to 2 h. Transdermal 25 mcg/h every 72 h.	
<b>Methadone</b>	(PO) 2.5 to 10 mg every 3 to 4 h (acute). (PO) 5 to 20 mg every 6 to 8 h (chronic).	
<b>ADJUVANT ANALGESICS</b>		
<b>Corticosteroids</b>		
The mechanism of analgesia probably relates to reduction of tumour-related edema, anti-inflammatory effects, and direct effects on nociceptive neural systems.		Agents that have no intrinsic analgesic properties, but increase the effectiveness of opioids.
<b>Dexamethasone</b>	(PO/IV) 4 to 20 mg every 4 to 24 h.	Useful for treatment of neuropathic pain.
<b>Antidepressants</b>		
Inhibition of norepinephrine reuptake appears to be the most important mode of action, but serotonergic and dopaminergic effects also may play a role in analgesia.		
<b>Amitriptyline</b>	(PO) 10 to 25 mg → 150 mg at bedtime.	
<b>Nortriptyline</b>	(PO) 10 mg → 150 mg at bedtime.	
<b>Anticonvulsants</b>		
Represent a diverse group of drugs that vary in mechanisms and clinical effects. Generally decrease neuronal excitability.		
<b>Gabapentin</b>	(PO) 100 to 1200 mg 3 times daily.	
<b>Pregabalin</b>	(PO) 75 to 300 mg daily in 3 divided doses.	

\*COX-2 Selective NSAIDs; IM: Intramuscular; IV: Intravenous; PO: Oral; SR: Sustained Release; Max.: Maximum

these different opioids have increased. Opioid switching refers to the use of an alternative opioid for the purpose of improving analgesia and reducing intolerable side-effects. It is associated with better clinical outcomes in terms of better response to opioids and better side effect profile.<sup>23,24</sup>

**Challenges of Pain Pharmacotherapy:** The use of pharmacology agents is fraught with challenges. There is tremendous inter-individual variability in the response to analgesics. Pharmacogenetics may potentially allow prospective prediction of response to different opioids and facilitate choosing of the correct dose of the correct drug for the correct patient, guiding personalised prescribing.<sup>27</sup> Although there is no clear evidence that genetic markers can be used to predict opioid efficacy or adverse effects in

cancer patients, a recent review has offered insights into pharmacogenomic targets for the management of opioid pain, including efflux transporters, proteins that metabolise drugs, enzymes that regulate the neurotransmitters that modulate pain, and opioid receptors.<sup>28</sup>

**Pain Management: Complementary Approaches and Recent Advances**

**Acupuncture Therapy:** Complementary approaches used for pain management in cancer patients include acupuncture, Chinese herbal medicine and reflexology. Acupuncture is seen as one of the most well-established non-pharmacological or complementary therapies. It is an ancient form of traditional Chinese medicine (TCM) or Oriental medicine, using needles to stimulate specific

acupuncture “anatomical” points in the body to relieve pain. In patients, it has been found that acupuncture increased adrenaline secretion.<sup>29</sup> Animal studies have shown that the needling can modulate substance P,<sup>30</sup> increase secretion of endogenous opioids,<sup>31</sup> normalise catecholamines,<sup>32</sup> and serotonin.<sup>33</sup> Even so, much investigation is still needed to understand the mechanism of actions of acupuncture analgesic effects.<sup>34</sup>

The use of acupuncture for different types of pain such as low back pain, sinusitis, herpes zoster and allergic rhinitis, is well-documented.<sup>35,36</sup> Thus far, very few randomised controlled trials have been performed and reported for the management of cancer pain. Alimi et al<sup>37</sup> have reported a randomised, blinded controlled study in 2003. This trial involved 90 patients who were randomly divided into 3 groups; 1 group received 2 courses of auricular acupuncture, and 2 placebo groups received auricular acupuncture at placebo points and one with auricular seeds fixed at placebo points. Pain intensity decreased by 36% at 2 months from baseline in the group receiving acupuncture; there was little change for patients receiving placebo (2%). There was statistically significant difference between the real acupuncture and placebo groups ( $P < 0.0001$ ). Another single-blinded, randomised, placebo-controlled pilot study, which was the first to test the use of electroacupuncture for neuropathic pain in cancer or palliative care patients, showed high attrition rate and reduction in neuropathic pain in 3 patients receiving electroacupuncture whereas the other 4 patients receiving sham treatment reported little change.<sup>38</sup> This suggests further research is needed.

