Accepted Manuscript

Postoperative pain management in Spanish hospitals. A cohort study using the PAIN-OUT registry

Mauricio Polanco-García, MD, Jaume García-Lopez, PhD, Neus Fàbregas, MD, PhD, Windfried Meissner, MD, PhD, Margarita M. Puig, MD, PhD

PII: S1526-5900(17)30611-9

DOI: [10.1016/j.jpain.2017.05.006](https://doi.org/10.1016/j.jpain.2017.05.006)

Reference: YJPAI 3427

To appear in: *Journal of Pain*

Received Date: 28 April 2017

Accepted Date: 31 May 2017

Please cite this article as: Polanco-García M, García-Lopez J, Fàbregas N, Meissner W, Puig MM, On behalf of the PAIN-OUT-Spain Consortium, Postoperative pain management in Spanish hospitals. A cohort study using the PAIN-OUT registry, *Journal of Pain* (2017), doi: 10.1016/j.jpain.2017.05.006.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Postoperative pain management in Spanish hospitals. A cohort study using the PAIN-OUT registry

Mauricio Polanco-García, MD^{*†}, Jaume García-Lopez, PhD[†], Neus Fàbregas, MD, PhD[†], Windfried Meissner MD, PhD[‡], Margarita M Puig, MD, PhD[†] On behalf of the PAIN-OUT-Spain Consortium.

[†]Department of Anesthesiology and Intensive Care, Hospital Clínic, Barcelona, Spain.

^{*} Present Address Department of Anesthesiology Hospital Comarcal de l'Alt Penedès, Barcelona, Spain.

[†]Department of Anesthesiology IMIM-Hospital del Mar-UAB, Barcelona, Spain.

[‡]Department of Anaesthesiology and Intensive Care, Friedrich-Schiller-University, Jena, Germany.

Corresponding autor: Mauricio Polanco, MD. Department of Anesthesiology. Hospital Comarcal de l'Alt Penedès, Carrer de l'Espirall, s/n, 08720. Barcelona. Spain. Tel +34622050101. Email: polmauricio@gmail.com

Disclosures

Research funding: This work was funded by the 7th framework program of the European Union. Grant Agreement No. 223590, and the Endowed Chair in Pain Management, Universitat Autònoma de Barcelona-Parc de Salut Mar-Menarini (MMP).

Conflicts of interest: For WM: Receipt of grants/research supports: Pzifer; Receipt of honoraria or consultation fees: AcelRx Pharmaceuticals, Menarini, BioQ, Pharma, Grünenthal, Medicines Company, Mundipharma; Participation in a company sponsored speaker's bureau: Menarini, Grünenthal, Mundipharma, BioQ, Pharma

ABSTRACT

Pain after surgery remains a problem worldwide, though there is no published data on postoperative outcomes in Spain. We evaluated 2922 patients in the first day after surgery in thirteen tertiary care Spanish Hospitals, using the PAIN-OUT questionnaire. Aims were to: assess postoperative outcomes, and anesthetic/analgesic management in orthopedics (ORT) and general (GEN) surgery patients; explore the influence of the analgesic—therapy on outcomes and opioid requirements; evaluate and compare outcomes and analgesic management by surgical procedure.

Mean worst-pain and % patients in severe pain were 5.6 (NRS 0-10) and 39.4%, slightly lower than those reported in Western countries (range 5.0-8.4 and 33%-55%). Patients' pain assessment (83.1%) and information were high (63.3%), but participation in decision-making (4.8) was lower than in the US (7.0) and Europe (Germany, France, Norway and Denmark, mean 5.9). Patients after ORT had worst outcomes. General anesthesia was more frequent in GEN, while regional (central and peripheral) in ORT. Mean opioid consumption ($20.2 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$, oral morphine equivalents), was lower than reported and decreased >50% after regional analgesia. Intravenous morphine-PCA was seldom used (6.2%). Acute opioids were associated with worsened outcomes while multimodal analgesia (mainly Antipyretic Analgesics-NSAIDs-Opioids) with improved results. Epidurals in abdominal surgery (16.7%) also associated with better outcomes. Pre-surgical chronic pain (>7) and/or chronic opioid consumption, were associated with worsened pain-outcomes; the latter with a 50% increase in postoperative opioid requirements. Tibia/fibula and foot surgeries (ORT), and gastric, small intestine and anterior abdominal wall procedures (GEN) were the most painful. Rigorous control of chronic pain before surgery, and combining opioids

with adjuvants and other analgesics perioperatively, might improve postoperative outcomes.

Perspective

We analyzed postoperative outcomes and analgesic-management in patients from tertiary care Spanish Hospitals. The study serves as a point of comparison with other Western countries and shows that pain intensity outcomes and opioid consumption were slightly better in the Spanish population. Chronic pain before surgery (NRS >7) and/or chronic opioid consumption, were associated with worsened pain-outcomes, suggesting that rigorous control of chronic pain before surgery, and combining opioids with adjuvants and other analgesics perioperatively, might improve outcomes. Patients' pain participation in decision-making was inadequate and should be improved in Spanish hospitals.

Key words: Postoperative pain, postoperative outcomes, pre-surgical chronic pain, postoperative analgesia, opioid consumption, patient satisfaction.

Introduction

Pain after surgery remains an unsolved problem^{8,26}, and large population studies on postoperative pain outcomes will help to improve the current practice.^{15,19,35,51} Data from six national surveys,¹¹ published from 1994 to 2011, on acute surgical and non-surgical pain reported that: 1) over half of the patients in all surveys presented moderate (from 4 to 6 in a 0–10 numeric rating scale, NRS) to severe ($\text{NRS} \geq 7$) pain, and 2) no evidence of progress in acute pain outcomes was observed despite the availability of new treatments. In an attempt to address this stagnation, several national agencies have implemented new standards in postoperative pain management^{8,14,31,45}, including multidimensional pain assessments.^{22,43} At present, there is no data available that substantiates postoperative pain outcomes in the Spanish population.

Multidimensional pain assessment is considered the best tool to measure pain outcomes.⁸ In addition to pain intensity, other pain-related outcomes such as interference with sleep and daily activities, adverse effects of analgesic medication, and satisfaction with pain management can be evaluated.^{21,45} Some recent studies assessed postoperative outcomes in several European countries and the USA, using a multidimensional self-administered questionnaire which correlates pain outcomes with analgesic management.^{15,19,33,35} All of them consistently show a high prevalence of postoperative pain with a worst-pain intensity ranging between 5.0 and 8.4 (NRS 0-10). Postoperative pain (POP) negatively affects patient's short and long term recovery and can contribute to the development of acute medical complications and to increase hospital stay.³ In addition, several studies show that after common surgeries, 30-50% of

the patients can develop persistent pain that may be severe in 2-10% of them.^{30,34} Among other factors, moderate to severe acute POP has been shown to be associated with persistent pain after surgery.^{30,34} It has been proposed that decreasing POP intensity, by means of distinct treatment modalities, may prevent the development of persistent pain after surgery.^{27,48} However, at present, there is insufficient information about the most effective analgesic therapies to control POP, and the beneficial and untoward effects of acute and chronic opioid administration.⁸

The present report addresses these issues in an observational study performed in a large sample of Spanish patients, using the PAIN-OUT registry. The observational data from the PAIN-OUT registry allows mirroring daily practice and inter-country comparison, but only associations, not causal relationships can be derived.^{16,19} PAIN-OUT is a web-based database that registers pain management and outcomes from hospitals in Europe (and around the world) with the aim of improving clinical decision making and postoperative outcomes.⁵¹ In order to obtain an overview of the actual postoperative care in Spain, we evaluated outcomes in thirteen tertiary care Spanish hospitals using PAIN-OUT implements. Our aims were to 1) assess and compare postoperative outcomes, and anesthetic / analgesic management in orthopedics (ORT) general (GEN) surgery patients; 2) explore the influence of the analgesic-therapy on outcomes and opioid requirements; and 3) evaluate and compare outcomes and analgesic management by surgical procedure

Methods

Sample and Study Design

This is a cohort study that analyzes data obtained in 13 Spanish hospitals. From an initial sample of 4011 patients enrolled, 509 of them (12.7%) did not fulfill the

inclusion criteria, and only 2922 could be incorporated in the analysis (Figure 1). Patients underwent GEN or ORT procedures and completed the PAIN-OUT questionnaire within the first day after surgery.⁵⁰ The methodology of PAIN-OUT, an European Commission funded project supported by the International Association for the Study of Pain (IASP), has been described elsewhere.⁵¹ The protocol was approved by the Research Ethic Committee of each participant hospital. Centers involved were public university Hospitals (300-1000 beds), distributed all over Spain (7 different regions) (Supplemental Table 1), having an acute pain service.

Data were collected from February 2010 to December 2013 by trained research assistants (RA). The RAs were not in charge of clinical decisions or pain treatments. The RA enrolled all patients who accepted to participate and fulfilled the inclusion criteria. If the volume of surgeries outnumbered the capacity of the RA, patients were randomized by a computer sequence. Within the first postoperative day patients, who voluntarily gave their verbal consent, after explanation by the RA, completed the questionnaire (rigorously anonymous) which included in the first page a letter of information and request of participation. Exceptionally, patients were verbally interviewed when too weak or tired (due to the surgery), or unable to read or write (illiterate).

Inclusion and Exclusion Criteria

PAIN-OUT inclusion criteria: surgical patient >18 years who gave informed consent, was in the first postoperative day, and back in the ward for a minimum of 6 hours. Exclusion criteria: refused to participate, sedated, asleep, not in the ward at the time of data collection, or impossible to communicate due to cognitive impairment or poor management of the Spanish language. Additional exclusion criteria were: 1) did not complete > 50% of the International Pain Outcome (IPO) Questionnaire; 2) did not

answer the “worst pain” question; 3) the ICD-9 (International Classification of Disease, 9 Revision) code (type of surgery) was not recorded in the Process Questionnaire (PQ); and 4) underwent surgeries other than GEN or ORT such as gynecologic, urologic, ENT, etc. (4.1% of the sample, Figure 1).

