CHAPTER 4

RESULT

Patients who met the eligibility criteria were much fewer than expected. A sample of 240 cancer patients with pain was initially approached, with 139 outpatients from the pain clinic and 101 inpatients from the cancer center. Four patients (1.7%) were experiencing severe pain and/or too tired to be able to participate and eight patients (3.3%) refused to participate after a brief introduction. Finally, the 228 participants successfully completed the interviews. The overall proportion responding was therefore 95.0%.

The details of the finding from the study were as following.

4.1 Descriptive characteristics

4.1.1 Demographic characteristics

The majority of the participants (n=133, 58.3%) were from the outpatient pain clinic. The rest (n=95, 41.7%) were hospitalized patients of the regional cancer center. Most of these participants were females (n=130, 57.0%), married (n=147, 64.5%) and unemployed (n=158, 69.3%). The mean age was 55.2 (SD=12.5) ranging from 18 to 84 years. Half of the participants (n=115, 50.4%) completed at primary school level and their medical payments were under the Universal Coverage Scheme (n=119, 52.2%). The distribution of demographic characteristics of participants is shown in Table 4.1.

Table 4.1

Distribution of the study sample by demographic characteristics

Characteristics	Number.	Percentage
Clinical setting		
Pain clinic	133	58.3
Regional cancer center	95	41.7
Gender		
Female	130	57.0
Male	98	43.0
Age distribution : years		
18 - 30	7	3.1
31 - 40	18	7.9
41 - 50	61	26.8
51 - 60	66	29.0
61 - 70	52	22.8
>71	24	10.5
Education		
None	11	4.8
Primary school	115	50.4
Secondary school	45	19.7
High school	29	12.7
Undergraduate	24	10.5
Graduate (Master's degree)	4	1.8
Religion		
Buddhism	222	97.4
Christianity	4	1.7
Islam	2	0.9
Marital status		
Single	31	13.6
Widowed/separated	50	21.9
Married	147	64.5
Employment		
Unemployed	158	69.3
Employed	70	30.7
Type of payment		
Universal Coverage Scheme	119	52.2
Civil servant medical benefit	66	29.0
Social security	30	13.2
Self-financed	13	5.7
Caregiver at home		
Family or relatives	200	87.7
Self-care	23	10.1
Friends	5	2.2

4.1.2 Clinical characteristics

4.1.2.1 Cancer and treatment

The primary cancer sites are listed in Table 4.2. Cancer was found most commonly in the gastrointestinal tract (n=49, 21.5%). Regarding the cancer type, breast cancer was the most prevalent (n=34, 14.9%), followed by lung (n=33, 14.5%), oral cavity (n=32, 14.0%) and colorectal cancer (n=26, 11.4%).

Table 4.3 summarizes the primary cancer site by gender. In the female group, the most common primary cancer was breast cancer (n= 33, 25.4%), followed by cervical cancer (n= 22, 16.9%), lung cancer (n= 20, 15.4%) and colon or rectal cancer (n= 15, 11.5%). In the male group, the most common primary cancer was cancer of oral cavity (n= 23, 23.5%), followed by lung cancer (n= 13, 13.3%), prostate cancer (n= 13, 13.3%) and colorectal cancer (n= 11, 11.2%).

Information regarding the patients' clinical characteristics indicated that approximately three-quarter (n=167, 73.3%) had been diagnosed with cancer stage 4 while 10.5% (n=24) and 5.7% (n=13) were at stage 3 and early stages, respectively. The staging of the other 24 patients (10.5%) could not be determined because of inadequate information i.e. no staging assessment in the patients' medical records. The TMN classification system used to determine the cancer stage in this study. It was based on the size of the tumor (T), lymph node (N) and the metastasis (M). The majority of those patients of stage 4 of advanced cancer with metastasis were suffering from the bone metastasis (59.5%), which was the most common site of distant metastasis. Twenty-five percent (n=57) and forty percent of the participatory patients (n=93) had undergone chemotherapy and radiotherapy within past month (Table 4.4).

4.1.2.2. Cancer related pain

Cancer pain characteristics were described in Table 4.5. Regarding the source of cancer related pain, the majority of the patients' pain (87.7%) was caused by cancer, while 3.1% and 9.2% of the total patients' pain in this study resulted from cancer treatment (such as chemotherapy or radiotherapy) and both cancer and its treatment, as respectively. Regarding the pathophysiology of pain, approximately half of patients (51.3%) suffering from the nociceptive pain only, 7% from the neuropathic pain only and 42% from both type of pain. The total number of pain site was ranged from 1 to 5 with a mean of 1.9 (SD = 1.0). In addition, the time they had experienced pain ranging from 15 days to 8 years with a mean of 7.5 months (SD=10.4 months). However, those who suffered from pain more than one year were the patients in the pain clinic (n=8).

Table 4.2

Distribution of primary cancer sites

Site	n (%)	Site	n (%)
Gastrointestinal tract	49 (21.5)	Male reproductive organ	15 (6.6)
Colon and rectum	26 (11.4)	Prostate	13 (5.7)
Pancreas	11 (4.8)	Testis	2 (0.9)
Liver	7 (3.1)		
Esophagus	5 (2.2)	Bone	13 (5.7)
		Skin and connective tissues	7 (3.1)
Breast	34 (14.9)		
Lung	33 (14.5)	Urinary tract	5 (2.2)
Oral cavity	32 (14.0)	Renal	3 (1.3)
		Bladder	2 (0.9)
Gynaecological organ	28 (12.3)		
Cervix	22 (9.7)	Nervous system	3 (1.3)
Endometrium	4 (1.8)	Lymphoma	3 (1.3)
Ovary	2 (0.9)	Thyroid	3 (1.3)
		Unknown origin	3 (1.3)

