ONCOLOGY PATIENTS' BELIEFS IN SUPPORTIVE CARE AND THEIR ADHERENCE

CASPER KEEGAN LIN RONGGUI

NATIONAL UNIVERSITY OF SINGAPORE

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CASPER KEEGAN LIN RONGGUI
B.Sc. (Pharm.) (Hons.)
National University of Singapore

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Yours Sincerely,

Dr WEE Hwee Lin
Assistant Professor
Supervisor

Miss Lita Chew
Assistant Professor
Co-supervisor

18 Science Drive 4, Singapore 117543
Tel: (65) 6516 5530
Website: www.nus.edu.sg
Company Registration No: 200604346E

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DECLARATION

I hereby declare that the thesis is my original

work and it has been written by me in its entirety.

I have duly acknowledged all the sources of

information which have been used in the thesis.

This thesis has also not been submitted for any degree

in any university previously.

Casper Keegan Lin Ronggui
13 July 2016

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EXECUTIVE SUMMARY

Pain is a common symptom of cancer and it significantly affects the diagnosis, quality of life and survival of patients with cancer. Opioids are the mainstay in managing cancer-related pain. However, cancer patients' adherence to opioid analgesics were reported to be less-than-desirable (63.6% for around-the-clock opioid analgesics and 30.9% for as-needed opioid analgesics in a study among Taiwanese oncology patients)[1]. Without proper adherence to prescribed opioid regimen, severe cancer pain cannot be adequately controlled[2].

Beliefs about opioids are rooted in their use and misuse in history, resulting in social stigma attached even to their legitimate use in cancer-related pain. As a consequence, they evolved to become significant barriers to cancer pain management by contributing to opioid medication non-adherence[3].

Self-management with prescribed opioid regimen has become an integral part of cancer pain experience at home[4]. Thus, the specific skills and behaviors needed by patients to effectively manage their opioid pain relievers has also become critically important in determining the degree to which opioids are adhered to. As a result, an understanding of this potentially modifiable variable may allow us to predict and hopefully serve as points of interventions to improve opioid medication adherence.

Patients' beliefs regarding opioid usage and their self-efficacy are largely unstudied in Singapore. Their relationships to opioid medication adherence have been evaluated only in limited studies in other countries such as the United States and Taiwan[5-7].

The work in this thesis will allow us to strengthen the understanding of how these patient attributes affect opioid adherence in the local context, specifically in cancer patients.

This thesis began with a systematic literature review that identified the contexts in which studies related to cancer patients' beliefs have been performed. In the systematic literature review, we also described and appraised the content and psychometric properties of the measurement tools for assessing cancer patient beliefs. This led us to single out the POABS-CA as a potentially valuable instrument to use in our population to understand how these patient attributes can affect opioid adherence. While several instruments, such as Beliefs in Medicines Questionnaire (BMQ) and the Barriers Questionnaire (BQ), have been developed to study patients' beliefs affecting medication adherence, only the Pain Opioid Analgesics Beliefs Scale-Cancer (POABS-CA) is specific to both cancer patients and to opioid medications. The POABS-CA, based on Agency for Health Care Policy and Research (AHCPR) cancer pain guidelines and culturally related pain beliefs observed in clinical settings, was designed by a Taiwanese research team to measure negative effect beliefs about opioids (belief that opioids will have negative effects on the body) and pain endurance beliefs (belief that one should endure as much pain as possible). Validation of the POABS-CA in our local setting will enable us to ascertain if the domains identified by the Taiwanese research group is similarly regarded as important and relevant by our patients. Hence, part of the thesis reported on the evaluation of the validity and reliability of the POABS-CA, which was found to show satisfactory feasibility

and reliability. However, unlike the Taiwanese study, the same construct validity

was not observed.

We acquired the trend of opioid usage in a local ambulatory cancer center to

obtain baseline understanding of our opioid consumption. We have found that,

despite increases in cancers diagnosed, our usage of opioids remained relatively

stable. However, a rise in the use of stronger opioids such as oxycodone is

observed. As serious problems associated with increased usage of stronger

opioids overseas have been reported, we should watch our population closely as

we continue to prescribe suitable analgesics for our patients .

In conclusion , this thesis has laid the groundwork by providing an

understanding of opioid usage trends and issues in Singapore among cancer

patients, particularly in the area of cancer pain beliefs and the consequent

adherence to opioid painkillers. The impact of cancer patients' beliefs has been

studied in a variety of contexts but there is a general lack of well-designed

studies. Several other contexts where cancer patient beliefs may play a role has

not been explored and could be areas for future research . Much needs to be

done to gain a better understanding of these issues and to develop strategies to

address them. Although the POABS-CA may not be readily useable in our patient

population, our results are nevertheless useful in informing the design of future

studies to understand cancer pain beliefs in relation to patients' adherence to

opioid painkiller medications.

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Specific Aims

Long-term objective

    i.   To enhance understanding of how patients' beliefs affect adherence to supportive care. Supportive care here refers to medical and surgical issues concerning supportive therapy and care, which may supplement basic treatment of the disease[8].

Goals of research

    i.   To broadly outline the contexts in which studies related to cancer patients' beliefs have been performed via a systematic review.

    ii.   To identify a valid and reliable questionnaire for assessing cancer patients' opioid medication beliefs in the local context

    iii.   To ascertain the trends in opioid use in a large local ambulatory cancer center to enable us to obtain a baseline understanding of opioid usage in our local setting

    iv.   To ascertain the reliability and validity of existing instrument identified in (ii) for opioid beliefs among Singaporean patients with cancer.

    v.   To determine the association between cancer patients' medication beliefs and cancer therapy adherence among local patients using the questionnaire identified in (ii).

Literature Review

Patients' beliefs as an important component in the total concept of care in oncology

Cancer is a complex and varied disease. For cancer care to be dependable and efficient, it has to be considered as a structure, functioning as an interconnected organization of operations with the same goal[9]. As a result, multidisciplinary cancer care is now viewed as necessary in delivering the total concept of care in oncology[10]. Total concept of care in oncology refers to holistic view of medical care that is relevant to a cancer patient, including anti-cancer treatment, supportive care, attention to mental health, emotional health, as well as spiritual needs. This patient management system increasingly involve representation of healthcare professionals from various disciplines as patient management continue to expand to envelop areas such as treatment, management of side effects, psychosocial support and end-of-life issues. Previous studies have reported that cancer patients' beliefs regarding pain and pain medications affected the way they viewed cancer-related pain and opioids[7], spiritual aspects of coping with cancer[11] and even the way they viewed their own illness[12]. Hence, we hypothesized that patients' beliefs are critical in the total concept of care in oncology, where every part of medical care in a cancer patient is relevant. We then embarked on a systematic literature review (study #1) to identify research gaps in this subject area. Specifically, we sought to (i) identify any component of the total concept of care in oncology where patients' beliefs have not been well studied and (ii) either cross culturally adapt or develop new measures of patients' belief to plug the research gap in the local context.

Patients' beliefs in Supportive Care

As stated earlier, we are also interested to evaluate how patient's beliefs may impact on the receipt of supportive care in cancer, specifically in the area of pain management.

Pain is a common symptom of the disease process in a patient's journey in cancer. World Health Organization (WHO) recommends that analgesics should be given "by the clock" rather than "on demand" in order to maintain a pain-free condition in cancer patients [13]. In support of this recommendation, WHO has developed a three-step cancer pain ladder for adult patients, where prompt oral administration of drugs is advised in the following manner: first non-opioids, followed by mild opioids such as codeine phosphate, and finally strong opioids such as morphine sulphate, until a pain-free state has been achieved in each cancer patient. Despite the World Health Organisation's (WHO) recommendations, inadequate management of cancer pain remains a major problem. The prevalence of chronic pain is about 30–50% among patients with cancer who are undergoing active treatment for a solid tumour[14-16] and 70–90% among those with advanced disease[17-21]. The prevailing health care provider-related impediments include inadequate pain assessment, dearth of expertise and doctor's hesitancy at prescribing opioids[22, 23]. System-related obstacles restrict patients' or physicians' access to opioid analgesics or even limit availability of pain experts. However, most pertinent to our study are patient-related barriers, which include mental and emotional factors as well as adherence to pain management plans[24].

Opioids are established as the cornerstone of cancer pain treatment by the WHO since 1990[25] and morphine is recommended by the European Association for Palliative Care as the benchmark "step 3" opioid according to the WHO ladder[26].

Despite opioid analgesics being the mainstay for management of cancer-related pain, there have been reported barriers to the use of opioids for pain relief[23, 27-29], particularly concerns with potential addiction, the perceived need to tolerate cancer pain without use of opioids and that opioids should only be reserved for use later in the course of cancer due to the belief that use of opioids earlier would render them less effective in the advanced stages of the disease. There were also reports of patients' beliefs that the introduction of morphine was a metaphor for impending death, as patients and their caregivers commonly viewed the use of morphine as a last resort in their treatment[29].

Significance of Proposed Studies

Systematic review of measures of cancer patients' beliefs

Identified knowledge gaps

We performed a systematic literature review (Chapter 1) of studies published in MEDLINE and Cochrane Trials before July 2015. From this systematic literature review of cancer patients' beliefs we confirmed that the relationship between cancer patients' beliefs and their adherence to both cancer therapy and supportive care are current knowledge gaps in the study of cancer patients' beliefs. This led us to propose several related studies to further contribute to this subject area.

Prevalence data on opioid consumption patterns in NCCS

Reported local data

We reported local data on trends in current opioid usage. This information is important in several ways. The International Narcotics Control Board (INCB) provides national-level opioid usage data which includes both cancer and non-cancer usage patterns. Our study is pertinent to our interest to acquire opioid usage patterns specific to cancer use. This information can be important to allow decision makers to anticipate associated harms with increased consumption of opioids and to potentially mitigate by increasing emphasis on adherence to opioids.

Evaluation of validity and reliability of POABS-CA

A valid and reliable tool for assessing cancer patients' beliefs on opioid analgesics is required as we seek to evaluate the association between patients' beliefs and opioid usage.

Measure of cancer patients' opioid beliefs and their adherence to opioid analgesics

<u>Lack of local data</u>

The NCCS has a busy specialist outpatient clinic (SOC) with more than 100,000 patient attendances annually. To date the Centre has limited resources and services that specifically cater to medication management needs of cancer patients. With regards to opioid analgesic use, we assumed that patients and their caregivers are able to manage their own medication safely. We do not have a system that actively seeks patients who potentially have problems with their treatment or handling of drugs. Little is also known about the medication adherence of patients who receive opioid analgesics for cancer pain.

The findings from this study will be used as baseline information for future resource and service allocations to cater to the needs of patients on opioid analgesics. By understanding the association between patients' beliefs on opioid analgesics and how this influences their adherence to opioids, we will be able to identify patients at risk for opioid analgesic non-adherence as well as improve the rate at which these patients adhere to their cancer pain regimen.

By enhancing our understanding of patients' opioid beliefs and their adherence to opioid analgesics, we will be able to identify patients at risk for opioid non-adherence. This will allow the future design of tailored interventions targeted at these patients and would be a more cost-effective approach than a one-size-fits-all intervention.

Chapter 1. Systematic review of measures of cancer patients' beliefs

1.1   Introduction

Cancer is a leading cause of death in many societies globally, with approximately 14 million new cases and 8.2 million cancer related deaths in 2012[30]. The annual cancer cases is expected to continue to increase from 14 million in 2012 to 22 million within the next two decades[30].

Approach to dealing with cancer by health care professionals have conventionally involved first a clinical diagnosis of the patient's condition followed by structured plans for treatment and ancillary care by consulting with evidence-based, consensus-driven management guidelines that serve to ensure that their patients receive treatment and supportive services that are most likely to lead to optimal outcomes. However, patients themselves deal with the disease very differently and their preferences and decisions should not be overlooked.

Patients' perspectives can play critical roles in the management of their own illness [31]. A patient's cancer beliefs can potentially influence how an individual perceives treatment modalities, likely courses of the disease journey, as well as the significance of the disease on their lives. For example, in a study[32] among 425 patients with diverse malignancies treated at a large academic oncology center, perceived disease severity was a significant predictor of participation in patient support groups after adjusting for disease site and other potential confounders [32]. Likewise, these inherent qualities[33] that patients harbor were also shown to effect the outcome of patients' mindset and behavior in their disease management. For example, in a study[33] among 1075 childhood cancer survivors, the perception that regular follow-up is not necessary was the only significant predictor of follow-up attendance after adjusting for other health beliefs, medical and demographic variables[33]. Hence, patients' beliefs are important in the potential success of cancer management.

However, most of the literature has focused on the understanding of how health beliefs of the general population influence cancer-screening uptake[34-36] in various parts of the world, such as among Hispanics, immigrant and ethnic minorities in the US and globally. A review identified a body of knowledge in the area of Indigenous beliefs about biomedical and bush medicine treatment efficacy for Australian indigenous cancer patients[37]. To the best of our knowledge, there is no other systematic review that summarizes current literature with regards to the areas of focus in which cancer patients' beliefs have been studied. The areas of focus are the common primary objectives of the individual studies in this review, of which we have segregated into five distinct groups. We are particularly interested to evaluate if the current measurement tools for assessing cancer patient beliefs are sufficiently comprehensive and robust for their intended purposes within each context. Hence, the purpose of this systematic literature review is to broadly outline the contexts by summarizing the studies within each area of focus in which studies related to cancer patients' beliefs have been performed. In addition, we would critically appraise the content and psychometric properties of the measurement tools for assessing cancer patient beliefs within each context. Suggestions for priorities in future research will be provided.

1.2   Methods

A literature search of studies published in MEDLINE and Cochrane Trials before July 2015 was undertaken. The search terms and study inclusion criteria were intentionally broad. We included studies of participants diagnosed with cancer, who were asked for their own beliefs regarding any aspect of cancer. The inclusion criteria are studies of participants diagnosed with cancer, who were asked for their own beliefs regarding

any aspect of cancer. The exclusion criteria are studies unrelated to cancer or related

to cancer screening, as well as studies that did not measure patients' beliefs, or that

the measurement of beliefs were those of the general public or health care

professionals instead of patients. Non-English articles are also excluded. Articles

published only as abstracts were excluded. The time frame was 10 years from 2006

to 2015.

The keywords "belief", "questionnaire" and "cancer" were used, with the following

search details: (("culture"[MeSH Terms] OR "culture"[All Fields] OR "belief"[All

Fields]) AND ("questionnaires"[MeSH Terms] OR "questionnaires"[All Fields] OR

"questionnaire"[All Fields]) AND ("neoplasms"[MeSH Terms] OR "neoplasms"[All

Fields] OR "cancer"[All Fields])) NOT "quality of life"[All Fields] AND ((Clinical

Trial[ptyp] OR Journal Article[ptyp] OR Review[ptyp] OR systematic[sb] OR Meta-

Analysis[ptyp] OR Randomized Controlled Trial[ptyp]) AND "2005/08/06"[PDat] :

"2015/08/03"[PDat] AND "humans"[MeSH Terms] AND English[lang] AND

cancer[sb]). While randomized controlled trials (RCTs) and controlled trials are the

most robust, it is not anticipated that many studies of these designs will be available

in this field. Therefore, if information from controlled trials is not available, other

studies such as cohort and cross-sectional studies as well as meta-analyses and

systematic reviews are eligible for inclusion. Besides conducting database analysis,

we hand-searched the bibliography of included articles for additional articles.