Questionnaires

Questionnaires for data collection were: 1) the self-administered validated IPO, a modified version of the Revised American Pain Society-Patient Outcome Questionnaire (APS-POQ-R), with good psychometric qualities.⁴³ The IPO Spanish version was constructed with a forward-backward translation according to international standards,⁴³ and 2) the PQ, completed by the RA with data from the patient medical history (Supplemental Material 1 and 2). The IPO is designed to evaluate five aspects of pain: 1) pain severity and relief, including worst pain, least pain, percentage of time with severe pain, and percentage of pain relief with treatment; 2) pain interference with sleep, in bed and out of bed activities, breathing, and emotional status; 3) side effects of the analgesic treatment including nausea, drowsiness, dizziness and itching; 4) ability to participate in pain treatment decisions, perception of quality of care and satisfaction, and 5) use of non-pharmacological strategies for pain relief. Questions about pain and pain intensity during the 3 months previous to surgery are also included (see Supplemental Material 1). NRS (0-10) or dichotomous selection and multiple choice questions (i.e. for non-pharmacological methods for pain management) were used. The percentage of patients with side effects was recorded and their intensity, as well as that of chronic pain before surgery, was measured in a 0-10 NRS scale. Severe pain was defined as a pain greater than 6 ($\text{NRS} \geq 7$), and moderate from 4 to 6 in the NRS. The PQ includes demographic information: gender, year and country of birth, weight, height, nationality, and comorbidities; type of surgical procedure (ICD-9 codes) and

anesthesia; analgesics and sedatives administered in the preoperative, intraoperative, and postoperative periods, with the name of the drug, dose and route of administration.

Data input

Data from the questionnaires were entered in a protected multi-institutional web-based database: The PAIN-OUT database is hosted and maintained by the Institute of Medical Informatics, Statistics, and Epidemiology, University of Leipzig, Germany, that periodically monitor data quality.⁵¹ To maintain anonymity, a unique code (unrelated to personal data, institution, or file number) was assigned to each patient. The feasibility of a large patient's data registry such as PAIN-OUT was shown by Rothaug and Zaslansky et al., when reporting that only 0.06% of the outcome data, and 2% of the process data were missing in most of the questionnaires.^{43,51}

Definition of Surgical Groups

All types of surgical procedures (major, moderate, minor) of each specialty (ORT, GEN) were included in the study. Procedures included in ORT and GEN surgeries are listed in Tables 7 and 8, respectively. Due to the confirmed discriminatory validity of the IPO questionnaire showing significant differences between GEN and ORT surgeries, the results were analysed both globally and separately by type of surgery⁴³. Surgical procedures were coded using the ICD-9 and assigned to ORT (11 subgroups) or GEN (13 subgroups) groups, based on the first two digits of the ICD-9 code. Procedures with ICD-9 codes that were not specific to any anatomic location were excluded (11.2% of the sample). Infrequent surgeries were included only if the number of patients > 10, and data was registered from > 2 hospitals.

Analgesic drugs

Postoperative analgesic drugs and doses were obtained from the PQs. Remifentanyl and intraoperative fentanyl were not considered postoperative analgesics, as they were used as part of the anesthetic protocol. Intraoperative intravenous (iv) morphine (MS) was included in the analysis considering that it was administered to provide postoperative analgesia. All iv opioids were converted first into iv MS and then multiplied by a factor of 3, while oral opioids were directly converted to oral MS. Postoperative opioid requirements were converted into oral morphine according to published equianalgesic tables.^{1,38} Multimodal analgesia was defined as the administration of more than one analgesic or adjuvant drug with a different mechanism of action.²⁸ Regional analgesia including epidural drugs, peripheral nerve blocks (PNB), and wound infiltration were assessed independently.

Sample size

Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, at least 561 subjects are necessary in each surgery group to recognize a between-group statistically significant difference in pain intensity greater than or equal to 0.5 units. The common standard deviation (SD) is assumed to be 2.5.¹⁹ A drop-out rate of 30% was anticipated.

Data analysis

Qualitative variables were expressed as absolute frequencies and percentages. For quantitative variables, the mean and SD or median and interquartile range (IQR) was used, according to their distribution. For ordinal variables, depending on the number of categories, percentage and absolute frequencies or median and IQR values were used. To compare categorical independent continuous variables, the Fisher's exact test and the Student's t test, with Bonferroni's correction for multiple comparisons, if required, were

used. Leastwise deletion of missing data were used for analysis. If they did not meet the assumption of applicability for ordinal variables, nonparametric methods for independent data were used (Mann-Whitney test or Kruskal-Wallis).

The effect size is a quantitative measure of the strength of a phenomenon and is classified as small ($d = 0-0.2$), medium ($0.3-0.5$) or large (>0.5).⁹ To measure the effect size when comparing ORT and GEN patients, we used the Cohen's d coefficient with Confidence Interval 95 (CI95). Cohen's d was also used to correlate continuous variables from the outcomes questionnaire. In our report, values were considered clinically relevant when Cohen's $d > 0.3$, this value remaining the principal criteria for reporting changes throughout the Results and Discussion in this work. Comparisons between groups < 10 patients were not performed because the statistical power is very low and conclusions can be falsely true. IBM SPSS Statistics 20.0 (SPSS Inc, Chicago, IL) was used for data analysis.

Results

Patient characteristics and comorbidities.

A total of 4011 patients from Spanish Hospitals distributed in seven regions of the country, were registered from February 2010 to November 2013 (Supplementary Table I). Inclusion criteria were met in 3502 (87.3%). After applying all exclusion criteria (Fig. 1), 2922 patients (72.8%) entered the study. Patients excluded were older (67.9 vs 59.5 years, $p < 0.001$, $d = 0.51$), leaner (body mass index, 26.8 vs 28.7, $p = 0.024$, $d = -0.29$), with more psychiatric disorders (24.7% vs 13.3%, $p = 0.006$, $d = 0.42$) and comorbidities (92.2% vs 72.3%, $p < 0.001$, $d = 0.83$). Patients' characteristics were similar in ORT and GEN surgery (Table 1). Cancer, renal, and gastrointestinal comorbidities were more

frequent in GEN than in ORT patients ($p < 0.001$) with effect sizes > 0.4 . In our sample, the median time from the end of the surgery until the patients completed the questionnaire was 25.16 hours (IQR 8.625).

Postoperative outcomes

Postoperative outcomes are listed in Table 2. Mean worst pain intensity in the whole sample was 5.6. Orthopedic patients had worse pain intensity and were more time in severe pain than GEN patients, whereas interference with breathing was notably greater in GEN (effect size 0.95). Adverse effects (AE) were observed in 72.4% of the patients. Most frequent AE were: anxiety, drowsiness, and helplessness. Adverse effects and perception of care was similar in both surgery groups. The mean satisfaction value with pain treatment was 7.9, although 19.2% of the patients requested more treatment. Pain assessment in the ward was obtained from 83.1% of the patients. Percentage of patients who received information about pain treatment options or were allowed to participate in decision making were 63.3%, and 71.6%, respectively (Table 2).

Anesthetic management

Premedication was administered to 2886 patients (78.2%) (Supplementary Table II). Sedatives (benzodiazepines) and opioids were more often used in ORT than GEN. General and combined anesthesia (general + epidural) were more frequently used in GEN than ORT, and regional anesthesia (central and peripheral) in ORT. Mean time of surgical procedures was similar in ORT (1.71 h) and GEN (2.04 h).

Postoperative outcomes according to anesthetic management

Premedication

Premedication did not alter pain outcomes but was associated with a significant decrease in the frequency of itching (16.1% vs 25.3%, $p<0.001$, $d=-0.31$)

Regional, general and combined anesthesia

Regional anesthesia was more frequently used in ORT surgery, but no clinically significant differences in pain outcomes were observed according to type of anesthesia. Patients receiving combined anesthesia felt less anxiety (43.1% vs 59.8%, $p<0.001$, $d=0.37$) and helplessness (37.3% vs 50.5%, $p<0.001$, $d=0.30$) compared with those who had only regional anesthesia. Opioid consumption, as oral morphine (MS) equivalents, was higher after general than regional or combined anesthesia ($26.8\text{mg}\cdot\text{patient}^{-1}\cdot 24\text{h}^{-1}$ vs $15.1\text{mg}\cdot\text{patient}^{-1}\cdot 24\text{h}^{-1}$ vs $12.3\text{mg}\cdot\text{patient}^{-1}\cdot 24\text{h}^{-1}$, $p<0.001$, $d=-0.34$). Variables related to satisfaction did not differ between groups (data not shown).

Epidural anesthesia

Epidurals (single bolus or infusion) and PNB were administered before or after surgical incision to provide both intra- and postoperative analgesia. An epidural technique was performed in 3.5% (56/1564) of ORT patients and 13.4% (179/1338) of GEN, and were applied mainly in the intraoperative period ($n=221$, 94%). Globally, pain outcomes in ORT or GEN patients receiving (or not) an epidural were similar. In the ORT group, global AE, and particularly itching, were more frequent in patients with an epidural ($p=0.04$, $d=0.39$). However, in GEN patients, drowsiness ($p<0.001$, $d=0.32$), anxiety ($p<0.001$, $d=-0.36$), and helplessness ($p<0.001$, $d=0.43$) were lower in patients with an epidural (data not shown).

As epidural blocks are often used for abdominal procedures, the outcomes of this subgroup of patients (65.0% of GEN) were analyzed separately (Supplementary Table

III). The epidural block was associated with a decreased percentage of time in severe pain, increased pain relief with treatment, and a reduced frequency of AE.

Intraoperative Opioids

Intraoperative opioids were used for both surgical and postoperative analgesia. During surgery, iv opioids were administered to 60.4% of the patients and were given more frequently to GEN than ORT patients (80.9% vs 43.0%, $p<0.001$, $d=0.95$). Fentanyl (54.1% of patients), remifentanyl (10.2%) or alfentanil (0.8%) were administered as part of a balanced general anesthesia protocol. Within patients who underwent general anesthesia, the administration of remifentanyl was associated with less interference with in bed activities (mean 3.3(SD2.6) vs 4.3(3.0), $p=0.02$, $d=-0.34$) and a lower number of patients that requested more treatment (6.4% vs 13.8%, $p<0.001$, $d=-0.47$). No change in opioid consumption in patients receiving remifentanyl was observed, although they were treated more frequently with the combination of opioid, AA and NSAIDs (54.3% vs 38.7%, $p<0.01$, $d=-0.35$). Intraoperative fentanyl was not associated with changes in outcomes.

Postoperative Analgesia

Analgesic-drugs were administered to 97.1% of the patients (Table 3). Those patients who had no systemic analgesia ($n=94$, 3.2%) received epidural analgesia ($n=7$), PNB ($n=37$), or no analgesic treatment ($n=50$). Opioids and non-opioids were administered intravenously before the closure of surgical wound (60.4% and 48.0% of patients, respectively) to obtain transitional and postoperative analgesia.

Opioids

Opioids at any time during the process, were given to 59% of the patients (Table 3); iv tramadol (TRM) and iv MS being the most frequently used. Intravenous TRM was

similarly administered to ORT and GEN patients, but doses were higher in ORT. Intravenous MS was more often administered in GEN versus ORT patients, the opposite occurring for subcutaneous (sc) MS. Mean dose of opioids (in oral MS equivalents) was $20.2 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$.

