CHAPTER 3

METHODOLOGY

This chapter describes the methodological approach adopted for developing this thesis. It covers in detail the study setting, pilot study, fieldwork procedures, sample size calculation, data management and analysis.

3.1 Study settings and samples

Before the main study was conducted, a pilot study was carried out to evaluate the feasibility of recruiting study samples (patients with cancer pain who diagnosed with either lung cancer, liver cancer, breast cancer, or cervix cancer) in two government hospitals, one with a pain clinic and the other without pain clinic. Finally, the result of the pilot study revealed that the patients from a university-based pain clinic and a regional cancer center who were diagnosed with cancer would be feasible for this study. The methodology and the results from the pilot study that be rendered to modify the methodology of the main study were presented in the part of the pilot study.

3.2 Study design and justification

A cross-sectional study was carried out in the selected settings due to the consideration on the logistic, the time and cost efficiency, the evaluation of the wide range of exposure related to the pain treatment outcomes, and the interrelationship among these factors. Furthermore, the information provided by the cross-sectional studies was essential for public health administrators.

3.3 Assessment

All questionnaires, including the Thai-BPI (Cleeland, 1988), the Thai-HADS (Nilchaikovit, Lortrakul, & Phisansuthideth, 1996), The Thai-FACT-G

(Rattanatharathorn et al., 2001), the BQ-II (Gunnarsdottir, Donovan, Serlin, Voge, & Ward, 2002), and the physicians' questionnaire (Ger, Ho, & Wang, 2000), were used in this study with permission.

3.3.1 Main outcome variables:

Pain intensity was measured by the BPI (Appendix B)

The single item of worst pain from BPI is categorized into 2 levels of pain control as adequate (score 0-3) vs inadequate (score 4-10).

Pain management index (calculation method was described in the operation definition)

Quality of life was measured by the Thai- FACT-G (Appendix D)

Depression was measured by the Thai-HADS (Appendix E)

The sum scores of 11 or higher of even numbers was considered a indicative of depression.

3.3.2 Main exposure variable: Clinical settings included

3.3.2.1 Institutional barriers involved opioid drugs availability and other barriers. An in-depth interview with pharmacists and physicians in two study settings was used to refine the issues of their institution barriers to cancer pain management.

3.3.2.2 Physicians' factors including knowledge and attitudes of opioids prescribing were measured by the questionnaire modified in part from the previous study (Ger, Ho, & Wang, 2000) (Appendix F- I). Regularity of pain assessment was also observed from each patient's medical record indicating whether the treating physician had recorded his/her own pain assessment on each visit.

3.3.3 Potential confounders: Patients' factors included

Demographic variables included age, gender

Clinical factors included stage of cancer, presence of bone metastasis, number of pain sites, duration of pain, dosage of opioid prescribed per day.

Patients' barriers was measured by the modified BQ-II (Gunnarsdottir, Donovan, Serlin, Voge, & Ward, 2002) (Appendix C)

Stage of cancer: Cancer staging was classified based on the TNM system (International Union Against Cancer (UICC), 1987). This system uses three significant events in the life history of a cancer. First, tumor size (T) refers to the extent of primary tumor. Second, regional lymph node involvement (N) indicates the absence or presence and extent of regional lymph node metastasis. Third, distant metastasis (M) is an important marker for the advanced disease that indicates the absence or presence of distant metastasis. A number (1-4) is added to each letter to indicate the size or extent of the tumor and the extent of spread. The higher number indicated the more advanced stage of disease. The stage of cancer information in this study was obtained from each patient medical record.

Presence of bone metastasis was obtained from each patient medical record

Number of pain site: The number of cancer-related pain sites was reported by the patient in the BPI instrument.

Duration of pain: The length of time which a patient had experienced pain related to cancer reported by the patient.

Opioids dosages: Average dosage of opioid analgesic prescribed were calculated to equianalgesic oral morphine doses for each patient, do not include rescue doses. The opioid analgesic medications were obtained from the patient's medical record.

3.4 Study procedure

3.4.1 Pilot study (June 2007- February 2008)

3.4.1.1 Objectives

1. To assess the feasibility of recruiting subjects and sample size
2. To prepare and pretest the instruments that were not available in Thai versions

3. To develop and refine concepts of institutional barriers to cancer pain management by using in-depth interview techniques with healthcare providers.

4. To measure the physicians' knowledge and attitudes toward the optimal use of analgesics as well as their perceived barriers to cancer pain management.

3.4.1.2 Procedures

1. A study of pilot fieldwork

In order to assess the feasibility of the methodology, the pilot was first carried out at the outpatient clinic of Gynecological and Surgical department of a university hospital. Samples were recruited through the registration list at the study site. During the first two weeks in June 2007, all of patients with cervix or breast cancer (N=12) were approached. All of them had reported no pain within previous 7 days. This may have been due to the patients were mostly in an early cancer stage on curable treatment, resulting in no pain developed. This observation also explained a small amount of opioid analgesic consumption within this hospital. Consequently, it was unlikely to recruit an adequate sample within a time constraint. However, effort was made to change the study setting to the regional cancer center, located in the suburb of Bangkok Metropolitan.

At the regional cancer center, the pilot was made to assess the possibility of recruiting a sample with the same methodology above. It was found that most referral cancer patients were hospitalized during their treatment such as chemotherapy or radiotherapy. After a completion of such treatment course, they would be referred back to their host hospital. Most cancer out-patients were newly treated patients and were about to be placed on chemotherapy or radiotherapy. Therefore, hospitalized patients were easier and more suitable to recruit than the out-patients.

