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The Experience of Cancer Pain: Developing Integrated Support Systems for Breast Cancer Patients with Chronic Pain informed by Patient and Caregiver Insights

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To patients and family members,
To my family and my partner,
To my best friend,
To all who made this dream come true.

List of Abbreviations

AGNES: Agglomerative Nesting

CP: Chronic Pain

FCR: Fear of Cancer Recurrence

FHIR: Fast Healthcare Interoperability Resources

IASP: International Association for the Study of Pain

IEO: European Institute of Oncology

MAP: Multimodal Assessment Model of Pain

MARS: Mobile Application Rating Scale

NRS: Numeric Rating Scale

PSEQ: Pain Self-Efficacy Questionnaire

SDM: Shared Decision-Making

SDM-Q-9-item: 9-item Shared Decision-Making Questionnaire

STM: The Systemic Transactional Model

QoL: Quality of Life

WHO: World Health Organization

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Abstract

Introduction: Chronic pain (CP) significantly affects the quality of life (QoL) of cancer patients and their caregivers, necessitating a multidimensional approach to understand and address the diverse impacts. This doctoral thesis synthesizes findings from a series of studies conducted over four years, focusing on the evolving understanding and management of cancer-related CP, particularly in breast cancer survivors and their caregivers.

Methods: The research began with a narrative review (Study 1) that synthesized existing data on the impacts of CP on both patients' and caregivers' QoL. Subsequent studies utilized a mix of qualitative and quantitative methods. Online platforms (Study 2) and focus groups (Study 3) were employed to collect data on the patients' and caregivers' unmet needs, emotional responses, and treatment preferences concerning CP. This focus has been further narrowed down to breast cancer survivorship (Study 3). The final study (Study 4) evaluated the usability of a novel digital health tool, PainRELife, in managing breast cancer CP and enhancing patient engagement in treatment decisions.

Results: Study 1 highlighted an overall reduction in QoL and underscored the importance of adopting a bidirectional perspective to fully comprehend the impact of CP on both patients and caregivers. Study 2 identified distinct emotional and practical needs between the two groups, drawing on data from online communities. Study 3's focus groups with breast cancer survivors uncovered significant barriers to pain management, the necessity for psycho-social support, and preferences for specific treatment modalities. Meanwhile, focus groups involving caregivers revealed profound emotional challenges and highlighted the complexities of providing emotional support during chronic conditions. The pilot implementation of the PainRELife app in Study 4 demonstrated promising results. Usability testing indicated good user engagement, functionality, and information quality, significantly improving pain self-efficacy and reducing pain intensity observed among breast cancer patients. The app was particularly effective in enhancing patient engagement and supporting shared decision-making processes.

Discussion: Across the studies, the complexity of CP management in cancer care was evident, particularly in breast cancer, revealing diverse needs and perceptions between patients and caregivers. As demonstrated by the PainRELife app, incorporating digital tools has shown the potential to enhance CP self-management and lead to better clinical outcomes, specifically in breast cancer care. This research emphasizes the critical need for holistic and customized approaches that address medical and emotional needs, promoting technology to support continuous care and informed decision-making. Future research should continue to explore innovative care models that integrate technology and patient-centered strategies to tackle the complex challenges of CP in cancer survivorship, with particular attention to developing support mechanisms specifically designed for breast cancer caregivers.

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Chapter 1

General Introduction

1.1 Understanding Cancer Pain

1.1.1 Cancer Pain Definition and Its Impact

Pain remains a significant challenge for cancer patients at various stages of their medical journey, from diagnosis through long-term survivorship and palliative care. In recent decades, we have observed changes in this domain: a recent meta-analysis [1] indicates a trend toward declining prevalence and severity of pain, yet the overall prevalence is still high. Notably, the incidence of pain following curative treatment has decreased to 35.8% [1] from the previously reported 39.3% [2]. During anti-cancer treatments, the prevalence has decreased from 55.0% to 44.5%. This decline is even more significant in advanced, metastatic, or terminal stages of cancer, with the current prevalence at 54.6% compared to the formerly reported 66.4%. Further analysis reveals that moderate to severe pain has followed this downward trend, now at 30.6% overall and only 22.8% post-curative treatment. However, the highest incidence of moderate to severe pain remains in patients without viable anti-cancer treatments, at 43.3% [1]. These findings underscore a persistent challenge: despite a reduction in reported instances, pain management in cancer care continues to be both undertreated and underreported, leading to approximately one-third of patients receiving inadequate treatment for their pain, highlighting a significant gap between pain experiences and therapeutic responses [3,4].

According to the International Association for the Study of Pain (IASP) [5], pain is defined as:

> "*An unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage*" (p.1977)

Expanding upon the revised definition of pain, cancer-related pain should be viewed as a multifaceted phenomenon comprising physical sensations (i.e., conscious awareness of a painful stimulus) and emotional experiences (i.e., intense discomfort that leads to reactive behavior) [6]. Pain is always a subjective experience, influenced by emotional, social, cultural, spiritual, and environmental components, and it is what the patient reports. This complexity is encapsulated in the concept of "total pain", as proposed by Dame Cicely

Saunders [7,8], which suggests that pain encompasses various biopsychosocial dimensions, making it difficult to measure and treat effectively [9]. The term "total pain" can be contextualized within the modern concept of quality of life (QoL), which ultimately should be the primary goal of pain management [10].

Therefore, comprehending and treating this suffering requires a thorough bio-psycho-social approach, in which psychological and social factors are considered to provide a comprehensive understanding of cancer patients' needs concerning cancer pain and its management (including all stages from assessment, diagnosis, and prognosis to treatment and beyond). See paragraph 1.1.3 and paragraph 1.1.4.

1.1.2 Mechanisms in Cancer Pain: Causes and Types

The experience of cancer-related pain varies among individuals, prompting the need for standardized classifications to enhance comprehension [11,12]. These classifications encompass temporal, locational, and intensity-related aspects.

Temporally, pain is categorized as either acute or chronic. Acute pain arises promptly following medical interventions or diagnostic procedures and typically resolves within a short duration as the causative factor heals. Conversely, chronic pain (CP) persists beyond three months, drastically impacting the QoL of patients [12], and it's maintained and catalyzed by the presence of psycho-social factors [13]. A specific type of CP is breakthrough pain, which refers to sporadic surges in pain intensity that cancer patients may experience, even when their pain is generally well-managed with opioid medications [14]. Additionally, with regard to temporal variation, pain can be either continuous or intermittent [11].

Regarding *localization* or *pathophysiological criteria*, pain is delineated as nociceptive, neuropathic, nociplastic, or mixed. Nociceptive pain originates from direct stimulation of pain receptors (either visceral – which originates from the internal organs, or somatic – which originates from the outer body structures like skin and muscles) due to tissue damage by tumor or metastasis or tissue injury resulting from anticancer treatments; while, neuropathic results from nervous system impairment (either peripheral – which originates from a damaged or dysfunction of the peripheral nervous system, or central which nerves damaged are inside the central nervous system and include the spinal cord) due to tumor growth or treatments [15].

Nociplastic pain has been recognized as a third mechanistic descriptor, introduced by the IASP in 2017. It refers to pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors, or evidence for disease or lesion of the somatosensory system causing the pain [16]. Unlike nociceptive and neuropathic pain, nociplastic pain involves a central sensitization mechanism, with heightened sensitivity to pain and a broad distribution of pain without apparent tissue or nerve damage. This type of pain is often seen in chronic conditions such as fibromyalgia and may co-occur with nociceptive and neuropathic pain mechanisms, particularly in cancer patients who have experienced prolonged nociceptive pain.

A mix of nociceptive, neuropathic, and nociplastic pain is common in cancer patients, representing a multifaceted phenomenon resulting from the simultaneous occurrence of various factors, including inflammatory, neuropathic, nociplastic, and ischemic elements, often distributed across multiple locations simultaneously.

In terms of *intensity*, pain is assessed on a scale of 0 to 10 (Numeric Rating Scale (NRS); [17]) or through a color gradient (Visual Analogue Scale) using the question : "What has been your worst pain in the last 24 hours?", where 0 (green) signifies the absence of pain, 1-3 (yellow) denotes mild pain, 4-6 (orange) indicates moderate pain, and 7-10 (red) represents severe pain.

While the mechanisms of cancer pain are well-defined and standardized classifications help in understanding its complexity, the experience of pain is highly individualized, and one significant factor contributing to this variability is the influence of sex and gender. It is crucial to correctly distinguish between sex and gender, as both biological aspects (such as differences in pain sensitivity) and cultural aspects (such as gender norms and identity) play a role in how pain is experienced and reported [18]. For this reason, the term sex/gender is used to encompass the complex interplay of biological and sociocultural factors influencing pain perception.

Studies have shown that women generally have lower pain thresholds and increased pain sensitivity compared to men, a difference often attributed to biological and hormonal factors such as estrogen, which modulate pain pathways [19–21]. Women are also disproportionately affected by CP conditions, with about half of CP conditions being more common in women, further complicating their pain experience in cancer [22,23].

Recent research has highlighted that certain pain pathways vary considerably between sexes/genders, with immune cells and hormones playing key roles in these differing responses [24]. For example, studies on rodents have shown that male and female mice use distinct immune mechanisms in response to CP, with microglia being more involved in males, while T cells play a more significant role in females [24]. Moreover, gender norms and relations can influence both the reporting of pain and the treatment received. For instance, clinicians may perceive women's pain as more psychological, leading to nonspecific diagnoses, longer wait times for treatment, and the prescription of more antidepressants and fewer analgesics compared to men [18].

Despite these complexities, a meta-analysis by Ahmed et al. [25] specifically examined sex/gender differences in perceived pain intensity among cancer patients and found no significant differences between men and women. This suggests that, despite the biological predispositions that may heighten pain sensitivity in women, the reported intensity of cancer pain does not consistently differ by sex/gender in clinical settings. These findings highlight the necessity for personalized pain management strategies that consider the unique influences of both sex and gender on cancer pain, while also addressing the broader socio-cultural factors that impact patient care [18,25].

Pain experienced by cancer patients typically arises from multiple sources [6,26]:

- The tumor itself and any accompanying comorbidities.
- Anticancer therapies aimed at either curative or palliative purposes, including surgery, radiotherapy, chemotherapy, biological therapy, or endocrine therapy.
- Supportive care interventions designed to alleviate the toxicity of oncologic treatments.
- Diagnostic or therapeutic procedures such as radiological examinations, soft tissue/bone biopsies, lumbar punctures, and venous injections.

These classifications serve to characterize cancer pain. However, these classifications do not consider the psycho-emotional impact of pain and patients' needs, making it more difficult to tailor management strategies effectively. Assessing pain and other physical and emotional symptoms is integral to clinical practice at every stage of cancer care. Symptom management should be guided by a comprehensive evaluation that recognizes the symptoms' multidimensional and subjective nature, the patient's sense of well-being, QoL, and functional status [6]. In this line, the biopsychosocial model of cancer pain must be applied to cancer pain management.

1.1.3 The Biopsychosocial Model of Cancer Pain

The biopsychosocial model of cancer pain is a theoretical framework for understanding how biological (e.g., injury, infection), psycho-emotional (e.g., negative mood, mindsets), and social/environmental (e.g., social support, access to services) factors can interact to influence a person’s overall experience of pain [27,28]. The physical and psychological processes are highly intertwined and function together as a system [13]. But how do these processes work? From a *physical perspective*, cancer pain is influenced by various physiological, biological, and clinical factors, including the tumor's type, stage, grade, metastasis, anticancer treatments (such as chemotherapy, radiotherapy, biological and hormonal therapy), and surgical outcomes (both destructive and reconstructive outcomes) [6,29].

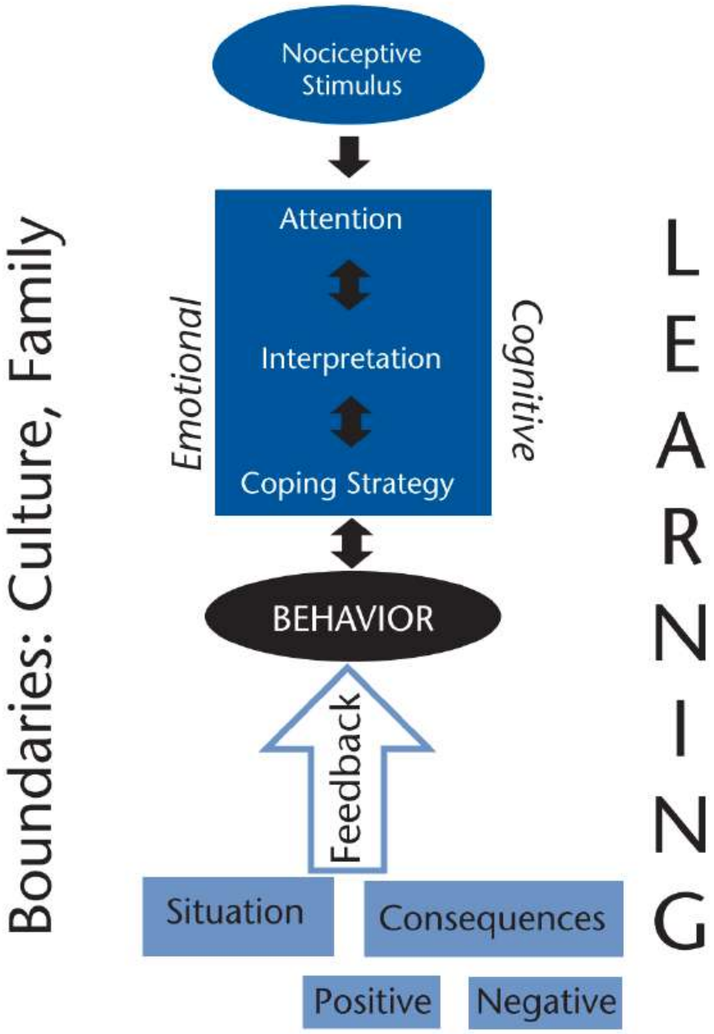

Figure 1. A contemporary perspective on pain perception from a psychological standpoint, as articulated by Linton [13]

Based on the Linton model (refer to Figure 1) [13], the process starts with the initial perception of the noxious stimulus (i.e., a stimulus that is actually, or potentially, damaging to tissue and liable to cause pain), followed by cognitive (attention, interpretation, coping strategies) and emotional processing, ultimately prompting individuals to respond to their pain (referred to as pain behavior).

From a *psychological perspective*, psycho-emotional factors may act as maintaining and catalyzing factors that influence pain (including its intensity, degree of interference, perceived uncontrollability, and duration) and facilitate the transition from acute to CP [13]. Regarding cognitive processing, the prerequisite for pain perception is that the noxious stimulus attracts our attention, viewing it as a warning signal (i.e., something is happening in the body) [30]. When pain is perceived as a "threat", the level of threat posed by the (noxious) stimulus guides the level of awareness: the higher the threat, the more attention is directed towards it [13]. Once the stimulus is attended to, cognitive processes interpret what it means. Mindsets (i.e., core beliefs about the nature and workings of things in the world [31]) play a crucial role in this phase. The cancer threat interpretation model [32] situates the occurrence of post-cancer pain within the framework of uncertainty related to survival. According to this model, cancer survivors navigate an environment characterized by uncertainty about symptoms, wherein experiencing pain can signal a threat, leading to fear of cancer recurrence (FCR) [33,34], heightened vigilance regarding bodily threats, and help-seeking behaviors (e.g., asking for help) [32]. Recent research [35] showed that bodily threat monitoring is associated with greater pain, FCR, and help-seeking behavior. This association depended on individuals' mindsets toward their bodies: when the body is perceived as an “adversary”, the outcomes were higher; when the body is “responsive”, they were lower.

Once a painful stimulus has been acknowledged and perceived as a “threat”, coping strategies are initiated. These strategies encompass both behavioral coping strategies (e.g., resting, applying moist heat, changing position, pacing activities, or using relaxation methods) and cognitive ones that alter one’s thought pattern (e.g., focusing on something distracting, visualizing, repeating calming self-statements, or practicing meditation or prayer) [13,36]. All these strategies are aimed at mitigating the perceived threat of pain and are often used by patients as coping mechanisms [37,38]. However, if employed maladaptively (such as denial or excessive prolongation of self-distraction from pain or catastrophizing the situation), these strategies may inadvertently worsen the impact of pain [39]. For instance, pain catastrophizing leads to a misinterpretation of bodily signals. It is characterized by irrational assumptions about pain, resulting in heightened rumination (“I can't stop thinking about how much it hurts”), magnification of the perceived threat (“I worry that something serious may happen”), and a sense of helplessness (e.g., “it is terrible, and I think it is never going to get any better”) [40]. According to the fear-avoidance model [13], catastrophizing thoughts contribute to the development of fear of pain, an emotional response that redirects attention to all potential negative signals from the body through hypervigilance, ultimately leading to avoidance behaviors (e.g., avoiding physical activity, social withdrawal). These behaviors can result in pain-related disability, depression, negative affect, anxiety, and higher pain perception and facilitate the transition from acute to CP [41]. Therefore, all these cognitive processes (attention, mindsets, coping) are deeply interconnected with emotional processes, laying the groundwork for subsequent behavior. The emotional distress caused by pain is one of its most disruptive aspects, embodying a broad and complex spectrum of feelings. This spectrum ranges from anxiety and depression to fear, anger, guilt, and frustration [13,38]. Such diverse emotional responses underscore the profound psychological impact that pain can exert on individuals. Specifically, a negative mood can precipitate alterations in pain behaviors, such as reduced activity levels, potentially resulting in deconditioning among certain patients and heightening the body's vulnerability to illness and injury. Moreover, pain can also impact mood states. For instance, an individual's interpretation of their pain condition (e.g., the extent to which they perceive pain will disrupt their daily life) can contribute to the onset of depressive symptoms and even suicidal thoughts [42–44].

As for the *social perspective*, social support constitutes a crucial element within the biopsychosocial model and has been observed to correlate with symptom burden among individuals diagnosed with cancer [28]. A social network's presence is pivotal in providing emotional and concrete support in times of crisis [45]. Existing literature has consistently shown links between increased cancer pain and diminished levels of social support, social activities, social functioning, and resilience, making it a risk factor when it is not perceived [38]. For instance, studies focusing on cancer patients and their partners indicate that individuals with avoidant attachment styles (marked by discomfort with intimacy and reliance on others) and anxious attachment styles (characterized by concerns about the availability and responsiveness of others) are associated with heightened reports of pain and diminished well-being among patients [46,47]. Additionally, social factors can give rise to different forms of social loss (including the loss of social roles, status, connections, or employment), financial burden, concerns about the family's future, and dependency [7,38,44].

Ultimately, cancer pain appears to prompt patients to confront existential reflections. It has been linked to spiritual considerations, such as finding meaning, losing faith, fear of uncertainty, and anger directed toward fate or God [7].

Given the multifaceted nature of cancer pain, which encompasses physical, psychological, social, and spiritual dimensions, it is crucial to capture its entire spectrum. Doing so is essential for developing and tailoring interventions that can effectively address and manage this complex condition in all its aspects.

1.1.4 Cancer Pain Management: From Assessment to Treatments

Understanding pain's nature and underlying causes is essential for informed medical management in cancer care. This assessment is intricate, combining subjective experiences with biological and psychosocial factors and requiring active participation from patients and, where necessary, from caregivers [48]. The Multimodal Assessment Model of Pain (MAP) [9] further emphasizes the value of integrating subjective pain narratives into this assessment, recognizing pain's individual and often unobservable nature. MAP advocates for a compassionate approach, validating all pain reports as legitimate experiences, which aligns with our emphasis on a holistic assessment framework. The evaluation should embrace the unpredictable aspects of cancer pain and the varied mechanisms and syndromes associated with different cancers [6,11]. A comprehensive assessment, considering intensity, location, duration, pattern, quality, and exacerbating factors, is crucial to plan an effective management strategy [11].

While guideline-based treatments for cancer pain effectively control it in 70–90% of cases [49], many patients still struggle with inadequate pain management. This is often due to patients' reluctance to report pain, misconceptions about its significance, or fears surrounding analgesics and dependence [3,50–53]. According to MAP, addressing these misconceptions and fears involves not only education but also ensuring that pain assessments are empathetic and patient-focused, thus fostering a better understanding of the subjective experience of pain [9]. Healthcare providers must address these misconceptions and fears and educate patients early in their diagnosis about pain manifestations, their meanings, and the efficacy of treatment options [54]. For instance, particular attention should be focused on the FCR and/or progression demonstrated to increase pain perception [33,55].

A preventive approach, utilizing validated assessment tools, is essential for timely and accurate pain management. Nevertheless, there is a compelling need for standardized protocols that holistically integrate pain's physical aspects with psychosocial domains, such as psychological distress, sleep-related issues, depression, anxiety, pain catastrophizing, and FCR [54,56]. Moreover, MAP enhances this holistic approach by advocating for the inclusion of diverse assessment methodologies that prioritize patient narratives and behaviors as central components [9]. This aligns closely with ESMO guidelines [57], which underscore the necessity for continuous and comprehensive pain assessments. These assessments are not just about quantifying pain characteristics but also about understanding their impact on the patient's life, including daily activities, psychological distress, QoL, caregiver presence, and the broader psychosocial context. The role of healthcare providers extends beyond clinical assessment to include effective communication with patients and families. They should dedicate time to discern and meet their needs and preferences for a clear, empathetic, and thorough care experience.

Following the assessment of pain, the treatment of cancer pain is a critical component of patient care. It involves a variety of approaches that should be adapted to the findings of the comprehensive pain evaluation, and patients should be well-informed about the pros and cons of each treatment option. It is important to note that not all interventions are suitable for every patient, and decisions must be made individually, guided by the detailed assessment process.

Treatment approaches for cancer pain can be categorized into two main categories:

1) Pharmacological treatments, which adhere to the World Health Organization (WHO)'s analgesic ladder for pain management [58];
2) Non-pharmacological therapies, which encompass a variety of approaches beyond painkiller prescription.

Focusing on the non-pharmacological or alternative therapies [59–62], subdivisions arise based on the nature and goals of the intervention:

- Psychological therapies include psychoeducation and social skills training, cognitive behavioral techniques that range from relaxation and distraction to reframing thoughts, acceptance and commitment therapy, mindfulness, supportive-expressive group therapy, and body-mind interventions such as guided imagery, biofeedback, and hypnosis.
- Physical and social rehabilitation treatments, including physical exercises and occupational therapy.
- Integrative treatments, including acupuncture, music or art therapy, massage, and yoga.

All these treatments can be considered either complementary (i.e., used in addition to other conventional treatments such as pharmacological interventions) or alternative treatments (i.e., used in place of traditional medicine) [59].

The treatment choice must be evidence-based and patient-centered, considering the patient's personal and cultural values and specific medical circumstances. Ongoing reassessment and adjustment of pain management strategies are vital, as pain can change over time or with disease progression.

In summary, a comprehensive cancer pain management plan should integrate various treatment modalities, informed by a detailed pain assessment, to alleviate pain, enhance QoL, and empower patients in their care process. It is about choosing the right treatment and providing patients with the necessary knowledge to make informed decisions about their pain management options. In this path, caregivers should also be considered an essential part of the cancer pain management process. See paragraph 1.2.2

1.2 Living with Cancer-related Chronic Pain: Setting the Stage

1.2.1 Chronic Pain in Cancer Survivorship: A Focus on Breast Cancer

Cancer survivorship, originally delineated through three phases from diagnosis to long-term survival, now encapsulates a broad spectrum of experiences ranging from living cancer-free to managing chronic conditions or facing recurrence [63,64]. Survivorship care emphasizes monitoring for recurrence, managing long-term side effects, and providing psychosocial support [64,65]. Recent findings from the Lancet [66] highlight the importance of addressing common issues for cancer survivors, such as pain, fatigue, FCR, and uncertainty about their future, which significantly impact their well-being and QoL.

In Italy, there are over 1.29 million cancer survivors [67], while globally, the number reaches approximately 53.5 million [68]. Despite the substantial survivor population, there are significant gaps in both oncological and primary care, which are highlighted by the overuse and underuse of services, especially in the context of cancer-related CP [69–71]. Notable side effects encompass CP, fatigue, and emotional distress, yet data on long-term consequences remain limited [72,73]. Conditions like CP, FCR, depression, anxiety, and cognitive limitations often diminish the QoL for survivors, emphasizing the need for more holistic care approaches. Moreover, patients who consistently use opioids from diagnosis to the index date face a heightened risk of continued use five years after survival [71].

This indicates a critical survivorship issue: the need for safe and appropriate pain management strategies that do not solely rely on opioids, particularly in cases where pain is not primarily opioid responsive. While self-management interventions offer effective strategies to enhance self-efficacy and improve mental health and pain management, ensuring that all cancer survivors have access to these valuable resources remains a challenge [74]. Self-management interventions, including those based on the Stanford model, acceptance and commitment therapy, or cognitive–behavioral therapy, are effective in not only reducing pain but also improving health-related QoL in CP groups [74].

For cancer survivors, a global review of National Cancer Control Plans by Mullen et al. [75] underscores the critical need for integrating psychosocial care into cancer survivorship. This includes comprehensive assessment and management of pain and distress, vocational support, and caregiver assistance [64,66,75]. These psychosocial interventions are essential for improving overall QoL and addressing the comprehensive needs of cancer survivors in the post-treatment phase. Effective pain management strategies should include both pharmacological and non-pharmacological methods [66]. Emphasis should be placed on non-pharmacological approaches such as self-management interventions, exercise, acupuncture, and support group therapies. Additionally, the judicious use of analgesics is important to reduce side effects and improve daily functioning.

Among women, breast cancer is especially significant, being the second most diagnosed cancer globally, with approximately 2.3 million new cases in 2022 [76]. In Italy, breast cancer continues to represent a major challenge, accounting for about 28% of all female neoplasms diagnosed in 2022 [67]. Despite advancements in treatment, the annual incidence rate slightly increases (+0.3%), indicating persistent prevalence. Regarding cancer pain, the prevalence of persistent pain following surgery in breast cancer survivors ranges from 27% to 46%, depending on location and severity [77]. This pain typically persists beyond the three-month mark, becoming chronic, and tends to remain stable for up to two years without significant improvement in prevalence or intensity [77,78]. Furthermore, research by Bredal et al. [78] has shown that factors such as young age, combined treatments involving axillary lymph node dissection followed by chemotherapy and radiotherapy, as well as comorbid conditions like depression and anxiety significantly predict CP. Andersen's and Kehlet’s review [79] corroborates these findings and further identifies nerve damage and radiotherapy as particularly impactful, marking them as critical risk factors for CP post-treatment. Additionally, their review aligns with findings from other surgical fields, identifying the severity of acute postoperative pain as a predictor for developing persistent pain. Their analysis, focusing on breast cancer treatments, reveals a positive correlation between the intensity of acute post-surgical pain and the development of CP, although they note that these studies often rely on recalled pain experiences, which may introduce bias.

In breast cancer survivors, cancer-related CP can be categorized into several key areas [80]:

- Post-operative pain, often experienced after surgical interventions such as mastectomy, is characterized by localized sensations and may exhibit neuropathic qualities. Jud et al. [81] found a higher incidence of CP among patients who underwent modified radical mastectomy compared to those who underwent breast-conserving surgery. Interestingly, tumor size did not influence pain incidence, but the lymphedema group showed a larger pain area than the non-lymphedema group. The breast and surrounding region (chest, armpit) are typically the most affected areas.
- Chemotherapy-induced pain, resulting from medication side effects or infusion techniques, often presents as peripheral neuropathy syndrome. This syndrome involves nerve damage from the brain to the spinal cord, typically beginning in the extremities (fingers and toes) and progressing towards the body. Symptoms include tingling or pins and needles sensation, burning or numbness, sensitivity to hot and cold, and difficulties with motor skills [82].

- Radiation therapy-related pain may manifest acutely during treatment or chronically months after treatment cessation. Patients often report experiencing aches, twinges, or sharp pains in the tissue, skin, or muscle area, indicative of somatic pain symptoms. Unlike somatic pain, which typically affects surface tissues, visceral pain is described as squeezing, crampy, or pressure-like and originates from internal organs. Additionally, neuropathic pain may occur, characterized by sensations such as burning, shooting, dysesthesia, and hyperalgesia. These pain sensations are localized to the treatment area, including the breast and surrounding regions (chest, armpit) [83].
- Pain following endocrine therapy often presents as musculoskeletal or joint discomfort and typically represents somatic pain symptoms [84].
- Bone pain, primarily observed in cases of locally advanced or metastatic breast cancer, typically represents a somatic pain symptom [57].

Recent studies have further classified CP in breast cancer survivors into distinct phenotypes, with mixed pain being the most prevalent at 40.7%, followed by neuropathic pain at 22.1%, nociceptive pain at 20.9%, and nociplastic pain at 16.3% [85]. This classification is crucial for understanding the complex pain profiles in breast cancer survivors, as each phenotype can have distinct impacts on health-related QoL. For example, breast cancer survivors with predominant nociplastic pain tend to experience lower QoL, particularly in areas related to bodily pain and social functioning, compared to those with other pain types. Moreover, hormone therapy, commonly administered as part of breast cancer treatment, has been associated with a higher likelihood of developing nociplastic pain, suggesting a need for tailored pain management strategies in this population.

The pain issue is often “hidden” by breast cancer patients and, to some extent, neglected by healthcare providers [86]. Some authors suggest that the lack of attention is partly because, to date, studies on pain have focused mainly on the advanced and terminal phases of the disease, with little or poor attention on pain during the extended period of cancer survivorship [87]. Lovelace et al. [88] further highlight that breast cancer survivors have multiple physical, emotional, and psychological needs that are often unmet by current healthcare systems, pointing to the failure to provide thorough assessments and education on interventions and treatment options to optimize health-promoting strategies. CP significantly interferes with psychological and emotional well-being, as well as with relationships—including family, social, and romantic partnerships—and work maintenance [89,90]. If not promptly recognized and managed, it can significantly alter QoL. Moreover, patients experiencing CP often show a marked reduction in the perceived utility of cancer treatments and adherence, such as to hormonal therapy, which negatively impacts the five-year survival rate [91]. This underscores the urgent need for comprehensive pain management and supportive care tailored to breast cancer survivors and their caregivers, aligning with broader survivorship care goals.

1.2.2 Chronic Pain as a “We Disease”: The Systemic Transactional Model

CP poses a significant challenge not only for the individuals directly affected but also for their family systems, especially their romantic partners. The onset and progression of a chronic condition led to substantial changes within family dynamics, including shifts in roles (e.g., one partner assuming the caregiver responsibilities) and increased stress [92], which necessitates a deeper exploration of how couples cope with such life-altering circumstances. The systemic transactional model (STM), developed by Bodenmann [93,94], offers a framework to understand these interactions more comprehensively, positing that illness is not merely an individual challenge but a dyadic one that impacts both partners.

The STM fundamentally shifts the understanding of stress and coping to a relational dimension, asserting that these processes are inherently interdependent within intimate relationships [93]. Defined by the interdependence theory [95], interdependence is the process by which individuals interacting with each other influence one another’s experiences through their actions, personality characteristics, and the dynamics of their relationship, emphasizing the significant reliance partners have on each other. This theory posits that in stressful situations, the experiences of one partner can significantly enhance (or deplete) the coping resources of the other, highlighting the profound impact of shared relational dynamics on individual coping mechanisms [94,96,97]. The research underscores the crucial role of mutual stress regulation in managing chronic conditions where the psychological well-being of both partners is closely intertwined [96–98]. Specifically, studies on cancer-related CP show that effective pain management in patients is deeply linked to the coping strategies and emotional responses of their caregivers [99,100].

Further, STM illustrates how partners’ emotional and behavioral reactions are intricately connected, affecting each other significantly. This interconnection forms the basis of the “we-disease” scenario in chronic illness cases [101], where the coping actions of one partner impact the other, influencing how stressors—particularly a chronic condition like CP—are managed through shared coping mechanisms. Unlike traditional models focusing on individual coping strategies, STM integrates a dyadic perspective based on the stress appraisal processes described by Lazarus and Folkman [102]. It redefines primary (i.e., the evaluation of the significance of the situation for one’s well-being) and secondary (i.e., the evaluation of the demands of the situation and one’s resources to respond to these demands) appraisals to consider both partners' stressors and resources, thereby enhancing stress management within the relationship [94]. This dyadic framework underscores the importance of joint appraisals, where partners collaboratively evaluate stressors using a “we-stress” approach, which is crucial for effective dyadic coping and significantly enhances the support exchanged between partners [103].

The responses to stress are pivotal; they can either be positive, promoting a return to stability within the relationship, or negative, exacerbating stress. STM specifically highlights two primary forms of dyadic coping: supportive and joint [94]. Supportive coping involves one partner actively assisting the other to alleviate stress, while joint coping sees both partners working collaboratively to address the stressor. Both methods strengthen relationship dynamics and enhance individual well-being by fostering intimacy and mutual support [104]. Each type of dyadic coping, whether targeting problem-solving or emotion regulation, can lead to negative outcomes such as hostile, ambivalent, or superficial coping, especially when a partner is unable or unwilling to provide effective support due to personal stress or emotional depletion. These negative behaviors, including withdrawal or hostility, can intensify stress and significantly diminish relationship quality [93,94].

Facing cancer-related CP as a “we-disease” can significantly enhance the strength and cohesion of relationships between partners. Concerning cancer, for example, 42% of couples dealing with non-metastatic breast cancer reported increased cohesion up to a year after diagnosis [105]. Similarly, Badr et al. [106] found that patients and partners who engaged in frequent discussions about their relationship exhibited higher relationship functioning over a six-month period post-diagnosis. This connection between effective communication and relationship functioning is robustly supported by a range of cross-sectional and qualitative studies, highlighting that constructive communication fosters relationship satisfaction, life satisfaction, and mutual responsiveness, as reported in a recent systematic review [96]. Additionally, research by Manne, Siegel, Kashy, and Heckman [107] on women with early-stage breast cancer supports the beneficial impact of shared awareness of the relationship's role in managing cancer, which was linked to higher levels of intimacy, mutual trust, and overall physical well-being. These positive outcomes underscore the value of “we-appraisals” in facilitating effective adjustment to illness, whereas discrepancies in these appraisals can lead to increased depressive symptoms among partners, highlighting the critical role of unified perceptions in disease management and emotional health [108]. However, despite these insights, there is a notable lack of specific studies addressing the management of CP within the context of cancer, a gap that, if addressed, could further improve support and outcomes for affected couples.

Moreover, to enhance our understanding of dyadic coping within the STM framework, it is crucial to consider the developmental-contextual model [98], which recognizes that coping strategies evolve across the lifespan and in response to changing daily circumstances and broader sociocultural contexts. Recent studies further underscored this by emphasizing the role of proximal contextual factors, such as relationship quality, in influencing dyadic coping and adjustment [103]. High relational quality enhances mutual support and effective joint coping strategies, facilitating better chronic conditions management. Moreover, as couples navigate through different stages of an illness, their coping mechanisms may require adaptation to meet changing needs and challenges. This aligns with findings that partners' perceptions of illness interference can significantly affect their coping responses, highlighting the importance of accurate and supportive dyadic appraisals in managing chronic illnesses [103].

1.2.3 The Role of Caregivers in the Chronic Pain Journey: The Emotional Toll

Caregiving plays an indispensable yet often overlooked role in cancer treatment, imposing significant demands on those who assume these responsibilities [109,110]. In this dissertation, “caregivers” refers to informal caregivers—partners, family members, or close friends—who often step into this role without formal preparation, providing essential support to individuals with cancer [110,111].

Unlike healthcare providers, who are trained professionals, these informal caregivers offer both emotional and practical assistance, often balancing these responsibilities with other aspects of their lives. This support becomes particularly critical in managing chronic conditions such as cancer-related CP.

Caregivers are crucial in offering physical and emotional support and overseeing healthcare transitions, such as moving from hospital to home care or between specialist and primary care providers [110]. Poorly handled transitions can result in worsened health conditions, heightened complication risks, and increased hospital readmissions [112]. Furthermore, caregivers are pivotal in helping with essential communication duties, including respecting patient preferences for information disclosure and navigating family dynamics during medical consultations. These responsibilities often require mediating between differing treatment options and managing difficult behaviors from family members [110].

The caregiving experience encompasses both challenges and growth opportunities. Studies indicate that caregiving can lead to elevated distress, burden, and marital strain [113–115], yet it also provides a stand for resilience and enhanced familial bonds [116,117]. The dyadic nature of caregiving often categorizes primary caregivers as “second-order patients”, who not only share the patient's suffering but also have significant emotional distress themselves, influenced heavily by the patient’s pain [100,118]. Girgis et al. [119] underscore the profound physical, psychosocial, relational, and economic burdens faced by caregivers of cancer patients, highlighting that caregiving is often a full-time job taken on without choice. The psychological and social stressors, including anxiety and depressive symptoms, intensify as caregivers struggle with their increasing responsibilities [114,120]. Additionally, dependency and financial worries are risk factors for emotional strain, whereas self-efficacy, accessible social support, and knowledge of pain management act as protective factors [99,117,121–123].

Empirical evidence suggests that the quality of the caregiving relationship can significantly influence patient outcomes. Northouse et al. [124] have shown that well-prepared and supported caregivers can improve patient outcomes, while Girgis et al. [119] emphasize the importance of caregivers' physical, psychosocial, relational, and economic support. The emotional impact on caregivers can also be influenced by the closeness of their relationship with the patient, which may either mitigate or exacerbate emotional strain [117]. These adjustments to CP affect not only the QoL of patients but also of caregivers [100], who face numerous physical, psychological, and social challenges. Insights from West et al. [125] highlight the adaptations within family systems to CP, revealing the multifaceted impact on family dynamics, including financial and social losses and the struggles of balancing work with caregiving duties.

Emotional tolls are particularly pronounced among caregivers who often feel unprepared for the caregiving role, resulting in feelings of guilt, fear, and anxiety about future uncertainties associated with CP [100,125]. These burdens manifest as depression, frustration, and grief but also extend to a spectrum of overwhelming emotions, including desperation, fear, denial, and helplessness [126,127]. Additionally, caregivers experience irritability, sadness, and a significant loss of interest in daily activities, all of which further compound their emotional distress [100,127]. These emotional challenges were further exacerbated during crises such as the COVID-19 pandemic, which not only magnified the challenges in pain management but also heightened feelings of hopelessness and isolation among caregivers [128]. A recent systematic review [115] has quantified these emotional strains, revealing significant percentages of caregivers experiencing existential distress, such as hopelessness (18%), fear of death (57%), and loneliness (35%).

Furthermore, FCR remains a pervasive concern among caregivers, similar to that experienced by survivors, and is influenced by factors like younger age, sex/gender (women more at risk than men), and the presence of physical symptoms such as pain and fatigue [129–132]. A qualitative study [133] has identified key themes of FCR among caregivers, including fears of patient suffering and the burden of responsibility they feel for the patient’s well-being. This shared emotional experience between caregivers and patients highlights the intertwined nature of their journey, underscoring the need for targeted interventions to manage FCR in both groups [131,134–137]. Additionally, characteristics such as spiritual uncertainty and limited social resources (social support from friends or family) are linked to increased distress and burden among caregivers, regardless of the patient’s stage of disease [138–140].

Despite the profound impacts, research remains limited in recognizing and addressing the wide range of emotions experienced by caregivers within the context of cancer pain. Particularly, there is a notable deficit in mixed-methods research that quantitatively and qualitatively explores caregivers' emotions within their lived experiences, indicating an urgent need for deeper investigation. Understanding these emotional dynamics is crucial as they significantly influence caregivers' well-being and ability to provide effective care. Recent studies have shown that psychosocial interventions that include caregivers enhance the emotional health of patients and caregivers and improve the overall quality of care [28,141,142]. Thus, caregiving in the context of cancer-related CP is a complex, multifaceted role that demands more comprehensive support from both medical and psychological communities to alleviate its emotional burden and elevate the care standard for patients.

1.2.4 Advancing Cancer Pain Management: Integrating Innovative Technologies and Shared Decision-Making

Technological innovations such as mobile health apps, wearable devices, and telehealth platforms provide essential real-time monitoring and feedback capabilities for managing CP. A systematic review by Zheng et al.[143], which included 13 studies involving a total of 915 patients, demonstrated that mobile applications significantly aid in monitoring and reducing cancer pain, thereby improving self-management skills and enhancing the QoL for cancer patients. The review highlighted that apps with instant messaging modules were particularly effective in reducing pain scores and improving patient satisfaction. Similarly, a systematic review by Gyawali et al. [144] focused on breast cancer patients, including 43 studies with a total of 6,285 patients, found that mobile health applications significantly improve outcomes by reducing pain disability, enhancing pain self-efficacy, and improving overall patient satisfaction. The studies evaluated various eHealth interventions, including mobile apps, online patient portals, and text messaging, highlighting substantial improvements in patient symptoms, lifestyle factors, and satisfaction. Moreover, it has been demonstrated that patients newly diagnosed with breast cancer have different needs than those undergoing active treatment or follow-up. The authors identified five studies focused on newly diagnosed patients, all utilizing online patient portals to provide information and supportive education. These interventions aimed to help patients understand their disease and navigate the medical system, addressing their immediate informational and emotional needs.

Advances in information and communication technology and the widespread availability of portable devices offer a unique opportunity to design supportive interventions for CP management that integrate all stakeholders involved in a patient's care. For example, An de Groef et al. [145] emphasize the importance of patient education in recognizing and managing symptoms, particularly the often-under-addressed psychosocial aspects, in clinical practice. Their work highlights the need for healthcare providers to engage in more comprehensive education and training to better support breast cancer survivors in managing CP after cancer treatment, integrating medical and psychological perspectives to optimize care. Specifically, the eHealth intervention developed includes pain science education and self-management interventions, personalized and delivered through an interactive platform. This platform engages patients actively in their care process, with educational sessions designed to improve understanding of pain, manage pain-related functioning, and ultimately enhance QoL. Personalization is achieved through an automated decision-tree algorithm that tailors the educational content to each patient’s specific treatment history and current needs, significantly improving engagement and adherence to self-managed care plans.

Furthermore, advancements in technology offer considerable benefits not only to patients but also to their family caregivers in managing conditions such as cancer pain. The deployment of the Behavioral and Environmental Sensing and Intervention for Cancer [146] underlines the transformative potential of integrated tech solutions. This system focuses on cancer pain management by employing a package of sensing technologies that collect real-time data on physiological (heart rate and activity level) and environmental (room temperature, light, humidity, barometric pressure, ambient noise) variables. These technologies include smartwatches for active patient and caregiver engagement through ecological momentary assessments and sensor stations for passive environmental monitoring. This comprehensive approach not only aids in pain management but also empowers caregivers by providing them with immediate data on the patient's condition, enabling proactive management and effective communication with healthcare providers. Integrating such technology into daily care routines enhances caregiver capabilities, reduces emotional burden, and improves patient outcomes.

eHealth tools also facilitate the shared decision-making (SDM) process between patients and doctors, mitigating decisional conflicts and improving patient satisfaction, which is central to a more patient-centered approach to healthcare [147–149]. SDM, the essence of patient-centered medicine [147], involves patients and doctors considering the best available evidence when making decisions while supporting patients in exploring options to achieve informed preferences. This approach helps prevent future regret associated with these decisions [150]. Especially in chronic conditions like CP, it includes integrating clinical guidance with patient preferences and values to ensure informed decision-making.

Decision aids are particularly effective in the context of SDM, providing patients with evidence-based information about their condition, available treatment options, and the associated benefits and risks. These tools help patients better understand their medical situation and empower them to make informed decisions that align with their values and family life implications [151]. They play a crucial role in the SDM process, as they not only enhance patient knowledge and reduce decisional conflict but also improve the accuracy of risk perceptions and the alignment of decisions with patient values, leading to more active patient participation in decision-making [151,152]. Furthermore, when implemented through mobile applications, decision aids can significantly enhance patient engagement. They facilitate a deeper understanding of treatment preferences, reduce decisional conflict, and improve adherence to chosen treatments [153,154].

Clinical decision support tools also play a significant role in SDM. Apathy et al. [155] conducted a study on the effectiveness of the OneSheet clinical support system in supporting primary care providers in managing noncancer CP by synthesizing patient information and treatment options. The study involved 69 providers who accessed OneSheet 2,411 times over 16 months, showing significant variability in usage. The tool helped them complete guideline-recommended tasks, review treatments, and monitor patient outcomes, thereby supporting SDM and improving patient outcomes by aligning clinical guidance with patient preferences and values. Similarly, Adam et al. [156] developed the Can-Pain digital intervention specifically aimed at optimizing cancer pain control for patients with advanced cancer. This intervention addresses challenges such as balancing pain levels with opioid intake, managing side effects, and improving communication about pain management with healthcare professionals. Can-Pain includes educational resources, opioid tracking, and patient-reported outcome monitoring, which have been shown to promote shared understanding and support SDM between patients and healthcare providers.

Using innovative technologies and decision aids in managing cancer pain represents a significant advancement in oncology. These tools enhance patient autonomy and improve clinical outcomes by fostering an environment of SDM.

Introduction to Research Studies

This doctoral dissertation delves into the dynamics of CP management in cancer, transitioning from broad inquiries about the impact of pain on QoL from the dual perspectives of patients and caregivers to targeted studies on breast cancer survivors and their informal caregivers. The ultimate goal is to elucidate their emotional and practical needs to inform the development of a digital health ecosystem designed to overcome barriers in pain management.

Throughout this dissertation, the term "caregiver" exclusively refers to informal caregivers—family members, partners, or close friends who provide ongoing physical, emotional, and social support to the patient outside of a clinical setting. Healthcare providers, such as doctors, nurses, and allied health professionals, will be explicitly referred to as "healthcare providers" or "HCPs" and not as caregivers.

Following the introduction, each chapter of the dissertation addresses specific gaps and associated research questions.

Chapter 2, which comprises two distinct studies, delves into the broader impacts and personal experiences of chronic cancer pain.

The first study delves into how CP affects the QoL for both patients and caregivers. The primary research question posed is:

- *How does cancer-related chronic pain affect the patients' and caregivers' quality of life?*

This study sheds light on the systemic failures in current pain management protocols that result in the underreporting and undertreatment of pain. It highlights the often-overlooked issue of how inadequately managed pain can severely impact daily living and overall well-being. Moreover, by focusing on caregivers' experiences, this study addresses a significant gap in the literature where caregivers' QoL and their role in pain management plans are often neglected. By advocating for the inclusion of caregivers' perspectives, this study aims to promote a more holistic approach to pain management that recognizes the critical role of caregivers.