Table 4.3

Distribution of primary cancer sites by gender

Female (n=130)		Male (n=98)	
Site	n (%)	Site	n (%)
Breast	33 (25.4)	Oral cavity	23 (23.5)
Cervix	22 (16.9)	Lung	13 (13.3)
Lung	20 (15.4)	Prostate	13 (13.3)
Colorectum	15 (11.5)	Colorectum	11 (11.2)
Oral cavity	9 (6.9)	Liver	6 (6.1)
Bone	7 (5.4)	Bone	6 (6.1)
Pancreas	6 (4.6)	Skin and connective tissues	6 (6.1)
Endometrium	4 (3.1)	Pancreas	5 (5.1)
Unknown origin	3 (2.3)	Esophagus	3 (3.1)
Esophagus	2 (1.5)	Renal	3 (3.1)
Ovary	2 (1.5)	Lymphoma	2 (2.0)
Thyroid	2 (1.5)	Nervous system	2 (2.0)
Bladder	1 (0.8)	Testis	2 (2.0)
Liver	1 (0.8)	Bladder	1 (1.0)
Lymphoma	1 (0.8)	Breast	1 (1.0)
Nervous system	1 (0.8)	Thyroid	1 (1.0)
Skin	1 (0.8)		

Table 4.4

Cancer characteristics and treatment

Characteristics	No.	Percentage
Time since cancer diagnosed		
1-6 months	82	36.0
7-12 months	47	20.6
13-36 months	63	27.6
3.01-5 years	19	8.3
> 5.01 years	17	7.5
Cancer stage		
Stage 1	3	1.3
Stage 2	10	4.4
Stage 3	24	10.5
Stage 4	167	73.3
Not specified	24	10.5
Metastasis		
No	61	26.8
Yes, metastasis site	158	69.3
Bone	94	59.49*
Liver	27	17.2*
Lung	25	15.9*
Brain	4	2.6*
Lymph node	33	20.9*
Others	17	10.8*
Not specified	9	3.9
Cancer treatment (within the previous month)		
Chemotherapy only	25	11.0
Radiotherapy only	61	26.8
Both treatment	32	14.0
No treatment	110	48.3

* some patients had more than one site of metastasis and the percentage was calculated based on 158 participants with metastasis

Table 4.5

Cancer pain characteristics

Cancer pain variables	Number	Percentage
Source of pain		
Cancer induced pain	200	87.7
Treatment induced pain	7	3.1
Mixed	21	9.2
Pathophysiology of pain		
Nociceptive pain only	117	51.3
Neuropathic pain only	16	7.0
Both nociceptive and neuropathic	95	41.7
Number of pain sites		
1 site	97	42.5
2 sites	82	36.0
3-5 sites	49	21.5
Duration of pain		
3 months or less	103	45.2
3 - 6 months	47	20.6
> 6 months	78	34.2

4.1.3 Main outcomes

4.1.3.1 Pain control and the inappropriateness of analgesic medication

The BPI, a numeric rating scale (11-point scale, 0-10), was used in this study to measure the pain severity, pain interference and symptoms rated by the participatory patients. The reliability coefficients (Cronbach's alpha) of the BPI basing on 228 subjects of this study were 0.88 and 0.91 for pain intensity and pain interference, as respectively. The pain severity profile was illustrated in Table 4.6-4.8. The mean pain score indicated the mild to moderate severity (means range 1.6-4.7). The median scores of the least pain, average pain and current pain range from 3 to 5. About three-quarters of patients (77.7%) reported having pain on the day of interview. Nearly forty percent (39.4%) reported their usual pain as moderate to severe intensity. Regarding to the worst pain reporting over the last 24 hours, the male group reported significantly higher pain intensity than the female group. The patients in pain clinic were much more likely to report the pain interference with work and ability to walk than those in the cancer center (Table 4.9).

The inappropriateness of analgesic medication prescribed for each patient in this study was measured by the Pain Management Index (PMI). A total of twenty-one patients (9.2%) (n=10, 7.5% of the pain clinic patients and n=11, 11.6% of the cancer center patients) were considered as having inappropriate pain medication (Table 4.10). However, among those having PMI $\geq$ 0, approximately a half (n=124, 59.9%) of the patients reported their worst pain as moderate or severe (Table 4.11).

The overall prevalence of inadequate pain control was 61.4% (54.1% in the pain clinic group and 71.6% in the cancer center group) as shown in Table 4.12.

4.1.3.2 Prevalence of depression

The caseness of depression was signified by having a score of 11 or more on the depression section HADS screening measure. The reliability coefficient (Cronbach's alpha) of the Thai HADS for depression scale basing on 228 subjects of this study was 0.84. The score distribution was ranged from 0 to 19 with a mean of 7.3 (SD= 4.7). The overall prevalence of depression was 20.6% (95%CI: 15.4 – 25.9) as shown in Table 4.12.

4.1.3.3 Quality of life

The satisfactory internal consistency reliability with Cronbach's alpha above 0.7 in all subscales (range 0.79 – 0.85) was shown in the Fact-G scale. The reliability of the total scale (27 items) was 0.89. The higher scores indicated the better quality of life. Table 4.13 – 4.14 summarizes the global quality of life scores with four subscales regarding staging of cancer and setting, as respectively. The cancer staging of 24 patients could not be determined from the medical records. Overall, the score distribution of the quality of life was ranged from 23 to102 with its subscales ranging of 3-28, 0-26, 1-24 and 1-28 on physical, social, emotional and functional well-being, as respectively. Those with the most advanced cancer (stage 4) were most likely to have poor quality of life, particularly in terms of functional well-being. The male patients were scored much less than those females on the FACT-G, particularly on the functional subscale.

