



**HAL**  
open science

# Assessment of pain prevalence in cancer patients undergoing anticancer treatments and in cancer survivors after completion of anticancer treatments: A French nationwide cross-sectional study

Charles Ragusa, Bruno Pereira, David Balayssac

## ► To cite this version:

Charles Ragusa, Bruno Pereira, David Balayssac. Assessment of pain prevalence in cancer patients undergoing anticancer treatments and in cancer survivors after completion of anticancer treatments: A French nationwide cross-sectional study. *International Journal of Cancer*, 2024, Online ahead of print. 10.1002/ijc.35280 . hal-04817552

**HAL Id: hal-04817552**

**<https://hal.science/hal-04817552v1>**

Submitted on 3 Dec 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

# Assessment of pain prevalence in cancer patients undergoing anticancer treatments and in cancer survivors after completion of anticancer treatments: a French nationwide cross-sectional study

Charles RAGUSA <sup>1</sup>, Bruno PEREIRA <sup>2</sup>, David BALAYSSAC <sup>1\*</sup>

1. Université Clermont Auvergne, INSERM U1107, NEURO-DOL, CHU Clermont-Ferrand, Direction de la Recherche Clinique et de l'Innovation, Clermont-Ferrand, France.

2. CHU Clermont-Ferrand, Direction de la Recherche Clinique et de l'Innovation, Clermont-Ferrand, France.

\* Corresponding author: David BALAYSSAC, INSERM U1107 – NEURO-DOL, UFR de Pharmacie – Laboratoire de Toxicologie, TSA 50400, 28 place Henri Dunant, 63001 Clermont-Ferrand cedex 1, France, Tel: +33 4 73 17 80 41, and email: [dbalayssac@chu-clermontferrand.fr](mailto:dbalayssac@chu-clermontferrand.fr)

**Keywords:** pain; cancer patients; cancer survivors; quality of life

## Abbreviations

BMI: Body mass index

BPI-SF: Brief Pain Inventory – short form

DN4: Douleur neuropathique 4 questions

ES: Effect size

HADS: Hospital Anxiety and Depression Scale

ICD-11: International Classification of Diseases 11th Revision

INCa: Institut National du Cancer

INSEE: National Institute of Statistics and Economic Studies

QLQ-C30: Quality of life questionnaire – core 30

QoL: quality of life

SD: Standard deviation

VAS: Visual analogue scale

VICAN : Vie après le CANcer

WHO: World Health Organization

95% CI: 95% confidence interval

## Category

Cancer Therapy and Prevention

## Novelty & Impact Statements

Pain prevalence in France during and after cancer tends to remain stable, with nearly 50% of individuals still reporting pain (pain score  $\geq 4/10$ ). Pain had a negative impact on QoL in both groups, but the impact on global health status, functioning, symptom severity, and depression was greater among cancer patients.

## **Abstract**

Pain is a common and disabling symptom of cancer and its treatment. This study aimed to provide an update on the prevalence, characteristics, and impact of pain on quality of life (QoL) in cancer patients and survivors in France. Data were collected using self-assessment questionnaires as part of a nationwide web-based survey conducted between January and March 2023. Pain was reported by 44.7% of the study population (n=1029), including by 49.2% (95% CI [44.8; 53.6]) of cancer patients (n=255/518) and 40.1% (95% CI [35.8; 44.5]) of cancer survivors (n=205/511). Chronic pain was more prevalent among survivors (99.0%) than patients (87%), but no between-group differences in the prevalence of neuropathic pain (66.8% vs 67.5%, respectively) or other pain characteristics (pain intensity, location, etc.) were observed. Pain had a negative impact on QoL in both groups, but the impact on global health status, functioning, symptom severity, and depression was greater among cancer patients. Analgesic use was also more frequent among patients than survivors. Breast cancer, being overweight or obese, and having a poorer global health status were identified as main factors increasing the likelihood of pain. Pain therefore remains a common symptom among cancer patients and survivors in France. Further improvements to management are needed, including strategies to target chronic and neuropathic pain, and the high frequency of pain associated with breast cancer. Multimodal interventions to improve global health status, help individuals maintain a healthy weight, and reduce the impact of cancer pain on QoL could also be evaluated.

## 1. Introduction

Pain is a common symptom of cancer, occurring at diagnosis and during and after treatment with an estimated prevalence of 44.5%<sup>1</sup>. As the global cancer burden continues to rise<sup>2</sup>, cancer pain is a growing worldwide public health concern. Cancer pain is classed as moderate-to-severe in around a third of cases<sup>1</sup>, and can be acute, episodic, or chronic, with or without a neuropathic component<sup>3,4</sup>. The pain can be caused by the tumor or metastases, diagnostic procedures, or cancer treatment<sup>5,6</sup>. Insufficient management of cancer pain interferes with activities of daily living, has a major impact on quality of life (QoL), and is associated with anxiety, depression, and sleep disturbances<sup>7-10</sup>.

Strategies for cancer pain management have evolved considerably in recent years. A new classification for chronic cancer-related pain has been included in the International Classification of Diseases (ICD-11)<sup>5</sup>. The 1996 World Health Organization (WHO) cancer pain management guidelines, which included recommendations for a three-step therapeutic ladder from non-opioids to weak opioids to strong opioids when pain was severe<sup>11</sup>, were updated in 2018<sup>12</sup>. The new recommendations advocate the use of nonsteroidal anti-inflammatory drugs (NSAIDs), paracetamol, and opioids, either alone or in combination, during both treatment initiation and maintenance to relieve pain to a level that allows for an acceptable QoL<sup>12</sup>. While pharmacologic treatment remains the mainstay of management, clinical practice guidelines and standards developed by national and international health bodies also highlight the importance of regular pain assessments, invasive management of refractory pain, and the use of a multimodal approach including non-pharmacologic interventions (e.g. physical or occupational therapy, psychosocial support, and patient education programs)<sup>6,12-14</sup>.

Despite these advances, undertreatment of cancer pain remains common, affecting around 40% of patients<sup>15</sup>. Various barriers to effective pain management have been identified among patients and health care professionals, including lack of knowledge and training about cancer pain and management, inadequate pain assessment by physicians and patient reluctance to report persistent pain, late or inadequate access to opioids, and reluctance to initiate or adhere to opioid therapy due to fear of addiction and side effects<sup>13,16-18</sup>.

Continuing to assess pain prevalence in cancer patients and survivors, and increasing knowledge of the characteristics and impact of pain is therefore essential for improving pain management. In France, the most recent national survey that collected data on the prevalence of cancer-related pain at all disease stages was conducted by the French national cancer institute (Institut National du Cancer; INCa) in 2010. Since this survey, the only other data published on cancer pain prevalence in France have been restricted to cancer survivors (the *Vie après le CANcer* [VICAN] survey<sup>19-21</sup>), or focused on chronic and neuropathic pain in patients undergoing cancer treatment<sup>22</sup>. Thus, the current study was conducted to provide an update on pain prevalence among both French cancer patients (undergoing anticancer treatments) and cancer survivors (after completion of anticancer treatments), and to investigate distinctions in pain characteristics, as well as the impact of pain on health-related QoL and psychological distress, in these two groups.

## **2. Methods**

### **2.1. Study design and setting**

This nationwide, cross-sectional, observational study was an ancillary study to the study<sup>23</sup>. The study was conducted in France using data collected from a web-based questionnaire distributed through collaboration with 12 French associations of cancer patients and 12 French Facebook groups, including approximately 61 700 individuals (supplement 1). Participant inclusion and data collection took place between January 27, 2023, and March 20, 2023. Questionnaire responses were collected online using the REDCap<sup>TM</sup> electronic data capture tools<sup>24</sup>. The study adhered to the STROBE guideline<sup>25</sup>.

### **2.2. Participants**

All members of the participating French associations of cancer patients and Facebook groups were invited by email to take part in the study. Individuals aged  $\geq 18$  years, who self-identified as currently undergoing cancer treatment or having received such treatment in the past, were eligible for inclusion. Individuals who did not provide responses to essential items in the questionnaire (age, gender, cancer type, time since diagnosis) were excluded. In addition, individuals who did not speak French, resided outside of France, were caregivers of cancer patients, or were legally protected adults were considered ineligible.

### **2.3. Data collection and assessment methods**

The questionnaire collected data on the sociodemographic and cancer characteristics of the participants, as well as on pain, health-related QoL, anxiety, and depression (supplement 2).

#### **2.3.1 Sociodemographic data**

The sociodemographic data included age, gender, height, weight, body mass index (BMI, as defined by the WHO<sup>26</sup>) socioeconomic status (according to the National Institute of Statistics and Economic Studies [INSEE] classification<sup>27</sup>), and French department of residence.

#### **2.3.2 Cancer characteristics**

The cancer characteristics included cancer type, date of cancer diagnosis, ongoing cancer management (yes/no), and type of ongoing or previous anticancer treatments. Individuals currently undergoing cancer management were categorized as “cancer patients” (active phase of the disease), while those who had received cancer management in the past and were no longer undergoing any anticancer treatment were classified as “cancer survivors”.

