Development and pilot test of a new set of good practice indicators for chronic cancer pain management.

ABSTRACT

Background
Pain is among the most important of symptoms in terms of prevalence and cause of distress in cancer patients and their families. However, there is a lack of clearly defined measures of quality pain management which could be used to identify problems and monitor changes in improvement initiatives.

Methods
We built a comprehensive set of evidence-based indicators, following a 4-step model: (i) Review and systematization of existing guidelines, to list evidence-based recommendations; (ii) Review and systematization of existing indicators matching the recommendations; (iii) Development of new indicators, to complete a set of measures for the identified recommendations; and (iv) pilot test for feasibility, reliability (with kappa index), and usefulness for quality problems identification in two hospitals and one primary care center, using the Lot Quality Acceptance (LQAS) method for 95% and 75% compliance standards (threshold 70% and 40% respectively, α≤5%, β≤10% in both cases), and estimates of compliance with exact binomial 95% Confidence Interval.

Results
A twenty-two indicator set was eventually pilot-tested. Seventeen were feasible in hospitals and twelve in all settings. Feasibility barriers included difficulties in identifying target patients, deficient clinical records, and low prevalence of cases for some indicators dependent on the compliance of other indicators. Reliability was mostly very good or excellent (k>0.8). Four indicators, all of them related to medication and prevention of side effects, had acceptable compliance at 75%/40% level. Other important medication-related indicators (i.e. adjustment to pain intensity, prescription for breakthrough pain) had very low compliance, highlighting the existence of specific quality gaps. Indicators concerning patient-centered care (i.e. attention to psychological distress and education needs) were massively problematic.

Conclusions
A set of good practice indicators has been built and pilot-tested as feasible, reliable, and useful quality monitoring tool, underscoring specific areas for improvement.
Introduction

The International Agency for Research on Cancer (IARC) estimated 12.7 million of new cancer diagnoses in 2008 around the world\(^1\). If recent trends in major cancers are confirmed in the future, the burden of cancer will reach 22 million of new cases each year by 2030. This represents an average increase of 75% compared to 2008 data, with a higher rate (81%) in low and middle Human Development Index countries\(^2\).

Pain is among the most important of symptoms in term of prevalence and cause of distress in cancer patients and their families. A meta-analysis in adult cancer patients found that 59% of cancer patients under treatment, 64% of patients with advanced, metastatic or terminal disease, and 33% of patients after curative treatment suffer pain. More than one-third of cancer patients rate their pain in a Visual Analogue Scale (VAS) as moderate or severe\(^3\), and it has been estimated that more than 80% of the patients around the world with moderate or severe pain are inadequately treated even though science has the capacity to relieve this situation\(^4\). In the case of cancer patients, a review suggested that an average of 43% receive inappropriate care for pain\(^5\).

Not surprisingly, the management of pain has raised interest among the clinician and research communities in recent decades. Several efforts have been developed to change a situation perceived as deficient in terms of the quality and results achieved in relation to pain management in general and in cancer patients in particular. Strategies include interventions against identified barriers\(^6\),\(^7\),\(^8\),\(^9\), the promotion of a clear policy shift\(^10\), new guidelines development\(^11\), and some attempts to overcome the challenges for quality improvement (QI), one of which is the lack of clearly defined measurable attributes of quality pain management\(^12\).

Initiatives using the QI approach have included\(^12\) the pain assessment and accreditation standards used by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), build on the work of the Agency for Healthcare Research and Quality (AHRQ) and the American Pain Society, the national nursing home quality improvement initiative launched by the United States Centers for Medicare and Medicare Services, which included improvement activities on pain management, and some multi-center initiatives, particularly on post-operative pain. More recently, some quality indicators on pain management have been included in a set of indicators for palliative care in general\(^13\), for cancer pain management in older adults in hospice care\(^14\), and for advanced cancer patients\(^15\),\(^16\). However, a specific and yet comprehensive set of measures to define cancer pain management is still lacking.