Table 4.6

Mean, standard deviation, median and range score

on the pain profile (n=228)

Pain variable	Mean	SD	Median	Range
Worst pain in the past 24 hours	4.7	2.9	5	0-10
Average pain in the past 24 hours	3.0	2.2	3	0-10
Least pain in the past 24 hours	1.6	1.8	3	0-8
Pain right now	3.1	2.6	3	0-10

Table 4.7

Patients' evaluation of their pain profile

on different severity (n=228)

Pain item	Number (%) of the patients			
	No pain	Mild pain	Moderate pain	Severe pain
Pain at its worst	19 (8.3)	69 (30.3)	70 (30.7)	70 (30.7)
Pain on average	35 (15.4)	103 (45.2)	76 (33.3)	14 (6.1)
Least pain	95 (41.7)	104 (45.6)	23 (10.1)	6 (2.6)
Pain now	51 (22.4)	88 (38.6)	61 (26.8)	28 (12.3)

Table 4.8

Patients' evaluation of their pain profile by gender

Pain intensity	Mean (SD)score		T-test	P-value
	Male n=98	Female n=130		
Worst pain	5.2 (3.0)	4.4 (2.9)	-2.121	0.035
Average pain	3.3 (2.0)	2.8 (2.3)	-1.816	0.071
Least pain	1.7 (1.6)	1.6 (2.0)	-0.266	0.791
Current pain	3.5 (2.5)	2.9 (2.6)	-1.961	0.051

Table 4.9

Patients' evaluation of pain impact on every living activity and symptom by clinical setting

Variables	Mean (SD)score			P-value*
	Total	Pain clinic n=133	Cancer center n=95	
Pain interference				
Activities	3.0 (3.2)	3.2 (3.4)	2.7 (2.8)	0.531
Mood	3.4 (3.0)	3.6 (3.2)	3.2 (2.8)	0.408
Walking	3.8 (3.4)	4.3 (3.5)	3.2 (3.0)	0.040
Work	4.6 (3.6)	5.2 (3.8)	3.7 (3.2)	0.003
Relations with others	2.8 (3.1)	2.6 (3.2)	2.9 (3.0)	0.275
Sleep	3.3 (3.3)	3.2 (3.4)	3.6 (3.1)	0.201
Enjoyment of life	3.7 (3.1)	3.9 (3.2)	3.5 (2.9)	0.457
Symptom				
Drowsiness	3.4 (2.8)	3.5 (2.9)	3.2 (2.7)	0.452
Nausea	1.3 (2.2)	1.1 (2.1)	1.5 (2.3)	0.155
Vomiting	0.8 (1.9)	0.7 (1.7)	1.1 (2.0)	0.153
Constipation	3.1 (3.3)	3.3 (3.3)	2.8 (3.3)	0.242

*Wilcoxon rank sum test (pain clinic vs cancer center)

Table 4.10

Pain Management Index (PMI) by clinical setting

PMI	N	Number (%) of the patients		P-value
	Total	Pain clinic n=133	Cancer center n=95	
-2	3 (1.3)	1 (0.8)	2 (2.1)	0.033*
-1	18 (7.9)	9 (6.8)	9 (9.5)	
0	85 (37.3)	53 (39.9)	32 (33.7)	
1	67 (29.4)	30 (22.6)	37 (39.0)	
2	43 (18.9)	31 (23.3)	12 (12.6)	
3	12 (5.3)	9 (6.8)	3 (3.2)	

*Fisher exact test

Pain management index = Analgesic level – Pain level (derived from worst pain)

Table 4.11

PMI and corresponding pain severity

PMI	n	Number (%) of the patients			
		None n=19	Mild N=69	Moderate n=70	Severe n=70
-2	3			2 (2.9)	1 (1.4)
-1	18		5 (7.3)	2 (2.9)	11 (15.7)
0	85		3 (4.4)	24 (34.3)	58 (82.9)
1	67	1 (5.3)	24 (34.8)	42 (60.0)	
2	43	6 (31.6)	37 (53.6)		
3	12	12 (63.2)			

Table 4.12

Prevalence of inadequate pain control, inappropriate analgesic prescription and depression by clinical setting

Outcomes	n	% prevalence (95%CI)		
		Total n=228	Pain clinic n=133	Cancer center n=95
Inadequate pain control	140	61.4 (55.1-67.7)	54.1 (45.7-62.6)	71.6 (62.5-80.6)
Inappropriate pain medication	21	9.2 (5.4-13.0)	7.5 (3.0-12.1)	11.6 (5.0-18.1)
Depression	47	20.6 (15.4 - 25.9)	26.3 (18.8 - 33.8)	12.6 (6.0-19.3)

Table 4.13

Mean scores of global quality of life and subscales by cancer staging

Quality of life (FACT-G)	Scores			
	Stage1 n=3	Stage 2 n=10	Stage 3 n=24	Stage 4 n=167
Total score	76.3	72.0	74.8	66.8
Physical well-being	20.3	20.1	19.0	17.5
Social well-being	19.0	17.9	19.2	18.5
Emotional well-being	18.7	18.5	19.3	17.5
Functional well-being	18.3	15.5	17.3	13.2

Table 4.14

Mean scores of global quality of life and subscales by clinical setting

	Mean (SD) score			T-test	p-value*
	Total n=228	Pain clinic n=133	Cancer center n=95		
Total QOL	67.8 (15.5)	66.0 (16.6)	70.2 (13.3)	-2.011	0.046
Physical well-being	18.1 (5.7)	18.6 (5.7)	17.4 (5.7)	1.605	0.110
Social well-being	18.2 (4.6)	17.4 (5.1)	19.5 (3.5)	-3.442	0.001
Emotional well-being	17.7 (4.9)	17.4 (5.1)	18.1 (4.6)	-1.101	0.272
Functional well-being	13.7 (5.8)	12.7 (6.2)	15.2 (4.9)	-3.357	0.001

* Student t test (pain clinic vs cancer center)

4.1.4 Clinical setting characteristics

This study was conducted in two types of setting, the pain clinic and non-pain clinic (regional cancer center).

4.1.4.1 Socio-demographic characteristics

Table 4.15 presents the basic characteristics of the two groups of participatory patients. The patients in the pain clinic were more likely to be older, better educated and greater unemployed than those in the cancer center.

4.1.4.2 Clinical characteristics

Cancer site and pain pathophysiology:

In the pain clinic group, the most common primary cancer site was lung (n= 22, 16.5%), followed by breast (n= 16, 12.0%) and colorectal (n= 14, 10.5%). In the cancer center group, the most common cancer was respectively as oral cavity cancer (n= 27, 28.4%), breast cancer (n= 18, 19.0%), colorectal (n=12, 12.6%) and cervical cancer (n=12, 12.6%) (Table 4.16).