At the pain clinic, the pilot was carried out on the out-patients in order to assess the feasibility of recruiting a sample. The cancer patients at this setting all had experienced pain and were receiving pain treatment. Although cancer of lung, liver, breast and cervix are the most prevalent forms of cancer in Thailand, fewer of

them were seen at the out-patient pain clinic. However, there were varieties of cancer sites formed among the pain clinic patients. Due to the time constraint and limited resources, we decided to recruit all those with cancer pain regardless of their primary cancer site. The pilot was carried out between June 2007 and October 2007

It was found that most of the participants were not able to answer the questions regarding their certain medical characteristics including cancer staging, metastasis status and analgesic drug prescription. Therefore, we used the patients' medical records to obtain those data with the permission from both the patients and their physicians.

2. Instruments preparation

The instruments to be used in this study were originally developed in the English language. The Brief Pain Inventory (BPI), the Functional Assessment of Cancer Therapy-General Scale (FACT-G), the Hospital Anxiety and Depression (HADS) were already available in Thai versions. But the Barriers Questionnaire (BQII) was not available in Thai versions. The original BQ-II was translated into Thai by using the Cross-Cultural Adaptation techniques (Gullemin, Bombardier, & Beaton, 1993). There are three steps including (1) Translation: the process of translation from English to Thai by two Thai mother tongue translators. One was aware of the objects underlying the material to be translated and the concepts involved. The other was an English language expert, (2) Back translation: the process of translation of the Thai questionnaire from the first step to an English questionnaire by two English mother tongue translators who were also Thai language experts, (3) Committee review: the process of comparison between the original English questionnaire and the back translated English questionnaire. This process was carried out by three English experts. They considered the introduction/instruction, content and scaling of response of the questionnaire.

During the translation process, the word "cancer", when translated is "มะเร็ง" read "MA-RENG" which has a very strong negative connotation for Thai people. Whether or not subjects knew their diagnosis of cancer, they usually did not acknowledge it (Petpichetchian, 2001). Both patients and healthcare professionals in Thailand avoid the use of the term "มะเร็ง". They use another term, "เนื้องอก", read

"NUE-NGOK", that is similar to the term "tumor" in English. Therefore, the latter Thai word was used in the Thai version of the instruments to refer to cancer and cancer pain.

3. A study of healthcare institutional barriers

Two pharmacists from each of the two settings who were responsible for opioid drugs administration and three physicians in the pain clinic were invited to participate in the interview. However, the physicians in the cancer center refused to participate.

Each in-depth interview was performed by the researcher. Discussions were recorded on tape and transcribed. The topics focused on the healthcare institution barriers to cancer pain treatment including the opioids adequacy and the pain treatment facility. All participants gave informed consent for their participation and they were assured that all information would be treated confidentially. All the interviews were held in their settings between November 2007 and January 2008. The duration of each interview was approximately thirty minutes.

The interview topic guidance centered on the following key facets.

1. The general questions for all participants were as follows:

- What are the obstacles to opioid analgesics availability in their hospitals? For example, a shortage of opioid analgesics, a small variety of opioid drug forms
- How often did the obstacles take place?

2. The specific questions for the physicians were as follows:

- What are the roles of the pain clinic in cancer pain management?"

4. A study of physicians' factors

Physicians from the two settings were approached to complete a self administered questionnaire ((Appendix F-I) after giving their written informed consents. All of them were providing cancer patient care in the present study. All physicians of the cancer center completed the questionnaire.

3.4.1.3 Pilot results and discussion

1. Pilot fieldwork results

Changes made to the study setting

Given concerns to look for another hospital with no pain treatment facility available, a regional cancer center in the suburb of Bangkok Metropolitan was selected to replace. The regional cancer center is a specialized oncology provided particularly chemotherapy and radiotherapy covering 5 surrounding provinces in the suburb of Bangkok metropolitan. Referral cancer patients at this setting are mostly attending to receive cancer treatment and soon turn back to their referred hospital. The majority of patients appear to be hospitalized during their course of treatment either chemotherapy or radiotherapy. As a result, hospitalized unit at this hospital was carried out to ensure adequate samples for the main study.

Changes in the primary cancer:

Although the pain clinic and the cancer center were a specialized setting for cancer patients, fewer patients with specific primary cancer at lung, liver, breast or cervix were found. Concerned the time constrain, any types of primary cancer should be recruit in order to obtain more samples without reflecting to the objective of the study.

Results of pilot fieldwork study

Sample characteristics:

Ninety-four patients who experienced cancer related pain, with 71 patients from the pain clinic and 23 patients from the cancer center were eligible. Six eligible patients felt exhausted and refused to participate, leaving 88 successfully completed interviews. The mean age was 57.1 years ranging from 32 to 84 years. Sixty-three percent of patients were female. The majority religion was Buddhism (95.5%) (Table 3.1)

The distribution of primary cancer sites by gender is described in Table 3.2. Lung cancer was the most common of the primary cancer sites (n=16, 18.2%). Seventy percent were at stage 4. Subjects experienced cancer related pain for 9.8 months ranging from 1 to 96 months. At least one site cancer-related pain was identified (30.7%) with the mean of 2.2 sites ranging from 1 to 5 sites (see Table 3.3)

The main outcomes:

The three main outcomes are summarized by setting in Table 3.4. Between the pain clinic and the cancer center patient group, using the classification of pain control into adequate (worst pain score ≤ 3) vs inadequate (worst pain score >3), inadequate pain control was found 46.2 % and 60.9% respectively. The pain clinic group had better quality of life and less prevalent of depression than in those in the cancer center group.

