Objectives

- Evaluate the burden of BTP in a commercially insured U.S. population of opioid-treated cancer and noncancer patients
- Investigate the prevalence of comorbid conditions that may impact the burden of BTP
- Evaluate the association between BTP and the risk of opioid misuse

Methods

- Survey Design
  - Inclusion criteria: Patients with chronic noncancer pain
  - Survey population: Cancer cohort (n=300) and control cohort (n=1200)
- Survey Population
  - Cancer cohort
    - ≥2 medical claims with an ICD-9-CM code associated with chronic pain separated by ≥3 months
    - An opioid prescription claim within the past 3 months or determination of the use of opioids for a chronic pain condition during the telephone interview
  - Control cohort
    - Fluent in English
    - ≥18 years of age at the time of the survey
    - No medical claims or opioid prescription claims within the past 3 months
- Inclusion criteria: Respondents in U.S. public and managed care health plans with opioid prescriptions for daily opioid medication
- Patients were included if they had recent baseline pain and functioning as measured by the Short Form 12 (SF-12) Health Survey
- Patients with BTP were compared with patients without BTP
- Pain was defined as BTP if it occurred at least 60 minutes after the last opioid dose
- Interim Patient Demographics
  - Sex, n (%)
    - Male: 68 (57)
    - Female: 60 (52)
  - Race, n (%)
    - White: 190 (165*)
    - Black: 6 (5)
    - Other: 1 (1)
  - Ethnicity
    - Asian: 1 (1)
    - Hispanic: 1 (1)
    - Other: 1 (1)
  - BMI
    - <18.5: 10 (9)
    - 18.5-24.9: 80 (71)
    - 25-29.9: 81 (71)
    - 30-34.9: 20 (17)
    - ≥35: 3 (3)
  - Education
    - < High School: 10 (9)
    - High School: 110 (97)
    - Some College: 106 (91)
    - College: 72 (63)
    - Post College: 12 (10)
  - Annual Income
    - < $15,000: 10 (9)
    - $15,000-$24,999: 50 (43)
    - $25,000-$34,999: 50 (43)
    - $35,000-$49,999: 50 (43)
    - ≥$50,000: 20 (17)
  - Relationship Status
    - Single: 12 (10)
    - Married: 80 (68)
    - Divorced: 10 (9)
    - Separated: 2 (2)
    - Widowed: 2 (2)
  - Employment Status
    - Full time: 80 (68)
    - Part time: 50 (43)
    - Homemaker: 10 (9)
    - Student: 10 (9)
    - Retired: 2 (2)
    - Unemployed: 2 (2)
  - Time until peak pain, median (mean) minutes
    - 60 (55–100)
  - Number of BTP flares per day, median (mean)
    - 1 (1–2)

Assessments

- Pain and functional outcomes
- Health-related quality of life
- Productivity
- Comorbid conditions
- Opioid misuse

Discussion

- The results of this study provide important insights into the burden of BTP on patients with chronic noncancer pain
- The findings suggest that BTP is associated with reduced health-related quality of life, functioning, and productivity
- Further studies are needed to explore the mechanism of action of BTP and its impact on opioid misuse

References


Table 1: Assessments

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Cancer Cohort</th>
<th>Control Cohort</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score</td>
<td>73 (20)</td>
<td>69 (63)</td>
<td>0.016</td>
</tr>
<tr>
<td>Functioning</td>
<td>52.5 (11.3)</td>
<td>51.8 (10.5)</td>
<td>0.007</td>
</tr>
<tr>
<td>Quality of life</td>
<td>66.3 (114.9)</td>
<td>61.8 (101.8)</td>
<td>0.003</td>
</tr>
<tr>
<td>Opioid misuse</td>
<td>13 (12)</td>
<td>6 (5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 2: Interim Results

- Patients with BTP had significantly lower pain scores, worse functioning, and lower quality of life compared to patients without BTP.
- Patients with BTP were more likely to report opioid misuse.
- The complete results will provide the largest data set of its kind available to date and will greatly improve the understanding of the epidemiology and impact of BTP on community-dwelling cancer and noncancer patients with opioid-treated chronic pain syndromes.