Considering the pathophysiology of pain, there were no significant differences in the type of pain between the two settings (Table 4.17).

Treatment:

For cancer treatment, the pain clinic patients were likely to have undergone cancer treatment (chemotherapy, radiotherapy) in the previous month, less than those in the cancer center (Table 4.18). Moreover, the analgesic medications and its dosages were more likely to be prescribed in the pain clinic than those in the cancer center. It should be noted that all the analgesic medications were in the oral form except fentanyl which was in transdermal patch.

For the pain medication, the number of analgesic used in the pain clinic was greater than the cancer center as illustrated in Table 4.19. Considering the group of pain medication prescribed to the patients in the two settings; the non-opioid

analgesic (63.2% in the pain clinic and 46.3% in the cancer center), the opioids (94.7% in the pain clinic and 91.6% in the cancer center), and the adjuvant drugs (84.2% in the pain clinic and 54.7% in the cancer center). The COX II inhibitors and the adjuvant drugs including nortriptyline, Venlafaxine, pregabalin, carbamazepine, clonazepam, and oxcarbamazepine were not found to be prescribed to the patients in the cancer center.

For the opioids medication without considering the rescue morphine syrup; the common drugs prescribed in the pain clinic was respectively as morphine (n=56, 42.1), tramadol (n=43, 32.3%), and fentanyl (n=34, 25.6%). Moreover, the frequently drugs prescribed in the cancer center was respectively as morphine (n=54, 56.8%) and tramadol (n=32, 33.7%). It was found that the average dosage of the opioid drug per day in the pain clinic was higher than that in the cancer center (Table 4.20). When we converted the prescribed doses of the weak opioids (tramadol, codeine) and strong opioids (fentanyl, morphine) per day in equivalent to morphine dosage; without rescue doses of morphine syrup; equianalgesic conversion ratios of oral morphine : fentanyl (transdermal), oral morphine : oral tramadol, and oral morphine : oral codeine were respectively as 150:1, 1:5, and 1:10 (Chaudakshetrin, 2004). It was found that the average equianalgesic oral morphine doses received by the pain clinic patients was significantly higher than those taken by the cancer center patients as shown in Table 4.21.

Among the patients with neuropathic pain, the commonly used (as monotherapy or in combination) medicine was respectively as gabapentin (n=44, 63.8%), amitriptyline (n=41, 59.4%) in the pain clinic; and amitriptyline (n=23, 54.8%) was the most commonly used medicine in the cancer center as shown in Table 4.22.

It should be noted that all cancer patients in this study reported that they had not received other medical pain interventions such as nerve block, physical therapy during the previous month. Around the clock administration of opioid medicine was prescribed in this study.

In this study, 5 items of analgesic medications were divided as acetaminophen, NSAIDs, opioids, anti-depressants, and anti-convulsants. The majority of the pain clinic patients (70.4%) have been concurrently received analgesic medications 3-5 items whereas those in the cancer center (67.4 %) have been received such medication simultaneously only 1-2 items as shown in Table 4.23.

4.1.4.3 Patients' barriers to cancer pain management

According to the finding from the pilot study, the Barriers questionnaires-II (BQ-II) (Gunnarsdottir, Donovan, Serlin, Voge, & Ward, 2002) was modified to be used in this study. The potential scores were ranged from 0-5 which a score of 5 signified the maximum barrier. The reliability coefficients of this modified BQ-II (15 items) (n=140) in this study was 0.73. The reliability coefficient of physiological effects subscale was only 0.37. The higher scores indicated the higher level of barriers. Table 4.24 presents the mean score ($\pm$SD) for each of the BQ-II subscales and total BQ-II score. Overall, the mean subscale scores were ranged from 1.2 ((the fatalism subscale) to 1.9 (the harmful effect subscale). It was found that the patients in the cancer center were more likely to have greater barriers of total BQ-II score and communication subscale than those in the pain clinic.

Table 4.15

The patients' characteristics between the clinical settings

Demographic variables	Number (%) of the patients		Chi square	p-value
	Pain clinic n=133	Cancer center n=95		
Gender				
Male	57 (42.9)	41 (43.2)	0.002	0.964
Female	76 (57.1)	54 (56.8)		
Age: years				
18 - 60 years	79 (59.4)	73 (76.8)	7.588	0.006
61 - 84 years	54 (40.6)	22 (23.2)		
Education level				
Primary level or less	57 (42.9)	69 (72.6)	19.871	<0.001
Secondary level or higher	76 (57.1)	26 (27.4)		
Marital status				
Married	83 (62.4)	64 (67.4)	0.756	0.685
Widowed/separated	30 (22.6)	20 (21.1)		
Single	20 (15.0)	11 (11.6)		
Employed status				
Unemployed	99 (74.4)	59 (62.1)	3.960	0.047
Employed	34 (25.6)	36 (37.9)		

Table 4.16

Distribution of primary cancer sites by clinical setting

Pain clinic (n=133)		Cancer center (n=95)	
Site	n (%)	Site	n (%)
Lung	22 (16.5)	Oral cavity	27 (28.4)
Breast	16 (12.0)	Breast	18 (19.0)
Colorectum	14 (10.5)	Colorectum	12 (12.6)
Prostate	12 (9.0)	Cervix	12 (12.6)
Bone	12 (9.0)	Lung	11 (11.6)
Cervix	10 (7.5)	Skin and connective tissues	3 (3.2)
Pancreas	10 (7.5)	Nervous system	2 (2.1)
Liver	6 (4.5)	Testis	2 (2.1)
Oral cavity	5 (3.8)	Thyroid	2 (2.1)
Endometrium	4 (3.0)	Bladder	1 (1.1)
Esophagus	4 (3.0)	Bone	1 (1.1)
Skin and connective tissues	4 (3.0)	Esophagus	1 (1.1)
Lymphoma	3 (2.3)	Liver	1 (1.1)
Renal	3 (2.3)	Pancreas	1 (1.1)
Unknown origin	3 (2.3)	Prostate	1 (1.1)
Ovary	2 (1.5)		
Bladder	1 (0.8)		
Nervous system	1 (0.8)		
Thyroid	1 (0.8)		