The second study investigates the perceptions, unmet needs, and emotional responses to cancer pain among patients and caregivers. The questions posed in this study are:

- *How do patients and caregivers perceive cancer pain? What are their unmet needs?*
- *What are the main emotions and sentiments experienced by patients and caregivers in relation to cancer pain?*

This research integrates psychological and social dimensions into the assessment models of pain management, thus addressing the exclusion of psycho-social factors from traditional pain management paradigms. The study provides a comprehensive understanding of CP's emotional and psychological impact, acknowledging that pain is not only a physical experience but also profoundly influenced by psychological and social contexts. Additionally, by assessing the unmet needs and perceptions of patients and caregivers, the study further underscores the importance of including caregivers in pain management strategies, recognizing them as essential stakeholders whose insights are crucial for developing effective pain management plans.

Chapter 3 consists of a comprehensive study divided into two interrelated parts. It specifically focuses on breast cancer survivors and their informal caregivers. The questions guiding this study are:

- *What are the unique needs, experiences, and preferences of breast cancer survivors with chronic pain?* (Part A)
- *What are the basic and complex emotions experienced by caregivers supporting breast cancer survivors with chronic pain?* (Part B)

This study addresses the significant gap between underreporting and undertreatment of pain by examining the specific needs and preferences of breast cancer survivors who suffer from CP. It highlights the unique and often complex emotional burdens faced by caregivers, thereby integrating psycho-social factors into the discussion of pain management. This dual focus not only sheds light on the survivors' struggles with pain management but also brings to the forefront the basic and complex emotions experienced by caregivers, which are frequently overlooked in pain management plans. The study promotes a more inclusive approach that considers survivors' and caregivers' perspectives.

Chapter 4 evaluates the usability and impact of the PainRELife Digital Health Ecosystem on breast cancer patients who exhibit pain post-surgery. The questions posed are:

- *What associations are observed between the use of the PainRELife app and changes in pain management practices among breast cancer patients with pain?*
- *How is using the PainRELife ecosystem associated with changes in engagement and decision-making processes among breast cancer patients?*

This study specifically targets the inadequate knowledge and education gap by assessing how a digital health platform can enhance pain management practices among healthcare providers and patients. By examining the associations between the use of the PainRELife app and changes in pain management practices, this study addresses the urgent need for tailored decision-making support in pain management. It evaluates how the ecosystem facilitates personalized pain management plans by incorporating patient-specific data, thereby promoting a more individualized approach to pain management. Additionally, the study investigates how the use of the PainRELife ecosystem influences engagement and decision-making processes among breast cancer patients, aiming to improve the overall management and reporting of pain.

The dissertation adopts a mixed-methods approach to explore the multifaceted experiences of cancer pain comprehensively. The research thoroughly examines cancer pain's broad impacts and personal experiences through narrative reviews, quantitative analyses, and qualitative methodologies. The conclusion integrates all findings, advancing scientific understanding and practical approaches for managing CP in cancer, focusing on enhancing outcomes for breast cancer survivors and their caregivers. By addressing these critical gaps, the dissertation aims to provide actionable insights for oncology pain management and clinical practice, ultimately advocating for a more holistic and inclusive approach to pain management.

Chapter 2

Navigating Cancer Pain: A Dual Perspective

2.1 *Study 1: The Impact of Cancer-Related Chronic Pain on the Patients' and Caregivers' Quality of Life: A Narrative Review*

The following section introduces the first study of my doctoral thesis published in 2022[1], focusing on the impact of cancer-related CP on the patients' and caregivers' QoL. In this chapter, "caregivers" refers exclusively to informal caregivers—such as partners, family members, or close friends—who support cancer patients outside of a clinical setting. This distinction is crucial for understanding the unique challenges these caregivers face and the significant impact of their role on their own QoL.

Focusing solely on personal characteristics proves inadequate for a comprehensive understanding of the cancer-related CP experience and its effects on health status and QoL. Consistent with the biopsychosocial paradigm [27,28], which posits health status as the result of interactions among physical, psychological, and social dimensions, several factors are instrumental in shaping the CP experience and QoL in cancer patients. These include familial context and personal relationships. Predominantly, illness poses a substantial challenge to the patient and their family, transforming the family system and the roles of its members [96,157]. Moreover, the behavioral and emotional responses of family members are intricately linked. As postulated by the STM, the interdependence of partners is crucial in managing stress and adapting to life changes [93,94], particularly in the context of cancer [96]. This interdependence implies that stressors can impact both partners directly or indirectly, with the intrapersonal resources of one partner potentially enhancing (or reducing) those of the other, thus fostering a synergistic effect and facilitating positive (or negative) dyadic coping [94,96,97]. Consequently, patients' and caregivers' perception and management of pain play vital roles in influencing the persistence, exacerbation, or alleviation of the patient's pain experience and QoL [157,158].

Despite the evidence supporting these dynamics, no review has thoroughly examined the literature on cancer-related CP and its multifaceted impact on QoL from the perspectives of patients, caregivers, and the dyadic relationship between them. Existing studies have

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[1] Filipponi C, Masiero M, Pizzoli SFM, Grasso R, Ferrucci R, Pravettoni G. A Comprehensive Analysis of the Cancer Chronic Pain Experience: A Narrative Review. Cancer Manag Res. 2022 Jul 12;14:2173-2184. doi: 10.2147/CMAR.S355653

predominantly focused on how CP alters QoL in patients by assessing general domains such as physical, emotional, functional, social, and family well-being. However, these studies have not delved into specific functional alterations (e.g., self-esteem, beliefs about pain, pain coping strategies) and their repercussions on QoL. Additionally, there is a notable shortage of studies addressing the subdomains of QoL impacted by CP, including anxiety, depression, pain catastrophizing, attachment styles, social support, sexuality, employment status, and return to work. Research into the potential interrelations among these subdomains and their effect on the individuals involved in the caregiving process also remains limited.

2.1.1 Aim of the Study

The study was guided by the following aims:

1. To gather evidence on the impact of cancer-related CP from three distinct perspectives: patients, caregivers, and the combined patient-caregiver perspective.
2. To analyze the impact of cancer-related CP through a comprehensive and multidimensional lens, considering both the general domains and sub-domains of QoL and the interactions among these domains.

The narrative discussion of the data collected was framed by the WHO's definition of QoL [159], which defined it as:

> *"An individual's perception of their position in life, within the context of the culture in which they live and in relation to their goals, expectations, standards, and concerns"* (p.1405).

In conducting this review, a narrative approach was adopted, following the guidelines provided by Demiris et al.[160] without adhering to a strict search strategy protocol. The literature search was carried out until August 2021.

2.1.2 Impact of Chronic Pain on Quality of Life

Patients' Perspective

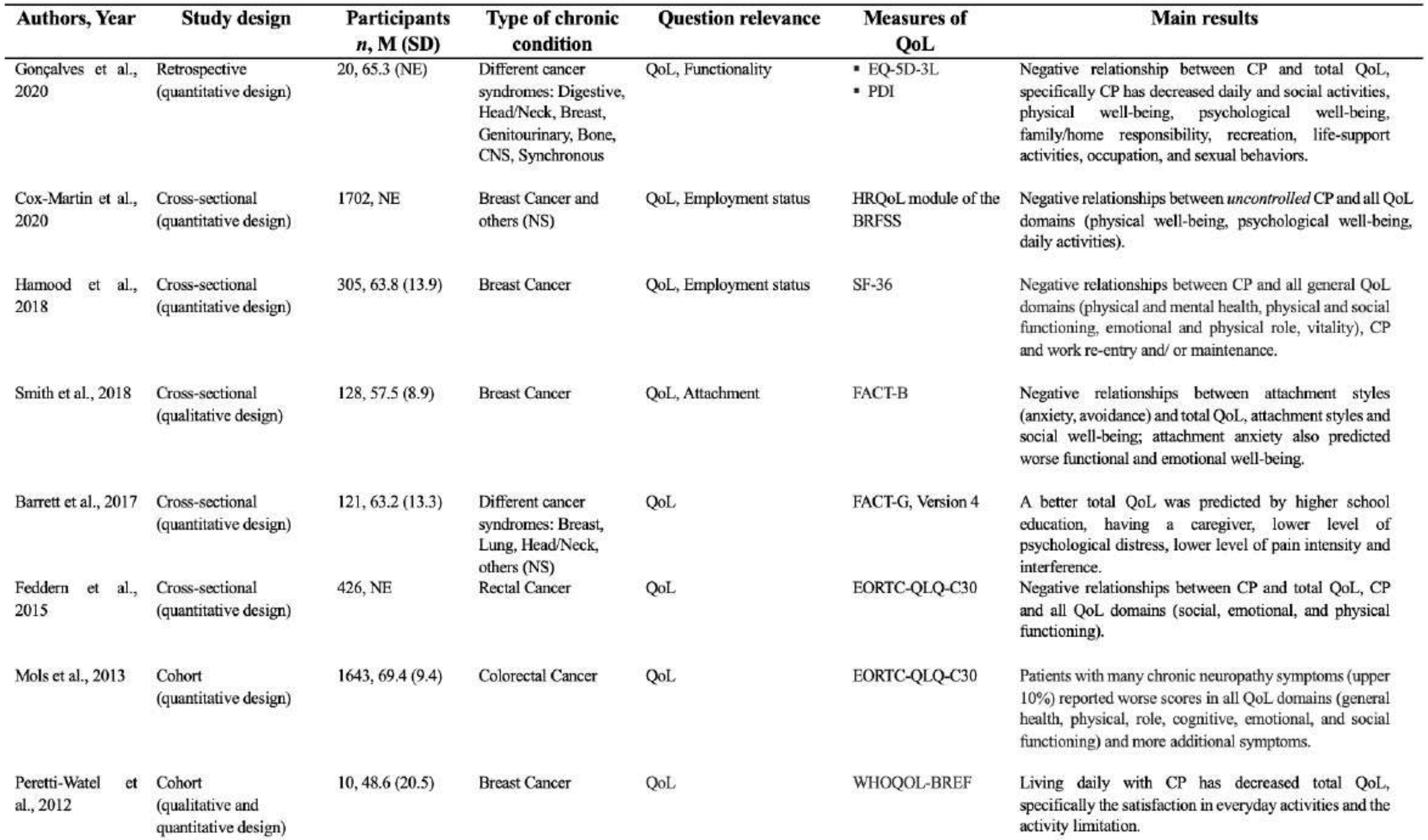
In cancer research, a significant body of literature has explored the CP experience, particularly focusing on its effects on patients' QoL across general domains such as physical, emotional, functional, social, and family well-being [89,90,161–169]. However, a smaller subset of these studies has delved deeper into the influence of CP on specific sub-domains of patients' QoL [90,161–164], along with additional insights from two other studies [170,171].

Overall, research indicates that CP critically impairs QoL across various cancer types during the cancer trajectory [89,90,161–169].

In breast cancer research, there is robust evidence highlighting sex/gender-specific variations in the pain experience. Studies consistently show that women report more frequent pain, increased severity of pain, and higher levels of depression compared to men [89,161,163]. Additionally, research conducted by Caffo and colleagues [167] has further differentiated the impact of pain based on its continuity. Specifically, women enduring continuous pain demonstrated significantly worse outcomes in terms of physical health, psychological well-being, and autonomy than those with intermittent CP. The nature of the pain also plays a critical role in the severity of its impact: widespread pain occurring post-surgery is associated with more severe effects on QoL compared to more localized, regional pain [89].

Similar sex/gender-specific differences in response to cancer-related CP are also evident in rectal cancer patients. Feddern et al. [168] demonstrated that a higher frequency of CP, particularly caused by radiotherapy and chemotherapy, severely affected all dimensions of QoL but expressed differently between sexes/genders. In particular, women patients experienced reduced emotional functionality, increased instances of constipation, and more frequent sleep disruptions than their male counterparts, who experienced lower scores in physical and role functioning along with a higher level of fatigue and dyspnea. Additionally, a distinct impact based on treatment type was observed, as patients undergoing chemotherapy frequently reported neuropathy symptoms—such as trouble hearing, difficulty opening jars or bottles, and trouble walking up stairs or standing—which particularly affected sensory functions like tingling in the toes/feet, numbness, or a burning sensation. These symptoms negatively impacted all QoL domains [169]. See Table 1, adapted from Filipponi et al. [172].

Table 1. A descriptive overview of studies included focused on patients' perspectives



Authors, Year	Study design	Participants *n*, M (SD)	Type of chronic condition	Question relevance	Measures of QoL	Main results
Gonçalves et al., 2020	Retrospective (quantitative design)	20, 65.3 (NE)	Different cancer syndromes: Digestive, Head/Neck, Breast, Genitourinary, Bone, CNS, Synchronous	QoL, Functionality	▪ EQ-5D-3L ▪ PDI	Negative relationship between CP and total QoL, specifically CP has decreased daily and social activities, physical well-being, psychological well-being, family/home responsibility, recreation, life-support activities, occupation, and sexual behaviors.
Cox-Martin et al., 2020	Cross-sectional (quantitative design)	1702, NE	Breast Cancer and others (NS)	QoL, Employment status	HRQoL module of the BRFSS	Negative relationships between *uncontrolled* CP and all QoL domains (physical well-being, psychological well-being, daily activities).
Hamood et al., 2018	Cross-sectional (quantitative design)	305, 63.8 (13.9)	Breast Cancer	QoL, Employment status	SF-36	Negative relationships between CP and all general QoL domains (physical and mental health, physical and social functioning, emotional and physical role, vitality), CP and work re-entry and/ or maintenance.
Smith et al., 2018	Cross-sectional (qualitative design)	128, 57.5 (8.9)	Breast Cancer	QoL, Attachment	FACT-B	Negative relationships between attachment styles (anxiety, avoidance) and total QoL, attachment styles and social well-being; attachment anxiety also predicted worse functional and emotional well-being.
Barrett et al., 2017	Cross-sectional (quantitative design)	121, 63.2 (13.3)	Different cancer syndromes: Breast, Lung, Head/Neck, others (NS)	QoL	FACT-G, Version 4	A better total QoL was predicted by higher school education, having a caregiver, lower level of psychological distress, lower level of pain intensity and interference.
Feddern et al., 2015	Cross-sectional (quantitative design)	426, NE	Rectal Cancer	QoL	EORTC-QLQ-C30	Negative relationships between CP and total QoL, CP and all QoL domains (social, emotional, and physical functioning).
Mols et al., 2013	Cohort (quantitative design)	1643, 69.4 (9.4)	Colorectal Cancer	QoL	EORTC-QLQ-C30	Patients with many chronic neuropathy symptoms (upper 10%) reported worse scores in all QoL domains (general health, physical, role, cognitive, emotional, and social functioning) and more additional symptoms.
Peretti-Watel et al., 2012	Cohort (qualitative and quantitative design)	10, 48.6 (20.5)	Breast Cancer	QoL	WHOQOL-BREF	Living daily with CP has decreased total QoL, specifically the satisfaction in everyday activities and the activity limitation.

Pühse et al., 2012	Cohort (quantitative design)	238, 35.2 (9.3)	Testis Cancer	Sexuality	▪ BSFI ▪ IIEF-5	Negative correlation between chronic testicular pain and sexual dysfunctions.
Green et al., 2011	Cross-sectional (quantitative design)	40 (current CP) 80 (CP since diagnosis), NE	Different cancer syndromes: Breast Prostate, Colorectal, Lung, Others (NS), Multiple Myeloma	QoL, Depression, Functionality	▪ EORTC-QLQ-C30 ▪ PDI ▪ CES-D	*Current* CP has decreased several domains of QoL (general health, physical, social, and role functioning); while additional symptoms and financial difficulties were increased. CP *since diagnosis* has decreased all QoL domains (general health, physical, role, emotional, cognitive, and social functioning; while depression, additional symptoms, and financial difficulties were increased.
Burckhardt et al., 2005	Cross-sectional (quantitative design)	23, 56.8 (5.5) patients with regional pain 58.7 (8.6) patients with widespread pain	Breast Cancer	QoL	▪ FACT-B ▪ SF-36	Poorer scores on all QoL domains (physical, emotional, functional well-being, additional concerns) in patients with *widespread* CP compared to patients with *regional* one.
Caffo et al., 2003	Retrospective (quantitative design)	210, NE	Breast Cancer	QoL	QoLQ	Poorer scores on all QoL domains (physical, social, and psychological well-being, physical autonomy).
Monga et al., 1998	Cross-sectional (quantitative design)	70, 49.9 (NE)	Different types of chronic illness: Cancer, Arthritis, Neuralgia, Headache, Diabetic Neuropathy	Sexuality, Depression	▪ DISF ▪ CES-D ▪ HSCL-21	Negative correlations between CP and sexual functioning (drive, arousal, behaviour, orgasm), except for fantasy. More sexual problems were experienced in patients with depression, distress, and those who adopted passive coping strategies than patients with active ones.

Notes: [†]with chronic pain.

Abbreviations: NE, not estimable; NS, not specified; CP, Chronic Pain; CNS, Central Nervous System; QoL, Quality of Life; RT, Radiotherapy; ChT, Chemotherapy; QoLQ, Quality of Life Questionnaire; FACT-B, Functional Assessment of Cancer Therapy-Breast; FACT-G, Functional Assessment of Cancer Therapy-General; WHOQOL-BREF, World Health Organization Quality of Life; EQ-5D-3L, European Quality of Life Five Dimensions Questionnaire; PDI, Pain Disability Index; EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer – 30-item Quality of Life Questionnaire; IIEF-5, International Index of Erectile Function; BSFI, Brief Sexual Functioning Inventory; DISF, Derogatis Inventory of Sexual Functioning; CES-D, Center for Epidemiological Studies Depression Scale; HSCL-21, Hopkins Symptom Checklist.

Sub-Domains of Quality of Life

A subset of studies [90,161–164,170,171] has delved into specific sub-domains of QoL that are critically influenced by patients' experiences of CP. These investigations have highlighted the significant effects of CP on various aspects, including sexuality, employment, return to work, and psycho-emotional (e.g., anxiety, depression, pain catastrophizing, attachment styles) and social factors (e.g., social support). For instance, Gonçalves et al. [162]observed that long-term cancer survivors suffering from CP not only experienced a deterioration in their overall QoL but also faced declines in several specific functionalities such as family and home responsibilities, recreational activities, support initiatives, employment conditions, personal care practices, community engagements, and sexual conduct. The authors noted that the adverse impacts of CP might exceed those caused by the cancer diagnosis itself. Furthermore, it was found that only thirty-eight (45%) out of 85 patients received adequate long-term pain management and surveillance.

Sexuality. CP significantly impacts intimacy and sexual functionality within romantic relationships, particularly affecting the sexuality of the ill partner. Research by Pühse et al. [171] indicates that patients with testicular cancer suffer from decreased sexual desire, erectile dysfunction, and ejaculation disorders, adversely affecting intimacy with their partners.

Similarly, Monga et al. [170] report that CP compromises various aspects of sexuality in different types of illness, including cancer, encompassing arousal, behaviors, orgasm, and satisfaction in relationships, with the exclusion of sexual fantasies. Furthermore, the research demonstrated a distinct negative association between sexual performance and psychological factors. Higher levels of depression, distress, and pain catastrophizing were all associated with lower scores in sexual behaviors, orgasm intensity, and libido. In particular, higher levels of depression and distress negatively impacted sexual behaviors and libido, while pain catastrophizing also reduced orgasm intensity. Conversely, the authors identified certain psychological factors as strongly correlated with enhanced sexual functioning, acting as protective factors. These encompass a positive evaluation of control over pain and life, self-directed coping declarations, an internal locus of control, and active participation in domestic duties and outdoor pursuits, all connected to enhanced sexual fantasies, arousal, behaviors, and libido. Conversely, passive coping methods and overattentive reactions were pinpointed as risk factors, exhibiting a negative association with sexual fantasies, the intensity of orgasms, and libido.

Psycho-emotional and social factors. Psychological and social factors are crucial sub-domains of QoL that significantly influence the experience of CP. Smith et al. [164]

identified that attachment styles and pain catastrophizing play a pivotal role in moderating the CP experience. Specifically, they found that breast cancer patients undergoing treatment were more prone to display higher levels of anxious attachment and catastrophizing thoughts. Conversely, women with avoidant attachment styles were less likely to report pain, a phenomenon possibly linked to their tendency to restrict the expression of negative emotions. Such attachment styles were found to negatively affect overall QoL, especially the social dimension. Moreover, a negative correlation was found between attachment avoidance and the perceived effectiveness of pain management, with avoidant individuals reporting poorer pain control, after adjusting for age and pain catastrophizing.

Further exploring the impact of CP, Green et al. [161] noted that patients enduring CP, from the time of diagnosis to the present, tended to exhibit more severe depressive symptoms, diminished general functioning, financial hardships, and a range of physical symptoms, including fatigue, discomfort, sleep disturbances, and altered appetite, spanning various cancer types.

Conversely, Barrett et al. [165] underscored several protective factors that contribute to preserving a better QoL. Specifically, they categorized these factors into three main groups:

1. Pain-Related Factors: Lower intensity and frequency of pain.
2. Personal Characteristics: Higher level of education and lower levels of current psychological distress.
3. Social Context: Receiving support from a caregiver and having good social and relational well-being.

Employment and/or returning to work. The experience of CP has been shown to temporarily affect employment status and the ability to return to work. For instance, Cox-Martin et al. [163] demonstrated that uncontrolled CP, particularly in women, reduced the likelihood of remaining employed due to the interference of neuropathy or lymphedema with job performance. These findings are consistent with those of a previous study [90], where CP was identified as an independent predictor of a downgrade in work status. Specifically, women who were previously working full-time were often downgraded to part-time positions, while those who were part-time were more likely to quit, retire, or lose their jobs after treatment.

Caregivers' Perspective

CP significantly impacts not just the QoL of patients but also those of their caregivers. Caregivers of cancer patients frequently face stress adjustment challenges that can manifest as physical, psychological, and social health impairments, as well as disruptions in family dynamics [122]. However, most studies [99,125,173] have focused on general QoL domains without addressing specific areas, such as the relationship between patients and caregivers, or considering the synergistic interrelations between all domains and sub-domains of QoL involved.

A limited number of studies have explored the main themes and sub-themes related to caregivers' QoL and the protective factors that can mitigate the impact of CP. These investigations highlight how CP significantly compromises caregivers' QoL across multiple domains. For instance, Ferrell et al. [173] observed that cancer-related CP adversely affects caregivers’ social well-being—evidenced by increased distress from chronic illness, reduced participation in household activities, greater financial burden, lower perceived support, and more employment interference. Psychologically, caregivers reported greater difficulties in managing chronic illness, along with heightened anxiety, depression, challenges in finding happiness, feeling in control, satisfied, concentrated, and useful. From a spiritual perspective, caregivers faced increased uncertainty, decreased involvement in personal spiritual practices, changes in their spiritual lives, fewer positive transformations, reduced hope, lower participation in communal religious events, and a diminished sense of purpose. Physically, caregivers faced more issues with sleep, fatigue, appetite, and pain. See Table 2, adapted from Filipponi et al. [172].

Table 2. A descriptive overview of studies included focused on caregivers' perspectives

Authors, Year	Study design	Participants[†] *n*, M (SD)	Type of chronic condition	Question relevance	Measures of QoL	Main results
Kizza & Muliira, 2020	Cross-sectional (quantitative design)	284, 36 (13.8)	Cancer (NS)	Family	CQoL-I-C	The key determinants of better overall caregivers' QoL were their knowledge and self-efficacy for cancer pain management. Burden, disruptiveness, and support were the most afflicted areas damaged of caregivers' QoL; conversely, positive adaptation and lower financial concerns enhanced their QoL.
West et al., 2012	Cross-sectional (qualitative design)	9, NE	NS	Family	Interviews	The impact of CP is extended on the entire family, resulting in physical, social, and emotional changes. Four themes were captured: family losses; life changes; emotional impact; future plans' concerns.
Ferrell et al., 1999	Quasi-experimental (quantitative design)	231, 21-86	Different cancer syndromes: Lung, Others (NS), Breast, Prostate, Pancreatic, Colorectal, Myeloma, Liver, Bladder, Ovarian, Renal, Melanoma, Uterine/Cervical, Oesophageal	Family	QoLFT	The impact of CP is extended on the entire family, resulting in poorer scores on all caregivers' QoL domains (social, psychological, spiritual, and physical well-being).

Notes: [†]with chronic pain.

Abbreviations: NE, not estimable; NS, not specified; CP, Chronic Pain; QoL, Quality of Life; QoLFT, Quality of Life Family Tool; CQoL-I-C, Caregiver Quality of Life-Index-Cancer.

Sub-Domains of Quality of Life

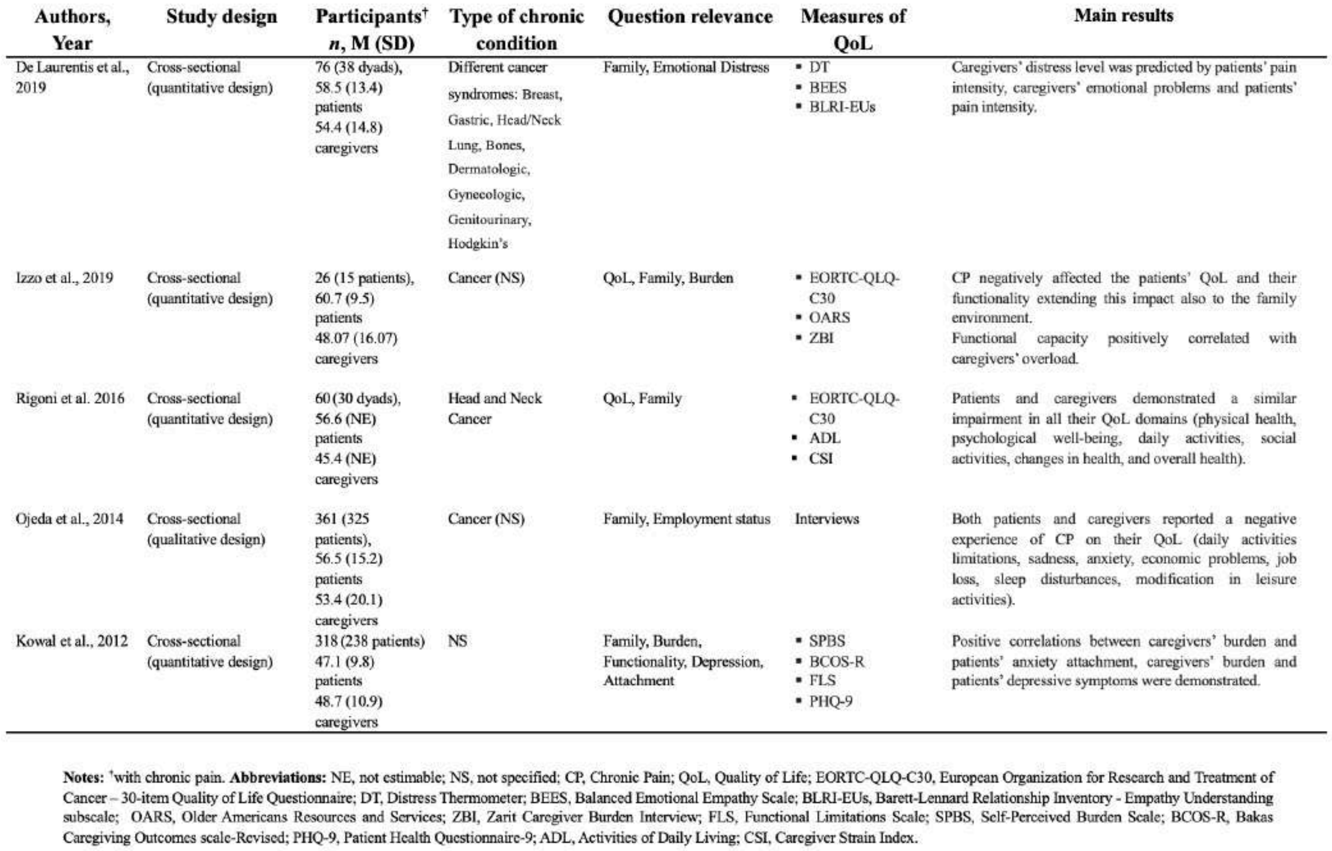
West et al. [125] conducted interviews with 9 caregivers, primarily romantic partners, of individuals living daily with CP, identifying four main themes reflecting changes within the family: family losses, life changes, emotional impacts, and concerns about future plans. The theme of family losses highlighted the financial and social consequences, ranging from minor inconveniences to significant, life-altering disruptions. Families reported reduced interactions with other family members and friends and diminished participation in social activities, often leading to social isolation due to fewer invitations to events like birthdays and dinners. The life changes’ theme encompassed substantial shifts in family roles, relationships, and career prospects, necessitating a readaptation within the family unit. Notable were role reversals, decreased work capacity, and altered care responsibilities, including those affecting emotional and sexual relationships. The emotional impacts’ theme captured feelings of self-blame, anger, and fear among caregivers, who often hide negative emotions related to their partner's pain. These caregivers frequently attributed these emotional strains to the pain itself, and they expressed feelings of guilt when overwhelmed or desiring a break from caregiving responsibilities. Last but not least, concerns about future plans’ theme involved anxiety over the ill partner's health outcomes, future life planning, and the caregiver’s capacity to manage ongoing pain challenges.

Despite these difficulties, certain protective factors can mitigate the adverse effects of CP on caregivers' QoL. Kizza et al. [99] found that positive adaptation and reduced financial worries significantly enhanced caregivers' QoL. Furthermore, a deeper understanding of pain management and increased self-efficacy in managing cancer pain were crucial for improving caregivers’ well-being. Conversely, the absence of these protective factors typically resulted in a poorer QoL for caregivers, characterized by increased burdens (impacting physical well-being and influenced by the patient’s level of pain and the caregiver’s self-efficacy in managing it), disruptiveness (affecting physical well-being), and a perceived lack of social support (linked to the hours spent providing care each week).

A Systemic and Integrated Perspective

While CP and its management are clearly concerns involving the entire family [132], shaped by an intricate interplay of biopsychosocial factors [27,28], research examining the perspectives of patients and their caregivers is still in its infancy. The existing literature suggests that CP negatively impacts patients' and caregivers' general QoL domains. However, most studies have focused on the impact of CP on patients' and caregivers' QoL separately, neglecting to address the reciprocal influences between their experiences adequately. Furthermore, only a limited number of studies have explored specific aspects of QoL worsening, such as daily activities, lifestyle changes, burden, and emotional distress [123,174], and even fewer have investigated the bidirectional impact between patients' and caregivers' QoL [100,127,175]. See Table 3, adapted from Filipponi et al. [172].

Table 3. A descriptive overview of studies included focused on the patient-caregiver perspective



Authors, Year	Study design	Participants† n, M (SD)	Type of chronic condition	Question relevance	Measures of QoL	Main results
De Laurentis et al., 2019	Cross-sectional (quantitative design)	76 (38 dyads), 58.5 (13.4) patients 54.4 (14.8) caregivers	Different cancer syndromes: Breast, Gastric, Head/Neck Lung, Bones, Dermatologic, Gynecologic, Genitourinary, Hodgkin's	Family, Emotional Distress	▪ DT ▪ BEES ▪ BLRI-EUs	Caregivers' distress level was predicted by patients' pain intensity, caregivers' emotional problems and patients' pain intensity.
Izzo et al., 2019	Cross-sectional (quantitative design)	26 (15 patients), 60.7 (9.5) patients 48.07 (16.07) caregivers	Cancer (NS)	QoL, Family, Burden	▪ EORTC-QLQ-C30 ▪ OARS ▪ ZBI	CP negatively affected the patients' QoL and their functionality extending this impact also to the family environment. Functional capacity positively correlated with caregivers' overload.
Rigoni et al. 2016	Cross-sectional (quantitative design)	60 (30 dyads), 56.6 (NE) patients 45.4 (NE) caregivers	Head and Neck Cancer	QoL, Family	▪ EORTC-QLQ-C30 ▪ ADL ▪ CSI	Patients and caregivers demonstrated a similar impairment in all their QoL domains (physical health, psychological well-being, daily activities, social activities, changes in health, and overall health).
Ojeda et al., 2014	Cross-sectional (qualitative design)	361 (325 patients), 56.5 (15.2) patients 53.4 (20.1) caregivers	Cancer (NS)	Family, Employment status	Interviews	Both patients and caregivers reported a negative experience of CP on their QoL (daily activities limitations, sadness, anxiety, economic problems, job loss, sleep disturbances, modification in leisure activities).
Kowal et al., 2012	Cross-sectional (quantitative design)	318 (238 patients) 47.1 (9.8) patients 48.7 (10.9) caregivers	NS	Family, Burden, Functionality, Depression, Attachment	▪ SPBS ▪ BCOS-R ▪ FLS ▪ PHQ-9	Positive correlations between caregivers' burden and patients' anxiety attachment, caregivers' burden and patients' depressive symptoms were demonstrated.

Notes: †with chronic pain. **Abbreviations:** NE, not estimable; NS, not specified; CP, Chronic Pain; QoL, Quality of Life; EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer – 30-item Quality of Life Questionnaire; DT, Distress Thermometer; BEES, Balanced Emotional Empathy Scale; BLRI-EUs, Barett-Lennard Relationship Inventory - Empathy Understanding subscale; OARS, Older Americans Resources and Services; ZBI, Zarit Caregiver Burden Interview; FLS, Functional Limitations Scale; SPBS, Self-Perceived Burden Scale; BCOS-R, Bakas Caregiving Outcomes scale-Revised; PHQ-9, Patient Health Questionnaire-9; ADL, Activities of Daily Living; CSI, Caregiver Strain Index.

Sub-Domains of Quality of Life

The primary sub-dimensions of QoL, including daily activities, lifestyle changes, burden, and emotional distress, are critically impacted by CP and can be grouped into the social and psychological domains of QoL. For example, research by Izzo et al. [123] indicates that male cancer patients with CP exhibit significantly less independence from their caregivers than their female counterparts, especially in carrying out instrumental tasks like housekeeping and shopping, as well as in performing essential personal activities such as eating and maintaining hygiene. This increased dependency intensifies the caregiving burden, potentially leading to a decrease in caregivers' ability to manage their own daily tasks.

Moreover, the lifestyle adjustments required when living with a chronically ill partner detrimentally affect caregivers' QoL and significantly heighten their stress levels. Rigoni et al. [174] emphasize that this stress is primarily linked to caregivers' feelings of incapacity, disruptions to personal plans, and sleep disturbances, which underscore the pervasive impact of CP on both the psychological and social aspects of caregivers' lives.

A Co-Dependence Effect Behind Patients' and Caregivers' Quality of Life

The studies reviewed often do not consider the family or the dyad as the unit of analysis despite evidence showing that illness deeply transforms family dynamics and affects all members involved [96,157]. This neglect is significant considering the documented *co-dependence* in the pain experience and associated QoL between patients and caregivers, evident in both physical and psychological dimensions. For instance, De Laurentis et al. [100] found a positive correlation between the intensity of patients' pain experiences and their caregivers' emotional distress. They noted that caregivers with higher emotional distress tended to be associated with patients experiencing more intense pain across four subcategories: sensory, affective, evaluative, and miscellaneous. Additionally, caregivers' emotional distress was influenced by their personal and social challenges, with increased depression symptoms, fear, irritability, sadness, and disinterest in daily activities correlating with a higher level of burden.

Schultz et al. [176] and Kowal et al. [175] highlighted the significant role of patients' perceived pain in contributing to caregivers' emotional burden. Specifically, patients who viewed themselves as a burden were more likely to exhibit insecurity, dependency, and increased anxiety and depressive symptoms, which, in turn, exacerbated caregivers' distress. However, the perception of pain's impact may differ between patients and caregivers. Ojeda et al. [127] reported that patients often feel sadness and anxiety due to restrictions in daily activities and job performance caused by pain, but they perceive only a moderate impact on their family and leisure activities. In contrast, caregivers perceive the pain experienced by their loved ones as having a more profound effect on the family system, particularly noting sleep disturbances and changes in leisure activities as significant consequences. This discrepancy suggests that the perception of pain and its impact on family dynamics can influence, and be influenced by, the broader context in which CP is experienced.

2.1.3 Discussion

The present narrative review has qualitatively integrated assessments of how cancer-related CP influences QoL, utilizing a comprehensive, tripartite framework encompassing the perspectives of patients, caregivers, and their interactions. This broader perspective aims to enrich our understanding of the cancer pain landscape. While the contributions of healthcare professionals to pain management are clearly defined [177,178], the role of the family as a vital care component remains underexplored; this review seeks to address this gap in the literature.

The gathered data consistently reveal that CP profoundly compromises QoL across all dimensions for both patients and caregivers, including physical, emotional, functional, social, and familial aspects.

Further analysis highlights two primary theoretical and methodological challenges. Initially, the literature underscores the necessity of a bidirectional approach (patient–caregiver) for a deeper comprehension of the pain experience along the disease continuum and its repercussions on QoL. The way CP is managed within the family context can significantly alter the patient's perception of pain and reciprocally affect the caregiver's emotional state. For instance, the involvement of a supportive and engaging partner serving as the primary caregiver has been shown to decrease pain perception and emotional distress in patients with chronic lymphocytic leukemia [179], metastatic [180], and non-metastatic breast cancer [181]. Additionally, caregiving responsibilities can lead to significant physical, emotional, and social strain on caregivers, significantly diminishing their QoL and potentially intensifying the patient's experience of pain. Typically, caregivers' emotional distress escalates as their dependent partner's autonomy and functionality decline [157]. This interdependency is critical for understanding the mutual influence of pain experiences and QoL outcomes, suggesting a *co-dependence effect* between the partners. Moreover, social and relational factors are pivotal in managing adversity and fostering positive psycho-emotional well-being [96,182,183]. This aligns with the STM [93,94], which elucidates how romantic partners' emotional and behavioral responses are intricately linked and influence each other in stress and CP management. The outcomes of family dynamics rely on the individual characteristics of each member, thus necessitating dyadic or family-based analysis to explore these reciprocal influences [183–187].

Secondly, the biopsychosocial model [27,28] proposes that illness results from complex physical, psychological, and social interactions. Therefore, understanding the intertwined influences among these domains is essential. Specifically, disruptions in one domain can influence others, modulating the overall experience of CP and its related aspects within the familial context. However, existing studies often fail to examine the interconnectedness between these dimensions, highlighting the necessity for a comprehensive and multifaceted approach to investigating cancer-related CP and its effects on the QoL for both patients and their caregivers [57,188]. Such an approach could enhance cancer pain management and inform decision-making regarding care strategies.

In conclusion, relational factors are crucial in navigating adversity and promoting health and well-being among cancer patients with CP. These dynamics can shape pain experiences and provide support through treatment phases, survivorship, and care decisions. Thus, it is vital that both clinical and psychological interventions addressing cancer-related CP consider the patient and their significant others (e.g., romantic partners) [189–191]. A stable, supportive relationship is immensely advantageous as it facilitates better coping mechanisms, fosters adaptation, and improves QoL [117,121,122,182]. Hence, enhancing awareness and knowledge about the physical and psychosocial factors involved in cancer pain and its impact on both patients' and caregivers' QoL is crucial for guiding healthcare professionals toward more effective cancer pain management. The findings from a recent study underscore the significant role that caregivers' understanding of pain and patients' self-perceived performance status play in the congruence of pain experiences. This congruence is essential for accurate pain assessment and effective management, directly affecting QoL [192]. Therefore, educational interventions to improve patients' and caregivers' pain knowledge and communication about pain experiences between patients and caregivers are recommended to enhance the effectiveness of cancer pain management strategies.

2.2 Study 2: Exploring Cancer Pain Representations: A Mixed-Methods Social Media Analysis from Patient and Caregiver Perspectives

The following section introduces the second study of my doctoral thesis, published in 2023[2], which focuses on analyzing representations of cancer pain from patients and informal caregivers using social media data in a mixed-methods approach.

Previously, we discussed how cancer-related CP significantly impacts patients' QoL and reverberates within the family dynamic. Building upon existing research, this study incorporates the biopsychosocial paradigm [27,28] and the STM [93,94], as its core frameworks. These frameworks view illness as a multidimensional “we disease” [101], highlighting the complex interactions among biological, psychological, and social health dimensions. Notably, within a relational context, the stress of cancer pain affects both patients and caregivers, engendering a cycle of mutual dependence and emotional strain [172,175].

Despite advancements in pain management, significant gaps remain in the reporting and treatment of cancer pain, often leaving it undertreated [3,4] and highlighting a critical unmet need in psycho-oncology [193]. One significant obstacle is the difficulty patients face in communicating their pain, stemming from insufficient knowledge and misconceptions about pain management – for example, concerns about expressing pain, prioritizing cancer treatment over pain relief, or the belief that pain is inevitable [51,53]. Caregivers face similar challenges and need appropriate education to effectively manage their responsibilities and emotional burdens [194,195]. A study by Ma et al. [192] reinforces this point, demonstrating that caregivers' knowledge about pain significantly influences the congruence of cancer pain experiences between patients and caregivers. When caregivers are well-educated about cancer pain, their perceptions align more closely with the patients, leading to more effective pain management.

Research consistently shows that both patients and caregivers experience substantial emotional distress in the context of cancer-related pain. Studies have highlighted the association between pain and psycho-emotional distress in cancer patients, including symptoms like depression, anxiety, worry, and fear [38,44]. Although the focus has been primarily on anxiety and depression [38,196,197], other specific negative emotions triggered by pain include frustration, exhaustion, anger, helplessness, fear of further suffering, and

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[2] Filipponi C, Chichua M, Masiero M, Mazzoni D, Pravettoni G. Cancer Pain Experience Through the Lens of Patients and Caregivers: Mixed Methods Social Media Study. JMIR Cancer. 2023 Jul 3;9:e41594. doi: 10.2196/41594.

hopelessness [198]. Despite this, it remains challenging for patients to articulate their feelings, leading to some emotions (e.g., fear, panic, helplessness) being overshadowed by others (e.g., anger) [199]. In fact, anger may be directed at the cancer itself, at caregivers, or even at God, particularly if the patient holds religious beliefs [7,199].

Regarding caregivers, several studies [125,126,173,200] have examined their emotional responses in the context of cancer-related pain, most of which are dated, with only two recent studies [100,127]. Being close to someone in pain can lead to empathetic responses, increasing susceptibility to psychological symptoms such as distress, fatigue, pain [175], anxiety and depression [173,200]. The emotional weight and assumed caregiving responsibilities can impair caregivers' ability to support their loved ones effectively [7,18,19], promoting feelings of incapacity [174] and often leading to heightened feelings of guilt, blame, anger, fear about the future [125] and/or FCR [129–131]. They may also experience a spectrum of overwhelming emotions such as desperation, fear, denial, grief, burden, and helplessness [126,127], along with depression, irritability, sadness, worry, and a loss of interest in daily activities [100,127].

In a recent systematic review, Wang et al. [201] noted that qualitative data provide invaluable insights into the unmet needs of patients and caregivers related to a disease experience, such as cancer pain. Online social platforms denote a source for qualitative data by giving users a forum to discuss their personal experiences and get guidance and support from others. It has been shown that these platforms foster a sense of community that makes users—caregivers and patients—feel less alone and more understood while providing them with the information they require [202,203]. Using such data, this study offers a window into the cancer pain representations, including the complex emotional experiences of patients and caregivers, which are sometimes difficult to convey through traditional medical consultation [204].

2.2.1 Aim of the Study

This study aimed to capture the whole representation of cancer pain from the perspective of patients and caregivers. We were interested in the perceptions of these two groups separately since patients experience the pain directly while caregivers respond to it.

Specifically, the primary aim was to identify the unmet needs of cancer patients and caregivers regarding cancer pain management. Second, by examining the textual patterns of patients and caregivers, this study aimed to identify the emotional and sentimental responses to cancer pain. Comparisons were conducted to detect the variations in responses to cancer pain experiences between these two groups.

2.2.2 Material and Methods

Data collection

Data collection occurred in November 2021, guided by the Pushshift Reddit API Documentation [205]. We focused on comments within the Reddit cancer patient support group, which claimed 45,900 subscribers [206]. Specific keywords associated with cancer pain classifications [11,207] were used to extract the data, including temporal patterns ("acute*pain", "chronic*pain"), pathophysiological types ("somatic*pain", "visceral*pain", "neuropathic*pain", and "nociceptive*pain"), and descriptors characteristic of neuropathic pain (terms like "pain*sensation", "burning*sensation", "numbness", "soreness", "tingling", "shooting", "pricking", and "pins/or needles"). Additionally, commonly used terms by users describing pain such as "pain", "hurting", "aching", and "discomfort" were manually included. CP and MC independently screened all collected posts, discarding duplicates and filtering out posts not pertinent to cancer pain.

For each relevant post, we documented the creation date, the number of comments, and the poster's username. The posting years were identified to translate epochs into human-readable formats. Our analysis excluded any mentions of names or people to maintain user anonymity. Since the data gathering and analysis included publicly accessible web resources, no request for ethical committee permission was made.

Statistical analysis

Descriptive Statistics and Word Frequency

This study employed a manual categorization method, where posts were read and classified into established categories. The two reviewers (authors CF and MC) initially formed these categories from a sample of 100 posts, randomly selected using Google's random generator. The reviewers utilized initial coding frameworks to categorize all the posts (n=783). Where these initial codes did not align with the post content, new codes were incorporated into the broader categories following mutual consensus between the reviewers. Any discrepancies in coding were resolved through discussion, culminating in the creation of the final coding list. Both reviewers were involved in coding all the posts.

Quantitative data analyses were conducted using RStudio version 2022.02.3 [208]. The interrater reliability was evaluated by calculating the Cohen kappa coefficient. This scale interprets values as follows: less than 0 signifies no agreement, 0.01 to 0.20 denotes slight agreement, 0.21 to 0.40 suggests fair agreement, 0.41 to 0.60 reflects moderate agreement, 0.61 to 0.80 corresponds to substantial agreement, and 0.81 to 1.00 indicates almost perfect agreement [209].

Text mining was utilized to preprocess the data and analyze the differences in descriptions of cancer pain between patients and caregivers. A word cloud, which identifies the most frequently used words in a text, was created using the “tm” [210] and “word cloud” [211] packages in R.