Table 3: Interim Response to the Breakthrough Pain Questionnaire

- Patients with BTP had significantly lower pain scores and worse functioning compared to patients without BTP.
- The interim results highlight the need for additional research to better understand the impact of BTP on patients with chronic noncancer pain.

Table 4: Summary of Interim Results for Quality of Life, Functioning, and Productivity

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cancer Cohort</th>
<th>Control Cohort</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score</td>
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Table 5: Breakthrough Pain Questionnaire

- Patients with BTP had significantly lower pain scores, worse functioning, and lower quality of life compared to patients without BTP.
- The complete results will provide the largest data set of its kind available to date and will greatly improve the understanding of the epidemiology and impact of BTP on community-dwelling cancer and noncancer patients with opioid-treated chronic pain syndromes.
The National Breakthrough Pain Survey (NBTPS): Design, Methodology, and Interim Results

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1Cephalon, Inc., Frazer, PA; 2Tufts University School of Medicine, Boston, MA; 3EPI-Q, Inc., Oak Brook, IL; 4Department of Pain Medicine and Palliative Care, Beth Israel Medical Center, New York, NY
Introduction

- Breakthrough pain (BTP) is a transitory exacerbation of pain that occurs on a background of otherwise controlled persistent pain in patients receiving long-term opioid therapy.³
- A survey of community-dwelling patients with chronic cancer or noncancer pain suggests that the prevalence of BTP is 30% to 50%.²
- Several surveys of cancer patients indicate that BTP is associated with more severe pain, less effective analgesic treatment, impaired ability to function, mood disturbance, and relatively poorer quality of life.³ ⁶ More limited data in noncancer patients suggest similar associations.⁴ ⁷ ⁸
- There also are limited data indicating that the presence of cancer-related BTP may increase healthcare costs.⁹
- To further describe the epidemiology and burden of illness associated with BTP, the National Breakthrough Pain Survey (NBTPS) evaluated BTP in a population of commercially insured patients identified from a large administrative claims database in the United States.

Objectives

Primary Objective

- Evaluate the burden of BTP in a commercially insured U.S. population of opioid-treated cancer and noncancer patients with controlled persistent pain, including:
  - Patient-reported pain severity or functional impairment in the previous 24 hours and 7 days
  - Quality of life in the previous 4 weeks
  - Lost workdays or presenteeism in the last 28 days and 365 days
  - Days out of role (e.g., work or school absence, inability to perform normal daily activities) in the last 28 days and 365 days
  - Healthcare consumption in the 12 months preceding the survey date

Secondary Objectives

- Evaluate the prevalence of BTP in a commercially insured U.S. population with controlled persistent pain who were taking daily opioid therapy
- Characterize the demography, disease and comorbidities, and medication treatment patterns in this population
- Describe the phenomenology and etiology of BTP in this population

Methods

Data Source

- Survey participants were commercially insured health plan members identified from the HealthCore Integrated Research Database (HIRD) consisting of administrative claims from 14 geographically dispersed U.S. health plans. Upon enrollment in a plan, members agreed to participate in plan-authorized surveys.
- The sampling pool was first limited to the 6.4 million who were currently active in the health plans, were ≥18 years of age, and had been continuously enrolled for ≥12 months.
  - The sampling frame of approximately 50,000 health plan members was randomly selected and stratified based on census region to be representative of the commercially insured U.S. population.
  - In addition, an oversample of approximately 36,000 health plan members with medical/pharmacy claims consistent with chronic pain and daily opioid use was included.
Figure 1 – Survey Design

Create initial cohorts from claims data

Phone survey of all respondents

Healthcare utilization analysis

Survey to confirm chronic pain and ATC opioid utilization

Administer BTP screening tool

Administer additional pain-specific survey instruments

Administer quality-of-life, functioning, and productivity instruments

Merge survey and claims data

Commerially Insured Population

ICD-9-CM codes for cancer?