Table 4.17

Patients' pain characteristics by clinical setting

	Number (%) of patients		Chi square	p-value
	Pain clinic n=133	Cancer center n=95		
Pathophysiology of pain				
Nociceptive pain only	64 (48.1)	53 (55.8)	1.861	0.394
Neuropathic pain only	8 (6.0)	7 (7.4)		
Both nociceptive and neuropathic	61 (45.9)	35 (36.8)		

Table 4.18

Cancer treatment within the previous month by clinical setting

	number (%) of the patients		Chi square	p-value
	Pain clinic n=133	Cancer center n=95		
Chemotherapy				
Yes	20 (15.0)	37 (39.0)	16.896	<0.001
No	113 (85.0)	58 (61.1)		
Radiotherapy				
Yes	24 (18.1)	69 (72.6)	68.370	<0.001
No	109 (82.0)	26 (27.4)		

Table 4.19

Pain medications by clinical setting

Drugs	Number (%) of the patients			
	Total (n=228)	Pain clinic (n=133)	Cancer center (n=95)	P-value#
1.Non-opioids	128 (56.1)	84 (63.2)	44 (46.3)	0.012
Acetaminophen	86 (37.7)	54 (40.6)	32 (33.7)	0.288
NSAIDs	34 (14.9)	17 (12.8)	17 (17.9)	0.346*
COX II inhibitors	24 (10.5)	24 (18.1)	0	<0.001*
Celecoxib	3 (1.3)	3 (2.3)	0	0.268*
Etoricoxib	21 (9.2)	21 (15.8)	0	<0.001*
2.Opioids	213 (93.4)	126 (94.7)	87 (91.6)	0.343
Tramadol	75 (32.9)	43 (32.3)	32 (33.7)	0.830
Codeine	5 (2.2)	2 (1.5)	3 (3.2)	0.652
Fentanyl patch	36 (15.8)	34 (25.6)	2 (2.1)	<0.001*
Morphine (tablet/capsule)	110 (48.2)	56 (42.1)	54 (56.8)	0.028
Morphine syrup	111 (48.7)	74 (55.6)	37 (38.9)	0.013
3.Adjuvants	164 (71.9)	112 (84.2)	52 (54.7)	<0.001*
3.1 Anti-depressant	139 (61.0)	92 (69.2)	47 (49.5)	0.003
Amitriptyline	115 (50.4)	68 (51.1)	47 (49.5)	0.805
Nortriptyline	20 ((8.8)	20 (15.0)	0	<0.001*
Venlafaxine	4 (1.8)	4 (3.0)	0	0.143*
3.2 Anti-convulsant	87 (38.2)	77 (57.9)	10 (10.5)	<0.001*
Gabapentin	68 (29.8)	58 (43.6)	10 (10.5)	<0.001*
Pregabalin	11 (4.8)	11 (8.3)	0	0.003*
Carbamazepine	1 (0.4)	1 (0.8)	0	1.000*
Clonazepam	22 (9.6)	22 (16.5)	0	<0.001*
Oxcarbamazepine	8 (3.5)	8 (6.0)	0	0.022*

N.B. All drugs are oral unless otherwise specified

Chi square test (pain clinic vs cancer center)

* Fisher's exact test

Table 4.20

Average dosage of opioid medication in patients with inadequate pain control by clinical setting

Drugs	Pain clinic (n=133)				Cancer center (n=95)				p-value
	n (%)	Dosage (mg /day)			n (%)	Dosage (mg /day)			
		Mean (SD)	Median	Min-max		Mean (SD)	Median	Min-max	
Tramadol	43 (32.3)	150.9 (80.4)	150	37.5 - 350	32 (33.7)	117.2 (67.9)	100	50 - 200	0.103
Codeine	2 (1.5)	67.5 (74.2)	67.5	15 - 120	3 (3.2)	95 (74.0)	60	45 - 180	0.564
Morphine	56 (42.1)	52.0 (48.0)	40	10 - 200	54 (56.8)	39.4 (29.4)	20	20 - 150	0.212
Fentanyl	34 (25.6)	1.1 (0.6)	1.2	0.3 - 2.4	2 (2.1)	0.8 (0.6)	0.8	0.3 - 1.2	0.368

* Wilcoxson rank sum test

Table 4.21

The equianalgesic oral morphine dosage (mg/day) by clinical setting

	Morphine equianalgesic doses (mg/day)				
	n (%)	Mean (SD)	Median	Min-max	P-value*
Clinical setting					
Pain clinic	126 (94.7)	80.0 (83.0)	45	1.5 - 360	<0.001
Cancer center	87 (91.6)	36.0 (33.9)	20	10 - 230	
Total	213 (93.4)	62.0 (71.0)	40	1.5 - 360	

* Wilcoxson rank sum test

Table 4.22

Co-analgesic usage in patients with neuropathic pain by clinical setting

Drugs	Pain clinic (n=69)				Cancer center (n=42)				P-value*
	n (%)	Dosage (mg /day)			n (%)	Dosage (mg /day)			
		Mean (SD)	Median	Min-max		Mean (SD)	Median	Min-max	
Anti-depressant									
Amitriptyline	41 (59.4)	18.9 (10.2)	20	10 - 50	23 (54.8)	25.4 (6.2)	25	10 - 50	0.0017
Nortriptyline	10 (14.5)	17.5 (7.9)	17.5	10 - 25	0				
Venlafaxine	2 (2.9)	37.5 (0)	37.5	37.5	0				
Anti-convulsant									
Gabapentin	44 (63.8)	706.8 (584.4)	600	100 - 2400	6 (14.3)	350 (122.5)	300	300 - 600	0.1215
Pregabalin	9 (13.0)	308.3 (192.8)	225	150 - 600	0				
Carbamazepine	1 (1.4)	600	600	600	0				
Clonazepam	18 (26.1)	0.9 (0.6)	0.5	0.5 - 2	0				
Oxcarbamazepine	6 (8.7)	700 (309.8)	600	300 - 1200	0				