Two investigators independently reviewed the abstracts and full-text articles against

the pre-specified eligibility criteria. One investigator extracted details about the study

design, patient sample, setting, and results. Another investigator verified the extracted

data for accuracy. Two investigators independently assessed the quality of each study

by applying Newcastle-Ottawa quality assessment scale in terms of the number of

stars accrued, where appropriate. Discrepancies were resolved through a consensus

process. We then organized the included articles according to the contexts of inquiry

(subsequently referred to as areas of focus), according to the articles' primary

objectives as our guiding principle. This process involved both investigators

separately categorizing the articles with similar focus as identified by their primary

objectives under their relevant categories. Discrepancies were resolved through a

consensus process. Within each context, we summarize the work that has been done

and provide a list of measurement tools for cancer patient beliefs that is available. We

will then critique the content and psychometric properties of each tool.

1.3   Results

The literature search, exclusion and selection are summarized in Figure 1. Database searches resulted in 657 potentially relevant articles, whose titles and abstracts were dual-reviewed, leaving 29 articles that met our inclusion and exclusion criteria. 423 articles were rejected due to their titles being unrelated to cancer or were related to cancer screening. 172 articles were further rejected due to their abstracts showing that the studies did not measure patients' beliefs, or that the measurement of beliefs were those of the general public or health care professionals instead of patients'. Finally, 30 articles rejected after the investigators read the full text and found that the studies did not measure patients' beliefs, or that the measurement of beliefs were those of the general public or health care professionals instead of patients. We identified no studies conducted as randomized controlled trials and other than two large, good-quality cohort studies, the rest of the studies were cross-sectional in nature. The resultant articles were then grouped according to the focus of their studies and will be subsequently discussed. Table 1.2 shows a summary of the studies reviewed while Table 1.3 compiles the questionnaires measuring cancer patients' beliefs found in the studies.

Figure 1: Literature search, exclusion and selection
Areas of focus

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The shortlisted studies may be organized into five areas of focus, namely: views on

treatment acceptance, health status, adherence, coping with cancer and

traditional/complementary medicine (Table 1.1).

Table 1.1 - Studies on cancer patients' beliefs

Focus	Number of studies
Cancer Beliefs and Treatment Acceptance	3
Cancer Beliefs and Health Status or Health Behavior	9
Cancer Beliefs and Treatment Adherence	7
Cancer Beliefs and Coping with Cancer	7
Cancer Beliefs and Traditional/Complementary Medicine	3

Cancer Beliefs and Treatment Acceptance

A total of three studies evaluated the association between cancer patient beliefs and treatment acceptance. Negative beliefs about cancer treatments have been associated with patients' low acceptance of recommended cancer management plans. A study in Australia by Cohen et al (n = 126) found that a significant proportion of the patients surveyed (41%) possessed strong negative beliefs about the addictive potential of opioid analgesics [5]. The authors postulated that the strong negative beliefs might explain why only 40.4% of patients decided to receive a portion of painkillers available to them despite experiencing moderate to severe pain in the 24 hours prior to being interviewed. In a cross-sectional study by Liang et al in Taiwan (n = 92), 33.7% believed that "opioid medicine should only be used at the last stage of an illness" and 68.5% believed that "opioid medication is not good for a person's body". This showed that a similarly large proportion of respondents had misconceptions about opioid analgesics and the concept of pain management[7]. However, the

Taiwanese study did not evaluate if the misconceptions were associated with treatment acceptance.

Akiyama et al conducted a nation-wide survey in Japan to study advanced cancer patients' perception, knowledge as well as concerns about use of opioid painkillers, palliative care and homecare[27]. While 1,619 questionnaires were sent, 925 responses have been received. In particular, 30% of patients were shown to believe that use of opioid painkillers can result in addiction or reduce one's lifespan. About half also erroneously believed palliative care to be reserved only for those in the final stages of the disease.

Cohen et al utilized the American Pain Society's (APS) Patient Outcome Questionnaire, which has been established as a valid and reliable instrument to measure pain[38-40] and has been translated into various languages[39, 40]. It is a patient-reported outcome (PRO) on pain intensity, the degree to which pain affects their mood and daily living activities, pain beliefs and attitudes and their management, and their satisfaction with inpatient pain management.

Liang et al used the Pain Opioid Analgesic Beliefs Scale – Cancer (POABS-CA) to measure cancer patients' beliefs in pain and opioid analgesics using 10 items on a 5-point Likert-type scale. Cronbach's alpha was calculated to be 0.70 and test-retest reliability was 0.94. Factor structure was confirmed and known group, as well as face, validities were supported. It was also shown to possess satisfactory reliability and validity, and consists of two factors, pain endurance beliefs and negative effect beliefs. Using this instrument, Liang et al found association between patients' negative beliefs in opioids and their treatment adherence to opioid analgesics. It was however validated only among Taiwanese cancer patients.

Akiyama et al's survey consisted of two items to assess opioid knowledge and belief: "opioids can relieve most pain caused by cancer" and "opioids are addictive and/or shorten life". Three items were utilized to measure patients' beliefs about palliative care: "palliative care relieves pain and distress", "palliative care is provided along chemotherapy and/or radiation therapy" and "palliative care is only for terminally ill patients". Each of these five items was answered along a 5-point Likert scale (1: strongly disagree, 2: disagree, 3: unsure, 4: agree, 5: strongly agree).

Cancer Beliefs and Health Status or Health Behavior

A total of nine studies evaluated the relationship between cancer patient beliefs and health status. Among these, six studies evaluated beliefs about the etiology of cancer and health status. For example, one large, fair-quality cohort study (n = 1489) by Panjari et al found that stress (58.1%) was the most common cause attributed to the development of cancer[41]. Women who believed in this had lower Psychological General Well-being Index (PGWB) scores than others (70.9±16.1, n=361 versus 77.3±14.9, n=1071, mean difference=6.4, 95% CI: 4.6–8.2 p<0.0001). Interestingly, they were also more inclined to adopt strategies to reduce stress. In another study, Costanzo et al showed that women with cervical or endometrial cancer reported stress as the second most important cause of cancer, preceded by genetics[42]. It was found that stronger causal attributions tended to be associated with symptoms of depression and anxiety. As with the previous study, women with stronger causal attributions also tend to be more inclined to practise healthy behaviors. In a third study, Thuné-Boyle et al demonstrated that belief of the consequence of their illness was found to be a critical determinant of distress in patients, explaining 15% of the variance in anxiety and 5% of that in depression[43]. A small study (n = 28) by Obeidat showed that fear

played a dominant role in Jordanian women's breast cancer journey, where it shaped

their experience with their illness and its associated treatment[44]. Another study in

UK by Lord K et al found that a minority of British South Asian (BSA) patients held

strong beliefs in supernatural causes of cancer[45].

Besides belief about etiology of cancer, two other studies evaluated the belief on

cancer severity and health behavior. For example, Ermiah et al discovered that the

seemingly lackadaisical belief on the gravity of cancer has contributed to the view

that breast cancer symptoms are not serious and this has been shown to result in

delays in clinical diagnosis of breast cancers in Libya, where the median diagnosis

time was 7.5 months and only 30% of patients were diagnosed within 3 months upon

presentation of symptoms[46]. Another study in the USA by Costanzo et al found that

among women treated with adjuvant chemotherapy and/or radiotherapy, those who

viewed their cancer to have graver consequences were also the most likely to develop

positive changes in their lifestyles[47].

Kumar et al showed that cancer patients in Pakistan possessed unique beliefs and

concerns about the disease that physicians should be aware of[48]. A significant

proportion of patients in the study (27%) were of the opinion that cancer was

contagious and majority (75.2%) sought alternative treatments (faith healing,

homeopathy) prior to an appointment with their oncologists.

A study in Canada by Nadler et al on osteoporosis knowledge and beliefs among men

with prostate cancer on androgen-deprivation therapy (ADT) revealed that patients

lack knowledge on osteoporosis as well as self-efficacy[49]. These patients also

neither view themselves as susceptible to osteoporosis nor approached the issue

(osteoporosis) with the appropriate gravity due to the condition. As a result, many

failed to practice healthy bone behaviors.

Ermiah et al used a semi-structured interview conducted by a physician to collect data including patients' sociodemographics and medical history.

Kumar et al designed a set of questionnaire themselves from review of studies done in South Asia. It covered themes of current cultural practices and religious beliefs, and also included patient-level information on education levels, employment statuses, as well as knowledge and beliefs regarding cancer risk and treatments.

Lord K et al utilized six questionnaires in his study: which include the Mini- Mental Adjustment to Cancer (Mini-MAC) and the Physician/Patient Trust and Cancer Beliefs questionnaire, a questionnaire on patient's opinions on confidentiality outcome and cancer management. The Mini-MAC is a revised version of the Mental Adjustment to Cancer (MAC) and its purpose is to measure the coping styles that cancer patients have when diagnosed with the disease.

The set of questionnaires employed by Nadler et al included the Osteoporosis Health Belief Scale (OHBS) to measure health beliefs in the domains of perceived osteoporosis susceptibility, seriousness about osteoporosis and general motivation to health.

Panjari et al administered three separate questionnaires to her subjects: enrollment questionnaire (EQ) about 41 weeks upon diagnosis of breast cancer, follow-up questionnaires 1 (FQ1) 12 months from EQ, and FQ2 which was administered 24 months from completing EQ. The EQ consisted of background information such as demographics and details of the disease as well its treatment. FQs record ongoing medical management of the disease as well as changes in lifestyles. FQ2 additionally included the Psychological General Well-Being Index (PGWB), a 22-item questionnaire to assess psychological well-being.

Thuné-Boyle et al used the Illness Perception Questionnaire (IPQ) in his study. More accurately, the study used two subscales from IPQ that was adapted for breast cancer patients, to measure breast cancer patients' beliefs about the potential for cure of the disease, as well as the ramifications of cancer and its management.

Costanzo et al, in the study on breast cancer patients, attempted to measure two aspects: health practices and common-sense models of cancer. To perform the former, the research group asked the patients, via the questionnaire, on health behavior changes after the cancer diagnosis as well as the degree to which the patients participated in the health practices. The Illness Perception Questionnaire-Revised (IPQ-R) was utilized to measure the patients' beliefs about their disease.

In a separate study on gynecologic cancer survivors, Costanzo et al used a set of questionnaires. The were two that measured cancer patients' beliefs: cancer attributions was measured by asking patients to rate the importance of several factors in how they contribute to cancer development as well as prevent recurrence; cancer-related worry was assessed by using the Concerns About Recurrence Scale (CARS), of which only measures general fear of recurrence of cancer (4 items) was used in this study.

Cancer Beliefs and Treatment Adherence

Seven studies evaluated the association between cancer beliefs and treatment adherence. One large, good-quality cohort study (n = 1075) by Michel et al on adherence to follow-up care for survivors of childhood cancers in Switzerland found that belief about the importance of follow-up was the single most important predictor to self-reported attendance at follow-up after adjusting for other health beliefs, sociodemographic and clinical variables[33].A Taiwanese study by Liang et al

showed that patients' beliefs about pain and opioid analgesics were significantly associated with adherence to these opioids (r = -0.30, p < 0.01)[24]. Patients were also noted to have worse adherence to around-the-clock (ATC) pain management regimens when they reported more misconceptions about pain and opioids. This is cogent as opioids, despite being the mainstay of cancer pain management, bring with them significant negative social stigma such as fear of addiction, side effects, as well as its reputation as a herald of impending death[29].

This was contradicted in a Norwegian study by Valeberg et al where their patients' barrier scores as measured using the Barriers Questionnaire–II (BQ-II) were not associated with their adherence scores[50]. The authors postulated that this could be due to patients not always reacting to their own concerns about how they felt about opioids by not being adherent to their pain regimen.

In terms of oral chemotherapy, one Greek study by Sarasiotou et al found that unintentional non-adherence to oral chemotherapy was most prevalent among those patients who believed that their treatment was ineffective (62.5%, p=0.03)[51]. As a result, it was concluded that patients' beliefs about treatment efficacy seemed to be a significant determinant of adherence to oral chemotherapy.

As part of oral anticancer treatment, adjuvant endocrine therapy has also seen problems related to patients' beliefs. Tamoxifen non-adherers were more inclined to also hold the belief that taking the medication would not benefit them[52], as illustrated in a UK study of breast cancer patients performed by Grunfeld et al. Sherman et al found that adherence to lymphedema risk minimization strategies by cancer patients who have undergone breast surgery was associated with belief in gravity of consequences of not adopting this practice[53].

Salz et al in a study in USA[54] found that while colorectal cancer survivors remain at risk of recurrence, not all continue with follow up colonoscopies. The research team found that a greater perceived susceptibility to colorectal cancer among these patients was associated with greater motivation to have a colonoscopy (OR=2.00, 95% CI=1.16–3.44). In addition, those who already had a colonoscopy since their diagnoses were associated with greater motivation to have a colonoscopy in the future (OR=9.47, 95% CI=2.08–43.16).

Sherman et al adapted a questionnaire that was originally created for genetic testing research for his study on lymphedema risk minimization. It consisted of four subscales that measured different cognitive facets that affect adherence to lymphedema risk minimization recommendations.

Michel et al used a questionnaire to answer mainly two questions: follow-up care and health beliefs. The health belief portion included measures of perceived susceptibility to late effects of past cancer treatments on a 10cm visual analogue scale, while severity of late effects was measured on 4-point Likert-type scale. In addition, benefits and barriers to follow-up care were assessed, as well as importance of health to the individual and beliefs on detecting and treating late effects of cancer treatments early.

Sarasiotou et al utilized a 7-page questionnaire that asked the following aspects of cancer care: demographics, belief in objective of oral chemotherapy, self-report adherence to treatment, intentional/unintentional missing of dose, reasons for missing dose, ways to improve adherence and side effects experienced from treatment, among other questions.

The study by Valeberg et al employed the use of the Brief Pain Inventory (BPI), two self-report instruments to measure adherence with pain management regimen, a 22-

item self-efficacy questionnaire and the Barriers Questionnaire-II (BQ-II). The BPI

measures pain intensity, pain relief from medications as well as the extent to which

pain has interfered with daily life. The 2 questionnaires on medication adherence

were the 4-item Morisky's Medication Adherence Scale (MMAS-4) and a single-item

adherence question with five response options developed by Lai Y H et al[55]. The

self-efficacy questionnaire was originally developed for arthritic patients and included

three subscales: self-efficacy for pain management, self-efficacy for physical function

and self-efficacy for coping with pain as well as other symptoms.