Non-opioid analgesia

Antipyretic Analgesics (AA) were administered to 94.3% of patients (Table 3), iv paracetamol (PCT) and iv metamizol (MET) being the most used. Oral (po) PCT was similarly used in ORT and GEN, but doses were higher in ORT. Dexketoprofen (DEX) iv was the most frequent nonsteroidal anti-inflammatory drug (NSAID, 55.7% of patients) administered in both surgeries. Oral DEX was more often used, and at higher doses, in ORT than in GEN, the opposite occurring with ketorolac iv.

Multimodal analgesia (MA)

Drug combinations or MA was used in 82.3% of the patients (Supplementary Table IV). Opioids + AA+NSAIDs were the combinations most frequently prescribed as MS, PCT and DEX (31.3%) followed by AA + NSAIDs (21,6 %), and opioids + AA (19,6 %). Intravenous PCA and PNB were more often used in ORT than in GEN, whereas the opposite occurred for LA-PCA and wound infiltration. The most frequent PNB performed were: femoral (13.5% of the total sample), sciatic (10.5%) and braquial plexus (7.6%); continuous PNB catheter infusion was used in 3.3% of patients. When PNB were administered, NSAIDs were given less frequently (31.0% vs 51.2%, $d=-0.46$, $p<0.001$). Outcomes and frequency of analgesic modalities according to location and procedure are shown in Tables 7 and 8.

Non-pharmacological methods for pain control were reported to be used in 27.8% of patients, the more frequent being talking with friends and relatives (50.5%)

and non-medical hospital staff (44.4%), distraction (i.e. watching TV or reading) (43.3%), and cold packs (25.7%). In our sample, only imagery and visualization (1.6%) or transcutaneous electrical nerve stimulation (1.0%) were associated with a lower intensity of worst pain ($d=0.31$).

Postoperative outcomes according to the type of analgesia

When opioids were used as postoperative analgesics (Table 4), more patients had severe pain, a higher intensity of worst pain, and more interference with in-bed activities. Frequency of AE and satisfaction outcomes were similar. Patients receiving MA reported more pain relief and more satisfaction, although the percentage of patients in severe pain was higher (Table 4). Other pain outcomes and frequency of AE were similar. Patients who received less than two analgesics in the ward (15.9% of the sample), although they had less patients in severe pain ($p<0.001$, $d=-0.33$), showed less pain relief ($p<0.001$, $d=-0.68$) and less satisfaction ($p<0.001$, $d=-0.53$).

Patients who received PNB or LA-PCA had similar pain intensity, interferences, and satisfaction outcomes compared to patients who did not, and the frequency of AE was also similar. The same occurs for iv PCA, but in this case global AE were increased ($p<0.001$, $d=0.30$) (data not shown). Wound infiltration was mainly used in gastric, hand, and knee surgeries that comprised the 7.9% of a non-representative sample from only 3 hospitals (comparisons not performed).

Postoperative outcomes in patients with chronic preoperative pain

A 52.7 % of patients had chronic pain before surgery (mean intensity of 6.9). Frequency of chronic pain ($p<0.001$, $d=0.86$), its intensity ($p<0.001$, $d=0.56$), and chronic use of opioids before surgery ($p<0.001$, $d=0.83$), were higher in patients undergoing ORT than GEN. Chronic pain was more frequent in patients who had more comorbidities

($p < 0.001$, $d = 0.47$), and was mainly located at the site of surgery. Frequency of chronic pain was high in spine (89.7%), knee (87.2%), shoulder (78.4%) and hip procedures (76.8%) (data not shown).

Table 5 shows postoperative outcomes per chronic pain and per chronic opioid administration before surgery. Among patients with chronic pain ($n = 1487$), 60.3% scored its intensity as severe ($\text{NRS} \geq 7$). In these patients outcomes were significantly worse than in the group of non-chronic pain ($p < 0.001$, $d = 0.39$). No differences were observed among other groups, thus, patients with non-severe preoperative chronic pain (39.7%, $\text{NRS } 1-6$) (mild + moderate) had similar outcomes than those without preoperative pain. The coefficient correlation between the intensity of chronic pain and worst-pain after surgery was $r = 0.2$ ($p < 0.001$).

The frequency of AE was similar in all groups of patients. Only 5.8% of patients with chronic pain received chronic opioids, and this group also presented worse pain outcomes (Table 5): they requested more analgesia after surgery, and required 50% more opioid-analgesics postoperatively (Table 6). The frequency of AE was alike in all groups.

Perioperative procedures that affect opioid requirements during the first day after surgery

Table 6 shows perioperative procedures which could modify opioid requirements in the first 24h postoperatively. Chronic opioid administration before surgery was associated with a 50% increase in postoperative acute opioid requirements. On the contrary, epidural blocks, particularly during abdominal surgery, were associated with an opioid sparing effect, decreasing opioid requirements approximately 2-3 fold. Globally, regional procedures were associated with decreased doses of opioids by more than 70%.

Peripheral nerve blocks, or the use of non-pharmacological treatments did not affect opioid requirements in our sample.

Postoperative outcomes and analgesic management by surgical procedure

Tables 7 and 8 show postoperative outcomes and analgesic management by surgical procedure. Worst pain and the requirement for more analgesic treatment were selected as best indicators for the presence of pain and its inadequate management.^{21,46} Opioid consumption was considered high when oral morphine equivalents exceed percentile 75 ($30 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$).

In ORT patients (Table 7), tibia/fibula and foot/ankle interventions were the most painful surgeries, requesting more analgesic treatment. Shoulder and hand procedures, with a high percentage patients receiving PNB, were the least painful. Spine surgery, knee, and hip replacement presented the highest incidence of AE. Epidural block, both for analgesia and anesthesia, was frequently used in femur, knee, and hip surgery. In ORT patients, wound infiltration was only used in knee and hand surgery. Mean total opioid consumption was above $30 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$ in spine surgery.

Among GEN procedures (Table 8), gastric, small intestine and anterior abdominal wall procedures were the most painful, where patients had more adverse events and also would like to receive more treatment. Despite anal surgery procedure were painful, both frequency of multimodal analgesia and opioid dose were low. The least painful procedures were thyroid and breast surgery, the latter where MA was less frequently used. Mean total opioid consumption was above $30 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$ in liver and gastric surgeries, cholecystectomy, and anterior abdominal wall repair. Appendectomy patients received lower doses of postoperative opioids ($10.9 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$ of oral MS equivalents) despite of a high request for more treatment (16.1%).

Epidural blocks were frequently used in colo-rectal, liver, gastric, and small bowel surgeries, and PNB in breast surgery and umbilical hernia repair. PCA (iv) and LA-PCA were mostly used in liver surgery.

According to the variable number of patients in severe pain (>7 , NRS 0-10), the most painful ICD-9 procedures were observed in ORT patients after foot and spine surgeries. In agreement with data from Schwenkglenks et al,⁴¹ in our cohort we found a positive relation between requesting more pain treatment and both, worst pain intensity ($d=0.99$ (CI95 0.89-1.08)) and percentage of patients with severe pain ($d=0.98$ (CI95 0.87-0.95)); a negative association with satisfaction was also observed ($d=-1.12$ (CI95 -1.21;-1.01) (Figure 2).

Discussion

This is the first study on quality of care and outcomes in postoperative Spanish patients using a multidimensional self-administered validated scale. As in similar studies,^{19,33,35} the percentage of women was higher than that of men (57.9/42.1), mean age and mean time of surgery being approximately 55 years and 2h. Since patients enrolled were from tertiary care hospitals, higher levels of pain were expected when comparing to surveys that included patients from primary and secondary centers. Comparison of the outcomes observed in the present survey with those reported by other Western countries (Germany, France, Denmark, and U.S.A)^{15,19,21,33,35} shows a similar postoperative pain intensity (global). Nevertheless, our mean worst-pain of 5.6, was lower than in France (6.4),¹⁵ Denmark (6.5),³³ and U.S.A. (range 6.17-8.37),²¹ although higher than the reported in Germany (4.8).¹⁹ Also, the percentage of patients (39.4%) with severe pain in our study (≥ 7 , NRS 0-10) was comparable, even slightly lower, than the reported in

Europe and U.S.A. (33%-55%).^{15,19,33,35}. Other detected divergences were: Lower doses of acute opioid analgesics consumed in the Spanish population, and lower frequency of administration of morphine by iv-PCA. The low levels of postoperative pain in Spain, when compared to other countries (except Germany) could be partially explained by a lower pain sensibility⁴, the surgical population and practice patterns, or cultural/religious idiosyncrasies. Another factor not yet investigated, is the diet: Oxidation and inflammation are inter-twined phenomenon, and the richness of antioxidants in the Mediterranean diet could promote a high protective status during in the presence of inflammation.⁴⁷

Similar to other reports,²⁵ the most painful surgeries were associated with orthopedic surgery, particularly fractures of extremities; spine, hip, and knee procedures with a high frequency of preoperative chronic pain, repeated surgeries, and also bariatric surgeries (results not shown). Interference with breathing was much higher in GEN surgeries. Incidence of AE was also comparable to other countries. As already reported¹⁹, orthopedic procedures registered worst pain outcomes than general surgery.

In the analysis of the results, Cohen's "d" coefficient was valuable to substantiate differences between ORT and GEN patients, considering medium values of d (>0.3) an indication of the strength of the results. However, the terms 'small,' 'medium,' and 'large' for Cohen Coefficients may be considered relative, and there is a certain risk when using them in power analysis in health research. Accordingly, the relevance of the results cannot be exclusively established by the size of the coefficient, but should be based on its contribution to improve postoperative outcomes and patient well-being. There are a number of instances in our study, that illustrate the usefulness of calculating the level of Cohen's coefficient. As examples of data with high values of d, we observed that ORT patients presented more frequently pre-surgical chronic pain

($d=0.86$) and it was of greater intensity than in GEN surgery patients ($d=0.56$). Likewise, general anesthesia was more frequent during GEN surgery ($d= -1.36$), while intrathecal ($d=1.52$) and PNB ($d=1.85$) were more often used in ORT; interestingly, PNB were not associated with better pain outcomes ($d=-0.15$ for worst pain) but with an important decrease in NSAIDS consumption ($d=-0.46$).

Chronic pain before surgery has been associated with greater postoperative pain intensity, both at rest and during movement.^{20,25} We observed that only *severe* chronic pain (≥ 7) was associated with poor pain outcomes, with effect sizes >0.4 in pain variables, when comparing with mild or no pain before surgery. Despite the high prevalence (52.7%) of chronic pain, it appears to be insufficiently treated, given its high intensity (mean 6.9) and the limited use of chronic opioids (5.8%). It is noteworthy that patients with severe chronic pain are more likely to receive chronic opioids, a practice that is not influenced by intra or postoperative events or procedures.