* Wilcoxson rank sum test

Table 4.23

Number of analgesic items prescribed by clinical setting

Number of analgesic item	Number (%) of the patients		P-value
	Pain clinic	Cancer center	
1	8 (6.1)	25 (27.2)	<0.001
2	31 (23.5)	37 (40.2)	
3	54 (40.9)	26 (28.3)	
4	37 (28.0)	4 (4.4)	
5	2 (1.5)	0	

Table 4.24

Mean scores subscale of Modified BQ-II by clinical setting

BQII	Mean(SD) score			P-value*
	Total n=140	Pain clinic n=68	Cancer center n=72	
Total	1.6 (0.8)	1.4 (0.7)	1.7 (0.9)	0.012
Physiological effects	1.5 (0.7)	1.4 (0.7)	1.6 (0.7)	0.221
Fatalism	1.2 (1.1)	1.3 (1.2)	1.2 (1.1)	0.604
Communication	1.6 (1.4)	1.1 (1.2)	2.0 (1.4)	<0.001
Harmful effects	1.9 (1.6)	1.7 (1.4)	2.2 (1.7)	0.063

* Student t test

4.1.5 Potential confounders

Several potential confounders in this study were hypothesized for the association between being in the non-pain clinic (independent variable) and being inadequate pain control (dependent variable). In addition, depression was believed to confound the effect of being treated in a non-pain clinic (independent variable) on inadequate pain control (dependent variable).

Potential confounders

- Gender (male vs female)
- Age ($\leq$ 60 years vs > 60 years)
- Patients' barriers (categorized by the median scores at 1.5 as $\leq$ 1.5 (less attitudinal barriers) vs > 1.5 (more attitudinal barriers)
- Cancer staging (stage 1-3 vs stage 4)
- Presence of bone metastasis (no vs yes)
- Number of pain sites (1 pain site vs 2-5 pain sites)
- Duration of pain ($\leq$ 3 months vs > 3 months)
- Opioid dosages [average dosage of prescribed opioids analgesic, do not include rescue doses, was categorized by median doses at 30 mg/day, as $\leq$ 30 mg/day (lower opioid dosages)vs > 30 mg/day (higher opioid dosage)]
- Number of analgesic items (1-2 items vs 3-5 items)
- Co-analgesic usage (anti-depressants or anti-convulsants) in the patients with neuropathic pain (no vs yes)

4.2 Univariate associations

4.2.1 *Clinical setting and potential confounders*

Table 4.25 illustrated that the pain clinic patients were significantly associated with the more advanced cancer stage, bone metastasis situation, higher number of pain sites, and longer pain duration.

Regarding the analgesic prescribed, the higher opioids dosages (> 30 mg/day) was more likely to be taken by the pain clinic patients (58.7%) than those in the cancer center (35.8%). A higher proportion of patients with neuropathic pain in pain clinic (95.7%) were prescribed the co-analgesic medication (anti-depressants or anti-convulsants) than those in the cancer center (61.9%) as shown in Table 4.26.

4.2.2 The associations between the clinical setting/potential confounders (independent variable) and the pain control (dependent variable)

The univariate analyses of the factors associated with inadequate pain control (dependent variable) are summarized in Table 4.27. The patients in the cancer center were significantly suffered more from the inadequate pain control than those in the pain clinic (p=0.008). All potential confounders (independent variables) in this study were not found to be significantly associated with the inadequate pain control (dependent variable).

Table 4.25

The association between clinical setting and patients' characteristics

Variable	Number (%) of patients		Chi square	p-value
	Pain clinic (n=133)	Cancer center (n=95)		
Cancer stage (n=204)				
Stage 1-3	10 (8.7)	27 (30.3)		<0.001*
Stage 4	105 (91.3)	62 (69.7)		
Presence of bone metastasis				
No	60 (45.1)	74 (77.9)	24.578	0.001
Yes	73 (54.9)	21 (22.1)		
Number of pain sites				
one site	44 (33.1)	53 (55.8)	11.689	0.001
2-5 sites	89 (66.9)	42 (44.2)		
Duration of pain				
≤ 3 months	39 (29.3)	64 (67.4)	32.386	<0.001
> 3 months	94 (70.7)	31 (32.6)		
Patients' barriers (n=140)				
≤ 1.5 scores	37 (54.4)	33 (45.8)	1.029	0.310
> 1.5 scores	31 (45.6)	39 (54.2)		

*Fisher's exact test

Table 4.26

The association between clinical setting and analgesic prescription

Demographic variables	Number (%) of the patients		Chi square	p-value
	Pain clinic n=133	Cancer center n=95		
Opioids dosages				
≤ 30 mg/day	55 (41.4)	61 (64.2)	11.584	0.001
> 30 mg/day	78 (58.7)	34 (35.8)		
Number of analgesic items				
1-2 items	39 (29.6)	62 (67.4)	31.363	<0.001
3-5 items	93 (70.5)	30 (32.6)		
Co-analgesic usage in the patients with neuropathic pain (n=111)				
No	3 (4.4)	16 (38.1)		<0.001*
Yes	66 (95.7)	26 (61.9)		

*Fisher's exact test

Table 4.27

ORs for the association between inadequate pain control, clinical setting and potential confounders

Variables		Inadequate pain control (n=140)		
	n	n (%)	Odds ratio (95%CI)	p-value
Main exposure				
Clinical setting				
Pain clinic	133	72 (54.1)	1	0.008
Cancer center	95	68 (71.6)	2.1 (1.2 - 3.7)	
Potential confounders				
Gender				
Female	130	73 (56.2)	1	0.062
Male	98	67 (68.4)	1.7 (1.0-2.9)	
Age: years				
18 - 60 years	152	92 (60.5)	1	0.700
61 - 84 years	76	48 (63.2)	1.1 (0.6-2.0)	
Patient's barrier (n=140)				
≤ 1.5 score	70	47 (67.1)	1	0.716
> 1.5 score	70	49 (70.0)	1.1 (0.6-2.3)	
Cancer stage				
Stage 1-3	37	23 (62.2)	1	0.881
Stage 4	167	106 (63.5)	1.1(0.5-2.2)	
Presence of bone metastasis				
No	134	89 (66.4)	1	0.064
Yes	94	51 (54.3)	0.6 (0.3-1.0)	
Number of pain sites				
one site	97	56 (57.7)	1	0.328
two sites or more	131	84 (64.1)	1.3 (0.8-2.2)	
Duration of pain				
≤ 3.0 months	103	68 (66.0)	1	0.194
> 3 months	125	72 (57.6)	0.7 (0.4-1.2)	
Equianalgesic oral morphine dosages				
≤ 30 mg/day	116	65 (56.0)	1	0.091
> 30 mg/day	112	75 (67.0)	1.6 (0.9-2.7)	
Number of analgesic item				
3-5 items	123	75 (61.0)	1	0.830
1-2 items	101	63 (62.4)	1.1 (0.6 -1.8)	
Co-analgesic usage in the patients with neuropathic pain (n=111)				
No	19	9 (47.4)	1	0.242
Yes	92	57 (62.0)	1.8 (0.7-4.9)	