At the same time, research has shown that QI initiatives are more successful in significant reductions of pain intensity when they include treatment-focused strategies\(^12\), and that evidence-based practice is more cost-effective than usual care\(^17\). It seems essential then for QI to complement the usual focus on improving pain assessment and documentation with efforts to increase implementation of effective evidence-based treatment approaches, in a field where much of conventionally accepted practice seem to remain supported by clinical observation only\(^18\). All these factors underscore the need to develop, test and eventually use comprehensive, valid and reliable indicators of quality cancer pain management, in order to improve, measure changes, and assure the best practice for these patients.

This paper reports on the construction process and pilot test results regarding feasibility, reliability and capacity to identify quality problems, of a set of evidence-based indicators for...
cancer pain management (SICPM). The proposed indicator set focuses on an integral approach to chronic cancer pain (CCP) management, and measurement data from the pilot test sites provide an estimation of the baseline situation regarding good practice in the control of cancer pain.

Methods

A multidisciplinary working group was assembled, including experts from the disciplines of anesthesiology, pharmacology, nursing, family medicine, physiotherapy and rehabilitation, and quality management. The mandate was to define evidence-based indicators in relation to assessment, initial treatment and follow-up of patients with cancer pain.

We followed an overall 4-step process, flowcharted in Figure 1, including: (i) review and systematization of evidence-based recommendations, in relation to the three main building blocks of cancer pain care (assessment, initial treatment and follow-up); (ii) review, systematization and critical analysis of existing indicators, and identification of evidence-based recommendations not covered by existing indicators; (iii) new indicators development to cover all evidence-based recommendations; and (iv) pilot test in hospital and primary care settings of the accepted set.

Review and systematization of evidence-based recommendations

We performed a comprehensive search of literature in Medline, Cochrane and Ovid databases looking mainly for systematic reviews and clinical guidelines in relation to cancer care or cancer pain management, published within the last ten years (2001-2011). Additionally, a search of clinical guidelines was performed using the National Guideline Clearinghouse of the AHRQ, the Scottish Intercollegiate Guidelines Network (SIGN), the New Zealand Guidelines Group (NZGG), National Institute for Health and Clinical Excellence (NICE), BMJ Evidence, and GuiaSalud (a Spanish database of clinical guidelines). When the level of evidence of relevant recommendations was not stated or was unclear, we reviewed the articles quoted in the reference lists of the identified clinical guidelines.

To harmonize the different scales used in the published literature, we established our own unified scale for level of evidence and strength of recommendation, based mainly on the GRADE19,20, SIGN21, and U.S. Preventive Services Task Force proposals22,23. The group retained recommendations which had supporting evidence level A (one or more randomized controlled trials, with or without meta-analysis) or B (significant observational studies), with a strength of recommendation A (must do), B (could be done: benefit is higher than potential adverse effects) and D (must not do: adverse effects are higher than benefit), but prioritizing evidence A and strength of recommendation A or D.

Review and systematization of existing indicators

We performed a comprehensive search of quality indicators for cancer pain management in the National Quality Measures Clearinghouse of the AHRQ, and in articles indexed the Medline, Scopus, Psycinfo, and Academic Premium databases for 10 previous years (2001-2011), containing the key words “Quality indicators, Health Care” [MESH] AND “Pain” [MESH]. An additional search for potentially non-indexed literature was done using Google, and extracted also the indicators, if any, proposed in the reviewed clinical practice guidelines. We tried to match the found indicators with the evidence-based recommendations we had listed,
and made an assessment of the level of evidence supporting them. Those not related to any of the recommendations were discarded.