Table 3.1

Clinical setting and demographic factors

Demographic variables	Number (%) of the patients			Chi square	P-value
	Total n=88	Pain clinic n=65	Cancer center n=23		
Gender					
Male	32 (36.4)	27 (41.5)	5 (21.7)	2.878	0.09
Female	56 (63.6)	38 (58.5)	18 (78.3)		
Education level					
Primary level or less	42 (47.7)	29 (44.6)	13 (56.5)	0.965	0.326
Secondary level or higher	46 (52.3)	36 (55.4)	10 (43.5)		
Marital status					
Married	64 (72.7)	47 (72.3)	17 (73.9)	0.758	0.684
Widowed/separated	19 (21.6)	15 (23.1)	4 (17.4)		
Single	5 (5.7)	3 (4.6)	2 (8.7)		
Religion					
Buddhism	84 (95.5)	64 (98.5)	20 (87.0)	5.183	0.023
Christian/Islam	4 (4.6)	1 (1.5)	3 (13.0)		

Table 3.2

Distribution of primary cancer sites by gender

Primary cancer Site	Number (%) of the patients		
	Female n =56	Male n=32	Total n=88
Lung	10 (17.9)	6 (18.8)	16 (18.2)
Breast	13 (23.2)	0	13 (14.8)
Cervix	9 (16.1)	0	9 (10.2)
Colon & rectum	7 (12.5)	2 (6.3)	9 (10.2)
Liver	5 (8.9)	2 (6.3)	7 (8.0)
Prostate	0	5 (15.6)	5 (5.7)
Other	12 (21.4)	17 (53.1)	29 (33.0)

Table 3.3

Clinical setting and oncological factors

Variables	Total N=88	Pain clinic n=65	Cancer center n=23	Chi square	P-value
Cancer stage					
Stage 1-3	16 (18.2)	8 (12.3)	8 (34.8)	7.391	0.025
Stage 4	61 (69.3)	50 (76.9)	11 (47.8)		
Not specified	11 (12.5)	7 (10.8)	4 (17.4)		
Number of pain sites					
One site	27 (30.7)	14 (21.5)	13 (56.5)	11.249	0.004
Two sites	30 (34.1)	23 (35.4)	7 (30.4)		
3- 5 sites	31 (35.2)	28 (43.1)	3 (13.0)		
Duration of pain : months					
Mean $\pm$ SD	9.8 $\pm$ 12.8	11.7 $\pm$ 14.3	4.3 $\pm$ 3.5	T=2.428	0.0173
Range	1 - 96	1 - 96	1 -12		

Table 3.4

The percentage of pain control, depression and quality of life score by setting

Variables	Total n=88	Pain clinic n=65	Cancer center n=23
Pain control (% patients)			
Inadequate	44 (50.0)	30 (46.2)	14 (60.9)
Adequate	44 (50.0)	35 (53.9)	9 (39.1)
Depression (%prevalence)			
No depressed	76 (86.4)	54 (83.1)	22 (95.7)
Depression	12 (13.6)	11 (16.9)	1 (4.4)
Quality of life (score)			
Mean total score	72.9	71.5	77

2. Instrumental preparation results

The instrument preparation results were made to change several aspects.

Changes to the eligibility criteria with regard to the drug titration period:

According to the pilot fieldwork process, hospitalized cancer patients of the regional cancer center were selected as a recruiting site instead of the out-patients of a university hospital. Given concerned about the adequacy period for drug titration, surveys suggest that one week probably is adequate to assess the effectiveness of cancer pain management (Hagen, Elwood, & Ernst, 1997; Klepstad, Kaasa, Skauge, & Borchgrevink, 2000). It was found that hospitalized patients in the cancer center were seen by their physician every morning. Therefore, the hospitalized patients would be approached if they were treated at this center for at least one week. But this criterion could not be used with the pain clinic out-patient, since the time interval between follow-up appointments for out-patients by their responsible physicians were usually on a two weeks follow-up during the beginning of drug titration period. Most patients' pain was expected to be stabilized by the first or second visit. Consequently, samples would be conducted if they have received treatment at the pain clinic for at least one month.

Changes made to the BQ-II instrument:

A pretest of all measures in Thai version was conducted on 65 pain clinic outpatients and 23 cancer center inpatients. It was found that patients found it difficult to answer many questions of the translated Thai version of the BQ-II and asked to why some items that had similar meaning. Finally, we simplified and shortened the BQ-II from 27 items into 14 items and 2 additional questions as shown in Table 3.5. One was suggested by the respondents "Pain medicine can harm your kidney or liver" and the other was an open-ended question "Do you have any additional concerns, not addressed in this questionnaire, that might prevent you from using pain medication to treat pain, or that might prevent you from wanting someone close to you using pain medication to treat pain?".

Table 3.5

Comparison of BQ-II between original version and modified version using in the main study with its reasons

Original version	Modified version	reason
3. Drowsiness from pain medicine is difficult to control 5. Confusion from pain medicine can not be controlled. 10. Nausea from pain medicine can not be relieved. 14. Pain medicine makes you say or do embarrassing things. 17. Constipation from pain medicine can not be relieved. 20. It is easier to put up with pain than with the side effects that come from pain medicine.	1. Similar to the original version. 2. Similar to the original version. 3. Similar to the original version. 4. Similar to the original version. 5. Similar to the original version. 6. Similar to the original version.	
6. When you use pain medication your body becomes used to its effects and pretty soon it won't work any more 15. If you take pain medicine when you have some pain, then it might not work as well if the pain becomes worse. 21. If you use pain medicine now, it won't work as well if you need it later.	7. Using pain medicine frequently, you then become drug tolerance.	Same meaning
7. Using pain medicine blocks your ability to know if you have any new pain. 16. Pain medicine can keep you from knowing what's going on in your body. 22. Pain medicine can mask changes in your health.	8. Pain medicine can mask change in your body, for example, it blocks you from knowing whether disease is better or worse.	Same meaning

Table 3.5 (Continued)