Acute (mainly short acting opioids) or chronic opioid exposure induces pain sensitization and hyperalgesia in animal models and humans (Opioid Induced Hyperalgesia, OIH). In a preclinical model of surgical (incisional) pain, we reported dose-dependent remifentanyl-induced pain sensitization in the postoperative period.⁵⁻⁷ Increased pain hypersensitivity after chronic exposure to opioids has also been reported³⁷. In our study, acute and chronic opioids were associated with comparable poor pain outcomes, supporting other reports.^{10,37} This could be related to reduced pain thresholds (OIH), a diminished potency of the drugs (tolerance), or both. Clinically, opioid-tolerant patients obtain analgesia when increasing the doses of opioids, but during OIH, increasing the opioid dosage does not reduce pain, but may even increase it. In the survey, chronic opioids were associated with a 50% increase in acute opioid consumption (suggesting tolerance), but these high doses (mean $37.6 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$

oral morphine equivalents) were also associated with poor pain outcomes (suggesting OIH). The association could be influenced by the temporal relationship with acute opioid administration which was not registered, and consequently, pain outcomes may not reflect treatment effectiveness. Unfortunately, these hypotheses cannot be confirmed (or disproved), on the basis of the present study, where postoperative hyperalgesia was not assessed. Since subjects exposed to chronic opioids require distinct protocols for POP management,^{8,49} patients undergoing surgery should be carefully questioned about the use of opioid-analgesics prior to surgery.

Genetic variations leading to lower opioid efficacy could be relevant in some patients⁴¹, and opioid-receptor gene analyses may help to devise individualized protocols for postoperative pain. It is unlikely that acute opioids would induce acute tolerance or hyperalgesia, the latter occurring when high doses of intraoperative short acting opioids (mainly remifentanyl) are administered²³. No clinically significant influence of remifentanyl administration on outcomes could be detected in our survey.

Acute opioids for postoperative analgesia were administered to 59% of the sample at a mean dose of $20.2 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$ (oral morphine equivalents). The dose is lower than the reported in the Norwegian survey ($60 \text{ mg} \cdot \text{patient}^{-1} \cdot 24\text{h}^{-1}$)¹³ and higher than in the German report when comparing the same surgeries.¹⁹ The use of regional analgesia and other opioid-sparing analgesic procedures (i.e. drug-combinations) could be responsible for the low doses of opioids given in our sample. Opioids (MS, TRM) by iv-PCA were only used in 10.5% of patients, and morphine-PCA (MS-PCA) in 6.2% of the sample; a low percentage when compared with France (21.4%)¹⁵ and U.S.A (16%).¹⁷

Patient information and pain assessment are essential components for the quality of pain management.²¹ Frequent pain evaluation and individual education about

pain treatment options, has been associated with better outcomes, and improved patient-physician relationship.^{24,36} In the study, pain assessment in the ward was performed in 83.1% of patients, and 63.3% felt informed. These results are better than those reported in PATHOS, a survey performed in 7 European countries,² in which, according to the acute pain team, percentages of patients receiving pain information and assessment were 48.5% and 44%, respectively. The participation of our patients in pain treatment decision-making (mean 4.8) was lower than in U.S.A. (mean 7.9) and other European countries (median 7),^{22,43} an aspect that should be improved. The process of care and appropriateness of treatment are also important factors in quality improvement.^{8,21} The high scores in satisfaction reported could be related to a good quality of information and perception of care.^{21,39,46} Also, the administration of ≥ 2 analgesics in the ward (mainly AA+NSAID) was associated with higher satisfaction and pain relief despite having more severe pain, what could be related to a perceived better care.⁴⁶ In the study, premedication did not alter outcomes but was associated with decreased itching (16.1% vs 25.3%), a finding that could be explained by the administration of sedatives (i.e. benzodiazepines), drugs reported to decrease pruritus of different etiologies.³²

Recent postoperative pain guidelines advise the use of analgesic techniques with opioid-sparing effects such as multimodal analgesia (MA) or epidural and PNBs.^{8,29,45} In agreement with this, in our study, MA was associated with better pain relief, although acute opioid-analgesics were associated with worse outcomes. The analgesic combination most frequently prescribed was NSAIDs+antipyretics+opioids, according to the optimal analgesic-drug combinations described;^{12,31,45} the drugs most frequently used were MS, DEX, and PCT (31.6%). Nerve blocks were used in half of orthopedics patients, while the use of epidurals was low when compared to other European countries.² From our results, epidural blocks should be part of the anesthetic protocol in

abdominal surgery, although this conclusion is buffered by the low number of cases involved (145 patients); however, our results support those reported by Roeb et al.⁴² in 646 cases of abdominal surgery.

Our study has strengths and limitations. One strength is the use of the IPO questionnaire whose consistency, reliability, construct, and discriminative validity, has been previously established as satisfactory.⁴³ From our own and others' data, self-administration of the questionnaire reduces the bias of an external interviewer.^{8,18} Also, data collection was done by trained personnel, and introduced in a protected, periodically monitored database that assured homogeneity across centers. As limitations, participation from hospitals and patients was voluntary, what can produce a bias toward a willingness for assessing pain outcomes. We were unable to compare our results with the findings of other anesthesia practice surveys in Spain^{40,44}, since in these reports there was a predominance of low complex surgeries. Most of our patients (72.5%) belonged to four hospitals, and this could affect the generalization of the results. Moreover, there was a single measure of pain in the afternoon, and answers could be influenced by the analgesic schedule of the ward and the pain suffered when answering the questionnaire.

In summary, the study shows that in our Spanish tertiary care hospital cohort, despite the low dose of opioids administered, mean pain intensity 24hours postoperatively and the percentage in severe pain were quite similar, and even in the low range, to those reported in other Western countries. From our data, severe chronic preoperative pain (>7 NRS), but not mild-moderate chronic pain (1-6, NRS), was associated with worsened pain outcomes. Treatment with chronic opioids also concurred with worsened outcomes and increased opioid requirements (50%). A more effective control of the intensity of chronic pain before surgery, combining opioids with

adjuvants and other analgesics, and adjusting the doses of chronic opioids to individual needs, could be useful. Our data also reinforces that epidural anesthesia should be part of the anesthetic protocol in abdominal surgery, and reveals that premedication is associated with less postoperative pruritus. The administration of ≥ 2 different analgesics in the ward, improves the perception of care. Patient information and pain assessment in our hospitals could be improved, and patients' participation in treatment decisions must be revised.

Acknowledgements

The PAIN OUT project was funded by the European Commission 7th Framework Programme, Call HEALTH-2007- 3.1 4: Improving Clinical Decision-Making, and endorsed by the International Association for the Study of Pain.

The authors thank the members of the PAIN-OUT Spanish Consortium who took part in the study: Dr. Montes, Hospital del Mar, Barcelona. Dr Bogdanovich and Dr Gómez, Hospital Clínic, Barcelona. Drs. Martinez, Pons, Cortell, Femenía, and Peláez, Hospital Universitario La Fe, Valencia. Drs. Aguilar, Sastre, Nohel and Carbayo, Hospital Son Llatzer, Palma de Mallorca. Dr. Pascual, Hospital de Ciudad Real. Dr Martínez and Dr Cano, Hospital Virgen de las Nieves, Granada. Dr. García-Filoso, Hospital San Juan, Alicante. Drs. Telletxea, Ortega. and Pérez, Hospital de Galdakao Usansolo. Dr. Crespo, Hospital Sant Joan de Deu, Sant Boi de Llobregat. Drs. Pérez, Conejo, Cicuéndez, Beltrán, Zorrilla and Martín, Hospital Clínico Universitario, Valladolid. Drs. Rodriguez, Hernández, Yáñez, Túñez, and Mancuso, Hospital Universitario Insular, Gran Canaria. Drs. Guadalix, Romero, Hinojosa, and Medina, Hospital Regional Universitario Carlos Haya, Málaga. Drs, Atiénzar, Mansilla,

Mercado, Orta, Massó, Sarabia, Sánchez, Pardo and Muñoz, Hospital General de Castellón.

References

1. Anderson R, Saiers JH, Abram S, Schlicht C: Accuracy in Equianalgesic Dosing : Conversion Dilemmas. *J Pain Symptom Manage* 21:397–406, 2001.
2. Benhamou D, Berti M, Brodner G, De Andres J, Draisci G, Moreno-Azcoita M, Neugebauer EAM, Schwenk W, Torres LM, Viel E: Postoperative Analgesic THERapy Observational Survey (PATHOS): a practice pattern study in 7 central/southern European countries. *Pain* 136:134–41, 2008.
3. Breivik H: Postoperative pain management: why is it difficult to show that it improves outcome? *Eur J Anaesthesiol* 15:748–51, 1998.
4. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D: Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain* 10:287–333, 2006.
5. Cabañero D, Campillo A, Célérrier E, Romero A, Puig MM: Pronociceptive effects of remifentanyl in a mouse model of postsurgical pain: effect of a second surgery. *Anesthesiology* 111:1334–45, 2009.
6. Campillo A, Cabañero D, Romero A, García-Nogales P, Puig MM: Delayed postoperative latent pain sensitization revealed by the systemic administration of opioid antagonists in mice. *Eur J Pharmacol* 657:89–96, 2011.
7. Célérrier E, González JR, Maldonado R, Cabañero D, Puig MM: Opioid-induced

- hyperalgesia in a murine model of postoperative pain: role of nitric oxide generated from the inducible nitric oxide synthase. *Anesthesiology* 104:546–55, 2006.
8. Chou R, Gordon DB, Leon-casasola OA De, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden H, Degenhardt E, Griffith S, Manworren R, Mccarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL: Guidelines on the Management of Postoperative Pain. *J Pain* 17:131–57, 2016.
 9. Cohen J: A power primer. *Psychol Bull* 112:155–9, 1992.
 10. Cohen SP, Christo PJ, Wang S, Chen L, Stojanovic MP, Shields CH, Brummett C, Mao J: The Effect of Opioid Dose and Treatment Duration on the Perception of a Painful Standardized Clinical Stimulus. *Reg Anesth Pain Med* 33:199–206, 2008.
 11. Correll DJ, Vlassakov K V., Kissin I: No evidence of real progress in treatment of acute pain, 1993-2012: Scientometric analysis. *J Pain Res* 7:199–210, 2014.
 12. Curatolo M, Sveticic G: Drug combinations in pain treatment: a review of the published evidence and a method for finding the optimal combination. *Best Pract Res Clin Anaesthesiol* 16:507–19, 2002.
 13. Dihle A, Helseth S, Kongsgaard UE, Paul SM, Miaskowski C: Using the American Pain Society's patient outcome questionnaire to evaluate the quality of postoperative pain management in a sample of Norwegian patients. *J Pain* 7:272–80, 2006.
 14. Dolin SJ, Cashman JN, Bland JM, Clinic P, Richard S, Po C: Effectiveness of

