



# Prevalence of pain in patients with breast cancer post-treatment: A systematic review

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## ABSTRACT

**Purpose:** To evaluate the prevalence and severity of persistent pain after breast cancer treatment (PPBCT) in patients who received surgery, radiotherapy or a combination of treatments and to explore how different treatments and techniques impact pain.

**Methods:** Medline, Embase and Cochrane Central databases were searched for articles which evaluated the prevalence of PPBCT. Search results were limited to studies addressing chronic post-surgical pain (CPSP), persistent post-surgical pain (PPSP), post-mastectomy pain syndrome (PMPS) or radiotherapy (RT) related pain in breast cancer patients and published in the English language. The primary outcome was the incidence or severity of PPBCT. Descriptive analyses were performed.

**Results:** A total of 177 studies were included in this review. Overall, pain prevalence was 29.8% amongst 3746 patients (Group 1: 30 studies) post-surgery, 27.3% post-RT (Group 2: 41 studies, n = 15 019), and 21.8% amongst BC survivors who reported on the general prevalence of after receiving various combinations of BC treatment (Group 3: 106 studies, n = 135 437).

**Conclusion:** PPBCT remains to be a prevalent and complex clinical issue, despite a variety of different techniques and treatments. Various factors such as varying definitions of pain, inconsistent use of assessment tools and differences in methodology between studies may contribute to discrepancies in reports of PPBCT. A greater understanding of BC treatments and their impact on PPBCT may help identify potential risk factors, prevention and pain management strategies.

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## 1. Introduction

Persistent pain following treatment for breast cancer (BC) is a common occurrence, affecting 25–60% of patients, and has been linked to decreased quality of life (QoL) [1,2]. BC patients with persistent pain after breast cancer treatment (PPBCT) tend to experience greater anxiety and depressive symptoms, and also have higher levels of perceived stress than patients without<sup>1</sup>. BC therapy can be comprised of various combinations of treatment; therefore, the resulting pain is multifactorial and may be complicated by inherent risk factors in patients and the therapy they receive [2–4].

Persistent post-surgical pain (pain >3 months post-surgery) (PPSP) affects approximately 40% of patients and several risk factors have been identified, such as the presence of preceding pain, psychosocial factors, age, sex, type of surgery, analgesic used and genetics [2,5]. For example, axillary lymph node dissections (ALND) have been consistently associated with greater upper limb morbidities than sentinel lymph node biopsies (SLNB) [6]. Breast-conserving therapy for early BC patients presents a less extensive treatment option relative to radical mastectomies, but is still associated with significant upper limb morbidities such as reduced range of motion in the shoulder, muscle weakness of the arm and hand, lymphoedema, numbness and pain [6].

In addition to surgery, adjuvant therapies such as radiation and systemic treatments can also affect the development of persistent post-treatment pain, for example through severe radiation-induced skin reactions and damage to nerve fibers, which can all contribute to poorer health-related QoL outcomes [1,2,7]. Other types of patient-reported pain post-treatment include phantom breast syndrome, lymphoedema-related pain and pain associated with side effects of BC treatment, such as brachial plexopathy [8–11].

Although various factors have been proposed as predictors of increased persistent post-treatment pain in breast cancer patients, the incidence and severity of pain resulting from different breast cancer treatments are still not well-understood [2,3,11,12]. The purpose of this systematic review was to summarize findings in the literature to present our current understanding of the prevalence of PPBCT and to explore how different treatment and techniques may affect PPBCT.

## 2. Methods

### 2.1. Search strategy

Medline, Embase, and Cochrane Central databases were searched from inception to August 2017 for records using the following keywords: “breast neoplasms” or “breast cancer” or “breast tumor”, “radiotherapy”, “surgery”, “pain”, “pain management”, and “analgesia”. These records were independently screened for eligibility by two authors (CY, LD) first by title, then by

abstract, and subsequently by full text. Discrepancies in screening results were discussed until a consensus was reached. Data extraction was conducted by one author (CY) and verified by another (KW).

### 2.2. Study eligibility criteria

Articles addressing chronic post-surgical pain (CPSP), persistent post-surgical pain (PPSP), post-mastectomy pain syndrome (PMPS) or radiotherapy (RT) related pain for BC were eligible. According to The International Association for the Study of Pain, pain may be considered chronic when it has exceeded the normal time of healing with 3 months being the division between acute and chronic pain [13]. Therefore, studies that evaluated pain at 3 months or more were eligible. Studies were limited to those conducted in humans and published in the English language. Only studies specifically evaluating BC patients were eligible. Review articles, commentaries or editorials, case reports and case series were excluded. Studies that did not report on the incidence and/or severity of pain following BC treatment were ineligible. Studies only reporting on chemotherapy-induced pain, acute post-surgical pain (pain within 3 months of surgery) and studies specifically evaluating pain associated with breast reconstruction (including tissue expanders) were excluded unless they also reported on CPSP from breast conserving surgery (BCS), mastectomy or lymph node surgery.

### 2.3. Data collection

The following study characteristics were recorded: publication date, sample size, follow-up period, and pain assessment tool used. Treatment information was obtained, including treatment type (surgery, systemic therapy, and radiotherapy), interventions or rescue treatments for pain, treatment groups (control or treatment), pain prevalence and pain severity. Sample sizes used for analysis reflect the cohort analyzed for pain prevalence and/or severity only.

Any reported incidence of pain associated with BC-therapy was used for analysis, regardless of where the pain was located. However, in studies that independently reported the incidence of pain in separate areas of the body, only results for breast pain were used for analysis. For studies that presented both patient- and physician-reported results, only patient-reported values were used for analysis. Where pain severity was reported as “mild to moderate” or “moderate to severe”, it was analyzed as moderate or severe pain, respectively. For studies that reported only the overall prevalence of pain and the prevalence of severe pain, the incidence of mild or moderate pain was determined by subtracting the number of patients experiencing severe pain from the total number of patients reporting pain.

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