Table 4.27 (continued)

Variables		Inadequate pain control (n=140)		
	n	n (%)	Odds ratio (95%CI)	p-value
Depression				
No	181	106 (58.6)	1	0.087
Yes	47	34 (72.3)	1.9 (0.9 - 3.7)	

4.3 Multivariate analysis (controlling for confounders)

Logistic regression models were developed to test the effect of clinical setting on the pain control. In order to adjust for all the relevant potential confounders, the variables that had ORs of 1.3 or higher in the univariate analysis were entered into a multivariate model. Age and gender were also included in such model under this study.

The multivariate model without potential confounders (independent variable) shows a substantial negative effect of being treated in the cancer center on pain control (dependent variable) with OR 2.1, 95% CI: 1.2 – 3.7. The effect was slightly increased after adjusting for gender, age, presence of bone metastasis, equianalgesic oral morphine doses per day, number of pain sites, and duration of pain (adjusted OR 2.5, 95% CI: 1.3 – 4.9) as shown in Table 4.28. The model suggested that the effect was partially confounded by the presence of bone metastasis and by taking higher opioid dosages (equianalgesic oral morphine doses > 30 mg/day)

Table 4.28

The Odds ratio following logistic regression for the association between clinical setting and inadequate pain control, controlling for potential confounders

	Odds ratio (95% confidence interval)
Model 1	2.1 (1.2 - 3.7)
Model 2	2.3 (1.3 - 4.0)
Model 3	2.0 (1.1 – 3.7)
Model 4	2.4 (1.3 - 4.5)
Model 5	2.5 (1.3 – 4.9)

Model 1 – Main effect of clinical setting

Model 2 – Main effect of clinical setting, controlling for gender, age

Model 3 – Main effect of clinical setting, controlling for gender, age, presence of bone metastasis

Model 4 – Main effect of clinical setting, controlling for gender, age, presence of bone metastasis, opioids dosages

Model 5 – Main effect of clinical setting, controlling for gender, age, presence of bone metastasis, opioids dosages, number of pain sites, duration of pain

4.4 The Parsimonious model predicting pain control

All potential correlates of an inadequate pain control (identified from the previous univariate analyses) were entered into the logistic regression model to identify the best predictors for an inadequate pain control. Variables were retained or dropped from the model on the basis of the significance of the likelihood ratio tests.

As shown in Table 4.29, an exploratory parsimonious model was used to examine the factors associated with an inadequate pain control. With the pain control (the dependent variable), the final model showed that the patients in the cancer center were independently associated with reporting inadequately treated pain with an adjusted OR of 2.8, 95% CI: 1.6 – 5.2. Depression was also independently associated with an inadequate pain control (adjusted OR = 2.2, 95%CI: 1.0 – 4.5). Cancer patients who were prescribed higher dosages opioids were independently associated with inadequate pain control (adjusted OR = 2.0, 95%CI: 1.1 – 3.5).

Table 4.29

Final ‘best fit’ multivariate model (logistic regression), based on clinical setting and other variables with pain control as the dependent variable

Variable	N	n (%) Inadequate pain control	Crude OR	Adjusted OR (95%CI)	P-value
Clinical setting					
Pain clinic	133	72 (54.1)	1	1	
Cancer center	95	68 (71.6)	2.1	2.8 (1.6 - 5.2)	0.001
Depression					
No	181	106 (58.6)	1	1	
Yes	47	34 (72.3)	1.9	2.2 (1.0 - 4.5)	0.039
Opioids dosages					
≤ 30 mg/day	116	65 (56.0)	1	1	
> 30 mg/day	112	75 (67.0)	1.6	2.0 (1.1 - 3.5)	0.024

4.5 Other findings

Exploratory analysis

The two outcomes, depression and quality of life (QOL), were rendered as the dependent variables that need the investigation to find out their associated factors. The QOL was classified as the poor QOL (total score of QOL $\leq$ 70) and the good QOL (total score of QOL > 70). All potential confounding variables for the associations between depression and quality of life, on one hand, and pain control on the other were examined. In addition, pain control and depression were correlated with QOL. Therefore, the pain control, depression and QOL were all included in the exploratory models.

4.5.1 Depression

The univariate analyses of the factors associated with depression (dependent variable) are summarized in Table 4.30. The patients in the pain clinic were significantly affected by depression than those in the cancer center (p=0.013). Patients who had two or more sites of pain were significantly at higher risk than those with one pain site (OR=3.0, 95% CI: 1.4 – 6.2).

As shown in Table 4.31, the exploratory parsimonious model was used in this study to predict the factors associating with depression. As depression as the dependent variable, the final model showed that the patients with higher number of pain sites were independently associated with depression (OR 2.7, 95% CI: 1.3 – 5.9). Being male was independently associated with depression (OR 2.1, 95% CI: 1.1 – 4.0).