- acute postoperative pain management : I . Evidence from published data. *Br J Anaesth* 89:409–23, 2002.
15. Fletcher D, Fermanian C, Mardaye A, Aegerter P: A patient-based national survey on postoperative pain management in France reveals significant achievements and persistent challenges. *Pain* 137:441–51, 2008.
 16. Fleurence RL, Naci H, Jansen JP: The critical role of observational evidence in comparative effectiveness research. *Health Aff (Millwood)* 29:1826–33, 2010.
 17. Gan TJ, Habib AS, Miller TE, White W, Apfelbaum JL: Incidence, patient satisfaction, and perceptions of post-surgical pain: results from a US national survey. *Curr Med Res Opin* 30:149–60, 2014.
 18. García-López J, Domingo Vicent F, Montes PA, Dürsteler C, Puig Riera de Conías MM: [Comparison of 2 methods of clinical data collection, one using the PAINOUT questionnaire (a European database for the management of postoperative pain)]. *Rev Esp Anesthesiol Reanim* 58:273–8, 2011.
 19. Gerbershagen HJ, Aduckathil S, van Wijck AJM, Peelen LM, Kalkman CJ, Meissner W, Ph D, Kalkman CJ, Meissner W: Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. *Anesthesiology* 118:934–44, 2013.
 20. Gerbershagen HJ, Pogatzki-Zahn E, Aduckathil S, Peelen LM, Kappen TH, van Wijck AJM, Kalkman CJ, Meissner W, Ph D, Kappen TH, Wijck AJM Van, Kalkman CJ, Meissner W: Procedure-specific risk factor analysis for the development of severe postoperative pain. *Anesthesiology* 120:1237–45, 2014.
 21. Gordon DB, Pellino T a., Miaskowski C, McNeill JA, Paice J a., Laferriere D,

- Bookbinder M: A 10-year review of quality improvement monitoring in pain management: Recommendations for standardized outcome measures. *Pain Manag Nurs* 3:116–30, 2002.
22. Gordon DB, Polomano RC, Pellino TA, Turk DC, Mccracken LM, Sherwood G, Paice JA, Wallace MS, Strassels SA, Farrar JT: Revised American Pain Society Patient Outcome Questionnaire (APS-POQ-R) for Quality Improvement of Pain Management in Hospitalized Adults: Preliminary Psychometric Evaluation. *J Pain* 11:1172–86, 2010.
 23. Hayhurst CJ, Durieux ME: Differential Opioid Tolerance and Opioid-induced Hyperalgesia: A Clinical Reality. *Anesthesiology* 124:483–8, 2016.
 24. Hibbard JH: Engaging health care consumers to improve the quality of care. *Med Care* 41:I61-70, 2003.
 25. Ip HYV, Abrishami A, Peng PWH, Wong J, Chung F: Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology* 111:657–77, 2009.
 26. Joshi GP, Kehlet H, Healthcare B, Pharmaceuticals C: Procedure-specific pain management: the road to improve postsurgical pain management? *Anesthesiology* 118:780–2, 2013.
 27. Kairaluoma PM, Bachmann MS, Rosenberg PH, Pere PJ: Preincisional paravertebral block reduces the prevalence of chronic pain after breast surgery. *Anesth Analg* 103:703–8, 2006.
 28. Kehlet H: Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth* 78:606–17, 1997.

29. Kehlet H: Updated pain guidelines: what is new? *Anesthesiology* 117:1397–8; author reply 1398, 2012.
30. Kehlet H, Jensen TS, Woolf CJ: Persistent postsurgical pain: risk factors and prevention. *Lancet* 367:1618–25, 2006.
31. Larue F, Lehet P, Lejus C, Macaire P, Marret E, Richebé P: Expert panel guidelines (2008). Postoperative pain management in adults and children. SFAR Committees on Pain and Local Regional Anaesthesia and on Standards. *Ann Fr Anesth Reanim* 28:403–9, 2009.
32. Leslie TA, Greaves MW, Yosipovitch G: Current topical and systemic therapies for itch. *Handb Exp Pharmacol* 226:337–56, 2015.
33. Lorentzen V, Hermansen IL, Botti M: A prospective analysis of pain experience, beliefs and attitudes, and pain management of a cohort of Danish surgical patients. *Eur J Pain* 16:278–88, 2012.
34. Macrae WA: Chronic post-surgical pain: 10 Years on. *Br J Anaesth* 101:77–86, 2008.
35. Maier C, Nestler N, Richter H, Hardinghaus W, Pogatzki-Zahn E, Zenz M, Osterbrink J: The quality of pain management in German hospitals. *Dtsch Arztebl Int* 107:607–14, 2010.
36. McDonald S, Page MJ, Beringer K, Wasiak J, Sprowson A: Preoperative education for hip or knee replacement. *Cochrane database Syst Rev* 5:CD003526, 2014.
37. Patanwala AE, Jarzyna DL, Miller MD, Erstad BL: Comparison of opioid requirements and analgesic response in opioid-tolerant versus opioid-naïve

- patients after total knee arthroplasty. *Pharmacotherapy* 28:1453–60, 2008.
38. Pereira J, Lawlor P, Vigano A, Dorgan M, Bruera E, Chb MB: Equianalgesic dose ratios for opioids. a critical review and proposals for long-term dosing. *J Pain Symptom Manage* 22:672–87, 2001.
 39. Phillips S, Gift M, Gelot S, Duong M, Tapp H: Assessing the relationship between the level of pain control and patient satisfaction. *J Pain Res* 6:683–9, 2013.
 40. Puig MM, Montes A, Marrugat J: Management of postoperative pain in Spain. *Acta Anaesthesiol Scand* 45:465–70, 2001.
 41. Ren Z-Y, Xu X-Q, Bao Y-P, He J, Shi L, Deng J-H, Gao X-J, Tang H-L, Wang Y-M, Lu L: The impact of genetic variation on sensitivity to opioid analgesics in patients with postoperative pain: a systematic review and meta-analysis. *Pain Physician* 18:131–52.
 42. Roeb MM, Wolf A, Gräber SS, Meiner W, Volk T: Epidural versus Systemic Analgesia: An International Registry Analysis on Postoperative Pain and Related Perceptions after Abdominal Surgery. *Clin J Pain* :1, 2016.
 43. Rothaug J, Zaslansky R, Schwenkglenks M, Komann M, Allvin R, Backström R, Brill S, Buchholz I, Engel C, Fletcher D, Fodor L, Funk P, Gerbershagen HJ, Gordon DB, Konrad C, Kopf A, Leykin Y, Pogatzki-Zahn E, Puig M, Rawal N, Taylor RS, Ullrich K, Volk T, Yahiaoui-Doktor M, Meissner W: Patients' perception of postoperative pain management: validation of the International Pain Outcomes (IPO) questionnaire. *J Pain* 14:1361–70, 2013.
 44. Sabaté S, Canet J, Muñoz S, Castillo J, Lucas M, Mayoral V: [Epidemiology of

- anesthesia in Catalonia, Spain, in 2003]. *Med Clin (Barc)* 126 Suppl:13–8, 2006.
45. Schug SA, Palmer GM, Scott DA, Halliwell R, Trinca J: Acute pain management: scientific evidence, fourth edition, 2015. *Med J Aust* 204:315–7, 2016.
 46. Schwenkglenks M, Gerbershagen HJ, Taylor RS, Pogatzki-Zahn E, Komann M, Rothaug J, Volk T, Yahiaoui-Doktor M, Zaslansky R, Brill S, Ullrich K, Gordon DB, Meissner W: Correlates of satisfaction with pain treatment in the acute postoperative period: results from the international PAIN OUT registry. *Pain International Association for the Study of Pain*; 155:1401–11, 2014.
 47. Schwingshackl L, Hoffmann G: Mediterranean dietary pattern, inflammation and endothelial function: A systematic review and meta-analysis of intervention trials. *Nutr Metab Cardiovasc Dis* 24:929–39, 2014.
 48. Sentürk M, Ozcan PE, Talu GK, Kiyani E, Camci E, Ozyalçin S, Dilege S, Pembeci K: The effects of three different analgesia techniques on long-term postthoracotomy pain. *Anesth Analg* 94:11–5, 2002.
 49. Shah S, Kapoor S, Durkin B: Analgesic management of acute pain in the opioid-tolerant patient. *Curr Opin Anaesthesiol* 28:398–402, 2015.
 50. Zaslansky R, Chapman CR, Rothaug J, Bäckström R, Brill S, Davidson E, Elessi K, Fletcher D, Fodor L, Karanja E, Konrad C, Kopf a, Leykin Y, Lipman a, Puig M, Rawal N, Schug S, Ullrich K, Volk T, Meissner W: Feasibility of international data collection and feedback on post-operative pain data: proof of concept. *Eur J Pain* 16:430–8, 2012.
 51. Zaslansky R, Rothaug J, Chapman CR, Bäckström R, Brill S, Fletcher D, Fodor

L, Gordon DB, Komann M, Konrad C, Leykin Y, Pogatski-Zahn E, Puig MM, Rawal N, Ullrich K, Volk T, Meissner W: PAIN OUT: The making of an international acute pain registry. Eur J Pain :1–13, 2014.

Figure Legends

Figure 1. Flow-chart of the study

Table 1. Patients characteristics and comorbidities

	Total (N=2922)	Orthopedics (N=1584)	General Surgery (N=1338)	Effect size (95CI)
Female Sex, n (%) ^a	1683 (57.9)	941 (59.7)	742 (55.8) [*]	0.09 (0.01 - 0.17)
Age (years), mean (SD)	59.1 (16.5)	60.9 (16.6)	57.0 (16.3) [†]	0.23 (0.16 - 0.31)
BMI (kg/m ²), mean (SD) ^b	28.8 (6.6)	28.4 (5.3)	29.2 (8.0) [†]	-0.12 (-0.20 - -0.04)
Height (cm), mean (SD) ^b	164.3 (10.0)	163.9 (10.4)	164.8 (9.6) [†]	-0.09 (-0.17 - -0.01)
Weight (kg), mean (SD)	77.3 (18.5)	76.2 (15.6)	78.6 (21.4) [†]	-0.13 (-0.21 - -0.06)
Comorbidities, n (%)	2083 (71.9)	1127 (71.7)	956 (72.0)	-0.01 (-0.10 - 0.08)
Cancer	252 (8.7)	36 (2.3)	216 (16.3) [†]	-1.17 (-1.37 - -0.97)
Renal	69 (2.4)	24 (1.5)	45 (3.4) [*]	-0.45 (-0.73 - -0.17)
Psychiatric	398 (13.7)	249 (15.8)	149 (11.2) [†]	0.22 (0.10 - 0.34)
Addictive disorders	373 (12.9)	186 (11.8)	187 (14.1)	-0.11 (-0.23 - 0.01)
Cardiovascular	1190 (41.0)	678 (43.1)	512 (38.6) [*]	0.10 (0.02 - 0.19)
Gastrointestinal disease	87 (3.0)	26 (1.7)	61 (4.6) [†]	-0.58 (-0.84 - -0.32)
Respiratory	404 (13.9)	192 (12.2)	212 (16.0) [*]	-0.17 (-0.29 - -0.06)
Fibromyalgia	39 (1.3)	25 (1.6)	14 (1.1)	0.23 (-0.13 - 0.59)

Data displayed as mean (SD). ^{*}p<0.05; [†]p<0.001 versus Orthopedics. P values obtained by Mann-Whitney U test and effect size by Cohen's d (95% CI). ^aData available only on 2095 patients. BMI, body mass index. ^bData available only on 2527 patients. Significant effect sizes are shown in bold letters.