Emotion and Sentiment Analysis

Emotion and sentiment analysis on the posts from patients and caregivers was conducted using the "syuzhet" package in R [212]. This analysis considered eight basic emotions (anger, fear, anticipation, trust, surprise, sadness, joy, and disgust) and two sentiments (positive and negative), as defined by the NRC Emotion Lexicon [213,214]. The lexicon assigns each word an emotional and sentiment association, marked as 0 (no association) or 1 (association present). Words can be linked to multiple emotions and exhibit a positive, negative, or neutral polarity. Typically, negative words are associated with emotions such as anger, fear, disgust, and sadness, while positive words often relate to anticipation, joy, and trust. The emotion of surprise can be associated with either positive or negative sentiments, depending on the context of the target words.

To evaluate the distribution of our data, we implemented several steps using R software. Initially, relevant posts were selected, and the text was “unnested” to segment it into individual sentence units, resulting in 5577 sentences from patients and 2052 from caregivers. Each sentence was then analyzed as an independent data point within R. Subsequently, we conducted emotion and sentiment analysis on these sentences utilizing the “get_nrc_sentiment” function. This produced a dataset where rows represented individual sentences and columns corresponded to various emotions. An association between a sentence and a specific emotion was determined whenever one or more words corresponded to that emotion, assigning a numerical value to each sentence to represent its emotional intensity. The structured dataset was then analyzed to determine if the distribution of emotions across sentences conformed to a normal distribution. We applied the Shapiro test, a statistical tool designed to check for normal distribution conformity. The results indicated that the P value from the Shapiro test was below the set significance level of .05, leading us to conclude that the emotion distribution among the sentences did not fit a normal distribution. Given that the data did not display a normal distribution, we opted to conduct the Wilcoxon rank sum test, a nonparametric alternative suitable for data that do not meet the normality assumption. This test is also effective when dealing with unequal sample sizes [215].

Hierarchical Clustering

Hierarchical clustering was conducted on comments from caregivers and patients using the “dendexten” R package [216]. Based on the k-means algorithm, this method organizes data into clusters without a preset number of groups and visualizes them through a dendrogram, a tree-like data representation. We employed the Agglomerative Nesting (AGNES) method, an agglomerative clustering technique that starts by treating each data point as an individual cluster and then progressively merges clusters based on a similarity metric until it meets a specific criterion, like a desired number of clusters.

Additionally, we calculated the agglomerative coefficient, which assesses the extent of the clustering structure found, where a value closer to 1 indicates a strong structure. The Ward method optimized the dendrogram by minimizing the total within-cluster variance.

To compare dendrograms, we used the "tanglegram" function, which aligns two dendrograms side by side and connects their labels with lines. The quality of this alignment was assessed using the "entanglement" function, aiming for a lower entanglement coefficient, which indicates minimal overlap and clearer differentiation between clusters (range: 1 [complete entanglement] to 0 [no entanglement]).

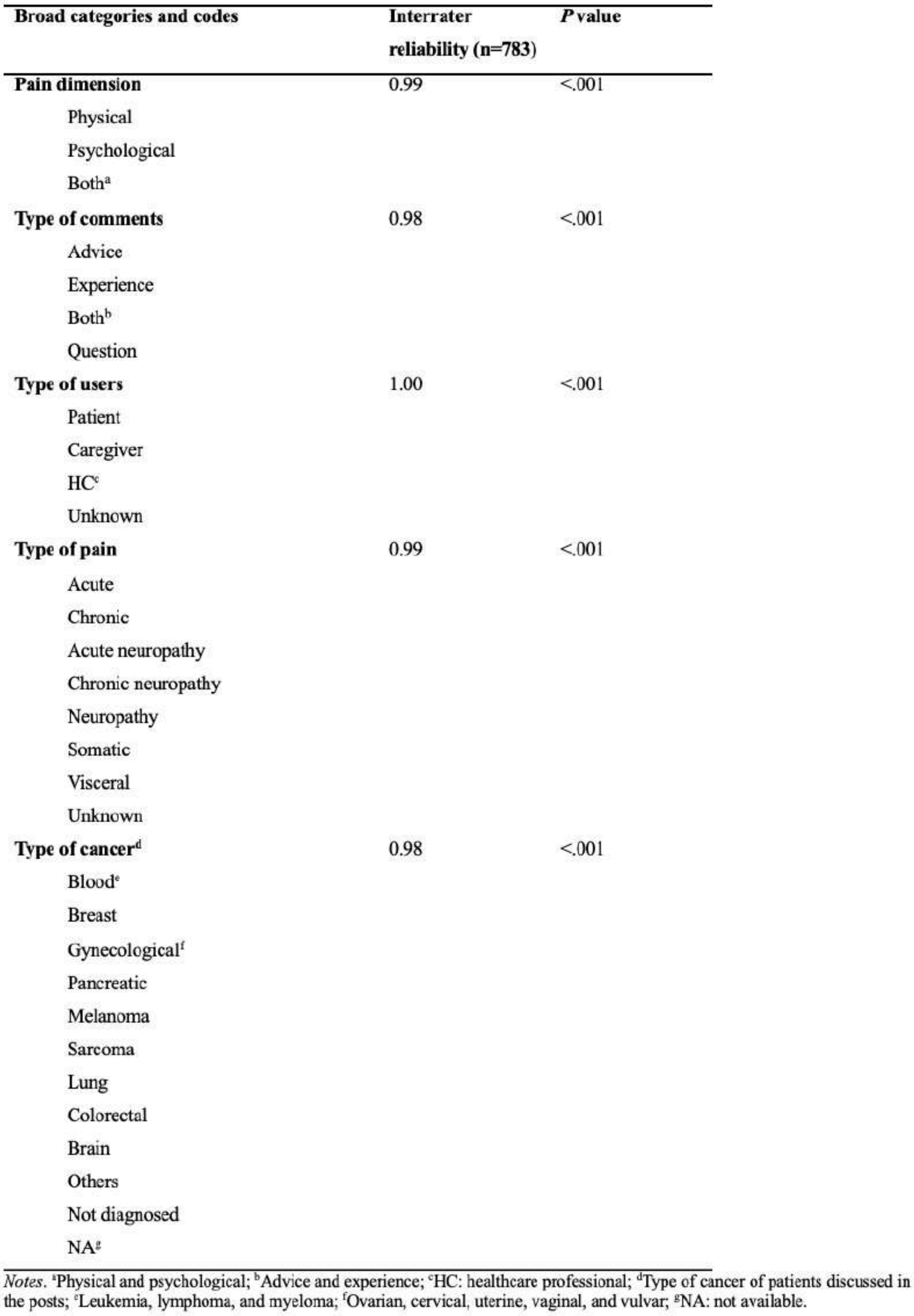
The naming of each cluster was determined through consensus between the two authors (CF and MC), following the guidelines by Galili [216] and Kassambara [217]. Ultimately, we interpreted and labeled the product clusters based on the hierarchical clustering results, considering the specific contexts of the derived words.

2.2.3 Results

Descriptive Statistics and Word Frequency

The interrater reliability for manual coding showed complete consensus, with agreement scores ranging from 0.98 to 1 across all major categories and codes. See Table 4, adapted from Filipponi et al. [218].

Table 4. List of broad categories, related codes, and interrater reliability results



Broad categories and codes	Interrater reliability (n=783)	*P* value
Pain dimension	0.99	<.001
Physical		
Psychological		
Both[a]		
Type of comments	0.98	<.001
Advice		
Experience		
Both[b]		
Question		
Type of users	1.00	<.001
Patient		
Caregiver		
HC[c]		
Unknown		
Type of pain	0.99	<.001
Acute		
Chronic		
Acute neuropathy		
Chronic neuropathy		
Neuropathy		
Somatic		
Visceral		
Unknown		
Type of cancer[d]	0.98	<.001
Blood[e]		
Breast		
Gynecological[f]		
Pancreatic		
Melanoma		
Sarcoma		
Lung		
Colorectal		
Brain		
Others		
Not diagnosed		
NA[g]		

Notes. [a]Physical and psychological; [b]Advice and experience; [c]HC: healthcare professional; [d]Type of cancer of patients discussed in the posts; [e]Leukemia, lymphoma, and myeloma; [f]Ovarian, cervical, uterine, vaginal, and vulvar; [g]NA: not available.

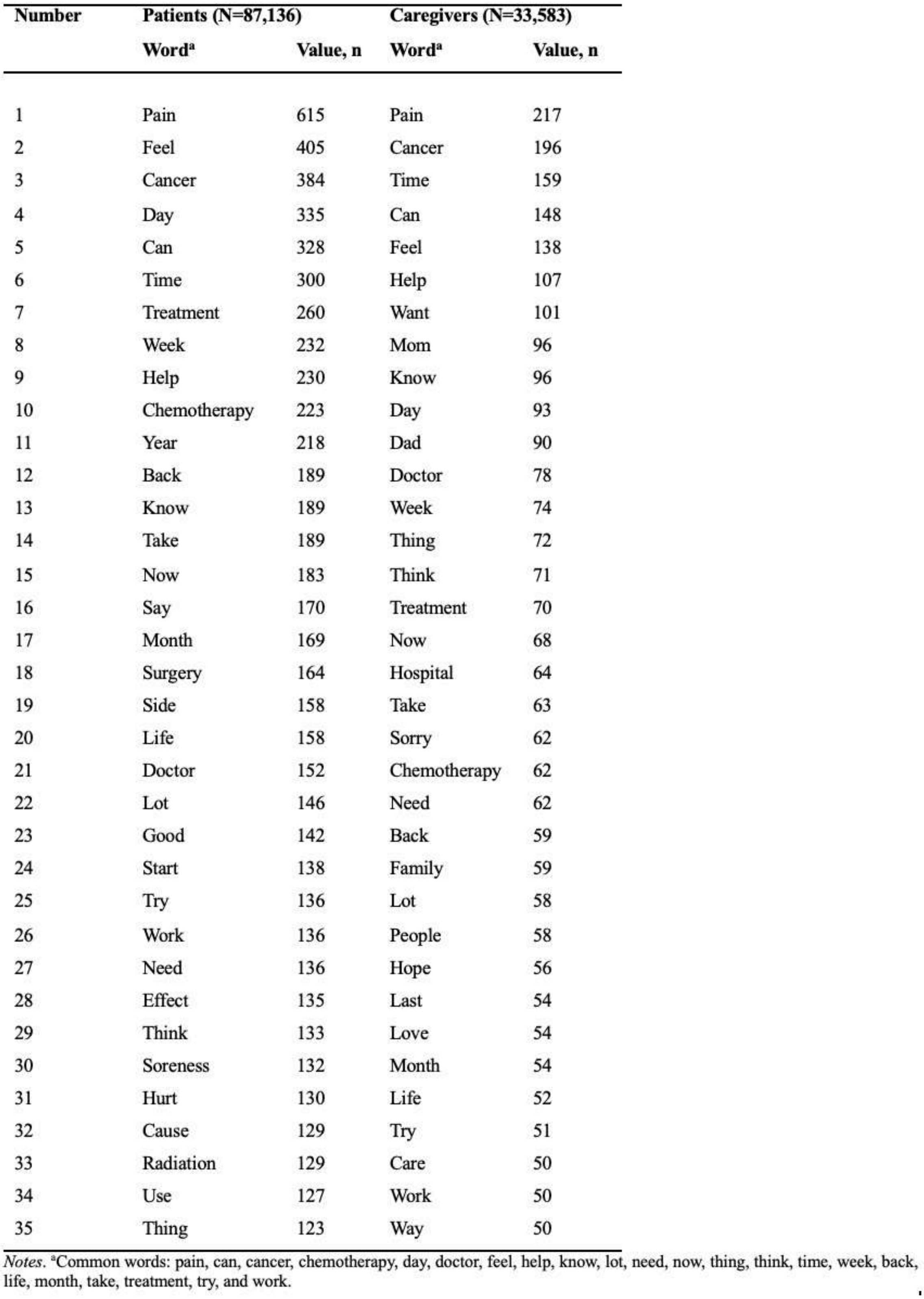
Between April 2011 and November 2021, 783 public comments were identified. Of these, 679 comments—161 from caregivers and 518 from patients—were selected for inclusion in the final database, aligning with our focus on patient and caregiver perspectives. Consequently, 104 comments were omitted from the analysis due to either unidentified user types (93 comments) or references to healthcare professionals (11 comments). Further details can be found in Appendix 1, adapted from Filipponi et al. [218].

Patients' Posts

Of the 679 comments analyzed, 518 (76.3%) were posted by patients. Within this subgroup, the predominant aspect of cancer pain discussed was the physical dimension, noted in 359 comments (69.3%). Additionally, 123 comments (23.7%) addressed physical and psychological dimensions of pain, whereas only 37 (7.1%) focused exclusively on the psychological aspect. Of the total comments from patients, 219 (42.3%) did not mention the specific type of pain. Among those that did, neuropathic pain was most frequently mentioned (95 comments, 18.3%), followed by chronic (80 comments, 15.4%), acute (51 comments, 9.8%), somatic (2 comments, 0.4%), and visceral pain (1 comment, 0.2%). Specifically for neuropathy, chronic and acute neuropathies were discussed in 52 (10.0%) and 18 (3.5%) of the comments, respectively.

Most posts (422/518, 81.5%) featured patients sharing their personal experiences and offering insights to others facing similar challenges. Fewer posts (53/518, 10.2%) provided advice, and a small number (9/518, 1.7%) posed questions. Additional information is available in Appendix 1 and Table 5, adapted from Filipponi et al. [218], which lists the top 35 most frequently used words and their frequencies.

Table 5. Most commonly used terms related to cancer pain by patients and caregivers: A top 35 overview



Number	Patients (N=87,136)		Caregivers (N=33,583)	
	Word[a]	Value, n	Word[a]	Value, n
1	Pain	615	Pain	217
2	Feel	405	Cancer	196
3	Cancer	384	Time	159
4	Day	335	Can	148
5	Can	328	Feel	138
6	Time	300	Help	107
7	Treatment	260	Want	101
8	Week	232	Mom	96
9	Help	230	Know	96
10	Chemotherapy	223	Day	93
11	Year	218	Dad	90
12	Back	189	Doctor	78
13	Know	189	Week	74
14	Take	189	Thing	72
15	Now	183	Think	71
16	Say	170	Treatment	70
17	Month	169	Now	68
18	Surgery	164	Hospital	64
19	Side	158	Take	63
20	Life	158	Sorry	62
21	Doctor	152	Chemotherapy	62
22	Lot	146	Need	62
23	Good	142	Back	59
24	Start	138	Family	59
25	Try	136	Lot	58
26	Work	136	People	58
27	Need	136	Hope	56
28	Effect	135	Last	54
29	Think	133	Love	54
30	Soreness	132	Month	54
31	Hurt	130	Life	52
32	Cause	129	Try	51
33	Radiation	129	Care	50
34	Use	127	Work	50
35	Thing	123	Way	50

Notes. [a]Common words: pain, can, cancer, chemotherapy, day, doctor, feel, help, know, lot, need, now, thing, think, time, week, back, life, month, take, treatment, try, and work.

Caregivers' Posts

Of the 679 comments analyzed, 161 (23.7%) were shared by caregivers. Many of these caregiver comments (67/161, 41.6%) discussed pain from psychological and physical perspectives. Others focused solely on the physical dimension (50/161, 31.1%) or exclusively on the psychological aspect (44/161, 27.3%). Of the 161 comments, 123 (76.4%) did not identify the type of pain experienced.

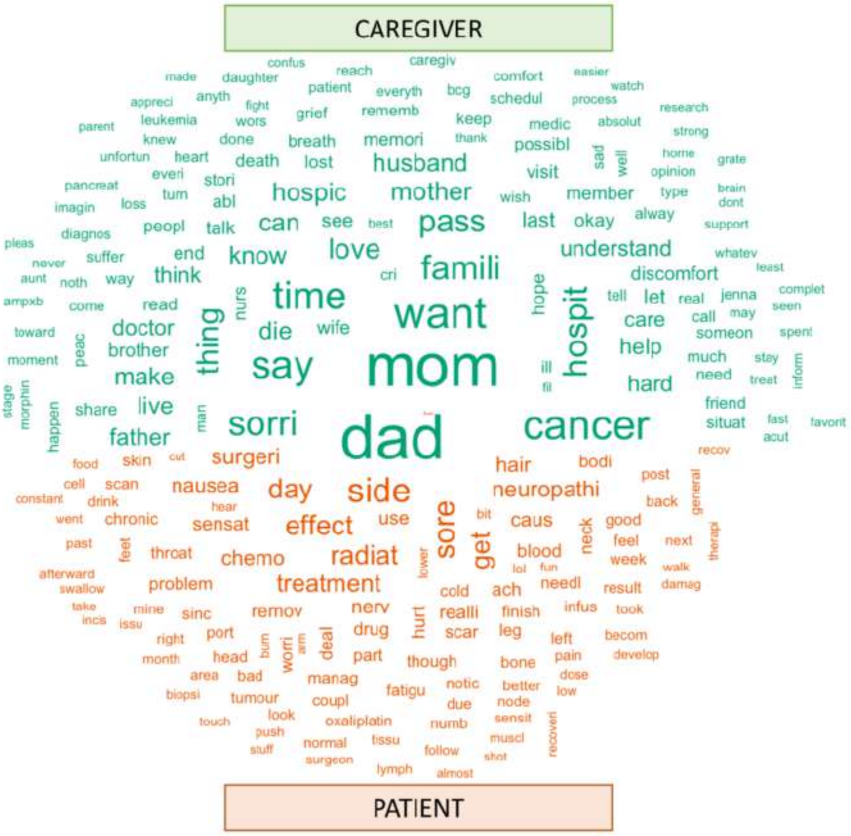
In the comments that did provide specifics, CP emerged as the most commonly cited issue (18/161, 11.2%), followed by neuropathy (12/161, 7.5%) and acute pain (4/161, 2.5%). These comments did not mention somatic or visceral pain. Regarding neuropathy, chronic neuropathy was referenced in only 2.5% (4/161) of the comments, while acute neuropathy was noted in 0.6% (1/161).

Generally, caregivers primarily relayed the experiences of their loved ones with cancer (130/161, 80.7%). They shared personal experiences, provided information in 11.2% (18/161) of posts, and offered advice in 8.1% (13/161) of the comments. Additional information is available in Appendix 1, and Table 5 details the top 35 most frequently used words and their frequencies.

Word Cloud Comparison

Figure 2, adapted from Filipponi et al. [218], features a word cloud that compares patients' and caregivers' words when discussing the cancer pain experience. This visualization was generated by analyzing the most used words.

Figure 2. Comparative word cloud analysis of terms used by patients and caregivers in describing cancer pain



Notes. Patient-related terms are highlighted in orange, while caregiver-associated words are displayed in green.

Patients often employed terms that describe the physical aspects of pain, such as "neuropathy", "sensation", "nerve", "hurt", and "fatigue". They also frequently mentioned terms associated with pain causes related to treatments like "radiation", "surgery", and "chemotherapy", as well as specific diagnostic procedures such as "biopsy" and "scan". Furthermore, patients discussed pharmacological treatments for pain management, including "drug", "oxaliplatin", "dose", and "addiction", along with their side effects like "nausea", "soreness", "hair loss", "scar", "numbness", and "cold sensation". Psychological terms related to pain, such as "worry" and "scary", were also commonly used by patients.

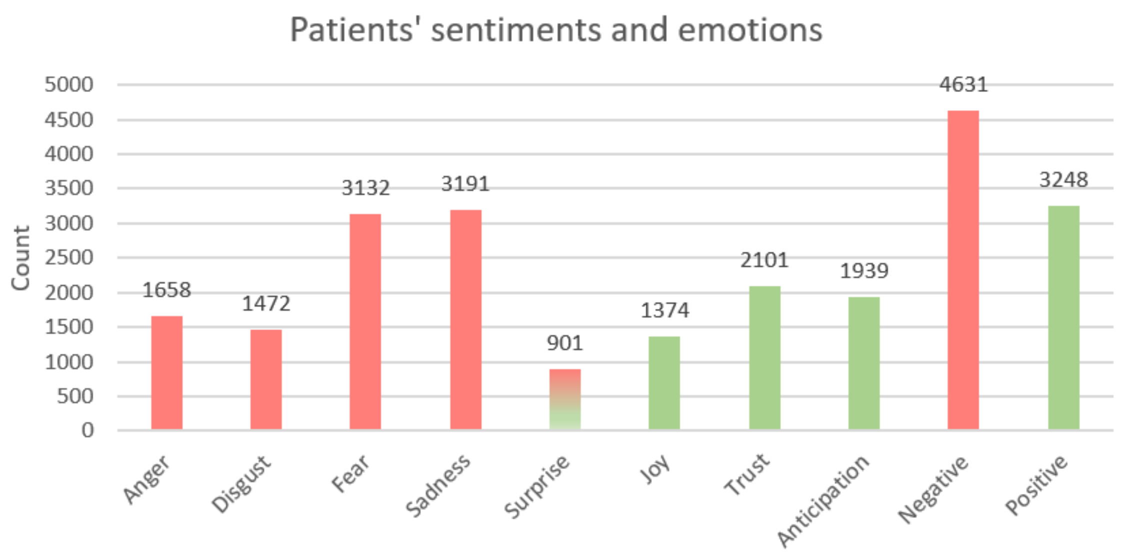
Conversely, caregivers more often used words that reflect the psychosocial dimensions of pain, including references to family members like "dad", "mom", and "wife", as well as terms such as "sorry", "help", "memories", "care", "doctor", "death", "understand", and "remember". In contrast to patients, caregivers less frequently mentioned the physical aspects or side effects of pain and treatments, with terms like "morphine", "stage", and "acute" appearing less often.

Emotion and Sentiment Analysis

Patients' Posts

The bar chart (see Figure 3), adapted from Filipponi et al. [218], illustrates eight emotions (anger, fear, anticipation, trust, surprise, sadness, joy, and disgust) along with two sentiments (positive and negative) related to the target words used by patients in discussions about cancer pain. The analysis was based on 87,136 words from patients and 5,577 extracted sentences.

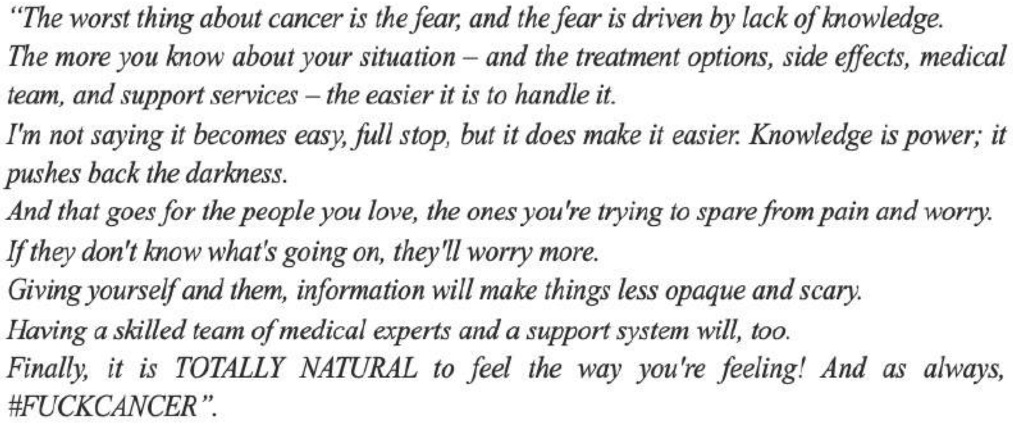
Figure 3. Patients' emotion and sentiment frequencies



Notes. Emotions and sentiments linked to negative affects are depicted in red, while those linked to positive affects appear in green. The emotion of surprise, which can reflect either positive or negative affects, is represented by a blend of red and green.

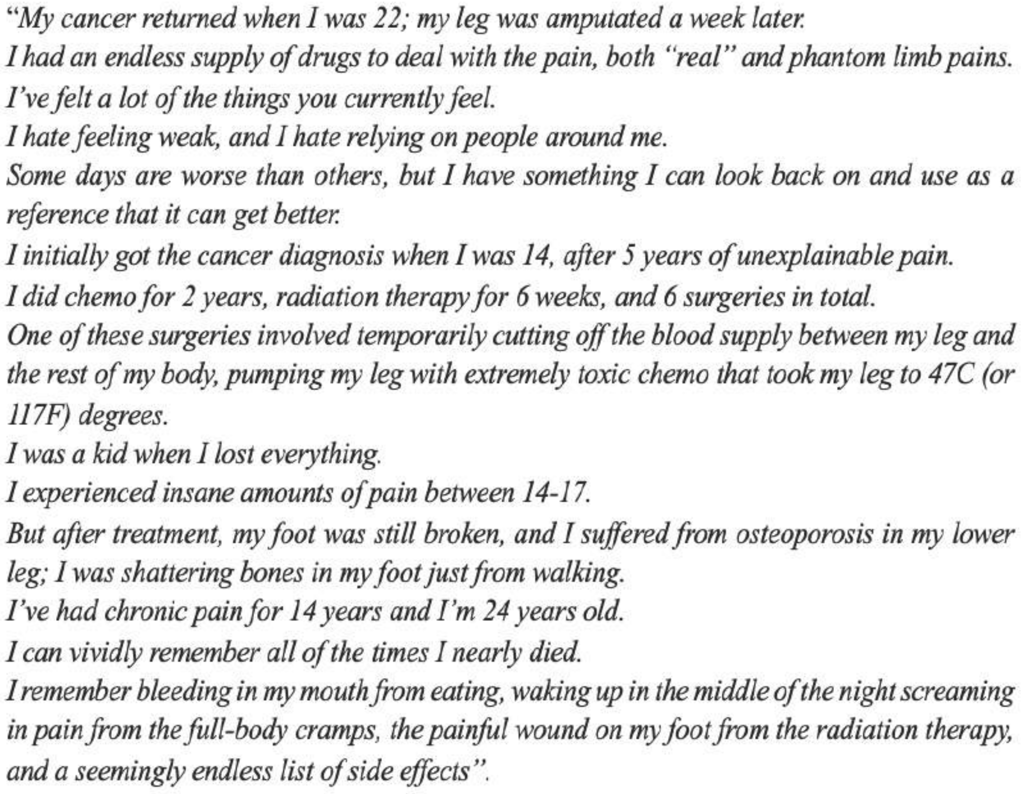
The analysis of target words revealed that negative sentiments averaged higher (mean=0.83) compared to positive sentiments (mean=0.58). Sadness (mean=0.57) and fear (mean=0.56) dominated the negative emotions, with anger (mean=0.30) and disgust (mean=0.26) appearing less frequently. On the positive side, trust (mean=0.40) and anticipation (mean=0.35) were more frequently observed, followed by joy (mean=0.25). Surprise was the least common emotion, with a mean of 0.17. Illustrative sentences from post IDs P2 and P258 demonstrate these emotional and sentimental nuances.

- Sentences extracted from post ID P2:



"The worst thing about cancer is the fear, and the fear is driven by lack of knowledge.
The more you know about your situation – and the treatment options, side effects, medical team, and support services – the easier it is to handle it.
I'm not saying it becomes easy, full stop, but it does make it easier. Knowledge is power; it pushes back the darkness.
And that goes for the people you love, the ones you're trying to spare from pain and worry.
If they don't know what's going on, they'll worry more.
Giving yourself and them, information will make things less opaque and scary.
Having a skilled team of medical experts and a support system will, too.
Finally, it is TOTALLY NATURAL to feel the way you're feeling! And as always, #FUCKCANCER".

- Sentences extracted from post ID P258:

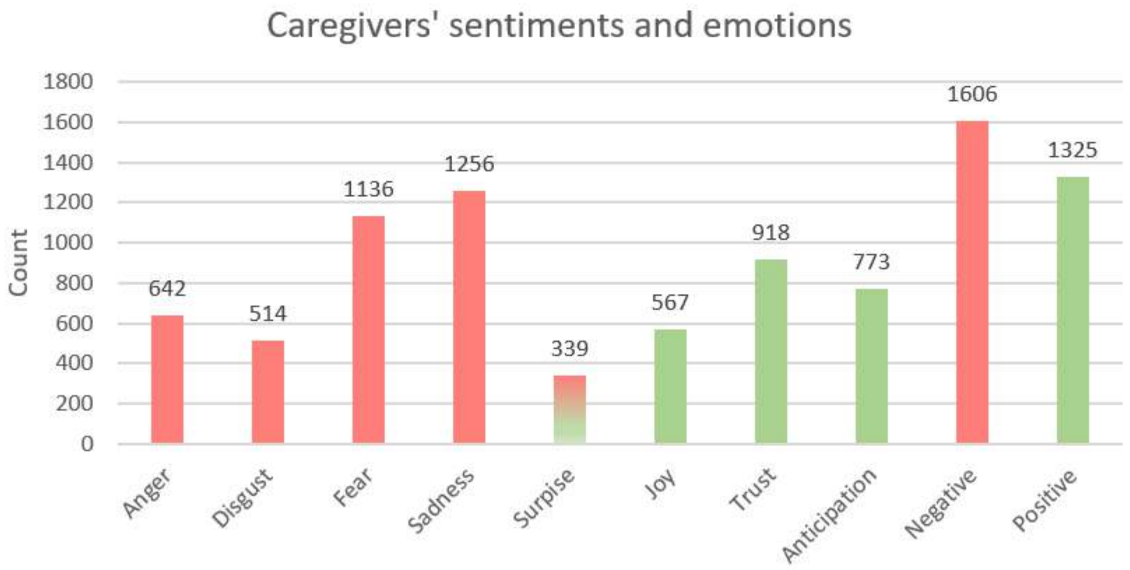


"*My cancer returned when I was 22; my leg was amputated a week later.*
I had an endless supply of drugs to deal with the pain, both "real" and phantom limb pains.
I've felt a lot of the things you currently feel.
I hate feeling weak, and I hate relying on people around me.
Some days are worse than others, but I have something I can look back on and use as a reference that it can get better.
I initially got the cancer diagnosis when I was 14, after 5 years of unexplainable pain.
I did chemo for 2 years, radiation therapy for 6 weeks, and 6 surgeries in total.
One of these surgeries involved temporarily cutting off the blood supply between my leg and the rest of my body, pumping my leg with extremely toxic chemo that took my leg to 47C (or 117F) degrees.
I was a kid when I lost everything.
I experienced insane amounts of pain between 14-17.
But after treatment, my foot was still broken, and I suffered from osteoporosis in my lower leg; I was shattering bones in my foot just from walking.
I've had chronic pain for 14 years and I'm 24 years old.
I can vividly remember all of the times I nearly died.
I remember bleeding in my mouth from eating, waking up in the middle of the night screaming in pain from the full-body cramps, the painful wound on my foot from the radiation therapy, and a seemingly endless list of side effects".

Caregivers' Posts

The bar chart (see Figure 4), adapted from Filipponi et al. [218], illustrates eight emotions (anger, fear, anticipation, trust, surprise, sadness, joy, and disgust) and two sentiments (positive and negative) related to the target words used by caregivers in discussions about cancer pain. This analysis encompassed 33,583 words and 2,052 sentences extracted from caregiver comments.

Figure 4. Caregivers' emotion and sentiment frequencies



Notes. Emotions and sentiments linked to negative affects are depicted in red, while those linked to positive affects appear in green. The emotion of surprise, which can reflect either positive or negative affects, is represented by a blend of red and green.

The analysis indicated negative sentiments (mean=0.78) more pronounced than positive sentiments (mean=0.64). Among the negative emotions, sadness (mean=0.61) and fear (mean=0.55) were the most prevalent, with anger (mean=0.31) and disgust (mean=0.25) also observed. Conversely, the leading positive emotions included trust (mean=0.45) and anticipation (mean=0.38), with joy (mean=0.28) being significant as well. The emotion of surprise was the least common, recorded at a mean of 0.16. Illustrative excerpts from post IDs C717 and C100 effectively showcase these sentiments and emotional states.

- Sentences extracted from post ID C717:

> *"My gf has stage IV lung cancer, and I cried a few times (I haven't cried for several years before that), but I feel like I am mostly in a "functioning" mode that keeps me going, but I am absolutely over the top overwhelmed with emotions and thoughts, but I know I am no good for my gf either if I just give up.*
> *With long times of sickness and going through all that with someone, some people even feel relieved when their loved ones die and feel very guilty, but I think in most cases, it is a relief that their loved one doesn't have to suffer anymore, I didn't cry when my dad died after months of being in and out of the hospital and intensive care, but it hit me later".*

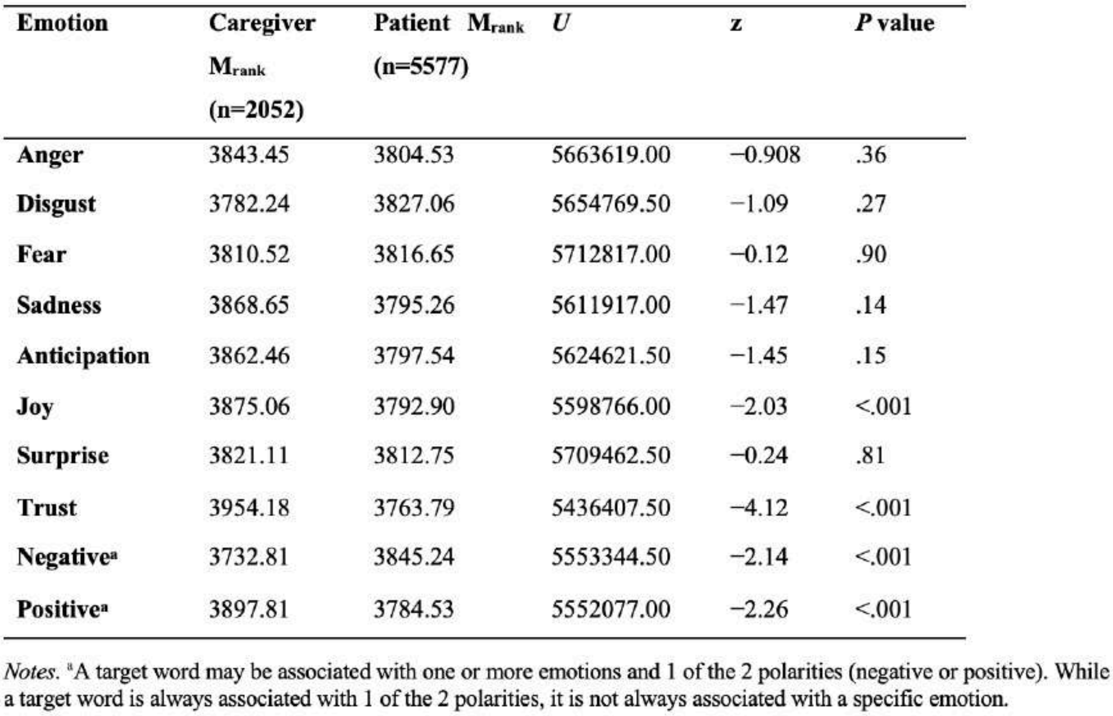
- Sentences extracted from post ID C100:

> *"I lost my husband 47 days ago (this is day 48), and as devastatingly painful as it was to lose him after 24 years together, every time I: 1) remember his struggles in the two months prior to losing him; 2) remember all the times he said he didn't want to be sicker from the treatment from the disease; 3) look at pictures and videos from his final days; it helps me accept that he is gone.*
> *I absolutely loathe the «he's no longer in pain» sentiment, but I've realized what I actually miss most of all are the times before he got sick.*
> *Truth be told, his last two months were increasingly terrible with every passing day.*
> *I can't tell you how many times he said to me, «This is not living.»*
> *I share this in case it helps.*
> *If your mom is not yet hospitalized and can take care of her own needs, there is still hope for her.*
> *In my husband's case, that hope evaporated early, though, and if and when it begins evaporating for your mom, the best thing you can do is remind yourself that «keeping her alive» doesn't mean she's actually «living».*
> *That could help you let her go".*

Wilcoxon Rank Sum Analysis of Emotional Scores Between Patients and Caregivers

The Wilcoxon rank sum test was applied to assess the variations in emotion and sentiment scores across patients and caregivers. The results indicated that patients more frequently exhibited negative sentiments than caregivers (meanP_rank=3845.24; meanC_rank=3732.81; z=−2.14; P<.001). Conversely, caregivers showed a higher frequency of positive sentiment than patients (meanP_rank=3784.53; meanC_rank=3897.81; z=−2.26; P<.001). Among positive emotions, trust (meanP_rank=3763.79; meanC_rank=3954.18; z=−4.12; P<.001) and joy (meanP_rank=3792.90; meanC_rank=3875.06; z=−2.03; P<.001) were most prevalent. Further details can be found in Table 6, adapted from Filipponi et al. [218].

Table 6. Wilcoxon rank sum test results comparing emotion and sentiment scores between patients and caregivers



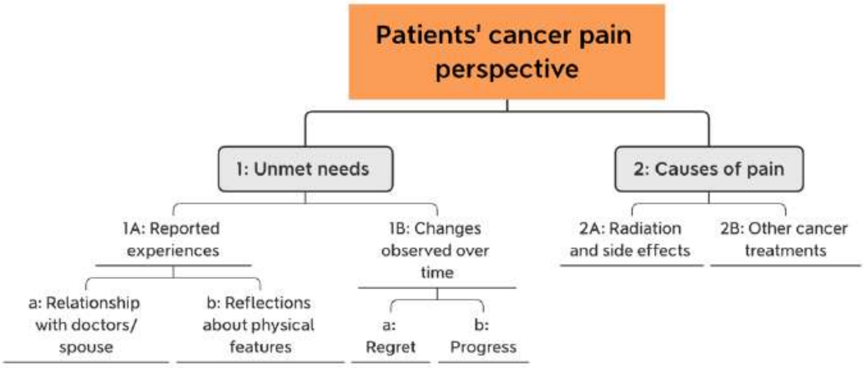
Emotion	Caregiver M_{rank} (n=2052)	Patient M_{rank} (n=5577)	*U*	z	*P* value
Anger	3843.45	3804.53	5663619.00	−0.908	.36
Disgust	3782.24	3827.06	5654769.50	−1.09	.27
Fear	3810.52	3816.65	5712817.00	−0.12	.90
Sadness	3868.65	3795.26	5611917.00	−1.47	.14
Anticipation	3862.46	3797.54	5624621.50	−1.45	.15
Joy	3875.06	3792.90	5598766.00	−2.03	<.001
Surprise	3821.11	3812.75	5709462.50	−0.24	.81
Trust	3954.18	3763.79	5436407.50	−4.12	<.001
Negative[a]	3732.81	3845.24	5553344.50	−2.14	<.001
Positive[a]	3897.81	3784.53	5552077.00	−2.26	<.001

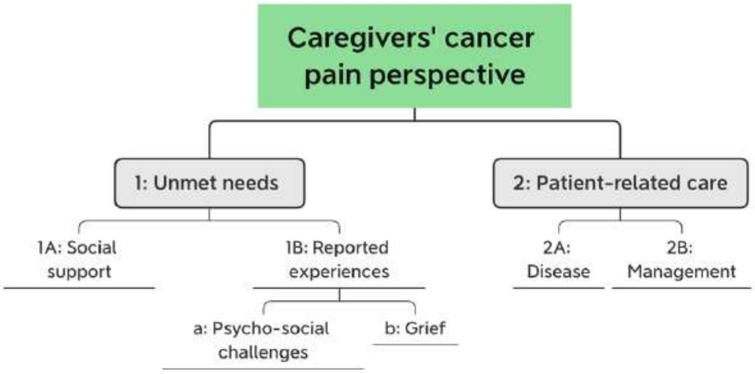
Notes. [a]A target word may be associated with one or more emotions and 1 of the 2 polarities (negative or positive). While a target word is always associated with 1 of the 2 polarities, it is not always associated with a specific emotion.

Hierarchical Clustering

Appendix 2, adapted from Filipponi et al. [218], shows the results of the hierarchical clustering analysis. It was determined that the best configuration involves two clusters for patients, linked to a single root reflecting the patients' view on pain. Using the Ward method, the agglomerative coefficient reached 0.72, indicating a robust cluster structure. Likewise, the analysis for caregivers also suggested two optimal clusters associated with a single root related to the caregivers' perception of pain, where the agglomerative coefficient was 0.80. Figure 5, adapted from Filipponi et al. [218], illustrates the labels used to interpret the product clusters.

Figure 5. Patients' and caregivers' perspectives about cancer pain





In the patients' group, the two main clusters were categorized as (1) unmet needs and (2) cause of pain. The "unmet needs" cluster consists of two nodes: (1A) reported experiences, with subclusters (a) relationships with doctors and spouses and (b) reflections on physical attributes; and (1B) observed changes over time, featuring subclusters (a) regret and (b) progress. The "cause of pain" cluster includes two subcategories: (2A) radiation and its side effects, and (2B) various other cancer treatments. The interactions with spouses, as described in subcluster (a) of the cluster (1A), are exemplified in the subsequent post (post ID P478):

> *"I got diagnosed about 5 weeks ago with stage IV. It has completely changed the relationship…From my end, I now see my spouse as a caregiver instead of a spouse. I feel horrible about it and try and remind myself that he is my sexy husband, who I adore, but when he is wiping my butt and stuff, it's hard to remember that. Sometimes, I see him and just cry because I want to see him as my sexy husband, but it just seems impossible right now."*

The relationship with doctors, detailed in subcluster (a) of the cluster (1A), was associated with the need for reassurance. This is clearly demonstrated in the following post (post ID P399):

> *"I know how bone cancer feels and how recovery feels. This is cancer. But everyone thinks I'm just "imagining" it because I'm afraid of it returning. But I truly know I'm not. I know my body. I'm just waiting for my doctor to tell me so I can get on with treatment."*

Concerning physical features, detailed in subcluster (b) of the cluster (1A), patients discussed the effects of pain on various body parts and detailed the physical symptoms they experienced, such as numbness and soreness.

> *"Had Stage 0 breast cancer (DCIS) and a lumpectomy with a scar on the side of my breast, but close to the armpit. It has been a year, and it was slightly painful/sensitive for many months afterward. Even now, I still get some pain where the scar tissue is (burning and/or aching). From what I have read in blogs/chatrooms online, this is normal and can last for many years .... Glad to hear you do NOT have cancer. :-)"* [Post ID P429]

Regarding the changes observed over time (cluster 1B), patients expressed regret, detailed in subcluster (a) of the cluster (1B), about the actions taken during recovery due to the challenges of waiting. They also expressed a desire for rapid progress (subcluster b of cluster 1B), focusing on the optimal timing and the need to return to their pre-diagnosis state.

> *"I'm hoping to move on to using a stationary bike soon, but like you said, I have to take it easy. I've been pushing myself and regretting it afterward. Progress is never fast enough." [Post ID P127]*

As for caregivers, the first major cluster was labeled (1) unmet needs. This cluster comprised two nodes: (1A) social support and (1B) reported experiences, with subclusters including (a) psychosocial challenges and (b) grief. The second cluster was labeled (2) patient-related care, consisting of two nodes: (2A) disease and (2B) management.

Concerning social support (cluster 1A), caregivers highlighted their need for this support stemming from the responsibility they carry in making decisions on behalf of the patients. For instance, one caregiver noted:

> *"I would ask for support and make his time as comfortable as possible. It is not your fault, and you need to remember that. It is no one's fault. I hope he is comfortable, and whatever choice you make, I'm sure it will be the right one." [Post ID C128]*

Regarding their experiences (cluster 1B), caregivers also expressed the need to be understood concerning the burden associated with the psychosocial challenges (subcluster a of cluster 1B) of managing pain, caring for their loved ones, and the grief associated with loss (subcluster b of cluster 1B).

The following posts are examples of what caregivers shared on the platform with their peers:

> *"I'm so terribly sorry for your loss. I lost my mom to cancer in August, too. I wish I could say it gets easier, but I found it comes to you in waves. One second, you'll be fine and the next second you'll be crying. Followed by numbness. It's hard to watch them slowly fade away from us. And there's nothing we could've done to help save them. It's hard. Reach out for help with extended family to see if they can help take some of the burden off you. If you ever need someone to talk to you can always shoot me a message here." [Post ID C697]*
>
> *"...Not many people can verbalize what I am feeling...Our pains and struggles are different but hauntingly similar.... Often people don't and cannot understand. Even worse, they often don't *want* to understand, especially when you're young....My grief and suffering make people uncomfortable. My husband's suffering and mortality make them uncomfortable...They don't want to see it, so they only see what they want to see. They see a young guy that looks good for having cancer. They dismiss his deficits as "well sometimes I forget things, get lost, or have brain farts! Totally normal!" This isn't a brain fart or a slight delay in finding words. This isn't a "shit I forgot to bring my lunch today." It's much deeper and more consistent than that. This isn't normal..." [Post ID C356]*

Furthermore, the comparison of the two dendrograms revealed significant entanglement (entanglement coefficient=0.28), showing only a partial similarity in the clade that contains the terms "help" and "may" in both dendrograms of patients and caregivers. According to the Loughran and McDonald dictionary [219], both words represent uncertainty. Consequently, we identified the textual node common to both dendrograms as "uncertainty". For example, patient ID 340 conveyed uncertainty in terms of "*what if*" regarding their health status and uncertain future. Such uncertainty can give rise to various worries and fears, including the FCR. However, the patient also noted that dwelling on the myriad what-ifs associated with the illness can lead to missing out on the joys of life.

> *"What I came to realize (with the help of therapy) is, that there are a lot of What-ifs attached to cancer and the anxiety that comes with it. What if my cancer spreads? What if it won't go away? What if it comes back? What if they find something on my next scan? or my personal favorite: What if they overlook something on my next scan? But for every What if we worry about, there is an infinite number of What-ifs we don't even think about. We can't predict the future or how it will develop, but if we worry about what bad could happen, we might miss the good that can happen, too. Or frankly speaking, if it's a beautiful sunny day outside, I won't run around with an open umbrella because it might start raining, or I could get shit on by a bird."*

Regarding caregivers, uncertainty was linked to the grief and fear of losing a loved one. For instance, caregiver ID 159 expressed these feelings while supporting another caregiver.

> *"Your story caught my attention immediately. I know the pain, fear, and uncertainty you are going through. You see, my daughter died 3 weeks ago after a 3 ½-year battle with leukemia. She was 12 years and 5 months old to the day. I will elaborate some, not to compound anything you are going through, but to let you know you are not alone."*

Refer to Appendix 2, adapted from Filipponi et al. [218], for additional information.