Original version	Modified version	reason
1. Cancer pain can be relieved 2. Pain medicine can effectively control cancer pain. 24. Medicine can relieve cancer pain.	9. Cancer pain can be treated to reduce pain.	Same meaning
11. It is important to be strong by not talking about pain 25. Doctors might find it annoying to be told about pain. 27. If I talk about pain, people will think I'm a complainer.	10. You will talk about pain until you are unbearable 11. Similar to the original version.	Same meaning
12. It is important for the doctor to focus on curing illness, and not waste time controlling pain. 18. If doctors have to deal with pain they won't concentrate on curing the disease. 26. Reports of pain could distract a doctor from curing the cancer.	12. It is important for the doctor to focus on curing illness, and not waste time controlling pain	Same meaning
2. There is a danger of becoming addicted to pain medicine. 9. Many people with cancer get addicted to pain medicine. 23. Pain medicine is very addictive.	13. If you have used pain medicine for a long time, you will become drug addict.	Same meaning

Table 3.5 (Continued)

Original version	Modified version	reason
4. Pain medicine weakens the immune system. 13. Using pain medicine can harm your immune system. 19. Pain medicine can hurt your immune system.	14. Pain medicine weaken the body and decreases the immune system	
	15. Pain medicine can harm your kidney or liver.	Same meaning
	16.Do you have any additional concerns, not addressed in this questionnaire, that might prevent you from using pain medication to treat pain, or that might prevent you from wanting someone close to you using pain medication to treat pain?”	Same meaning

3. Healthcare institutional barriers

Results

Five respondents included pharmacists from the two hospitals (one has been working with a comprehensive opioid drugs administration for more than 15 years at the pain clinic hospital while the other has been working for 2 years at the cancer center) and three physicians from the pain clinic (two were female instructors with 56 and 54 years of age and one was a fellow)

Regarding opioid analgesics availability:

All participants agreed that the opioid analgesics were available for prescribing at the two settings all the year. No shortages of such opioid analgesics were found. The Pharmacy Department in both hospitals can provide all items of opioid analgesics as supplied from the Thai FDA.

The two female instructors though that it is reasonable for the hospitals to have all the items of opioid analgesics supplied by the Thai FDA due to the high amount of patients. However, it should have more varieties of such drugs to serve the different needs of each patient in terms of response to opioid analgesics and the side effects of the drugs. Therefore, the drug items should depend on the facility of each hospital or the amount of patients.

The pain clinic hospital pharmacist:

"*Because opioid analgesics were necessary for particular cancer cases and there were not any other drugs to replace them. Therefore, any dosage form of opioid analgesics that the Thai FDA supplied would be available in the hospital. In recent year, there were no problems with the Thai FDA in purchasing drugs. We got all drugs as we want. In addition, we make a provision plan based on data when we make a decision to order drugs from the Thai FDA.……in recent 3-4 years, we have never received any complaints about the shortage of opioid analgesics caused by the Thai FDA or drug quality problems from the physicians and patients*"

The cancer center pharmacist:

"A*ll physicians in the hospital are appointed as members of the DTC (Drug and Therapeutic Committee) and they all agreed to include opioid analgesics on the hospital drug list. Because we have no pain specialist, cancer pain patients are treated by their oncologist. Therefore, we purchase all dosage forms of opioid analgesics that are allowed and supplied by the Thai FDA*".

The female instructor with 56 years old:

"*At present, the provision system of the Pharmacy Department is able to consistently supply the morphine to the patients……..According to WHO guidelines, morphine is the minimum requirement for cancer pain management. However, the quality of pain treatment is not so effective because each patient has individual difference in responding to the opioid analgesics in terms of the degree of their pain control and side effects. The more drugs the hospital has, the more effective treatment the patients will have……General speaking, it would be sufficient to have only one analgesic drug as a prototype, that is morphine……., However, if it is possible, the hospital should have more varieties of analgesic drugs because each drug has different benefit".*

The female instructor with 54 years old:

"*The hospital should have more varieties of opioid analgesics as other developed countries have for use by the physicians. Therefore, the physicians, the specialists in palliative can prescribe most appropriate opioid analgesics. This will give patients for better quality of life."*

Regarding the role of pain clinic in cancer pain management:

In order to achieve cancer pain management, the two out of three participants in the pain clinic suggested that pain control should ideally be managed with multimodality approach so the multidisciplinary care is necessary. Therefore, the characteristic of pain clinic should be as multidisciplinary team approach comprising of different specialized healthcare professionals, such as physician, psychiatrist,

physiologist and rehabilitation physician, and nurse, working together in the same place particular in the pain clinic. A physician compared multidisciplinary care as "one stop service." However, the pain management in the pain clinic in this study was not actually the multidisciplinary care. It is just as the interdisciplinary care and some cancer patients could suffer from referring system.

The female instructor with 56 years old:

"*Cancer pain needs to be treated as multimodality care. The pattern of cancer pain management provided by this hospital is as the interdisciplinary care, not as really the multidisciplinary care. After one modality at one department finished, the cancer patients would be referred to the next modality in the other department. For example, the cancer patient that had received the treatment from the pain clinic will be refused to the Oncology department. Unfortunately, some disadvantages could be obtained from such "inter-disciplinary care".*

The female instructor with 54 years old:

"*Because our setting is not really a desirable pain clinic like multidisciplinary approach, the cancer pain treatment plan could be interrupted and the patients must make a new appointment because there was neither special queue nor time for the follow-up patients at the referral department. Furthermore, the referring system could also make them trouble, exhausted and even more pain due to a long distance between departments".*

The pain clinic physician (fellow):

"*There are at least 2 anesthesiologists working at the pain clinic everyday, while a physician specialized in physiologist and rehabilitation is available twice a week on Tuesday and Friday. The other one psychiatrist is available only once on Wednesday."*

Discussion

Although less varieties of opioid analgesic items was considered as the barriers to cancer pain management**,** all items of them that were supplied by the

Thai FDA was fully available in the hospitals. The more drugs the hospital could possess, the better pain control the patients would have. All physicians of this study are entitled to prescribe the appropriate opioid analgesics to the particular patients. It could be concluded that there were not any problems related to institution restriction in particular shortage of opioid analgesics among physicians in this study. Therefore, no factors related to such barriers that could be influenced to pain outcomes for this study. As a result, the institution barriers to cancer pain management should be excluded from the analysis of the main study.