Table 2. Postoperative outcomes evaluated by using the Spanish version of the IPO Questionnaire

	Total		Orthopedics		General Surgery		
	N		N		N		Effect size (95CI)
Intensity of Pain outcomes (NRS)							
Worst Pain	2922	5.6 (2.5)	1584	6.0 (2.5)	1338	5.2 (2.4)[†]	0.34 (0.27 - 0.41)
Least Pain	2890	1.9 (1.9)	1562	2.1 (2.0)	1328	1.7 (1.7) [†]	0.17 (0.10 - 0.24)
How often in severe Pain ^a	2751	26.9 (24.1)	1492	30.5 (24.8)	1259	22.6 (22.5)[†]	0.33 (-0.08 - 0.07)
Interference with in bed activities	2569	4.5 (3.1)	1338	4.7 (3.2)	1231	4.4 (3.0) [*]	0.09 (0.02 - 0.17)
Interference with breathing or coughing	2641	2.4 (3.0)	1415	1.2 (2.3)	1226	3.8 (3.1)[†]	-0.95 (-1.03 - -0.87)
Interference with sleep	2769	3.0 (3.2)	1501	3.3 (3.4)	1268	2.7 (3.0) [†]	0.21 (0.14 - 0.29)
Interference with out of bed activities	1439	3.9 (2.9)	514	4.0 (3.0)	925	3.9 (2.8)	0.03 (-0.08 - 0.14)
Pain relief ^a	2503	63.0 (30.1)	1354	62.4 (29.7)	1149	63.7 (30.5)	-0.04 (-0.12 - 0.04)
Adverse events Frequency (N, %)							
Nausea	2884	1113 (38.6)	1564	569 (36.4)	1320	544 (41.2) [*]	-0.11 (-0.20 - -0.03)
Drowsiness,	2862	1494 (52.2)	1551	771 (49.7)	1311	723 (55.1) [*]	-0.12 (-0.20 - -0.04)
Itching	2854	526 (18.4)	1550	263 (17.0)	1304	263 (20.2) [*]	-0.12 (-0.22 - -0.01)
Dizziness	2860	1087 (38.0)	1550	517 (33.4)	1310	570 (43.5) [†]	-0.24 (-0.32 - -0.15)
Feeling Anxious	2811	1580 (56.2)	1527	894 (58.5)	1284	686 (53.4) [*]	0.11 (0.03 - 0.20)
Feeling Helpless	2744	1338 (48.8)	1493	750 (50.2)	1251	588 (47.0)	0.07 (-0.01 - 0.15)
Global adverse effects ^b	2907	2106 (72.4)	1575	1103 (70.0)	1332	1003 (75.3) [*]	-0.15 (-0.24 - -0.06)
Perception of care							
Request more treatment, N (%)	2848	548 (19.2)	1549	344 (22.2)	1299	204 (15.7) [†]	0.24 (0.13 - 0.34)
Info about treatment options, N (%)	2822	1785 (63.3)	1526	974 (63.8)	1296	811 (62.6)	0.03 (-0.06 - 0.11)
Allowed to participate in treatment, NRS (mean, SD)	2496	4.8 (3.9)	1363	4.8 (3.9)	1133	4.8 (3.9)	0.02 (-0.06 - 0.10)
Allowed to participate- in treatment, NRS, N(%)	2496	1788 (71.6)	1363	970 (71.2)	1133	818 (72.2)	-0.02 (-0.12 - 0.07)
Satisfaction, NRS mean,SD)	2660	7.9 (2.3)	1449	7.8 (2.3)	1211	8.0 (2.2)	-0.06 (-0.14 - 0.01)

IPO, International Pain Outcome Questionnaire. N, number of patients who registered the item. Intensity expressed as mean values (SD). NRS, numeric rating scale from 0-10; ^{*} p<0.05; [†] p<0.001 versus Orthopedics. ^aMean (SD) values from a 0-NRS are shown as a percentage. Frequency expressed as the ratio between the number of positive answers over the number of patients who registered the item in the questionnaire. Cohen's d was used to estimate the effect size. Severe pain defined as NRS ≥ 7 . ^c Global adverse events were defined as the presence of at least one adverse event. Significant effect sizes are in bold.

Table 3. Postoperative analgesic consumption (mg·patient⁻¹·24h⁻¹)

	Total (N=2919)		Orthopedics (N=1581)		General Surgery (N=1338)			
	% of patients	Dose (mean(SD))	% of patients	Dose (mean(SD))	% of patients	Dose (mean(SD))	Effect size for frequency	Effect size for doses
Opioids*	59.0	33.8 (35.0)	59.1	37.0 (39.1)	58.9	30.0 (29.0)	0.01 (-0.08-0.09)	0.2 (0.10 – 0.30)
Tramadol i.v.	33.6	231.2 (157)	37.8	275 (172)	28.6	163 (100) [†]	0.23 (0.14-0.31)	0.75 (0.62 - 0.89)
Morphine i.v.	29.5	8.9 (12.4)	21.8	9.0 (16.6)	38.6	8.8 (8.7) [†]	-0.45 (-0.54- -0.36)	0.02 (-0.12 -0.16)
Morphine s.c.	9.5	6.3 (4.0)	12.6	6.5 (4.3)	5.8	5.7 (2.9) [†]	0.47 (0.32 - 0.62)	0.21 (-0.05 - 0.48)
Meperidine i.v.	2.1	68.4 (58.5)	1.9	83.8 (71.1)	2.3	53.0 (37.5)	-0.11 (-0.39 - 0.17)	0.54 (0.03 - 1.06)
Morphine p.o.	1.1	37.5 (121)	1.3	10.6 (2.3)	0.9	82.3 (194)	0.22 (-0.17 - 0.61)	-0.61 (-1.34 - 0.12)
Tramadol s.c.	1.1	124.7 (75.5)	0.4	129 (75.1)	1.9%	124 (77.0) [†]	-0.91 (-1.4 - -0.42)	0.06 (-0.99 - 1.11)
Methadone i.v.	0.4	5.7 (3.2)	0.6	6.1 (2.9)	0.4	5.1 (3.7)	0.29 (-0.30 - 0.88)	0.33 (-0.82 - 1.49)
Total consumption ^a	100	20.2 (31.8)	100	22.1 (35.3)	100	18.1 (26.9) [*]	0.13 (0.05 - 0.20)	0.13 (0.05 – 0.20)
Non-Opioid	96.3		96.1		96.5		-0.06 (-0.27 - 0.15)	
AA	94.3		94.6		94.1		0.05 (-0.13 - 0.22)	
Paracetamol i.v.	85.6	2889 (1742)	82.3	2805 (1787)	89.5	2987 (1683) [†]	-0.34 (-0.46 - -0.22)	-0.10 (-0.18 - -0.03)
Metamizol i.v.	37.5	2106 (3179)	37.1	2138 (3174)	38.0	2068 (3184)	-0.02 (-0.10 - 0.06)	0.02 (-0.05 - 0.09)
Paracetamol p.o.	3.9	1637 (1102)	3.8	2076 (1144)	4.1	1157 (829)	-0.04 (-0.25- 0.16)	0.91 (0.53 - 1.30)
Metamizol p.o.	1.1	2233 (1617)	0.8	2039 (1994)	1.5	2340 (1415)	-0.38 (-0.77 - 0.02)	-0.18 (-0.92 - 0.55)
NSAIDs	44.1		40.5		48.2 [†]		-0.17 (-0.25 - -0.09)	
Dexketoprofen i.v.	55.7	103 (163)	53.1	102 (189)	58.8	103 (125) [*]	-0.13 (-0.21 - -0.05)	-0.01 (-0.08 - 0.06)
Ketorolac i.v.	6.2	3.5 (39.1)	4.7	3.7 (52.0)	8.1	3.2 (12.3) [†]	-0.32 (-0.49 - -0.15)	0.01 (-0.06 - 0.08)
Dexketoprofen p.o.	2.2	67.0 (32.0)	3.2	69.2 (30.8)	1.0	58.9 (36.2) [†]	0.62 (0.29 - 0.95)	0.32 (-0.27 - 0.92)

N indicates the number of patients who registered the item. Frequency expressed as the ratio between the number of patients who received the drug over the number of patients who registered the item in the questionnaire. Doses are displayed as mean values (SD). *p<0.05; †p<0.001 versus Orthopedics. P value for the comparison of mean doses in ORT and GEN was obtained by Mann-Whitney U test, and effect size by Cohen's d (95% CI). ^aResults are expressed in oral morphine equivalents per patient in 24 hours. All intraoperative analgesics were administered intravenously (iv); intrathecal and epidural drugs were not included in the analyses. AA: Antipyretic analgesics. NSAIDs: Nonsteroidal anti-inflammatory drugs. Significant effect sizes are in bold.