Grunfeld et al used a set of four questionnaires, of which the Beliefs in Medicines

Questionnaire (BMQ)[56] contains two sections: the BMQ-Specific and the BMQ-

General. These two sections can be used separately or in combination. It was

developed based on beliefs found to be common among patients suffering from

chronic illnesses such as asthma, diabetes and psychiatric conditions. The internal

consistency and test-retest reliability were found to be good, and the criterion and

discriminant validity were satisfactory.

The Barriers Questionnaire (BQ)[57] was developed in 1993 in USA to assess cancer

patients' reluctance to report pain and use analgesics. This was updated to the

Barriers Questionnaire–II (BQ-II)[58] which was used in this context, to more

accurately reflect current ideas with regards to cancer pain, its management and

current pain management practice. It consists of four factors namely, physiological

effects, fatalism, communication and harmful effects and was shown to be a reliable

and valid measure of cancer patients' obstacles to pain management.

Finally, the Pain Opioid Analgesic Beliefs Scale – Cancer (POABS-CA)[59] was

designed in 2003 by Taiwanese researchers Liang et al to measure cancer patients'

beliefs in pain and opioid analgesics using 10 items on a 5-point Likert-type scale.

The POABS-CA was also shown to possess satisfactory reliability and validity and consists of two factors: pain endurance beliefs and negative effect beliefs. It was however validated only among Taiwanese cancer patients.

Cancer Beliefs and Coping with Cancer

Seven studies evaluated how cancer beliefs affected the ways in which patients coped with their cancer. Several of these studies involved a qualitative analysis. A large, fair-quality study (n = 1043) by Johannessen-Henry et al found that among cancer patients, greater spiritual beliefs and hence, greater spiritual well-being, was significantly related to having less distress (β=- 0.79, CI - 0.92; - 0.66), as well as better adjustment to a cancer diagnosis in terms of having greater fighting spirit, less anxious preoccupation, helplessness-hopelessness[60]. Doumit et al performed a qualitative study among Lebanese breast cancer patients and found that these women were generally subscribed to the belief that cancer was supernaturally derived, possessed the constant fear of recurrence of the illness and generally preferred support in the manner that revealed no discrimination towards them from people around them[61]. Another qualitative study, this time among Chinese women by Cheng et al, revealed that a combination of fatalistic belief and acceptance of the diagnosis together with a personal motivation for self-care were ways in which these Chinese women coped with a breast cancer diagnosis[62]. A study by Thuné-Boyle in the UK on early-stage breast cancer patients revealed that the perception of being punished and abandoned by God as the cause of having cancer contributed to feelings of anxiety but this was partially moderated in their coping process by acceptance of their illness[63]. In a qualitative study by Banning et al in Pakistan among Muslim breast cancer patients, it was found that this group of patients responded to chemotherapy

with feelings of isolation and viewed it with aggression and anger[64]. Miccinesi et

al performed a study among Italian cancer patients with the resultant findings[11]: a

large proportion of Italian cancer patients have a personal spiritual life, with or

without any religious affiliation. Health care professionals were advised to be aware

of, and to place more emphasis on the metaphysical assets of cancer patients.

Alqaissi et al explored via phenomenological interviews that Jordanian breast cancer

women rely heavily on other women for support, mainly within the family[65]. In

addition, the research team recommended that health care professionals be aware of

the influence of culture and religion, as well as clinical and individual characteristics

of each woman on her requirements of social support.

Johannessen et al employed the use of a series of questionnaires in their study, of

which the Danish version of 12-item Functional Assessment of Chronic Illness

Therapy-Spiritual Well-being (FACIT-Sp-12) was administered to measure spiritual

well-being of patients. It contains three domains on personal harmony, significance

of self and personal belief. The Mini-MAC previously introduced was also used in

this study to measure mental adjustment style following a cancer diagnosis.

Miccinesi et al utilized the Systems of Belief Inventory (SBI-15R) to assess spiritual

needs among Italian patients. The SBI-15R contains a 10-item Beliefs subscale that

assesses religious beliefs and participation in religious activities, and a 5-item Support

subscale that assesses the support the patients received from the religious societies

they belonged to.

Thuné-Boyle et al utilized a number of questionnaires in their study. The team used

three single-item questions to assess cancer paitents' beliefs in God, and the degree to

which they perceived themselves as spiritual as well as the stability of their faiths.

The authors also examined private religious or spiritual practices using three items

from the "Multidimensional Measurement of Religiousness/ Spirituality for Use in Health Research: A Report by the Feltzer Institute/National Institute on Ageing Working Group"[66], with the items being rated on an 8-point Likert scale. From the same report, the authors extracted and used two items to assess patients' participation in religious practices and other religious activities with others. Religious coping was assessed using three items with the highest loadings from RCOPE, a measure of the role of religion an individual employ in coping with stress in life. The authors used a 12-item sub-scale of spiritual involvement scale to assess patients' private spiritual involvement. This tool measures the degree to which patients privately assimilate their relationship with God and use it to cope with stress due to their cancer diagnosis. A 3-item tool was used to measure patients' perceived spiritual support from God on a 5-point scale. Non-religious coping was assessed using the Brief COPE, which consists of 14 items with 4-point scales. The Life Orientation Test was utilized to measure patients' optimism on a 5-point scale for the 8 items. The three sources of emotional support as recognized by patients (friends, family and significant others) were examined by the Multidimensional Scale of Perceived Social Support. This tool consists of 12 items on a 5-point scale, with higher scores showing greater perceived levels of social support.

Banning et al used "semi-structured interviews" in an exploratory manner to elucidate Pakistani Muslim women's perception of breast cancer, how they lived their lives upon diagnosis, as well as potential ways in which "cultural, socio-psychological or religious factors" may have affected their experiences. However, there was no description of the questions asked during the interviews.

Cancer Beliefs and Traditional/Complementary Medicine

Three fair-quality studies showed popular use of CAM among cancer patients, ranging from 22.9% to 93.4% of those studied[67-69]. Many of these cancer patients' beliefs about CAM included the belief that CAM could cure them of cancer[68] and that they were effective[67].

In particular, Teng et al used a questionnaire that asked about patients' use of CAM[67]. In this instrument, patients were asked to recognize a list of CAMs and whether they have used any in the course of their illness. They were considered nonusers if they have not used any during their illness, even if they have previously used it before. Further, users of CAM were asked on the frequency of CAM usage, where they procured the medications, expectations from usage of CAMs, actual beneficial effects derived from CAMs, any ill-effects felt from CAMs, and the costs of CAMs.

Broom et al conducted a survey in Sri Lanka asking the cancer patients about their beliefs regarding CAM as well as their traditional medicine[68]. The survey consisted of reasons for using these traditional medicines and CAMs, as well as, reasons for not using them. It also asked whether patients used these alternative treatments prior to seeking professional advice at a hospital.

Takeda et al in Japan administered a self-report questionnaire to gynecologic cancer patients[69]. It consisted of three parts: general demographic information, an 8-item questionnaire about beliefs and attitudes about Japanese traditional medicine (Kampo) on a 5-point scale, and finally the third part is a Japanese version of the State-Trait Anxiety Inventory (STAI) which evaluates the level of anxiety of the patient at the point of answering the questionnaire and also the level of anxiety the patient normal felt.

1.4   Discussion

In this first systematic review of current knowledge landscape in patient's cancer beliefs, we found that some of the studies focused on how cancer belief is associated with treatment acceptance and treatment adherence. The belief that use of CAM can "cure their cancer"[68] is one that prevail in many cultures and are not limited to non-Western cultures. This myth appears to be particularly difficult to debunk despite considerable patient education effort. The use of CAM is intimately linked to cultural practices of cancer patients. In addition, the low incidences of adverse effects associated with CAM in comparison with Western medicine seem to affirm patients in their continued usage. The inability of current technology in Western medicine to cure advanced cancers further erode patients' faith. As a result, patients may choose to instead rely on CAM. As such, instead of seeking to abolish its practice, effort should perhaps be made to promote safer use of CAM, as well as encourage open discussion with their attending physicians when using CAM.

There is a general lack of longitudinal studies that evaluate how interventions designed to alter cancer patient beliefs influence future health status or health behavior. There is a need for future research focusing on how negative beliefs about opioids and cancer treatments can be ameliorated. This study is important because acceptance and maintenance of treatment ensure that patients obtain the best possible outcomes in their cancer care management.

Most of the studies were of fair quality. The best quality evidence we found were two large cohort studies with the rest being cross-sectional in design. There is clearly a need for good quality studies. Randomized trials evaluating effects of interventions on cancer patients' beliefs in terms of health outcomes may be challenging to conduct, but more malleable, large and well-designed controlled observation studies

with proper assessment of and control for potential confounders could better clarify and even advance knowledge in this field. In addition, we recommend that more qualitative studies should be performed to provide in-depth understanding of cancer patient beliefs. We have identified only a limited number of qualitative studies.

We identified a total of eighteen questionnaires that measure patient belief about cancer (Table 1.3). All of these evaluate cancer patient beliefs related to medications. Among these questionnaires, only POABS-CA is opioid specific. This has great potential for use in other cultures. A well-designed instrument should have a sound theoretical basis and should be relevant to the target patient group. In addition, it should possess good reliability and validity, and should be rigorously tested using relevant and current methodologies to justify its use. In this light, the POABS-CA, which was validated only in the Taiwanese population, is deserving of further testing in other cultures.

The Health Belief Model (HBM) proposed that an individual's perceived susceptibility to a condition and his/her perceived severity of having that condition, coupled with the perceived benefits of reducing the risk or seriousness of the condition in spite of the perceived barriers to taking such actions, could help to explain or predict engagement in health-promoting behaviors[70]. Construct of self-efficacy was added to the model to incorporate increasing evidence about its role in health behaviors and decision-making. From this review, we see that patients' cancer beliefs affected various aspects of the management of their disease. Cancer patients' negative beliefs about cancer treatments have been associated with low acceptance of recommended cancer management plans. We have also found several studies that evaluated the association between cancer beliefs and health status or health behavior. These beliefs affect the way patients attribute the cause of their illness, which in turn

affect how they went about addressing these believed attributions such as the adoption of healthier lifestyles for those who perceived exogenous factors to be contributing to their development of cancer. The belief in supernatural causes may have affected some patients to become more anxious but it also led them to be more accepting of their illness. Thus, cancer beliefs are consistent with the HBM, with particular regard to a patient's perception or beliefs of susceptibility, seriousness and barriers. This is explicitly manifest in the study on the development of the POABS-CA, whose results suggesting that negative opioid and cancer pain beliefs in cancer patients significantly determined their decisions on cancer pain management commensurate with the HBM, which assumes that a positive belief about illnesses and their treatments influenced people's sustained investment in health improvement behaviors[71].

The theory of reasoned action (TRA) is another popular health behavior model. The TRA strives to understand a person's voluntary behavior with the goal to explain the relationship between the individual's attitude and behavior in their actions[72]. Critical to this model are the individual's "belief towards an outcome" and "beliefs of what others think"[73]. These translate to an individual's attitude and subjective norm, respectively, which together contribute to behavioral intent[73]. Thus, a central theme of the TRA is an individual's perception or "belief", both on expected outcomes upon embarking on an improved health behavior as well as subjective norms with regards to such a health behavior. In this context, measuring cancer patients' beliefs become particularly relevant when we are attempting to understand these individuals' beliefs on expected outcomes of adhering to treatment such as chemotherapy or pain management plans, or how society and healthcare professionals (subject experts) perceive them using opioid analgesics for relief of cancer pain.

However, a more pragmatic and current model that is a good fit with cancer beliefs is the theory of planned behavior (TPB)[74]. The TPB is an extension of the TRA to account for involuntary behaviors, since behavioral intent may not be the sole determinant of an individual's behavior to take up a health intervention. In addition, much like the updated HBM, it also includes self-efficacy as part of its model. This is especially consistent with cancer beliefs when an intervention to, for example, improve adherence to opioid pain medication is introduced to cancer patients. In addition to understanding patients' negative beliefs about opioids, this model seeks to incorporate patients' perceived behavioral control beliefs in adhering to their pain management regimen, thereby allowing us to better explain or predict the rates at which these interventions are successfully accepted and practised by patients. Since introducing a health intervention is a logical follow-up to discovering patients' baseline beliefs, the TPB would seem to be a more consequential and relevant model to incorporate cancer beliefs.

While it is beyond the scope of this review, it should be mentioned that there should perhaps be a specific cognitive framework for cancer patients, and this should be segregated between curative and palliative patients. The motivations behind patients undergoing curative treatments as opposed to those receiving palliative care are very different. Thus, intentions of receiving medical care between these two groups can be expected to be diverse as well. Especially pertaining to palliative care patients, comfort and palliation of cancer symptoms, as well as possible burdens to family, are chief concerns among their considerations in their care. As such, current existing theoretical frameworks related to health beliefs may not be fully relevant to this special group. Regnant sociocultural influences have harvested individuals that harbor a strong sense of familialism, wishing to leave a legacy for their family units, or those

who are firmly entrenched in principlism. Or, more likely, many fall in the half-way point between these two extremes, hoping for assurances that their families will be adequately cared for and also for their own comfort in the dying process. Regardless of which camp one is invested in, a context-sensitive, patient-centered model to understanding palliative care patients' decision-making phenomena should be used. Accomplishing this may require a modification of current TPB to include patients' intentions on two subjects: internal (extents of comfort care), as well as external, (desire to leave a legacy). Future studies will be required to explore the feasibility of this cancer belief model for advanced cancer patients.

An important strength of this review lies in the identification of the contexts in which studies related to cancer patients' beliefs have been performed. This allows us to understand which aspects of cancer patients' beliefs may have the greatest value for further study or are lacking in information and require more research to better examine its impact. In addition, we also described and appraised the content and psychometric properties of the measurement tools for assessing cancer patient beliefs. We are aware that there are limitations to our review. We have only included English-language articles and excluded those published only as abstracts. We could not assess publication bias because of the lack of evidence.

1.5   Conclusion

In summary, the impact of cancer patients' beliefs has been studied in a variety of contexts but there is a general lack of well-designed studies. Several other contexts where cancer patient beliefs may play a role has not been explored and could be areas for future research.