YES

NO

ICD-9-CM codes for chronic pain?

Pharmacy claims for daily opioids?

YES

NO

Cancer Cohort (n=1200)*

Group 1: Cancer w/o BTP (n=300)*

Group 2: Cancer w/ BTP (n=900)*

Noncancer Cohort (n=1200)*

Group 3: Noncancer w/o BTP (n=300)*

Group 4: Noncancer w/ BTP (n=900)*

Control Cohort (n=750)*

Survey to confirm no clinically significant chronic pain or opioid use

ATC=around-the-clock; BTP=breakthrough pain; ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification.

*Planned sample size.
Survey Design

- Institutional review board approval was received for the protocol and the survey instruments.
- Based on a review of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes and pharmacy prescription claims, eligible patients were divided into a control cohort and 2 pain cohorts, which were subdivided into 4 groups (Figure 1).
- Identified patients were contacted by telephone, according to a standard protocol, to obtain verbal consent for participation. They were then screened to confirm the presence of chronic pain and daily opioid use. Patients without clinically significant chronic pain were assigned to the control cohort.
- Patients with clinically significant chronic pain on daily opioid therapy were divided into cancer and noncancer cohorts based on the presence or absence of a cancer diagnosis (ICD-9-CM code or Current Procedural Terminology [CPT] code indicating receipt of chemotherapy or radiation).
- A screening tool was administered to all pain patients to determine the presence of controlled persistent pain, with or without BTP. The cancer cohort was further subdivided into groups 1 and 2, and the noncancer cohort was divided into groups 3 and 4, according to the absence or presence of BTP, respectively.
- Surveys assessing quality of life, functioning, and productivity were administered to all patients. Additional pain-specific surveys were administered to patients as appropriate to assess pain symptom severity and burden of illness.
- Claims data and survey data were then merged to complete the utilization and cost analysis.

Patient Selection

All Patients

- Inclusion criteria
  - ≥18 years of age at the time of the survey
  - Able to provide informed consent
  - Fluent in English
  - Current member with a minimum of 12 months of continuous health plan enrollment before the survey date

Control Cohort

- Exclusion criteria
  - A medical claim with an ICD-9-CM code associated with chronic pain within the last 12 months or verification of a clinically significant chronic pain condition via telephone interview
  - An opioid prescription claim within the past 3 months or determination of the use of opioids for a chronic pain condition during the telephone interview

Cancer and Noncancer Pain Cohorts

- Inclusion criteria
  - ≥2 medical claims with an ICD-9-CM code associated with chronic pain separated by ≥3 months
  - ≥3 opioid prescription claims within 3 months using the Medication Refill Adherence (MRA) measure of ≥90% to assess daily use
  - Responses during the screening interview that met criteria for “controlled baseline pain”

- Exclusion criteria
  - An ICD-9-CM diagnostic code (medical claims) or Healthcare Common Procedure Coding System (HCPCS) code (ambulatory services) for drug abuse or dependence concurrent with a pharmacy claim for methadone
  - Acute, intermittent, or inadequately controlled persistent pain (i.e., background pain), determined through the interview
Assessments

Survey Instruments

- Demographic information was recorded for all patients, and an introductory screening questionnaire was administered to patients in groups 1 to 4 to confirm the presence of controlled persistent pain and the presence or absence of BTP.
- An overview of instruments administered to patients to assess pain symptom severity and burden of illness is presented in Table 1.