#### **2.3.3 Pain**

Data on pain (severity, location, analgesics used, and impact on daily living) were collected using the Brief Pain Inventory–Short Form (BPI-SF) questionnaire<sup>28</sup>. Visual analog scales (VAS) were used to indicate the severity of “pain at its worst in the last 24 hours”, “pain at its least in the last 24 hours”, “average pain”, and “pain right now” (scored from 0 = no pain to 10 = extreme pain). The impact of pain on daily activities was scored from 0 (does not interfere) to 10 (completely interferes). Information on pain duration was also collected, with pain lasting for  $\geq 3$  months classed as chronic pain<sup>5</sup>. The presence of neuropathic pain was assessed using the DN4 interview questionnaire<sup>29</sup>, with individuals scoring  $\geq 3$  out a possible total of 7 considered as having neuropathic pain.

### **2.3.4 Health-related quality of life**

Health-related QoL was assessed using the QLQ-C30 questionnaire<sup>30</sup>, covering global health status, functional scales (physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning), and symptomatic scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). All scale scores were linearly converted to range from 0 to 100, with higher scores for global health status and functioning indicating better outcomes and higher scores for symptoms indicating worse outcomes.

### **2.3.5 Anxiety and depression**

The Hospital Anxiety and Depression Scale (HADS) questionnaire<sup>31</sup> was used to assess the presence and severity of anxiety and depression (scored from 0-21, with scores  $\leq 7/21$  considered normal, 8–10/21 considered suggestive, and  $\geq 11/21$  considered indicative).

## **2.4. Evaluation criteria**

The primary evaluation criterion was comparison of the prevalence of pain between cancer patients and cancer survivors, with participants scoring  $\geq 4/10$  for the BPI-SF item “pain at its worst in the last 24 hours” classed as experiencing pain and those with a score  $< 4/10$  for this item classed as being without pain<sup>32</sup>.

Secondary evaluation criteria included comparisons of sociodemographic and cancer characteristics, pain characteristics, health-related QoL, anxiety, and depression between cancer patients and cancer survivors and between subgroups of individuals with and without pain, and the identification of factors associated with the presence or absence of pain in the whole study population.

## **2.5. Study size**

As this was an ancillary study<sup>23</sup>, no specific sample size was estimated for the primary evaluation criterion. However, given the inclusion of around 1000 participants in the primary study<sup>23</sup>, evenly distributed between cancer patients and cancer survivors, it was expected that the size of the population would be sufficient to allow the detection of a 10% absolute difference in pain prevalence between the two groups assuming a two-sided type I error at 5%, a satisfactory statistical power of around 90%, and an overall expected pain prevalence of 50%.

## **2.6. Statistical methods**

Quantitative data were presented as the mean and standard deviation (SD) or as the median and first and third quartile values ( $Q_1$ ;  $Q_3$ ). Normality was assessed using the Shapiro–Wilk test and confirmed by statistical distribution plots. Quantitative data were compared between independent groups (cancer patients vs. cancer survivors, and those with pain vs. those without pain) using the unpaired Student t-test or the Mann–Whitney test, as appropriate. The magnitude of between-group differences was analyzed using 95% confidence intervals (95% CI) and Hedge's effect sizes (ES), with the effect size being defined as small ( $ES \geq |0.2|$ ), medium ( $ES \geq |0.5|$ ), or large ( $ES \geq |0.8|$ )<sup>33,34</sup>.

Categorical data comparisons between groups were performed using the Chi<sup>2</sup> or Fisher's exact tests. The relationship between time since cancer diagnosis and pain was analyzed using the Spearman correlation coefficient ( $\rho$ ).

Factors associated with pain status (presence or absence of pain) were identified using two multivariate logistic regression models. Covariates were chosen based on clinical relevance,

and multicollinearity was assessed. In the first model, cancer status (cancer patients vs. cancer survivors), gender, age, BMI, and type of cancer were included as covariates. In the second model, the number of factors was expanded to include anxiety, depression, and global health status in addition to the previous covariates. Interactions between cancer status and other covariates were also examined. Results were expressed as odds ratios and 95% CI.

Statistical analyses were performed using Stata 14 (StataCorp, College Station, TX). Two-sided tests were conducted with a type I error set at 5%. No adjustment for multiple testing was applied. The presence of missing data was considered negligible (less than 5%), and no data imputation method was employed.

### **3. Results**

#### **3.1. Study population**

A total of 1029 individuals were included in the study (Supplement 3, Figure S1). The study population primarily consisted of females (82.7%) and had an average age of  $55.1 \pm 11.2$  years. Around half of the participants (51.4%) had a normal BMI and the majority ( $n=691$ ; 67.7%) were employed. Breast cancer was the most common form of cancer (61.4% of participants), and the median time since cancer diagnosis was 40 months (Table 1). The cohort included 518 (50.3%) cancer patients (undergoing anticancer treatments) and 511 (49.7%) cancer survivors (after completion of anticancer treatments) (Table 1). The cancer survivors were slightly older than the cancer patients (55.8 years vs 54.4 years). No other differences in sociodemographic characteristics were observed between the two groups. Although the frequency of breast cancer was similar in both groups, prostate and colorectal cancers were more frequent among cancer survivors (10.8% and 4.1%, respectively) than among cancer patients (6.6% and 1.5%, respectively). In contrast, lung cancer was more prevalent among cancer patients (9.9%) than among cancer survivors (5.3%). Analysis of anticancer treatment history showed that the proportion of individuals who had received oral anticancer drugs, oral targeted therapy, and immunotherapy was higher among cancer patients (14.1%, 11.6% and 16.0%, respectively) than among cancer survivors (8.0%, 2.2% and 9.2%, respectively), whereas the proportion of individuals who had received intravenous anticancer drugs was lower among cancer patients than cancer survivors (52.9% vs. 62.8%; Table 1).

#### **3.2. Pain**

Overall, 44.7% ( $n=460/1029$ ) of the study participants reported experiencing pain (VAS score of pain  $\geq 4/10$  for the BPI-SF item "pain at its worst in the last 24 hours"). Using the pain item (yes/no) from the BPI-SF, 58.7% ( $n=604/1029$ ) of individuals reported experiencing pain. Among all study participants, pain was classified as chronic (lasting  $\geq 3$  months) in 92.4% ( $n=425/460$ ) of cases and as neuropathic in 67.2% ( $n=309/460$ ) of cases. The proportion of individuals experiencing pain decreased with increasing time since cancer diagnosis ( $\rho: -0.66$ ,  $p = 0.014$ ; Figure 1).

The prevalence of pain was 49.2% (95% CI [44.8; 53.6]) among cancer patients ( $n=255/518$ ) and 40.1% (95% CI [35.8; 44.5]) among cancer survivors ( $n=205/511$ ;  $p = 0.004$ ). Among all individuals, the proportion of those reporting pain was higher among females than males (49.0% ( $n=417/851$ ) vs. 24.3% ( $n=43/177$ );  $p < 0.001$ ). The mean age of individuals with pain was lower than that of those without pain ( $54.1 \pm 10.2$  vs.  $55.9 \pm 11.8$ ;  $p = 0.008$ ). Similar results were observed across age groups for the proportions of individuals reporting pain (<

50 years: 49.0% (n=147/300) vs.  $\geq 50$  and  $< 55$  years: 53.5% (n=106/198) vs.  $\geq 55$  and  $< 60$  years: 41.9% (n=78/186) vs.  $\geq 60$  years: 37.3% (n=129/345);  $p = 0.001$ ).

Pain duration was shorter in cancer patients than in cancer survivors (Table 2). The proportion of individuals with pain classed as chronic was lower among cancer patients than cancer survivors (87.1% (n=222/255) vs. 99.0% (n=203/205),  $p < 0.001$ ). No significant difference in the frequency of neuropathic pain was observed between cancer patients with pain and cancer survivors with pain (67.5% (n=172/255) vs. 66.8% (n=137/205),  $p = 0.89$ ). Pain intensity scores did not differ between cancer patients and survivors with pain (Table 2). However, cancer patients reported that pain had a slightly greater impact on walking ability, relationships with other people, and enjoyment of life than cancer survivors (Table 2).

The most frequently reported pain location for both cancer patients and survivors was the lower limbs (Supplement 4, Table S1), with no notable difference in pain location between the two groups.

Among all participants, 419 individuals (40.7%) declared that they were using at least one analgesic drug. The proportion of individuals reporting that they used analgesics was higher for cancer patients than for cancer survivors (44.0% (n=228/518) vs. 37.4% (n=191/511),  $p = 0.03$ ). The most commonly used analgesics among all the participants were paracetamol (29.9%, n=308), opioids (12.1%, n=124), NSAIDs (7.8%, n=80), and gabapentinoids (2.9%, n=30), with the same pattern being observed in both cancer patients and survivors (Supplement 5, Table S2).