2.2.4 Discussion

General Overview of the Findings

This research aimed to examine the comprehensive representation of cancer pain from the perspectives of patients and caregivers. Our findings indicated that three distinct types of content were prevalent among Reddit cancer social group participants: experiences, advice, and questions. Both groups shared mostly experiences with advice followingly. Only patients posed questions. Additionally, the narratives of both user groups encompassed various pain types, with neuropathy, CP, and acute pain being the most frequently discussed. There was a noticeable difference in the language used to describe these experiences between the two groups, which was anticipated due to the differing nature of their experiences with cancer pain. Patients often focused on the physical aspects of pain, citing terms like "neuropathy", "sensation", "chronic", and "fatigue". They also discussed pain causes linked to treatments such as "radiation", "surgery", and "chemotherapy", or specific diagnostic procedures like "biopsy" and "scan". Side effects from treatments were commonly described using terms such as "nausea", "soreness", "hair loss", "scar", "numbness", and "cold sensation", alongside mentions of pharmacological interventions ("drug", "oxaliplatin", "dose").

In contrast, caregivers typically articulated their experiences in terms of their emotional responses to witnessing the pain and its overall impact on their lives, often touching on the psychosocial challenges faced when interacting with other caregivers using words like "family", "sorry", "help", "memories", and "grief".

Quantitatively, 69.3% (359 out of 518) of patients' posts exclusively addressed the physical manifestations of pain, while only 31.1% (50 out of 161) of caregivers' posts did the same. Regarding the psychological dimensions of pain, 27.3% (44 out of 161) of caregivers' posts discussed this aspect, compared to only 7.1% (37 out of 518) from patients.

According to the STM [93,94], each illness can be considered a "we disease" [101], impacting patients and their families and reflecting the interdependent nature of these relationships. In particular, patients with chronic conditions often rely on their caregivers [175], a reliance that might stem from the patients’ diminished autonomy and functionality. This dependence can foster a co-dependence between patients and their partners [172]. Such dependency often intensifies the care requirements, potentially leading to a perceived burden among family members [123,157]. An illustrative example from our dataset captures this dynamic: a caregiver expressing this burden while offering support and understanding to another caregiver.

> *“As for those witnessing his pain: I'm sorry, I am so sorry ... My only advice is to take turns. Everyone experiencing this needs some distance from it from time to time.... If I don't spend some time away from the pain, I will lose my mind.” [Post ID C261]*

The burden of caregiving, while significant, is also influenced by the quality of the relationship between the caregiver and the patient. Factors such as the closeness of the partners, the duration of time they spend together, and the overall robustness of their relationship can affect various facets of patients' and caregivers' experiences. As the STM [93,94] indicates, a caregiver's resources can augment the patient's resources, fostering new synergies for combating pain. This effect is particularly noticeable when there is a strong connection between the caregiver and the patient. For example, a caregiver noted:

> *“One could certainly have that reaction of hating every bit of the lifestyle change, and perhaps at times it may seem just 100% detestable and harrowing, but as is the case with any event that occurs in life, a significant amount depends on how you participate in it and how you experience it. I am 32 years old, and my husband was 31 when he passed away in early March. We were together for over ten years and got married just before he passed away. My one advice to you is to be the hero you can be. Our job isn’t to treat their cancer medically, that is. That’s the job of the doctors, rightfully so. Instead, focus on doing what you are capable of doing, which is being her partner, being her companion through this new life [...] So in a way, I wanted him to think that it was both of us who got diagnosed. He had to bear the brunt of it obviously... but no one can survive cancer alone. [...]. I was there to listen to him and empathize with him as he expressed the different types of pain he was feeling. We both knew I couldn’t cure his symptoms, but I did what I could— [...]. Reading through some of his notes he left behind, I realized I did the right thing. I was so relieved when I read how much it meant to him that I was there for him.” [Post ID C376]*

Although recent literature has increasingly attended to caregivers’ experiences [99,109,125,192], the unaddressed needs and the implicit emotional aspects of cancer pain among caregivers remain underexplored. This study acknowledges this oversight and emphasizes the significance of the mutual impact between patients and caregivers.

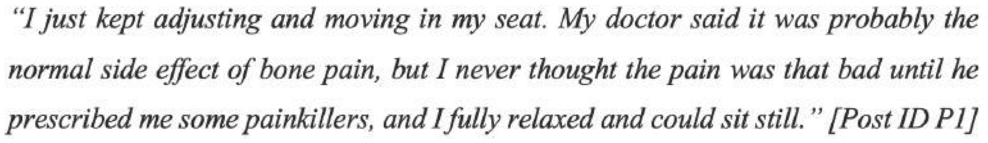
Living with Cancer Pain: Unmet Needs of Patients and Caregivers

An unmet need is a significant requirement of a person that remains unfulfilled [220]. The aim of the study here discussed was to explore the main concerns associated with cancer pain as expressed by patients and caregivers in their posts, along with the specific needs arising from those experiences.

Regarding the patients' group, the hierarchical cluster analysis identified as primary pain-related needs the relationships with doctors/spouses (i.e., seeking reassurance or opinions from physicians about pain and perceiving the spouse more as a caregiver than as a partner) and reflections on physical features of pain (e.g., location of pain, CP, stage of cancer, and bodily sensations like numbness and soreness). Consequently, patients predominantly emphasized the physical aspects of pain.

The primary reason for this focus stems from the inherently physical nature of the pain, often caused by tissue damage from oncological treatments, surgery, or the cancer itself [11]. This insight is aligned with the discussions in cluster 2 (causes of pain), where patients frequently mentioned radiation and its side effects, as well as other cancer treatments, such as chemotherapy, as the main causes of pain. This could lead patients to view their pain from a physical perspective intuitively.

However, the predominance of physical symptom discussion is not only due to the nature of the pain itself. During medical consultations, physicians often guide patients to concentrate on the physical characteristics of their pain, with questions like "*What was your pain intensity in the last 24 hours?*" posed during these sessions [11,221]. This medical focus can influence patients to be more aware of physical symptoms rather than exploring psychological aspects. Additionally, the typical medical response to pain, which often involves prescribing pharmacological treatments as recommended by the WHO's analgesic ladder [222], may reinforce the notion that pain is a purely biological concern to be managed physically. This issue is illustrated in the following patient statement extracted from our study:



> *"I just kept adjusting and moving in my seat. My doctor said it was probably the normal side effect of bone pain, but I never thought the pain was that bad until he prescribed me some painkillers, and I fully relaxed and could sit still." [Post ID P1]*

Interestingly, when patients looked back on their pain (within the cluster called "changes observed over time"), they delved deeper into their experiences. They not only recounted their physical experiences but also expressed their psychological needs, such as the desire to go back to how they were before experiencing pain. This reflection often led to a drive to be more active, and realizing their actions led to regrets and an acknowledgment that progress is often slower than desired.

Regarding caregivers, their primary discussions revolved around the psychosocial challenges resulting from their loved ones' conditions (e.g., economic and work-related issues, thoughts on the passage of time, disease progression, hopes for improved prognoses, and effectiveness of treatments) and experiences of grief (e.g., feeling numb after a death, self-blame, loss, and maintaining hope for their loved ones).

Grief, a common emotional response among caregivers, can persist for six months to a year after the loss of a loved one [223]. Furthermore, grief is not solely a reaction to death but also to the potential loss of loved ones. The burden of caregiving can lead to intense suffering, as well as grief from the real or anticipated loss. As noted by Allen et al. [223] to address this suffering by identifying caregivers at higher risk so that interventions can be tailored to their specific emotional needs.

Thus, caregivers predominantly focused on the psychological dimensions of pain rather than the physical aspects, which were only mentioned in relation to caring for the patient (referenced in cluster 2 of caregivers' words). Several factors contribute to the unique experiences of caregivers. Firstly, they do not experience cancer pain firsthand but rather through the perspective of a caregiver. Secondly, their main responsibility is to provide care and alleviate the patient's pain. However, if this objective is not achieved, caregivers might experience emotions such as anger, helplessness, powerlessness, exhaustion, spiritual distress, diminished confidence, self-blame, and the overall burden associated with caregiving [125,194]. These feelings highlight the psychological struggles caregivers endure daily while managing the suffering of their loved ones, as outlined in the cluster of psychological challenges. Thirdly, to manage these overwhelming responsibilities, caregivers often seek support from others, establishing a community network, as noted in the cluster of social support. It has been shown that social support is a critical unmet need for both caregivers and patients [201], yet it plays a significant role in reducing pain perception in cancer patients [38,181] and alleviating emotional distress in caregivers [194,224]. As the STM explains [93,94], addressing the needs of both patients and caregivers within the patient-caregiver dyad is essential to enhance overall well-being [225].

Despite the differing concerns and needs expressed by caregivers and patients, a common theme of uncertainty emerges. Uncertainty is a prevalent emotion among patients dealing with cancer pain [201,226,227], and according to the theory of uncertainty [228], it arises when the illness's course is unpredictable, the prognosis is poor, the disease progresses, and symptoms intensify. This uncertainty manifests in concerns about the disease's progression and future for patients. Studies have shown that cancer patients experiencing pain exhibit higher levels of uncertainty, which correlates with diminished hope [226]. This uncertainty can also lead patients to feel a loss of control, potentially exacerbating their pain management challenges [227]. For caregivers, uncertainty often pertains to the well-being of their loved ones, possibly leading to anticipatory grief and increasing the caregiving burden [229].

As highlighted in a recent systematic review [230], managing uncertainty involves various strategies where informational support is crucial. A common barrier to effective pain management is a lack of education, affecting patients, caregivers, and healthcare providers who may hold misconceptions about pain treatment, such as fears of addiction to painkillers or beliefs that cancer pain is inevitable and cannot be fully alleviated [51,53]. Prioritizing pain management education is vital, as it informs healthcare professionals about tailoring interventions to address the uncertainties patients and caregivers face, particularly those experiencing CP. eHealth tools have been identified as promising interventions to support these needs [143,144,231,232], suggesting a potential avenue for improving management strategies and support mechanisms for patients and caregivers.

Emotional Experiences of Patients and Caregivers

In this research, our secondary aim was to investigate the emotions and sentiments expressed in the textual responses of both patients and caregivers related to cancer pain. Notably, there was a disparity in the number of posts, with those from patients being twice as numerous as those from caregivers. In analyzing the outcomes, we focused not on numerical comparisons but on the proportional emotional distributions between the two groups. It was found that emotional activation was pronounced in the narratives of both groups, with patients exhibiting a significantly higher level of negative sentiment compared to caregivers, who more frequently expressed positive emotions. This trend aligns with existing literature indicating prevalent negative sentiments among cancer patients [38,44,198].

However, despite recognizing the importance of congruence in pain experiences between patients and caregivers [192], there is a notable gap in studies focusing specifically on the emotional responses to pain, distinct from the broader context of pain experience congruence. The observed differences in emotional sentiments might be attributed to patients' and caregivers' distinct experiences and roles in managing pain. Patients directly experience pain and the ongoing challenges of managing their disease from diagnosis through to long-term survivorship, including dealing with treatments and their side effects, which may lead them to focus more on the negative aspects. Conversely, caregivers often adopt a supportive role, maintaining optimism and sometimes underestimating potential difficulties along the medical journey. Our findings reveal significantly greater levels of trust and joy among caregivers, suggesting an optimistic perspective despite the demanding nature of their roles. According to Plutchik's theory [233], trust promotes openness, connection, and alliance, essential qualities for caregivers as they navigate the complexities of their roles. Similarly, joy, linked to energy and possibility, is crucial in maintaining caregivers' resilience by fostering creativity and connections. Additionally, the concept of family resilience, as discussed in the literature [234], supports the idea that these emotions play a critical role in how caregivers adapt to the challenges of their roles. Family resilience theories suggest that positive emotional activations are part of broader adaptive systems that help families manage and thrive in adversity. Thus, trust and joy are not merely basic emotions but are integral to the coping and adaptive strategies that fortify caregivers against the strains of their responsibilities.

Regarding specific negative emotions—anger, disgust, fear, and sadness—no significant differences were found between the groups, indicating a uniformity in the negative emotions experienced. When examining each group separately, sadness and fear emerged as the predominant negative emotions within the narratives of both patients and caregivers. This observation is consistent with the fear-avoidance model [13,235], which posits that fear and avoidant behaviors are primary responses to pain, potentially leading to depression and disability. Our data underscores that both firsthand (patients) and thirdhand (caregivers) experiences of pain seem to induce similar negative emotions as described in the fear-avoidance model (fear and sadness), although for different reasons. Patients often experience FCR, a concern driven by pain that may signal treatment failure or disease progression [33,34,55], and is frequently cited as an unmet need along with the need for more information [236]. On the other hand, caregivers might experience guilt over perceived inadequacies in their caregiving abilities or feel fear and uncertainty about the future well-being of their loved ones [100,125]. Importantly, caregivers also share the patients' anxiety that pain could indicate the return of cancer, underscoring a common emotional thread that both parties navigate in the context of ongoing cancer care [129].

Limitations

Our study presents several limitations. First, as the data were sourced from an online social network, demographic details and personal characteristics of users (e.g., personality traits, levels of anxiety, depression, etc.) were not included in our analysis.

Additionally, we could not match patients with their caregivers due to the nature of the data from the cancer subreddit, which did not provide such information. Although some comments included relationship descriptors (e.g., time spent together), the frequency of these comments was insufficient to establish separate variables for relationship characteristics.

Another consideration is the cultural backgrounds of the users. Most Reddit users are based in the United States, with a significant number from the United Kingdom and Canada. This geographic concentration should be considered when interpreting and generalizing our results, as cultural background significantly influences patients' and caregivers' expressions and experiences of pain. Consequently, some findings may not be applicable to individuals from different cultural backgrounds.

Furthermore, our study employed word clouds for descriptive analysis. While word clouds offer a visual representation of frequently mentioned words, they do not fully capture the complexities of individual experiences or the contextual factors and connotations associated with specific terms. Therefore, we advise caution when interpreting word clouds, as they might oversimplify or misrepresent the nuances of the data. By addressing these limitations, we intend to provide a comprehensive perspective on the advantages and disadvantages of utilizing word clouds. Finally, our analysis lacked information on treatment type, and some patients' cancer type data was incomplete. These variables could significantly impact patients' pain experiences and affect our findings' generalizability.

In summary, the primary limitation of our study, and many similar studies utilizing online public data, is the lack of participant characteristics. However, this type of data collection offers anonymity and invisibility, which have been shown to promote self-disclosure [237]. This is particularly beneficial for studying emotions and unmet needs.

Conclusion

Cancer pain is described as an “emotional provoker” [44], significantly diminishing the QoL for both patients and caregivers [172]. It is essential to include informal caregivers in pain management strategies, as they are also emotionally impacted by their loved ones' experiences. Patients and caregivers form an interconnected system, and addressing the needs of this entire system can enhance QoL and pain relief for both parties. Our study underscores the importance of considering patients' and caregivers' perspectives, as this helps identify their needs and emotions influencing pain management.

Improving awareness among patients, caregivers, and healthcare providers is crucial for better pain management and decision-making. eHealth solutions and technological advancements can greatly improve the cancer treatment experience by increasing understanding of treatment options and enhancing communication between patients and healthcare professionals [238]. These technologies can empower patients, enhance their participation in decision-making processes, and help bridge the communication gap between patients and healthcare providers, ensuring that patients are well-informed about their treatment options and actively engaged in their care decisions [143,144,155,156]. For instance, clinical decision support systems have been shown to help primary care providers and patients collaboratively manage noncancer CP and cancer pain in patients with advanced cancer by synthesizing patient information and treatment options and facilitating the SDM process [155,156].

Moreover, eHealth tools have been demonstrated to support the self-management of symptoms, improve lifestyle factors, and enhance the QoL for cancer patients [143,144]. Further research is required to understand the interconnected behavioral and emotional responses of caregivers and patients to cancer pain. Since these reactions develop within dyadic (or family) relationships (e.g., patient-caregiver), implementing dyadic analyses is crucial to exploring the mutual influence between two or more individuals [183–187].

Chapter 3

Chronic Pain in Breast Cancer Survivorship: Deepening Understanding Through Patients and Caregivers Lens

The third study of my doctoral thesis is divided into two parts: the first was published in 2024[3] and examines the challenges faced by breast cancer survivors living with CP; the second, also published in 2024[4], further explores the emotional experiences of caregivers supporting these survivors.

Regarding the first study, as mentioned in paragraph 1.2.1, breast cancer survivors often experience persistent pain following surgery, with a prevalence of 27% to 46%, depending on the location and severity of the pain. This pain typically persists beyond the three-month mark, becoming chronic, and remains stable for up to two years without significant improvement [77,78]. Although guideline-based treatments for cancer pain are effective in 70–90% of cases, many patients continue to face challenges with inadequate pain management [49]. This ongoing struggle is attributed to various difficulties in both pain communication and treatments.

Communicating about pain is challenging because pain is inherently complex, influenced by biological, psychological, and subjective factors, complicating its measurement and effective treatment [9]. Additionally, patient hesitancy in reporting pain results in about one-third of them not being prescribed necessary pain medications [53]. Particularly in breast cancer survivors, De Groef et al. [86] highlighted that pain is frequently underreported and under-assessed, often due to the discomfort patients feel in discussing their symptoms and the focus on other health issues by clinicians. Although self-management interventions provide effective methods to boost self-efficacy and enhance mental health and pain management, ensuring universal access to these important resources for all cancer survivors is still problematic [74]. Peretti-Watel et al. [166] have identified that optimal pain control

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[3] Filipponi C, Masiero M, Mazzoni D, Chichua M, Marceglia S, Ferrucci R, Fragale E, Didier F, Pravettoni G. The voices of breast cancer survivors with chronic pain: A qualitative thematic analysis of patients' challenges to pain management. J Psychosoc Oncol. 2024 May 15:1-25. doi: 10.1080/07347332.2024.2348595

[4] Filipponi, C., Masiero, M., Chichua, M. et al. Navigating the emotional landscape: exploring caregivers' journey alongside breast cancer survivors with chronic pain. Support Care Cancer 33, 32 (2025). https://doi.org/10.1007/s00520-024-09064-3

is often hindered by a lack of skills, knowledge, and prevailing misconceptions about pain and its management, making significant relief elusive for many patients. In this context, the psychosocial literature emphasizes improving pain communication and overcoming potential barriers, such as patients' hesitancy to report pain. In this line, the authors suggested mixed methods to assess pain experiences in breast cancer patients, revealing a notable incongruity between quantitative and qualitative results [166]. Although patients described their pain experiences vividly in interviews, they often minimized their pain on quantitative scales. This discrepancy might arise from a normalization of pain, influenced by misconceptions such as viewing pain as a necessary step for recovery or a perpetual condition [51,53]. This normalization could obstruct accurate reporting on self-report questionnaires, underlining the importance of qualitative methods in exploring sensitive psycho-oncological topics that require in-depth analysis [239].

The MAP [9] offers practical frameworks to address these challenges by integrating the subjective pain experience within research and practice. MAP delineates between identifying and assessing pain, emphasizing using narrative reports for identification and comprehensive assessments to understand why pain is reported. This model prioritizes validating pain reports as legitimate experiences, regardless of other findings, thereby promoting a more compassionate and comprehensive approach to pain assessment. This is vital as qualitative research continues to demonstrate that cancer patients deeply benefit from understanding the cause and significance of their pain and sharing these insights with their families and healthcare providers to enhance access to support and develop strategies to avoid isolation [240]. As pain management in specific populations gets more attention, the focus on CP in breast cancer survivors necessitates further exploration.

Regarding the second study, as mentioned in paragraph 1.2.3, caregiving is a critical yet often overlooked component of cancer care, imposing significant responsibilities on those involved [109,110]. In this context, "caregivers" refers exclusively to informal caregivers—such as partners, family members, or close friends—who, despite often feeling unprepared for the challenges, play a crucial role in supporting cancer patients [110,111]. These informal caregivers are essential in managing the daily care and emotional well-being of patients, particularly in chronic conditions.

However, they often experience significant emotional burdens, with many reporting feelings of hopelessness (18%), demoralization (13.9%), and fear of death (57%), alongside other profound emotional impacts such as pre-loss grief (24%), emotional unpreparedness (36%), and loneliness (35%) [115]. The strain of their responsibilities can lead to guilt, fear, and anxiety about future uncertainties, particularly in managing CP [100,125]. This emotional load often manifests in depression, frustration, grief, and a broader spectrum of overwhelming emotions like desperation and helplessness [126,127], further aggravated by irritability, sadness, and a disinterest in daily activities [100,127].

These challenges underscore the critical need for focused studies on the specific emotional impacts of caregiving in the context of cancer-related CP. Despite the pivotal role caregivers play in managing cancer pain, a significant gap remains in research aimed at understanding and addressing their emotional experiences. In particular, there is a lack of mixed-methods research that quantitatively and qualitatively analyzes caregivers' emotions within the contexts they are experienced. Understanding the specific emotions caregivers face in response to certain challenges can lead to developing targeted interventions to alleviate the perceived burdens. Such an approach promises to enhance caregiver well-being and improve the effectiveness of their care provision.

In the previous chapters, we examined CP from the perspectives of patients and informal caregivers, irrespective of the cancer diagnosis. The first study (paragraph 2.1) emphasized the biopsychosocial interactions affecting both patients and their caregivers, while the second study (paragraph 2.2) utilized social media data to explore the representations and communication challenges of cancer pain in general. Building on these foundations, the current study aims to delve deeper into the unique needs and obstacles related to pain management among breast cancer survivors and to explore the emotional experiences of caregivers supporting them, thereby addressing a critical gap in the existing research.

3.1 *Study 3, part A: Exploring Chronic Pain Narratives among Breast Cancer Survivors: A Qualitative Thematic Analysis*

3.1.1 Aim of the Study

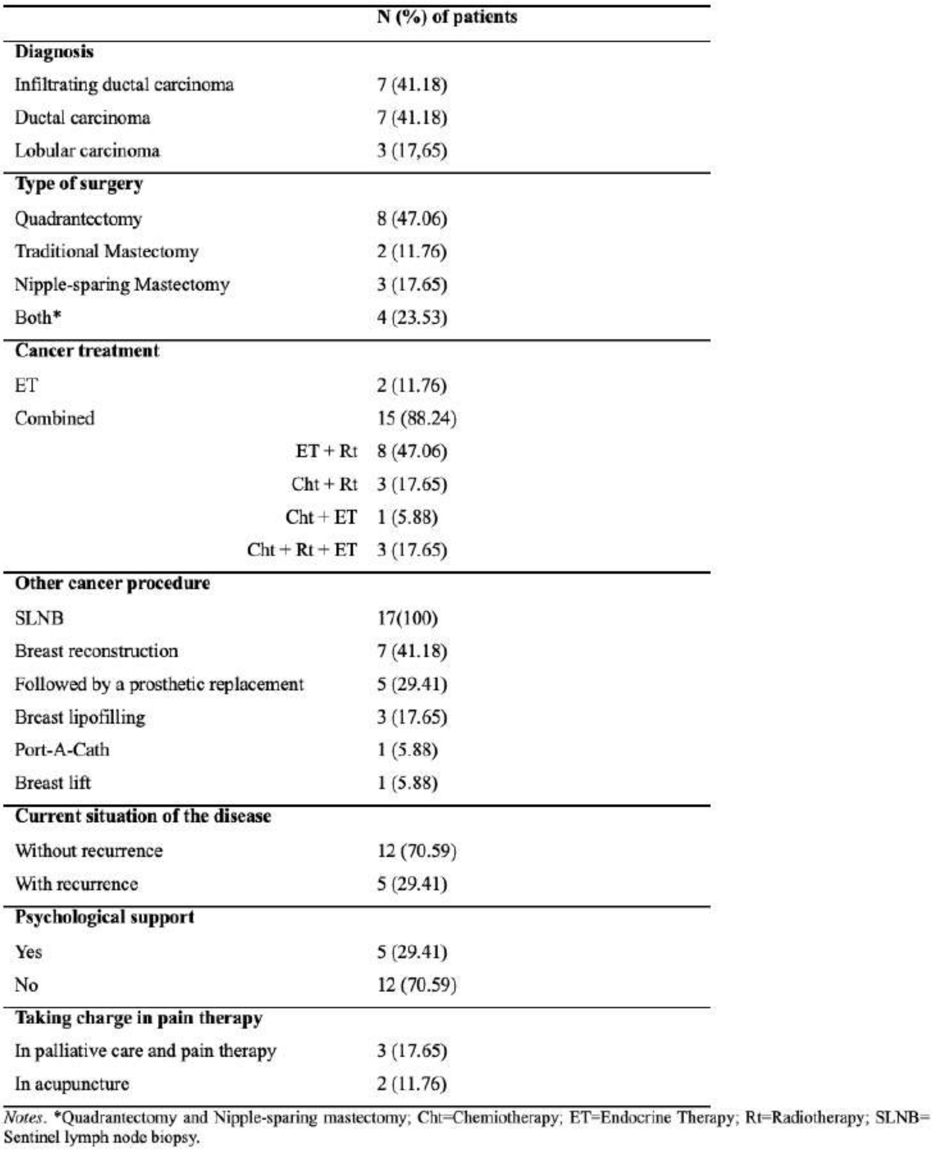
Given the evidence presented, this study aimed to explore the distinct needs and challenges associated with pain management among breast cancer survivors.

3.1.2 Material and Methods

Study design and recruitment

The current study conducted focus groups comprising breast cancer survivors with CP. Due to the COVID-19 pandemic and transportation limitations for some participants, these groups were facilitated online via Zoom video calls. We adhered to the focus group methodology outlined by Krueger and Casey [241] and adjusted for virtual environments [242]. Patients were recruited through phone calls. Exclusion criteria included patients with psychiatric or neurological disorders, other preexisting medical conditions that cause CP, and individuals who experienced CP before surgery or had other pain-related diseases. Additionally, individuals who declined to participate or did not sign the informed consent form (n=53) were excluded. The predominant reasons for non-participation were the absence of pain and difficulties with online engagement. The study ultimately included 17 breast cancer survivors with CP from the Breast Unit at the European Institute of Oncology (IEO). All participants were in the follow-up phase of their treatment and engaged in the discussion once. This study was conducted according to the principles outlined in the Declaration of Helsinki and received approval from the Ethics Committee of the IEO in July 2021 (R1508/21- IEO1594). Refer to Table 7, adapted from Filipponi et al. [243].

Table 7. Clinical characteristics of the sample (N = 17)



	N (%) of patients
Diagnosis	
Infiltrating ductal carcinoma	7 (41.18)
Ductal carcinoma	7 (41.18)
Lobular carcinoma	3 (17,65)
Type of surgery	
Quadrantectomy	8 (47.06)
Traditional Mastectomy	2 (11.76)
Nipple-sparing Mastectomy	3 (17.65)
Both*	4 (23.53)
Cancer treatment	
ET	2 (11.76)
Combined	15 (88.24)
ET + Rt	8 (47.06)
Cht + Rt	3 (17.65)
Cht + ET	1 (5.88)
Cht + Rt + ET	3 (17.65)
Other cancer procedure	
SLNB	17(100)
Breast reconstruction	7 (41.18)
Followed by a prosthetic replacement	5 (29.41)
Breast lipofilling	3 (17.65)
Port-A-Cath	1 (5.88)
Breast lift	1 (5.88)
Current situation of the disease	
Without recurrence	12 (70.59)
With recurrence	5 (29.41)
Psychological support	
Yes	5 (29.41)
No	12 (70.59)
Taking charge in pain therapy	
In palliative care and pain therapy	3 (17.65)
In acupuncture	2 (11.76)

Notes. *Quadrantectomy and Nipple-sparing mastectomy; Cht=Chemiotherapy; ET=Endocrine Therapy; Rt=Radiotherapy; SLNB= Sentinel lymph node biopsy.

Procedure

Before joining the focus groups, each participant provided their informed consent through digital and handwritten signatures. The participants were organized into four focus groups, each containing 4 to 5 patients. The sessions lasted between 60 and 90 minutes, including a break midway to prevent excessive fatigue. Three IEO psychologist-researchers (CF, ST, FD) experienced in leading focus groups facilitated the discussions. No additional individuals were present during the discussions, and no prior relationships were established before the commencement of the study.

The session began with a brief overview of the research objectives, and participants introduced themselves and shared their experiences. A series of key questions were then posed to the participants [244]:

1. *Thinking about yourself and your daily life, what are your difficulties in managing pain or barriers that hinder good pain management?*
2. *What are your needs in relation to pain and its management?*
3. *Have you discussed your treatment preferences with your doctor, caregiver, or anyone important to you?*
4. *Which treatment would you prefer to follow to treat pain?*

The focus group discussions were audio-recorded and transcribed verbatim by the first author, who also ensured the removal of any identifiable information. The number of focus groups was established based on existing literature [245,246] to ensure the capture of pertinent themes. Group composition was determined by the homogeneity of the pain experiences, considering the intensity of pain reported during the recruitment phone calls and the participants' preferences. Field notes were also taken throughout the discussions.

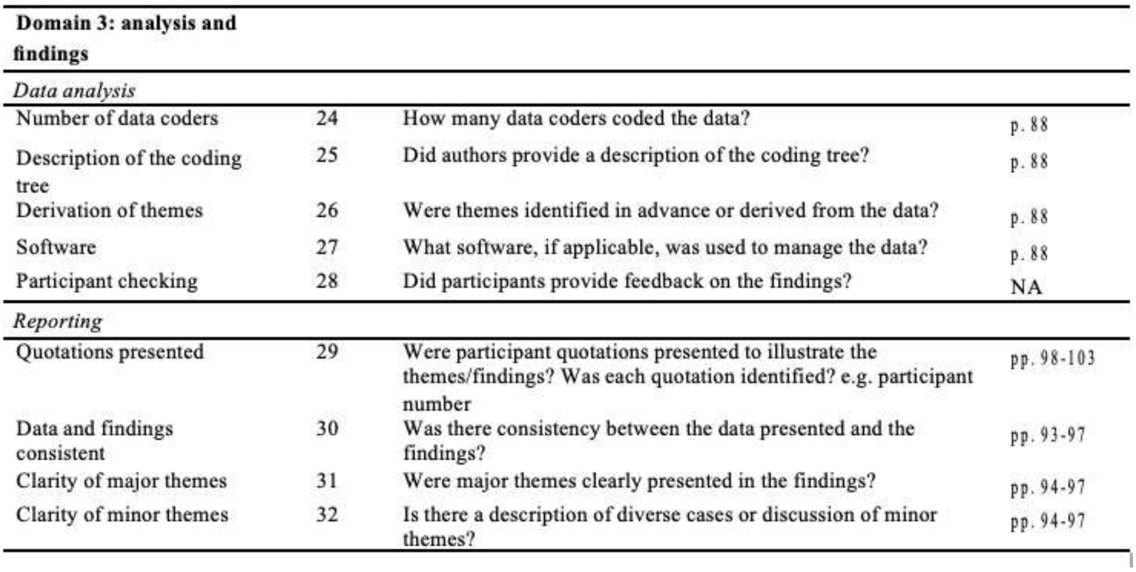
Data analysis

A descriptive analysis was conducted using clinical data obtained from patients' electronic health records and additional information collected during recruitment phone calls. The NRS was used to assess pain intensity during these calls [17]. In the focus group sessions, participants' self-reported pain characteristics, including type, semantics, and location, complemented this data. Subsequently, a body map was generated using the matplotlib library in Python.

Data analysis employed reflexive thematic analysis as described by Braun and Clarke [247,248]. The process of reflexive thematic analysis involved several steps, starting with becoming thoroughly familiar with the data. The coding process was collaborative and introspective. Initially, the primary coder (CF) carefully reviewed the transcripts, noting items of potential interest to better understand the data (step 1). From this, initial codes were developed (step 2), and transcripts were manually coded and organized into potential themes by CF (step 3). This was followed by iterative discussions with EF, MC, and DM to review and refine the themes (step 4), define and name the final themes (step 5), and ultimately prepare the final report (step 6). Throughout this process, the COREQ checklist for reporting qualitative research was adhered to [249]. Refer to Table 8, adapted from Filipponi et al. [243].

Table 8. The COREQ (COnsolidated criteria for REporting qualitative research) checklist

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	p. 87
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	NA
Occupation	3	What was their occupation at the time of the study?	p. 87
Sex/Gender	4	Was the researcher male or female?	NA
Experience and training	5	What experience or training did the researcher have?	p. 87
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	p. 87
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	p. 87
Interviewer characteristics	8	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	NA
Domain 2: Study design			
Theoretical framework			
Methodological orientationand Theory	9	What methodological orientation was stated to underpin the study? e.g.grounded theory, discourse analysis, ethnography, phenomenology, content analysis	p. 88
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	p. 86
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, email	p. 86
Sample size	12	How many participants were in the study?	p. 86
Non-participation	13	How many people refused to participate or dropped out? Reasons?	p. 86
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	p.86
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	p. 87
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data	pp. 87, 90-92
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	p. 88
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	p. 88
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	p. 88
Field notes	20	Were field notes made during and/or after the interview or focus group?	p. 88
Duration	21	What was the duration of the interviews or focus group?	p. 87
Data saturation	22	Was data saturation discussed?	p. 88
Transcripts returned	23	Were transcripts returned to participants for comment and/or correction?	NA



Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	p. 88
Description of the coding tree	25	Did authors provide a description of the coding tree?	p. 88
Derivation of themes	26	Were themes identified in advance or derived from the data?	p. 88
Software	27	What software, if applicable, was used to manage the data?	p. 88
Participant checking	28	Did participants provide feedback on the findings?	NA
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	pp. 98-103
Data and findings consistent	30	Was there consistency between the data presented and the findings?	pp. 93-97
Clarity of major themes	31	Were major themes clearly presented in the findings?	pp. 94-97
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	pp. 94-97

3.1.3 Results

The characteristics of the sample

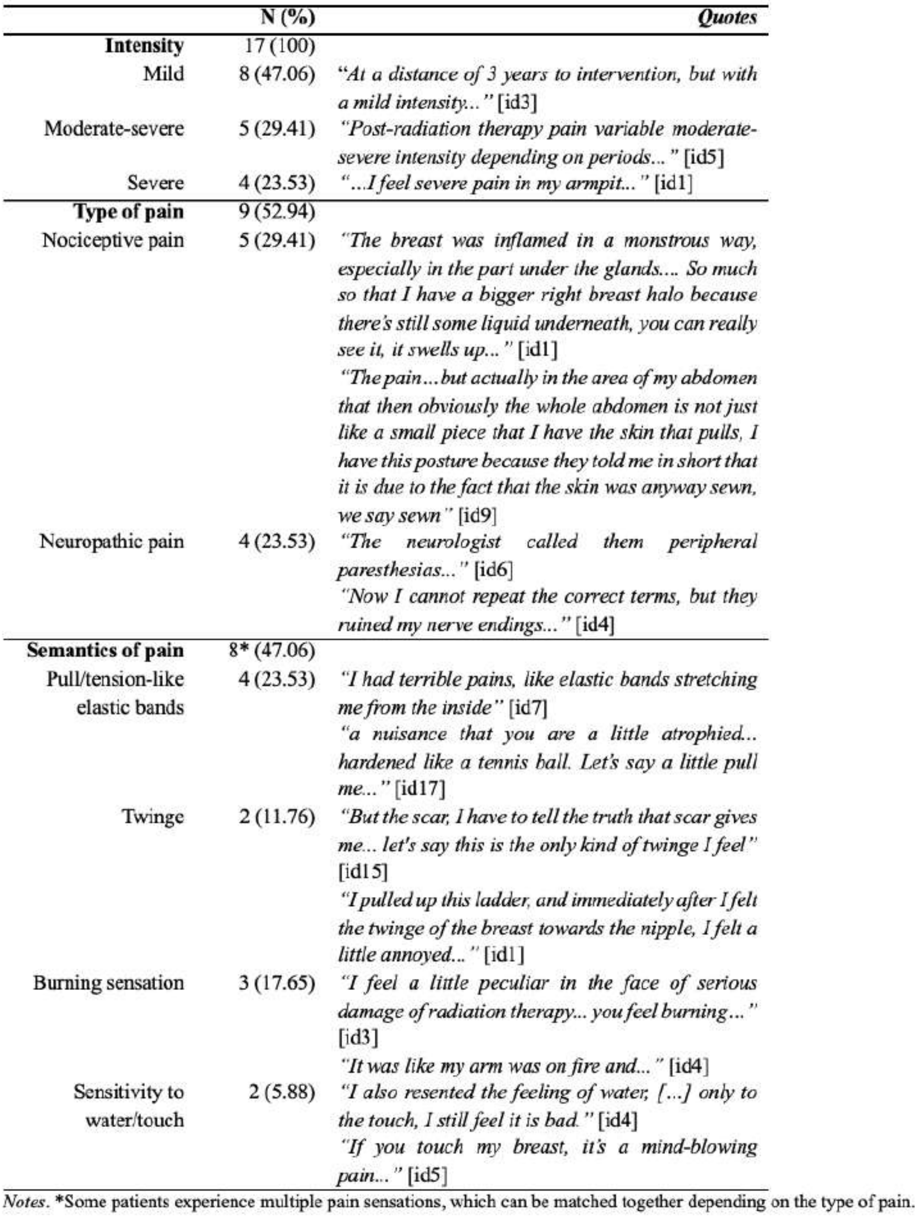
Table 7 illustrates the attributes of the 17 breast cancer survivors with CP, with a mean age of 51 years (SD=7.88). On average, participants were 7 years post-radiotherapy and/or chemotherapy, with durations ranging from less than 2 to 16 years. Most individuals underwent quadrantectomies (n=8, 47%) and combined therapies (n=15, 88%), specifically radiotherapy with five years of endocrine therapy (n=8, 47%). Sentinel lymph node biopsies were performed on all participants. Breast reconstruction was reported by 41% (n=7), with prosthetic replacements in 29% (n=5). Ductal carcinoma was the predominant diagnosis (n=14, 82%), with more than half experiencing no recurrences and review intervals typically between six months and one year.

29% of participants (n=5) utilized psychological support from the psycho-oncology division, while pain management included acupuncture for 12% (n=2) and palliative care for 18% (n=3), addressing various pains such as thoracic, lumbar, and neuropathic pain.

Table 9 details the pain characteristics concerning intensity, type, and sensations experienced by the participants. All reported ongoing CP were categorized as mild (n=8, 47%), moderate (n=5, 29%), or severe (n=4, 23%). The pain was primarily iatrogenic, with participants noting decreased pain thresholds following cancer-related procedures. Over half of the sample (n=9, 53%) described overlapping types and mechanisms of pain. Specifically, 29% (n=5) experienced nociceptive pain and 23% (n=4) neuropathic pain, with corresponding sensations such as burning (n=3, 18%) and increased sensitivity to touch and water (n=2, 6%). Conversely, 23% (n=4) of participants experienced pain akin to pull/tension via elastic bands, while 12% (n = 2) reported twinges associated with nociceptive pain.

In case of pain, all participants were medically advised to administer 1000 mg of paracetamol per dose, taking one tablet when needed with a maximum limit of three tables daily, spaced every eight hours (refer to Table 9, adapted from Filipponi et al. [243]).

Table 9. Features of chronic pain in breast cancer survivors



	N (%)	*Quotes*
Intensity	17 (100)	
Mild	8 (47.06)	*"At a distance of 3 years to intervention, but with a mild intensity..."* [id3]
Moderate-severe	5 (29.41)	*"Post-radiation therapy pain variable moderate-severe intensity depending on periods..."* [id5]
Severe	4 (23.53)	*"...I feel severe pain in my armpit..."* [id1]
Type of pain	9 (52.94)	
Nociceptive pain	5 (29.41)	*"The breast was inflamed in a monstrous way, especially in the part under the glands.... So much so that I have a bigger right breast halo because there's still some liquid underneath, you can really see it, it swells up..."* [id1] *"The pain...but actually in the area of my abdomen that then obviously the whole abdomen is not just like a small piece that I have the skin that pulls, I have this posture because they told me in short that it is due to the fact that the skin was anyway sewn, we say sewn"* [id9]
Neuropathic pain	4 (23.53)	*"The neurologist called them peripheral paresthesias..."* [id6] *"Now I cannot repeat the correct terms, but they ruined my nerve endings..."* [id4]
Semantics of pain	8* (47.06)	
Pull/tension-like elastic bands	4 (23.53)	*"I had terrible pains, like elastic bands stretching me from the inside"* [id7] *"a nuisance that you are a little atrophied... hardened like a tennis ball. Let's say a little pull me..."* [id17]
Twinge	2 (11.76)	*"But the scar, I have to tell the truth that scar gives me... let's say this is the only kind of twinge I feel"* [id15] *"I pulled up this ladder, and immediately after I felt the twinge of the breast towards the nipple, I felt a little annoyed..."* [id1]
Burning sensation	3 (17.65)	*"I feel a little peculiar in the face of serious damage of radiation therapy... you feel burning..."* [id3] *"It was like my arm was on fire and..."* [id4]
Sensitivity to water/touch	2 (5.88)	*"I also resented the feeling of water, [...] only to the touch, I still feel it is bad."* [id4] *"If you touch my breast, it's a mind-blowing pain..."* [id5]

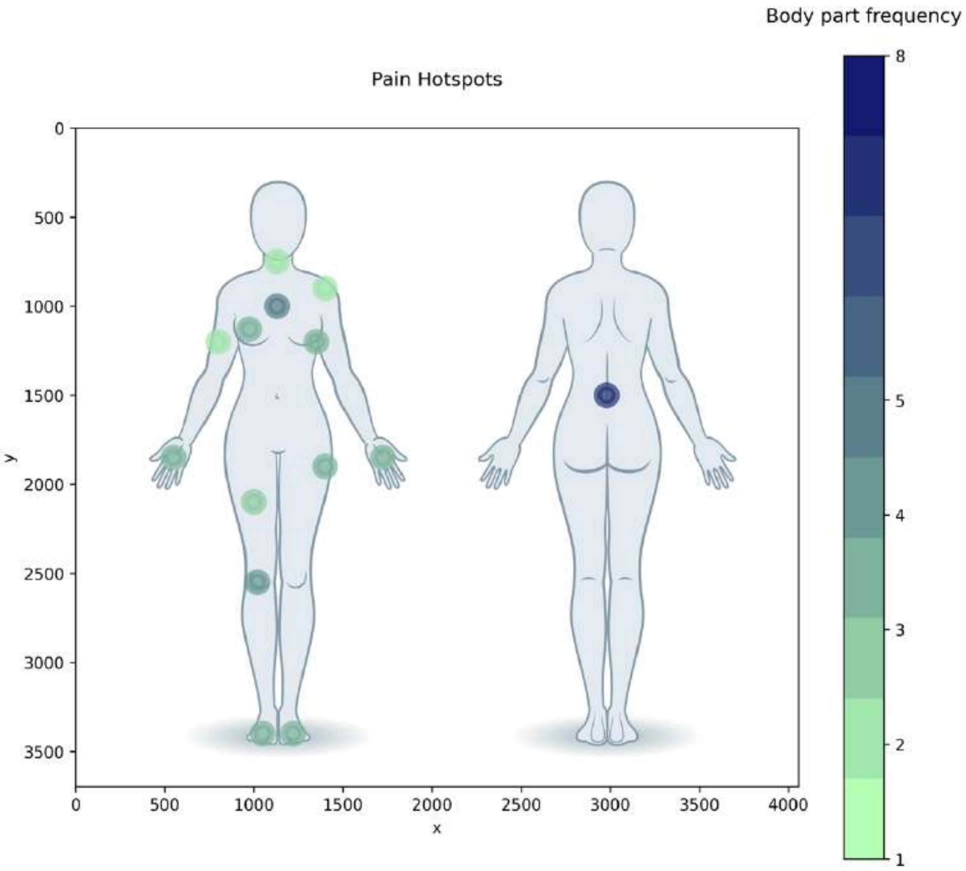
Notes. *Some patients experience multiple pain sensations, which can be matched together depending on the type of pain.

The body map

Figure 6 reveals the distribution of pain frequency across various body regions among the participants. The lumbar area emerged as the most reported location for pain (n=8, 47%), with the arm and chest each reported by 29% of participants (n=5 for each). Pain was also frequently noted in adjacent areas affected by surgical interventions, such as the breast and armpit.

Furthermore, 59% of the participants (n=10) identified joints as a prevalent source of discomfort, followed by bones (18%, n=3) and muscle retraction (6%, n=1). See Figure 6 (adapted from Filipponi et al. [243]).