Table 5. Postoperative outcomes according to the presence of **previous** chronic pain or **previous** chronic opioid administration

Table 4. Postoperative outcomes according to type of analgesia

Outcomes in patients who received opioids for postoperative analgesia								
	% of patients with Severe Pain	Worst Pain	How often in severe pain	Interference with in bed activities	Interference with sleep	Pain Relief	Desire of more Treatment	Satisfaction
Yes (N, %) 1723 (59.0%)	46.5 ± 49.9	6.0 ± 2.5 6 (4-8)	28.8 ± 24.8 20 (10-50)	4.9 ± 3.1 5 (2-7.5)	3.3 ± 3.4 2 (0-6)	65.6 ± 29.0 70 (50-90)	20.9 ± 40.7	8.0 ± 2.2 9 (7-10)
No (N, %) 1196 (41.0%)	29.2 ± 45.5	5.1 ± 2.4 5 (3-7)	24.2 ± 22.8 20 (10-40)	4.0 ± 3.0 4 (2-6)	2.7 ± 3.0 2 (0-5)	59.5 ± 31.1 60 (40-90)	16.8 ± 37.4	7.8 ± 2.3 8 (7-10)
<i>P value</i>	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
<i>Effect size</i>	0.41	0.36	0.19	0.30	0.17	0.20	0.15	0.10
<i>95 CI</i>	(0.33-0.50)	(0.29-0.44)	(0.12-0.27)	(0.22-0.38)	(0.10-0.25)	(0.12-0.28)	(0.04-0.25)	(0.02-0.18)
Outcomes in patients who received multimodal analgesia								
Yes (N, %) 2404 (82.3%)	41.8 ± 49.3	5.7 ± 2.5 6 (4-8)	27.1 ± 24.5 20 (10-40)	4.6 ± 3.1 5 (2-7)	3.1 ± 3.3 2 (0-6)	65.2 ± 29.6 70 (50-90)	19.6 ± 39.7	8.1 ± 2.2 9 (7-10)
No (N, %) 518 (17.7%)	28.2 ± 45.0	5.2 ± 2.2 5 (4-7)	25.8 ± 22.2 20 (10-40)	4.0 ± 2.8 4 (2-6)	2.7 ± 2.8 2 (0-5)	53.6 ± 30.3 60 (30-80)	17.6 ± 38.2	7.3 ± 2.5 8 (6-9)
<i>P value</i>	0.00	0.00	0.78	0.00	0.28	0.00	0.32	0.00
<i>Effect size</i>	0.33	0.19	0.05	0.21	0.11	0.39	0.07	0.33
<i>95 CI</i>	(0.22-0.45)	(0.10-0.29)	(-0.04-0.15)	(0.11-0.31)	(-0.01-0.21)	(0.28-0.48)	(-0.14-0.10)	(0.23-0.43)

For each item, N indicates the number of patients who registered the item. Postoperative outcomes measured as NRS (numeric rating scale from 0-10) with exception of request for more treatment (yes/no). Severe pain defined as NRS from 7 to 10. Values are displayed as mean (SD) and median (Interquartile range). P values were obtained by Mann-Whitney U test and effect size by Cohen's d (95% CI). Significant effect sizes are in bold.

Postoperative Outcomes in Patients with Chronic Pain

	Worst Pain	How often in severe pain	Interference with in bed activities	Interference with sleep	Pain relief	Request more Treatment (%)	Satisfaction
NO Chronic pain (N = 1352, 47.6%)	5.3 ± 2.4 5 (3-7)	24.0 ± 22.3 20 (10-40)	4.2 ± 2.9 4 (2-6.5)	2.7 ± 3.0 2 (0-5)	61.7 ± 29.9 60 (40-90)	18.1%	7.7 ± 2.4 8 (7-10)
Chronic mild pain (N=204, 7.2%)	5.1 ± 2.6 5 (3-7)	18.9 ± 18.7 10 (10-30)	3.8 ± 3.2 3 (1-7)	2.4 ± 3.2 1 (0-4)	66.1 ± 33.2 80 (40-90)	18.0%	7.7 ± 2.9 9 (7-10)
Chronic moderate pain (N=387, 13.6%)	5.6 ± 2.3 6 (4-7)	27.9 ± 23.5 20 (10-40)	4.2 ± 3.1 4 (2-7)	3.3 ± 3.3 2.5 (0-6)	58.3 ± 31.5 60 (40-90)	22.3%	7.9 ± 2.1 8 (7-10)
Chronic severe pain (N=896, 31.6%)	6.2 ± 2.6 7 (4-8)	32.4 ± 26.9 30 (10-50)	5.2 ± 3.2 5 (3-8)	3.6 ± 3.5 3 (0-6)	67.2 ± 28.6 70 (50-90)	20.3%	8.3 ± 2.0 9 (7-10)
P value *	<0.001	<0.001	<0.001	<0.001	<0.001	0.25	<0.001
Effect size	0.39	0.34	0.35	0.33	0.27	0.19	0.08
95 CI	(0.29-0.48)	(0.26-0.43)	(0.26-0.43)	(0.24-0.42)	(0.18-0.36)	(0.09-0.28)	(-0.04-0.20)
Postoperative Outcomes in Patients who received Chronic Opioids							
No (N=2691, 94.2%)	5.6 ± 2.5 6 (4-8)	26.4 ± 23.8 20 (10-40)	4.5 ± 3.1 5 (2-7)	3.0 ± 3.2 2 (0-5)	63.0 ± 30.2 70 (40-90)	18.8%	7.9 ± 2.3 9 (7-10)
Yes, (N =165, 5.8%)	6.2 ± 2.6 7 (4-8)	34.4 ± 27.3 30 (10-50)	5.5 ± 3.3 6 (3-8)	4.0 ± 3.5 4 (0-7)	62.7 ± 29.1 70 (50-90)	30.7%	7.8 ± 2.3 8 (6-10)
P value	<0.001	<0.001	<0.001	<0.001	0.76	<0.001	0.40
Effect size	0.25	0.33	0.35	0.31	-0.01	0.36	-0.08
95 CI	(0.10-0.41)	(0.17-0.49)	(0.18-0.52)	(0.15-0.47)	(-0.17-0.15)	(0.17-0.55)	(-0.24-0.09)

For each element, N = number of patients who registered the item. Postoperative outcomes measured with a NRS (numeric rating scale from 0-10) with exception of *request for more treatment* (yes/no). Severe pain defined as a NRS from 7 to 10; moderate pain as a NRS from 4 to 6; and mild pain as a NRS from 1 to 3. Values are displayed as mean (SD) and median (interquartile range). * P and “d” values obtained by Mann-Whitney U test and effect size by Cohen's d (95% CI) for the comparison between chronic severe and no chronic pain. Significant effect sizes are shown in bold.

Table 6. Perioperative procedures that affect opioid requirements during the first 24 hours after surgery

	Opioid consumption				change %	Effect size (95 CI)
	Yes		No			
	N	Dose	N	Dose		
Chronic pain	1352	22.7 (35.6)	1508	17.8 (27.0)	21.59 [†]	0.15 (0.08-0.23)
Chronic opioids	165	37.6 (53.0)	2691	19.1 (29.8)	49.20 [†]	0.59 (0.43-0.75)
Regional Techniques						
Intrathecal	1004	16.6 (23.3)	1804	22.3 (35.5)	-34.34 [†]	-0.17 (-0.25 - -0.10)
Epidural block	211	8.5 (15.8)	2592	21.2 (32.6)	-148.55 [†]	-0.40 (-0.54--0.26)
Epidural block in abdominal surgery	145	8.9 (16.6)	725	24.2 (28.8)	-171.88 [†]	-0.56 (-0.75--0.38)
Peripheral nerve block	626	16.2 (22.3)	529	20.7 (26.1)	-27.78 [†]	-0.19 (-0.30--0.07)
Total	1491	14.8 (22.0)	1317	26.4 (39.1)	-78.25 [†]	-0.37 (-0.44 - -0.30)
Non-pharmacological treatments	875	19.8 (32.6)	2173	21.2 (29.7)	-7.07*	0.04 (-0.04-0.12)

N indicates the number of patients who registered the item. Dose, mean (SD) of oral morphine equivalents in mg·patient⁻¹·24h⁻¹. *p<0.05; [†]p<0.001. P value was obtained by Mann-Whitney U test and effect size by Cohen's d (95% CI). Significant effect sizes are shown in bold letters.

Table 7. Outcomes and frequency of analgesic treatments according to location and procedure in orthopedic patients.

Procedure	Hospitals (N)	Patients (n)	Worst pain	More Treatment (%)	Adverse events (%)	Multimodal Analgesia (%)	Opioids* (%)	Total po Morphine Equivalents ** (mg·patient ⁻¹ ·24h ⁻¹)	Epidural Block (%)	Peripheral nerve block (%)	Wound Infiltration (%)	I.V. Opioids PCA (%)	L.A. PCA (%)
Tibia/Fibula surgery	6	69		32.4	53.6	83.8	69.6	25.1 (31.5)	1.4	26.1	0	4.3	0
Open reduction of fracture with internal fixation	5	35		34.3	51.4	76.5	65.7	17.3 (18.8)	2.9	20	0	2.9	2.9
Wedge osteotomy	3	12		50	50	91.7	83.3	24.7(15.1)	0	33.3	0	16.7	0
Other (ICD-9: 79.16, 77.37, 79.06, 78.47, 78.57, 78.67)	5	22		19	59.1	90.9	68.2	37.9 (47.5)	0	31.8	0	0	0
Foot surgery	8	83		29.1	63.9	69.9	51.8	12.0 (0.5)	0	31.3	1.2	0	0
Bunionectomy	5	39		29.7	64.1	66.7	56.4	10.8 (12.9)	0	48.7	2.6	0	0
Arthrodesis and fusion	4	21		38.1	66.7	57.1	33.3	8.6 (15.2)	0	19	0	0	0
Other (ICD-9:79.33, 77.3, 77.6, 78.0, 79.8, 84.26, 78.1, 81.5, 84.1)	5	23		19	60.9	87	60.9	17.3 (17.2)	0	13	0	0	0
Humerus surgery	6	38		19.4	57.9	81.6	73.7	22.3 (18.2)	0	63.2	0	13.2	2.6
Open reduction of fracture with internal fixation	3	21		25	57.1	95.2	90.5	29.5 (16.6)	0	57.1	0	19	4.8
Spine surgery	9	206		21.7	77.1	91.2	84.9	48.1 (65.3)	0.5	1.5	2.9	48.1	0
Spinal fusion	7	126		18.5	76.8	96.8	89.7	49.1 (43.0)	0.8	0.8	1.6	54	0
Excision, destruction and other repair of intervertebral disc	6	29		34.5	79.3	79.3	65.5	24.5 (37.4)	0	6.9	6.9	31	0
Refusion of spine	5	16		25	75	100	100	43.5 (31.5)	0	0	6.3	43.8	0
Exploration and decompression of spinal canal structures	4	12		18.2	75	90.9	81.8	110.9 (215.0)	0	0	0	41.7	0
Replacement of spinal disc	4	12		0	83.3	75	83.3	63.8 (59.4)	0	0	0	58.3	0
Other (ICD-9: 84.6, 81.6, 03.5, 03.9, 80.8, 84.5, 84.8)	5	11		45.5	72.7	63.6	63.6	25.2 (26.1)	0	0	9.1	27.3	0
Hip surgery	11	223		21.4	72.5	78.4	71.7	24.4 (23.3)	4	42.2	0.5	26	5.4
Total hip replacement	7	165		22.1	71.3	77	73.9	24.5 (22.9)	0.6	47.9	0	29.7	3
Revision of hip replacement	7	35		20	80	91.2	85.7	32.1(23.3)	5.7	34.3	0	14.3	2.9
Other (ICD-9: 81.21, 81.52, 81.40, 79.85, 80.05)	6	23		18.2	69.6	69.6	34.8	10.8 (21.4)	26.1	13	4.5	17.4	26.1
Knee surgery	11	495		21.9	72.4	72.7	52.3	17.3 (23.9)	6.1	63.2	7.6	9.5	12.9
Total knee replacement	10	387		20.9	69.9	71.3	52.7	17.2 (23.7)	3.4	74.4	9.5	11.4	10.6
Revision of knee replacement	6	37		27	81.1	89.2	67.6	20.0 (20.8)	13.5	37.8	2.8	2.7	10.8
Other repair of joint of lower extremity (ICD-9: 81.4)	6	22		40	86.4	68.2	50	16.6 (21.8)	9.1	18.2	0	4.5	13.6
Arthroscopy knee	5	22		18.2	72.7	68.2	31.8	7.0 (12.2)	4.5	9.1	0	0	4.5
Other (ICD-9: 81.22, 80.6, 84.17, 84.46, 77.26, 77.86)	5	27		18.5	85.2	77.8	44.4	24.0 (36.0)	33.3	18.5	0	3.7	55.6
Radio/Ulna surgery	6	50		26	62	59.2	50	16.3 (25.2)	0	82	0	0	0
Open reduction of fracture with internal fixation	5	34		26.5	58.8	66.7	61.8	19.4 (21.7)	0	79.4	0	0	0
Femur surgery	6	84		20.5	65.9	71.1	58.3	18.9 (31.3)	7.1	13.1	2.4	2.4	1.2
Open reduction of fracture with internal fixation	3	43		18.6	51.2	76.2	67.4	19.9 (38.7)	0	11.6	2.3	2.3	0
Ankle surgery (ICD-9: 79.87, 81.11, 81.49, 80.27)	6	22		28.6	77.3	77.3	50	23.6 (14.0)	0	13.6	0	4.6	0
Shoulder surgery	6	78		16.9	71.4	56.4	34.6	12.1(20.5)	0	88.5	0	3.8	7.7
Other repair of shoulder (ICD-9: 81.83)	3	20		20	73.7	20	15	3.8 (9.8)	0	90	0	5	0
Shoulder replacement	3	23		13.6	65.2	95.7	65.2	25.2 (27.4)	0	87	0	8.7	21.7
Arthroscopy shoulder	3	11		9.1	81.8	27.3	18.2	4.5 (12.1)	0	90.9	0	0	9.1
Other (ICD-9: 83.63, 81.82, 79.71, 79.81, 81.23)	4	18		11.1	66.7	62.5	29.2	9.7 (16.4)	0	83.3	0	0	0
Hand surgery	6	35		15.2	54.3	29.4	22.9	4.2 (9.2)	0	85.7	5.9	0	2.9