Table 1.2 - Cancer patients' beliefs

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
Treatment							
Liang et al 2013 [7]	Cross-sectional; Taiwan	4/0/2=6*	Cancer patients with an average pain intensity score of 3 or more on a 0-10 scale in the past 24 hours; had been prescribed opioid analgesics for cancer-related pain on an around-the-clock (ATC) and/or as needed (PRN) basis and had taken them for at least the past week; were 18 years of age; and were conscious	n = 92, Male (58.7%) Mean age = 56.4 years ±12.2 (30 – 92) Majority of subjects (89.1%) lived with others (families/relatives/friends) Overall mean education level = 9.2 years±4.5	POABS-CA	Age, sex, living with others, education level	Large numbers of patients had misconceptions about using opioids for pain. 33.7% - 68.5% of the patients had negative beliefs about opioids and beliefs about pain, as quantified using the POABS-CA.
Akiyama et al 2012 [27]	Cross-sectional; Japan	4/1/2=7	Cancer patients with metastasis or recurrent cancer. Patients with incapacity to complete the questionnaire, severe emotional distress poor physical condition or language difficulty were excluded.	n = 925, Mean age = 67±11 years, Men = 57%, ECOG 0 or 1 = 70%, Receiving treatment (chemotherapy or radiotherapy) = 60%	Non-validated questionnaire on advanced cancer patients' perception, knowledge as well as concerns about use of opioid painkillers, palliative care and homecare	Knowledge about opioids, beliefs about palliative care, concerns about homecare, sense of security about cancer care, pain intensity, patient-perceived quality of pallaitive care	Advanced cancer patients frequently had incorrect knowledge about opioids, a belief that palliative care is only for terminally ill patients, and concerns about homecare, especially the family burden and responses to sudden changes.
Cohen et al 2008 [5]	Cross-sectional; Australia	3/0/2=5*	Cancer patients older than 18 years who had been inpatients for a minimum of 48 hours	n = 126 Median age (age in this study was not normally distributed) = 56.06 years±15.98 Males = 53.9% 62.7% had 12 years of education or less.	American Pain Society (APS) Patient Outcome Questionnaire	Age, gender, education, cancer type, pain intensity, pain beliefs	47.6% of patients had experienced moderate to severe pain in the previous 24 hours but had only received 40.4% of available analgesic. Patients held varying beliefs about pain and pain treatments in particular, 41% held strong beliefs about the potential for addiction to narcotics. Patients who held

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
				Solid tumors = 46% 38% reported pain 70.1% of those who reported pain had pain episodes in the 24 hours before interview			this belief reported higher current pain, worst pain intensity, and higher average pain intensity in the previous 24 hours, even though they did not have any difference statistically in opioid usage compared to other groups.
Cancer Beliefs and Health Status or Health Behavior							
Obeidat, R. F. 2013 [44]	Cross-sectional; Jordan	3/0/2=5*	Jordanian women who had surgical treatment for early stage breast cancer (clinical stages 0-II) within 6 months of the interview, were 18 years or older and were physically and mentally able to consent and participate in the study	n = 28 Mean age = 48.5 years (29 – 70) Majority were married, had high school education or less, with a diagnosis of stage II breast cancer, and had mastectomy as their initial surgical treatment	Non-validated questionnaire using Heidegger interpretive phenomenology to uncover patients' meaning of lived experiences via their narratives of their diagnoses and treatments, and the impact of sociocultural backgrounds on these aspects	Quality of care at various health institutions, age, education	Fear had a profound effect on Jordanian women's stories of diagnosis and surgical treatment of early-stage breast cancer. Women's experience with breast cancer and its treatment was shaped by their preexisting fear of breast cancer, the disparity in the quality of care at various healthcare institutions, and sociodemographic factors (e.g., education, age). When surgeons provided information and support, several of these patients made their own treatment choices. Lack of healthcare system support in Jordan did not prepare these women for and managing changes after treatment.
Kumar S et. al.2010 [48]	Cross-sectional; Pakistan		Cancer patients undergoing treatment, excluding terminally ill patients and those with other serious medical conditions	n = 230 Mean age = 46 years (13-77) Females = 63% Married = 77.4% Formal education = 83% Bachelor degree = 33.5%	Non-validated questionnaire asking current cultural practices, religious beliefs, education, employment status, previous treatment for disease, knowledge, beliefs and myths regarding risk factors for disease and its	Various perceptions of cancer by patients	Cancer was thought to be a contagious disease by 27.5% of patients. 63.5% thought cancer is not related to any social habits like alcohol consumption. 89.6% thought cancer was potentially curable. 60% believed rituals can bring about positive outcome.39.6% thought that regular religious activity can

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
					treatment, role in decision making, satisfaction with provided knowledge and treatment		prevent cancer. Only 39.6% were fully informed of their disease, treatment and side effects. Pakistani patients have unique beliefs in myths that physicians should be aware of
Nadler et al 2013[49]	Cross-sectional; Canada	4/1/2=7	Prostate cancer patients on androgen-deprivation therapy (ADT) by injection, able to communicate in English. Patients receiving chemotherapy or have symptomatic metastatic disease were excluded.	n = 175, Mean age = 72.6 (51-90) years, Married = 80%, Retired = 68%, College or university education = 66%, Median duration of ADT = 30 (1-221) months, Recevied bone mineral density (BMD) testing = 38%. Based on BMD testing, 46% had osteopenia and 6% had osteoporosis	16-item Food Frequency Questionnaire, 3-item Godin Leisure-Time Exercise Questionnaire (GLTEQ), 19-item form of the Facts on Osteoporosis Quiz-Revised (FOOQ), Osteoporosis Self-Efficacy Scale (OSES), and Osteoporosis Health Belief Scale (OHBS)	Knowledge on osteoporosis, self-efficacy and health beliefs, healthy bone behaviors,	Most patients who are receiving ADT are not receiving appropriate screening, lack basic information about bone health, and are not engaging in the appropriate healhy bone behaviors
Ermiah et al. 2012[46]	Cross-sectional; Libya	2/0/2=4*	Breast cancer patients diagnosed during the period from Jan 1, 2008 to Dec 31, 2009.	n = 200 Mean age = 45.4 years (22–75). 62% (n = 124) were literate. 79% (n = 158) were married.	Non-validated questionnaire. The data collection included social and demographic data, medical and obstetric history, symptom-related questions, and consultation-related questions. Dates of the chronological events (first recognition of symptoms, first consultation, referral and first hospital appoint-ment) were included. Diagnosis time and delays were estimated in days.	Age, literacy, clinical staging at time of diagnosis, not considering symptoms as serious (patient's perspective)	The median of diagnosis time was 7.5 months. Only 30.0% of patients were diagnosed within 3 months after symptoms. 14% of patients were diagnosed within 3– 6 months and 56% within a period longer than 6 months.
Lord, K. 2012 [45]	Cross-sectional;	4/0/2=6*	Patients newly diagnosed with	n = 279 (British South Asian, BSA = 94, British	Hospital Anxiety and Depression Scale (HADS),	Ethnicity, age, education, religion, cancer site, HADS	232/279; 83.2% believed cancer was curable. However, significantly more

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
	UK		cancer	White, BW = 185) Median age for BSA = 57.1 years ±19 Median age for BW = 61 years ± 14	a version of the Patient Health Questionnaire (PHQ-9), which had been adapted and validated for use in India and translated into Gujarati and Hindi, Mini-Mental Adjustment to Cancer (MAC), Distress Thermometer, Cancer Insight and Denial, and Physician/Patient Trust and Cancer Beliefs questionnaires (non-validated). And a non-validated tool on patients' views on confidentiality, outcome and cancer treatment and beliefs about the causes of cancer.	subscales, type of treatment	BSA (10.6% versus 2.7% BW P < 0.001) believed cancer was incurable. While 86.4% agreed that smoking can cause cancer, there was a widespread lack of knowledge of the importance of diet and obesity as contributing causes of cancer. There was a strong belief in supernatural involvement in the development of cancer among a minority of BSA patients. 20% of this sample believed that treatment, especially surgery, caused the cancer to spread and this was associated with significant depression in BSAs (P = 0.019) and anxiety in both BW (P = 0.006) and BSA (P = 0.0134) patients.
Panjari, M. 2012 [41]	Cohort study; Australia	3/1/2=6*	Women were recruited within 12 months of their first diagnosis with invasive breast cancer	n = 1489 43.5% (647/1489) of women answered "Yes" when asked if they believed their cancers to be attributable to a cause. They were more likely to be younger than women who did not report a specific contributing factor to their breast cancer (mean age = 56.6 years ± 11.2 versus 61.2 years± 12.2, p<0.0001) and educated beyond high school (37 versus 57.8%, p<0.0001)	The Psychological General Well-being Index (PGWB) and non-validated questionnaires on demographics, investigations and treatments, general medical conditions, partnership status and body image.	Age, likelihood of reporting a belief in a reason for breast cancer, education, being at > stage 1 at diagnosis, reporting stress as reason for developing breast cancer, PGWB total score	Stress (58.1%) was the most common reason. Many women with breast cancer believe that stress has contributed to their condition and they had lower PGWB scores than other study participants (70.9±16.1, n=361 versus 77.3± 14.9, n=1071, mean difference=6.4, 95% CI: 4.6–8.2 p<0.0001) Women who held this belief were more likely to adopt strategies to reduce stress than those who did not.
Costanzo, E. S. 2011 [47]	Cross-sectional;	3/0/2=5*	Stages 0-III breast cancer patients who	n = 71 Median age = 55.0 years	Non-validated questionnaire and Illness	Age and duration of treatments	Survivors reported behavior changes directed toward improving physical,

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
	USA		were treated with adjuvant chemotherapy and/or radiation therapy	±10.8 (32-89)	Perception Questionnaire-Revised (IPQ-R). Patients post adjuvant chemotherapy and/or radiotherapy were assessed for changes in health practices and other behaviors, as well as beliefs about the causes, course, personal control, and consequences of their cancer		emotional, and spiritual well-being. Those who believed their cancer had more severe consequences and those who attributed the development of cancer or the prevention of recurrence to health behaviors or stress were most likely to report improvement in diet or physical activity and reduction in alcohol use or stress.
Thune-Boyle, I. C. et al, 2006 [43]	Cross-sectional; UK	5/0/2=7*	Cancer patients receiving 3 cycles or more intravenous chemotherapy as outpatients.	n = 72 Mean age = 55 years (22-83) Female = 54% Married = 61% Education = 43% preschool leaving Employment status = paid employed (39%)	Illness Perception Questionnaire (IPQ), Hospital Anxiety and Depression (HAD) Scale	Age, gender, no. of treatments, new or relapsed cancer, no of symptoms reported, mean perceived symptom severity, no. of symptoms attributed to treatment, consequence beliefs	Consequence beliefs serve as important mediators between number of symptoms and distress, explaining 15% of the variance in anxious mood and 5% of the variance in depressed mood. Perceived severity of symptoms is an independent predictor of anxious mood, explaining 7% of the variance. Its role in predicting depressed mood was not significant.
Costanzo, E. S. et al, 2005 [42]	Cross-sectional; USA	5/0/2=7*	Cancer patients who had completed treatment for cervical or endometrial cancer 5 or more years previously	n = 134 Mean age = 60 years (23-90) White ethnicity = 95% Married = 51% High school education = 40% Employed = 47%	Functional Assessment of Cancer Therapy (FACT) version 3, Center for Epidemiological Studies Depression Scale (CES-D), Impact of Events Scale (IES), Concerns About Recurrence Scale (CARS)	Age, cancer site, stage, treatment received, years since diagnosis, current physical well-being, and education, cancer attributions, health behavior changes	Genetics/heredity was rated as the most important cancer cause, followed by stress, God's will, hormones, and environmental factors. Medical screening was rated as most important in preventing recurrence, followed by positive attitude and prayer. Stronger causal attributions were generally associated with elevated depressive symptomatology and anxiety, but women citing potentially controllable causes were more likely to be practicing healthy behaviors. Similarly, women citing health behaviors as important in preventing recurrence reported greater anxiety but were more likely to practice positive health behaviors. Health behavior and lifestyle

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
							attributions interacted with health practices in predicting distress. For example, among women who had not made positive dietary changes, rating lifestyle as important in preventing recurrence was associated with greater distress, whereas among women who had made a positive change in diet, this belief was associated with less distress.
Cancer Beliefs and Treatment Adherence							
Liang et al 2013 **[24]**	Cross-sectional; Taiwan	3/0/2=5*	Cancer patients with an average pain intensity score of 3 or more on a 0-10 scale in the past 24 hours; had been prescribed opioid analgesics for cancer-related pain on an around-the-clock (ATC) and/or as needed (PRN) basis and had taken them for at least the past week; were 18 years of age; and were conscious	n = 92, male (58.7%) Mean age = 56.4 years ±12.2 (30 – 92) Majority of subjects (89.1%) lived with others (families/relatives/friends) Overall mean education level = 9.2 years±4.5	POABS-CA	Age, sex, living with others, education level	Beliefs about pain and opioids demonstrated a significant relationship with patients' opioid adherence (r = -0.30, p < 0.01). However, no significant correlation between opioid belief and pain experience was found. There were also no significant relationships between adherence to opioid regimen and any of the measures of pain experience.
Salz et al. 2009 **[54]**	Cross-sectional; USA	4/2/2=8	Colorectal cancer survivors previously diagnosed with stage I-III colorectal cancer; patients not able to undergo colonoscopy were excluded	n = 601 (1-year interview), n = 277 (4-year follow-up), Female 53% (based on 4-year follow-up), Age < 65 = 52%, Education high school or more = 49%, Insured = 84%	Interview based on Health Belief Model (HBM)	Intention to undergo coloscopy, health beliefs in terms of likelihood of getting colorectal cancer again, perceived barriers and benefits to coloscopy, self-efficacy and any physician recommendation for colonoscopy; screening history, age , sex,	Greater perceived susceptibility to colorectal cancer (OR=2.00, 95% CI=1.16–3.44) among these patients was associated with greater motivation to have a colonoscopy. Survivors who already had a colonoscopy since diagnosis also had greater intentions of having a colonoscopy in the future (OR=9.47, 95% CI=2.08–43.16).