### **3.3. Quality of life, anxiety, and depression**

Scores for global health status and functioning dimensions were lower among cancer patients than cancer survivors, except for emotional functioning (Table 3). Additionally, symptom scale scores were higher among cancer patients than cancer survivors, except for insomnia.

Scores for global health status and functioning dimensions were lower in individuals experiencing pain compared to those without pain, with most items showing a large effect size. Similarly, scores for symptom scales were higher in those with pain. Notably, the largest effect sizes were observed for fatigue, and nausea and vomiting.

No significant differences in the presence or apparent severity of anxiety were observed between cancer patients and survivors. However, depression was more pronounced in cancer patients than in cancer survivors, with cancer patients having a higher overall mean score for depression and more cancer patients than survivors having indicative depression scores. Moreover, both anxiety and depression were more severe among individuals with pain than among those without pain (Table 3).

### **3.4. Multivariate analysis**

The first multivariate analysis, which incorporated factors including individual cancer status (cancer patients vs. cancer survivors), cancer type, gender, age, and BMI groups, revealed that the odds ratios for experiencing pain were lower for cancer survivors than for cancer patients. Lower odds ratios were also observed for individuals who had been diagnosed with prostate cancer. Conversely, higher odds ratios for pain were associated with being female, overweight, or obese (Figure 2A).

In the second multivariate analysis, which included the additional variables anxiety, depression, and global health status, no significant difference in the odds ratio for pain was observed between cancer patients and survivors (Figure 2B). A higher odds ratio for pain was



observed for individuals with breast cancer, and consistent with the findings of the initial analysis, for overweight and obese individuals. Pain was also found to be linked to indicative anxiety scores and lower global health status scores.

#### **4. Discussion**

This nationwide survey-based study provided updated information on the prevalence and impact of pain on both cancer patients and cancer survivors in France. The results showed that pain was a common cancer symptom in patients (49.2%) and survivors (40.1%), with no overall between-group difference in the risk of pain in the largest multivariate analysis. Pain was classed as chronic in most cases (> 90%) and as neuropathic in around two-thirds of cases. Chronic pain was more common among cancer survivors than cancer patients, but there were no significant between-group differences in other pain characteristics. Pain had a major impact on health status, daily functioning and symptom severity, and on levels of depression and anxiety in both groups, but its effects were generally greater in cancer patients. Individual characteristics such as breast cancer, being overweight or obese, a poorer global health status, and heightened anxiety were associated with an increased likelihood of pain.

The latest epidemiologic cancer data from France revealed an increase in cancer incidence (+0.9% per year in women and +0.3% in men between 1990 and 2023)<sup>35</sup> and reduction in cancer mortality (-2% in men and -0.7% in women between 2010 and 2018)<sup>36</sup>, indicating an overall increase in the number of people living with or surviving cancer. Despite the public health interest of monitoring pain prevalence in this population, prior to the current study, the most recent nationwide survey data on cancer pain prevalence in France were based on information from patients diagnosed, treated, or followed up for cancer between 2010 and 2017. Data from the 2010 INCa survey, which included 1507 oncology outpatients with a range of different cancer types and stages, indicated that cancer pain prevalence in France was 53%<sup>37</sup>. For patients diagnosed with cancer in France in 2010, the results of the VICAN study indicated that 69.9% of survivors at 2 years post-diagnosis and 73.4% of those at 5 years post-diagnosis experienced some type of pain in the 2 weeks prior to the follow-up survey<sup>21,38</sup>. Although pain assessment methods and pain threshold criteria differ between studies reported in the literature, a comparison of these data with those of the current study suggests that the prevalence of pain among individuals affected by cancer in France has tended to remain stable over the past 10 to 15 years. The overall prevalence of pain in our population (44.7%) was within the range cited in the recent systematic review and meta-analysis conducted by Snijders et al., which reported a pooled cancer pain prevalence of 44.5% (95% CI 41.1; 47.9%), as well as decreases in pain prevalence among cancer patients and cancer survivors between the periods 2005-2014 and 2014-2021<sup>1,39</sup>. However, the presence of pain in nearly half of individuals affected by cancer demonstrates that pain continues to be a frequent symptom of the disease and its treatment, despite advances in cancer therapy and updates to guidelines for cancer pain management<sup>6,13</sup>.

Our analysis of pain characteristics showed that the prevalence rates for chronic pain and neuropathic pain (92.34% and 67.2% of participants with pain, respectively) were much higher than those reported in the 2010 INCa survey (56% and 43% of the outpatients with pain had chronic pain or neuropathic pain, respectively)<sup>37</sup>. Our prevalence rate for chronic pain in cancer survivors (99.0%) was also higher than that reported at 5 years post-diagnosis in the VICAN study: 86.5% of the survivors with pain had chronic pain and in 92.8% of these cases the chronic pain had a neuropathic component<sup>21</sup>. As reported previously, increases in the proportion of individuals with chronic and neuropathic cancer pain are a consequence of

advances in treatment and improved survival<sup>3,5,40</sup>. However, as indicated by our study and in previous publications, these types of persistent cancer pain have a major impact on QoL, daily functioning, and depression and anxiety [4,6,15,26]. Moreover, a study conducted by Bouhassira et al.<sup>22</sup> evaluating the impact of chronic pain with and without a neuropathic component in French outpatients undergoing cancer treatment revealed that chronic neuropathic pain (lasting > 6 months) was associated with higher pain intensity scores and had a greater impact on functioning and QoL than chronic pain without a neuropathic component<sup>22</sup>. These findings highlight the importance of monitoring not only the overall prevalence of pain in cancer patients and survivors, but also the prevalence of the different types of pain experienced by these individuals. Indeed, this distinction is particularly important given the shift in the pattern of cancer treatments toward newer classes of chemotherapeutic agents, targeted treatments and immunotherapy, and evidence that some of these therapies are associated with the development of specific nociceptive musculoskeletal pain syndromes or with predominantly neuropathic pain, which may require alternative therapeutic approaches, such as antidepressants and anticonvulsants, to achieve adequate pain management<sup>3,6</sup>.

According to the latest cancer pain management guidelines, the goal of treatment is to minimize the effect of cancer pain on QoL<sup>13</sup>. In our study, 44.0% of cancer patients and 37.4% of survivors reported using analgesics to manage their pain. However, our findings indicated that the levels of pain experienced by the participants were sufficient to have an impact on global health status, functioning, and levels of depression and anxiety. The analysis of the types of analgesics being used by our study population suggests the burden of pain in cancer patients and survivors in France could be reduced by further optimizing the therapeutic strategies used for pain management. Only 22.8% of our participants with pain reported using opioids, whereas updated guidelines indicate that opioids, either alone or in combination with non-opioid drugs, should be now considered for all stages of cancer pain management [36]. Relatively low rates opioid use (notably step III opioids as defined in the original WHO analgesic ladder<sup>11</sup>) were reported among French cancer patients in a European-wide survey assessing the prevalence, treatment and patient attitudes to cancer pain<sup>41</sup>. Moreover, under-prescription of step III opioids was identified as likely factor contributing to the high prevalence of chronic pain reported in cancer survivors 5 years post-diagnosis in the VICAN study, and may have been associated with health care provider and patient concerns over the risks of long-term opioid therapy in this population<sup>21</sup>. In addition to the apparent under-use of opioid therapy, our findings suggested that management strategies in France also need to incorporate the more widespread use of treatments indicated for the relief of neuropathic pain. Although neuropathic pain was common in our population, the proportion of individuals using recommended first-line treatments for this type of pain was low (5.3% for gabapentinoids, 2.4% for amitriptyline, and 1.1% for serotonin noradrenaline reuptake inhibitors).

Our analysis also allowed us to identify gaps in pain management among specific groups in our population. The impact of pain on QoL indicators was more severe in cancer patients than cancer survivors, although pain characteristics were similar between the two groups and analgesic use was more frequent among cancer patients. Taken together, these findings suggest that pain management in patients still undergoing treatment in France needs to be improved, perhaps not only through adjustments to pharmacological treatments, but also, as recommended in the European guidelines, through the earlier introduction of more tailored and patient-centered approaches that include patient education and support for better self-management<sup>6,13</sup>. A similar multimodal approach may also help to improve the

management of chronic pain in cancer survivors. Our study also identified breast cancer, poorer global health status, increased anxiety, and being overweight or obese as factors associated with an increased risk of pain, and therefore provided valuable information to health care professionals in France on the cancer patient and survivor populations that would most likely benefit from additional pharmacological and non-pharmacological support for pain management.