Figure 6. Mapping body pain in breast cancer survivors

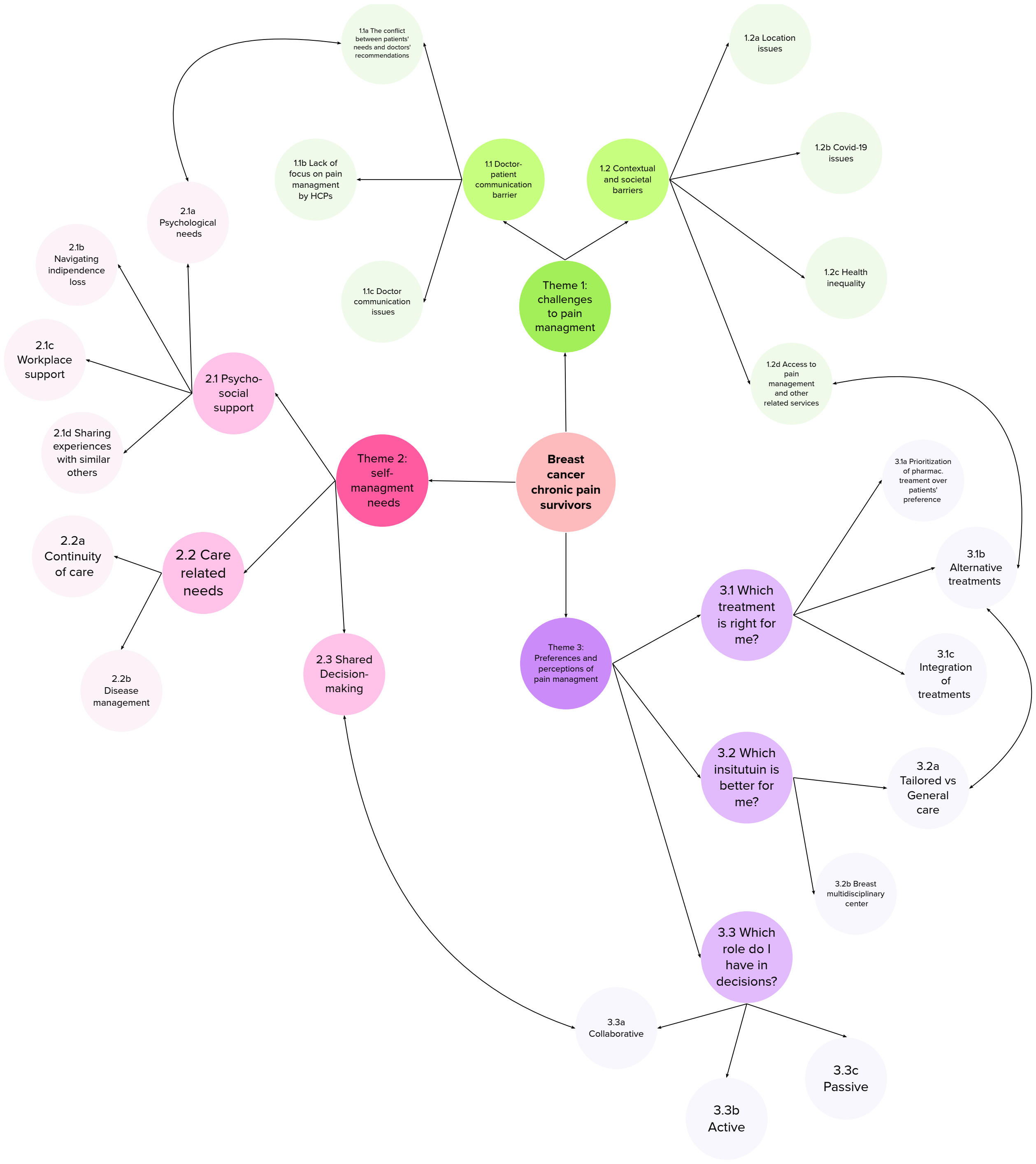


Notes. The figure utilizes a color spectrum ranging from light green to dark blue to demonstrate the prevalence of pain across various body regions. Lighter hues represent less frequent pain reports, while darker tones indicate areas with more frequent pain occurrences. The horizontal and vertical axes of the diagram serve as coordinates for the reported pain locations. It should be noted that the color intensity represents the count of pain reports per area, not the severity of the pain. The visual does not differentiate between the body's left and right sides in depicting pain locations. Additionally, although the diagram acknowledges pain originating from joints, bones, and muscle retractions, these details are not visually represented on the map.

The thematic analysis

The analysis identified three primary themes encapsulating patients' perspectives on pain and its management. Details of each theme are outlined below and visually represented in Figure 7 (adapted from Filipponi et al. [243]).

Figure 7. Map of themes derived from the qualitative thematic analysis



Notes. HCPs = Healthcare providers; Pharmac. = Pharmacological. The diagram employs a range of colors (green, purple, violet) to differentiate the three primary themes extracted from the thematic analysis. Unidirectional arrows connect each primary theme to its respective subthemes, whereas bidirectional arrows illustrate interactions between subthemes across different main themes. This use of color and directional arrows adeptly illustrates the linkages and interrelationships among the established themes and subthemes. Importantly, the diagram's organization places the main themes and subthemes on the first two levels, with a third level dedicated to associated topics.

Theme 1: Patients' challengers to pain management

Theme 1 addresses the multifaceted challenges patients encounter in pain management, categorized under two main sub-themes: (1.1) "Doctor-patient communication barriers" and (1.2) "Contextual and societal barriers".

Sub-theme 1.1 highlights the conflict between patients' needs and doctors' recommendations (1.1a). Patients have expressed significant concern about their hesitancy to adhere to painful cancer treatment protocols prescribed by doctors. A key element contributing to the barriers in doctor-patient communication is how doctors communicate (1.1c). As participants recounted their experiences, two primary concerns surfaced. First, they are frustrated that physicians often view pain solely as a physical issue, which restricts their ability to discuss the psychological aspects associated with their pain. This compartmentalization of knowledge and expertise limits how patients can express their emotions. Second, participants have noted a significant lack of empathy from doctors, feeling treated more like case numbers or hypothetical cases rather than as individuals enduring genuine suffering. Conversely, participants who experienced empathy and support from their doctors reported gratitude. This support has reduced their anxiety and enhanced their openness in discussing their concerns, thereby fostering a deeper trust in their healthcare relationships.

In sub-theme 1.2, patients deal with location-related issues (1.2a), COVID-19 restrictions (1.2b), and health inequalities (1.2c) that contribute to their distress and the financial burden of accessing care. Patients reported that transportation costs, healthcare delays, and the closure of physical facilities like gyms during lockdowns have negatively impacted the way in which they cope with pain. Health inequality also presents challenges, including fears of medical malpractice, treatment disparities, and prolonged waiting periods within public health services, all of which influence the patient-doctor relationship. Another problem identified by patients is inadequate access to pain management services (1.2d), characterized by insufficient information and a lack of practical tools. Patients advocated for more informative resources, such as brochures, booklets, and educational videos, to better understand and manage their pain. For a detailed summary, refer to Table 10 (adapted from Filipponi et al. [243]).

Theme 2: Patients' self-management needs

Theme 2 delves deeply into the challenges and needs of patients managing pain from their cancer treatments, categorized into three distinct sub-themes that reflect the patients' diverse experiences during the study: (2.1) "Psycho-social support", (2.2) "Care-related needs", and (2.3) "Shared decision-making".

Within the first sub-theme, (2.1) Psycho-social Support, the narrative unfolds around the psychological needs of the patients (2.1a), often under-addressed during their medical consultations. Participants articulated profound dissatisfaction with their interactions with healthcare providers, who frequently failed to acknowledge, understand, trust, or reassure them. This lack of emotional support led to heightened feelings of frustration and anger. Amidst their struggles, the concept of hope emerged as a beacon, with patients expressing a desire for more accessible information about available psycho-oncology services, advocating for these services to be a standard part of cancer care. They highlighted the dual necessity of psychological support for themselves and their caregivers, acknowledging the significant emotional toll the cancer journey exerts on all involved.

The discourse around independence (2.1b) revealed that patients grappled with their evolving dependency on partners, feeling burdensome and concerned about the impact on their relationships. The dialogue also turned to the workplace (2.1c), where participants voiced a need for better support and accommodations to help balance their health needs with professional obligations, thus maintaining their employment and dignity.

Community support and sharing were identified as therapeutic, with participants finding solace in connecting with others who had undergone similar experiences (2.1d). They stressed the importance of having a safe space for emotional expression and community building, suggesting the creation of online social groups to facilitate such exchanges.

The second sub-theme, (2.2) Care-Related Needs, highlighted the importance of continuity of care following recovery (2.2a). Participants stressed the need for ongoing support, including home assistance and physical rehabilitation recommendations, underscoring the critical role of physical activity in managing pain—sometimes in contradiction to advice from their romantic partners. Concerns about disease management (2.2b) surfaced as a significant stressor, with participants overwhelmed by the sheer number of medical appointments. This led to the proposal of a mobile application to aid in long-term monitoring and providing information aligned with their preferences, aiming to alleviate some of their burdens.

The third sub-theme, (2.3) Shared Decision-Making, discusses the need for more inclusive and collaborative approaches in healthcare interactions (2.3a). Participants voiced their frustration with the brief consultations, which frequently hindered their ability to communicate their symptoms and worries fully. They advocated for a more inclusive decision-making process that actively involves them and considers their perspectives and choices, ultimately improving the quality of their care. See Table 10.

Theme 3: Patients' preferences and perceptions of pain management

Theme 3 focuses on the preferences and perceptions of patients regarding their pain management, structured into three nuanced sub-themes: (3.1) "Treatment preferences", (3.2) "Institution preference", and (3.3) "Decision role perception".

Under sub-theme (3.1) Treatment preferences, the discussion centers on patients grappling with the decision to prioritize pharmacological treatments over their personal preferences (3.1a). They reflected on various prescribed medications, such as antibiotics, cortisone, ointments, morphine plasters, and other painkillers, voicing concerns over the side effects, which often intensified irritability, frustration, and dissatisfaction rather than mitigating pain. Additionally, the fleeting relief provided by these painkillers left patients uneasy as they faced persistent daily pain.

When pharmacological treatments fall short, patients often consider alternative treatments (3.1b), like acupuncture, psychological support, and holistic practices, including reiki, yoga, and pilates—though not all patients have access to these options. The alternatives mentioned in medical reports usually include physical activities such as walking, swimming, and massage. The accessibility of these treatments varies based on individual circumstances and the effectiveness of painkillers. Patients also highlighted the challenge posed by a lack of awareness about available services, often introduced only after other methods fail, complicating the treatment landscape.

Some patients advocated for an integrated approach to treatment (3.1c), perceiving pharmacological treatments as merely one component of a broader care regimen. In this view, pharmacological methods are considered necessary but not the primary focus, allowing other personal health desires to take precedence.

In the second sub-theme, (3.2) Institution preference, the narrative extends to the desire for personalized interventions (3.2a) rather than a standardized approach. Patients praised the tailored care provided at breast unit multidisciplinary centers (3.2b), where a team of specialists dedicated to breast cancer offers comprehensive, specialized, and coordinated care, valuing the collaboration and expertise of healthcare professionals.

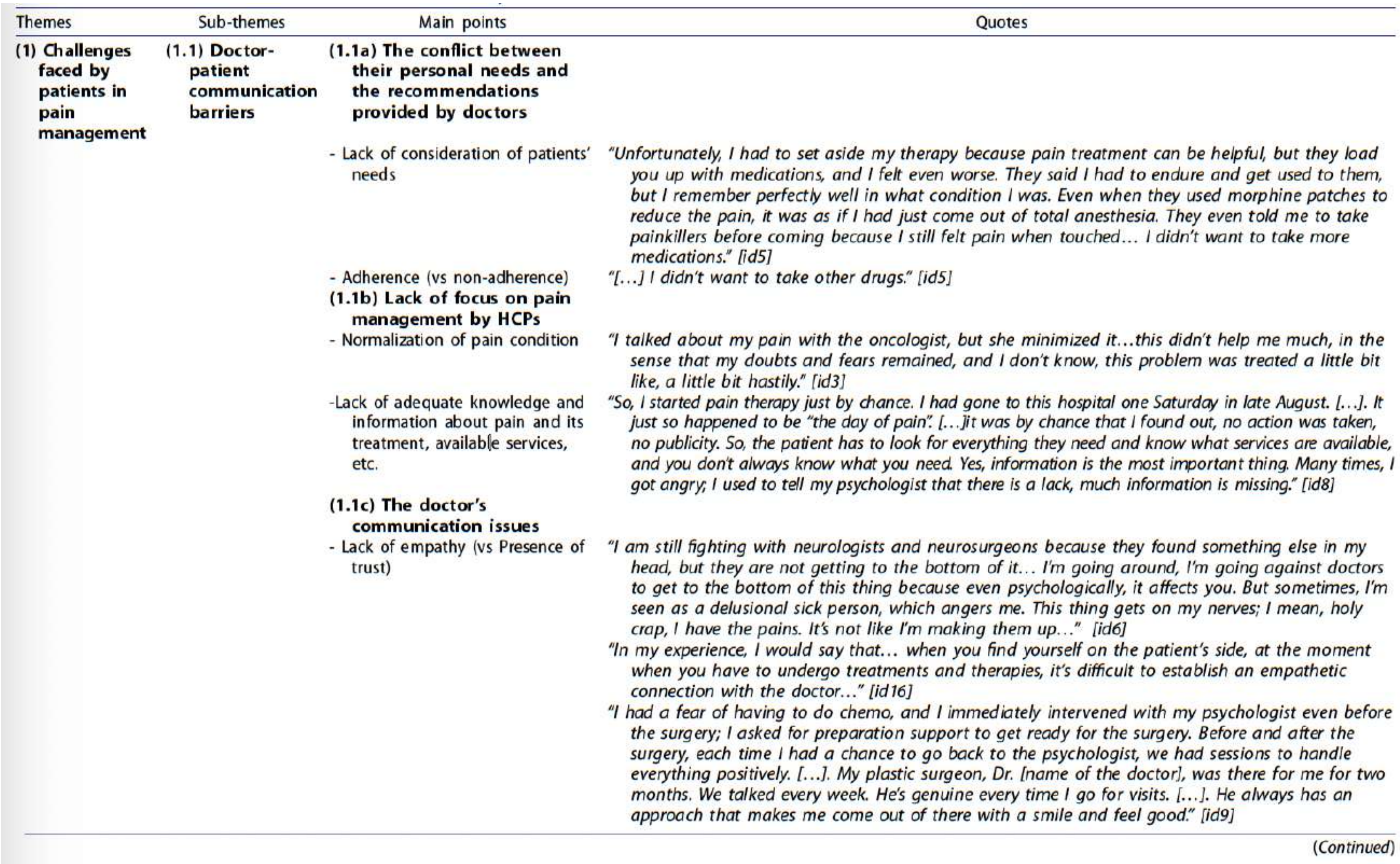
The final sub-theme, (3.3) Decision role perception, explores patients' various roles in their decision-making process. Many favored a collaborative role (3.3a), where patients prefer a SDM approach, actively engaging with their doctors beyond merely agreeing or disagreeing. They appreciated it when doctors understood their detailed concerns, even in the face of time constraints that might rush decisions.

An active role (3.3b) saw some patients playing "devil's advocate", like patient 16, who questioned and challenged proposed options, actively participating in decision-making.

However, this patient later regretted rejecting a reconstruction procedure, recognizing the potential negative outcomes of such decisions.

Conversely, the passive role (3.3c) was characterized by patients who accepted medical decisions with resignation, often expressing their experiences through passive narratives. See Table 10.

Table 10. Themes and subthemes of the thematic analysis



Themes	Sub-themes	Main points	Quotes
(1) Challenges faced by patients in pain management	**(1.1) Doctor-patient communication barriers**	**(1.1a) The conflict between their personal needs and the recommendations provided by doctors**	
		- Lack of consideration of patients' needs	*"Unfortunately, I had to set aside my therapy because pain treatment can be helpful, but they load you up with medications, and I felt even worse. They said I had to endure and get used to them, but I remember perfectly well in what condition I was. Even when they used morphine patches to reduce the pain, it was as if I had just come out of total anesthesia. They even told me to take painkillers before coming because I still felt pain when touched… I didn't want to take more medications." [id5]*
		- Adherence (vs non-adherence)	*"[…] I didn't want to take other drugs." [id5]*
		(1.1b) Lack of focus on pain management by HCPs	
		- Normalization of pain condition	*"I talked about my pain with the oncologist, but she minimized it…this didn't help me much, in the sense that my doubts and fears remained, and I don't know, this problem was treated a little bit like, a little bit hastily." [id3]*
		-Lack of adequate knowledge and information about pain and its treatment, available services, etc.	*"So, I started pain therapy just by chance. I had gone to this hospital one Saturday in late August. […]. It just so happened to be "the day of pain". […]it was by chance that I found out, no action was taken, no publicity. So, the patient has to look for everything they need and know what services are available, and you don't always know what you need. Yes, information is the most important thing. Many times, I got angry; I used to tell my psychologist that there is a lack, much information is missing." [id8]*
		(1.1c) The doctor's communication issues	
		- Lack of empathy (vs Presence of trust)	*"I am still fighting with neurologists and neurosurgeons because they found something else in my head, but they are not getting to the bottom of it… I'm going around, I'm going against doctors to get to the bottom of this thing because even psychologically, it affects you. But sometimes, I'm seen as a delusional sick person, which angers me. This thing gets on my nerves; I mean, holy crap, I have the pains. It's not like I'm making them up…" [id6]* *"In my experience, I would say that… when you find yourself on the patient's side, at the moment when you have to undergo treatments and therapies, it's difficult to establish an empathetic connection with the doctor…" [id16]* *"I had a fear of having to do chemo, and I immediately intervened with my psychologist even before the surgery; I asked for preparation support to get ready for the surgery. Before and after the surgery, each time I had a chance to go back to the psychologist, we had sessions to handle everything positively. […]. My plastic surgeon, Dr. [name of the doctor], was there for me for two months. We talked every week. He's genuine every time I go for visits. […]. He always has an approach that makes me come out of there with a smile and feel good." [id9]*

(*Continued*)

Themes	Sub-themes	Main points	Quotes
		- Compartmentalization of physician's expertise	*"When I go to the oncologist, I tell him everything; if there is something that worries me a little bit, I try, however, to stay in his field because, as all others said, their expertise is limited to one field, the field of pathology."[id4]*
	(1.2) Contextual and societal barriers	**(1.2a) Location issues**	
		-Far away from home -Transport cost -Roadblocks	*"[…]. I live in Sardinia. This represents a problem because I must always cross the sea to visit this hospital. […]. During chemotherapy and radiation therapy, I had to move for a month to Milan because then we were in full lockdown [COVID-19]. I started it [referring to therapy] in March 2020 and moved there, but not everybody can afford to do something like that, so I don't know." [id6]*
		(1.2b) Covid-19 issues - Gym closed	*"You could not go in the gym because it was closed for a while […]. After starting hormone therapy, I put on 2 kg. This bothers me very, very much." [id16]*
		-Lockdown: Sense of abandonment and healthcare slowdowns due to emergency	*"Among other things, the second surgery, unfortunately, was the mastectomy with dorsal flap reconstruction, and it happened just near the beginning of the pandemic. So I found myself in Umbria, and I had to return to Milan for medication. It was disappointing because here in Perugia, they did not allow me to go anywhere. I really had a moment of crisis. […] During this pandemic, it's really difficult to have meaningful conversations with the family doctor. Ah, this hospital is always there, but with the family doctor, I feel somewhat abandoned to myself. We hope this situation will improve." [id9]*
		(1.2c) Health inequality -Medical malpractice -Disparities -Long waiting list in health public services	*"I started a consultation here earlier [referring to the hospital in her country], and I must say that I didn't feel well at all with the doctor-patient approach. It made me quite alarmed, and things were already at their worst, to be honest. I preferred coming to your hospital because there's a noticeable difference in the way you handle things. Even though we might say that the same procedures are available, they don't always follow the protocol. But I wanted to address another issue as well, which is what I mentioned at the beginning. Unfortunately, there's a significant disparity in healthcare between the South and the North. That's been my experience, and it remains a significant problem." [id11]*
		(1.2d) Lack of access to pain management and related services -Lack of knowledge/awareness about services offered/available -Lack of instruments to better management	*"I was fortunate to learn about this service, as [name of another patient] mentioned. I have a friend who works at this hospital as a psycho-oncologist. She came to visit me when I had surgery and said, 'Did you know about this service here?' If she hadn't been there, I probably wouldn't have known about it." [id7]*

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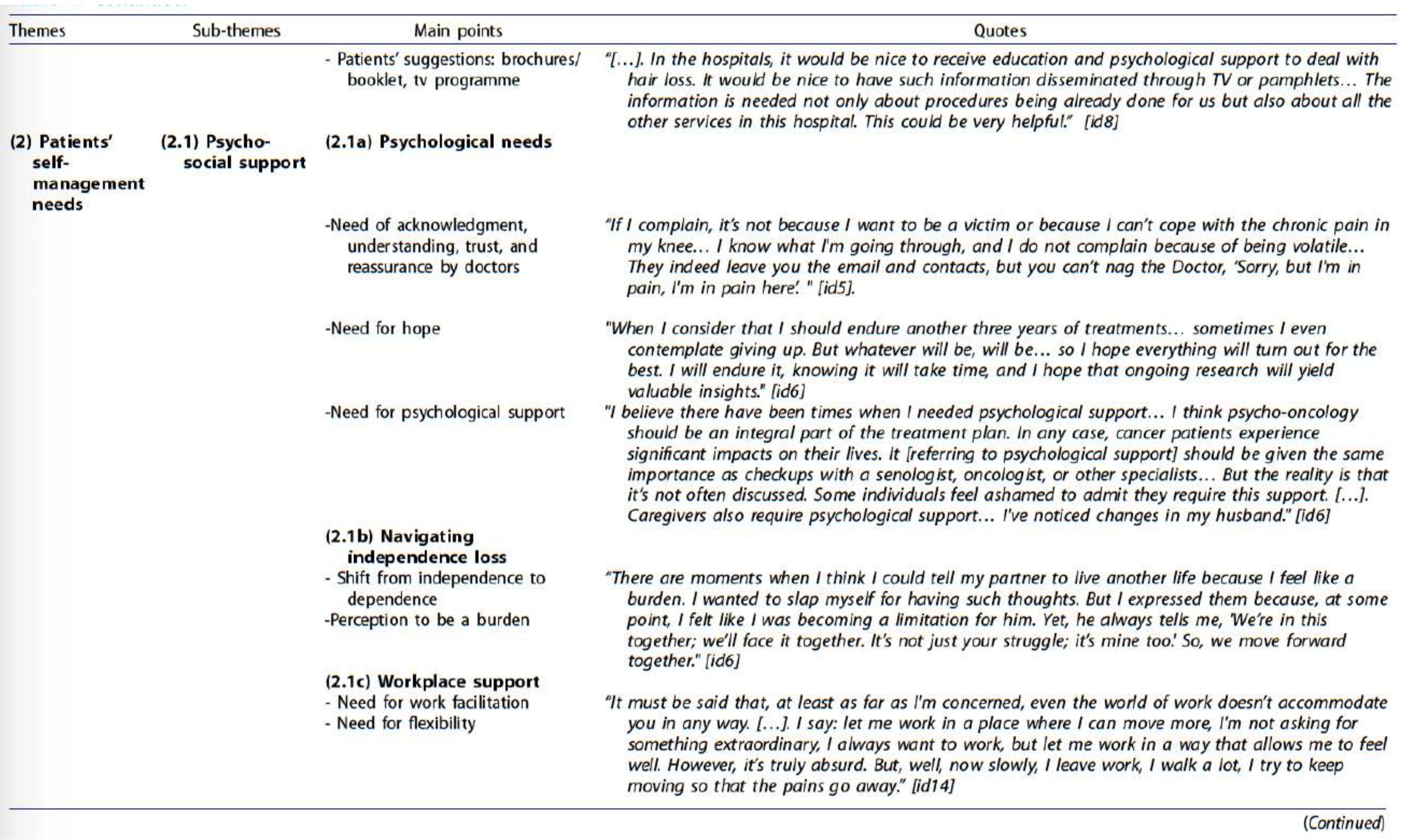

Themes	Sub-themes	Main points	Quotes
		- Patients' suggestions: brochures/ booklet, tv programme	"[…]. In the hospitals, it would be nice to receive education and psychological support to deal with hair loss. It would be nice to have such information disseminated through TV or pamphlets… The information is needed not only about procedures being already done for us but also about all the other services in this hospital. This could be very helpful." [id8]
(2) Patients' self-management needs	**(2.1) Psycho-social support**	**(2.1a) Psychological needs**	
		-Need of acknowledgment, understanding, trust, and reassurance by doctors	"If I complain, it's not because I want to be a victim or because I can't cope with the chronic pain in my knee… I know what I'm going through, and I do not complain because of being volatile… They indeed leave you the email and contacts, but you can't nag the Doctor, 'Sorry, but I'm in pain, I'm in pain here'. " [id5].
		-Need for hope	"When I consider that I should endure another three years of treatments… sometimes I even contemplate giving up. But whatever will be, will be… so I hope everything will turn out for the best. I will endure it, knowing it will take time, and I hope that ongoing research will yield valuable insights." [id6]
		-Need for psychological support	"I believe there have been times when I needed psychological support… I think psycho-oncology should be an integral part of the treatment plan. In any case, cancer patients experience significant impacts on their lives. It [referring to psychological support] should be given the same importance as checkups with a senologist, oncologist, or other specialists… But the reality is that it's not often discussed. Some individuals feel ashamed to admit they require this support. […]. Caregivers also require psychological support… I've noticed changes in my husband." [id6]
		(2.1b) Navigating independence loss - Shift from independence to dependence -Perception to be a burden	"There are moments when I think I could tell my partner to live another life because I feel like a burden. I wanted to slap myself for having such thoughts. But I expressed them because, at some point, I felt like I was becoming a limitation for him. Yet, he always tells me, 'We're in this together; we'll face it together. It's not just your struggle; it's mine too.' So, we move forward together." [id6]
		(2.1c) Workplace support - Need for work facilitation - Need for flexibility	"It must be said that, at least as far as I'm concerned, even the world of work doesn't accommodate you in any way. […]. I say: let me work in a place where I can move more, I'm not asking for something extraordinary, I always want to work, but let me work in a way that allows me to feel well. However, it's truly absurd. But, well, now slowly, I leave work, I walk a lot, I try to keep moving so that the pains go away." [id14]

(Continued)

Themes	Sub-themes	Main points	Quotes
		(2.1d) Sharing experiences with similar others	
		- Reduction of the reluctance to report their feelings and emotions -Sense of community -Emotional exposure -Patients' suggestion: online social group	*"In the family, they all reacted badly, even friends; however, over time, I realized that it's one thing to talk to a person who has gone through a similar experience as you. […] It's another thing to discuss with someone with no such experience, even if they are family members. Because nobody besides you [referring to other patients in the focus group] can understand what I'm going through, what we're going through." [id4]* *"I think it would be beneficial to have forums specifically for patients of this hospital categorized by diseases. We could have sections for breast problems, uterine problems, and other areas. It would be beneficial not just for psychological support but also to alert each other if there are any alarming signs. For example, if someone says, 'I had the same experience, and it turned out to be serious,' it could prompt others to seek medical attention. Having such a forum would be truly valuable." [id1]*
	(2.2) Care-related needs	**(2.2a) The continuity of care**	
		- Home assistance: ongoing support after recovery - Physical rehabilitation from home	*"When I keep moving, walking, even just around the house, my husband tells me to take a break. Paradoxically, it's worse because if I truly stop, it's the end. That's why the only solution is to stay active, even on Sundays." [id14].*
		(2.2b) Concerns about disease management	
		- Healthcare agenda - Patient-centered management - Patients' suggestion: App	*"[…] some apps that would ask me to make notes in the form of a diary in which I would also speak about psychological aspects rather than physical, the pain, etc., […]. This could also indicate some alarming changes happening in you. Knowing there is communication, even if indirect or technological, would make us feel better. The perception that someone has taken us by the hand carries on, even if they are not there. […] An app where I could report perceptions or experiences related to various states of my being." [id4]* *"I made a pain diary. I had just pages and pages with dates, hours, and activities. I did it because when you go to the doctor, you cannot tell them: 'I have pain'. I had the pain of getting in the car to go up the stairs. I mean, I was prevented from doing several daily activities. So, I believe an app where you can write about all of this could be helpful." [id17]*
	(2.3) Shared decision-making	**(2.3a) Collaborative-active approach**	
		-Need for active involvement in decisions	*"They don't tell you what will be waiting for you in the short term, in a month, in the long term, 24 months. […] They speak of the present, but sometimes it's not enough. If I had known, if I had been made aware, of the trouble I was heading to, I would have made different choices." [id4]*

(Continued)

Themes	Sub-themes	Main points	Quotes
(3) Patents' preferences and perceptions of pain management	**(3.1) Treatment preferences**	**(3.1a) Prioritizing of pharmacological treatments over patients' preferences**	
		-Concerns and Unsatisfaction with drugs prescribed -Worries about side effects -Immediate relief, but then?	*"I cannot go on anymore with all the drugs." [id13]* *"[…] the only side effect that deteriorates the bones." [id14]*
		(3.1b) Alternative treatments - Attempts due to drug failure - Discovered by chance	*"[…] and then with the help of the physiotherapist I did a lot of pain therapy…* *I had physical therapy at home […]. .I remember I used to tell the physical therapist: 'Take my arm', because, as [name of another patient] said, I had a piece of cement instead of an arm. I used to say: 'Take my arm and move it because if I have to do it myself, I stop right away due to pain'. So, you would say in these services: 'Okay, it's the first time for me, I'm hurting; whom can I lean on, what do I need?' and the answer would be: 'Here's this; here's what we offer'." [id5]*
		(3.1c) Integration of treatments -Attempts with a combination of treatments It's not for everyone: you must discuss it with your physician	*"My life companion for ten years now is physical activity. It's not so much, but I always walk and avoid taking the elevator…if I go somewhere within walking distance, I walk. It's my life partner: physical activity. […] I do it along with other drugs. So, I took it as a medicine." [id13]*
	(3.2) Institution preferences	**(3.2a) Tailored vs General care**	
		-Better take charge -Being seen as a person instead of a disease	*"I preferred to come to this hospital since there is a significant difference in treatment between hospitals. Even though they say you can do the same things at their place [referring to the general hospital], they sometimes need to follow the protocol. They follow the existing general protocol, whereas, at this hospital, it can be tailored. So, it is more specific." [id11]*
		(3.2b) Breast multidisciplinary center - Multidisciplinary of the care	*"I would have really preferred it because when I joined doctors at this hospital for various health issues, they were more attuned to our needs and our medical conditions rather than a generic psychologist, using this term - mine is excellent, okay - but I find that even the physiotherapist, in simple terms, was much more in tune, forgive the expression, than the physiotherapist I've been seeing for twenty years when they treated me… no, I mean, I would have preferred it, maybe, well, there's distance, but there's technology that helps us, as in this case, right."[id4]*

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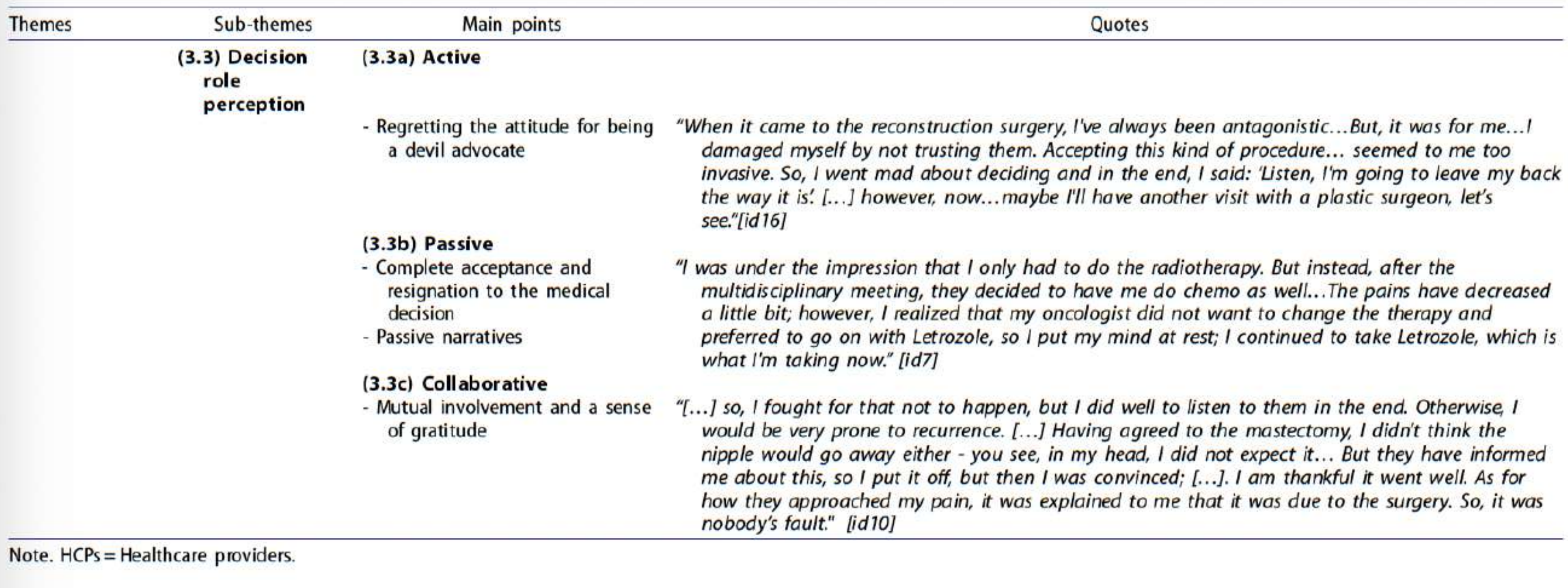


Themes	Sub-themes	Main points	Quotes
	(3.3) Decision role perception	**(3.3a) Active**	
		- Regretting the attitude for being a devil advocate	*"When it came to the reconstruction surgery, I've always been antagonistic…But, it was for me…I damaged myself by not trusting them. Accepting this kind of procedure… seemed to me too invasive. So, I went mad about deciding and in the end, I said: 'Listen, I'm going to leave my back the way it is'. […] however, now…maybe I'll have another visit with a plastic surgeon, let's see."[id16]*
		(3.3b) Passive	
		- Complete acceptance and resignation to the medical decision - Passive narratives	*"I was under the impression that I only had to do the radiotherapy. But instead, after the multidisciplinary meeting, they decided to have me do chemo as well…The pains have decreased a little bit; however, I realized that my oncologist did not want to change the therapy and preferred to go on with Letrozole, so I put my mind at rest; I continued to take Letrozole, which is what I'm taking now." [id7]*
		(3.3c) Collaborative	
		- Mutual involvement and a sense of gratitude	*"[…] so, I fought for that not to happen, but I did well to listen to them in the end. Otherwise, I would be very prone to recurrence. […] Having agreed to the mastectomy, I didn't think the nipple would go away either - you see, in my head, I did not expect it… But they have informed me about this, so I put it off, but then I was convinced; […]. I am thankful it went well. As for how they approached my pain, it was explained to me that it was due to the surgery. So, it was nobody's fault." [id10]*

Note. HCPs = Healthcare providers.

3.1.4 Discussion

This study explores three integral themes: the challenges, self-management needs, and treatment preferences and perceptions among breast cancer survivors with CP. It's vital to consider these themes and their subthemes as interconnected parts of a continuum, as this perspective elucidates how the patient's needs and preferences emerge in response to the barriers faced in managing breast cancer pain.

Utilizing focus groups allowed us to delve deeply into patients' needs and emotional states, often elusive in quantitative methodologies such as self-reports [250]. As Peretti-Watel [166] noted, patients are more likely to openly discuss their pain in spoken conversations rather than in written assessments, frequently underestimating their pain and dismissing it as a "normal nuisance". This tendency was also evident in our findings. While few participants reported high pain levels when responding to questionnaires, most described significant pain experiences during focus group discussions. Moreover, during the recruitment phase, several individuals declined to participate, citing no pain, yet later discussed their pain with the recruiting researchers. This behavior may indicate a normalization of pain and a denial of the pain experience.

The hesitance to address experienced pain can be traced to two main factors: misconceptions held by patients and the attitudes of doctors. Patients often view pain as an inevitable part of recovery or a persistent condition that must be tolerated, a sentiment supported by their personal experiences and corroborated by the literature [51,53,166,251]. Conversely, doctors may minimize the significance of pain, viewing it as a minor symptom expected to decrease over time [252]. This attitude contributes to barriers in doctor-patient communication, particularly concerning pain management. Moreover, the literature underscores an ongoing need to address the gaps in knowledge regarding cancer pain management among healthcare providers [53,253,254]. A lack of adequate education is identified as a major barrier to effective pain management, impacting both providers and patients. For instance, another qualitative study [255] revealed that breast cancer patients did not anticipate the persistence of pain post-surgery, voicing concerns over the lack of information provided about pain management or the risk of ongoing pain during recovery and subsequent follow-ups.

Moreover, it is essential to consider the influence of sex/gender bias in patient-provider interactions. Research has shown that female patients with CP often face invalidation and dismissive attitudes from healthcare providers, which can lead to discrediting, silencing, and stereotyping of their pain experiences [256,257]. This disenfranchising talk can harm patients' agency, credibility, access to care, and support, ultimately affecting the patient-provider relationship. By recognizing and addressing these biases, healthcare providers can foster more supportive and empathetic communication, thereby improving pain management outcomes for female patients.

Participants also highlighted the critical need for patients to know the available pain management services, tools, and options, including pharmacological and nonpharmacological treatments. This requirement is supported by the literature [9,28], which stresses the importance of a multidisciplinary and biopsychosocial approach to cancer pain. This method guarantees that patients' preferences are acknowledged and that their cultural and belief systems are respected. It is vital to move beyond the conventional view that cancer pain is purely a physical and biological phenomenon and to investigate the psychosocial elements that also influence pain. Examining the fundamental causes of physical and mental pain and understanding its unique impacts on individuals can address the needs highlighted by participants in this research. Embracing the biopsychosocial model transforms the understanding of cancer pain from mere tissue damage to a comprehensive experience that encompasses various aspects of QoL.

Patients frequently face uncertainty regarding various aspects of pain management [201,226,227], as evidenced by our study. This uncertainty manifests as a series of "what-if" scenarios related to cancer, which are filled with dread and anxiety [218]. For instance, patients may ponder whether their cancer will spread, reduce, or return. They also face uncertainty about the variety of cancer treatments, the procedures involved, and the nature and duration of the pain they experience. A recent systematic review [230] indicates that managing such uncertainties involves several components, with informational support being crucial. In this context, eHealth tools emerge as a promising method for implementing these interventions [143,144,232], as suggested by our participants. These tools can aid in smoothing the transition from hospital to home care, thus maintaining an uninterrupted continuum of care. By facilitating this transition, eHealth tools help to bridge the gaps between these healthcare environments, reducing disparities in healthcare access and ensuring that all patients, irrespective of contextual or societal barriers, receive care. Nonetheless, as our participants emphasized, while these tools are valuable, they should not supplant the essential doctor-patient relationship, which is fundamental to achieving satisfactory care management.

The results of this study demonstrate that when patients feel supported and empathized with by their doctors, it effectively dismantles barriers within the doctor-patient relationship, creating a secure environment where patients can easily share their emotions and feelings. In this setting, participants expressed their appreciation for the comprehensive support provided by their doctors, which alleviated their concerns and encouraged open discussions about their pain-related worries. This, in turn, reinforced their trust in their healthcare providers. These findings are consistent with a recent meta-analysis [258] that showed significant improvements in cancer patients' outcomes, including decreased psychological distress and enhanced satisfaction with care, which were associated with physician empathy as reported by patients.

The necessity for support extends beyond medical professionals to include primary caregivers. The study reveals that although a chronic condition may disrupt patients' sense of independence, they recognize they are not alone. This recognition of what we have termed the *co-dependence effect* in our previous study [172] underscores the importance of relational dynamics. According to the STM [93,94], interdependence and mutuality play critical roles when two partners manage a chronic illness together. This not only means that the stress experienced by one partner affects the other but also that the resources of one partner enhance those of the other, creating new dynamics that help both cope more effectively with the illness.

Another source of support identified in this study comes from individuals who have experienced similar health challenges. Participants found group discussions immensely beneficial for expressing emotions, noting that those who have faced similar struggles truly comprehend their journey. This process, which we describe as emotional exposure, enables patients to genuinely share their emotions, thoughts, and experiences. Such shared experiences cultivate a sense of community, providing reassurance and support during difficult times, as corroborated by other research [202,218,259]. Participants proposed the creation of a social media group as a viable option for fostering connections with peers, enhancing mutual understanding and empathy, and facilitating the exchange of knowledge and support. It has also been shown that such online social groups can effectively empower patients to manage their chronic conditions [260].

In summary, this research underscores the importance of addressing patients' needs and preferences in pain management and actively involving them in decision-making. A recent meta-synthesis of qualitative studies [240] highlights that healthcare providers should prioritize supporting patients by considering their needs and preferences rather than merely attempting to manage them. A fundamental practice in medicine should involve providing patients with comprehensive information, enabling them to participate actively in their medical decisions. This approach is foundational to SDM, which embodies the core of patient-centered medicine [147]. SDM entails patients and doctors evaluating the best available evidence when making decisions while aiding patients in exploring their options to form well-informed preferences. Considering patients' preferences is essential as it may help prevent future regret associated with these decisions [150]. In this study, participants voiced a strong desire for collaborative decision-making with their healthcare providers, emphasizing the importance of being actively involved. This engagement is vital to ensure patients' concerns are fully addressed and their voices are effectively heard.

This study highlights critical clinical implications that warrant attention. Firstly, it underscores the importance of a multidisciplinary team of social workers, psychologists, and other healthcare providers to effectively treat patients with chronic illnesses. For example, Melanie McDonald and Hardeep Gill from Pain BC [261] have developed free resources tailored for British Columbian breast cancer patients experiencing CP. These resources encompass a broad spectrum of support services, including establishing a dedicated pain support line, providing at-home activity options, educating healthcare providers on the subjective nature of pain experiences, and organizing support groups and coaching sessions. Social workers, driven by their professional ethos, are urged to proactively prioritize pain management, consider patients' holistic needs, and foster collaboration within relationship models to empower patients [262].

Maintaining continuity of care beyond five years of survival poses significant challenges following hospital discharge, thus emphasizing the need for innovative facilities that integrate seamlessly into patients' daily lives. Profiling patients based on their treatment preferences and clinical features is crucial for empowering them, enhancing their understanding of available treatments, and facilitating collaborative decision-making in their care. In this dynamic, the role of a psychologist is paramount. Our recent work [263,264] demonstrates that this approach can be implemented by developing a new digital health ecosystem that integrates mobile applications to ensure a seamless transition and continuity of care from hospital to home. This ecosystem is specifically designed to overcome barriers to effective pain management and cater to the unique needs of patients with breast cancer and post-stroke conditions. It also addresses the needs of caregivers, but this support is exclusively for the post-stroke groups. See Chapter 4.

Limitations

This study has several limitations that should be considered. First, it lacks detailed socio-demographic information, such as the participant's education level, marital status, and employment status. Moreover, all participants were solely Italian and shared a homogeneous cultural background, potentially restricting the generalizability of the results to different cultural settings. It should also be mentioned that the descriptions and reports of pain characteristics relied on participants' self-reports, not clinical assessments. Due to the intricate nature of cancer treatment, which encompasses multiple medical procedures, accurately identifying the precise origin of pain for each participant proved difficult. Nonetheless, our focus on the iatrogenic nature of reported pain is intended to shed light on the unique pain experiences of individuals undergoing cancer treatments, highlighting the necessity for tailored pain management strategies in the post-treatment phase.

Moreover, the data concerning the type of pain, sensations experienced, specific body parts affected, and medications administered were all derived solely from patient narratives. It should be acknowledged that these narratives might not encompass the experiences of all individuals, introducing complexity into the interpretation of pain experiences within the study group. Although these constraints impact our results' broad applicability and thoroughness, they also establish a foundation for future studies designed to delve into the subtler aspects of pain experiences across varied populations in cancer treatment contexts.

3.2 *Study 3, part B: Exploring the Emotional Experiences of Caregivers in the Journey of Breast Cancer Survivors with Chronic Pain: A Mixed Methods Analysis*

3.2.1 Aim of the Study

The second part of the third study focused on examining the linguistic expressions that depict the emotional experiences of caregivers. In this context, "caregivers" refers specifically to informal caregivers—such as partners, family members, or close friends—who provide support to individuals living with CP who are breast cancer survivors. The objective was to uncover both basic and complex emotions associated with these caregiving roles, highlighting the emotional challenges informal caregivers face in assisting their loved ones.

3.2.2 Material and Methods

Study design and recruitment

The research utilized focus groups to explore the emotional landscape of caregivers who assist breast cancer survivors with CP. Owing to COVID-19 restrictions, these discussions were facilitated through Zoom video calls. We followed the guidelines by Krueger and Casey [241] to adjust to the virtual format [242]. Only participants free from psychiatric or neurological disorders were eligible, and those who opted out were excluded. The study ultimately included 13 caregivers (M_{age}=43.17, SD=10.97), although two recruited individuals did not attend on the designated day without providing a reason. The caregivers were primarily family members (predominantly husbands, N=8, 62%) and friends of the breast cancer survivors with CP. Ethical approval was secured from the Ethics Committee of IEO (ID: R1508/21-IEO1594).

Procedure

Before participating, each participant gave informed consent via digital and hand-written signatures. The participants were organized into three focus groups, each containing 4 or 5 members. The discussions lasted between 60 and 90 minutes. Two experienced psychologist-researchers (CF, ST), skilled in managing focus groups, led the discussions. There were no prior relationships between the moderators and the participants. Following an introductory overview of the research objectives and initial self-introductions by the participants, a sequence of fundamental questions was presented, consistent with the established thematic guidelines:

1. Barriers in cancer pain management: *Thinking about yourself and your daily life, what difficulties do you face in managing the pain of the person you care for, or what barriers do you perceive hinder effective pain management?*
2. Needs in cancer pain management: *When assisting the person you care for, what are your needs regarding the care and its management?*
3. Involvement in the cancer treatment decision-making process: *Have you discussed the treatment preferences of the person you care for with the doctor, other caregivers, or anyone significant to you?*
4. Treatment preferences in cancer pain management: *Which treatment would you prefer to pursue for managing the pain of the person you care for?*

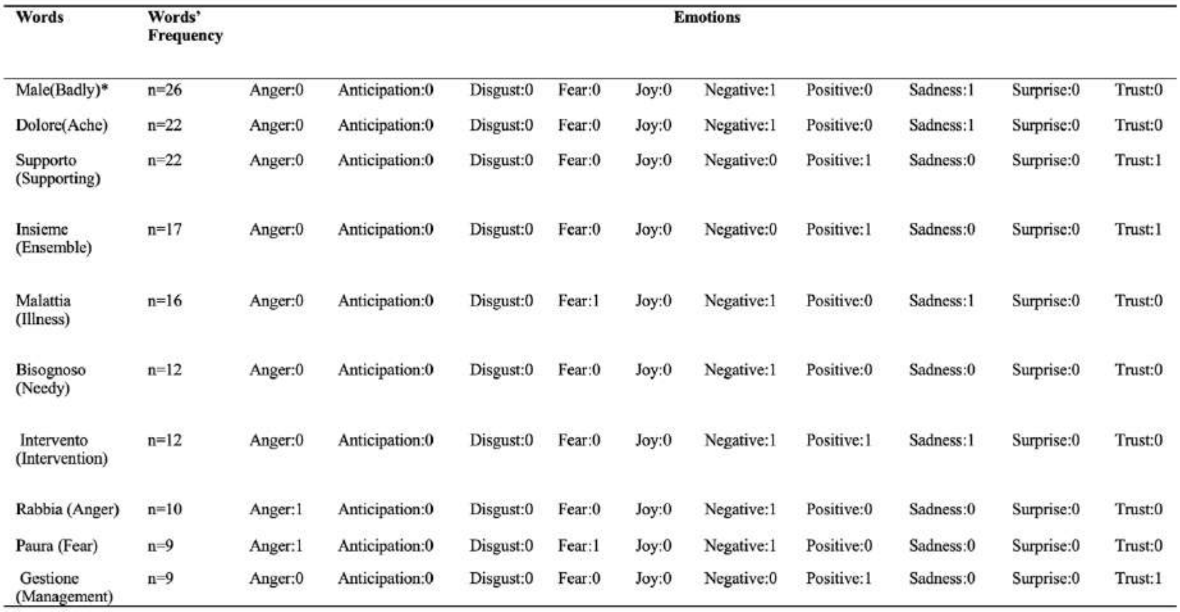
The focus groups were comprehensively audio-recorded, and the first author performed a verbatim transcription, meticulously ensuring the removal of all identifiable details. The number of focus groups was determined by established literature recommendations [245]. Field notes were consistently taken during the discussions.