**Massage Therapy:** Massage is also a component of TCM, and commonly used with acupuncture. It is popular in cancer palliation in the US.<sup>13</sup> It involves manipulating, applying pressure, rubbing or stroking soft tissue and skin to promote relaxation, well-being and circulation. Massage brings about a range of psychological and physiological changes including improvements in cerebral blood flow that provides a comfortable sensation,<sup>39</sup> reduction of pain and muscle relaxation.<sup>40</sup> Similar to acupuncture, the mechanism of how massage works is still being investigated.<sup>41</sup> A recent randomised controlled trial shows that providing massage and acupuncture in addition to usual care resulted in significant decreased pain and depressive mood among postoperative cancer patients when compared with usual care alone.<sup>42</sup> Fourteen trials were included in a systematic review of randomised clinical trials on massage therapy for cancer palliation and supportive care. Despite limitations in design quality, the evidence is encouraging.<sup>43</sup>

**Dietary-Herbal Therapy:** Dietary-herbal therapy refers

to the non-pharmacological approach use of dietary supplements and herbs to manage cancer pain. While few papers are available on herbal use for pain relief,<sup>44,45</sup> even fewer papers focus on cancer pain, and most of the works done are not published in English literature, except for a rather extensive recent review published by Ling Xu et al<sup>46</sup> that suggests that Chinese herbal medicine may be useful for managing cancer pain, at least for short-term application. This review surveyed a total of 115 articles and suggests that Chinese herbal medicine may have similar analgesic effects as Western pharmacological pain killers, where the herbs may reduce the side effects of the conventional analgesics and the various formulations are suitable for cancer patients. Other herbs such as devil’s claw, cat’s claw, camphor and capsicum species are also effective mostly by their analgesic and anti-inflammatory activities,<sup>44</sup> which are similar to the conventional analgesics (Table 6). Readers are encouraged to refer to the relevant reviews and papers for more details.

## Discussion

Among the complementary therapies, acupuncture has been well-documented for relieving of cancer pain. Surprisingly, we found that only 2% reported the use of acupuncture. This is similar to a study in American cancer survivors which found that 1.2% reported the use of acupuncture/acupressure.<sup>13</sup> Pharmacological means was still the major way for patients to relieve their pain; as medicated oil, cream or gel was used by about 50% and only 3.0% reported use of Chinese herbs. The percentage that reported use of massage (35.5%) was higher as compared to the American study which was 11.2% among cancer survivors<sup>13</sup> and less than 10% in a hospice setting.<sup>47</sup> The present study defined the prevalence of pain in the past week which ranged between 41.2% (overall responders, 279/677) and 64% (patients who had pain in the past week and had pain that lasted for more than a week, Fig. 2). This finding is similar to Cleeland’s who reported that 41% of the outpatients with metastatic cancer had pain attributed to the disease process.<sup>48</sup> The Cleeland’s Eastern Cooperative Oncology Group (ECOG) survey showed 67% of the patients reported that they had had pain or had taken analgesic drugs daily during the week preceding the study, and 36% had pain severe enough to impair their function ability. In our Singaporean study population, when patients reported to have had pain in the past week, their pain experience affected their quality of life to a more severe extent (Fig. 2).

There are several issues which need to be attended to. Firstly, although majority of patients who experienced pain were prescribed pain medications, a significant number of more than 60% of these still reported that they had pain in the past week (Fig. 2). Secondly, 37.4% of patients had

difficulties taking pain medication as instructed. The top reasons (Table 4) could be solved by proper patient education on pain management to alleviate the unnecessary fear of ineffectiveness of pain medication, which could still exist in a previous opioid study among cancer patients at the end of life in our Singapore context.<sup>49</sup> The other challenges might be overcome by changing dosage form of pain medications, reducing the number of medications to be taken or improving affordability and accessibility of medications to patients. As this study was done before taking the pain as the fifth vital sign in Singapore health facilities, which was implemented in 2005, it is hoped that in future, patients would be better taken care of, especially for pain problem, as we strive to provide better quality of life to them.