This study had several strengths and limitations. It involved a large population from regions all over France and included survivors and patients diagnosed with different types of cancer. The cancer patients and survivors were well balanced in terms of their sociodemographic and socioeconomic characteristics, allowing for meaningful comparison of the prevalence and impact of pain in these two groups. The use of a web-based questionnaire containing validated self-assessment tools allowed the prevalence and impact of pain to be assessed from a patient perspective. However, this cross-sectional, self-reporting design may be subject to the common limitations of these types of observational studies (e.g., subject selection, respondent recall, and social desirability bias). In particular, comparison of cancer characteristics of our population with the latest data on the incidence of the different types of cancer in France <sup>35</sup>, indicates that female subjects and breast cancer were over-represented in our population. This over-representation of females is also a consequence of the higher number of female cancer patient associations participating in the study. Moreover, females generally have a longer life expectancy compared to men <sup>42</sup>, which may lead to a higher proportion of female cancer patients and survivors in the population. This demographic trend could explain the overrepresentation of females in our sample. Previous studies have indicated that women are more likely to participate in surveys and research studies than men, but this result may vary across different studies <sup>43</sup>. This tendency may be influenced by greater expressiveness or comfort in discussing health-related issues, including pain experiences, which could result in a higher response rate among female participants <sup>44,45</sup>. Women are generally more proactive about health management and are more likely to seek medical advice, attend follow-up appointments, and engage in health-related activities <sup>46</sup>. This increased health awareness and engagement could lead to a higher likelihood of participating in health-related research. In addition, data on several potentially valuable aspects of pain were not collected during our survey, including information on pain etiology, whether the analgesics being used were prescribed or the subjects were self-medicating, and whether the participants were using specific types of nonconventional or non-pharmacological interventions to help manage their pain.

In conclusion, this study indicated that the prevalence of pain during and after cancer in France has tended to remain stable over the past 10-15 years. Pain was still a common symptom in both cancer patients and survivors, and had a significant impact on QoL, daily functioning and mental wellbeing, particularly in patients still undergoing treatment. Adjustments and improvements to cancer pain management are therefore required to reduce the burden of cancer pain in France, particularly to address the high prevalence of chronic pain and neuropathic pain. Breast cancer, anxiety, and being overweight or obese were identified as risk factors for experiencing pain, suggesting that these populations of cancer patients and survivors may require closer monitoring and additional interventions to achieve optimal pain management.

### **Author contributions**

Conceptualization, D.B.; methodology, D.B. and B.P.; software, D.B. and C.R.; validation, D.B. and C.R.; formal analysis, D.B., C.R., and B.P.; investigation, C.R.; resources, D.B.; data curation, D.B. and C.R.; writing—original draft preparation, D.B., C.R., and B.P.; writing—review and editing, D.B., C.R., B.P., and Santé Active Edition-Synergy Pharm; visualization, D.B., C.R., and B.P.; supervision, D.B.; project administration, D.B.; funding acquisition, D.B. All authors have read and agreed to the published version of the manuscript. The work reported in the paper has been performed by the authors, unless clearly specified in the text.

### **Acknowledgments**

The authors extend their sincere gratitude to the French associations of cancer patients (ANAMACaP, Vivre comme avant, ARTuR, De l'air, Patients en reseau, Laurette FUGAIN, Jeune et rose, Toujours femme, Rose Up, Corasso, Odyssea, and Vaincre le mélanome), as well as the Facebook groups (Ensemble contre le cancer, Cancer du sein, Cancer de l'ovaire, parlons-en en toute liberté, Cancer alimentation et cie, Le cancer et les proches, La vie après le cancer, Les roses : soutiens, infos et humour autour du cancer du sein, Cancer du rectum, Laurette FUGAIN, Cancer / immunothérapie, Cancer du pancréas - Groupe de soutien, and Vivre avec un cancer du poumon) for their valuable participation.

They also thank Emma Pilling (PhD) and Marielle Romet (PhD) from Santé Active Edition-Synergy Pharm for language revision and medical writing assistance.

During the preparation of this work the authors used ChatGPT-3.5 in order to improve language and readability. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication.

### **Conflict of Interest**

The authors declare that they have no conflict of interest.

### **Ethics Statement**

The study received ethical approval (Comité de protection des personnes Ile de France VII, 2022-A02460-43, December 12, 2022). Informed consent was obtained from all participants along with their questionnaire responses. The study protocol has been registered on ClinicalTrials.gov (NCT05684939).

### **Funding**

The study was funded with the support of the National Institute of cancer (INCa) and Institut pour la recherche en santé publique (IReSP), grant number INCa/IReSP-16651.

### **Data availability statement**

Supporting data for the study will be made available upon request to the corresponding author.

## 5. References

1. Snijders RAH, Brom L, Theunissen M, van den Beuken-van Everdingen MHJ. Update on Prevalence of Pain in Patients with Cancer 2022: A Systematic Literature Review and Meta-Analysis. *Cancers (Basel)*. 2023;15(3). doi:10.3390/cancers15030591
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2021;71(3):209-249.
3. Glare P, Aubrey K, Gulati A, Lee YC, Moryl N, Overton S. Pharmacologic management of persistent pain in cancer survivors. *Drugs*. 2022;82(3):275-291.
4. Yoon SY, Oh J. Neuropathic cancer pain: prevalence, pathophysiology, and management. *The Korean journal of internal medicine*. 2018;33(6):1058.
5. Bennett MI, Kaasa S, Barke A, Korwisi B, Rief W, Treede RD. The IASP classification of chronic pain for ICD-11: chronic cancer-related pain. *Pain*. 2019;160(1):38-44.
6. Fallon M, Giusti R, Aielli F, et al. Management of cancer pain in adult patients: ESMO Clinical Practice Guidelines. *Annals of Oncology*. 2018;29:iv166-iv191.
7. Niedzwiedz CL, Knifton L, Robb KA, Katikireddi SV, Smith DJ. Depression and anxiety among people living with and beyond cancer: a growing clinical and research priority. *BMC cancer*. 2019;19(1):1-8.
8. Pitman A, Suleman S, Hyde N, Hodgkiss A. Depression and anxiety in patients with cancer. *BMJ*. Published online April 25, 2018;k1415. doi:10.1136/bmj.k1415
9. Rodriguez C, Ji M, Wang HL, Padhya T, McMillan SC. Cancer pain and quality of life. *Journal of Hospice & Palliative Nursing*. 2019;21(2):116-123.
10. Te Boveldt N, Vernooij-Dassen M, Burger N, Vissers K, Engels Y. Pain and its interference with daily activities in medical oncology outpatients. *Pain Physician*. 2013;16(4):379.
11. World Health Organization. *World Health Organization. Cancer Pain Relief: With a Guide to Opioid Availability*. World Health Organization; 1996.
12. World Health Organization. WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. Published online 2018.
13. Bennett MI, Eisenberg E, Ahmedzai SH, et al. Standards for the management of cancer-related pain across Europe—A position paper from the EFIC Task Force on Cancer Pain. *European journal of pain*. 2019;23(4):660-668.
14. Swarm RA, Paice JA, Anghelescu DL, et al. Adult cancer pain, version 3.2019, NCCN clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network*. 2019;17(8):977-1007.
15. Roberto A, Greco MT, Uggeri S, et al. Living systematic review to assess the analgesic undertreatment in cancer patients. *Pain Practice*. 2022;22(4):487-496.
16. Breuer B, Fleishman SB, Cruciani RA, Portenoy RK. Medical oncologists' attitudes and practice in cancer pain management: a national survey. *J Clin Oncol*. 2011;29(36):4769-4775.
17. Kwon JH. Overcoming barriers in cancer pain management. *Journal of Clinical Oncology*. 2014;32(16):1727-1733.
18. Makhoulouf SM, Pini S, Ahmed S, Bennett MI. Managing pain in people with cancer—a systematic review of the attitudes and knowledge of professionals, patients, caregivers and public. *Journal of Cancer Education*. 2020;35:214-240.
19. Bouhnik AD, Bendiane MK, Cortaredona S, et al. The labour market, psychosocial outcomes and health conditions in cancer survivors: protocol for a nationwide longitudinal survey 2 and 5 years after cancer diagnosis (the VICAN survey). *BMJ open*. 2015;5(3):e005971.
20. Dugué J, Humbert M, Bendiane MK, Bouhnik AD, Babin E, Licaj I. Head and neck cancer survivors' pain in France: the VICAN study. *J Cancer Surviv*. 2022;16(1):119-131. doi:10.1007/s11764-021-01010-0
21. Janah A, Bouhnik AD, Touzani R, Bendiane MK, Peretti-Watel P. Underprescription of Step III Opioids in French Cancer Survivors With Chronic Pain: A Call for Integrated Early Palliative Care in