Data analysis

The statistical analysis was executed using R Studio version 4.1.2 (2021-11-01) [208]. To analyze the caregiver transcripts, we utilized the “Syuzhet” R package [212]. The analysis of emotions and sentiments was conducted using the “get_nrc_sentiment” function, which incorporates eight primary emotions and two sentiments based on the NRC Emotion Lexicon [213,214]. This lexicon includes a compilation of words, each linked to primary emotions (anger, fear, anticipation, trust, surprise, sadness, joy, and disgust) and sentiments (positive and negative), consistent with Plutchik's wheel of emotions [233]. In this framework, sadness is identified by a feeling of weight and terms such as “drained” or “loss” and arises from perceived reduced interactions with a close person. Fear is characterized by nervousness with words like “stressed” or “scared” and occurs when a treasured aspect seems at risk. Disgust, linked with feelings of revulsion and words such as “distrust” or “rejecting”, is triggered when something appears fundamentally incorrect or breaches usual standards, possibly in relation to a loved one’s state. Anger is generally marked by a sense of power and heat, with terms like “mad” or “fierce” signaling an obstacle to progress. Surprise involves a racing heart and terms like “shocked” or “unexpected”, indicating an unforeseen event that demands immediate attention. Trust is felt as warmth and described with words like “accepting” or “safe”, denoting reliability and safety in a relationship, which helps build bonds with others. Anticipation, characterized by eagerness and vigilance, suggests a readiness for change and a willingness to embrace new experiences. Joy brings excitement and potential, providing positive moments amidst difficulties, which fuels creativity, deepens relationships, and boosts enduring energy.

Through the “get_nrc_sentiment” function, the NRC lexicon aligned words in the dataset with those in the lexicon, identifying their associated emotions and sentiments. Each association is labeled as either “0” or “1”, where “0” denotes no connection and “1” represents a clear link. Words can align with several emotions and possess a positive, negative, or neutral tone. For instance, terms associated with anger, fear, disgust, and sadness often convey negative feelings, while those linked to anticipation, joy, and trust usually reflect positive sentiments. Words denoting surprise can have either positive or negative polarity, depending on the context. Table 11 lists ten words from the dataset, showing their assignment to the eight fundamental emotions of the lexicon (adapted from Filipponi et al. [265]). The lexicon also highlighted sentences with the most intense emotions, uncovering key themes and discussions. It provided a foundational structure for narratively detailing the most emotionally compelling topics, supported by quotes from caregivers, allowing for an explanation of each emotion within its specific context.

Table 11. A snapshot from the data: Analysis of 10 words using the NRC lexicon



Words	Words' Frequency	Emotions									
Male(Badly)*	n=26	Anger:0	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:1	Positive:0	Sadness:1	Surprise:0	Trust:0
Dolore(Ache)	n=22	Anger:0	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:1	Positive:0	Sadness:1	Surprise:0	Trust:0
Supporto (Supporting)	n=22	Anger:0	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:0	Positive:1	Sadness:0	Surprise:0	Trust:1
Insieme (Ensemble)	n=17	Anger:0	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:0	Positive:1	Sadness:0	Surprise:0	Trust:1
Malattia (Illness)	n=16	Anger:0	Anticipation:0	Disgust:0	Fear:1	Joy:0	Negative:1	Positive:0	Sadness:1	Surprise:0	Trust:0
Bisognoso (Needy)	n=12	Anger:0	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:1	Positive:0	Sadness:0	Surprise:0	Trust:0
Intervento (Intervention)	n=12	Anger:0	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:1	Positive:1	Sadness:1	Surprise:0	Trust:0
Rabbia (Anger)	n=10	Anger:1	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:1	Positive:0	Sadness:0	Surprise:0	Trust:0
Paura (Fear)	n=9	Anger:1	Anticipation:0	Disgust:0	Fear:1	Joy:0	Negative:1	Positive:0	Sadness:0	Surprise:0	Trust:0
Gestione (Management)	n=9	Anger:0	Anticipation:0	Disgust:0	Fear:0	Joy:0	Negative:0	Positive:1	Sadness:0	Surprise:0	Trust:1

Note. *In () we reported the English words.

Plutchick's Spectrum of Emotional States

Based on Plutchik's model [233], the eight basic emotions can combine to create complex emotions, or dyads, when they pair with one of the other seven basic emotions. Plutchik's wheel visually represents these emotions and their interactions, facilitating understanding of their relationships through spatial organization and identifying primary, secondary, tertiary, or opposite dyads based on their spatial proximity. Leveraging this model, we analyzed the frequencies of basic emotions to identify co-occurrences and establish various types of emotion dyads. Co-occurrence within a sentence was noted when specific emotions appeared in conjunction with others. For example, the combination of fear and anger, which are opposites, results in the complex emotion of “frozenness”. If fear appears twice and anger three times in a sentence, then the occurrence of “frozenness” is recorded as two.

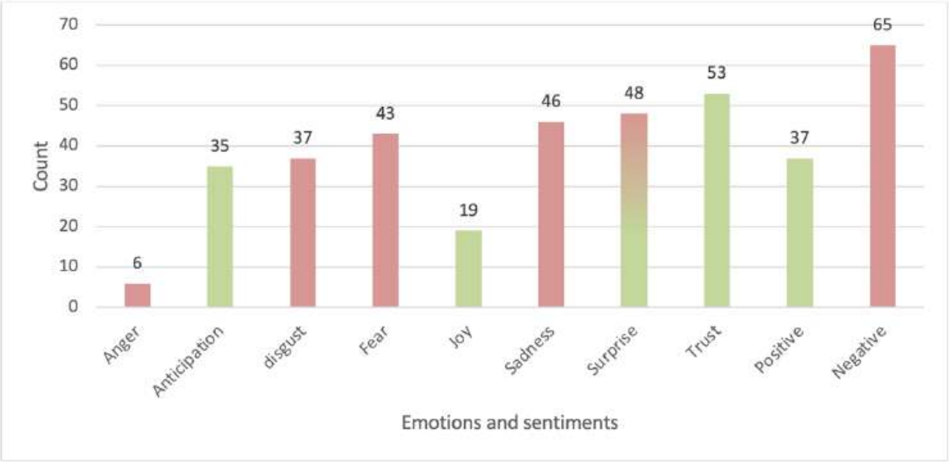
The overall co-occurrences within sentences were quantified to determine the prevalence of specific dyads. The wheel was visualized using Python 3.10.5 [266] with the “PyPlutchik” package [267], which allows for a graphical depiction of Plutchik's wheel of emotions. In the visualizations of each wheel (basic emotions, primary dyads, secondary dyads, tertiary dyads, opposites), the most frequent emotion was scaled to 1, with other emotions adjusted relative to this benchmark. Thus, the emotional scale on the wheel ranges from 0 to 1, where 1 represents the most prevalent emotion.

3.2.3 Results

Sentiment and emotions analysis

The bar chart (see Figure 8, adapted from Filipponi et al. [265]) illustrates the predominant basic emotions and sentiments in the caregivers' verbatim transcripts.

Figure 8. Sentiment and emotion frequencies expressed by caregivers discussing breast cancer and chronic pain care



Notes. Emotions and sentiments linked to negative affects are depicted in red, while those linked to positive affects appear in green. The emotion of surprise, which can reflect either positive or negative affects, is represented by a blend of red and green.

The analysis included a total of 642 sentences and 15,847 words. The frequency of negative sentiment (N=65; M =.06, SD =.25) was higher than that of positive sentiment (N=37; M=.10, SD=.31). Among the negative emotions, sadness (N=46; M =.07; SD=.27) and fear

(N=43; M=.07, SD=.25) were the most common, followed by disgust (N=37; M=.06, SD=.23). Surprise was slightly more prevalent than sadness, with a frequency nearly equal to that of trust (N=48; M=.07, SD=.28).

Caregivers emphasized the difficulties stemming from insufficient preparation in managing CP, frequently experiencing feelings of being overwhelmed by their inability to offer the needed support. This situation could lead to patients feeling inadequately cared for, both within the family and as part of a couple. For instance, a 22-year-old caregiver, the daughter of a 51-year-old woman with lobular carcinoma in her breast, expressed the intense emotions she experienced while assisting her mother. She described the situation as frightening and uncertain due to inadequate information. However, she also recognized the possibility of a positive shift when armed with reliable information:

> *"I mean, my mother, for example, once had her drain slightly occluded, and at night, she was full of blood, and at that time, you get scared, but maybe if you get an answer right away, without having to run somewhere, you can calm down enough to say...OK, we can go slowly; there's nothing deadly right now."*

Among the positive emotions, trust (N=53; M=.08, SD=.28) and anticipation (N=35; M=.05, SD=.23) emerged as the most prevalent, with joy (N=19; M=.03, SD=.18) following. For instance, Caregiver 5, a 45-year-old husband, vividly articulated feelings of trust, anticipation, and joy while discussing the challenges of managing a chronic illness. Although initially comparing the experience to an *unexpected atomic bomb explosion*, which posed daily struggles that could disrupt marital harmony, he acknowledged that facing these challenges could also foster an opportunity to discover new strengths together:

> *"Clearly, this can also change certain dynamics in the couple because it is inevitable...there are times when you say maybe our relationship will be destroyed or maybe it will be strengthened."*

According to the findings from the lexicon-based analysis, caregivers showed minimal expressions of anger (N=6; M=.01, SD=.10). Although the quantitative data indicated rare instances of anger, a more thorough qualitative analysis of caregivers' narratives revealed underlying irritability and frustration. For example, one mother (caregiver 11, aged 59) of a 27-year-old daughter diagnosed with early-stage breast cancer clearly articulated her anger. This emotion was primarily directed towards the medical professionals but stemmed more profoundly from her feelings of frustration and vulnerability while supporting her daughter through additional invasive procedures.

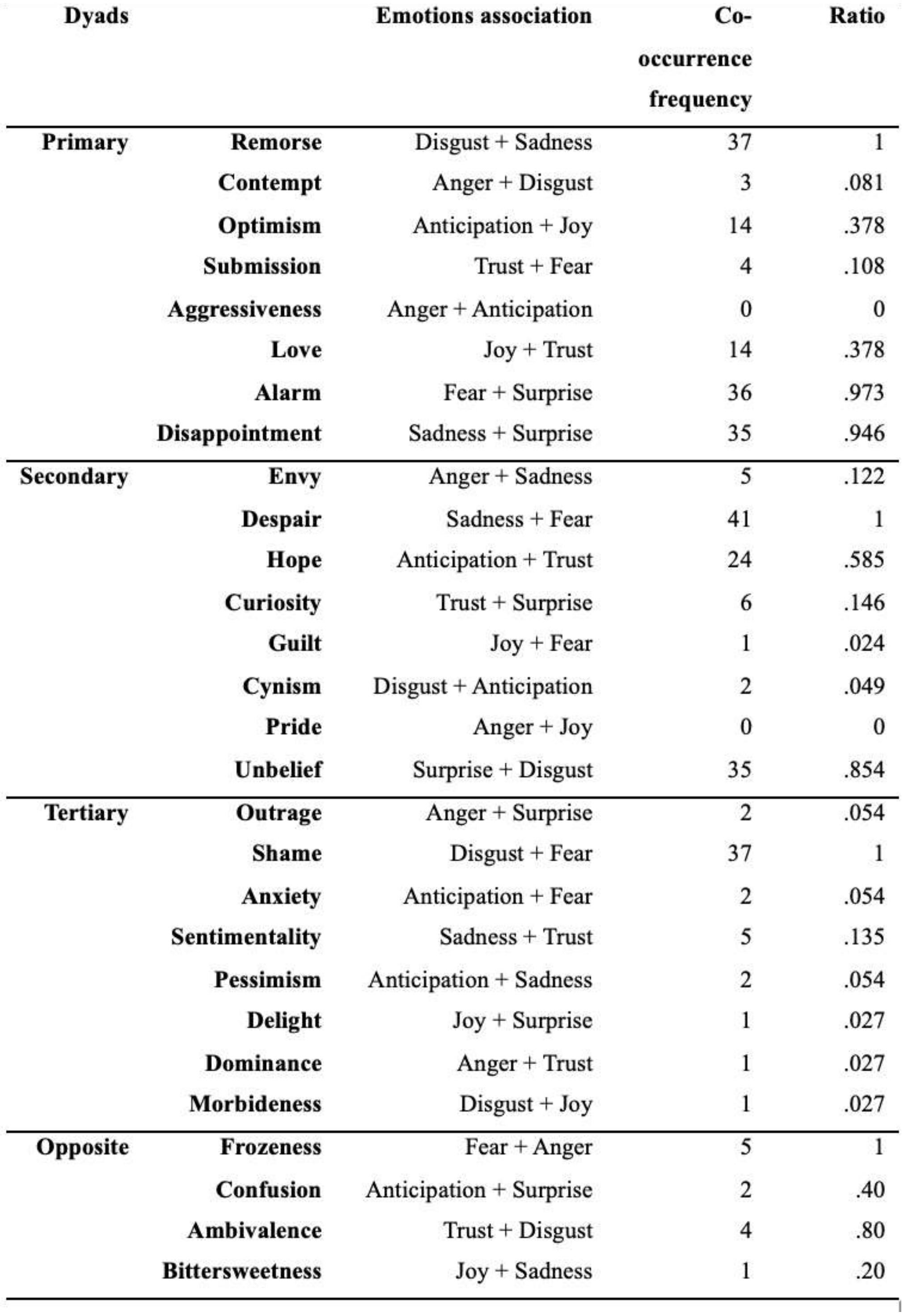
She vividly described her emotions in a narrative that portrayed a highly distressing scenario:

> *"She fainted, excruciating pain because the only thing they could tell us: she now has 11 bruises in her ovaries because we took 11 eggs."*

Plutchick's wheel of emotions

Table 12 illustrates the frequency with which pairs of basic emotions co-occur, forming complex dyads (adapted from Filipponi et al. [265]).

Table 12. The co-occurrence of complex emotions



Dyads		Emotions association	Co-occurrence frequency	Ratio
Primary	**Remorse**	Disgust + Sadness	37	1
	Contempt	Anger + Disgust	3	.081
	Optimism	Anticipation + Joy	14	.378
	Submission	Trust + Fear	4	.108
	Aggressiveness	Anger + Anticipation	0	0
	Love	Joy + Trust	14	.378
	Alarm	Fear + Surprise	36	.973
	Disappointment	Sadness + Surprise	35	.946
Secondary	**Envy**	Anger + Sadness	5	.122
	Despair	Sadness + Fear	41	1
	Hope	Anticipation + Trust	24	.585
	Curiosity	Trust + Surprise	6	.146
	Guilt	Joy + Fear	1	.024
	Cynism	Disgust + Anticipation	2	.049
	Pride	Anger + Joy	0	0
	Unbelief	Surprise + Disgust	35	.854
Tertiary	**Outrage**	Anger + Surprise	2	.054
	Shame	Disgust + Fear	37	1
	Anxiety	Anticipation + Fear	2	.054
	Sentimentality	Sadness + Trust	5	.135
	Pessimism	Anticipation + Sadness	2	.054
	Delight	Joy + Surprise	1	.027
	Dominance	Anger + Trust	1	.027
	Morbideness	Disgust + Joy	1	.027
Opposite	**Frozeness**	Fear + Anger	5	1
	Confusion	Anticipation + Surprise	2	.40
	Ambivalence	Trust + Disgust	4	.80
	Bittersweetness	Joy + Sadness	1	.20

The most common primary dyads identified were remorse (N=37), alarm (N=36), and disappointment (N=35). These complex emotions are vividly depicted in the narrative of a mother's anger (referenced above), highlighting related emotions. She felt driven to find solutions (remorse), recognized an external problem (disappointment), and was shocked (alarm) by the unexpected nature of the event. Similarly frequent were the primary dyads of optimism (N=14) and love (N=14). These emotions were effectively conveyed in scenarios where caregivers emphasized the necessity for support and precise information. Specifically, they highlighted the role of online social groups in enhancing their understanding and management of caregiving responsibilities:

> *"But then if I can also add a video call, a call or make a group like today, where in half an hour we take out the things that we've written down and that are perhaps more urgent there [...]."* (Caregiver 5, 45 years old, husband)

In terms of secondary dyads, despair (N=41) and unbelief (N=35) emerged as the most prevalent, with hope (N=24) following closely. These feelings of despair and disbelief were often articulated as significant emotional responses triggered by the emotional distress within the family dynamics. However, as exemplified by a son (caregiver 2, 27 years old), maintaining family unity was emphasized as crucial in navigating these challenges:

> "*Me, my sister, dad, and the whole family were always united, and yes, I must say that there was physical pain, but the psychological one definitely prevails."*

Shame (N=37) was identified as the most common tertiary dyad among caregivers, particularly when they were unable to provide physical or emotional support to patients due to COVID-19 restrictions. Caregivers discussed using eHealth tools, which they described as *double-edged swords*: although these tools helped bridge communication gaps between patients and doctors, they also posed a risk of depersonalizing the care process. Participants emphasized the importance of treating patients with respect and dignity rather than merely as clinical cases:

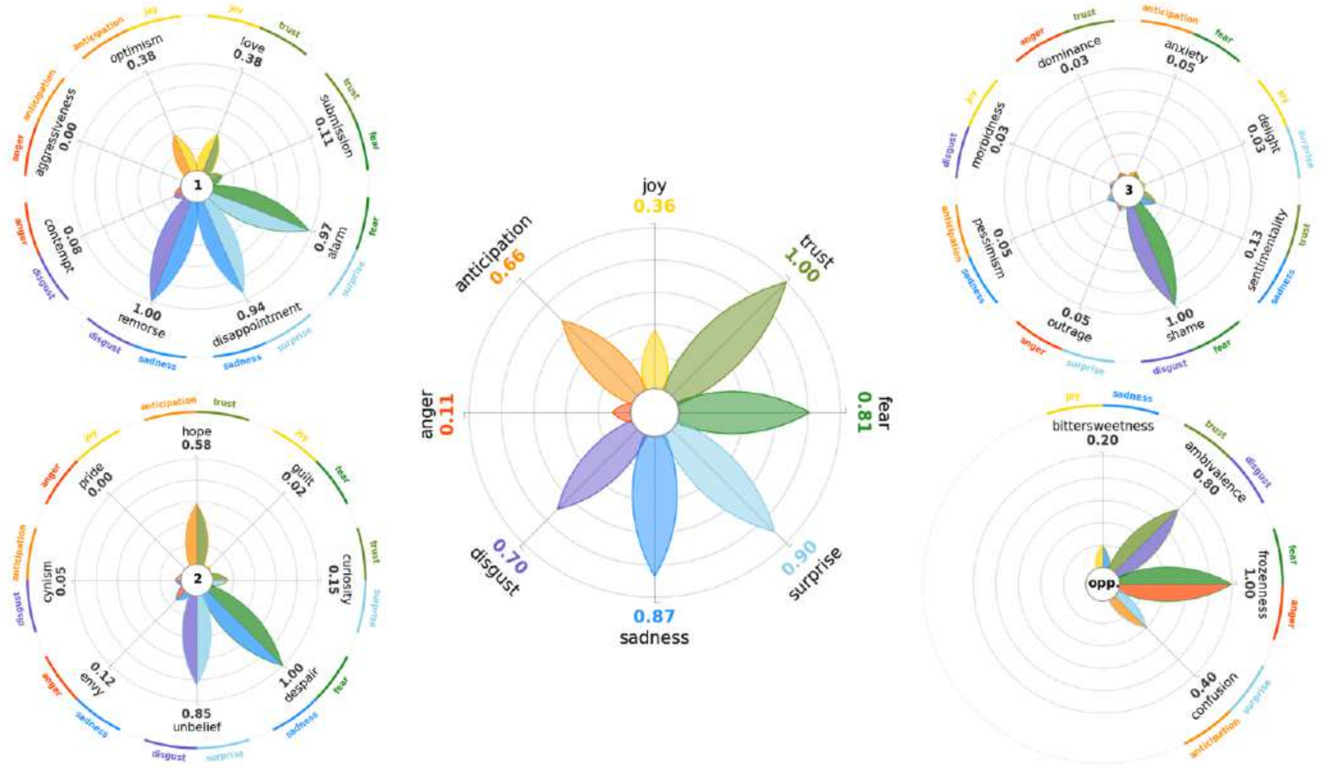
> *"I can't fully express it, but it's like, you know, trying to offer help just through words on a screen feels so distant. In moments like these, just having someone physically present means a lot. It's not just about what's written here; it's about having someone to lean on, someone real."* (Caregiver 1, 22 years old, daughter)

The lack of personal connection intensified emotions such as frozenness (N=5) and ambivalence (N=4), the most commonly noted conflicting pairs. The uncertainty about how to provide effective support from a distance, combined with an overwhelming sense of helplessness and emotional inadequacy, further intensified the caregivers' feelings of being immobilized. Caregivers also faced significant ambivalence; while feeling excluded and disheartened by their circumstances, they understood the necessity of relying on medical professionals to ensure the well-being of their loved ones, given the lack of alternatives. Despite some comfort found in physical distancing, caregivers wrestled with guilt and shame, caught between relief and remorse for harboring such mixed feelings:

> *"I believe that this COVID situation has been truly disastrous for certain dynamics because, in the end, you also have a sort of... you want to stay away from certain places a bit because you think they're all dangerous...So, even more so, everything was very distant, very detached. So, this certainly didn't help us to participate as we could have done in another historical moment."* (Caregiver 5, 45 years old, husband)

Refer to Figure 9 to view Plutchick's wheel of emotions, adapted from Filipponi et al. [265]).

Figure 9. The wheels of emotions by Plutchik's model



Notes. The eight basic emotions are in the center. Starting from the left and following a counterclockwise turn, 1 represents the primary dyads, 2 represents the secondary dyads, opp. represents the opposite dyads, and 3 represents the tertiary dyads.

3.2.4 Discussion

This study explores the emotional journey of caregivers who support breast cancer survivors living CP. Primarily, negative sentiments were more pronounced than positive ones, spanning from basic individual emotions such as sadness, fear, and disgust to more complex emotions like remorse, alarm, disappointment, despair, and unbelief. The research also examines social emotions, including shame and feeling overwhelmed (frozenness). Consistent with existing literature [125,172,218], cancer-related CP necessitates various adjustments in family dynamics, often leading to role reversals within the family and diminished connections both within the family unit and the wider social network. These changes frequently result in significant uncertainty, concerns about the future, and profound existential distress [115].

Uncertainty is a pervasive experience among both cancer patients and their caregivers, often linked with FCR [129,134], anticipated grief, and the escalating burden of caregiving [218,229]. These sentiments were effectively articulated by a 45-year-old husband (caregiver 5):

> "*Many fears come crashing down on you. Why, when, and maybe not will it end?... This stuff devastates you because you don't know how to help this person except for being beside them and maybe even acting as a lightning rod in certain situations.*"

Caregivers often grapple with blame and guilt due to their perceived lack of preparation when facing uncertain situations, leading them to believe they did something wrong for their loved ones [100,127,218]. Our research also indicates that such experiences trigger profound emotions like remorse, which foster empathetic concern for the actions they did not take toward their loved ones.

Our findings reveal that emotions such as shame, frozenness, and ambivalence have been intensified by the COVID-19 pandemic. Caregivers often grapple with shame over perceived deficiencies in their ability to support, coupled with feelings of ambivalence and immobilization. These emotional states are frequently attributed to external pressures, including pandemic-related restrictions or the limitations of eHealth tools, which are seen as inadequate replacements for face-to-face medical interactions. Shame, which reflects a sense of personal inadequacy ("I am inadequate in providing help") and differs from guilt ("I did something wrong"), often arises from perceived external judgment during group interactions. This prompts defensive reactions and emotional withdrawal [268]. It has been identified as a poorly managed emotion that can significantly augment the perceived burden among caregivers [269–271].

A related study conducted during the pandemic [128] underscored the amplified challenges caregivers faced, especially in pain management and navigating pervasive emotions such as hopelessness and uncertainty. The caregiving restrictions imposed by the pandemic, which curtailed access to hospital settings, amplified caregivers' fears of potentially missing the chance to say goodbye or reunite with their family members. This situation often precipitated heightened anticipatory grief. The authors also observed that disruptions in clinical routines and diminished social interactions due to these restrictions exacerbated feelings of loneliness. Additionally, the inability to alleviate the suffering of loved ones not only intensified feelings of isolation but also fostered a sense of social alienation [114].

Despite the prevalence of negative sentiments, caregivers consistently reported high trust in their relationships with partners and/or doctors. This finding aligns with results from our previous study [218], in which caregivers frequently took on the role of supporters, charged with upholding a positive attitude for themselves and their loved ones. The challenge of managing CP was seen by caregivers as an opportunity to forge new synergies with loved as underlined by STM [93,94]. When combined with anticipation, trust nurtures a sense of hope, serving as a vital resource in times of crisis. This hope was further bolstered when caregivers perceived their families as united and engaged with others facing similar challenges. The discussions within the focus group exemplified this dynamic, illustrating how participation in a support group with peers can alleviate stress and improve QoL, as evidenced in the literature [202,203,218]. However, when trust intersects with feelings of disgust, it can lead to ambivalence, a common emotional trigger among caregivers. Ambivalence regarding emotional expression—such as feeling unable to discuss emotional struggles because expressing needs might be viewed as a weakness—has been shown to increase the caregiving burden, exacerbate depressive symptoms, and reduce caregiver self-efficacy [272].

Overall, it is essential to recognize caregivers' deep emotional experiences and their influence on their own well-being and that of the patients they assist. Developing interventions that address caregivers' specific emotional requirements is crucial for enhancing the overall care and QoL for all involved. According to findings from our prior study [218], concerns such as uncertainty and the fear that symptoms may indicate a cancer recurrence are prevalent among both patients and caregivers. A recent systematic review [230] suggests that addressing this uncertainty requires several elements, with informational support being key. A significant obstacle to effective pain management is the lack of education, impacting patients, caregivers, and healthcare providers alike. Although eHealth tools offer promising support for empowering patients and caregivers in managing cancer pain [131], they are not substitutes for the doctor-patient relationship, which caregivers in our study highlighted as crucial. Some caregivers suggested using eHealth tools to facilitate the transition from hospital to home care and to monitor conditions remotely, recognizing their potential utility. Additionally, interventions that address specific outcomes, such as the FCR among family caregivers through group interactions, have demonstrated the potential to foster understanding, build trust, and enhance communication with partners, thus reducing uncertainty [134]. However, these interventions still need additional validation to verify their effectiveness.

In summary, neglecting caregivers' emotional needs can compromise the quality of care and support delivered at home, which may result in less effective pain management for the patient. Consequently, it is crucial to acknowledge caregivers and offer them the requisite emotional support, as this directly impacts the overall quality of care that cancer patients receive.

Limitations

While this study provides valuable insights, it is essential to recognize certain limitations. While natural language processing provides advantages in collecting and analyzing text data, it might not completely capture the subtle complexities of human emotions. For example, trust is generally considered a positive emotion but can also have negative connotations, such as the fear that a relationship might deteriorate due to betrayal by a partner. Moreover, distinguishing between basic and complex emotions can be challenging, as complex emotions are frequently implied rather than directly expressed. For instance, anger, despite its apparent intensity, can be difficult to quantify using solely quantitative methods. To address these challenges, we adopted a qualitative method to narratively detail participants' experiences within their specific contexts to gain a deeper understanding of their emotional journeys.

Chapter 4

Breaking Barriers in Chronic Pain Management for Breast Cancer Survivorship

4.1 *Study 4: Usability Testing of the PainRELife Digital Health Ecosystem for Managing Chronic Pain in Early Breast Cancer Patients: A Pilot Study*

The management of CP in breast cancer survivors represents a significant challenge within the healthcare system. Despite advances in cancer treatment, many survivors continue to face persistent pain that significantly impacts their QoL [77,78]. This chapter explores the development and testing of the PainRELife digital health ecosystem, a novel integrated platform designed to enhance CP management for early breast cancer patients. This ecosystem integrates various digital health tools, including mobile apps and cloud technology, to provide a comprehensive approach to pain management, aligning with modern healthcare strategies emphasizing patient-centered care and self-management.

A rigorous protocol published in 2023[5] guided the design and preliminary testing of the PainRELife ecosystem, and a subsequent study focused on its usability was published in 2024[6]. These studies were foundational in addressing the technological and patient-care aspects of the ecosystem, highlighting its potential to facilitate better pain management outcomes through an integrated care approach. Prior studies, including comprehensive focus group analyses (Chapter 3), informed this project, identifying specific barriers to pain management and tailoring the ecosystem to effectively meet the unique needs of breast cancer patients.

In digital health, the usability of technological solutions is not merely a supplementary feature but a core determinant of their success and efficacy in clinical settings. Assessing the usability experience of users is a crucial step toward enhancing the integration of these

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[5] Masiero M, Filipponi C, Pizzoli SFM, Munzone E, Guido L, Guardamagna VA, Marceglia S, Caruso A, Prandin R, Prenassi M, Manzelli V, Savino C, Conti C, Rizzi F, Casalino A, Candiani G, Memini F, Chiveri L, Vitali AL, Corbo M, Milani A, Grasso R, Traversoni S, Fragale E, Didier F, Pravettoni G. Usability Testing of a New Digital Integrated Health Ecosystem (PainRELife) for the Clinical Management of Chronic Pain in Patients With Early Breast Cancer: Protocol for a Pilot Study. JMIR Res Protoc. 2023 May 12;12:e41216. doi: 10.2196/4121

[6] Masiero M, Filipponi C, Fragale E, Pizzoli SFM, Munzone E, Milani A, Guido L, Guardamagna V, Marceglia S, Prandin R, Prenassi M, Caruso A, Manzelli V, Savino C, Conti C, Rizzi F, Casalino A, Candiani G, Memini F, Chiveri L, Vitali AL, Corbo M, Grasso R, Didier F, Ferrucci R, Pravettoni G. Support for Chronic Pain Management for Breast Cancer Survivors Through Novel Digital Health Ecosystems: Pilot Usability Study of the PainRELife Mobile App. JMIR Form Res. 2024 Feb 2;8:e51021. doi: 10.2196/51021

technologies into daily clinical practice. It provides essential quantitative data on the effectiveness of electronic tools and is fundamental to ensuring that new mobile health applications meet the practical needs of end-users [273]. Grounding the development of these applications in thorough usability evaluations is essential to tailor these tools around the user's needs, thereby maximizing their effectiveness and fostering greater acceptance and compliance with the intended medical protocols [274].

This chapter will delve into the usability testing of the PainRELife platform, examining its effectiveness in real-world settings and its impact on patient self-efficacy and engagement in managing pain. This project is part of a national initiative funded by the Lombardy Region, identified under project number "*PainRELife, Sustainable and integrated big data ecosystem for continuity of care and decision support for patients with pain*" (ID: 1173269). The following sections will detail the methodology employed in the pilot study, discuss the results obtained, and explore the implications of these findings for future interventions to improve the QoL of breast cancer patients with CP.

4.1.1 Aim of the Study

This pilot study investigates the user experience with the PainRELife digital health ecosystem, specifically designed for early breast cancer patients managing CP. The primary objective is to evaluate the usability of the PainRELife system, which aims to bridge the gap between inpatient care and ongoing outpatient or home care, thus ensuring a continuous flow of patient-centered data. Three months after implementing this digital health platform, the patients' usability experiences were assessed. The comprehensive evaluation covered multiple dimensions, including user engagement, usability metrics, aesthetic quality, accuracy and relevance of information provided, personal user perceptions, and the impact on behavioral modifications. These assessments were carried out using the Mobile Application Rating Scale (MARS).

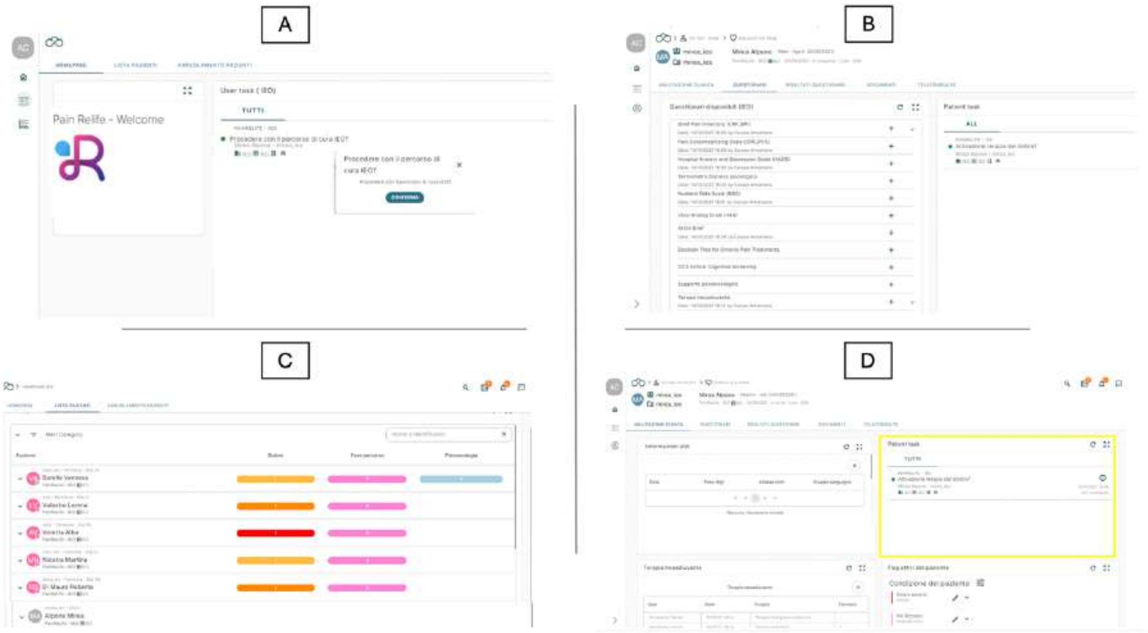
Additionally, the study explored secondary objectives such as app usage frequency, pain self-efficacy improvements, pain intensity changes, and the effectiveness of SDM processes.

4.1.2 Material and Methods

Brief Description of the PainReLife Digital Health Ecosystem

The PainRELife ecosystem integrates a cloud technology platform, the Nu Platform, with electronic health records to enhance data analysis pertinent to the patient care pathway. This integration is facilitated by connecting to the Fast Healthcare Interoperability Resources (FHIR) server, enabling advanced data analysis capabilities. Healthcare providers (doctors, psychologists) utilize the Nu Platform for the comprehensive collection and storage of clinical data, supporting continuous monitoring of various patient health parameters such as pain levels, psychological well-being, and treatment decision preferences throughout the patient's journey—from initial diagnosis to active treatment and follow-up stages (refer to Figures 10A, 10B, 10C, and 10D).

Figure 10. Interface design for healthcare professionals on the Nu Platform



Notes: All names in this image are fictional and used for illustrative purposes only. (A) Main screen showcasing a comprehensive list of activities available for healthcare professionals; (B) Overview of patient questionnaires detailing the tools utilized to evaluate both psychological and physical conditions via the PainRELife mobile app; (C) A comprehensive roster of patients enrolled on the Nu Platform, providing an accessible directory; (D) A dedicated page for clinical assessments, featuring in-depth insights into clinical occurrences and recommended therapeutic actions.

Additionally, the ecosystem leverages a robust big data infrastructure connected to the FHIR server, which provides dynamic dashboards. These dashboards offer healthcare professionals, researchers, and other stakeholders an intuitive and systematic visualization of patient population characteristics.

The PainRELife mobile app, designed for patient use, is connected to the Nu Platform. This app facilitates data collection and supports bidirectional communication between patients and healthcare providers. Data gathered via the mobile app are stored on the Nu Platform and accessible to healthcare professionals for ongoing oversight.

For further details on the implementation and impact of these technologies, refer to Masiero et al. 2023 [263] and 2024 [264].

Functionality of the PainRELife Mobile App

The PainRELife app has multiple features to educate patients and collect patient-reported outcomes (see figure 11A). It includes an educational section that provides resources to help patients understand CP across various stages of cancer survivorship (acute, extended, and permanent phases; see Figure 11D). A dedicated assessment section within the app offers validated questionnaires to measure aspects like pain intensity and interference, anxiety, and depression (see Figure 11B).

Additionally, the app features an electronic diary (see Figure 11C) and contains exercises tailored for pain and emotional-body mapping (see Figures 11E and 11F), enabling a comprehensive evaluation of the patient's psychological well-being and pain experience. The app also incorporates a decision aid section, divided into two modules: profiling patient preferences and a decision tree for healthcare choices (see Figure 11G). These tools empower patients by enhancing their understanding of treatment options, including the benefits and drawbacks of pharmacological and non-pharmacological interventions, and by supporting SDM. The decision tree module utilizes a subjective expected utility approach to tailor healthcare preferences, thus aligning treatment choices with patients' unique needs and objectives.

All figures are adapted from Masiero et al. [264]. The protocol [263] provides more details regarding the psychological assessment through the app and the questionnaires.

Figure 11. User interface design of the PainRELife mobile app for patients

All'interno dell'app troverai una ricca sezione educativa: una maggiore conoscenza porterà a una gestione più consapevole del dolore.

Notes: (A) Homepage presenting a summary of all sections within the mobile app; (B) Section for assessing pain and psychological well-being, featuring the required questionnaires for patient completion; (C) A digital diary accessible to the patient for daily entries; (D) Educational module showcasing a selection of content available on the mobile app; (E) and (F) Exercises designed for mapping pain and emotional responses within the body; (G) Decision support module displaying options for pharmacological and non-pharmacological treatment preferences.

Study Design and Procedure

Participants

This pilot usability study encompassed 25 individuals diagnosed with breast cancer experiencing pain post-surgery. Patients were recruited from the Division of Medical Senology and the Division of Pain Therapy and Palliative Care at IEO. The mean age of the participants was 47.12 years, with a standard deviation of 8.41 years. After their clinical consultation, participants were introduced to the mobile app and instructed to engage with it for over three months consistently.

Eligibility for participation was determined based on a specific set of criteria: individuals had to be over 18 years old, diagnosed with early breast cancer, have undergone surgical treatment for breast carcinoma, and be experiencing post-surgical pain with a severity of at least 3 on NRS [17]. Additionally, candidates were required to have internet access and own a personal smartphone. Exclusion criteria included patients with a history or current diagnosis of psychiatric or neurological disorders or any other condition necessitating active analgesic treatment.

Measurement Tools

Sociodemographic and medical data from patients were collected via electronic medical records and specifically designed questions during the initial consultation. Pain levels were assessed using the NRS, which ranges from 0 (no pain) to 10 (severe pain) [17]. Additionally, validated self-report measures were employed to evaluate primary and secondary outcomes:

- *Usability Evaluation*: The Italian version of the MARS [275] was used to assess the usability of the eHealth platform. It includes a description/classification section and 23 items, rated using a 5-point Likert-type scale, which evaluates the quality of apps across four objective quality dimensions: engagement (5 items), functionality (4 items), aesthetics (3 items), and information (7 items). Additionally, there is a subjective quality dimension consisting of 4 items. Several items within the information subscale provide a 'Not applicable' (N/A) option. The scores from individual items are averaged to derive a mean quality score for each dimension; these are further averaged to calculate a total MARS score. All mean quality scores range from 1 (poor) to 5 (excellent). Furthermore, MARS features an app-specific section with 6 items tailored to assess the impact of the app on user knowledge, intentions, and related outcomes, which can be customized to align with specific research objectives. The MARS total and subscale scores demonstrate very high internal consistency with Cronbach's alpha coefficients ranging from .80 to .89 for subscales and .90 for the total score, and they show acceptable inter-rater reliability, agreement, and convergent validity with app-store star ratings.

- *Pain self-efficacy*: The Pain Self-Efficacy Questionnaire (PSEQ) [276] assesses patients' confidence in managing pain while performing daily activities despite ongoing discomfort. Comprising 10 items that evaluate aspects such as handling household chores or achieving personal goals, the PSEQ employs a 7-point Likert scale for responses, ranging from 0 (not at all confident) to 6 (completely confident). This scale allows for scores between 0 and 60, with higher scores indicating greater self-efficacy in pain management. The PSEQ demonstrates excellent internal consistency, with a Cronbach's alpha of .94, and it also exhibits good test-retest reliability (ICC_agreement = 0.82), confirming its robustness as a measurement tool.
- *SDM*: The Italian version of the 9-item Shared Decision-Making Questionnaire (SDM-Q-9) [277] assessed facets of achieving a collaborative decision-making process. It also showed good reliability with a Cronbach's alpha of α = .86.

Statistical Analysis

Data analysis was performed using SPSS version 29.0 (IBM Corp). Descriptive statistical analyses and correlations of psychological variables collected through the app were conducted to outline the participants' characteristics and usage patterns comprehensively. It is important to note that the analyses of psychological aspects collected through the app were conducted to provide a comprehensive understanding of the sample and are not directly related to the study's primary objectives.

To assess the primary endpoint, the mean and standard deviation for each MARS subscale—including engagement, functionality, aesthetics, information quality, subjective app quality, and the app's expected impact on user knowledge, attitudes, and behaviors—were calculated at the three-month mark. A composite measure termed "total app quality" was derived by averaging the mean scores from the engagement, functionality, aesthetics, and information quality subscales of MARS.

The total number of participants who had access to the PainRELife mobile app was recorded to create a new binary variable, "app usage", defined based on the total app accesses (mean 22.92, SD 15.60; range 2-73). A threshold of 21 accesses was set as the minimum required for completing the study's tasks, categorizing participants into higher—or lower-frequency groups.

To assess the relationship between pain self-efficacy and app usage frequency, participants were divided into two groups based on their pain self-efficacy scores at the three-month follow-up (T2). The median score of 50 was used as the threshold to create two groups:

lower pain self-efficacy (scores below 50) and higher pain self-efficacy (scores of 50 and above). An independent samples t-test was conducted to compare the number of app accesses between these two groups. The mean and standard deviation of app accesses were reported for both groups, along with the t-test results and effect size measures. Additionally, a repeated measures ANOVA was performed to examine the changes in pain self-efficacy over time (from baseline T0 to the three-month follow-up T2) and to investigate the interaction between app usage frequency and changes in pain self-efficacy. This analysis included within-subject factors (time) and between-subject factors (app usage groups). Partial eta squared (η^2) was used to measure the effect size for ANOVA.

The variable "pain reduction" was calculated as the difference between pain intensity at baseline (T0) and pain intensity at the three-month follow-up (T2). This was achieved by subtracting each participant's NRS score at T2 from the NRS score at T0. This derived variable evaluated the Pearson correlation between initial pain levels and the relationship between app usage frequency and pain reduction. Other correlation analyses were conducted to explore relationships among self-report measures (NRS, PSEQ, SDM-Q-9, MARS) and the frequency of app usage over the three-month period. Variation in pain intensity, as measured by the NRS from baseline (T0) to three months (T2), was examined using repeated measures ANOVA.

Ethical Considerations and Participant Consent

The Ethical Committee of the IEO granted ethical approval for this study in December 2021 (R1597/21-IEO 1701), adhering to the principles of the Declaration of Helsinki and the guidelines for Good Clinical Practice. Before providing written informed consent, participants were thoroughly briefed on the study's objectives, procedures, potential risks, and benefits. No compensation was offered for participation, and participants retained the right to withdraw at any point without consequence.

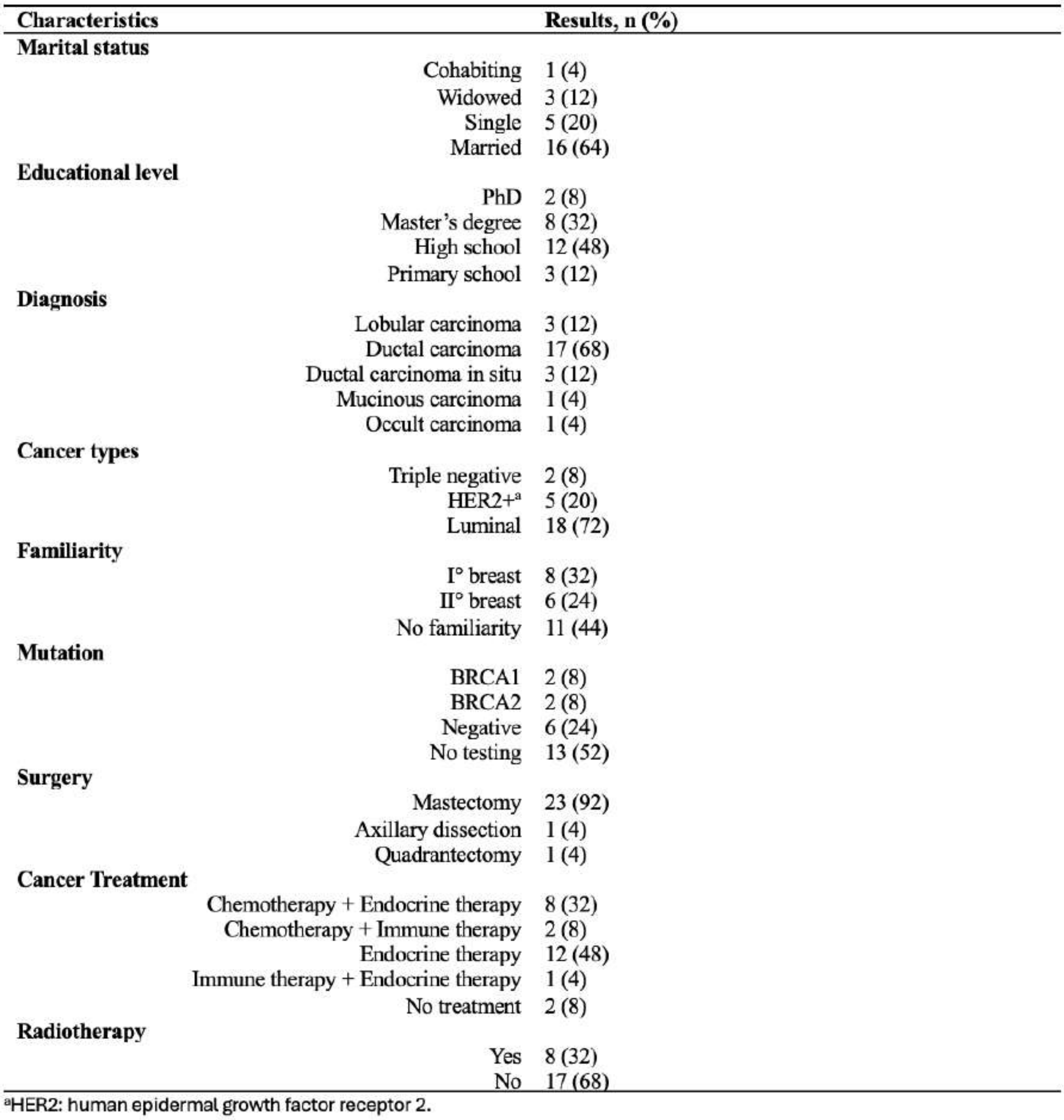
To ensure privacy and confidentiality, all personal identifiers were removed from the data, which was anonymized by national data protection laws. The anonymized data will be retained in the IEO databases for a duration of ten years.