There were some limitations in the prospective survey of NCC patients. As there is a lack of information on the prevalence of pain among the cancer outpatients in Singapore context, the survey was conducted in a nationally representative sample of outpatients. Due to the nature of the study, we tried to capture all patients who attended NCC in both the medical oncology and radiation oncology departments. We did not rule out those patients whose diagnosis were not confirmed when they were first approached to take part in the survey. The main reason we treated all outpatients equally and sensitively was because we did not want to impose stress to the patients, and we did not want to cause further fear and distress for those who had yet to confirm diagnosis. For analysis that involves diagnosis, subjects with 'benign', 'not confirmed' and 'no data' diagnosis were excluded (Table 2). Although including all patients would have increased the capture rate, we did not manage to capture all of the patients as this was a voluntary study. There is a possibility that a greater capture rate may affect the findings. However, in our study, a large majority (92.6%) of patients returned the survey form. We believe that this is a representative sample because the medical oncology and radiation oncology departments of NCC treat the most cancer patients in Singapore. Nonetheless, we did not investigate the aetiology of pain the patients described. It could be due to the disease, the treatment or non-malignant causes, but we managed to identify that 87% of patients were with malignant diagnosis (data not shown). Bearing in mind these limitations, 92.6% returned rate among the responders could be considered remarkable. This leads us to believe that the data can be of assistance for the initiatives to improve pain management in cancer outpatients which is still lacking currently.

The current prospective survey has adopted a non-pharmacological definition for the term 'non-drug methods', which did not itemise other herbal or traditional medicines working as pain medications. The survey could also be improved by itemising the alternative medicines, or

traditional Chinese medicines as additional options to the non-drug methods that had been included in the survey form, such as acupuncture, rubbing oil, and massage. It was postulated that non-drug use methods among the study population were under-reported. As patients would like to try all options regardless of its pain-relieving efficacy, respecting patients' right to well-being and using pain management requires an open mind and sincere communication. Healthcare providers such as physicians, pharmacists and nurses should discuss with the patients with regards to other alternative medicines patients are taking, so as to reduce potential side effects due to drug interactions or polypharmacy problems.

## Conclusion

The percentages of Singapore patients attending NCC who had pain lasting more than a week, normal daily activities affected, appetite affected and sleep affected were 64.4%, 47.3%, 43.4% and 55.8% respectively. Pain is a significant symptom in outpatients attending a cancer centre, affecting almost half of patients. Over one-third of patients had difficulty taking the pain medication as instructed. Self-medication using non-pharmacological methods to relieve pain was reported and reveals that pain may be not adequately treated. Although majority of patients who suffered from pain reported to doctors, much medical effort is still needed to help patients to relieve their pain.

Recently, due to the paucity of quality trials involving acupuncture for chronic pain, a trialists' collaboration has been formed and hopefully such collaboration can provide the most reliable basis for treatment decisions about acupuncture using individual patient data meta-analysis of high-quality trials.<sup>50,51</sup> It is also expected that such approach can serve as a model for future studies in acupuncture and other complementary therapies. Acupuncture has been integrated into palliative care settings in the United Kingdom but is yet to be widely offered in the United States and Singapore. However, it is underutilised in the United States<sup>52</sup> and also Singapore. Lately, acupuncture has also been tested in a randomised controlled trial to treat aromatase inhibitors associated musculoskeletal pain and it has been found that the breast cancer patients who received acupuncture had significant improvement of joint pain and stiffness.<sup>53</sup> Moreover, acupuncture can be potentially used as adjunctive care in palliative and end-of-life care.<sup>54</sup> It is also effective against chemotherapy induced nausea and vomiting,<sup>55,56</sup> including paediatric patients in a randomised pilot trial.<sup>57</sup> The most recent review suggested that it is effective and presents low risk in children when used properly.<sup>58</sup> Therefore, there is good evidence of the benefit of using acupuncture, and this may warrant its inclusion into the mainstream medical treatment. The benefit of

combining Chinese medicines, Western medicine such as morphine and acupuncture has yet to be fully explored while benefits has been shown.<sup>59</sup>

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