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
						education, income	
Valeberg et al 2008 [75]	Cross-sectional; Norway	4/0/2=6*	Cancer patients over18 years of age, had self-reported pain of any intensity and/or use of analgesics; and were able to read, write, and understand Norwegian.	n = 174 Females = 79% Mean age = 58 years ±11.4 Had college or university education = 35% Married = 70% Not working = 84% Most common diagnosis = breast cancer (42%) Metastatic cancer = 43%	Brief Pain Inventory (BPI), Barriers Questionnaire (BQ-II), non-validated questionnaires on adherence and self-efficacy	Age, gender, education, clinical and pain characteristics, levels of adherence	41% of the patients were adherent with their analgesic regimen. In the regression analysis, 29.9% of the variance in adherence was explained. Higher adherence scores were associated with male sex, and also lower SE for physical function scores, higher average pain intensity scores, higher pain relief scores, and the use of strong opioid analgesics.
Grunfeld, E. A. et al, 2005 [52]	Cross-sectional; UK	4/0/2=6*	Women aged 35–65 years who were in remission from primary breast cancer with no recurrence and currently prescribed tamoxifen	n = 110 Mean age 56.3 years ±7.0 (38-65) White ethnicity = 93% Married or cohabiting = 67% Employed = 44% Mean time taking tamoxifen = 2 years 9 months±1 year 7 months	Women's Health Questionnaire (WHQ), Beliefs about medicines questionnaire (BMQ), Medication Adherence Report Scale (MARS-5), non-validated single question ''In the past week have you taken your, tamoxifen every day?'', non-validated hot flushes and night sweats questionnaire	Age, individual components of MARS-5, necessity, concerns, overuse and harms subscale of BMQ, MARS-5 scores,	Non-adherers were more likely to report a belief that there was nothing to be gained from taking tamoxifen whereas adherers were more likely to report that tamoxifen would stop them from developing breast cancer. Main reason for not taking tamoxifen was side effects. No differences between adherers and non-adherers with regard to the strategies used to remember to take tamoxifen or with regard to the time of day tamoxifen was taken.
Sherman, K. A. et al 2013 [53]	Cross-sectional; Australia	2/0/2=4*	Breast cancer patients over 18 years of age and were scheduled for breast and lymph node surgery	n = 98 Mean age = 55.3 years ±10.6 Married or partnered = 70.5% 10 years of education = 28.6%	Non-validated questionnaire. Patients were surveyed regarding utilization rates, health beliefs, and medical and demographic characteristics, using a questionnaire constructed based on the Health Belief Model.	Age, lymphedema-related knowledge and trait anxiety	Levels of adherence to risk management strategies were moderate (M=9.53, SD=2.95; range 0–12), and knowledge was high (M= 9.53, SD= 2.95). Perceived consequences, controllability, self-efficacy and self-regulatory ability subscales were significantly positively correlated with adherence. Trait anxiety (r =_0.27, p = 0.009) and knowledge (r=0.29, p = 0.005) were significantly associated with adherence; hence, both variables were treated as covariates in analyses. Demographic, medical status, family breast cancer history and family/friend

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
							lymphedema history variables were not associated with adherence. Greater adherence was associated bivariately with greater beliefs in lymphedema controllability, self-efficacy, perceived consequences and perceived self-regulatory ability. Linear regression analyses revealed that greater beliefs in the controllability of lymphedema and self-regulatory ability, as well as greater knowledge, were predictive of greater adherence to risk management strategies.
Saratsiotou, I. 2011 [51]	Cross-sectional; Greece	3/0/2=5*	Patients on oral chemotherapy.	n = 99 Median age = 61 years (30-91) Female = 62 Most common tumor type was breast cancer.	Non –validated questionnaire, asking patients on their treatment profiles, attitudes about oral chemotherapy, whether they were adherent, whether they were intentionally nonadherent, and suggestions to improve adherence	Treatment profile, type of drug, age, sex, education, tumor type, adherence, nonadherence, causes of unintentional nonadherence	Greek patients have similar non-adherence pattern as in other countries. Confidence in treatment efficacy appeared as a significant adherence determinant.
G. Michel et al. 2011 [33]	Cohort study; Switzerland	4/2/3=9*	All patients registered at the Swiss Childhood Cancer Registry (SCCR) between 1976 and 2003, who survived for 5 years or more	n = 1075 Median age at study = 26.3 years (19-49) Median age at diagnosis = 8.5 years (0-16) Median time since diagnosis = 19.5 years (6-36)	Swiss Census questionnaire for demographics and non-validated questionnaire for health beliefs	Health beliefs, demographic, medical variables	More survivors at high risk of cancer- and treatment-related late effects attend follow-up care in Switzerland. Patient-perceived barriers hinder attendance even after accounting for medical variables.
Cancer Beliefs and Coping with Cancer							
Banning et al. 2009 [64]	Cross-sectional; Pakistan	3/0/1=4*	Breast cancer patients at age range of 22 to 60 years, receipt of treatment as a hospital inpatient for breast cancer, of Muslim belief and	n = 30 3 were single, 2 widows, 2 living separate from husbands, 1's husband had second wife, 22 living with husbands. Married woman have	Non-validated questionnaire, where patients were asked, via a self-reported 7-page questionnaire about their demographic profile, disease and treat- ment	No statistical analysis performed in the study (qualitative design)	The data not only highlight the role of religion and family support as essential coping strategies but also emphasize the issues of isolation, aggression, and anger as common responses to chemotherapy. Unique features of this study are

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
			Pakistani origin	average of 3 children (2-5). Most were housewives.	characteristics, and side-effects and adherence information, both intentional and non-intentional.		women's need to seek spiritual support for their illness and the overriding innate characteristic of maternal responsibility
Thune-Boyle, I. C. et al. 2013 [63]	Cross-sectional; UK	5/0/2=7*	Newly diagnosed breast cancer patients with subsequent surgery	n = 140 with early stage (I & II) breast cancer.	Brief RCOPE, scale to measure public religious/spiritual practice from Multidimensional Measurement of Religiousness/ Spirituality for Use in Health Research: A Report by the Feltzer Institute/National Institute on Ageing Working Group, spiritual involvement scale, spiritual support scale, Life Orientation Test, Multidimensional Scale of Perceived Social Support, Hospital Anxiety and Depression Scale	Religious/Spiritual variables, age, type of surgery, whether patients had had a reconstruction or not, feeling punished and abandoned by God, optimism, denial, self-blame and venting	'Feeling punished and abandoned by God' significantly explained 5% of the variance in increased levels of anxiety but was partially mediated by denial coping. I t was partially mediated by acceptance coping, lowering levels of anxiety. Feeling punished and abandoned by God was a significant independent predictor of depressed mood, explaining 4% of the variance.
Miccinesi G et al. 2012 [11]	Cross-sectional; Italy	5/1/2=8	Cancer patients undergoing treatment	n = 252, Mean age = 53.6 (±12.2) years, Females = 74%, Believers and church-goers = 49%, Believers but not church-goers = 43%, Non-believers = 8%	Systems of Belief Inventory (SBI-15R)	SBI-15R items as measure of spirituality, belief status	A large proportion of Italian cancer patients have a personal spiritual life, with or without any religious affiliation. Health care professionals may wish to pay more attention to spiritual resources for cancer patients.
Alqaissi et al 2010 [65]	Cross-sectional; Jordan	2/0/1=3	Jordanian breast cancer women diagnosed with Stage I to III cancer and are completing their treatments or have completed their	n = 20, Mean age = 45.8 (±7.3) years, Mean years of formal education = 11.7 (2 - 16) years	Phenomenological interview on the meaning of social support for Jordanian women with breast cancer	No statical analysis performed	Jordanian breast cancer women rely heavily on other women for support, mainly within the family. Health care professionals need to be aware of influence of culture, religion, as well as clinical and personal characterristics of each woman on her

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
			treatments				requirements of social support
Johannessen-Henry, C. T.et al 2013 [60]	Cross-sectional; Denmark	5/0/2=7*	Adult cancer patients who had completed primary treatment, who needed rehabilitation, were capable of participating in the physical activities offered and who had an expected survival of at least six months	n = 1043 Women = 76%, Mean age = 58 years (10-90% range, 43-72 years). Most were diagnosed with cancer of the breast, colorectum, female genital organs or prostate. Generally, the participants had higher education (515), and most were working (57%) and living with a partner (68%) at the time of enrolment into the study. Most were members of the Evangelical Lutheran Church (83%), but only 3% attended services weekly. 60% of the participants, mostly women, characterized themselves as believing in a god	Danish versions of Functional Assessment of Chronic Illness Therapy — Spiritual Well-being 12 items [FACIT-Sp-12 (version 4)], Profile of Mood States Short Form (POMS-SF), Mental adjustment style Mini-MAC, Functional Assessment of Cancer Therapy — General (FACT-G, version 4)	Faith, distress, mental adjustment to cancer, gender, age and cancer diagnosis, social and physical well-being	Higher spiritual well-being was associated with less total distress (β=-0.79, CI - 0.92; - 0.66) and increased adjustment to cancer (fighting spirit, anxious preoccupation, helplessness-hopelessness). Specific aspects of faith were associated with high confusion-bewilderment and tension-anxiety, but also lower score on vigor-activity, and with higher anxious-preoccupation, both higher and lower cognitive avoidance, but also more fighting spirit.
Cheng, H. et al 2013 [62]	Cross-sectional; China	3/0/2=5*	18 years or older, with a first diagnosis of breast cancer; had completed surgery and systematic treatments; and were able to communicate in Mandarin.	n = 29 25 were married or had a partner, and their ages ranged from 41 to 69 years (mean, 53.9 years ± 7.24).	Non-validated questionnaire on breast cancer patients' experience of survivorship which explored the role of fatalism in coping with the disease experience	Qualitative study, only descriptive statistics	Median length of survivorship since the completion of treatment for these study participants was 45months (interquartile range, 23-60 months); 62.1% were diagnosed at stage II. All participants received either modified radical mastectomy or radical mastectomy and completed chemotherapy. Findings suggest that fatalism related to coping in the Chinese context combined 2 elements: fatalistic belief in and acceptance of the way things are as well as the exertion of personal efforts over the situation.

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
Doumit et al 2010 [61]	Cross-sectional; Lebanon	3/0/1=4*	Lebanese Arabic speaking stage I-III breast cancer patients living in Lebanon at an age of 25 years or older, without distant metastases, previous history of mental disorders, or the existence of other forms of cancer or other chronic diseases and agreed to be interviewed without the presence of a third person to ensure liberty for the participant to express her feelings	n = 10 Mean age = 51.3 years (36-63) Patients' experience with breast cancer ranged = 4 months to 9 years. 8 remained married, 2 widowed.	Non-validated questionnaire using a phenomenological approach to study how breast cancer patients cope with with disease	Statistical analysis not done in study	The negative stigma of cancer in the Lebanese culture, the role of women in the Lebanese families, and the embedded role of religion in Lebanese society are bases of the differences in the coping strategies of Lebanese women with breast cancer as compared to women with breast cancer from other cultures.
Cancer Beliefs and Traditional/Complementary Medicine							
Takeda, T. 2012 [69]	Cross-sectional; Japan	3/0/2=5*	Gynecologic cancer patients who were treated and followed at Tohoku University Hospital in Sendai, Japan	n = 420 Median age = 53 (19=76) 96 (22.9%) Kampo users vs 324 (77.1%) nonusers.	Non-validated questionnaire, which consisted of general profile factors such as demographics, usage of traditional Kampo and dietary supplements, side effects of western treatment and beliefs and attitudes about Kampo.	Age, time from diagnosis to screening, cancer site, treatment, dietary supplements, side effects of treatment, satisfaction with conventional treatment, state anxiety, trait anxiety	Kampo users made more favorable comments on Kampo medicine than nonusers. Psychological characteristics of individual patients is one of the factors that can influence the usage of Kampo.
Broom, A. 2010 [68]	Cross-sectional; Sri Lanka	4/0/2=6*	Cancer patients who were currently undergoing or had previously received cancer treatment	n = 500 Female = 53% Average age = 45.6 ±15.4 years	Non-validated questionnaire that asked patients on use of traditional medicine and reasons for using them.	Gender, marital status, religion, area of Sri Lanka, cancer site, treatment, time since diagnosis	67.4% of those surveyed used one or more TCAM in conjunction with biomedicine for cancer treatment. The most common were Sinhala, Ayurveda and traditional religious practices. Of those patients who used TCAM, 95.0% gave the main reason for usage as 'they thought it would cure their cancer'.

Study, Year (Reference)	Design; Country	Quality (Max; 10*)	Eligibility Criteria	Patient Characteristics	Method for assessing outcomes and confounders	Variables adjusted for statistical analysis	Primary results
							The strongest reason for not using TCAM was on advice from their doctor (80.5%).
Teng et al. 2010 [67]	Cross-sectional; China	3/0/2=5*	Adult cancer patients who were aware of their diagnosis, able to understand the questions, were free from any condition that would make completing the questionnaire inappropriate or overburdening for the patients	n = 121 Males = 64 (52.9%) Mean age = 57.31 years ±12.78 (19-85)	Non-validated questionnaire that asked patients on use of complementary medicine, their level of satisfaction using them and the benefits derived.	Age, marital status, socioeconomic status, educational level, occupation, cancer site, treatment received previously, current treatment	93.4% used CAM at some point during their cancer illness (of these 54.0% were male). Over 71.7% of those who used CAM were satisfied, only 28.3% were disappointed. Twenty-eight users (24.8%) did not see any benefit from the CAM, but eighty-one patients (71.7%) could describe some specific benefits. Only one patient will use orthodox medicine instead of CAM in the future, almost all patients will continue to use CAM in the future

Table 1.3 - Questionnaires used to measure patients' beliefs

Instrument	Year	Country	Objective	Specific to cancer patients?	Reliability	Validity
Pain Opioid Analgesic Beliefs Scale – Cancer (POABS-CA)[59]	2003	Taiwan	10 items to assess cancer patients' beliefs about opioid analgesics	Yes	Cronbach's alpha = 0.70 Cohen's kappa = NA Test-retest = 0.94	Factor structure = confirmed Known group validity = supported Convergent validity = NA Divergent validity = NA Face validity = supported Concurrent validity = NA Predictive validity = NA
Beliefs in Medicines Questionnaire (BMQ)[56]	1999	UK	Two sections (18 items): 1) BMQ-Specific (two parts): a) Specific-Necessity (5 items): - assesses beliefs about the necessity of prescribed medication b) Specific-Concern (5 items): - assesses beliefs about concerns about prescribed medication based on beliefs about dangers of dependence and long-term toxicity and the disruptive effects of medication 2) BMQ-General (two parts): a) General-Harm (4 items): - assesses beliefs that medicines are harmful, addictive poisons which should not be taken continuously b) General-Overuse (4 items): - assesses beliefs that medicines are overused by doctors These two sections can be used separately or in combination.	No	*Specific-Necessity* Cronbach's alpha = performed across 6 chronic diseas groups Cohen's kappa = NA *Specific-Concern* Cronbach's alpha = performed across 6 chronic diseas groups Cohen's kappa = NA *General-Harm* Cronbach's alpha = performed across 6 chronic diseas groups Cohen's kappa = NA *General-Overuse* Cronbach's alpha = performed across 6 chronic diseas groups Cohen's kappa = NA Test-retest = NA	Factor structure = confirmed Known group validity = supported Convergent validity = NA Divergent validity = supported Face validity = NA Concurrent validity = NA Predictive validity = NA
Akiyama et al [27]	2012	Japan	To study advanced cancer patients' perception, knowledge as well as concerns about use of opioid painkillers, palliative care and homecare	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Kumar et al [48]	2010	Pakistan	A set of questionnaires that examined themes of current cultural practices and religious beliefs, and also included patient-level information on education levels, employment statuses, as well as knowledge and beliefs regarding cancer risk and treatments.	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA

Instrument	Year	Country	Objective	Specific to cancer patients?	Reliability	Validity
						Face validity = NA Concurrent validity = NA Predictive validity = NA
Mini- Mental Adjustment to Cancer (Mini-MAC) [76]	1994	UK	To measure the coping styles that cancer patients have when diagnosed with the disease with 29 items	Yes	Cronbach's alpha = 0.51 to 0.79 Cohen's kappa = NA Test-retest = NA	Factor structure = confirmed Known group validity = supported Convergent validity = supported Divergent validity = NA Face validity = NA Concurrent validity = supported Predictive validity = NA
Physician/Patient Trust and Cancer Beliefs [45]	2012	UK	To assess patient's opinions on confidentiality outcome and cancer management	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Osteoporosis Health Belief Scale (OHBS)[77]	1991	USA	To measure health beliefs in the domains of perceived osteoporosis susceptibility, seriousness about osteoporosis and general motivation to health	No	Cronbach's alpha = 0.61 to 0.80 Cohen's kappa = NA Test-retest = NA	Factor structure = confirmed Known group validity = supported Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = supported Predictive validity = NA
Costanzo et al [42]	2005	USA	To understand patients' cancer cause attribution and prevention of recurrence	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Concerns About Recurrence Scale (CARS) [78]	2003	USA	To assess the extent and nature of women's fears about possibility of recurrence of breast cancer	Yes	Cronbach's alpha = 0.89 to 0.94 among four subscales Cohen's kappa = NA Test-retest = NA	Factor structure = confirmed Known group validity = NA Convergent validity = supported Divergent validity = NA Face validity = supported Concurrent validity = NA Predictive validity = NA
Illness Perception Questionnaire (IPQ) [79]	1996	New Zealand	To measure cancer patients' beliefs about the potential for cure of the disease, as well as the ramifications of cancer and its management.	Yes	Cronbach's alpha = 0.73 to 0.82 Cohen's kappa = NA	Factor structure = NA Known group validity = supported Convergent validity = NA

Instrument	Year	Country	Objective	Specific to cancer patients?	Reliability	Validity
					Test-retest = 0.49 to 0.84	Divergent validity = NA Face validity = NA Concurrent validity = supported Predictive validity = supported
Michel et al [33]	2011	Switzerland	Measures of perceived susceptibility to late effects of past cancer treatments on a 10cm visual analogue scale, perceived benefits and barriers to follow-up care, importance of health to the individual and beliefs on detecting and treating late effects of cancer treatments early	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Sarasiotou et al [51]	2011	Greece	To measure belief in objective of oral chemotherapy	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Functional Assessment of Chronic Illness Therapy-Spiritual Well-being (FACIT-Sp-12) [80]	2013	Denmark	To assess the spiritual well-being of patients	Yes	Cronbach's alpha = 0.81 to 0.88 Cohen's kappa = NA Test-retest = NA	Factor structure = confirmed Known group validity = NA Convergent validity = supported Divergent validity = supported Face validity = supported Concurrent validity = supported Predictive validity = NA
Systems of Belief Inventory (SBI-15R) [81]	1998	Italy	To assess spiritual needs among Italian patients: - Beliefs subscale has 10 items that assess religious beliefs and participation in religious activities - Support subscale has 5 items to assess the support the patients received from the religious societies they belonged to	Yes	Cronbach's alpha = 0.93 overall and 0.92 and 0.89 for Beliefs and Practices Subscale and Social Support Subscale, respectively Cohen's kappa = NA Test-retest = 0.95	Factor structure = confirmed Known group validity = supported Convergent validity = supported Divergent validity = supported Face validity = NA Concurrent validity = NA Predictive validity = NA
Thuné-Boyle et al [63]	2013	UK	A set of questionnaires: - three single-item questions to assess cancer paitents' beliefs in God, and the degree to which they perceived themselves as spiritual as well as the stability of their faiths - a 12-item sub-scale of spiritual involvement scale to assess patients' private spiritual involvement which measures the degree to which patients privately assimilate their relationship with God and use it to cope with stress due to their cancer diagnosis	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA

Instrument	Year	Country	Objective	Specific to cancer patients?	Reliability	Validity
			- a 3-item tool was used to measure patients' perceived spiritual support from God on a 5-point scale			
Teng et al [67]	2010	China	To measure expectations from use of CAM	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Broom et al [68]	2010	Sri Lanka	To measure cancer patients about their beliefs regarding CAM as well as their traditional medicine	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Takeda et al [69]	2012	Japan	An 8-item questionnaire about beliefs and attitudes about Japanese traditional medicine (Kampo) on a 5-point scale	Yes	Cronbach's alpha = NA Cohen's kappa = NA Test-retest = NA	Factor structure = NA Known group validity = NA Convergent validity = NA Divergent validity = NA Face validity = NA Concurrent validity = NA Predictive validity = NA
Barriers Questionnaire –II (BQ-II)[82]	2002	USA	Update of BQ to more accurately reflect current ideas with regards to cancer pain, its management and current pain management practice.	Yes	Cronbach's alpha = 0.89 overall and 0.75 to 0.85 for the four subscales Cohen's kappa = NA Test-retest = NA (only done for original BQ, ranging 0.53 to 0.90)	Factor structure = confirmed Known group validity = supported Convergent validity = supported Divergent validity = NA Face validity = supported Concurrent validity = NA Predictive validity = NA

Chapter 2. Prevalence data on opioid consumption patterns in NCCS

2.1   Introduction

The International Association for the Study of Pain announced in its Declaration of Montreal[83] that a patient's access to medications for the relief of pain is an elementary human right. Further, the autonomous authorities that practice United Nations drug rules, the World Health Organization (WHO) and International Narcotics Control Board (INCB), have untiringly advocated that various controlled drugs are necessary analgesics in the treatment of many ailments. It was not coincidence that there was a notable sustained increase in use of opioids in the world, where prior to 1987 use of opioids were below Global Morphine Equivalent (ME) of 5mg/capita, to beyond 45mg/capita in 2011[84]. In the United States itself, as the largest consumer of opioids in the Regional Office for the Americas (AMRO) which in turn far surpasses all other WHO regions, a 1448% increase in medical use of opioids was seen between 1996 and 2011, and this was accompanied by an even more dramatic increase in opioid abuse (4680%) as well[85].

Age-adjusted rate for opioid-analgesic related deaths in the United States was reported to have almost quadrupled from 1.4/100,000 in 1999 to 5.4/100,000 in 2011[86]. In Australia, although morphine use declined while oxycodone use increased, number of treatments for morphine poisoning maintained while that for oxycodone expectedly increased between 2001 and 2009[87].

While INCB provides national-level data on opioid usage, this collective information includes both cancer and non-cancer use. While opioids are widely accepted as treatment for cancer pain, their use in non-cancer treatments is more controversial: the risk of opioid misuse, abuse and diversion in the treatment of non-cancer pain is a potential problem[88]. Non-adherence patterns from these two groups of patients can be quite different: cancer patients tend to refuse opioids[24] while non-cancer patients

may use more than is prescribed for them[88]. Thus, due to these different groups of patients having potentially different profiles of non-adherence, it is imperative to our interest to acquire opioid usage patterns for cancer-use only.

Opioids are categorized according to their strengths. Weak opioids such as codeine and tramadol are differentiated from stronger opioids such as morphine and oxycodone. The stronger the opioid, the greater its potency as a central nervous system (CNS) depressant and a consequent higher risk of lethal toxicity if recommended doses are exceeded, especially in combination with other CNS depressants such as alcohol or benzodiazepines[89]. Hence, an increase in prevalence of use of stronger opioids would be of concern.

A study in Canada found consistent correlations between increased use of prescription opioid analgesics and mortality, particularly strong opioids such as hydromorphone and oxycodone[90].

In addition, there are associations between prescribing of strong opioids such as oxycodone and non-medical use as well as emergency department (ED) visits in USA[91]. Thus, increasing the availability and consumption of strong opioids raise the likelihood of harms: as more individuals have exposure to opioid analgesics, more people may develop dependence to opioids and possibly look for more opioids for diversion or abuse[92]. Mortality due to overdose of opioids have also seen a surge in USA alongside an increase in opioid doses prescribed[93].

These problems can be expected to be potentiated in strong opioids such as oxycodone. Case in point, oxycodone-related death was found to increase 21-fold

over 10 years in Victoria, Australia, and is associated with an increased supply of the specific opioid[89].

The objective of this study is to acquire trend of opioid usage in a local ambulatory cancer center to obtain baseline understanding of our opioid consumption. Should the results of this study be similar to trends experienced in Australia and United States, this will in turn allow decision makers to anticipate associated harms with increased consumption of opioids and to allow potential future mitigation by increasing emphasis on the understanding of patients' adherence to opioids.

2.2   Methods

The study will be conducted in an ambulatory cancer centre in NCCS using 5-year consumption data (Jan 2010-Dec 2014) from MaxCare®, an institution-wide dispensing software used by NCCS pharmacy.

Inclusion criteria are all dispensed opioids from NCCS during the eligible period (Jan 2010-Dec 2014). These are: codeine, tramadol, morphine, fentanyl and oxycodone. Samples of opioids will not be excluded.

The MaxCare® program was used to generate a list of opioids dispensed from NCCS in period stipulated (Jan 2010 – Dec 2014) from its transaction history. These were segregated as different opioids in its various dosage forms, in chronological order. Opioid use was not differentiated between as-needed and around-the-clock usage.

Data cross checking

Total cost of each opioid was present in the report. The total quantity of each opioid was summed and then multiplied by its unit cost. This information is cross-checked

against the total cost of each opioid to ensure that quantity of each opioid was

accurately tabulated. If total costs derived do not match the total costs stated for each

opioid, a mistake must have occurred in tabulating the quantities.

Morphine equivalents

Each opioid's strength was divided by its corresponding equivalent morphine strength

to obtain morphine equivalents (ME). Using ME allows us to equate different opioids

and their varying potencies into a standard morphine equivalent value. A high ME is

an indicator of a strong opioid.

As MaxCare® only codes opioids by their generic names, trades names were not

used.

Data analysis will be presented in the form of a line chart of opioid use (morphine

equivalents on the y-axis vs the years 2010-2014 on the x-axis) in NCCS.

2.3   Results

The study results are summarized in line charts as Figure 2.

The numbers of patients prescribed opioids over the years of 2010 to 2014 were as

follows: 5766, 6840, 6230, 6275 and 6241.

From 2010 to 2014, a general decline was seen for both codeine and morphine.

Fentanyl use was observed to increase from 2010 and then decline over 2014. Use of

oxycodone and tramadol saw a steady increase from 2012 to 2014.

2.4   Discussion

Although cancer diagnoses in Singapore rose over the years, use of opioids remained

stable. Despite more cancer diagnoses in 2014, there was a decrease in opioid usage

compared to in 2011, which could be due to greater awareness in cancer screening,

leading to detection of cancers at earlier stages. These patients of early stage cancers have may have presented with lower incidence of cancer-related pain. According to a systematic review, although cancer pain was reported in 59% of cancers of various stages, this prevalence increased to 64% in advanced stages[94]. However, use of oxycodone increased steadily from 2012 and increased use of such strong opioids is of concern, regardless of disease and pain severity. The degree of damage to society from misuse of opioids is reasonably potentiated when the opioid of concern is a stronger one.

A sharp decline in use of morphine, and a gentler drop in use of oxycodone and tramadol after 2011 accompanied the rise in use of fentanyl (Figure 2). The increased use of convenient, long-acting fentanyl patches may have resulted in a reduced need to supplement our patients with immediate-acting opioids for breakthrough pain. However, even as fentanyl usage continued to rise, use of oxycodone and tramadol also rose, albeit much more slowly. A flip of tables occurred in 2013, which saw a sharp decline in use of fentanyl, with an accompanying rise in use of tramadol, morphine and oxycodone. While it may be valuable to investigate this change in opioid prescribing pattern, it is beyond the scope of this study. Codeine appeared to have been gradually replaced by stronger opioids.

A strength in our study is that it allows us to observe the changing trends of opioid use in cancer-related pain in our cancer center. Although use of weaker opioids like codeine and morphine declined from 2010 to 2014, the steady rise in use of stronger opioids like oxycodone was seen from 2012 to 2014. This seems to mimic the trends seen in other developed countries like USA and Australia[89, 93]. It is logical to anticipate the same problems faced by these countries. This finding may grant

decision makers valuable time to address this potential problem while it is still in its infancy.

However, there are several limitations to this study. Consumption data does not directly account for amount of drug actually administered. Patients may in reality be taking more (by obtaining opioids from other clinics) or less (prescription may not be completely filled) opioid medications than are currently reported. There were no longitudinal data on opioid prescribing and outcomes in individual patients such as ED visits and mortality. As such, we were unable to draw correlational relationships between amount of opioids prescribed and health-related outcomes such as hospitalizations and deaths. Since information source is dispensing data, we were unable to measure prescribed dosages and days of opioid supplied. As a result, it was neither possible to ascertain trends of adherence to opioids nor whether prescriptions were completely filled. Lastly, the findings of this study do not include possible co-prescribing if patients attended pain clinic outside of NCCS. Hence, actual use of opioid analgesic by patients may be higher than reported.

2.5   Conclusion

In conclusion, despite increases in cancers diagnosed, our usage of opioids remained relatively stable. However, a rise in use of stronger opioids such as oxycodone is observed. As there are serious associated problems with increased usage of stronger opioids overseas, we should watch our population closely as we continue to prescribe suitable analgesics for our patients.