4.1.3 Results

Sample Characteristics Summary

The sample comprised 25 breast cancer patients (M_{age}=47.12, SD=8.41), primarily married (16/25, 64%) and with high school education (12/25, 48%). Most were diagnosed with ductal carcinoma (17/25, 68%), with the majority having luminal cancer types (18/25, 72%). A significant portion had no family history of breast cancer (11/25, 44%), and half did not undergo genetic testing for BRCA mutations (13/25, 52%). The predominant surgery type was mastectomy (23/25, 92%). Treatments included chemotherapy combined with endocrine therapy (8/25, 32%) or immune therapy (2/25, 8%), endocrine therapy alone (12/25, 48%), and some received radiotherapy (8/25, 32%). Refer to Table 13, adapted from Masiero et al. [264].

Table 13. Characteristics and treatment details of the sample (n=25)



Characteristics	Results, n (%)
Marital status	
Cohabiting	1 (4)
Widowed	3 (12)
Single	5 (20)
Married	16 (64)
Educational level	
PhD	2 (8)
Master's degree	8 (32)
High school	12 (48)
Primary school	3 (12)
Diagnosis	
Lobular carcinoma	3 (12)
Ductal carcinoma	17 (68)
Ductal carcinoma in situ	3 (12)
Mucinous carcinoma	1 (4)
Occult carcinoma	1 (4)
Cancer types	
Triple negative	2 (8)
HER2+[a]	5 (20)
Luminal	18 (72)
Familiarity	
I° breast	8 (32)
II° breast	6 (24)
No familiarity	11 (44)
Mutation	
BRCA1	2 (8)
BRCA2	2 (8)
Negative	6 (24)
No testing	13 (52)
Surgery	
Mastectomy	23 (92)
Axillary dissection	1 (4)
Quadrantectomy	1 (4)
Cancer Treatment	
Chemotherapy + Endocrine therapy	8 (32)
Chemotherapy + Immune therapy	2 (8)
Endocrine therapy	12 (48)
Immune therapy + Endocrine therapy	1 (4)
No treatment	2 (8)
Radiotherapy	
Yes	8 (32)
No	17 (68)

[a]HER2: human epidermal growth factor receptor 2.

Summary of Psychological Variables Measured Through the App

Appendix 3 provides an overview of the psychological variables assessed through the PainRELife app. The data encompass various psychological and pain-related measures taken at baseline (T0), one month (T1), and three months (T2). The baseline pain intensity had a mean of 5.00 (SD = 1.68), which decreased to 3.72 (SD = 2.59) at the three-month follow-up. Pain self-efficacy improved from a baseline mean of 40.92 (SD = 8.95) to 44.80 (SD = 11.99) at the three-month follow-up. Additionally, patients reported that they generally preferred a passive-collaborative role in decision-making, with a mean of 4.28 (SD = 1.49). The high values observed in SDM (mean=80.89, SD=22.45) suggest that participants valued and engaged in collaborative decision-making processes, aligning with their preference for a passive-collaborative role. Other measured variables include the pain severity ($\text{mean}_{T0}=3.71$, $\text{SD}_{T0}=1.25$; $\text{mean}_{T2}=3.13$, $\text{SD}_{T2}=2.11$), interference scores ($\text{mean}_{T0} = 4.42$, $\text{SD}_{T0}=1.98$; $\text{mean}_{T2} = 3.89$, $\text{SD}_{T2}=3.12$), pain catastrophizing thinking ($\text{mean}_{T0}= 15.12$, $\text{SD}_{T0}=8.11$; $\text{mean}_{T2}=12.84$, $\text{SD}_{T2}=9.15$), anxiety ($\text{mean}_{T0}=8.52$, $\text{SD}_{T0}=4.58$; $\text{mean}_{T2}=7.12$, $\text{SD}_{T2}=3.82$) and depression scores ($\text{mean}_{T0}=7.24$, $\text{SD}_{T0}=4.53$; $\text{Mean}_{T2}=5.96$, $\text{SD}_{T2}=4.40$), indicating reductions from baseline to three months. Particularly, baseline scores of anxiety and depression indicated borderline abnormal to abnormal cases, while body dissatisfaction (mean=3.36, SD=10.76) and self-efficacy in daily life (mean=2.42, SD=0.46) measured at baseline were moderate.

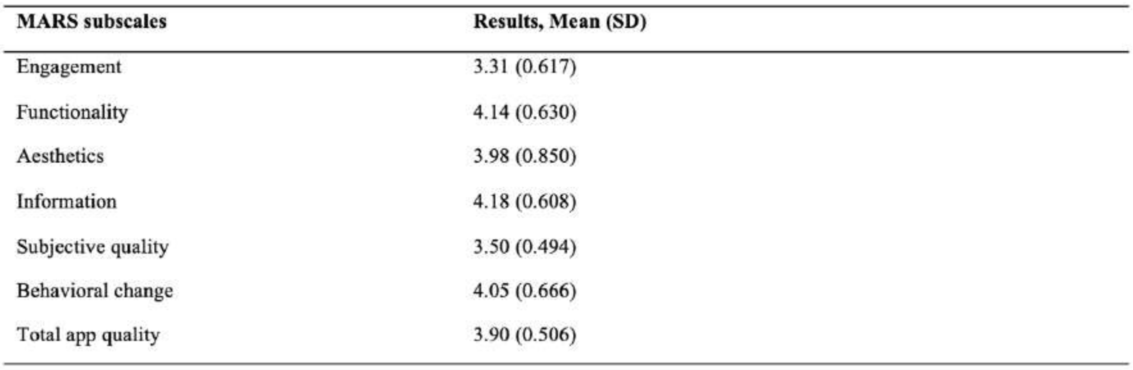
Significant correlations were observed in the study. Baseline pain intensity was negatively correlated with perceived self-efficacy in daily life ($r=-0.408$, $p<.05$). Pain intensity at the one-month follow-up showed positive correlations with body dissatisfaction ($r=0.480$, $p<.01$) and pain self-efficacy at three months ($r=0.543$, $p<.01$). Furthermore, anxiety at baseline was positively correlated with depression at baseline ($r=0.595$, $p<.01$) and pain intensity at one month ($r=0.444$, $p<.05$). Pain intensity at the three-month follow-up positively correlated with baseline anxiety ($r=0.400$, $p<.05$) and body dissatisfaction ($r= 0.464$, $p<.05$). The severity of pain interference at three months was also significantly correlated with various psychological measures, including anxiety ($r=.732$, $p<.01$) and depression ($r=.813$, $p<.01$) scores at three months. Finally, SDM was negatively correlated with body dissatisfaction ($r=-0.409$, $p<.05$), suggesting that higher SDM scores are associated with lower patient body dissatisfaction.

Usability Evaluation of the Mobile App

Usability and App Quality

The total MARS score, ranging from 1 to 5, showed medium-to-high mean values across all subscales (range 3.31-4.18; refer to Table 14, adapted from Masiero et al. [264]). The overall mean score for app quality was 3.90 (SD=0.506), indicating good usability as perceived by the participants. This finding is further supported by the mean number of app accesses throughout the study (mean=22.92, SD=15.60; range 2-73). It is important to note that the statistics on app usage are based on the entire sample of 25 patients, while the MARS scale is evaluated based on 23 responses, as 2 patients did not respond. Notably, three out of five subscales received the highest scores: functionality (mean=4.14, SD=0.630), information (mean=4.18, SD=0.608), and behavioral change (mean=4.05, SD=0.666).

Table 14. Mean and standard deviation for MARS subscales



MARS subscales	Results, Mean (SD)
Engagement	3.31 (0.617)
Functionality	4.14 (0.630)
Aesthetics	3.98 (0.850)
Information	4.18 (0.608)
Subjective quality	3.50 (0.494)
Behavioral change	4.05 (0.666)
Total app quality	3.90 (0.506)

Functionality

In the functionality subscale, 57% (15/23) of participants found the mobile app easy to use. Additionally, 91% (21/23) reported that interactions within the app were reliable and intuitive (ease of use: 8/23, 35% agree; 13/23, 57% strongly agree). Positive evaluations were also given for the app's design (gestural design: 8/23, 35% agree; 12/23, 52% strongly agree) and navigation properties (navigation: 12/23, 52% agree; 8/23, 35% strongly agree). Despite 52% of participants finding the app to perform well (performance: 7/23, 30% agree; 5/23, 22% strongly agree), there were some uncertainties regarding the speed of the app's features and components (performance: 8/23, 35% undecided; 3/23, 13% disagree).

Information Quality

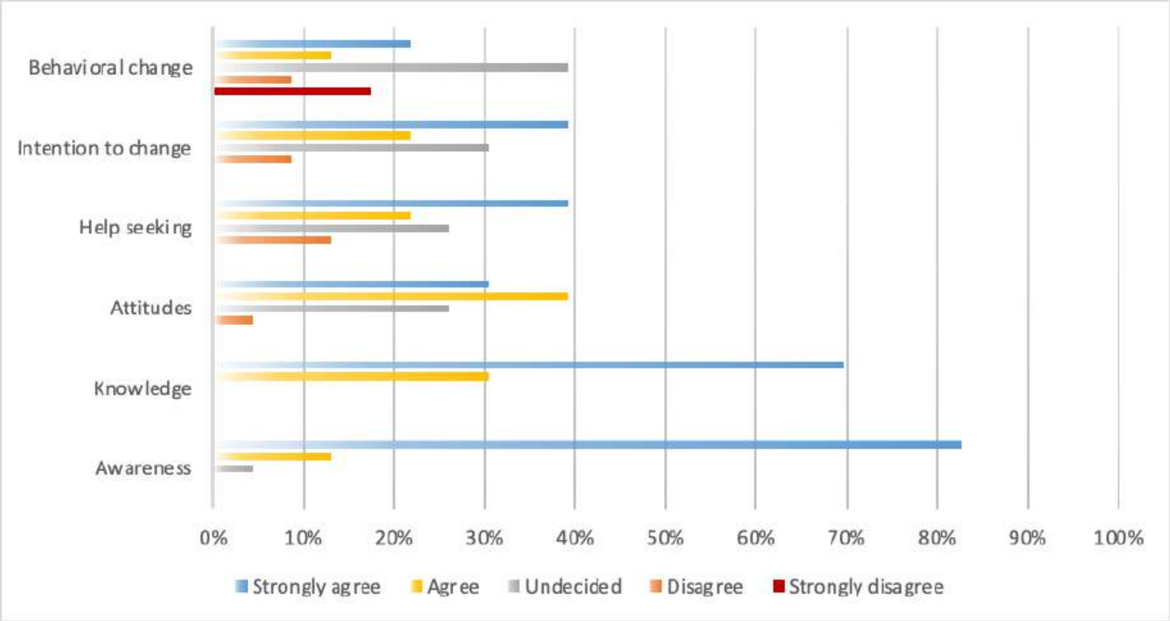
Regarding the information subscale, 78% (18/23) of participants agreed that the information provided in the app is evidence-based (information: 9/23, 39% agree; 9/23, 39% strongly agree), relevant to CP in breast cancer, and useful for its management (quality of information: 9/23, 39% agree; 11/23, 48% strongly agree). The app was also deemed trustworthy (credibility: 22/23, 96% strongly agree). Participants positively rated the quantity of information (quantity of information: 7/23, 30% agree; 9/23, 39% strongly agree) and how it was presented (visual information: 11/23, 48% agree; 9/23, 39% strongly agree). Most participants (goals: 11/23, 48% agree; 3/23, 13% strongly agree) felt that the app's goals were achievable, though 30% (7/23) expressed some concerns.

Behavioral Change

In the behavioral change subscale (see Figure 12), 83% (19/23) strongly agreed that the app improved awareness about CP in the cancer pathway, and 70% (16/23) strongly agreed it increased CP-related knowledge. Similarly, 69% (16/23) believed the app might influence attitudes toward CP (attitudes: 9/23, 39% agree; 7/23, 30% strongly agree). Furthermore, most participants believed the app could potentially support help-seeking behaviors (help-seeking: 5/23, 22% agree; 9/23, 39% strongly agree) and intention to change (intention to change: 5/23, 22% agree; 9/23, 39% strongly agree). However, 52% (15/23) had concerns about the app's ability to convert intentions into significant behavioral changes (behavioral change: 9/23, 39% undecided; 2/23, 9% disagree; 4/23, 17% strongly disagree).

Overall, participants felt the app was well-targeted (engagement subscale: mean=3.31, SD=0.617), with a satisfactory layout (aesthetics subscale: mean=3.98, SD=0.850) and subjective quality (subjective quality subscale: mean=3.50, SD=0.494).

Figure 12. Distribution of responses for behavioral change



App Usage Patterns and Impact on Pain Self-Efficacy

Analyzing pain self-efficacy levels between high and low app usage groups reveals insightful trends. At baseline, there was no significant difference between the groups in terms of pain self-efficacy scores (High Usage: mean=41.85, SD=8.375; Low Usage: mean=39.92, SD=9.811; t(23)=0.530, p=0.301). However, at the three-month follow-up, a trend was observed where participants in the low app usage group (mean=48.46, SD=7.90) reported higher pain self-efficacy than those in the high app usage group (mean=40.83, SD=14.58) (t(23)=1.644, p=0.057; d=0.658). Although this difference did not reach statistical significance (p=0.057), the medium effect size (d=0.658) suggests practical significance, implying that participants with high self-efficacy might not feel the need to use the app as much as those with low self-efficacy.

A negative correlation was found between the number of app accesses and self-efficacy measured at time T2 (r=-0.460, p<.05), indicating that participants with lower self-efficacy at T2 used the app more frequently. When dividing participants based on self-efficacy at T2, it was observed that those with low self-efficacy made more app accesses (mean=27.71, SD=17.35) than those with high self-efficacy (mean=16.82, SD=10.95). This difference was significant (t(23)=1.814, p<.05; d=0.731), and the moderate effect size (d=0.731) suggests practical significance, indicating that participants who feel less confident in managing their pain seek more support through the app.

Further analysis using repeated measure ANOVA revealed important results. There was a significant main effect of time on pain self-efficacy, F(1,23)=4.651, p<.05, η^2=.168, indicating that self-efficacy scores significantly changed from T0 to T2. Additionally, app usage significantly affected pain self-efficacy, F(1, 23)=4.391, p<.05, η^2=.160. Although the interaction between time and app usage was not statistically significant, F(1, 23)=3.099, p=.092, η^2=.119, the moderate effect size suggests a potential trend worth further investigation. These findings highlight the importance of personalized interventions based on initial self-efficacy levels.

Changes in Pain Intensity and Effects on Decision-Making

A significant positive correlation was found between pain reduction and baseline pain levels (r=0.474, p<.05), suggesting that participants with higher initial pain levels tended to experience greater pain reduction. Additionally, baseline pain showed a significant positive correlation with the number of app accesses (r=0.425, p<.05), suggesting that those with higher initial pain accessed the app more frequently.

The repeated measures ANOVA revealed a significant reduction in pain intensity from baseline (T0) to the three-month follow-up (T2). Specifically, the mean pain intensity decreased from 5.00 (SD = 1.68) at T0 to 3.72 (SD = 2.59) at T2, with an F-value of 3.407 (p<.05). The partial eta squared value was 0.124, indicating a moderate effect size.

Significant correlations were also observed between certain MARS subscales and other measures. For instance, SDM-Q-9 scores showed significant positive correlations with engagement mean scores (r=0.445, p<.05), information mean scores (r=0.427, p<.05), and subjective quality mean scores (r=0.548, p<.01). However, no significant correlations were detected between the MARS subscales and PSEQ or NRS scores.

4.1.4 Discussion

This study evaluated the usability of the PainRELife digital health ecosystem designed to enhance CP management for early breast cancer patients. The primary objective was to assess the app's usability, while the secondary objective was to investigate the relationships between app usage, pain self-efficacy, pain intensity, and SDM.

Regarding the primary objective, most participants rated the app favorably, with three out of five subscales—functionality, information, and behavioral change—receiving the highest scores. Participants believed the app could increase knowledge and awareness about CP and positively influence attitudes towards CP, thereby supporting help-seeking behaviors and the intention to change. These findings suggest that the PainRELife app is well-designed and user-friendly, effectively meeting the needs of breast cancer patients managing CP.

Insufficient education is a significant obstacle to effective pain management, affecting both healthcare providers and patients. For example, a qualitative study [255] found that breast cancer patients were often unprepared for the persistence of pain after surgery, expressing concerns about the lack of guidance on pain management and the potential for enduring pain during recovery and follow-up periods. This was confirmed by our focus group discussions with breast cancer patients [243].

In another previous research [218], along with other studies [201,226,227], it was identified that cancer patients frequently encounter significant uncertainty regarding various aspects of pain management, leading to numerous "what-if" scenarios about their cancer and pain, causing considerable anxiety and fear. Patients may worry about whether their cancer will spread, shrink, or recur, and they also face uncertainties about the different types of treatments, the procedures involved, and the nature and duration of their pain [218]. A recent systematic review emphasizes that addressing these uncertainties requires several components, with informational support being crucial [230].

In this context, eHealth tools show great promise for delivering necessary interventions, as suggested by feedback from breast cancer patients during our focus group discussions [243]. These tools can facilitate smoother transitions from hospital to home care, maintaining a continuous care pathway. By bridging gaps between different healthcare settings, eHealth tools help reduce disparities in healthcare access, ensuring consistent care regardless of patients' contextual or societal circumstances. However, it is important to note that while these tools are beneficial, they should complement rather than replace the fundamental doctor-patient relationship, essential for achieving satisfactory care management, as noted by our participants [243].

These findings are particularly noteworthy given the challenges reported in the literature. CP syndrome in breast cancer patients is often undiagnosed and inadequately addressed by oncologists. De Groef et al. [86] highlighted that pain is frequently underreported, under-assessed, and undertreated in breast cancer survivors, often due to discomfort in discussing symptoms and clinicians focusing on other health issues. Additionally, Pas et al. [278] found that many cancer patients report poor knowledge about cancer-related CP, available interventions, and possible health system resources, significantly impacting their ability to manage pain effectively. This aligns with our previous study [243], which highlighted the attitude of healthcare providers to normalize pain, misconceptions about pain management due to inadequate education, and the inadequacy of doctor-patient communication as major barriers. The PainRELife app addresses these issues through features designed to enhance patient education, facilitate improved communication by providing an interconnected system between patients (PainRELife app) and doctors (Nu platform), and offer comprehensive pain management strategies tailored to patients' preferences.

As for the secondary objective, the focus on pain management significantly decreased baseline pain intensity at the three-month follow-up. Notably, patients with higher initial pain accessed the app more frequently. Additionally, pain self-efficacy improved significantly over this period. Our study showed that app usage affected pain self-efficacy: participants with lower self-efficacy used the app more frequently, while those with higher initial pain self-efficacy did not need to use the app as often. These improvements highlight the app's potential impact on pain management and self-efficacy among breast cancer patients.

Self-efficacy plays a crucial role in patients with cancer. Karademas et al. [279] showed that higher levels of coping self-efficacy are associated with better self-care, less psychological distress, and higher life satisfaction among breast cancer patients. Specifically, Fisher et al. [280] found that enhancing self-efficacy for pain management significantly reduced pain severity, pain catastrophizing thinking, and depressive symptoms in breast cancer patients, underscoring the importance of addressing self-efficacy in pain management interventions. Our findings, consistent with these studies, emphasize the importance of enhancing pain self-efficacy in interventions designed for breast cancer patients with pain to improve their psychological and physical health outcomes.

Evidence from other studies supports the potential of mobile health applications to help breast cancer patients manage CP and empower them effectively. The systematic review of Zheng et al. [143] demonstrated that mobile applications significantly aid in monitoring and reducing cancer pain, improving self-management skills, and enhancing the QoL for breast cancer patients. Similarly, Gyawali et al. [144] found that mobile health applications significantly improve outcomes by reducing pain disability, enhancing pain self-efficacy, and improving overall patient satisfaction.

The significant correlations observed between pain intensity, self-efficacy, and psychological variables such as body dissatisfaction, anxiety, and depression highlight the interconnectedness of physical and emotional well-being in breast cancer patients. These findings align with the biopsychosocial model of pain [28], underscoring the importance of addressing both physical and psychological aspects of pain to achieve comprehensive care. As the MAP framework [9] emphasizes, integrating narrative reports into comprehensive assessments can enhance understanding of the underlying reasons for pain reports and facilitate more effective pain management strategies. The PainRELife app incorporated these elements by offering educational resources, tracking pain and treatment progress, and supporting SDM processes. This integration of technological support aligns with the needs identified in the narratives of breast cancer survivors in our previous study [243], suggesting the app's potential to bridge gaps in pain assessment and management.

Despite the positive feedback, half of the participants in our study expressed concerns about the app's ability to convert intentions into significant behavioral changes. This could be attributed to the fact that a comprehensive intervention was not developed and tested in this study. Future research should focus on testing the app with a larger sample size and a control group to evaluate its effectiveness in facilitating behavioral change and improving pain management outcomes. For instance, De Groef et al. [145] demonstrated the preliminary efficacy of an eHealth intervention, which includes pain science education and self-management interventions, in improving the understanding of pain, managing pain-related functioning, and ultimately enhancing the QoL of breast cancer survivors.

Regarding SDM processes, significant correlations were observed between SDM scores and the MARS subscales for engagement, information quality, and subjective quality, suggesting that higher SDM scores were associated with better app engagement and perceived quality. Moreover, SDM was negatively correlated with body dissatisfaction, suggesting that patients who feel involved in decision-making tend to report lower levels of body dissatisfaction. The positive impact of SDM on patient outcomes is supported by various studies. For instance, research has shown that SDM significantly reduces clinician-controlled decision-making and increases patient-controlled decision-making, indicating that decision aids effectively enhance patient involvement in decisions [151,152]. This is crucial as patients who are more active in making decisions about their health generally have better health outcomes and healthcare experiences [151–153]. These studies have also highlighted that

SDM helps address decisional conflict and improve treatment adherence, which are key factors in patient satisfaction and engagement [151,152]. Moreover, patients participating in SDM processes report feeling more empowered and satisfied with their healthcare choices, positively affecting their overall treatment experience [151–153]. This highlights the importance of SDM in enhancing patient engagement and satisfaction with digital health interventions.

Additionally, our focus group study [243] showed that breast cancer survivors preferred to adopt a collaborative role in the decision-making process with their doctors, reducing the risk of regretting decisions by adopting an active role. This preference aligns with our finding that most patients preferred collaborative-passive roles in their decision-making process. We suggest that breast cancer patients actively involved in treatment decisions show greater engagement with the mobile app and improve their satisfaction with their body's perception. For these patients, the information provided by the app can reinforce and support their ability to make shared decisions throughout their care journey.

Limitations

Despite the promising results, this pilot usability study had several limitations that must be considered. The primary limitation is the relatively small sample size of patients with breast cancer (n=25) and the use of a single group to test usability. This design might have limited the capture of more comprehensive information about patients' perceptions of digital health technology. However, our sampling strategy is consistent with the pilot study design and methodological guidelines [281,282].

The inclusion criterion of a 3/10 NRS for pain intensity in this study was selected as it represents a level of pain that, while mild, approaches moderate levels, particularly when assessed shortly after surgery or other interventions. Clinicians have observed this threshold as a potential indicator of the development of CP. However, it's important to note that other guidelines, such as those in the British Journal of Anaesthesia, suggest using a 4/10 NRS as a more reliable predictor of significant pain and CP risk [283]. The choice of 3/10 in this study acknowledges the variability in patients' pain thresholds and the potential for early intervention but also highlights a limitation: pain intensity alone may not always provide a comprehensive picture. To enhance the assessment, it would be beneficial to complement the intensity criterion with an interference index, which could better capture the impact of pain on patients' daily functioning and QoL.

The reported statistical significance for pain self-efficacy should be considered a trend since it does not reach the threshold for statistical significance (P=.057). However, the medium-to-large effect size (d=0.65) supports the presence of a meaningful difference between groups, which may be due to the small sample size. According to Schmettow [284], small sample sizes in usability studies can lead to incomplete findings and variability, underscoring the need for larger sample sizes to confirm these results and ensure robustness.

Another limitation of this study is the moderately high standard deviation (15.60) in the "app usage" variable, indicating significant variability in how participants used the app. Additionally, despite the balanced distribution between low-frequency (n=13) and high-frequency (n=12) users, the overall sample size was small (n=25), which may limit the statistical power of the findings. Furthermore, there is a potential selection bias due to the inclusion criteria requiring internet access and a personal smartphone, possibly excluding certain vulnerable groups such as older adults and individuals with lower health literacy and socioeconomic challenges. When interpreting the results, these factors should be considered and underscore the need for further research with more diverse and larger samples.

Most patients reported medium-to-low pain levels and were in the acute stages of survivorship, which might have affected the frequency of mobile app use. Indeed, although the total number of times the mobile app was accessed was relatively high and satisfactory, some participants decreased their total usage in the last month of the study, with 2 out of 25 participants using the mobile app only at enrollment.

A limitation related to the timing of mobile app use was the collection and evaluation of only the total number of times the app was accessed without considering when the app was used during the study period.

Conclusions

This pilot study evaluated the usability of the PainRELife digital health ecosystem designed to enhance CP management for early breast cancer patients. The results indicate that the PainRELife app is well-designed and user-friendly, effectively meeting the needs of breast cancer patients managing CP. The use of the app was associated with significant improvements in pain self-efficacy and reductions in pain intensity. Additionally, patients who perceived their involvement in SDM were better engaged with the app and perceived it as of higher quality.

However, given the preliminary nature of this study, further research is needed to confirm these findings and evaluate the app's long-term effectiveness in a broader clinical context. Future research should also explore the integration of personalized interventions based on initial pain self-efficacy levels to maximize the PainRELife system's effectiveness. Additionally, it is crucial to address the specific needs of patients with CP who have decisions to make regarding their pain treatments. Tailoring the decision aids to provide more concrete and decision-relevant information could enhance their effectiveness and support patients in making informed pain treatment choices.

Chapter 5

General Discussion

5.1 Summary of Findings

This doctoral dissertation has delved into the dynamics of CP management in cancer, transitioning from broad inquiries about the impact of pain on QoL from the dual perspectives of patients and caregivers to targeted studies on breast cancer survivors and their informal caregivers. The ultimate goal has been to elucidate their emotional and practical needs to inform the development of a digital health ecosystem designed to overcome barriers in pain management.

Throughout this dissertation, the term “caregiver” has exclusively referred to informal caregivers—family members, partners, or close friends who provide ongoing physical, emotional, and social support to the patient outside of a clinical setting. Healthcare providers, such as doctors, nurses, and allied health professionals, have been referred to as "healthcare providers" or "HCPs" and not as caregivers.

The first study identified substantial challenges in managing cancer-related CP and its profound impact on patients and caregivers across all dimensions of QoL, including physical, emotional, functional, social, and family well-being (see Appendix 4). Regarding patients’ perceptions, the nature of the pain plays a critical role in its impact on QoL: widespread pain post-surgery, continuous pain, and pain that is persistent, uncontrollable, and intense are significant risk factors for poorer QoL. Sex/gender-specific differences were also observed, with women reporting higher levels of impairment compared to men. For example, breast cancer patients report more frequent and severe pain and higher levels of depression compared to men. Similarly, rectal cancer patients experience differences in pain perception, with women facing more emotional disturbances and sleep issues, while men report higher levels of fatigue and dyspnea. CP also affects specific sub-domains of QoL such as sexuality, employment, and psycho-emotional and social dimensions. Psychological factors such as attachment styles and pain catastrophizing significantly influence the experience of CP. Patients with anxious attachment styles and catastrophizing thoughts are more likely to experience severe pain and emotional distress, whereas those with avoidant attachment styles tend to report less pain but experience poorer overall QoL due to restricted emotional expression.

Additionally, social factors such as diminished general functioning, financial hardships, and a lack of social support exacerbate the challenges faced by patients with CP. Protective factors contributing to better QoL include lower intensity and frequency of pain, higher education levels, lower psychological distress, strong caregiver support, and robust social and relational well-being. Long-term cancer survivors suffering from CP not only experience deterioration in overall QoL but also face declines in family and home responsibilities, recreational activities, and employment conditions. This highlights the need for holistic pain management approaches that address both the physical and psychological aspects of pain.

In line with these findings, it is important to consider the emerging recognition of nociplastic pain as a distinct mechanistic descriptor in the pain experiences of cancer patients, particularly breast cancer survivors. Recent studies have classified CP in this population into distinct phenotypes, including nociplastic pain, which is characterized by central sensitization and altered nociception [16]. Notably, women are more likely to report nociplastic pain, which may contribute to the heightened pain sensitivity and complex pain profiles observed in female cancer patients [85]. These findings are consistent with broader research indicating that women experience and report pain differently due to a combination of biological, hormonal, and psychosocial factors [19,20]. This type of pain, often exacerbated by hormone therapy, is associated with poorer health-related QoL, particularly in areas related to bodily pain and social functioning [85]. These findings underscore the necessity for sex/gender-sensitive approaches to pain management that account for the unique impact of nociplastic pain in women [18,85].

Regarding caregivers' perspective, informal caregivers face stress adjustment challenges that manifest as physical, psychological, and social health impairments. CP significantly compromises caregivers' QoL, including social, psychological, spiritual, and physical aspects. Their well-being is influenced by the patient's pain level and their self-efficacy in managing it. Significant risk factors for caregivers include the intensity and persistence of the patient's pain, financial burden, and lack of social support. The study revealed significant emotional strain and physical exhaustion among caregivers, impacting their ability to provide effective care. Protective factors that can mitigate these impacts include positive adaptation strategies, adequate pain management education, strong social support networks, and a good knowledge of pain management. This underscores the need for comprehensive support systems and interventions that address caregivers' multifaceted challenges, promoting their health and well-being as they care for patients with CP.

From an integrative perspective, CP management involves the entire family, with mutual influences between patients' experiences and those of their caregivers. Persistent, uncontrollable, and intense cancer pain significantly deteriorates QoL for both patients and caregivers, causing heightened stress and emotional burden. Patients with chronic conditions often rely on their caregivers, fostering co-dependence that can intensify care requirements and lead to a perceived burden on family members. Relational factors are crucial in navigating the challenges of cancer-related CP and promoting health and well-being among patients and caregivers. Stable and supportive relationships significantly contribute to better coping mechanisms, adaptation, and improved QoL.

Building on these insights, it is important to consider the role of sex/gender dynamics in shaping the interactions between patients, caregivers, and healthcare professionals. Research has shown that gender biases can significantly influence these interactions, particularly in the context of CP management. For example, female patients are more likely to have their pain experiences invalidated or attributed to emotional causes, a process known as the "psychologization" of women's pain, which leads to disparities in treatment and care quality [256,257]. Additionally, a pattern of separation between men and women that is not rooted in biological differences but in gendered norms was emphasized. According to Samulowitz et al. [257], this dichotomy between men and women has been described as a mechanism to establish and maintain the gender order, allowing men's dominance over women.

These biases extend beyond patient-provider interactions to affect informal caregivers as well. As Bartley and Fillingim [20] highlighted, women often adopt coping strategies that involve seeking social support more frequently than men. This tendency could indirectly place a greater emotional and practical burden on male caregivers, who may feel less equipped to provide the needed emotional support. Additionally, healthcare providers might unconsciously perpetuate gender biases, influencing the quality of care delivered to patients and the support given to caregivers. These dynamics underscore the importance of developing gender-sensitive support systems for both informal caregivers and healthcare providers, recognizing the unique pressures that different sex/gender roles can create in caregiving relationships.

In continuation of these findings, the second study delved deeper into the comprehensive representation of cancer pain from the perspectives of both patients and caregivers, utilizing mixed methods (content analysis, hierarchical cluster analysis, and sentiment analysis) from Reddit cancer social groups. This approach allowed for a richer understanding of these groups' specific emotional and practical challenges in managing CP.

Three prevalent types of content were identified: experiences, advice, and questions, with patients sharing more physical aspects of pain and caregivers focusing on emotional and psychosocial challenges. Patients sought reassurance or opinions from physicians about their pain and often perceived their spouse more as a caregiver than as a partner. They emphasized the physical aspects of pain, including its location, chronicity, stage of cancer, and bodily sensations like numbness and soreness. Consequently, patients predominantly highlighted the physical dimensions of their pain experience. As for caregivers, the primary discussions revolved around the psychosocial challenges resulting from their loved ones' conditions. These included economic and work-related issues, thoughts on the passage of time, disease progression, hopes for improved prognoses, and the effectiveness of treatments. Caregivers also frequently shared their experiences of grief, such as feeling numb after a death, self-blame, loss, and maintaining hope for their loved ones. A common theme of uncertainty emerged, with patients expressing it about their health status and the unpredictability of their future, often contemplating "what if" scenarios. This uncertainty can lead to various worries and fears, including the FCR, which is also shared by caregivers. Moreover, caregivers experienced uncertainty primarily through grief and the fear of losing their loved ones, highlighting their emotional struggle in managing the patient's condition and its potential outcomes. These findings underscore the need for better informational support and education to manage cancer-related pain.

Emotion and sentiment analysis showed that negative sentiments were more prevalent among patients and caregivers, with fear and sadness being the most prevalent emotions in both groups. Patients' fear often revolved around cancer recurrence and the impact of pain on their treatment, while caregivers experienced fear and uncertainty about their loved one's future. However, patients exhibited higher negative emotions overall, particularly sadness and fear. In contrast, caregivers expressed higher positive emotions such as trust and joy, indicating a more optimistic perspective.

Technological advancements and eHealth tools offer significant opportunities to enhance pain management strategies, improve communication between patients and healthcare professionals, and empower patients in decision-making [143,144,155,156]. These innovations provide essential informational support and education and could address the uncertainty experienced by both patients and caregivers. By integrating these tools into pain management protocols, healthcare providers can offer more personalized and effective care, ultimately improving the QoL for both patients and their caregivers. In this context, we aimed to explore the specific needs of breast cancer survivors and their informal caregivers to provide solutions and tailored interventions based on patients' preferences and needs. Shifting the focus from general cancer pain to breast cancer pain, the findings from Studies 3 highlight the multifaceted challenges faced by breast cancer survivors and their caregivers in managing CP.

In the first part of the study, we explored the distinct needs and challenges associated with pain management among breast cancer survivors. Significant barriers in doctor-patient communication were revealed, where physicians often focus solely on the physical aspects of pain, neglecting its psychological dimensions. This lack of empathy and support exacerbates patients' distress, emphasizing the need for better communication and more empathetic care. Additionally, patients face contextual and societal barriers exacerbated by the COVID-19 pandemic, such as healthcare access issues due to restrictive measures, health inequality, and location issues, all of which lead to financial burdens and hinder effective pain management. Participants stressed the necessity for better informational resources and practical tools to manage their pain.

The study also revealed that patients require substantial psycho-social support, often inadequate during medical consultations. Emotional support from healthcare providers is crucial, as its absence increases patients' frustration and anger. Amidst their struggles, the concept of hope emerged as a beacon, with patients expressing a desire for more accessible information about available psycho-oncology services and advocating for these services to be a standard part of cancer care. They highlighted the dual necessity of psychological support for themselves and their caregivers, acknowledging the significant emotional toll the cancer journey exerts on all involved.

Patients grappled with evolving dependency on partners, feeling burdensome and concerned about the impact on their relationships. They also voiced the need for better support and accommodations in the workplace to balance health needs with professional obligations, thus maintaining their employment and dignity. Community support and sharing were identified as therapeutic, with participants finding solace in connecting with others who had undergone similar experiences. They emphasized the importance of having a safe space for emotional expression and community building, suggesting the creation of online social groups to facilitate such exchanges.

Last but not least, patients underscored the importance of continuous care post-recovery, including home assistance and physical rehabilitation. They expressed the need for a mobile app to aid long-term monitoring and support SDM processes. Patients strongly preferred an integrated approach to pain management, combining pharmacological and non-pharmacological methods. Concerns were raised about the side effects of painkillers, and the need for alternative treatments (e.g., acupuncture, psychological support, and holistic practices) was highlighted. Personalized care at multidisciplinary centers was highly valued, as was a collaborative role in decision-making, where patients appreciated when doctors understood their concerns and involved them in the process.

In the second part of the study, exploring the emotional journey of caregivers revealed that negative sentiments were more pronounced than positive ones, with emotions such as sadness, fear, and disgust being prevalent. Caregivers also experienced more complex emotions like remorse, alarm, disappointment, despair, and unbelief. Social emotions were also noteworthy, including shame and feeling overwhelmed (frozenness). Caregivers frequently struggle with feelings of blame and guilt due to a perceived lack of preparation to handle uncertain and challenging situations. This self-perception leads them to believe they have let down or failed the people they are caring for, resulting in self-criticism and emotional distress. Such feelings foster profound emotions like remorse and shame, fostering empathetic concern for the actions they did not take.

Our findings reveal that the COVID-19 pandemic has intensified emotions such as shame, frozenness, and ambivalence. Caregivers frequently felt shame over perceived deficiencies in their ability to provide support, coupled with feelings of ambivalence and immobilization. These emotional states were often attributed to external pressures, including pandemic-related restrictions or the limitations of eHealth tools, which were perceived as inadequate only when they replaced face-to-face medical interactions. Shame, reflecting a sense of personal inadequacy, often arose from perceived external judgment during group interactions, prompting defensive reactions and emotional withdrawal. This emotion significantly augmented the perceived burden among caregivers.

Despite the prevalence of negative sentiments, caregivers consistently reported high trust in their relationships with partners and doctors. This finding aligns with results from our previous study, where caregivers frequently took on the role of supporters, maintaining a positive attitude for themselves and their loved ones. The challenge of managing CP was seen by caregivers as an opportunity to forge new synergies with their loved ones. When combined with anticipation, trust nurtured a sense of hope, serving as a vital resource in times of crisis. This hope was further bolstered when caregivers perceived their families as united and engaged with others facing similar challenges. Participation in support groups with peers alleviates stress and improves QoL. Peer support was also identified as therapeutic by caregivers finding support in connecting with others who had undergone similar experiences. The study highlighted the importance of providing caregivers with emotional support, recognizing their crucial role in managing CP, and ensuring that they, too, receive the necessary care and attention.

Taking into consideration all these findings, specifically the barriers and needs raised by breast cancer patients and their informal caregivers, it is evident that managing CP requires a comprehensive and holistic approach. This approach must address not only the physical aspects of pain but also the psychological dimensions, involving patients in their own monitoring to increase their awareness and knowledge about pain and the choices available for pain treatments. This aligns with the biopsychosocial model of pain [28], which emphasizes addressing physical, psychological, and social aspects to achieve comprehensive care. The biopsychosocial model supports a multifaceted approach to cancer pain management, recognizing that illness and pain result from complex interactions among these domains. Disruptions in any domain can affect others, compounding the overall pain experience.

Current research often overlooks these interdependencies, focusing on isolated aspects of the patient or caregiver experience. Notably, applying the STM [93,94] provides a comprehensive framework for understanding the intricate interconnections between patients and caregivers in the context of cancer pain. According to the STM, the lives of patients and caregivers are deeply intertwined, with each party's stress and coping mechanisms influencing the other. These dynamics underscore the concept of cancer, including cancer pain, as a "we disease" [101], where the impact of pain extends beyond the individual to affect their immediate social environment, particularly caregivers. Furthermore, the STM posits that the emotional and behavioral responses of romantic partners or close family members are closely linked, especially under stress conditions like CP management. The outcomes of family dynamics are heavily influenced by the individual characteristics of each member, necessitating a dyadic or family-based analysis to explore these reciprocal influences fully [183–187]. For example, a caregiver's emotional stability and coping capacity can significantly shape the patient's pain experience and overall adaptation to the illness [100,123].

Integrating a biopsychosocial perspective provides deeper insights into these domains' interconnectedness and enhances the effectiveness of pain management interventions. As the MAP [9] framework emphasizes, integrating narrative reports into comprehensive assessments can enhance understanding of the underlying reasons for pain reports and facilitate more effective pain management strategies. The PainRELife app incorporated these elements by offering educational resources, tracking pain and treatment progress, and supporting SDM processes. This integration aligns with the needs identified in the narratives of breast cancer survivors in our previous study, suggesting the app's potential to bridge gaps in pain assessment and management.

Study 4 focused on usability testing the PainRELife digital health ecosystem for managing CP in early breast cancer patients. Several key findings emerged. The PainRELife app received high usability scores, particularly in functionality, information quality, and potential for behavioral change, with higher scores in awareness and knowledge. Patients found the app intuitive, reliable, and informative. Despite this positive feedback, there were concerns about the app's ability to convert increased knowledge and awareness about CP into significant behavioral changes.

However, significant improvements were observed in pain management over the three-month period, with reductions in pain intensity and enhancements in pain self-efficacy. Patients with lower initial self-efficacy used the app more frequently, suggesting its supportive role in boosting self-efficacy. Moreover, significant correlations were observed between SDM scores and pain management outcomes. Higher SDM scores were associated with better engagement with the PainRELife app and perceived quality of care, suggesting that involving patients in their treatment decisions can improve their satisfaction and involvement in their care, thereby enhancing overall treatment experiences and outcomes. Finally, significant correlations were found between pain intensity, self-efficacy, and psychological variables such as body dissatisfaction, anxiety, and depression. This underscores the interconnectedness of physical and emotional well-being in breast cancer patients.

Taken together all these findings, it is important to note that holistic pain management approaches are vital for addressing both physical and psychosocial aspects of pain. Effective doctor-patient communication, characterized by empathy and support, is crucial for improving pain management and patient satisfaction. Participants in our studies emphasized the importance of doctors recognizing and addressing their worries and concerns regarding pain. This approach could reduce patients' hesitancy in reporting pain. Moreover, providing comprehensive informational support to patients and caregivers is essential for managing uncertainty and enhancing self-efficacy. The PainRELife app shows promise, offering valuable resources and support for pain management. Engaging patients in SDM improves their satisfaction and involvement in their care, reducing feelings of helplessness and enhancing their overall treatment experience. Additionally, addressing the emotional needs of caregivers is vital for improving the quality of care provided to patients, as caregivers' emotional well-being directly impacts their ability to support their loved ones effectively.

These findings are consistent with the recommendations from Hewitt et al. [64], Mullen et al. [75], and Emery et al. [66], which highlight the necessity of comprehensive survivorship care. This includes monitoring for recurrence, managing long-term side effects, providing psychosocial support to address common issues (e.g., pain, fatigue, FCR, uncertainty about the future), and assisting caregivers. Integrating these recommendations into clinical practice can enhance the QoL for cancer survivors and their caregivers by ensuring their physical and emotional needs are met.

In this line, digital health tools like the PainRELife app, combined with empathetic healthcare practices and comprehensive informational support, can significantly enhance CP management for breast cancer survivors and their caregivers.

5.2 Implications for Clinical Practice and Future Research

Based on the detailed analysis and findings, the dissertation addresses several critical gaps in the literature review. These gaps include underreporting and undertreatment of pain, inadequate knowledge and education among healthcare providers, patients, and caregivers, exclusion of psycho-social factors in pain assessment, lack of tailored decision-making support, and the neglect of caregivers in pain management plans.

The underreporting and undertreatment of pain are significant issues despite existing clinical guidelines. This dissertation examines these systemic failures, highlighting the ineffectiveness of current reporting systems and treatment protocols. It advocates for a healthcare framework that fully recognizes the complex realities of patient experiences, ensuring pain management is both adequate and responsive to patient needs.

Inadequate knowledge and education among healthcare providers, patients, and caregivers are critical barriers to effective pain management. This dissertation's proposed digital health platform addresses these gaps by enhancing the knowledge and skills necessary for better pain assessment and management. The platform seeks to improve communication about pain experiences through targeted educational sections and empower patients with the information needed for effective pain management. However, a notable limitation of the study is that it did not include control and experimental groups to test the educational intervention, limiting the ability to draw definitive conclusions about its impact. Future research should include larger sample size and implement control and experimental groups to enhance the robustness of the findings.

Additionally, the study only involved patients and did not include all stakeholders, such as healthcare providers or informal caregivers. This is a critical weakness that future research should address to provide a more comprehensive evaluation of the platform's effectiveness. For instance, the Behavioral and Environmental Sensing and Intervention for Cancer [146] system discussed earlier demonstrates the transformative potential of integrated tech solutions that use real-time data collection and active patient and caregiver engagement to improve pain management. Moreover, it is essential to provide caregivers with better knowledge of the disease and support them emotionally, ensuring they are well-equipped to handle the challenges associated with cancer care.

An essential implication for clinical practice is the need for profiling cancer-related pain not just based on intensity or location, but also by understanding the underlying pain mechanisms—nociceptive, neuropathic, and nociplastic—and how these interact with sex and gender. Evidence suggests that women are more likely to experience certain types of pain, such as nociplastic pain, which is often associated with central sensitization. Recognizing these differences is crucial for developing targeted pain management strategies. However, this requires healthcare providers to be aware of and actively address potential sex-gender biases that may influence both pain assessment and treatment decisions. Such biases can lead to misdiagnosis, under-treatment, or inappropriate treatment, particularly in female patients. Therefore, integrating a sex-gender lens into the profiling of pain mechanisms should be a priority in clinical settings, ensuring that pain management is personalized, equitable, and effective for all patients.