- Oncology. *Journal of Pain and Symptom Management*. 2020;59(4):836-847. doi:10.1016/j.jpainsymman.2019.10.027
22. Bouhassira D, Luporsi E, Krakowski I. Prevalence and incidence of chronic pain with or without neuropathic characteristics in patients with cancer. *Pain*. 2017;158(6):1118-1125. doi:10.1097/j.pain.0000000000000895
  23. Ragusa C, Pereira B, Balayssac D. Study of the relationship between psychoactive substance use and pain in cancer patients and cancer survivors: A French nationwide cross-sectional study. *Intl Journal of Cancer*. Published online May 15, 2024:ijc.35006. doi:10.1002/ijc.35006
  24. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010
  25. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med*. 2007;147(8):573-577. doi:10.7326/0003-4819-147-8-200710160-00010
  26. World Health Organization (WHO). Obesity and overweight Fact Sheet, 2021. Accessed October 1, 2023. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>.
  27. National Institute of Statistics and Economic Studies [Institut National de la Statistique et des Études Économiques, INSEE]. Nomenclature of occupations and socioeconomic categories (PCS 2020). 2nd Edition 2024. Accessed October 1, 2023. [https://www.insee.fr/fr/statistiques/fichier/6051913/Guide\\_PCS\\_2020\\_version\\_2024.pdf](https://www.insee.fr/fr/statistiques/fichier/6051913/Guide_PCS_2020_version_2024.pdf).
  28. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singap*. 1994;23(2):129-138.
  29. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain*. 2005;114(1-2):29-36. doi:10.1016/j.pain.2004.12.010
  30. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365-376. doi:10.1093/jnci/85.5.365
  31. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370.
  32. Atkinson TM, Mendoza TR, Sit L, et al. The Brief Pain Inventory and Its "Pain At Its Worst in the Last 24 Hours" Item: Clinical Trial Endpoint Considerations. *Pain Med*. 2010;11(3):337-346. doi:10.1111/j.1526-4637.2009.00774.x
  33. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. L. Erlbaum Associates; 1988.
  34. Nuzzo R. Scientific method: statistical errors. *Nature*. 2014;506(7487):150-152. doi:10.1038/506150a
  35. Lapôtre-Ledoux B, Remontet L, Uhry Z, et al. Incidence des principaux cancers en France métropolitaine en 2023 et tendances depuis 1990. *Bull Épidémiologique Hebd*. Published online 2023:188-204.
  36. Institut national du cancer (INCa). Panorama des cancers en France - Edition 2022. Published online February 2022. Accessed February 21, 2022. <https://www.e-cancer.fr/content/download/336357/4805630/file/Panorama%20des%20cancers%20en%20France%20-%20C3%A9dition%202022.pdf>
  37. Synthèse de l'enquête nationale 2010 sur la prise en charge de la douleur chez des patients adultes atteints de cancer. INCa, mars 2012, [www.e-cancer.fr](http://www.e-cancer.fr).
  38. Matias M, Baciarello G, Neji M, et al. Fatigue and physical activity in cancer survivors: A cross-sectional population-based study. *Cancer medicine*. 2019;8(5):2535-2544.
  39. van den Beuken-van Everdingen MHJ, Hochstenbach LMJ, Joosten EAJ, Tjan-Heijnen VCG, Janssen DJA. Update on Prevalence of Pain in Patients With Cancer: Systematic Review and

- Meta-Analysis. *Journal of Pain and Symptom Management*. 2016;51(6):1070-1090.e9. doi:10.1016/j.jpainsymman.2015.12.340
40. Boland EG, Ahmedzai SH. Persistent pain in cancer survivors. *Current Opinion in Supportive & Palliative Care*. 2017;11(3):181-190. doi:10.1097/SPC.0000000000000292
  41. Breivik H, Cherny N, Collett B, et al. Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. *Annals of Oncology*. 2009;20(8):1420-1433. doi:10.1093/annonc/mdp001
  42. Austad SN, Fischer KE. Sex Differences in Lifespan. *Cell Metabolism*. 2016;23(6):1022-1033. doi:10.1016/j.cmet.2016.05.019
  43. Wu MJ, Zhao K, Fils-Aime F. Response rates of online surveys in published research: A meta-analysis. *Computers in Human Behavior Reports*. 2022;7:100206. doi:10.1016/j.chbr.2022.100206
  44. McLean CP, Anderson ER. Brave men and timid women? A review of the gender differences in fear and anxiety. *Clinical Psychology Review*. 2009;29(6):496-505. doi:10.1016/j.cpr.2009.05.003
  45. Hawke LJ, Nelson E, O'Brien P, et al. Influences on clinical trial participation: Enhancing recruitment through a gender lens - A scoping review. *Contemporary Clinical Trials Communications*. 2024;38:101283. doi:10.1016/j.conctc.2024.101283
  46. Thompson AE, Anisimowicz Y, Miedema B, Hogg W, Wodchis WP, Aubrey-Bassler K. The influence of gender and other patient characteristics on health care-seeking behaviour: a QUALICOPC study. *BMC Fam Pract*. 2016;17(1):38. doi:10.1186/s12875-016-0440-0

**Table 1. Characteristics of the study population**

Items	All (n=1029)	Cancer patients (n=518)	Cancer survivors (n=511)	P-values
<b>Gender, n (%)</b>	<i>n</i> =1029	<i>n</i> =518	<i>n</i> =511	
Male	177 (17.2)	90 (17.4)	87 (17.0)	0.6
Female	851 (82.7)	428 (82.6)	423 (82.8)	
Non-binary	1 (0.2)	0	1 (0.2)	
<b>Age</b> mean ± SD, years	<i>n</i> =1029 55.1 ± 11.2	<i>n</i> =518 54.4 ± 11	<i>n</i> =511 55.8 ± 11.3	0.04
<b>BMI</b> median [Q <sub>1</sub> ; Q <sub>3</sub> ], kg/m <sup>2</sup>	<i>n</i> =1023 24.2 [21.5; 27.6]	<i>n</i> =515 24.2 [21.6; 28.1]	<i>n</i> =508 24.2 [21.4; 27.5]	0.37
Normal weight	526 (51.4)	268 (52.0)	258 (50.8)	0.1
Underweight	54 (5.3)	23 (4.5)	31 (6.1)	
Overweight	290 (28.4)	136 (26.4)	154 (30.3)	
Obese	153 (15.0)	88 (17.1)	65 (12.8)	
<b>INSEE socioprofessional category, n (%)</b>	<i>n</i> =1020	<i>n</i> =514	<i>n</i> =506	0.4
Farmer	6 (0.6)	4 (0.8)	2 (0.4)	
Artisan	4 (0.4)	2 (0.4)	2 (0.4)	
Merchant/entrepreneur	32 (3.1)	15 (2.9)	17 (3.4)	
White-collar profession	309 (30.3)	160 (31.1)	149 (29.5)	
Intermediate profession	118 (11.6)	65 (12.7)	53 (10.5)	
Employee	206 (20.2)	94 (18.3)	112 (22.1)	
Worker	16 (1.6)	12 (2.3)	4 (0.8)	
Retired	241 (23.6)	115 (22.4)	226 (24.9)	
Unemployed	88 (8.6)	47 (9.1)	41 (8.1)	
<b>Cancer type, n (%)</b>	<i>n</i> =1029	<i>n</i> =518	<i>n</i> =511	
Breast	632 (61.4)	320 (61.8)	312 (61.1)	0.8
Prostate	89 (8.7)	34 (6.6)	55 (10.8)	0.02
Lung	78 (7.6)	51 (9.9)	27 (5.3)	0.007
Blood	67 (6.5)	37 (7.1)	30 (5.9)	0.4
Gynecological	66 (6.4)	27 (5.1)	39 (7.6)	0.1
Kidney	57 (5.5)	34 (6.6)	23 (4.5)	0.1
Colorectal	29 (2.8)	8 (1.5)	21 (4.1)	0.01
Other	11 (1.1)	8 (1.5)	3 (0.6)	0.1
<b>Time since diagnosis</b> median [Q <sub>1</sub> ; Q <sub>3</sub> ], months	<i>n</i> =1029 40 [17; 82]	<i>n</i> =518 28 [12; 57]	<i>n</i> =511 52 [28; 103]	< 0.001
<b>Anticancer treatment received, n (%)</b>	<i>n</i> =1029	<i>n</i> =518	<i>n</i> =511	
Oral anticancer drugs	114 (11.1)	73 (14.1)	41 (8.0)	0.002
Injectable anticancer drugs	595 (57.8)	274 (52.9)	321 (62.8)	0.001
Hormone therapy	345 (33.5)	161 (31.1)	184 (36.0)	0.09
Oral targeted therapy	71 (6.9)	60 (11.6)	11 (2.2)	< 0.001
Immunotherapy	130 (12.6)	83 (16.0)	47 (9.2)	0.001
Surgery	674 (65.5)	314 (60.6)	360 (70.5)	0.001
Radiotherapy	648 (63.0)	312 (60.2)	336 (65.8)	0.07
Hematopoietic stem cell transplantation	26 (2.5)	8 (1.5)	18 (3.2)	0.048
Other	71 (6.9)	35 (6.8)	36 (7.1)	0.9
<b>Anticancer treatment ongoing, n (%)</b>	<i>n</i> =1029	<i>n</i> =518		
Oral anticancer drugs	55 (5.3)	55 (10.6)		
Injectable anticancer drugs	81 (7.9)	81 (15.6)		
Hormonal therapy	255 (24.8)	255 (49.2)		
Targeted therapy (oral)	65 (6.3)	65 (12.6)		
Immunotherapy	62 (6.0)	62 (12.0)		
Surgery	10 (1.0)	10 (1.9)		
Radiotherapy	31 (3.0)	31 (6.0)		
Hematopoietic stem cell transplantation	1 (0.1)	1 (0.2)		
Other	38 (3.7)	38 (7.3)		

BMI, body mass index; INSEE, Institut National de la Statistique et des Études Économiques (French national institute for economic studies and statistics); Q<sub>1</sub>; Q<sub>3</sub>, first and third quartile values; SD, standard deviation.