4. Physicians' factors

Results

Physicians' characteristics

The demographic and practice characteristics of the 16 physicians who responded to the questionnaires are presented in Table 3.6. All specialists at the pain clinic were anesthesiologists whereas specialties at the cancer center consisted of 3 (50%) radiologists, 2 (33%) oncologists and 1 (17%) surgeon. Between the two groups of physicians at the pain clinic and the cancer center, the median (min/max) number of cancer patients cared for per physician within the recent month was 15 (10/60) and 55 (13/80) respectively. All of the physicians agreed that patient is the best judge of cancer pain intensity. All physicians have trained or attended cancer pain management workshops and also had experience of prescribing opioid of slow-released or skin patched form. They all informed that the WHO ladder is the guideline for treating cancer pain in their medical practice.

Regarding attitudes toward the optimal use of analgesics for cancer pain management

The responses of physicians to the attitude questions classified by medical settings are shown in Table 3.7. Between the pain clinic physicians and the cancer center physicians, most of them (80% vs 83%) felt that cancer pain in their settings relieve adequate pain treatment.

Regarding knowledge of opioid prescribing:

Between two groups of physicians at the pain clinic and the cancer center, the mean (SD) score was 4.2 (0.4; range 3.6 – 5.0) and 3.9 (0.4; range 3.1- 4.3) for the scale of knowledge to prescribe opioids respectively. The response of physicians to knowledge questions are shown in Table 3.8. Each individual mean score was higher than 3.0 out of a perfect mean score of 5.0, which probably displayed better knowledge of opioid prescribing.

Regarding attitudes toward opioid prescribing:

Between two groups of physicians at the pain clinic and the cancer center, the mean (SD) score was 4.1 (0.5; range 3.3 – 4.8) and 3.9 (0.7; range 3.3 – 4.8) for the scale of attitudes to prescribe opioids respectively. The response of physicians to each item is shown in Table 3.9. All respondents both in the pain clinic and the cancer center had each individual mean score over 3.0.

Regarding identified barriers to optimal pain management:

Physicians were asked to rank a list of 14 potential barriers to optimum cancer pain management in terms of how they might impede in their setting. Table 3.10 lists the number and percentage of physicians who ranked each item as one of the top three barriers. Among the pain clinic physicians, the most important barriers to adequate pain management identified were inadequate staff knowledge of pain management and inadequate type of analgesic opioids and fewer varieties. Among the cancer center physicians, the most important barriers to adequate pain management identified was lack of access to opioid analgesics because of its higher price.

Regarding pain assessment

Patients' medical records were observed whether there was documented pain assessment by their physicians. There was intensive pain assessment with detailed, including pain severity, pain characteristics in the pain clinic while only the cases with severe pain were assessed by the nurse not by physician in the cancer center.

Table 3.6

Background characteristics of physicians

by setting

Characteristics	Number (%) of the physicians		
	Total (n=16)	Pain clinic (n=10)	Cancer center (n=6)
Gender			
Male	5 (31.3)	1 (10.0)	4 (66.7)
Female	11 (68.8)	9 (90.0)	2 (33.3)
Age: years			
Mean ± SD(range)	36.5±9.3 (28-56)	36.8±10.4 (28-56)	36.0±7.9 (28-50)
28-40 years	13 (81.3)	8 (80.0)	5 (83.3)
41-50 years	1 (6.3)	0	1 (16.7)
51-58 years	20 (12.5)	2 (20.0)	0
Medical specialty			
Anesthesiologist with pain subspecialty	8 (50.0)	8 (80.0)	0
Anesthesiologist	2 (12.5)	2 (20.0)	0
Radiologist	3 (18.8)	0	3 (50.0)
Oncologist	2 (12.5)	0	2 (33.3)
Surgeon	1 (6.3)	0	1 (16.7)
Number of cancer patients being cared for in the past month			
Median (range)	35 (10-80)	15 (10-60)	55 (13-80)
Number of months in clinical practice to cancer patients			
Median (range)	10 (0.5 - > 240)	8 (0.5 - > 240)	28 (9 - > 240)

Table 3.7

Physicians' attitudes toward the optimal use of analgesic for cancer pain management

Attitudes	Number (%) of the physicians		
	Total (n=16)	Pain clinic (n=10)	Cancer center (n=6)
Cancer pain among cancer patients in your medical setting			
Most patients receive adequate pain treatment	13 (81.3)	8 (80.0)	5 (83.3)
Most patients in pain are under-medicated	3 (18.8)	2 (20.0)	1 (16.7)
The appropriate pain relief in your medical setting			
Pain is completely abated	2 (12.5)	-	2 (33.3)
Pain is diminished, noticed but not distressing	14 (87.5)	10 (100.0)	4 (66.7)
What percentage of pain can be relieved with pharmacological pain relievers?			
80%	15 (93.8)	10 (100.0)	5 (83.3)
100%	1 (6.3)	-	1 (16.7)
At what stage would you feel it is appropriate for a patient to receive maximal doses of analgesics for severe pain without consideration about tolerance?			
Prognosis < 24 months	3 (18.8)	2 (20.0)	1 (16.7)
Not concerned with survival time	13 (81.3)	8 (80.0)	5 (83.3)
The incidence of addiction to opioid analgesics in cancer patients is:			
< 0.1%	8 (50.0)	7 (70.0)	1 (16.7)
0.1 - 1 %	6 (37.5)	3 (30.0)	3 (50.0)
1 - 10 %	2 (12.5)	-	2 (33.3)
When a cancer patient requests increasing amounts of analgesic to control pain, this usually indicates:			
Patient is experiencing increased pain	12 (75.0)	8 (80.0)	4 (66.7)
Patient has developed tolerance to drug	2 (12.5)	1 (10.0)	1 (16.7)
All of the above	2 (12.5)	1 (10.0)	1 (16.7)
Who is the best judge of cancer pain intensity?			
Patients	16 (100.0)	10 (100.0)	6 (100.0)
Which measure was the most use in your setting?			
Visual analog scale	6 (37.5)	4 (40.0)	2 (33.3)
Numerical rating scale	10 (62.5)	6 (60.0)	4 (66.7)