Another critical gap is the exclusion of psychosocial factors from conventional pain management approaches. By integrating psychosocial factors into assessment models, this dissertation highlights the profound influence of psychological and social dimensions on pain perception and management. This holistic approach ensures that pain management strategies are not solely focused on physical symptoms but also consider the emotional and social aspects that significantly impact the patient's QoL and one of their caregivers.

Additionally, the dissertation addresses the lack of tailored decision-making support in current pain management practices. By promoting the development and evaluation of a decision-making framework that incorporates patient-specific data, the research underscores the need for personalized pain management plans. Tailoring the decision aids to provide more concrete and decision-relevant information could enhance their effectiveness and support patients in making informed pain treatment choices. However, our study had a notable limitation: the recruited patients were those experiencing acute post-operative pain with a baseline pain level of 3 or higher, rather than patients already dealing with CP. Consequently, these patients were not facing immediate decisions regarding pain treatment, which meant they had difficulty reporting the advantages and disadvantages of pharmacological versus non-pharmacological treatments. Their feedback could be influenced by personal biases or information provided through the app rather than imminent decision-making. Future studies should focus on breast cancer patients with CP to better demonstrate the effectiveness of the developed decision aids in supporting treatment choices.

Moreover, one of the most critical gaps identified is the neglect of caregivers in pain management plans. Caregivers are crucial stakeholders in CP management, yet their perspectives are often overlooked. The dissertation advocates for including informal caregivers in comprehensive pain management strategies, recognizing their vital role, and addressing their emotional and practical needs. During patient recruitment in the last study, we observed that husbands often accompanied their wives and supported using the app, especially in cases of cognitive complications arising from chemotherapy side effects. This underscores the need to include caregivers in future studies to better assess the platform's overall effectiveness. Additionally, providing caregivers with the necessary support and resources can significantly enhance the overall effectiveness of pain management plans.

The studies' strengths lie in their comprehensive approach to pain management, integrating physical, psychological, and social dimensions of pain. Using a mixed-methods approach further enriches the research, combining qualitative and quantitative data to provide a more nuanced understanding of pain management. Additionally, integrating digital health tools, such as the PainRELife app, demonstrates the potential for innovative technologies to improve pain management outcomes. The studies also emphasize the importance of educational interventions and the inclusion of caregivers, highlighting the multifaceted nature of effective pain management.

However, certain weaknesses of the studies remain. One significant limitation is the lack of dyadic analysis examining the reciprocal influences between patients and caregivers. Future research should implement dyadic or family-based analyses to provide a more comprehensive understanding of the interconnected nature of cancer pain. This approach could enhance our understanding of how patients and caregivers influence each other’s experiences and inform more effective, holistic interventions. Another limitation is the sample size and the absence of a control group for the app testing. Future studies should include larger sample sizes and control groups to validate the findings and assess the long-term effectiveness of the PainRELife app. Additionally, the study only involved patients and did not include all stakeholders, such as healthcare providers or caregivers. This is a critical weakness that future research should address to provide a more comprehensive evaluation of the platform's effectiveness.

5.2.1 Personal Reflections

Reflecting on my doctoral dissertation's findings, it is evident that future studies should delve deeper into intrapersonal factors (those occurring within the individual) and interpersonal factors (involving interactions between individuals) to enhance our understanding and management of cancer pain, as also shown by the model of Pietromonaco and Collins [182] in relation to health. At the intrapersonal level, one significant area for future research is patients' perception of identity changes. Many patients experience a profound sense of not being the same person they were before their cancer diagnosis and treatment, reported as one of the eight emotional concerns in cancer patients [285]. Notably, Charmaz described this phenomenon as a "*loss of self*", where individuals' former self-images disintegrate without simultaneously creating equally valued new ones [286]. During discussions with patients, this shift in identity was observed and noted to significantly impact their overall well-being, potentially increasing their perception of psychological pain. Specifically, about the shift from independence to dependence, many patients find themselves in a state of dependence reminiscent of the past, where they have to start anew in their struggle to regain autonomy. Studies have shown that the process of identity reconstruction, where survivors integrate their cancer experience into their self-concept, is essential for developing a sense of "*living through and beyond cancer*" [287]. Therefore, interventions should focus on addressing these identity-related issues, helping patients reconcile their new self-perception with their pre-cancer identity. This aspect, observed during patient discussions, merits further exploration in future studies.

Another crucial factor is sharing experiences with others who have undergone similar challenges. Patients often find solace and understanding in connecting with peers who share their journey. Encouraging patients to share their experiences can enhance their emotional support networks, fostering a sense of connection and reducing feelings of isolation. Research has found that cancer-related loneliness mediates the relationships between social constraints—such as avoidance and criticism—and symptoms like pain, fatigue, sleep disturbances, and cognitive complaints [288]. By addressing cancer-related loneliness and promoting peer support, interventions may help lessen the negative impact of these social constraints on patients' symptoms. It is important to note that several studies demonstrate how pain, in both its somatic and psychological components, is a significant risk factor for suicide [289,290], and this risk also involves patients with cancer [291]. Specifically, psychological pain (mental pain, psychic pain, or "psychache") has been defined as an unbearable feeling linked to the frustration of affiliation and protection needs [292]. In recent years, this concept has been investigated in numerous studies within the psychiatric population and has been associated with depression and suicide [293]. Recently, Naomi Eisenberger proposed the concept of social pain, which could be considered a subtype of psychological pain [294]. Social pain is "*the unpleasant experience associated with actual or potential damage to one's sense of social connection or value*" (following experiences of social rejection, exclusion, negative social evaluation, or loss of social value) and should be taken under control during assessment also for cancer patients.

The mindset about the body is also a critical factor. When pain is perceived as a threat, the threat posed by the noxious stimulus guides the level of awareness: the higher the threat, the more attention is directed towards it. Once the stimulus is attended to, cognitive processes interpret what it means [13]. Mindsets and core beliefs about the nature and workings of things in the world play a crucial role in this phase [31]. The cancer threat interpretation model [32] explains post-cancer pain within survival uncertainty. According to this model, cancer survivors often live in an environment filled with uncertainty about their symptoms, where experiencing pain can be perceived as a potential threat. Recent research has demonstrated that monitoring bodily threats is linked to higher levels of pain, FCR, and increased help-seeking behavior [35]. This connection is influenced by individuals' mindsets towards their bodies: those who see their body as an adversary experience worse outcomes, while those who view their body as responsive tend to fare better. Interventions should address the psychological impact of these changes, helping patients develop a healthier relationship with their bodies despite the physical alterations they have undergone and changing their mindset toward their bodies.

Equally important is ensuring patients feel continuously monitored throughout their treatment journey. Regular check-ins and follow-ups can provide patients with a sense of security and ongoing support, which is crucial for their mental and physical well-being. This approach can help mitigate FCR, avoiding or reducing uncertain experiences, a common stressor for cancer patients [201,226,227]. Future research should focus on managing this uncertainty, with strategies developed to help patients cope more effectively, thereby reducing anxiety and improving their overall QoL.

Regarding the interpersonal level, Pietromonaco et al. [182] emphasize that interpersonal dynamics in close relationships significantly affect individual health outcomes. They highlight how partners’ emotional support, shared coping strategies, and relationship quality can mitigate stress and improve psychological well-being. This model underlines the importance of addressing the dyadic processes and mutual influences between patients and caregivers in healthcare. In this line, future studies should consider the interdependent nature of patient and caregiver pain-related experiences. Dyadic or family-based interventions are particularly promising. These interventions should target patients and caregivers, assisting them in managing uncertainty, enhancing coping strategies, and addressing their emotions collectively. The benefits of this approach are well-documented in the literature. For example, Otto et al. [295] found that activities related to positive psychology—such as mindfulness, optimism, hope, meaning-making, and fostering positive relationships—are crucial for both patients and caregivers, aligning with our studies' findings.

Moreover, FCR is a common factor identified in both patients and caregivers, significantly impacting their emotional well-being [129,132], and should be considered an important outcome in future research for both groups. Hamama-Raz et al. [296] distinguish between intrapersonal and interpersonal aspects of FCR. They highlight that the shared fear within a dyad, particularly the FCR and the potential for death, combines both intrapersonal and interpersonal processes. This shared fear emphasizes the need for psycho-social treatment options tailored to address these intertwined factors in cancer survivors. For instance, the study by Lamarche et al. [134] adapted the Fear of Recurrence Therapy into a virtual format for family caregivers, known as FC-FORT. This intervention, involving 7 weekly virtual group therapy sessions, showed high usability and satisfaction among participants. Including caregivers in pain management strategies and addressing their emotional needs, as done with FC-FORT, can greatly enhance the effectiveness of the pain management plan. This plan could be promoted considering both patients and caregivers to reduce cognitive biases in interpreting threat signals as a cancer recurrence and improve their health.

In summary, future research should adopt a comprehensive approach, considering cancer pain management's individual and relational aspects. By addressing these intrapersonal and interpersonal factors, we can develop more effective interventions that enhance the overall well-being of cancer patients and their caregivers.

5.3 Concluding Remarks

The findings of this dissertation contribute to the growing body of knowledge on cancer-related CP and its management. By addressing critical gaps in pain reporting, education, the inclusion of psychosocial factors in pain assessment and management, and the integration of caregivers in care plans, this research advocates for a more holistic and inclusive approach to pain management. Integrating innovative technologies and recognizing caregiver roles highlight the potential for significant advancements in clinical practice and patient outcomes. As we move forward, we must continue exploring and developing comprehensive, patient-centered pain management strategies that enhance the QoL for cancer survivors and their caregivers.

This dissertation has shed light on the critical need for a more comprehensive approach to cancer pain management, emphasizing the integration of physical, psychological, and social dimensions of pain. By recognizing the unique challenges faced by patients and caregivers, this research underscores the importance of developing tailored interventions that address the specific needs of these groups.

Integrating digital health technologies, such as the PainRELife app, represents a promising avenue for improving pain management practices. These tools can enhance patient engagement, facilitate personalized care, and improve pain management outcomes. Future research should continue to explore the effectiveness of these technologies and how they can be integrated into existing pain management frameworks.

Furthermore, the importance of including caregivers in pain management strategies cannot be overstated. Caregivers play a vital role in supporting patients, and their emotional and practical needs must be addressed to ensure the overall effectiveness of pain management plans. By providing caregivers with the necessary support and resources, we can improve the quality of care for patients and enhance their well-being.

In conclusion, this dissertation highlights the urgent need for a holistic, patient-centered approach to cancer pain management. By addressing the physical, psychological, and social dimensions of pain, integrating innovative technologies, and including caregivers in pain management strategies, we can significantly improve the QoL for cancer survivors and their caregivers. The insights gained from this research provide a foundation for future studies and clinical practices to enhance pain management and overall patient care.

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Appendix

Appendix 1. Categorization of posts related to patients' and caregivers' comments

Broad categories	Code	Example of comments		Frequency (%)	
		Patients	Caregivers	Patients (n=518)	Caregivers (n=161)
Pain Dimension	Physical	*"[...] I have stage IV colon cancer which metastasized into my bones. The pain from bone cancer is crazy bad. I would shake and vomit due to how bad the pain would get...." P52*	*"My Aunt has stage IV. She's been on Keytruda for about a year now. Her symptoms were loss of appetite, vomiting, and tremors. The symptoms suck but her last MRI showed shrinkage in her main tumor and completely gone in the smaller ones that were giving her back pain [...]." C8*	359(69)	50(31)
	Psychological	*"[...] As for me, I have a recurrence of liver cancer. This time it's inoperable...I told my immediate family because we are close knit family. I told my best friend, and 2 other friends I can trust. I made the decision not to tell anyone else because I don't want to be treated differently. Also, when you drop the cancer bomb on people, you then have to comfort THEM instead of them comforting you. I can't deal with other people's emotions right now. For the first time in my life, I am being selfish and doing things my way [...]." P468*	*"My dad had prostatic cancer in 2016, he did surgery and radiotherapy. Last year the PSA levels started rising again. It took them 1 year (pandemic did not help) to realize that it might now be in the bones, so prognostic is not good. Apart from my dad who is pessimistic by nature (and so am I) out of everyone in the family I feel like I'm the one really suffering, I cry every night, I cannot sleep. My brothers seem relaxed. I don't know how I am going to handle seeing my dad in pain and getting worse and worse [...]." C37*	37(7)	44(27)
	Both[a]	*"[...] talk about anxiety and make sure you don't apologize or downplay it. Be anxious. Show anxiety. That doctor can refer you to an assortment of care providers AND some of them may be telemed so that helps me. Just getting to a doctor exhaust me....Cancer itself causes pain. Acute, scale of 7-10, needs immediate attention. Cancer treatment causes pain. Like chemo and neulastin. Radiation therapy causes still more. Nerve damage. And some time along the path, it might be acute, or drop down to moderate, scale 4-7, chronic, maybe it won't heal so how to manage it [...]. Ask for help. There are good sleep meds to help. And for talk therapy there are cancer specific psychologists. Make a list, then make them listen. If it's too much for you, bring your best advocate. Family. Best friend. Someone who knew you before your illness and can speak with truth about the old you and how cancer has changed you[...]." P104*	*"[...] My husband just passed away from his cancer which was diagnosed three years ago. It became stage iv two years ago...The prognosis is really just hopeless once it metastasizes. The day his routine checkup scan two summers ago revealed the inoperable metastasis in his lungs, has been the most devastating day of our lives. Far worse than the day he passed away. Because it changed our lives as we knew it. There was no going back to the "normal life". Living with cancer is a whole change in lifestyle [...].* *Whenever we had breakdowns after a bad news or he wasn't feeling well, I was there to listen to him and empathize with him as he expressed the different types of pain he was feeling. We both knew I couldn't cure his symptoms, but I did what I could [...] " C376*	123(23)	67(42)

Type of comments	Advice	*"I also had weird pain in my neck too and strangely my arm when I first got it. My advice is to fight through that weird discomfort and turn your neck/move your arm. It's normal for it to feel stiff because of the catheter placement, but when you keep moving your neck and arm it saves you trouble for doing extra physio for it in the future." P359*	*"Your own knowledge of your body should trump what the docs say. You've known it for a lot longer, and a lot more in detail than they can ever hope to... I'm not sure where you're located, or your access to healthcare. If it were me, or my loved ones, I'd recommends: see a specialist (Ear/nose/throat ask to otolaryngologist) and get the 'lump' in your throat checked. By seeing a brand-new doctor, they are more likely to work up a complete test, as opposed to a GP/family physician that sees you fairly frequently […]" C786*	53(10)	13(8)
	Experience	*"I had this horrible pain for over a year that eventually got to the point where I was on some strong pain meds and not able to sleep because it would constantly wake me up. I don't really know what I thought it was, but I never got checked out because I didn't have insurance. Finally realized something was serious when I ended up in the ER because I lost complete movement and feeling from my chest down." P5*	*"My mom was diagnosed with the same leukemia in January. I had a similar experience with her, she was diagnosed at the oncologist's office, and we admitted her to the hospital a few hours later. She's had three rounds of chemo and is now having her bone marrow transplant at Thomas Jefferson (she is having a half match donor transplant) […]. Chemo may not seem taxing now but it will probably get worse and she may not be up for the procedure of freezing her eggs. I'm not sure what that procedure is, but I've seen my mom go through 3 rounds of chemo and it's very tiring. […]. My mom complained a little bit about joint pain, but I haven't heard any doctor say that will be a lasting problem. My mom was in really great shape before she was diagnosed, she weights lifted and hiked all the time. But she's also 53 so her experience will probably be different than your wife's.[…]. " C163*	422(81)	130(81)
	Both[b]	*"I can honestly say I have been in pain every day for 18 years. Please get painkillers! They are absolutely lifesaving! If your doctor won't prescribe any then go find a pain clinic and bring all your medical records…Cancer is becoming more and more of a chronic disease for some people rather than a death sentence. If your cancer is being kept stable and you still have a semi-decent quality of life (you're still able to travel drink alcohol!) then it's just something, you'll have to live with…I'm on a targeted therapy drug that just got developed less than 10 years ago. Unless there are *significant* advances in healthcare in my lifetime, I can't be cured and it's likely that I'll just have to take the targeted therapy for the rest of my life. I'm currently 20 and I've been taking it for a couple years…I'm expected to have a half-decent lifespan if I continue dealing with the side effects and can afford it…I need to learn to live with this as a chronic disease and stop worrying*	*"[…] On to your questions. I'll answer them in the order asked. My father did the BCG treatment while the tumor was at stage 1. This is the default first defense urologist and oncologists usually consider for early-stage bladder cancer. The moment the first tumor was discovered, surgery was done to get it out of him. They pulled a 3cm. tumor out that was shaped like a cauliflower. This was the only surgery done prior to BCG to remove tumors. Experience with BCG was unpleasant. The virus is administered via a tube slipped into the urethra. It has a bad burning and itching sensation. My dad was told to hold it in for at least 1-2 hours if I remember right. It made the drive home from treatment hard, especially if there were bumps in the road. After the allotted time limit, my dad was allowed to urinate. What followed after the first day of treatment would be flu like symptoms. Aside from those, no hair loss. Just some nausea and the itchy/burning pain in the bladder. Urinating was a bitter/sweet sensation as the*	34(7)	18(11)

		about a cure. It's not killing me right now, it's just stable, so I'll be fine unless something goes super wrong. But accidents can happen all the time, not just with my cancer. Worrying all the time about mine getting aggressive would be as pointless as me worrying about getting run over. Chronic pain is a SIGNIFICANT deterrent in having a good quality of life." P222	*affects wore off over weekends. The symptoms could last 2-4 days [...]"C801*		
	Question	*"Did you have fatigue and neuropathic pain during all of Taxol? I'm doing 4x and have done 3, 3rd was today. Still haven't felt any side effects." P282*	*NA*	9(2)	0
Type of pain	Acute	*"[...]I know how it feels. My symptoms started with severe acute pancreatitis which sent me in an ambulance to the ER. Was admitted for 10 days and they removed my gall bladder. Gall stones had blocked the bile duct at the opening to the pancreas. After that I had periodic (about once a month) attacks of pain that typically required a visit to the ER because of severe pain." P103*	*"I know it doesn't sound healthy, but my mom (75, mouth cancer) spent a LOT of days on just Boost and Chocolate Milk...She's currently having mouth discomfort from the chemo but nothing like she had from the radiation" C355*	51(10)	4(2)
	Chronic	*"[...]We can affect our lives by making choices. Sometimes our choices are severely limited due to luck, chance and circumstance[...]. I've had cancer since I was 10 years old. I've had chronic pain for 15 years. I started balding when I was 15-16. My teeth took a huge toll during chemo. For 10 years my right leg was 4-5 inches shorter than my left, with my feet being 3 shoe sizes different from each other. I walked with a very noticeable limp. Then the cancer returned, and my leg was amputated. P252*	*"[...] It is hard to understand and accept that the process to solve chronic, cancer pain is complex, long, and difficult. They need to find a balance between keeping him alive and addressing his pain, and it's not easy. Trust the doctors but keep advocating for your dad. It's been five weeks for my wife and we're still working on it. One step forward and two backwards so far. In my wife's case, it was fundamental to understand anxiety and trauma from pain were making everything worse, were increasing her physical pain, or at least the perception of it, so including psychiatric medication is helping. As for those witnessing his pain: I'm sorry, I'm so sorry. I know how much it hurts and how much this affects you. It is extremely painful and difficult to live with. I am hugging you so tight. My heart is with you. My only advice is to take turns. Everyone experiencing this needs some distance from it from time to time. As much as it hurts and scares me to be away from my wife, I had to ask my Mil to come and stay with her at the hospital for a few days (I'll stay the nights). If I don't spend some time away from pain I will lose my mind, I know [...]" C261*	80(15)	18(11)
	Acute neuropathy	*"[...] I got 4 rounds of AC, spaced two weeks apart. I started getting sick at my stomach about 8hrs after treatment one. Then two days later felt sick all day. That pattern repeated for each of those courses. Felt*	*"[...] Experience with BCG was unpleasant. The virus is administered via a tube slipped into the urethra. It has a bad burning and itching sensation. My dad was told to hold it in for at least 1-2 hours if I remember*	18(3)	1(0.6)

	sore for several days after each of these. The soreness was probably caused by the neulasta, not the actual chemo. Hair fell out around 3 weeks after first treatment. Then I had 16 weeks of taxol. I didn't get sick to my stomach or ill feeling but the effects like weakness, neuropathy, and bleeding nails got worse the more of them I got." P590	*right. It made the drive home from treatment hard, especially if there were bumps in the road. After the allotted time limit, my dad was allowed to urinate. What followed after the first day of treatment would be flu like symptoms. Aside from those, no hair loss. Just some nausea and the itchy/burning pain in the bladder. Urinating was a bitter/sweet sensation as the affects wore off over weekends. The symptoms could last 2-4 days. C801*		
Chronic neuropathy	*"Acute pain in my prostate area starting at the end of May 2010, became chronic over the next few months...the worst pain has been a result of radiation and chemo induced neuropathy. I have a dependency on oxycontin now because I had to take it through the course of my treatment along with morphine and dilaudid. Lost feeling in both my feet at one point due to the effects of vincristine (aforementioned neuropathy)[...]. Pain and feeling like death sums it up nicely. Stage IV rhabdomyosarcoma btw." P166*	*"My husband is 65. Same diagnosis in May 2019. Did the 6 weeks of chemo and radiation followed about a month later by the esophagectomy. He actually did great. In hospital 6 days and no complications. Back to work 6 weeks later. Got the J tube out about 2 months after surgery. He was thin to start with so keeping weight on has been a struggle. They had to convert his laparoscopic procedure to open thoracotomy because when they went to separate his esophagus and trachea they were pretty well stuck and they made a hole in the trachea they had to repair urgently so converted to open. Still recovered really well though. Has had some persistent numbness and soreness right on the site of the big incision on his flank area [...]. He just started Opdivo and Folfox today." C554*	52(10)	3(2)
Neuropathy	*"[...] I also have incurable bone cancer (Ewing Sarcoma). Bone pain is so f* rough man. And I have neuropathy too. I'm gonna tell you my pain meds that I take every day.* *Gabapentin (nerve pain)* *Amitriptyline (nerve pain)* *Hydromorphone (opioid for overall body/bone pain)* *Celebrex (aleve works too) (NSAID drug which helps my bone pain)* *I'm telling you those so that when you talk to a palliative/pain doctor, you can advocate for him and ask questions about more specific drugs if you need to." P48*	*"[...] We tried Tube feeding, both NJ and J tube. I had so much hope on this last one. It didn't work for him. He gets a lot of bloating and inflammation, even connected 24 hrs at a slow drip, he couldn't tolerate it. The situation got worse with the leaking and skin burns. Doctor offered to try again, but I do think my dad is going through ptsd about it. He is suffering a lot just with the thought of it. I will try to bring it up again, I do almost every day, but he doesn't want to go through it." C300*	95(18)	12(7)
Somatic	*"[...] After my surgeries, I found it helpful to also work with someone who does somatic experiencing and somatic touch because of the trauma related to surgery and just the overall cancer experience [...] " P267*	*NA*	2(0.4)	0
Visceral	*"[...] Cancer pain is like no other. It's this visceral, holistic, constant overall pain no matter where it's located. The mucositis from radiation is particularly*	*NA*	1(0.2)	0

	sore for several days after each of these. The soreness was probably caused by the neulasta, not the actual chemo. Hair fell out around 3 weeks after first treatment. Then I had 16 weeks of taxol. I didn't get sick to my stomach or ill feeling but the effects like weakness, neuropathy, and bleeding nails got worse the more of them I got." P590	*right. It made the drive home from treatment hard, especially if there were bumps in the road. After the allotted time limit, my dad was allowed to urinate. What followed after the first day of treatment would be flu like symptoms. Aside from those, no hair loss. Just some nausea and the itchy/burning pain in the bladder. Urinating was a bitter/sweet sensation as the affects wore off over weekends. The symptoms could last 2-4 days. C801*		
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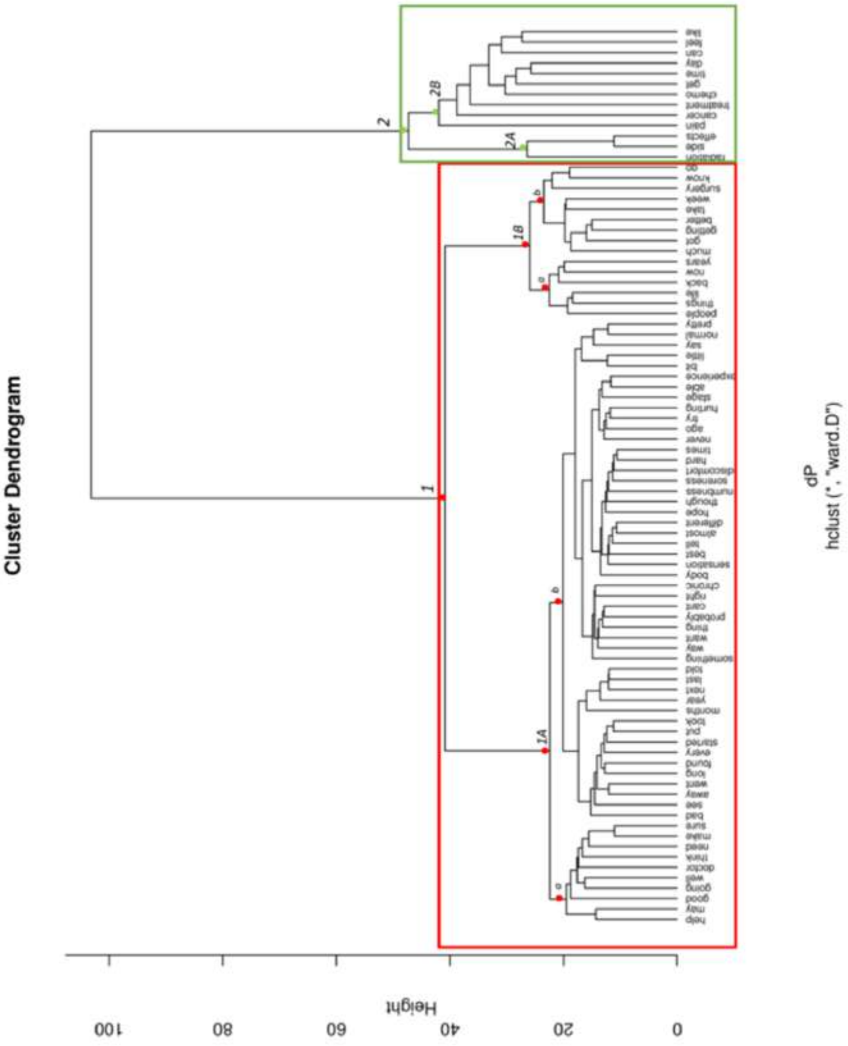
Neuropathy	*"[…] I also have incurable bone cancer (Ewing Sarcoma). Bone pain is so f* rough man. And I have neuropathy too. I'm gonna tell you my pain meds that I take every day.* *Gabapentin (nerve pain)* *Amitriptyline (nerve pain)* *Hydromorphone (opioid for overall body/bone pain)* *Celebrex (aleve works too) (NSAID drug which helps my bone pain)* *I'm telling you those so that when you talk to a palliative/pain doctor, you can advocate for him and ask questions about more specific drugs if you need to." P48*	*"[…] We tried Tube feeding, both NJ and J tube. I had so much hope on this last one. It didn't work for him. He gets a lot of bloating and inflammation, even connected 24 hrs at a slow drip, he couldn't tolerate it. The situation got worse with the leaking and skin burns. Doctor offered to try again, but I do think my dad is going through ptsd about it. He is suffering a lot just with the thought of it. I will try to bring it up again, I do almost every day, but he doesn't want to go through it." C300*	95(18)	12(7)
Somatic	*"[…] After my surgeries, I found it helpful to also work with someone who does somatic experiencing and somatic touch because of the trauma related to surgery and just the overall cancer experience […]" P267*	*NA*	2(0.4)	0
Visceral	*"[…] Cancer pain is like no other. It's this visceral, holistic, constant overall pain no matter where it's located. The mucositis from radiation is particularly*	*NA*	1(0.2)	0

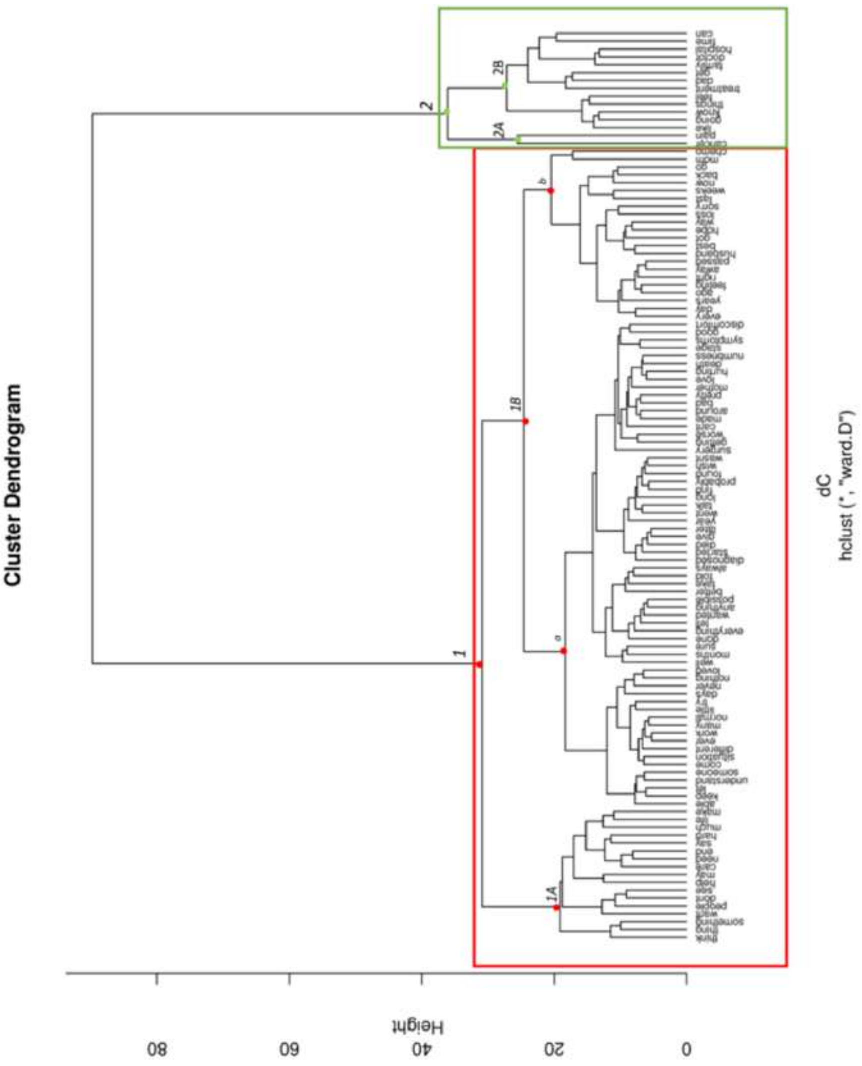
NA	*"I couldn't sit still. Not hyperactive or anything, I just kept adjusting and moving in my seat. My doctor said it was probably the normal side effect of bone pain, but I never thought the pain was that bad, until he prescribed me some pain killers and I full on relaxed and was able to sit still. It was my mum who said she noticed how suddenly I was sitting still." P1*	*"I am caring for my mother right now and what I would my friends to do is something I haven't found a way to ask them. I think of my mom every day at every moment, but some of my friends don't want to ask or inquire as much as they might be interested in, because they think it will upset me. So they ask about other things in my life and sometimes point out the good parts, but none, and I mean NONE, of it matters when your parent has cancer. I would want my friends to be comfortable with the situation. To be able to ask and sit with the silence when I say that I feel tremendous pain or weight on myself. I don't need them to lift the pain away. But just be there with me, weather those are texts or calls or meet ups. I would want constant reminder that they are there. Because even when they say they are and that I can absolutely reach out, I need them to do the reaching. So from my situation no gifts or food deliveries wouldn't help. It's the presence of a true friendship I need." C63*	270(52)	89(55)

Note. [a] physical and psychological; [b]advice and experience; [c]type of cancer of patients discussed in the posts; [d]leukemia, lymphoma, myeloma; [e]ovarian, cervical, uterine, vaginal, vulvar; NA=not available.

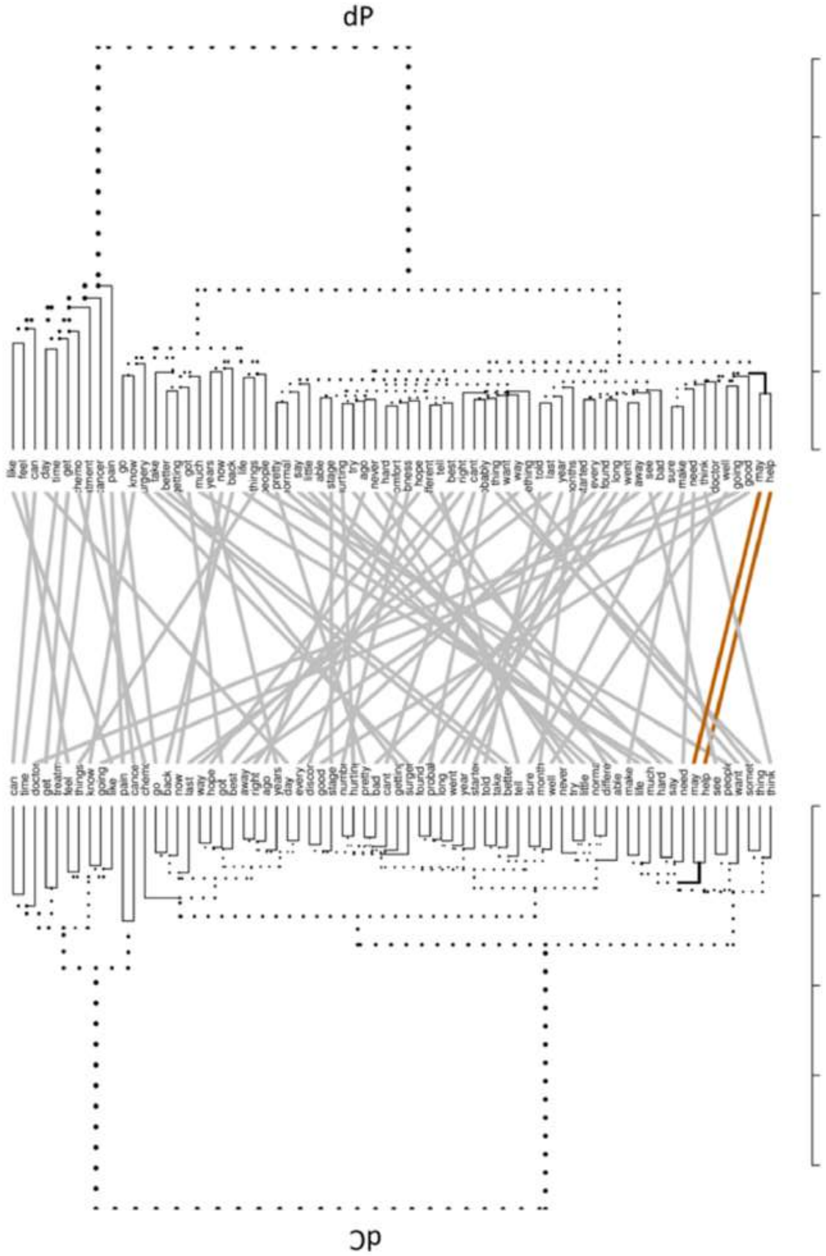
Appendix 2. Dendrogram analysis of patients' and caregivers' posts and their comparisons



Notes. Hierarchical clustering of patient comments.



Notes. Hierarchical clustering of caregiver comments.



Notes. Side-by-side comparison of patient and caregiver dendrograms using a tanglegram.

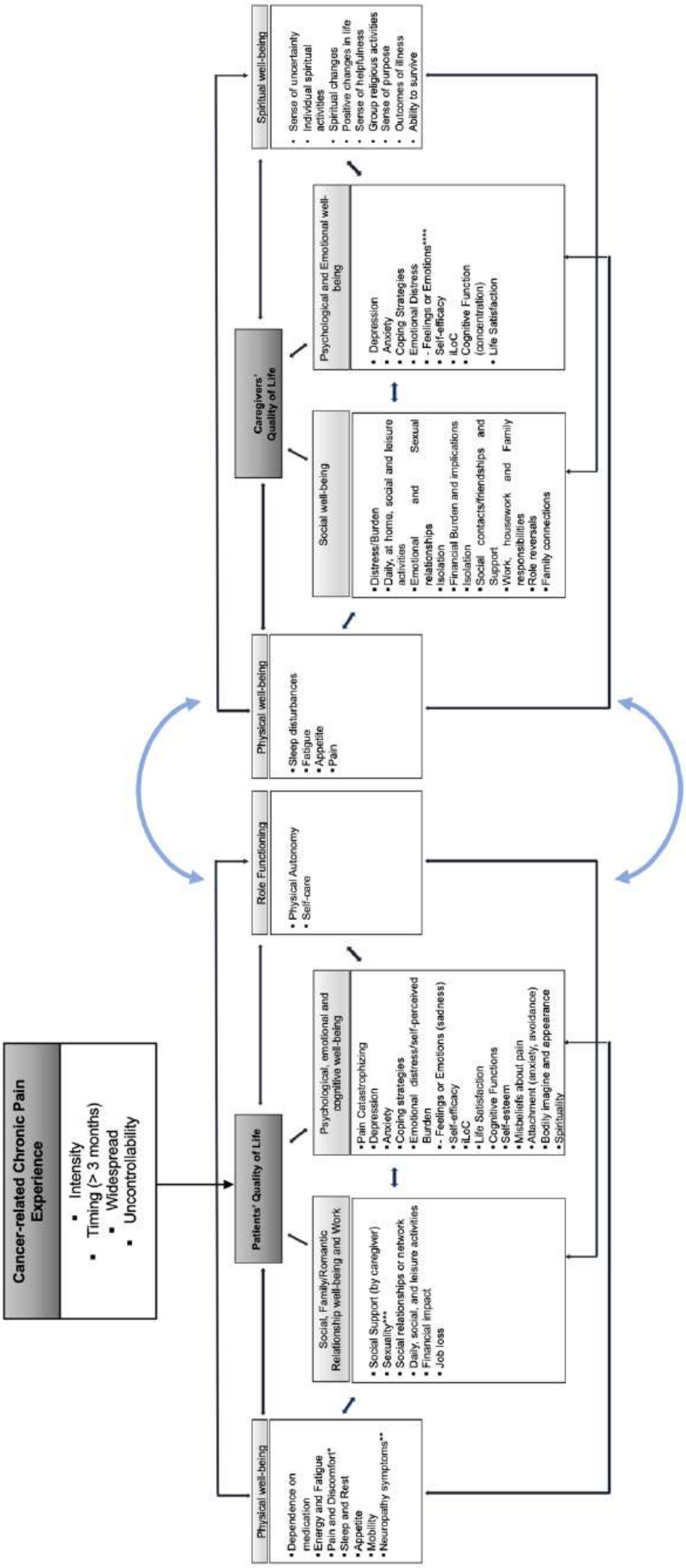
Appendix 3. Correlations between the psychological variables of the PainRELife App

Key variables	Results, Mean (SD)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
NRS_T0 (1)	5.00 (1.68)	-	-.050	.115	.307	.355	.241	-.047	-.055	.096	-.124	.026	.180	.081	-.088	-.225	.000	**-.408***	.000	-.032
NRS_T1 (2)	3.52 (2.49)		-	.192	.628	.477	.273	**.661***	**.595****	**.543****	**.444***	.379	.392	.612**	-.088	-.058	**.480***	.290	-.075	.013
NRS_T2 (3)	3.72 (2.59)			-	.675	.424	**.477***	.506	.329	.379	**.400***	.151	.172	.337	-.217	-.053	**.464***	.015	.097	.071
BPI_severity_T0 (4)	3.71 (1.25)				-	.807	.591	1.000**	.711	**.768***	.478	.547	**.902****	**.907****	.060	.598	.672	.458	-.525	-.498
BPI_severity_T2 (5)	3.13 (2.11)					-	.302	**.794****	.426	.497	.438	.212	**.869****	**.703****	-.116	-.107	.055	-.146	-.164	.098
BPI_interference_T0 (6)	4.42 (1.98)						-	.440	**.493***	**.483***	**.496***	.282	.257	.261	-.196	.033	**.518****	-.120	-.322	.104
BPI_Interference_T2 (7)	3.89 (3.12)							-	**.722****	**.813****	**.791****	**.732****	**.832****	**.803****	.097	-.145	.368	.077	-.382	.083
HADS_depression_T0 (8)	7.24 (4.53)								-	**.742****	**.601****	.393	.387	**.616****	.017	-.041	**.465***	.347	-.314	-.019
HADS_depression_T2 (9)	5.96 (4.40)									-	**.444***	**.627****	**.437***	**.721****	.147	-.306	**.575****	-.109	-.272	-.118
HADS_anxiety_T0 (10)	8.52 (4.58)										-	**.406***	**.452***	.387	-.117	-.066	**.485***	.186	**-.531****	-.014
HADS_anxiety_T2 (11)	7.12 (3.82)											-	.278	**.424***	**.480***	-.308	**.430***	-.130	-.358	-.111

Key variables	Results, Mean (SD)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
PCS_T0 (12)	15.12 (8.11)												-	**.599****	-.164	.104	.339	-.033	**-.546****	-.239
PCS_T2 (13)	12.84 (9.15)													-	-.042	-.202	**.561****	.058	-.337	-.179
PSEQ_T0 (14)	40.92 (8.95)														-	-.182	-.334	.026	-.023	.353
PSEQ_T2 (15)	44.80 (11.99)															-	-.186	**.415***	.036	-.222
ALGA_body-dissatisfaction_T0 (16)	3.36 (10.76)																-	-.083	-.391	**-.409***
ALGA_self-efficacy_T0 (17)	2.42 (0.46)																	-	-.054	-.098
CPS_T0 (18)	4.28 (1.49)																		-	.292
SDM-9-Q_T0 (19)	80.89 (22.45)																			-

Notes: *p<.05, **p<.01, ***p<.001. NRS = Numeric Rating Scale, T0 = baseline, T1 = one-month follow-up, T2 = three-month follow-up, BPI = Brief Pain Inventory, HADS = Hospital Anxiety and Depression Scale, ALGA = ALGA Brief Questionnaire, PCS = Pain Catastrophizing Scale, PSEQ = Pain Self-Efficacy Questionnaire, CPS = Control Preference Scale, SDM-9-Q = 9-item Shared Decision-Making Questionnaire.

Appendix 4. A comprehensive conceptual framework about the interrelation between cancer-related chronic pain and both patients' and caregivers' quality of life



The figure shows the impact of cancer-related chronic pain on patients' and caregivers' quality of life. As shown, all domains and sub-domains are affected and mutually interrelated, modulating the experience of chronic pain.

Notes: - = negative; *constipation, dyspnea, nausea/vomiting; **erectile problems, trouble hearing, opening jars or bottles, walking stairs or standing up, tingling toes/feet, numbness, aching, burning; ***desire/fantasy, activities/behavior, arousal, intensity of orgasm, ability to maintain an erection, erectile dysfunction or ejaculation disorder; ****sense of usefulness or incapacity, selfishness, self-blame, sense of guilty, frustration, anger, fears, sadness, irritability, loss of interest, iLoC = Internal Locus of Control.

Acknowledgments

These four years have finally come to an end. They have been long and challenging years, and it is now time to close this chapter to open a new one with a greater awareness of what I desire and a maturity gained also thanks to this journey. Therefore, it is now appropriate to thank and be grateful to the people who have helped me reach the final goal.

First and foremost, I must thank my Life Partner, who believed in me from the beginning and encouraged me not to give up. There have been many moments of crisis, and his words were fundamental in helping me get up and fight with greater strength and determination. He taught me to get back up and not throw in the towel, to see things from another perspective, and to fight for my dreams.

I also must thank my Babesina, also known as Crisi Isterica. We embarked on this journey together, but unfortunately, our acquaintance was initially limited by COVID-19. As soon as this great barrier was broken, she became my point of reference and still is. Over these long years, we have been each other's support, and her constant presence made me realize how essential she is to me because she allowed me never to feel alone, something I have often felt in my life, and capable of facing difficulties. She always told me: Devastata (oh yes, because this is my nickname), what are you saying? You have the fire inside you, let it out!

No one knows as much as we do about the challenges we have faced, the losses along the way, and the new acquaintances made, including our favorite confused animal. The flamingos were fundamental for us in the middle of our journey; they taught us to look beyond, stay, and move in a group. From there, the Jellyfishes were born, career beasts who never tried to reach the end of the rope (“Siamo alla frutta”, we often said).

We cannot forget the beloved Veronica from the SEMM office, who was always there for us and helped us untangle the knots that appeared on our path. Because everyone tells you that a Ph.D. is an enriching experience, but no one tells you that the journey is not linear but has great peaks up and down, and that the arrival along the way always seems endless.

But now we have reached this arrival, the queen of the pigeons Chiarina, we lost her along the way, and the other jelly Massimone, we leave to face another year, but he knows that we will always be there for him and that pizza will not be missing in the canteen.

And what I can say is that I must thank our beloved Confusa because she has been a source of inspiration. She doesn't know it, but she is super powerful with her wealth of knowledge. Who knows what she thought of me seeing help messages always sent and then deleted the second after in chat.

I thank my family because it is thanks to them that I am the person I am today. A special thanks goes to my therapist, who taught me what it means to be grateful and accept limits and imperfection.

A special thanks also to my big bro Gio, also known as @pensieroalsole, who taught me to look beyond the tangible with his poetry, and my little angels Vale and Robi, who have always been and will always be by my side. To my twin Chry Chry, with whom I share my ironic spirit, the fantasy of octopuses forming in our bellies, and our beloved Pausini.

To my friends Sofia, Tania, Silvia, and Susanna, who have always believed in me. Susi, thank you for instilling in me a passion for research and for making me understand that we must pursue what we desire without setting too many expectations.

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I want to extend my heartfelt thanks to all the patients and caregivers who have helped us achieve these results. Their courage in facing daily suffering has been greatly admired.

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I finally dedicate this achievement to myself and look forward to the next adventure!