**Table 2: Comparison of pain characteristics between the subgroups of cancer patients and cancer survivors who experienced pain**

Items	Cancer patients with pain (n=255)	Cancer survivors with pain (n=205)	Effect size [95% CI]	P-values
<b>Pain duration</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ], months	18 [6; 36]	31 [12; 60]	-0.45 [-0.61; -0.28]	< 0.001
<b>Pain intensity scores</b>				
Worst pain in last 24 h, median [Q <sub>1</sub> ; Q <sub>3</sub> ]	6 [4; 7]	6 [4; 7]	0.04 [-0.13; 0.20]	0.7
Least pain in last 24 h, median [Q <sub>1</sub> ; Q <sub>3</sub> ]	2 [1; 4]	2 [1; 4]	0.01 [-0.15; 0.17]	0.97
Average pain, mean ± SD	4.9 ± 1.9	4.9 ± 2.1	-0.01 [-0.17; 0.16]	0.95
Pain right now, median [Q <sub>1</sub> ; Q <sub>3</sub> ]	4 [2; 5]	3 [1; 5.5]	0.09 [-0.07; 0.25]	0.3
<b>Pain interference with daily life scores</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]				
General activity	5 [3; 7]	5 [3; 7]	0.04 [-0.12; 0.20]	0.61
Mood	5 [3; 7]	5 [3; 7]	-0.01 [-0.17; 0.15]	0.97
Walking ability	5 [1; 7]	3 [1; 6]	0.21 [0.05; 0.38]	0.01
Normal work	5 [3; 7.5]	5 [2; 7]	0.13 [-0.03; 0.29]	0.12
Relations with other people	4 [2; 6]	3 [1; 6]	0.17 [0.01; 0.33]	0.03
Sleep	5 [2; 8]	5 [2; 7]	0.11 [-0.05; 0.27]	0.17
Enjoyment of life	4 [1; 7]	3 [1; 6]	0.17 [0.01; 0.33]	0.03

The Brief Pain Inventory – Short Form (BPI-SF) questionnaire was used to assess pain intensity (scored from 0 = no pain to 10 = extreme pain) and interference with daily life (scored from 0 = does not interfere to 10 completely interferes).

BMI, body mass index; 95% CI, confidence interval at 95%; Q<sub>1</sub>; Q<sub>3</sub>; first and third quartile values; SD, standard deviation.

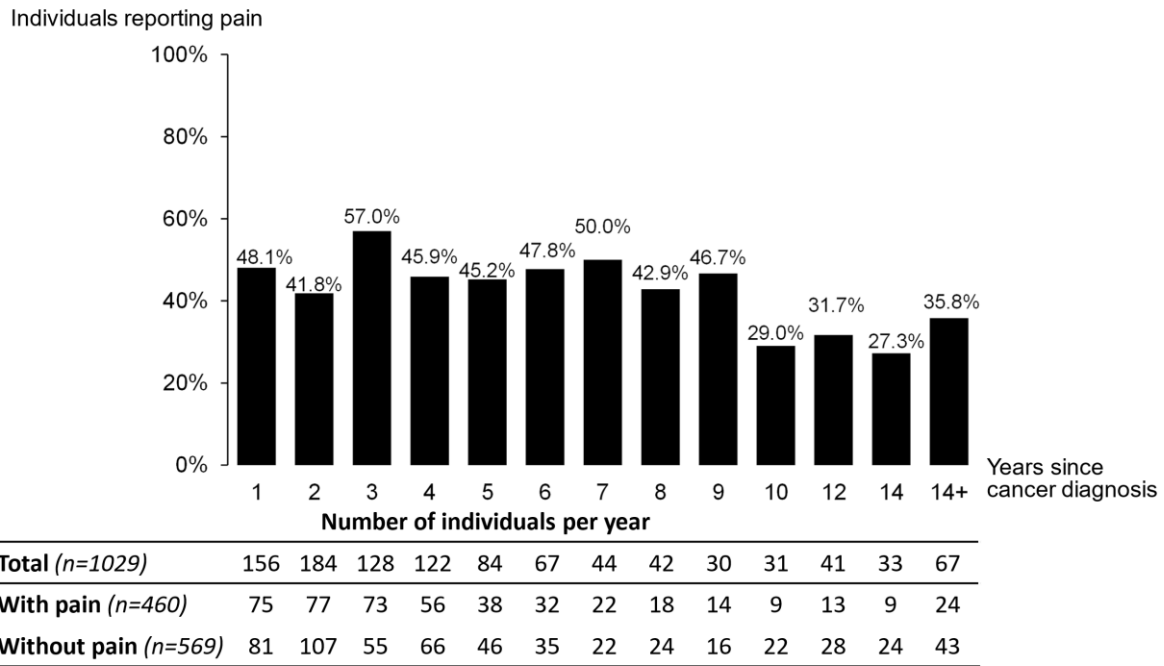
**Table 3. Comparison of health-related quality of life, and anxiety and depression between cancer patients and cancer survivors and between subgroups of individuals with and without pain.**

Items (scores)	Cancer patients (n=518)	Cancer survivors (n=511)	P-value	With pain (n=460)	Without pain (n=569)	P-value
<b>Global health status</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	58.3 [50; 66.7]	66.7 [50; 83.3]	< 0.001	50 [41.7; 66.7]	66.7 [58.3; 83.3]	< 0.001
Effect size [95% CI]	-0.44 [-0.56; -0.31]			-0.82 [-0.95; -0.70]		
<b>Physical functioning</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	80 [60; 93.3]	86.7 [73.3; 93.3]	< 0.001	73.3 [53.3; 86.7]	93.3 [80; 100]	< 0.001
Effect size [95% CI]	-0.44 [-0.56; -0.31]			-0.92 [-1.05; -0.79]		
<b>Role functioning</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	66.7 [50; 100]	83.3 [66.7; 100]	< 0.001	66.7 [33.3; 66.7]	83.3 [66.7; 100]	< 0.001
Effect size [95% CI]	-0.39 [-0.51; -0.23]			-0.90 [-1.03; 0.77]		
<b>Emotional functioning</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	66.7 [41.7; 75]	66.7 [41.7; 83.3]	0.08	58.3 [33.3; 75]	75 [58.3; 83.3]	< 0.001
Effect size [95% CI]	-0.11 [-0.23; 0.01]			-0.53 [-0.66; 0.41]		
<b>Cognitive functioning</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	66.7 [50; 83.3]	66.7 [50; 83.3]	<0.001	50 [33.3; 83.3]	66.7 [50; 83.3]	< 0.001
Effect size [95% CI]	-0.19 [-0.31; -0.07]			-0.66 [-0.79; -0.53]		
<b>Social functioning</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	66.7 [33.3; 83.3]	66.7 [50; 100]	< 0.001	58.3 [33.3; 75]	83.3 [50; 100]	< 0.001
Effect size [95% CI]	-0.26 [-0.38; -0.14]			-0.65 [-0.77; -0.52]		
<b>Fatigue</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	55.6 [33.3; 77.8]	44.4 [22.2; 66.7]	< 0.001	66.7 [44.4; 88.9]	33.3 [22.2; 55.6]	< 0.001
Effect size [95% CI]	0.45 [0.32; 0.57]			0.94 [0.81; 1.07]		
<b>Nausea and vomiting</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	0 [0; 16.7]	0 [0; 16.7]	< 0.001	0 [0; 16.7]	0 [0; 16.7]	< 0.001
Effect size [95% CI]	0.28 [0.16; 0.40]			0.30 [0.18; 0.42]		
<b>Pain</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	33.3 [16.7; 66.7]	33.3 [0; 50]	< 0.001	50 [33.3; 83.3]	16.7 [0; 33.3]	< 0.001
Effect size [95% CI]	0.31 [0.19; 0.44]			1.39 [1.25; 1.53]		
<b>Dyspnea</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	33.3 [0; 66.6]	0 [0; 33.3]	< 0.001	33.3 [0; 66.7]	0 [0; 33.3]	< 0.001
Effect size [95% CI]	0.32 [0.19; 0.44]			0.44 [0.31; 0.56]		
<b>Insomnia</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	33.3 [33.3; 66.7]	33.3 [33.3; 66.7]	0.1	66.7 [33.3; 100]	33.3 [0; 66.7]	< 0.001
Effect size [95% CI]	0.11 [-0.02; 0.23]			0.63 [0.50; 0.75]		
<b>Appetite loss</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	0 [0; 33.3]	0 [0; 33.3]	< 0.001	0 [0; 33.3]	0 [0; 33.3]	< 0.001
Effect size [95% CI]	0.25 [0.13; 0.37]			0.25 [0.13; 0.37]		
<b>Constipation</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	0 [0; 66.7]	0 [0; 33.3]	0.02	0 [0; 66.7]	0 [0; 33.3]	< 0.001
Effect size [95% CI]	0.17 [0.05; 0.30]			0.30 [0.17; 0.42]		
<b>Diarrhea</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	0 [0; 33.3]	0 [0; 33.3]	< 0.001	0 [0; 33.3]	0 [0; 33.3]	< 0.001
Effect size [95% CI]	0.25 [0.13; 0.38]			0.30 [0.18; 0.43]		
<b>Financial difficulties</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	0 [0; 33.3]	0 [0; 33.3]	0.001	33.3 [0; 33.3]	0 [0; 33.3]	< 0.001
Effect size [95% CI]	0.13 [0.004; 0.25]			0.45 [0.32; 0.57]		
<b>Anxiety</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	7 [5; 11]	7 [4; 10]	0.65	9 [6; 12]	6 [4; 9]	< 0.001
Effect size [95% CI]	0.03 [-0.09; 0.15]			0.52 [0.40; 0.65]		