Pain outcomes in the first 24 hours in the most common orthopaedic procedures organized in a descending order by **worst pain intensity in each location**. Horizontal box plot indicates worst pain during the first 24 hrs after surgery in a NRS 0 to 10 scale. **Data for the overall group is presented in green, and those for the specific procedure in yellow**. In each box, the vertical line represents median worst pain. Other variables are displayed as proportion of patients who registered a positive answer or received the analgesic treatment. *Opioids shows the percentage of patients who received opioids for postoperative analgesia; **Total oral morphine equivalents were obtained as explained in methods. IV PCA: Intravenous Patient-Controlled Analgesia. LA PCA: Local Anesthetic s Patient-Controlled Analgesia. Higher values in each item are highlighted in bold.

Table 8. Outcome and analgesic treatment according to location and procedure in general surgery patients.

Procedure	Hospitals (N)	Patients (n)	Worst pain	More Treatment (%)	Adverse events (%)	Multimodal Analgesia (%)	Opioids (%)	Total Morphine Equivalents (mg·patient ⁻¹ ·24h ⁻¹)	Epidural Block (%)	Peripheral nerve block (%)	Wound Infiltration (%)	I.V. Opioids PCA (%)	L.A. PCA (%)
Stomach surgery	7	162		27.2	87	96.3	78.4	33.2(28.8)	28.4	0.6	45	3.7	23.5
Sleeve resection of stomach.	3	112		26.6	87.5	97.3	81.3	37.2 (30.2)	25	0.9	58.4	1.8	21.4
Laparoscopic gastroenterostomy	3	18		29.4	72.2	100	61.1	18.1 (21.4)	77.8	0	0	5.6	61.1
Gastrectomy	3	9		11.1	88.9	88.9	44.4	13.4 (21.0)	22.2	0	11.1	33.3	22.2
Other (ICD-9: 44.3, 43.19, 43.4, 43.8, 44.4, 44.9)	4	23		34.8	95.7	91.3	91.3	33.0 (23.5)	8.7	0	33.3	0	4.3
Small intestine surgery	7	39		13.2	66.7	82.1	64.1	22.8 (35.6)	15.4	0	2.6	10.3	10.3
Closure of stoma of small intestine	4	14		14.3	78.6	100	85.7	19.4 (18.4)	0	0	0	0	0
Abdominal wall surgery	8	76		10.7	81.3	76	60.5	20.7 (26.3)	6.6	1.3	9.2	9.2	1.3
Incisional hernia repair	4	32		12.5	81.3	81.3	68.8	21.9 (28.4)	9.4	0	6.3	0	0
Anterior abdominal wall repair	6	27		7.4	74.1	88.9	81.5	31.6 (25.7)	3.7	0	3.7	25.9	0
Other (ICD-9: 53.72, 54.0, 53, 53.9)	4	17		12.5	93.8	43.8	11.8	2.1 (6.3)	5.9	5.9	23.5	0	5.9
Anal surgery	5	22		18.18	59.1	54.5	18.2	2.2 (6.1)	4.6	0	45.5	0	0
Diaphragm/Esophagogastric junction	6	24		4.30	83.3	95.8	79.2	22.0 (18.9)	4.2	0	4.2	0	4
Creation of esophagogastric sphincteric competence	3	18		0.00	77.8	100.0	77.8	24.2 (20.8)	5.6	0	0.0	0	6
Colo-rectal surgery	10	218		16.6	74.1	87.3	63.8	23.8 (32.6)	34.9	1.4	7.9	18.3	23.9
Open and other partial excision of large intestine	8	98		18.6	74.5	91.8	69.4	28.6 (34.4)	40.8	2	5.1	16.3	24.5
Laparoscopic partial excision of large intestine	6	45		13.3	75.6	86	68.9	24.1 (35.6)	22.2	2.2	11.6	22.2	17.8
Total intra-abdominal colectomy	5	15		15.4	80	64.3	40	11.4 (24.4)	33.3	0	33.3	6.7	20
Other resection of rectum	7	15		14.3	71.4	86.7	73.3	27.2 (33.1)	40	0	0	33.3	20
Abdominoperineal resection of rectum	3	14		14.3	71.4	83.3	50	15.1 (20.4)	64.3	0	0	14.3	57.1
Closure of intestinal stoma	4	11		18.2	81.8	100	72.7	31.1 (38.6)	27.3	0	0	27.3	27.3
Other (46.03, 46.1, 48.0, 48.1, 48.24, 48.3, 48.4, 48.7, 84.19)	6	20		17.6	63.2	80	40	8.1 (16.0)	15	0	10.5	15	15
Inguinal hernia	8	81		17.9	57.5	72.5	44.4	12.4 (20.2)	3.7	0	6.2	0	0
Other unilateral repair of inguinal hernia	8	61		20	58.3	68.9	41	12.1 (20.5)	3.3	0	4.9	0	0
Other bilateral repair of inguinal hernia	3	16		13.3	50	80	56.3	15.2 (21.7)	6.3	0	6.3	0	0
Gallbladder surgery	11	249		18.8	78.3	78.2	60.6	14.0 (19.6)	2	1.6	11.5	2.4	1.2
Cholecystectomy	9	32		25	81.3	87.5	71.9	33.8 (30.5)	6.3	3.1	6.5	12.5	3.1
Laparoscopic cholecystectomy	11	214		17.6	78	77.5	59.3	11.2 (15.5)	0.9	0.9	12.4	0.9	0.5
Appendix surgery	9	96		16.1	76.8	77.9	56.3	10.9 (13.4)	0	1	20.8	0	0
Laparoscopic appendectomy	7	51		16.3	86	66	41.2	9.5 (14.4)	0	2	35.3	0	0
Appendectomy	7	45		15.9	66.7	91.1	73.3	12.4 (12.3)	0	0	4.4	0	0
Liver surgery	5	30		10	76.7	86.7	76.7	35.5 (33.5)	30	0	33.3	46.7	30
Partial hepatectomy	4	19		5.3	89.5	89.5	78.9	40.3 (28.5)	21.1	0	47.4	63.2	21.1
Other (50.14, 50.24, 50.25, 50.29, 50.3, 50.4, 50.61)	4	11		18.2	54.5	81.8	72.7	27.2 (40.9)	45.5	0	9.1	18.2	45.5
Umbilical hernia	4	17		5.9	70.6	82.4	58.8	9.6 (11.8)	5.9	5.9	17.6	5.9	0
Thyroid surgery	4	112		5.5	68.8	72.3	50	9.2 (25.3)	0	0	0	0	0
Complete thyroidectomy	4	70		5.8	67.1	78.6	52.9	7.2 (8.9)	0	0	0	0	0
Other partial thyroidectomy	4	17		5.9	70.6	47.1	29.4	4.2 (8.2)	0	0	0	0	0
Unilateral thyroid lobectomy	3	11		0	63.6	81.8	72.7	13.1 (12.2)	0	0	0	0	0
Other (06.8, 06.51, 06.7)	2	14		7.7	78.6	64.3	42.9	21.9 (66.5)	0	0	0	0	0
Mama surgery	9	102		6.9	67.3	51	37.3	10.0 (30.9)	2	10.8	2	1	0
Unilateral mastectomy	6	46		8.7	56.5	52.2	37	12.7 (43.7)	0	19.6	2.2	2.2	0
Excision of lesion of breast	5	25		0	68	76	56	9.8 (11.3)	0	0	0	0	0
Other (85.22, 85.23, 85.42, 85.46, 85.0, 85.54, 85.79, 85.9)	3	31		10	83.3	29	22.6	6.5 (16.9)	6.5	6.5	3.2	0	0

Pain outcomes in the first 24 hours in the most frequent orthopaedics procedures organized in a descending order by **worst pain intensity in each location**. Horizontal box plot indicates worst pain during the first 24 hrs after surgery in a NRS 0 to 10 scale. **Data for the overall group is presented in green, and those for the specific procedure in yellow**". Vertical line represents median of global worst pain in GEN patients. Other variables are displayed as proportion of patients who registered a positive answer or received the analgesic treatment; * Total oral morphine equivalents dose were obtained as explain in methods. IV PCA: Intravenous Patient-Controlled Analgesia. LA PCA: Local Anesthetics Patient-Controlled Analgesia.

Highlights

- Postoperative outcomes in Spanish Hospitals were obtained with a multidimensional scale.
- Spanish Pain Outcomes were similar to those reported in Europe and USA.
- Patient's participation in pain management was poor.
- Pre-surgical chronic pain (NRS>7) was associated with worsened pain outcomes.
- Adequate control of chronic pain might improve postoperative outcomes.