Table 3.8

The number (%) of physicians' knowledge of opioid prescribing

Items	% physicians of the pain clinic					% physicians of the cancer center				
	Strongly agree	Agree	No opinion	Disagree	Strongly disagree	Strongly agree	Agree	No opinion	Disagree	Strongly disagree
1.When patients need potent opioids, I would prescribe meperidine rather than morphine.	-	-	-	3 (30.0)	7 (70.0)	-	-	1 (16.7)	3 (50.0)	2 (33.3)
2.Meperidine causes less harmful effects (such as tolerance. addiction. or side effect) in long-term opioid use.	-	-	-	1 (10.0)	9 (90.0)	-	-	-	4 (66.7)	2 (33.3)
3. For cancer patients with moderate or severe pain. I would prescribe meperidine 50 mg q 4 h.PRN.	-	1 (10.0)	-	3 (30.0)	6 (60.0)	-	-	2 (33.3)	3 (50.0)	1 (16.7)
4. For patients who using strong opioid and still experienced persistent and severe pain, I would increase that opioid dosage.	2 (20.0)	5 (50.0)	2 (20.0)	1 (10.0)	-	1 (16.7)	5 (83.3)	-	-	-
5. Administering opioids in a PRN dosing schedule can decrease the harmful effect of opioids, such as tolerance, addiction, or side effect.	-	1 (10.0)	1 (10.0)	3 (30.0)	5 (50.0)	-	2 (33.3)	-	2 (33.3)	2 (33.3)
6. Most patients prefer the parenteral administration to oral administration.	1 (10.0)	1 (10.0)	1 (10.0)	5 (50.0)	2 (20.0)	-	1 (16.7)	2 (33.3)	2 (33.3)	1 (16.7)
7. Parenteral administration is as efficacious as oral administration in pain management.	2 (20.0)	1 (10.0)	-	6 (60.0)	1 (10.0)	1 (16.7)	1 (16.7)	-	4 (66.7	-
8. The absorption of oral morphine in the GI tract is slow and incomplete. Even though my patients can eat food normally. I do not like them to take morphine orally.	-	-	-	4 (40.0)	6 (60.0)	-	-	-	3 (50.0)	3 (50.0)

Table 3.9
The number (%) of physicians' attitudes toward opioid prescribing

Items	% physicians of the pain clinic					% physicians of the cancer center				
	Strongly agree	Agree	No opinion	Disagree	Strongly disagree	Strongly agree	Agree	No opinion	Disagree	Strongly disagree
1. When prescribing opioids, I would be very careful in the control of dosage and frequency for the prevention of drug tolerance and addiction.	1 (10.0)	2 (20.0)	-	4 (40.0)	3 (30.0)	-	-	-	5 (83.3)	1 (16.7)
2. When I prescribe opioids, I would insinuate to patients or their relatives that they had better bear the pain as much as possible before using opioid drugs.	-	-	1 (10.0)	6 (60.0)	3 (30.0)	-	-	-	4 (66.7	2 (33.3)
3. When I find patients who bear severe pain and refuse the morphine injection. I would encourage their behavior.	-	-	1 (10.0)	5 (50.0)	4 (40.0)	-	2 (33.3)	1 (16.7)	1 (16.7)	2 (33.3)
4. I do not like to prescribe opioids because respiratory depression is a very severe side effect.	-	-	-	6 (60.0)	4 (40.0)	-	-	1 (16.7)	3 (50.0)	2 (33.3)
5.For patients with severe nausea or vomiting, I would prescribe opioids infrequently or with lower dosage only.	-	-	-	3 (30.0)	7 (70.0)	-	-	1 (16.7)	3 (50.0)	2 (33.3)
6. For patients with severe nausea or vomiting, it should be prescribed anti-vomiting drug.	4 (40.0)	3 (30.0)	2 (20.0)	1 (10.0)	-	1 (16.7)	3 (50.0)	-	2 (33.3)	-
7. For patients with severe drowsiness, I would stop prescribing opioid drugs.	1 (10.0)	2 (20.0)	3 (30.0)	4 (40.0)	-	-	2 (33.3)	-	4 (66.7	-
8. For patients with severe constipation, I would prescribe opioids infrequently or with lower dosage without considering re-occurred pain.	-	-	2 (20.0)	2 (20.0)	6 (60.0)	-	-	-	5 (83.3)	1 (16.7)

Table 3.10

Identified barriers to cancer pain management

by setting

Type of barriers	Number (%) of the physicians	
	Pain clinic (n=10)	Cancer center (n=6)
Physician reluctance to prescribe opioids	-	-
Inadequate staff knowledge of pain management	5 (50.0)	1 (16.7)
Inadequate pain assessment	1 (10.0)	2 (33.3)
Lack of oral strong opioids provided by pharmacy	1 (10.0)	0
Lack of pain specialists	-	2 (33.3)
Nursing staff reluctance to administer opioids	4 (40.0)	-
Patients' reluctance to take opioids	4 (40.0)	1 (16.7)
Patients' relatives' reluctance to permit patients to take opioids	3 (30.0)	-
Patients' reluctance to report pain	-	2 (33.3)
Excessive regulation of opioids in pharmacy	2 (20.0)	2 (33.3)
Excessive regulation of opioids prescribing in the Thai FDA	1 (10.0)	2 (33.3)
Inadequate type of analgesic opioids and fewer varieties	5 (50.0)	-
Lack of access to opioid analgesics because of its higher price	3 (30.0)	4 (66.7)
Lack of Clinical practice guidelines in your setting	1 (10.0)	1 (16.7)