**New indicators development**

In order to obtain a full set of tools for measuring the degree of implementation of the good practice recommendations we had found, we elaborated new clinical indicators when definitely valid indicators were not found for those recommendations. To facilitate discussion within the group, we defined and used a standardized format for describing both the adapted and the newly constructed indicators. This format included: name (overall description) of the indicator; component of health care quality to be covered by indicator (assessment, treatment, follow-up); data source and method for measurement (medical records review, inspection, direct observation, surveys); detailed description of the indicator, including definition of target patients for whom the quality indicator applies, and good practice to be assessed (inclusion and exclusion criteria for numerator and denominator); computation of the measure (presence/absence, rate or proportion); indicator origin (adapted or newly built); references supporting evidence; level of evidence and strength of the recommendation or recommendations used for the indicator; and observations, remarks or further specifications to assure reliability of measurements (i.e. list of commercial names of recommended drugs, precise definitions of recommended procedures, valid scales, etc.).

After iterative discussion sessions, the group redefined and retained indicators with the following characteristics: (i) adequate scientific evidence of the good practice measured; (ii) the indicator compliance is under control of health professionals and facilities providing care to cancer patients; and (iii) the measurement could be potentially feasible on a routine basis.

**Pilot testing**

The set of indicators was then pilot tested in two hospitals (one medium size: 200-500 beds, and one big: >500 beds) and one primary care center (staffed by 20 physicians and 16 nurses) providing home palliative care, all of them located in the Region of Murcia (Spain). One of the hospitals and the primary Health care center had electronic medical records. Formats for data abstraction and guidelines for the pilot test were devised, specifying the ICD codes (to identify cases for the Minimum Basic Data Set in hospitals), and the International Classification of Primary Care (for the Primary Health Care Center), sampling method, and Excel databases for calculation of reliability (kappa), problem identification using the Lot Quality Assurance method and estimated compliance of indicators.

The objectives of the pilot test were threefold: (i) feasibility of the measurement in the various settings and for the different type of cancer patients in which the indicators are applicable; (ii) reliability of the feasible indicators; and (iii) potential usefulness for quality improvement. Problems of feasibility may come from difficulties in identifying target patients, deficiencies in clinical records, very low prevalence of cases, or other circumstances in which it may not be possible to measure an indicator. Reliability was tested calculating inter-rater Kappa index for each clinical record-based indicator in samples of 15 cases, using assessment results from two independent raters not involved in designing the indicators. Reliability of inspection-based structure indicators was assessed looking at inter-raters concordance. Usefulness for problem identification and quality improvement was analyzed using LQAS (Lot Quality Acceptance Sampling), a quality control procedure promoted by the World Health Organization for rapid
assessments, that can be used in epidemiological studies, and that we had adapted as a problem identification tool for quality management\textsuperscript{24,25,26}. This technique allows identifying quality problems when the standard and threshold fixed for indicator compliance are not met. The parameters for acceptance (“good quality”) were set for two situations: a standard compliance of 75% (40% threshold); and a standard compliance of 95% (70% threshold), with $\alpha \leq 0.05$ and $\beta \leq 0.01$ for both instances. These conditions require a random sample of 15 patients and a minimum of 12 compliance cases for accepting a 95% compliance, or 8 compliance cases to accept a 75% compliance. Centers with $<12$ compliance cases in the sample may be identified as problematic for a 95% standard, and centers with $<8$ cases are problematic for a 75% compliance standard. Additionally, actual compliance level was estimated with 95% binomial exact confidence interval for each center individually, and using the formula for non-proportional stratified sampling for the aggregate estimate in more than one center.

**Results**

A set of twenty-two indicators was eventually proposed for the management of CCP, distributed by the aspects of care to which they apply (Assessment, Pharmacological, Psychological and Complementary Treatment, Education, and Perceived Quality/Patient Report), as listed in Table 1. The SICCP was piloted in several oncology-related services in hospitals, such as the oncologic outpatient unit, oncology service, and radiotherapy service; and general practitioner consultations and home care in the case of primary health care. Pilot test results in terms of feasibility of measurement, reliability, and usefulness to identify quality problems, are as follows:

**Feasibility of measurement**

Measurement was feasible for 17 of the 22 indicators in hospital care, and 12 of them in both hospital and primary health care. Structure indicators (5 in total, including existence and content of selected protocols and other pain management useful tools like patient education material, perceived quality questionnaires and equi-analgesic dose conversion tables) could be measured in all healthcare settings. The main reasons for non-feasible measurement were low incidence/prevalence of cases to evaluate (i.e. patients with pancreatic cancer and uncontrolled CCP), indicators subsequent or dependent on compliance of other indicators which resulted with very low or non-compliance (i.e. opioid rotation using equi-analgesic dose chart, where there is not such chart available, or adequate treatment of severe CCP, which requires first that pain severity is measured), and, particularly in primary and home care, difficulties to locate with the current information system either the cases or the information needed for measurement (i.e. patients with chronic neuropathic cancer-related pain). Detailed feasibility results are described Table 2.

**Indicators reliability**

Reliability results (last two columns of Table 2) were obtained from feasible chart reviewing-based indicators, and measured separately in the hospital and primary care settings. In hospitals, $kappa$ ranged from 0.65 (in one indicator) to 1 (in seven indicators); most of them had a $kappa$ index $>0.8$. Similar results were obtained in primary care, with only one indicator with moderate agreement ($k=0.53$) which was discussed and found to be due to ambiguity and confusing structure of clinical records. Agreement was at 100% for the 5 inspection-based structure indicators in both primary care and hospital settings.
Usefulness for problem identification and quality improvement

Although some variability was found, quality was low in the majority of indicators, pointing out to specific issues and areas for quality improvement (Table 3). Four indicators had acceptable quality compliance at the LQAS 75/40 standard/threshold level in at least one center. Two of them had also acceptable quality at LQAS 95/70 LQAS standard. All of these are medication-related indicators. Prevention of gastric side-effects in patients treated with NSAIDs was the least problematic (estimated overall compliance: 91.7±10.7 in hospitals, 53.3±17.8 in primary care), followed by the use of treatment with bisphosphonate in patients with bone metastasis (overall compliance: 51.4±in hospitals). The only one with acceptable LQAS 95/70 compliance in all centers (not use of cannabinoids as initial treatment) could be removed from the set considering that there was not variability, with 100% compliance in all centers, and that it is unlikely that it will be problematic in the future. Other important medication-related indicators such as the use of pain intensity scales and the consequent adjustment of medication, or the prescription for breakthrough pain had very low compliance levels, underscoring the existence of relevant quality gaps. However, the worse compliance and massive quality problems were found in relation to indicators concerning patient-centered care, including attention to psychological distress, educational needs, and the use of tools to measure patient experience/perceived quality. Structure indicators in relation to the existence of tools to support and help good practice (dose conversion tables for opioids, educational material or protocols about patient education, instruments to measure patients’ experience and perceived quality) were not present in any center.

Discussion

We have constructed and pilot tested a rather comprehensive set of good practice indicators for detecting problems and monitor changes in the management of CCP, considering current evidence-based knowledge, and assuring feasibility of measurement and reliability of feasible indicators. Lessons learnt along this project are manifold, including but not limited to the difficulties of summarizing existing evidence, the deficiencies of current recording and information systems to support an appropriate monitoring of good practices regarding cancer pain management, and ultimately the measurement results in the pilot sites showing that cancer pain management is a deficient, massively problematic area of health care. This finding reinforces the need of having the type of tools we propose, to support focused improvement initiatives.

Disparities in classifying evidence and the proposal of evidence-based recommendations

Our literature review has found that there is increasing interest in pain management and the building of guidelines to facilitate good practice. We may highlight the WHO initiative, WHO Normative Guidelines on Pain Management\textsuperscript{11}, as well as the initiatives of the American Pain Society\textsuperscript{29,30,31} and in other countries as diverse as Scotland\textsuperscript{32}, and Malaysia\textsuperscript{33}. However, the existing guidelines are not homogeneous regarding neither the particular recommendations they propose nor the scales used for grading the evidence and the strength of the recommendation. In some cases, such important information is lacking, making difficult to select what it would be the best recommended practice. Consequently, we had to find and define the common ground of all the scales for grading evidence, eventually keeping only those recommendations explicitly supported by controlled trials (preferably) or significant observational studies. In many instances we had to complement the information contained in
the guidelines by reviewing the original studies quoted in the guidelines, as well as other articles found in the literature search. In other cases, the recommendations were partial and left important aspects of the same issue or decision undefined. When this occurred, we tried to combine partial recommendations on the same issue into a single indicator, which was the case in nine of the twenty-two eventually proposed indicators. Most probably, these issues may explain at least partially why one of the gaps and challenges identified to improve quality of pain management has been the failure to define quality pain management itself.