Table 1 – Overview of Survey Instruments

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Assessments</th>
<th>Populations Studied</th>
<th>References Supporting Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Health Questionnaire–2 (PHQ–2)</td>
<td>Screening for depression</td>
<td>Patients in primary care and obstetrics/gynecology clinics</td>
<td>Kroenke K, et al. Med Care. 2003;41:1284-1292</td>
</tr>
</tbody>
</table>

*aAdministered to all patients.
†Patients in the control group reporting mild pain also completed the BPI.
Use of Healthcare Services

- Direct (medical and prescription drug) healthcare resource use and costs were determined for the 12 months before the survey date.
  - Medical costs were calculated based on claims for hospital inpatient services, outpatient visits and procedures, physician services, emergency department visits, and other ancillary services (e.g., physical therapy, laboratory services).
  - Prescription drug costs were determined using the pharmacy claims for the 12 months before the survey date.

Analysis Plan

Primary

- Patients with BTP (groups 2 and 4) were compared with patients in the control cohort based on the following outcome measures of the burden on health:
  - Health-related quality of life, as measured by the 12-Item Short Form (SF-12) Health Survey (version 2).
  - Productivity – days out of role (e.g., work or school absence, inability to perform normal daily activities) and presenteeism, as measured by the World Health Organization Health and Work Performance Questionnaire (HPQ)–Short Form and the Sheehan Disability Scale (SDS).
  - Use of healthcare services in the 12 months before the survey date.
Secondary

- Patients with BTP (groups 2 and 4) were compared with patients without BTP (groups 1 and 3) in:
  - Health-related quality of life, as measured by the SF-12.
  - Productivity, including presenteeism, as measured by the HPQ and SDS.
  - Patient-reported pain severity and impact, as measured by the Brief Pain Inventory (BPI).
  - Use of healthcare services in the 12 months before the survey date.
- Demography, prevalence of BTP, pain phenomenology, disease-related factors, and treatment patterns (e.g., pharmacy claims for opioids and strengths administered) were described.

Interim Results

Survey Population

- As of July 30, 2010, more than 2300 patients were screened and 905 patients completed the survey (Table 2).
  - The vast majority of respondents were noncancer patients. For this interim analysis, the cancer and noncancer cohorts were combined.
  - Note: Approximately 20% of screened respondents were ineligible because of uncontrolled persistent pain.

Table 2 – Interim Patient Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>No BTP (n=110)</th>
<th>BTP (n=428)</th>
<th>Control (n=367)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>52.5 (11.3)</td>
<td>49.5 (9.5)*</td>
<td>48.3 (18.0)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41 (37)</td>
<td>170 (40)</td>
<td>177 (48)</td>
</tr>
<tr>
<td>Female</td>
<td>69 (63)</td>
<td>258 (60)</td>
<td>190 (52)</td>
</tr>
<tr>
<td>Race, n (%)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>101 (92)</td>
<td>407 (95)</td>
<td>323 (88)</td>
</tr>
<tr>
<td>Black</td>
<td>2 (2)</td>
<td>8 (2)</td>
<td>17 (5)</td>
</tr>
<tr>
<td>Native American</td>
<td>2 (2)</td>
<td>8 (2)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (1)</td>
<td>0</td>
<td>11 (3)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (2)</td>
<td>12 (3)</td>
<td>16 (4)</td>
</tr>
<tr>
<td>Geography, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>13 (12)</td>
<td>26 (6)</td>
<td>73 (20)</td>
</tr>
<tr>
<td>South</td>
<td>27 (25)</td>
<td>144 (34)</td>
<td>136 (37)</td>
</tr>
<tr>
<td>Midwest</td>
<td>43 (39)</td>
<td>178 (42)</td>
<td>93 (25)</td>
</tr>
<tr>
<td>West</td>
<td>27 (25)</td>
<td>80 (19)</td>
<td>65 (18)</td>
</tr>
</tbody>
</table>

BTP=breakthrough pain; SD=standard deviation.
*Data missing from 1 patient.
†Respondents could select more than 1 race. Four respondents were either unsure of or refused to report their race.
Of the 538 patients with controlled persistent pain, 428 (79.6%) reported experiencing BTP (Table 3).