Discussion

Physicians' knowledge and attitudes

The study showed that a large majority of physicians (81%) believed that cancer pain control treatment in their practice setting (the pain clinic and the cancer center) was adequate for pain relief, in contrast to other studies (Ger, Ho, & Wang, 2000; Von Roenn, Cleeland, Gonin, Hatfield, & Pandya, 1993). They also displayed more positive attitudes toward analgesic medication than physicians in other studies (Ger, Ho, & Wang, 2000; Von Roenn, Cleeland, Gonin, Hatfield, & Pandya, 1993). All of them set the target of pain relief at complete pain relief (12%) or diminished level without distressing (87%). This result was quite similar to Ferrell et al's study, which showed that 98% healthcare professionals correctly believed that patients should not have to endure pain (Ferrell, Dean, Grant, & et al, 1995).

For assessing knowledge to prescribe opioids, the findings showed that no physicians had his/her mean score equal to or less than 3 out of a perfect mean score of 5. This indicated that no one had deficit knowledge of opioid prescribing. Similar to assess attitudes toward opioid prescribing, no physicians had his/her mean score equal to or less than 3 out of a perfect mean score of 5. This indicated that all of them were willing to prescribe opioid for the patients. Therefore, the fundamental knowledge and attitudes toward opioid prescribing of physicians in this study were not varied from person to person. We can not find any difference of the knowledge among physicians in different specialty, in contrast to other studies (Elliott & Elliott, 1992; Ger, Ho, & Wang, 2000; Von Roenn, Cleeland, Gonin, Hatfield, & Pandya, 1993).

Previous studies showed medical specialty has a profound effect on the knowledge of and the attitude toward appropriate morphine use in cancer pain management (Ger, Ho, & Wang, 2000; Von Roenn, Cleeland, Gonin, Hatfield, & Pandya, 1993). Anesthesiologists appeared more knowledgeable about opioid prescription in comparison to oncologists (Ger, Ho, & Wang, 2000). However, the results in this study were different to the above finding that the radiologists, oncologists and surgeon in the cancer center were as knowledgeable as anesthesiologist in the pain clinic. The underlying reason for better knowledge among

the physicians in the present study is in some way related to the personal past experience of cancer pain management such as training, the experience of using the advanced preparation of opioid (either sustain released morphine or transdermal fentanyl), the same standard WHO guideline.

Summary of the pilot study

What we achieved in the pilot study as set out earlier in the pilot study objectives can be summarized as follows:

1. The concepts for institutional barriers were refined through in-depth interview with both pharmacists and treating physicians. Based on opioid drugs that supplied by the Thai FDA, there were not any problems related to institution system to cancer pain management in the two settings. Therefore, no questions were generated for further measuring the two setting system barriers.

2. Each of individual physicians of the two settings has mean score higher than 3 out of a perfect mean score of 5 for measuring knowledge and attitudes scales, which indicated they all had adequate knowledge and appropriate attitude to prescribe opioids for each patient. We can not find any differences in basic knowledge and attitudes related to prescribe opioids among the physicians of the pain clinic and the cancer center.

3. Having translated and back-translated the instrument, all instruments were piloted in cancer patients at a selected hospitals for the main study.

4. Ninety-four percent of eligible patients agree to provide information about pain. All of the cancer center patients (n=23) agreed to participate while 6 out of 71 among the pain clinic patients refused to completed interviews.

5. Although the cancer patients were able to read the questionnaire, most of them were reluctant to read it by themselves. They would like the researcher to read the questionnaires for them. However, there were no missing data on the questionnaires with this approach.

6. A variety of cancer was found including lung cancer (18.2%), breast cancer (14.8%), cervix (10.25), colorectal cancer (10.2%), liver cancer (8.0%) and

prostate cancer (5.7). The most common cancer among males was lung cancer (18.8%) while breast cancer (23.2%) was the most common among females.

7. Using the definition of pain control and depression above, Inadequate pain control (worst pain score 4-10) among the cancer center patients were higher than those in the pain clinic (46.2% vs 60.9%). Conversely, depression was higher among participants in the pain clinic (16.9%) compared with the cancer center (4.4%).

3.4.2 Main study (October 2007 – July 2008)

Changes made to the main study as a result of the pilot study

3.4.2.1 Study settings

The two government hospitals were selected as the study site as the following reasons.

1. they were the tertiary care hospitals which are the places to which the cancer patients are referred;

2. they were the place providing pain relief for the cancer patients;

3. they locate in Bangkok and its vicinity where were feasible for the researcher to collect data;

4. they consisted of the multidisciplinary physicians related to the cancer patients such as oncologist, radiologist, and anesthesiologist with pain subspecialty is included;

5. In Thailand, most of the pain clinics were within the university hospital except for the National Cancer Institute, locating in Bangkok Metropolitan, but were not available in all of the seven regional cancer centers for special cancer treatment locating across the country. However, such regional cancer centers provide the pain relief concurrently by their responsible physicians who were not pain specialist. The quality of cancer pain treatment between the pain clinic and the non-pain clinic in the regional cancer centers is anticipated to be different from each other. Therefore, a research question was how well the cancer pain management was in each setting (the pain clinic and non-pain clinic). There were no previous studies in Thailand reporting

the cancer pain management in any subgroup of settings. Most studies revealed as a whole setting without stratification. The expected outcome of this study was the prevalence of inadequate pain control among the cancer patients being treated in the pain clinic and in the standard cancer treatment (the regional cancer center). It was the indicator to reflect the effect of the cancer pain management. Consequently, the pain clinic and the regional cancer center were selected for the study.