Figure 2: Opioid usage in NCCS over 5 years
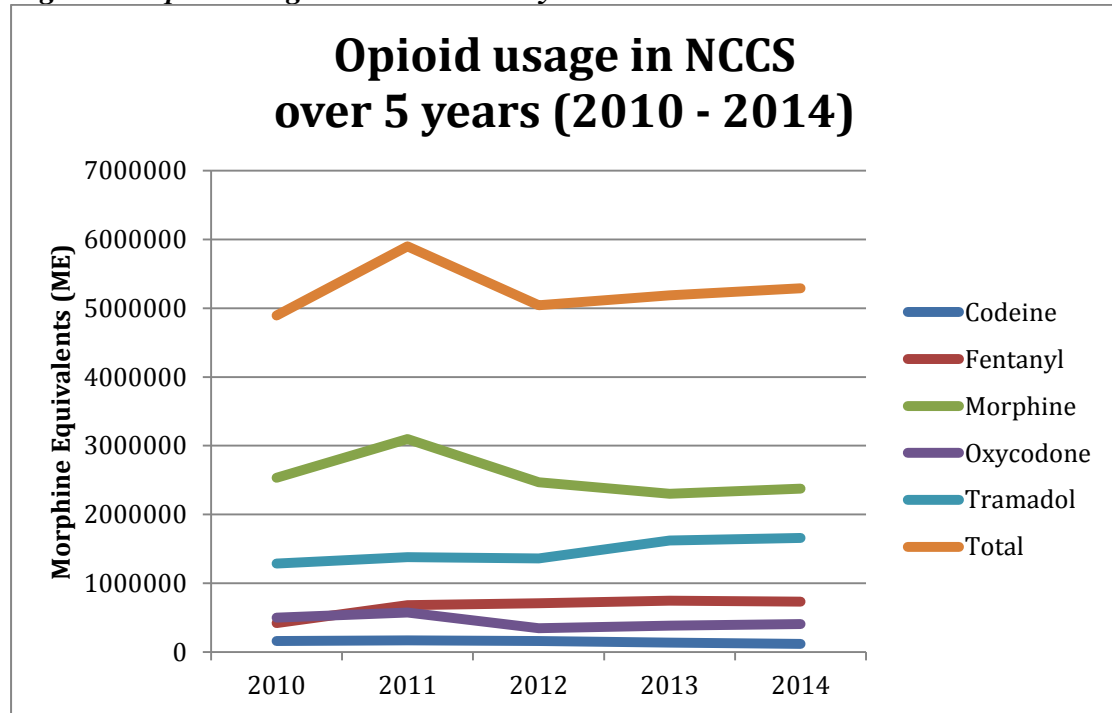
Chapter 3. Evaluation of validity and reliability of the Pain and Opioid Analgesic Beliefs Scale – Cancer (POABS-CA) instrument

3.1   Introduction

Despite remarkable advances in medical technology, cancer remains as one of the most feared diagnoses due to its accompanying short prognosis and debilitating symptoms. Of these, the most significant till date is pain. According to the American Cancer Society[95], about 80% of patients with advanced cancer have un-managed moderate to severe cancer pain. It argued that the simplest and most inexpensive solution to this is by increasing the ease with which patients can obtain necessary analgesics. Doing so can potentially increase prognosis, in addition to being the solution of greatest impact to reduce discomfort from cancer pain. However, when patients themselves refuse pain medications, ready access to analgesics cannot remain a potent solution to this problem.

Numerous barriers to pain management result in many patients not achieving optimal pain control. Patients' reluctance to report pain and poor adherence to pain medications have been reported as major culprits[57] obstructing adequate pain management. These patient-related barriers include erroneous concerns or beliefs about pain medications such as fears of side effects and addiction, as well as the perception that good patients should not report about pain[57]. Previous studies have shown that some pain beliefs, which are representative of a person's perception and evaluation of a pain episode, affect the way a patient reacts to pain[96, 97]. Therefore, misconceptions about opioid analgesics can potentially affect patients' receptivity to such pain medications.

Opioid analgesics are the cornerstone of cancer pain treatment. However, beliefs about use of opioids have been deeply polarizing. Negative beliefs about this class of

pain medications were frequently concerns about opioids' side effects and their

potential for addiction[57, 98]. Several instruments like the BQ (and BQ-II) and BMQ

have been designed to measure patients' beliefs about medicines. However Yeur-Hur

Lai et al developed the Pain Opioid Analgesics Beliefs Scale in Cancer patients

(POABS-CA)[59] to quantify this phenomenon specifically in opioid painkillers by

cancer patients. This instrument allows us to address the opportune and intimately

linked issues of cancer patients and their beliefs in opioids. The instrument attempts

to evaluate two factors, negative effect beliefs and pain endurance beliefs, using 10

items measured along a 5-point Likert-type scale. Developed and tested in Taiwan,

the POABS-CA was found to possess satisfactory validity, reliability and stability,

with Cronbach's alpha of 0.70 and test-retest reliability of 0.94. According to the

authors, all 10 items are intentionally worded using negative phraseology as this

phrasing imitates how people usually express their beliefs about opioids[59].

The purpose of this study is two-fold: (1) to explore the feasibility of the POABS-CA

in Singapore, and its (2) validity and reliability.

In addition, chapter 3, which is a study on cancer patients' adherence to opioid

analgesics, piggybacks on the same subjects used for the validation study of POABS-

CA. Thus, it was a concurrent study of two objectives with the same subjects being

administered an expanded list of questionnaires. As such, the discussion and

conclusion for both studies will be combined at the end of chapter 3.

3.2   Methods

A two-phase psychometric analysis was performed to test the feasibility, validity and

reliability of the POABS-CA using convenience sampling. Eligible subjects were (1)

oncology patients of the National Cancer Center Singapore (NCCS) who (2) were

above 21 years of age, (3) were prescribed opioid analgesics for cancer-related pain in

the prior week at least, (4) able to speak coherently and (5) were not cognitively

impaired as assessed by the recruiter. Institutional Review Board (IRB) approval was

obtained for both phases of the study. Diagnoses were captured from electronic

medical records. The researcher will be the person administering the questionnaires.

Phase I: Feasibility of POABS-CA

The specific aims of phase I were to ascertain the specificity and relevance of the

domains that were established in POABS-CA in our patients. Pilot data were collected

using a convenience sample of 30 cancer patients recruited at NCCS. POABS-CA

was used to measure pain beliefs. Subjects were asked to complete the POABS-CA

and then asked to comment on the ease of understanding the questions, the relevance

of the questions and whether they are suitable for use in the Singapore culture.

Specifically, the following questions were asked: (1) "Can you comment on the

clarity of the questions? If you feel they are not sufficiently clear, can you suggest a

way to improve it so it may be better understood?" (2) "Are you at any point

uncomfortable in answering any of the questions? If so, which ones are making you

feel uncomfortable and what do you suggest we can do about it?" (3) "Do you find

any questions irrelevant? How so?" (4) "Do you feel that additional relevant questions

should be added to the list? What are they?"

Phase II: Validity and reliability of POABS-CA

The specific aims of this phase were to test the (1) internal consistency reliability and

test-retest reliability of the POABS-CA and (2) examine its construct validity with

confirmatory factor analysis using the "confa" command in STATA and known-group

validity. A comparative fit index (CFI) of value 0.95 or greater is criteria for a good

fit of the data to the model. 300 patients from NCCS were recruited. The sampling

frame and inclusion criterion were the same as described previously for patients in

Phase I. The Brief Pain Inventory Short Form (BPI-SF) measured pain experience and

was interview-administered for the purpose of examining concurrent validity of the

POABS-CA. The BPI-SF comprised of four items to assess pain intensity (worst,

least, average, and current pain), seven items to assess pain interference, and one item

to assess pain relief in the past 24 hours. The validity and reliability of BPI-SF for

pain experience is well established[99, 100], with the instrument being used in many

studies in various parts of the world. Thus, we have reasonable confidence that it can

be applicable to our Singapore setting. In addition, it was developed for use in cancer

patients, which fit into our study population. Cancer patients' opioid beliefs is a

subjective latent variable and while there is no standard "gold standard" measure of

this phenomenon, we aimed to demonstrate the performance characteristics of the

POABS-CA in relation to the BPI-SF since the BPI-SF's validity and reliability is

well established and it is commonly used in various studies to ascertain the impact of

pain. Thus, BPI-SF was chosen as the "gold standard" in testing the validity of the

POABS-CA. The hypothesis that patients having greater pain intensity on the BPI-SF

will also report more negative beliefs on the POABS-CA will be tested and as such,

convergent validity will be examined between BPI-SF and the POABS-CA. In

addition, patients will be contacted by the researcher via telephone 2 days to one week

after completion of the questionnaires and be asked the 10 questions in the POABS-

CA. This is for the intention of assessing the test-retest reliability of the instrument

(POABS-CA). The patients themselves will be required to answer the questions independently.

The distributions of the level of agreements for each item in the POABS-CA were tabulated. As with the original Taiwanese POABS-CA development study, mean scores instead of summated scores were used because each of the POABS-CA items measure a unique portion of a person's beliefs about opioids as well as pain endurance.

Statistical analysis

Cronbach's alpha was calculated for internal consistency. Intra-class correlation coefficients were calculated for test re-test reliability. Pearson's product moment correlations were calculated among POABS-CA total score, subscales and age, education, pain intensity on average, worst pain intensity and least pain intensity. The *t*-test was used to examine gender differences. POABS-CA total score, as well as negative effect and pain endurance beliefs subscales differences among the different races were analyzed with ANOVA.

Confirmatory factor analysis was used to ascertain if the proposed beliefs subscales and factors were consistent. Pearson's correlation coefficient was determined to investigate the relationship of the two beliefs (negative effect belief and pain endurance belief) and criterion-related variables such as age and pain intensity. Previous studies have shown that patients who were older as well as those who had less education[57, 101] had more negative beliefs about pain medication. It was also suggested that these patients were more likely to embrace values of enduring pain[102]. Gender differences were subjected to the *t*-test.

3.3   Results
Subject Characteristics

A convenience sample of 300 subjects recruited from NCCS included 129 men (43%)

and 171 women (57%). Age ranged from 27 years to 89 years with a mean of 61

years. 34 received no formal education (11.33%) while the rest had education ranging

from primary school (*n*=90, 30%) to university and above (*n*=26, 8.67%).

Participants' diagnoses were most commonly breast cancer (29.67%), followed by

lung cancer (13%) and colorectal cancer (10.33%), and all others being detailed in

Table 3.1. POABS-CA total score ($F(3,3) = 1.73$, $p = 0.16$), as well as negative effect

beliefs ($F(3,3) = 2.07$, $p = 0.10$) and pain endurance beliefs subscales ($F(3,3) = 1.77$,

$p = 0.15$) did not differ among the difference races.

Table 3.1 - Demographic and Disease Characteristics (n = 300)			
Characteristics	Mean (SD)	*n*	Percent
Age (years)	61.0 (11.1)		
Ethnicity			
Chinese		246	82
Malay		34	11.33
Indian		18	6
Others		2	0.67
Education			
No education		34	11.33
Primary School		90	30
Secondary School		108	36
Pre-university/Junior college/A-level		22	7.33
Polytechnic/Diploma		20	6.67
University and above		26	8.67
Gender			
Male		129	43
Female		171	57
Diagnosis			
Breast cancer		89	29.67
Lung cancer		39	13

Colorectal cancer	31	10.33
Nasopharyngeal cancer	30	10
Head and neck cancer	26	8.67
Prostate cancer	14	4.67
Liver cancer	13	4.33
Lymphoma	13	4.33
Cervical cancer	8	2.67
Gastric cancer	7	2.33
Ovarian cancer	7	2.33
Pacreatic cancer	6	2
Anal cancer	5	1.67
Esophageal cancer	3	1
Kidney cancer	2	0.67
Uterine cancer	2	0.67
Appendix cancer	1	0.33
Bone cancer	1	0.33
Endometrial cancer	1	0.33
Gallblader cancer	1	0.33
Sacral chordoma	1	0.33

Feasibility of the POABS-CA

The participants took 1 to 5 minutes to complete the POABS-CA. All participants commented that they felt the questionnaire to be easy to understand, wording of the questions were clear and they were easy to answer.

Reliability of the POABS-CA

The POABS-CA is shown in Table 3.2. Cronbach's alpha for the POABS-CA was calculated to be 0.88. Item-to-total correlations for the 10 items were all above 0.5 (Table 3.3). The least correlated was item 2 "Opioid medicine should only be used at the last stage of an illness" with item to total correlation of 0.5364, while the most highly correlated was item 7 "Adult patients should not use opioid medicine frequently" with alpha = 0.6767. Test-retest reliability of total score of POABS-CA for all 300 subjects was 0.99 (p-value < 0.0001). As this high correlation may be due to the wide variation in time to retest (4 to 8 days), with a large proportion (n = 231,

77%) undergoing the retest after 4 or 5 days, a separate analysis for test-retest

reliability was performed for only subjects who did the retest beyond 7 days (n = 67)

with the following result: intra-class correlation of 0.96 (p-value < 0.001).

Table 3.2 - Pain Opioid Analgesics Belief Scale-Cancer (POABS-CA)

In the following 10 statements, we ask for your beliefs about the use of opioids in cancer pain. Opioids or opioid medicines are also called narcotics by some people. Please circle the number that best shows your belief about opioid medicine and its use.					
0 = I strongly disagree.					
1 = I disagree.					
2 = I neither agree nor disagree.					
3 = I agree.					
4 = I strongly agree.					
1. Opioid medicine is not good for a person's body.	0	1	2	3	4
2. Opioid medicine should only be used at the last stage of an illness.	0	1	2	3	4
3. If a person starts to use opioid medicine, it means health is already in serious condition.	0	1	2	3	4
4. Opioid medicines cause many side effects.	0	1	2	3	4
5. Side effects caused by opioid medicine are not easy to handle.	0	1	2	3	4
6. Adults should not ask frequently for pain medicine.	0	1	2	3	4
7. Adult patients should not use opioid medicine frequently.	0	1	2	3	4
8. The more opioid medicine a person uses, the greater the possibility that he or she might rely on the medicine forever.	0	1	2	3	4
9. If a person starts to use opioid medicine at too early a stage, the medicine will have less of an effect later.	0	1	2	3	4
10. An adult should endure as much pain as possible.	0	1	2	3	4

Table 3.3 - Mean Item Scores and Item to Total Correlations for POABS-CA (n=300)

Items	Mean	SD	Item to Total Correlation
1. Opioid medicine is not good for a person's body.	2.02	1.023	0.5989
2. Opioid medicine should only be used at the last stage of an illness.	1.74	1.035	0.5364
3. If a person starts to use opioid medicine, it means health is already in serious condition.	1.78	1.12	0.6161
4. Opioid medicines cause many side effects.	1.86	1.05	0.6226
5. Side effects caused by opioid medicine are not easy to handle.	1.82	1.03	0.6121
6. Adults should not ask frequently for pain medicine.	1.75	1.17	0.6527
7. Adult patients should not use opioid medicine frequently.	1.80	1.18	0.6767
8. The more opioid medicine a person uses, the greater the possibility that he or she might rely on the medicine forever.	2.07	1.15	0.5898
9. If a person starts to use opioid medicine at too early a stage, the medicine will have less of an effect later.	2.06	1.03	0.5579
10. An adult should endure as much pain as possible.	1.58	1.22	0.5419

Construct validity of the POABS-CA

Factor structures of the POABS-CA were examined using confirmatory factor analysis with the STATA command "confa".

The two factors, negative effect beliefs and pain endurance beliefs, have a moderate correlation (r = 0.51). Factor 1 contained 7 items from the negative effect beliefs subscale while factor 2 contained 3 items from the pain endurance beliefs subscale.

Items 1, 2, 3, 4, 5, 8 and 9 loaded correctly to Factor 1 (negative effect beliefs) while items 6, 7 and 10 loaded distinctly as well to Factor 2 (pain endurance beliefs).

CFI was found to be 0.8070.

Table 3.4 shows the Pearson's product moment correlation among POABS-CA total score, subscales and age, education, pain intensity on average, worst pain intensity and least pain intensity.