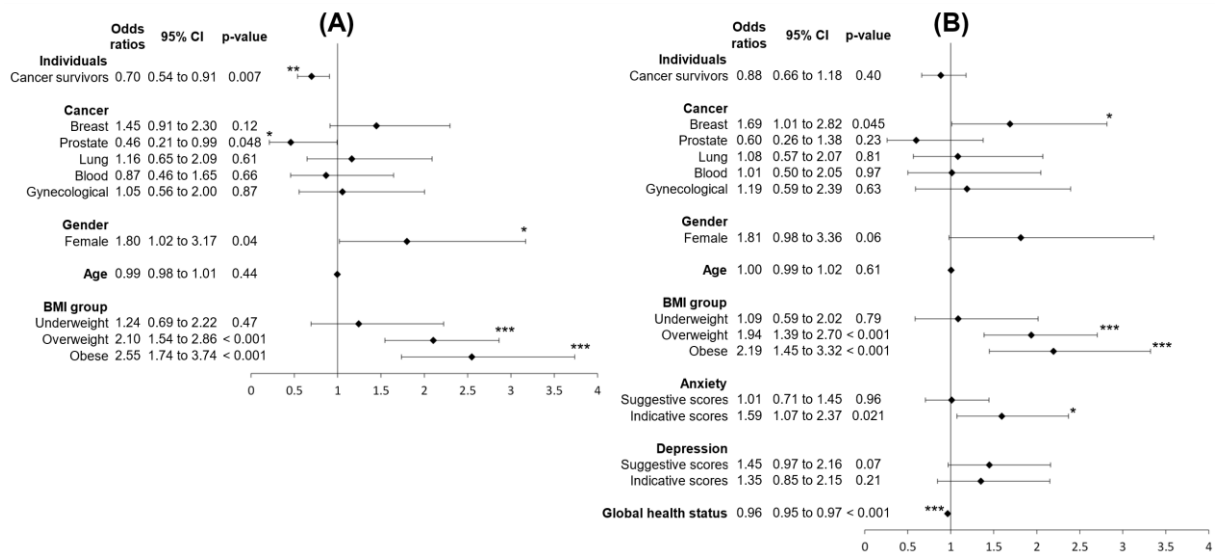
Normal, n (%)	263 (50.8)	261 (51.1)	0.65	181 (39.4)	343 (60.3)	< 0.001
Suggestive, n (%)	119 (23.0)	127 (24.9)		113 (24.6)	133 (23.4)	
Indicative, n (%)	136 (26.3)	123 (24.1)		166 (36.1)	93 (16.3)	
<b>Depression</b> , median [Q <sub>1</sub> ; Q <sub>3</sub> ]	6 [3; 9]	5 [2; 8]	< 0.001	7 [4; 10]	4 [2; 7]	< 0.001
Effect size [95% CI]	0.21 [0.09; 0.34]			0.65 [0.52; 0.77]		
Normal, n (%)	331 (63.9)	355 (69.5)	0.04	242 (52.6)	444 (78.0)	< 0.001
Suggestive, n (%)	91 (17.6)	90 (17.6)		108 (23.5)	73 (12.8)	
Indicative, n (%)	96 (18.5)	66 (12.9)		110 (23.9)	52 (9.1)	

The QLQ-C30 questionnaire was used to assess global health status (scored from 0-100 with higher scores indicating a better status), functional dimensions (scored from 0-100 with higher scores indicating better functioning) and symptom dimensions scores (scored from 0-100 with higher scores indicating more severe symptoms). The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression (scored from 0-21, with scores  $\leq 7/21$  considered normal, 8–10/21 considered suggestive, and  $\geq 11/21$  considered indicative).

BMI, body mass index; 95% CI, confidence interval at 95%; Q<sub>1</sub>; Q<sub>3</sub>; first and third quartile values; SD, standard deviation.



**Figure 1. Proportion of individuals with pain according to the time since cancer diagnosis**



**Figure 2. Multivariate analysis of factors associated with the presence or absence of pain.**  
 A: First logistic regression model. B: second logistic regression model including the additional covariates anxiety and depression scores (assessed using the Hospital Anxiety and Depression Scale; HADS) and global health status (assessed using the QLQ-C30 questionnaire). BMI, body mass index; 95% CI: 95% confidence interval. \* P < 0.05; \*\* P < 0.01, and \*\*\* P < 0.001.

## Supplement 1

### French associations of cancer patients and French Facebook groups

Associations of patients	Number of individuals
ANAMACaP	1300
Vivre comme avant	100
ARTuR	1500
De l'air	100
Patients en réseau	5000
Laurette FUGAIN	600
Jeune et rose	800
Toujours femme	250
Rose Up	2315
Corasso	423
Odyssea	?
Vaincre le mélanome	?

Facebook groups	Number of followers
Ensemble contre le cancer	1893
Cancer du sein	726
Cancer de l'ovaire, parlons-en en toute liberté	473
Cancer alimentation et cie	1525
Le cancer et les proches	1259
La vie après le cancer	1645
Les roses : soutiens, infos et humour autour du cancer du sein	256
Cancer du rectum	385
Association Laurette FUGAIN	39391
Cancer / immunothérapie	412
Cancer du pancréas. Groupe de soutien	934
Vivre avec un cancer du poumon	414

## **Supplement 2, Questionnaires and scoring**

### **Characteristics of cancer and treatments**

#### **Have you been or are you currently being treated for cancer?**

- Yes, I am currently being treated for cancer.
- Yes, I have been treated for cancer (currently in remission and treatments completed).
- No

#### **For what type of cancer are you or have you been treated?**

- Bladder
- Blood (leukemia, myeloma)
- Breast
- Colorectal
- ENT (head, neck, tongue, mouth, lip, nose...)
- Gynecological (cervix, endometrium, ovary)
- Kidney
- Liver
- Nervous system (brain, spinal cord)
- Pancreas
- Prostate
- Pulmonary (lung, bronchus, pleura)
- Skin (melanoma...)
- Stomach
- Thyroid
- Other

#### **When was the diagnosis of your cancer made? (approximate day)**

#### **What type of treatment have you already received (completed treatment)?**

- Oral chemotherapy
- Injectable chemotherapy
- Hormone therapy
- Targeted therapy (oral)
- Immunotherapy
- Surgery
- Radiotherapy
- Hematopoietic stem cell transplant
- Other
- None







**Sleep**

0 1 2 3 4 5 6 7 8 9 10  
Does not Interfere Completely Interferes

**Enjoyment of life**

0 1 2 3 4 5 6 7 8 9 10  
Does not Interfere Completely Interferes

---

**DN4 interview questionnaire (neuropathic pain)**

*Scoring of the DN4 interview is the sum of each answer (yes = 1 and no = 0). The maximum is 7 and the minimum 0.*

**Does the pain have one or more of the following characteristics?**

***Burning***

- Yes
- No

***Painful cold***

- Yes
- No

***Electric shocks***

- Yes
- No

**Is the pain associated with one or more of the following symptoms in the same area?**

***Tingling***

- Yes
- No

***Pins and needles***

- Yes
- No

***Numbness***

- Yes
- No

***Itching***

- Yes
- No

## **Anxiety and depression**

### **Hospital Anxiety and Depression Scale (HADS) questionnaire**

*For scoring see [2]*

#### **I feel tense or 'wound up':**

- Most of the time
- A lot of the time
- From time to time, occasionally
- Not at all

#### **I feel as if I am slowed down:**

- Nearly all the time
- Very often
- Sometimes
- Not at all

#### **I still enjoy the things I used to enjoy:**

- Definitely as much
- Not quite so much
- Only a little
- Hardly at all

#### **I get a sort of frightened feeling like 'butterflies' in the stomach:**

- Not at all
- Occasionally
- Quite Often
- Very Often

#### **I get a sort of frightened feeling as if something awful is about to happen:**

- Very definitely and quite badly
- Yes, but not too badly
- A little, but it doesn't worry me
- Not at all