A pain clinic was selected to be represented as a special pain treatment for cancer pain management whereas a regional cancer center was chosen to be represented as the standard cancer treatment for the cancer patients. This pain clinic in particular its outpatient area is managed by anesthesiologists specialized in pain treatment in daily morning. The staff is a multidisciplinary team, including anesthesiologists with subspecialty in pain management, psychiatrists, physical medicine and rehabilitation physician and nurses. At least two anesthesiologists with pain subspecialty work as core healthcare providers daily, whereas one physician with physical medicine and rehabilitation subspecialty sees the patients twice a week. One psychiatrist is available once a week. In this setting, fellows and residents were under supervision on the assessment and treatment of pain. No hospitalized pain clinic facility is available in this hospital. However, the pain clinic physicians usually provide services for hospitalized patients within the hospital in the afternoon, on request from other unit physicians from time to time. Therefore, the outpatients' pain clinic was a suitable setting to be recruited for this study.

This regional cancer center is a special cancer treatment with the chemotherapy and the radiotherapy covering 5 surrounding provinces in the suburb of Bangkok Metropolitan. It was found that most cancer out-patients of this regional cancer center were the newly or renewed treated patients and were during to be treated with chemotherapy or radiotherapy. Moreover, most referred cancer patients of this regional cancer center were hospitalized during their treatments with the chemotherapy or the radiotherapy. After the completion of such treatment courses, they would be referred back to their previous hospitals. Therefore, hospitalized patients were easier and more suitable to be recruited than the out-patients.

3.4.2.2. Study samples

The population used in this study was the patients with cancer pain in two selected settings. They were approached through the hospital registration lists of two selected settings. Inclusion criteria of the samples were as following:

(a) be diagnosed with cancer;

(b) be informed by their physicians for their diagnosis;

(c) having been experienced with the cancer pain in the previous 7 days or being currently taking analgesics;

(d) having been treated at that clinic at least one month or at least one week at the cancer center, prior to the interview;

(e) being 18 years old or older; and

(d) ability to effectively communicate.

Excluded criteria were those who were severely exhausted and consciously impaired. Moreover, the patients who undergone surgery within one month before the interview because the pain might be due to the possibility of post-surgical rather than cancer pain.

3.4.2.3 Procedures

The researcher recruited and trained one research assistant for each study setting to be an interviewer. Both of them were registered nurses who generally provided care for cancer patients at each of the study settings. After giving their written informed consents, the participants were interviewed by the researcher and/or research assistants with a structured questionnaire. The questions regarding medical data included cancer staging, metastasis status and analgesic drug prescription. We used the patients' medical records to obtain those data with the permission from both patients and physicians.

3.4.2.4 Sample size and power calculations

The formula was

$$n = \frac{\left[Z_{\alpha/2}\sqrt{2P(1-P)} + Z_{\beta}\sqrt{p_1q_1 + p_2q_2}\right]^2}{(p_2 - p_1)^2}$$

$$P = \frac{p_1 + p_2}{2}$$

n = Sample size of each group

$Z_{\alpha/2}$ = Critical value at $\alpha = 0.05$

Z_{β} = Critical value at $\beta = 0.20$

p_1 = the proportion of inadequate pain control among cancer patients in the pain clinic

p_2 = the proportion of inadequate pain control among cancer patients in the regional cancer center

q_1 = 1 - p_1

q_2 = 1 - p_2

From the pilot study, it was found that the proportion of inadequate pain control (worst pain score > 3) patients in the pain clinic and in the regional cancer center were approximately 45% (P1=0.45) and 60% (P2=0.6) respectively.

So,
$$P = \frac{0.45 + 0.6}{2} = 0.525$$

$$n = \frac{\left[1.96\sqrt{2*0.525(1-0.525)} + 0.84\sqrt{0.45*0.55 + 0.6*0.4}\right]^2}{(0.6-0.45)^2} = 172$$

An estimated sample size of each group was 172 with a total of 344 patients.

3.5 Analysis

Double data entry was conducted by the interviewers using EpiData, version 3 (Lauritsen & Bruus, 2003). The data were later transferred into Stata format and analyzed by Stata for windows, version 9.0

3.5.1 Sample description and prevalence estimate

Descriptive statistics, frequency and percentage for categorical variables and mean, median and standard deviation for continuous variables, were used for patients' characteristics, pain related factors and other principle pain outcomes (pain intensity, depression and quality of life).

Demographic, clinical characteristic and principle pain outcomes (depression and quality of life) between the two groups (the pain clinic group vs the cancer center group) were compared using Student's t test, Wilcoxon rank sum test, and Fisher exact tests for continuous and categorical variables respectively.

3.5.2 Univariate analysis

Odds ratio and 95% confidence intervals were calculated for the associations of the main outcomes and relevant study factors. The demographic, socio-economic status, disease status variables and other potential confounders were selected on the basis of an association with the outcomes for inclusion in the multivariate model.

3.5.3 Multivariate analysis

Multiple logistic regression model including demographic (sex, age), disease status variables (stage of cancer, presence of bone metastasis, number of pain sites and pain duration) and average opioids dosages was used to determine the adjusted effect of the clinical setting on inadequate pain control.

All statistical tests were considered significance at the level of 0.05.

3.6 Ethical consideration

Efforts were made to ensure the protection of human rights in this study. The proposal was submitted for approval from the two authorized ethic committee of the local institutions and the administrative committee of the regional cancer center prior to the data collection process. Once such permission was obtained, the researcher approached the chief of the participating clinics and provided information regarding the study‘s purposes, time frame, procedure and patient safeguards.

The researcher or the research assistants then approached potential subjects including pharmacists, physicians, and cancer patients. Each potential participant was informed, verbally and in writing, of procedures designed to ensure confidentiality, and was asked to sign a copy of the consent form.