Pain endurance beliefs had no significant correlation with any of the proposed criterion variables. However, higher negative effect beliefs were significantly correlated with lower pain intensity on average (r = -0.22, $P < 0.005$) and lower worst pain intensity (r = -0.24, $P < 0.0001$). Higher POABS-CA total score was associated with lower average pain intensity (r = -0.20, $P < 0.001$) and lower worst pain intensity (r = -0.22, $P < 0.001$). Previous studies have shown that patients who were older and those who received less education had more negative beliefs about pain medications[57, 101], which was not shown in our study. Gender differences were also different from the original study, with females having more negative effect beliefs (Mean = 2.10, SD = 0.77) than males (Mean = 1.65, SD = 0.70) ($t = -5.13$, df = 298, $P < 0.0001$). Likewise, females in our setting were found to have greater pain endurance beliefs (Mean = 1.82, SD = 1.14) than do males (Mean = 1.56, SD = 1.02) ($t = -2.05$, df = 298, $P < 0.05$).

Table 3.4 - Correlations: Pain Beliefs versus Pain Sensory and Demographic Factors

Variables	Age	Average Pain Intensity	Worst Pain Intensity	Least Pain Intensity	Education
Negative Effect Belief	-0.04 (0.4456)	-0.22[a] (0.0001)	-0.24[a] (0.0000)	-0.11 (0.0510)	0.01 (0.899)
Pain Endurance Belief	-0.06 (0.3238)	-0.11 (0.0583)	-0.11 (0.0582)	-0.07 (0.2443)	0.02 (0.7053)
Total Belief Score	-0.06 (0.3338)	-0.20[b] (0.0004)	-0.22[b] (0.0002)	-0.11 (0.0592)	0.01 (0.8002)

[a] $P < 0.0001$
[b] $P < 0.001$

Table 3.5 Frequency Distribution for Level of Agreement (%)
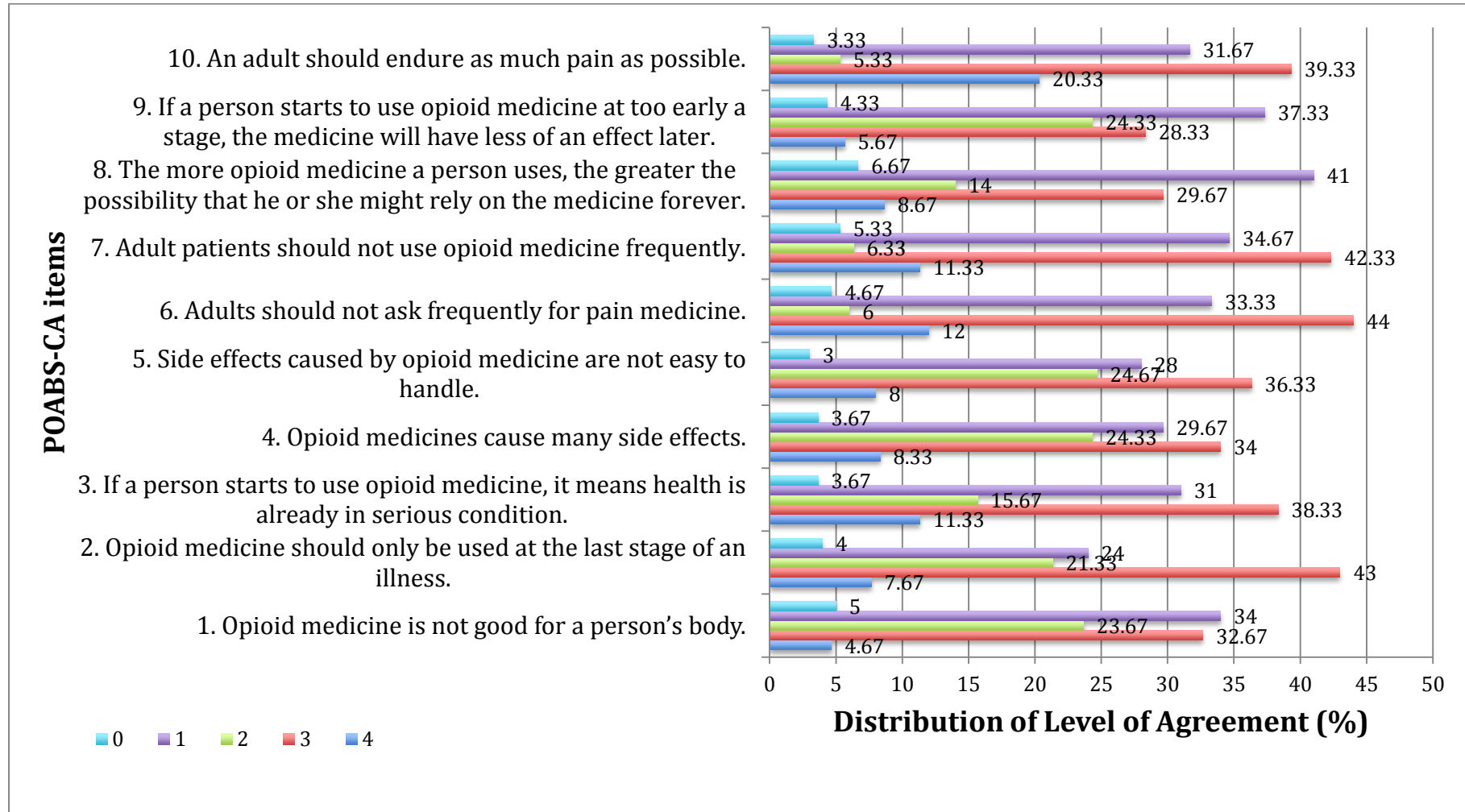
The distributions of the level of agreements for each item in the POABS-CA are shown in Table 3.5. Mean scores of each item are shown in Table 3.3. Range of means was 1.58 (SD = 1.22) to 2.07 (SD = 1.15).

3.4 Discussion

Psychometric analysis of the POABS-CA in our local setting supported its overall satisfactory internal consistency reliability. Cronbach's alpha for POABS-CA was 0.91 and item-to-total correlation of each of the 10 items was above 0.5. Test-retest reliability (r = 0.99) over a period of 2 to 7 days was satisfactory. All the items from the two subscales, negative effect beliefs and pain endurance beliefs, loaded on their original subscales. Negative effect beliefs among our patients were significantly correlated with lower pain intensity on average (r = -0.22, $P < 0.05$) and lower worst pain intensity (r = -0.24, $P < 0.05$). This is surprising as these findings suggest that the more negative beliefs our patients had of opioid effects, the lower their reported average pain intensity as well as worst pain intensity. While this may at first seem contradictory, our patients who possess negative beliefs regarding opioids could be reticent at reporting pain for fear of being sternly reminded again to consume opioid analgesics. There were, in fact, multiple occasions where patients asked interviewers during the study if their choices in the study would change their pain treatment plan.

Females in our study were found to score higher on both negative effect beliefs and pain endurance beliefs compared with males. This is again different from the original Taiwanese study, which showed males possessing greater pain endurance beliefs. This could be a reflection of true difference between both cultures with regard to attitudes about opioids, thereby strengthening the need to validate instruments despite

both cultures being superficially similar. Thus, the results of our study are consistent

with the Taiwanese report in all but one variable: gender differences with negative

effect beliefs. As with the original Taiwanese study[59], neither age nor education

were significantly correlated to negative effect beliefs. They were also not

significantly correlated with pain endurance beliefs. Authors of the original paper

suggested that their findings of negative effect beliefs not being significantly

correlated with variables of age, education and gender could be a universal

phenomenon[59], which our study proved to be otherwise, at least in terms of gender

differences. This may allow us to further streamline the phenomenon as such: that

beliefs about negative effects of opioids not having significant correlation with age

and education might be universal. Further research is needed to further refine these

relationships.

The multiracial setting in our population availed us the opportunity to analyze for

differences in the beliefs scores as well as adherence status among the different

ethnicities. It appears from our results that ethnicity is not a significant variable in

Singapore. This could be a reflection of the homogeneity of values held among the

races through lifetimes of acculturation.

Each item's mean score (Table 3.3) suggest that, unlike the original study, which had

more than 50% of the patients rating 8 out of the 10 items a 3 ("I agree") or 4 ("I

strongly agree")[59], our population was more evenly distributed with majority

(between 20% and 45%) either rating a 1 ("I disagree") or a 3 ("I agree") for each of

the items, with extreme choices being less popular. This may show that our

population is fairly balanced in their beliefs about opioids and the value of enduring

pain. This observation may explain to a certain extent the relatively high level of

adherence to opioid analgesics among our cancer patients. In addition, a significant

proportion of patients rated a 3 ("I agree") on questions about side effects (items 4

and 5), which could be a reflection of inadequate management of opioid-induced

adverse events in our setting.

Internal consistency reliability of the POABS-CA is satisfactory, with negative effect

beliefs subscale at 0.85, pain endurance beliefs at 0.90 and overall score at 0.88 as

well. While all subjects completed the retest, the interval between administration of

the first test and the retest was varied from 2 to 7 days. Test-retest reliability of total

score of POABS-CA was 0.99 (p-value < 0.0001). Subjects in which at least 7 days

have elapsed between first test to retest (n = 67), test-retest reliability was calculated

to be 0.96 (p=value < 0.0001). However, our study results did not show good fit of the

data to the model, as was observed from the CFI (0.8070), which was lower than our a

priori criteria of 0.95.

3.5   Conclusion

In conclusion, the 10-item POABS-CA is a simple measure of patients' negative

opioid beliefs with a short completion time. Although it has shown to possess good

internal consistency reliability and test-retest reliability, it does not exhibit concurrent

validity with BPI-SF, which is of concern as it may mean that one could be measuring

an unintended latent variable from what it was intended to measure. Thus, we need to

be critical in the usage of POABS-CA in our local setting.

Chapter 4. Measure of cancer patients' opioid beliefs and their adherence to opioid analgesics

Chapter 5. Conclusions

5.1   Major findings

In this thesis, we first performed a systematic review to summarize current literature with regards to the contexts in which cancer patients' beliefs have been studied (Chapter 1). In addition to broadly outlining these contexts, we identified the measurement tools used in the studies for assessing cancer patients' beliefs and critically appraised the content and psychometric properties of these instruments (Tables 1.2 and 1.3). We also found that the POABS-CA, a 10-item instrument developed to assess cancer patients' negative beliefs on opioid analgesic use, was a relevant tool that was relatively newly developed which would benefit from validation in our local setting, which was the direction this thesis took in the subsequent chapters. This instrument was chosen, as it was cancer specific and opioid specific, which fit our thesis objective of understanding cancer patients' beliefs in relation to their adherence to supportive care.

We next looked at the prevailing trend of opioid usage at a large local ambulatory cancer center (Chapter 2) to allow appreciation of the scope of our study we wished to undertake. This availed us with knowledge that while our opioid usage did not reach the levels experienced in US or Australia, a slow but steady rise in use of stronger opioids was observed which can potentially lead to the problems faced by these countries related to use and abuse of opioids. This is especially of concern, as the number of cancer patients using opioids did not significantly increase over the years, suggesting that our individual patients have been using more opioids over the years.

Following up to that, we explored the feasibility of the POABS-CA in Singapore as well as its construct validity and reliability (Chapter 3). From this validation study, we

found that the POABS-CA in our local setting exhibited satisfactory feasibility,

internal consistency reliability and test-retest reliability. The participants took only a

short time (1 to 5 minutes) to complete the POABS-CA and all commented that they

felt the questionnaire to be easy to understand, that the wording of the questions were

clear and that they were easy to answer during the interviewer-administered sessions.

However, the POABS-CA did not show convergent validity with the BPI-SF, which

brought up issues with interpretation of its results. This could either be due to actual

differences between the original Taiwanese population and our local population, or it

could be a manifestation of a more complex underlying cognitive reflex mechanism

among our patients. In addition, due to the study being interviewer-administered,

probable issues such as social desirability bias, which can obscure the intended

outcomes the instrument was designed to measure, could not be ruled out. While the

POABS-CA was originally devised as a self-report questionnaire, the low literacy of

our elderly (majority) patients necessitated the use of interviewers conducting the

study in various languages. Thus, the results of this study should be taken with this

consideration in mind.

Contents not disclosed due to copyright issues.

5.2   Contributions

In conclusion, this thesis has contributed to new knowledge to the understanding of cancer patients' beliefs in a few ways. Firstly, to the best of our knowledge, we have performed the first systematic review of current literature on studies done to measure cancer patients' beliefs. This allows us to appreciate the aspects of cancer patients' beliefs that are suitable and valuable for further study. Second, we have established the background opioid analgesic usage in our local ambulatory cancer center. Third, we isolated and performed validation studies on a relevant tool used to measure cancer patient's opioid beliefs in our local context.

5.3   Limitations

The limitations of the studies have been detailed in the preceding chapters and shall be summarized here. Firstly, our systematic review only included English-language articles and excluded those published only as abstracts. We also could not assess publication bias because of the lack of evidence. Second, as consumption data does not necessarily equate to amount of opioid actually taken, patients may in reality be taking more or less opioid medications than was reported. Third, as our validation and adherence studies were interviewer-led, social desirability bias could not be discounted. This potentially obscured, to an extent, the intended outcomes the instrument was designed to measure. Unfortunately, this could not be addressed in our

studies as a large proportion of our cancer patients were illiterate, necessitating the

need for an interviewer to both translate and verbalize the questions asked in the

instruments. Additionally, due to the self-report nature of both our measures of

adherence, biases may not be entirely mitigated by our use of 2 separate tools for this

purpose.

5.4   Recommendations for future studies

While carrying out the studies, several thoughts for further research arose. The following are some of the new research questions proposed:

1.   Do adjuvant pain medications significantly affect beliefs regarding opioid use?

Adjuvant pain medications lack the social stigma associated with opioids. As a result, their preferential use by cancer patients may help reduce cancer pain to such an extent as to affect response to questionnaires measuring opioid beliefs and their adherence. In order to make meaningful conclusions about opioid beliefs, we need to take into account patients who were using co-analgesics such as NSAIDs and anti-neuropathic agents. A separate study on patients not on these adjuvant treatments could potentially clarify our results.

2.   Do our patients possess the cognitive reflexes of favoring positive responses to POABS-CA items in order to avoid possible confrontation with interviewers who may sternly remind them to adhere to their opioid regimen?

In order to determine that this cognitive aspect did not corrupt the results from our POABS-CA study, we may need to ascertain whether our patients possess such attitudes in the first place. This can then lead to more meaningful data gathering and subsequent interpretation of results.

3.   Why do females among our cancer patients seem to possess more negative opioid beliefs than males?

Unraveling this phenomenon can bring us a step closer to understanding how cancer patients possess negative opioid beliefs and how culture and social constructs of gender roles contribute to this difference.

4.   What can be done for patients who possess negative opioid beliefs?

While our studies did not show a significant link between negative opioid beliefs and adherence, it is nevertheless worth having appropriate interventions in place to reduce such beliefs in our cancer patients, especially in light of the argument that there could be potential confounders due to administration of adjuvant analgesics and subject social desirability bias. A possible future work could be isolating interventions only to patients who score above a critical point in the POABS-CA to derive meaningful results.

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