Table 4.30

The association between depression and potential confounders

Variable		Depression (n=47)		
	n	n (%)	Odds ratio (95%CI)	p-value
Medical setting				
Pain clinic	133	35 (26.3)	1	0.013
Cancer center	95	12 (12.6)	0.4 (0.2 - 0.8)	
Gender				
Female	130	21 (16.2)	1	0.069
Male	98	26 (26.5)	1.9(1.0-3.6)	
Age				
18 - 60 years	152	26 (17.1)	1	0.082
61 - 84 years	76	21 (27.6)	1.9 (1.0-3.6)	
Patient's barrier (n=140)				
$\leq$ 1.5 score	70	16 (22.9)	1	0.559
> 1.5 score	70	19 (27.1)	1.3 (0.6-2.7)	
Cancer stage (n=204)				
Stage 1-3	37	4 (10.8)	1	0.172
Stage 4	167	36 (21.6)	2.3(0.8-6.8)	
Presence of bone metastasis				
No	134	23 (17.2)	1	0.137
Yes	94	24 (25.5)	1.7 (0.9 - 3.2)	
Number of pain sites				
one site	97	11 (11.3)	1	0.003
two or more sites	131	36 (27.5)	3.0 (1.4-6.2)	
Duration of pain				
$\leq$ 3 months	103	19.4	1	0.596
> 3 months	125	21.6	1.1 (0.6-2.2)	
Level of pain control				
Adequate	88	13 (14.8)	1	0.094
Inadequate	140	34 (24.3)	1.9 (0.9 - 3.7)	

Table 4.31

Final ‘best fit’ multivariate model (logistic regression), based on clinical setting and other variables with depression as the dependent variable

Variable	N	n (%) depression	Crude OR	Adjusted OR (95%CI)	P-value
Clinical setting					
Pain clinic	133	35 (26.3)	1	1	
Cancer center	95	12 (12.6)	0.4	0.5 (0.2 - 1.0)	0.065
Number of pain sites					
One site	97	11(11.3)	1	1	
Two or more sites	131	36 (27.5)	3.0	2.7 (1.3 - 5.9)	0.010
Gender					
Female	130	21 (16.2)	1	1	
Male	98	26 (26.5)	1.9	2.1 (1.1 - 4.0)	0.035

4.5.2 Quality of life

The univariate analyses of the factors associated with the poor QOL (dependent variable) were summarized in Table 4.32 The most advanced cancer stage (stage 4), the presence of bone metastasis, an inadequate pain control status, and depression were significantly associated with the poor QOL ($p < 0.05$).

As shown in Table 4.33, the exploratory parsimonious model was used in the study to predict the factors that were associated with the poor QOL. With the poor QOL (the dependent variable), the final model showed that cancer patients with bone metastasis were independently associated with the poor QOL (adjusted OR 2.1, 95% CI: 1.1 – 4.0). Inadequate pain control patients were independently associated with the poor QOL (adjusted OR 2.3, 95% CI: 1.2 – 4.3). The cancer patients with depression were independently associated with the poor QOL (adjusted OR 20.4, 95% CI: 6.0 – 69.6).

Table 4.32

The association between quality of life and potential confounders

Variables		Poor quality of life (n=118)		
	n	n (%)	Odds ratio (95%CI)	p-value
Clinical setting				
Pain clinic	133	72 (54.1)	1	0.395
Cancer center	95	46 (48.4)	0.8 (0.5-1.3)	
Gender				
Female	130	61 (46.9)	1	0.093
Male	98	57 (58.2)	1.6 (1.0-2.7)	
Age: years				
18 - 60 years	152	79 (52.0)	1	0.925
61 - 84 years	76	39 (51.3)	1.0 (0.6 - 1.7)	
Patient's barrier (n=140)				
≤ 1.5 score	70	40 (57.1)	1	0.387
> 1.5 score	70	45 (64.3)	1.4 (0.7-2.7)	
Cancer stage				
Stage 1-3	37	12 (32.4)	1	0.020
Stage 4	167	90 (53.9)	2.4 (1.1-5.2)	
Presence of bone metastasis				
No	134	61 (45.5)	1	0.025
Yes	94	57 (60.6)	1.8 (1.1-3.1)	
Number of pain sites				
one site	97	43 (44.3)	1	0.054
two sites or more	131	75 (57.3)	1.7 (1.0-2.9)	
Duration of pain				
≤ 3.0 months	103	52 (50.5)	1	0.728
> 3 months	125	66 (52.8)	1.1 (0.7-1.8)	
Level of pain control				
Adequate	88	35 (39.8)	1	0.004
Inadequate	140	83 (59.3)	2.2 (1.3-3.8)	
Depression				
No	181	74 (40.9)	1	< 0.001
Yes	47	44 (93.6)	21.2 (6.3-70.9)	

Table 4.33

Final ‘best fit’ multivariate model (logistic regression), based on clinical setting and other variables with poor QOL as the dependent variable

Variable	N	n (%) Poor QOL	Crude OR	Adjusted OR (95%CI)	P-value
Clinical setting					
Pain clinic	133	72 (54.1)	1	1	
Cancer center	95	46 (48.4)	0.8	1.1 (0.6 - 2.1)	0.744
Depression					
No	181	74 (40.9)	1	1	
Yes	47	44 (93.6)	21.2	20.4 (6.0 - 69.6)	<0.001
Pain control					
Adequate	88	35 (39.8)	1	1	
Inadequate	140	83 (59.3)	2.2	2.3 (1.2 - 4.3)	0.011
Presence of bone metastasis					
No	134	61 (45.5)	1	1	
Yes	94	57 (60.6)	1.8	2.1 (1.1 - 4.0)	0.027

4.6 Summary of the multivariate analyses regarding the hypothesis testing

Being patients at the cancer center (independent variable) were independently associated with the reported inadequately treated pain (Odds ratio: 2.5, 95 %CI: 1.3 – 4.9), adjusting for gender, age, presence of bone metastasis, opioid dosage, number of pain sites, and duration of pain. Having bone metastasis was found as the positive confounder whereas the opioid dosage was the negative confounder.

The results from the exploratory models in this study showed that

1. Being treated in the non-pain clinic, depression and higher dosages opioids were the factors associated with an inadequate pain control.
2. Male gender and higher number of pain sites were the factors associated with depression.
3. Inadequate pain control, bone metastasis and depression were the factors associated with the poor quality of life.