#### **I have lost interest in my appearance:**

- Definitely
- I don't take as much care as I should
- I may not take quite as much care
- I take just as much care as ever

#### **I can laugh and see the funny side of things:**

- As much as I always could
- Not quite so much now
- Definitely not so much now
- Not at all

**I feel restless as I have to be on the move:**

Very much indeed

Quite a lot

Not very much

Not at all

**Worrying thoughts go through my mind:**

- A great deal of the time

- A lot of the time

- From time to time, but not too often

- Only occasionally

**I look forward with enjoyment to things:**

- As much as I ever did

- Rather less than I used to

- Definitely less than I used to

- Hardly at all

**I feel cheerful:**

- Not at all

- Not often

- Sometimes

- Most of the time

**I get sudden feelings of panic:**

- Very often indeed

- Quite often

- Not very often

- Not at all

**I can sit at ease and feel relaxed:**

- Definitely

- Usually

- Not Often

- Not at all

**I can enjoy a good book or radio or TV program:**

- Often

- Sometimes

- Not often

- Very seldom

## **HRQoL and symptoms**

### **QLQ-C30 questionnaire**

*For scoring see [1]*

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

#### **Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?**

- Not at all
- A little
- Quite a bit
- Very Much

#### **Do you have any trouble taking a long walk?**

- Not at all
- A little
- Quite a bit
- Very Much

#### **Do you have any trouble taking a short walk outside of the house?**

- Not at all
- A little
- Quite a bit
- Very Much

#### **Do you need to stay in bed or a chair during the day?**

- Not at all
- A little
- Quite a bit
- Very Much

#### **During the past week**

##### **Do you need help with eating, dressing, washing yourself or using the toilet?**

- Not at all
- A little
- Quite a bit
- Very Much

##### **Were you limited in doing either your work or other daily activities?**

- Not at all
- A little
- Quite a bit
- Very Much

**Were you limited in pursuing your hobbies or other leisure time activities?**

- Not at all
- A little
- Quite a bit
- Very Much

**Were you short of breath?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you had pain?**

- Not at all
- A little
- Quite a bit
- Very Much

**Did you need to rest?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you had trouble sleeping?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you felt weak?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you lacked appetite?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you felt nauseated?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you vomited?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you been constipated?**

- Not at all
- A little
- Quite a bit
- Very Much

**Were you tired?**

- Not at all
- A little
- Quite a bit
- Very Much

**Did pain interfere with your daily activities?**

- Not at all
- A little
- Quite a bit
- Very Much

**Have you had difficulty in concentrating on things, like reading a newspaper or watching television?**

- Not at all
- A little
- Quite a bit
- Very Much

**Did you feel tense?**

- Not at all
- A little
- Quite a bit
- Very Much

**Did you worry?**

- Not at all
- A little
- Quite a bit
- Very Much



---

## Individual characteristics

**What is your age?**

**Gender**

- Male
- Female
- Non-binary

**What is your height (in cm)?**

**What is your weight (in kg)?**

**In which department do you live?**

**Socio-professional status (INSEE)**

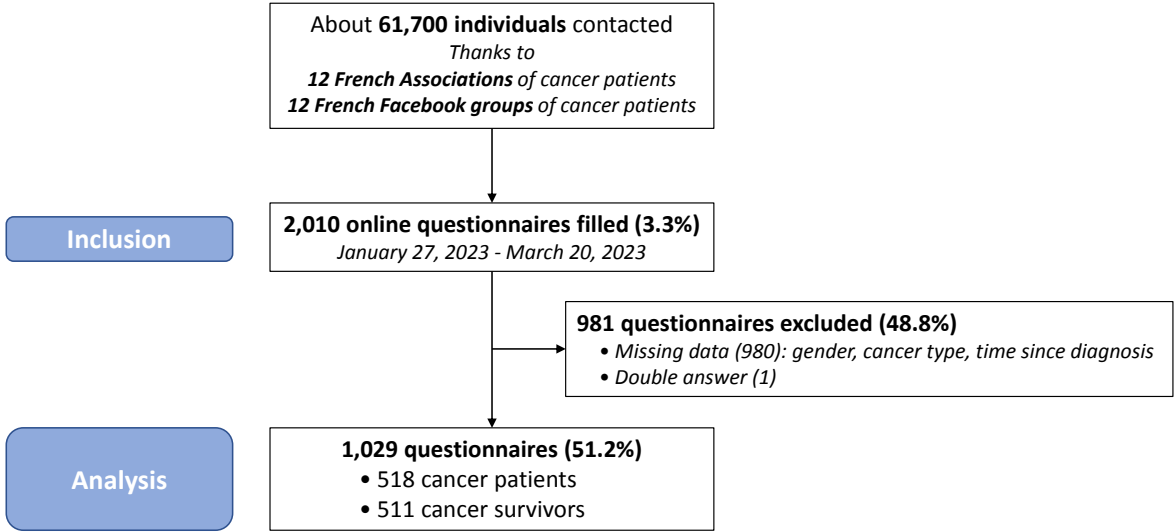
- Farmers and farm managers
- Craftsmen
- Shopkeepers and business owners
- Executives and higher intellectual professions
- Intermediate professions
- Employees
- Workers
- Retirees
- Other individuals without professional activity

**References**

- [1] Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365–376.
- [2] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–370.



**Supplement 3, Figure S1: Flow chart of participant inclusion in the study**



**Supplement 4, Table S1: Pain location in the subgroups of cancer patients and cancer survivors who experienced pain**

<b>Pain location, n (%)</b>	<b>Cancer patients with pain (n=255)</b>	<b>Cancer survivor with pain (n=205)</b>	<b>P-values</b>
Lower limb (including knee, ankle)	132 (51.8)	99 (48.3)	0.46
Feet (including toes)	98 (38.4)	68 (33.2)	0.24
Rachis (including neck, back)	96 (37.6)	80 (39.0)	0.76
Hands (including fingers)	96 (37.6)	70 (34.1)	0.44
Shoulders	82 (32.2)	65 (31.7)	0.92
Hips	74 (29.0)	44 (21.5)	0.07
Thorax (including breast, armpit, ribs...)	59 (23.1)	54 (26.3)	0.43
Head (including mouth, eyes, nose...)	36 (14.1)	27 (13.2)	0.77
Upper limb (including elbow, wrist)	36 (14.1)	27 (13.2)	0.77
Abdomen (including stomach, bladder)	35 (13.7)	20 (9.8)	0.19

**Supplement 5, Table S2: Comparison of analgesics used by cancer patients and cancer survivors and between subgroups of individuals with and without pain**

Analgesics, n (%)	Total (n=1029)		Cancer patients (n=518)		Cancer survivors (n=511)	
	With pain (n=460)	Without pain (n=569)	With pain (n=255)	Without pain (n=263)	With pain (n=205)	Without pain (n=306)
<b>Paracetamol</b>	254 (55.2)	54 (9.5)	139 (54.5)	27 (10.3)	115 (56.1)	27 (8.8)
<b>Opioids</b>	105 (22.8)	19 (3.3)	65 (25.5)	12 (4.6)	40 (19.5)	7 (2.3)
<b>NSAIDs</b>	62 (13.5)	18 (3.2)	28 (11.0)	6 (2.3)	34 (16.6)	12 (3.9)
<b>Gabapentinoids</b>	26 (5.3)	6 (1.1)	13 (5.1)	5 (1.9)	11 (5.4)	1 (0.3)
<b>Cannabidiol</b>	16 (3.5)	1 (0.2)	4 (1.6)	0 (0.0)	12 (5.9)	1 (0.3)
<b>Amitriptyline</b>	11 (2.4)	2 (0.4)	3 (1.2)	1 (0.4)	8 (3.9)	1 (0.3)
<b>Nefopam</b>	9 (2.0)	2 (0.4)	6 (2.4)	0 (0.0)	3 (1.5)	2 (0.7)
<b>Corticoids</b>	9 (2.0)	1 (0.2)	7 (2.7)	1 (0.4)	2 (1.0)	0 (0.0)
<b>Capsaicin patch</b>	6 (1.3)	0 (0.0)	4 (1.6)	0 (0.0)	2 (1.0)	0 (0.0)
<b>Medical cannabis</b>	6 (1.3)	0 (0.0)	5 (2.0)	0 (0.0)	1 (0.5)	0 (0.0)
<b>SNRIs</b>	5 (1.1)	2 (0.4)	3 (1.2)	2 (0.8)	2 (1.0)	0 (0.0)
<b>Lidocaine patch</b>	4 (0.9)	1 (0.2)	2 (0.8)	1 (0.4)	2 (1.0)	0 (0.0)
<b>Clonazepam</b>	3 (0.7)	2 (0.4)	1 (0.4)	1 (0.4)	2 (1.0)	1 (0.3)
<b>Triptans</b>	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)	0 (0.0)
<b>Botulinum toxin</b>	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)

NSAIDs: nonsteroidal anti-inflammatory drugs; SNRIs: serotonin noradrenaline reuptake inhibitors.