**Defining quality cancer pain management is not enough: the feasibility barrier**

We built a selected set of 22 evidence-based indicators, but, in spite of their potential relevance to monitor the quality of cancer pain management, measurement was not feasible for all of them. 17 indicators were feasible in hospitals and 12 in the primary care center where the set was pilot-tested. Feasibility differences between hospital and primary care were principally due to the kind of care provided (i.e. bisphosphonates are not prescribed in primary care), and then to some particular characteristics of the information system in primary health care, which uses a coding system for patients (*International Classification of Primary Care, ICPC-2*) less detailed than the *International Classification of Diseases* (ICD-9) used in hospital care, making more difficult to identify target cases for the assessments of particular good practices. In addition, there are the problems of sometimes disorganized or incomplete clinical records, which was the main reason, and the dependence of some indicators on the compliance of other indicators which resulted with low compliance (i.e. pain treatment adjusted to pain severity, opioids rotation using equianalgesic doses chart). The latter accounted for most of measuring difficulties in the hospital setting. However, It should be pointed out that the proposed set is meant to be used for internal QI (identification and understanding of the extent and nature of the quality problems, motivation for change, and comparisons after change has been made) rather than for external accountability, even though some indicators may be used for both purposes. Therefore, in different contexts where measurement may not be done externally, as it was the case in our project, or where the information system and clinical records are better organized feasibility barriers may be different or even not present. QI projects may choose also to prioritize the more generally applicable indicators, which are also the more feasible ones.

**The proposed set of indicators as a valuable quality problems identification tool.**

Cancer pain management is a complex issue which needs a multidimensional approach, be based on a comprehensive, not only intensity, pain assessment, and on drug, psychological and integrative interventions. At the same time, both the opioid and the not-opioid analgesic drugs (i.e. NSAID) used to control cancer pain need a close management of side effects, and a particular attention to their dosage, route of administration, the consideration of the need of rotation to adapt them to individual differences in the response to the various opioids drugs, and an anticipated plan for treating breakthrough pain. The set of indicators we propose include all these important aspects and their pilot test measurement with the LQAS technique and estimated level of compliance has shown which ones and to what extent they may constitute relevant quality problems. First, it is striking the low, virtually nil, compliance of the indicators addressing patient-centered care, including attention to psychological suffering and treatment education needs. The comprehensive approach to cancer pain management seems to be lacking. Second, important aspects of drug treatment such as the adjustment to measured pain intensity and planned treatment of breakthrough pain are problematic in all
pilot sites (LQAS results) and have a very low level of compliance (estimated 1.6 and 11.6% respectively), while dose conversion charts were also absent in all sites. Third, while treatment is not explicitly adjusted to patient needs, more attention is paid to the prevention of side effects such as gastric protection when NSAIDS are prescribed (the indicator with the highest level of compliance in the whole set: an estimated 91.7%), and constipation and emetic prophylaxis for opioids, even though there is a big room for improvement in both cases (estimated compliance of 33.3 and 38.6% respectively). These results may not be similar in other settings, but the measurement of the set of indicators we propose may highlight in any case the specific quality improvement challenges which should be addressed.