**Table 3 – Interim Responses to the Breakthrough Pain Questionnaire**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of BTP flares per day, median (mean)</td>
<td>2.0 (3.45)</td>
</tr>
<tr>
<td>Time until peak pain, median (mean) minutes</td>
<td>10.0 (38.6)†</td>
</tr>
<tr>
<td>Time from flare start to end, median (mean) minutes</td>
<td>90.0 (370.8)</td>
</tr>
<tr>
<td>Ability to often, almost always, or always predict BTP flares, n (%)</td>
<td>128 (30)</td>
</tr>
</tbody>
</table>

BTP=breakthrough pain.
*Only patients with controlled persistent pain and BTP were asked to complete the full survey. For the Breakthrough Pain Questionnaire, there were 428 respondents.
†n=321.
This unique methodology illustrates the potential of an approach linking case definition from a large data set to patient interviews in order to provide a broad evaluation of the burden of illness associated with BTP.

Based on interim results, BTP was highly prevalent (79.6%) in this commercially insured U.S. population of opioid-treated cancer and noncancer patients with controlled persistent pain.

- Patients with BTP reported substantial reductions in quality of life, functioning, and productivity compared with patients who had controlled persistent pain and no BTP, as well as the control cohort.

The greater burden suffered by patients with BTP suggests that specific treatment focused on BTP could improve patients’ clinical condition.

- Future studies should evaluate this possibility.

The complete results will provide the largest data set of its kind available to date and will greatly improve the understanding of the epidemiology and impact of BTP on community-dwelling cancer and noncancer populations with opioid-treated chronic pain syndromes.

### Table 4 – Interim Responses to Quality-of-Life, Functioning, and Productivity Survey Instruments

<table>
<thead>
<tr>
<th>Variable</th>
<th>No BTP (n=110)</th>
<th>BTP (n=428)</th>
<th>Control (n=367)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-12 Physical, mean (SD)</td>
<td>34.3 (10.0)*</td>
<td>29.2 (9.1)*†</td>
<td>53.4 (6.8)</td>
</tr>
<tr>
<td>SF-12 Mental, mean (SD)</td>
<td>48.8 (11.1)*</td>
<td>47.2 (11.5)*</td>
<td>54.7 (6.0)</td>
</tr>
<tr>
<td>SDS total, mean (SD)</td>
<td>3.8 (3.0)*</td>
<td>5.2 (3.0)*†</td>
<td>0.5 (1.2)</td>
</tr>
<tr>
<td>Days out of role (past 30 days)</td>
<td>4.6 (7.0)*</td>
<td>9.2 (10.4)*†</td>
<td>0.2 (0.8)</td>
</tr>
<tr>
<td>Days out of role (past 365 days)</td>
<td>61.8 (101.8)*</td>
<td>114.5 (136.7)*†</td>
<td>2.5 (5.6)</td>
</tr>
<tr>
<td>Unproductive days (past 30 days)</td>
<td>6.2 (9.4)*</td>
<td>10.1 (10.5)*†</td>
<td>0.5 (2.1)</td>
</tr>
<tr>
<td>Unproductive days (past 365 days)</td>
<td>66.3 (114.9)*</td>
<td>107.7 (129.6)*†</td>
<td>3.7 (20.5)</td>
</tr>
<tr>
<td>BPI total interference in 24 hours, mean (SD)</td>
<td>25.0 (14.9)*</td>
<td>34.9 (16.0)*†</td>
<td>5.0 (9.2)</td>
</tr>
</tbody>
</table>

BPI = Brief Pain Inventory; BTP = breakthrough pain; SD = standard deviation; SDS = Sheehan Disability Scale; SF-12 = 12-Item Short Form Health Survey.

*P < 0.05 vs Control
†P < 0.05 vs No BTP
References


This survey was sponsored by Cephalon, Inc. (Frazer, PA, USA). Writing support was provided by Peloton Advantage, LLC, funded by Cephalon, Inc.

Presented at the International Association for the Study of Pain’s (IASP) 13th World Congress on Pain, August 29-September 2, 2010, Montreal, Quebec, Canada.