The state of the art in indicators for cancer pain control and the contribution of the set we propose

Despite of the increasing interest in pain management, our literature search found only a few indicators which could be useful for our purposes. Most of the existing quality of cancer care indicators focus on palliative care\textsuperscript{34-38}, on breast cancer\textsuperscript{39,40}, or other limited populations groups\textsuperscript{41,42,43}. In many cases, some indicators on pain management are included as part of the set for specific target patients, but we did not found any evidence-based indicator set specifically or exclusively designed for cancer pain management in general. Therefore, most of the indicators we propose were purposely built for our project on the basis of the evidence-based recommendations we could locate and summarize.

More recently, some quality indicators on pain management have been included in a set of indicators for palliative care in general\textsuperscript{13}, for cancer pain management in older adults in hospice care\textsuperscript{14}, and for advanced cancer patients\textsuperscript{15,16}. In all these cases the authors try to follow a systematic approach to guarantee the validity of the indicators, but apart from their focus in particular type of patients or situations, they leave out some relevant aspects such as psychological assessment, a patient-centered view, adequate doses for pharmacological treatment, and opioid rotation\textsuperscript{14}, or some other issues like adequate dosage and drug rotation\textsuperscript{15,16}. However, they provide a somehow wider approach to the particular type of patients and situations they address, even though results on their usefulness as quality problems identification tools are not provided and both their level of evidence and strength of the recommendation, or the methods to assess them, are not always explicit. In general they rely heavily on the ratings of a group of experts.

Limitations

Although our set tries to be comprehensive, it has some limitations regarding palliative care, end-of-life treatment, and chronic cancer pain in children. General indicators, like patient assessment indicators, can be used by professionals in all these settings. Prevention of side-effects and most of pharmacological treatment indicators can be also used in palliative care and end-of-life care, but in general quality management for palliative care, end-of-life care or children population may need a specific attention and a complementary set of indicators.

In addition, the classification of chronic cancer pain is ambiguous. We have used the concept of chronic cancer pain as described in the document \textit{WHO Normative Guidelines on Pain Management} in which pain was arranged in three categories: acute pain, chronic malignant pain, and chronic non-malignant pain\textsuperscript{11}. Furthermore, given the operational ambiguity of most classifications of cancer pain\textsuperscript{19,44,45,46}, we just kept to the usually agreed three months limit to
include patients as chronic pain\textsuperscript{47}, which may not be completely adequate for cancer patients given that pain control may follow similar guidelines from the onset. However, the SICCP covers most of recommendations established by the American Pain Society for improving the quality of acute and cancer pain management\textsuperscript{30}.

Finally, the validation and pilot test results are context-dependent and may be different in other health care systems or health care institutions. We tried, however to include the more frequent type of settings where cancer patients are treated. The particular interest of a given institution or professional group may choose also to apply only part of the proposed set. In any case constant reviews may be useful to incorporate, replace or leave out some indicators when new evidence and recommendations are available.

**Conclusions**

We have built and pilot tested a set of evidence-based quality indicators for cancer pain management which may be used for monitoring and improvement of this important public health issue. The set has been tested for feasibility, reliability and usefulness for quality problem identification in the context of the Spanish health care system. Further refinements may come now from their actual use by committed professionals and institutions.

**Conflict of interest disclosures**

This project was carried out under contract between University of Murcia, Grünenthal Foundation, and Fundación para la Investigación en Salud (FUINSA).

The authors of this paper are responsible for its content. Statements in this paper should not be construed as endorsement by Grünenthal Foundation, and Fundación para la Investigación en Salud.
References


FIGURE 1. Flowchart of 4-steps process used

TABLE 1. Quality Indicators for Chronic Cancer Pain Management

A. Patient Assessment: 2 indicators
   - Pain assessment: 1 indicator *
   - Psychologic distress assessment: 1 indicator

B. Pharmacologic treatment of pain: 12 indicators
   - General: 3 indicators *
   - Specifics (additional) if opioid therapy: 5 indicators
   - Specific (additional) if NSAID therapy: 1 indicator
   - Complementary treatments in specific cases: 3 indicators

C. Psychological treatment: 1 indicator

D. Patient education: 3 indicators *

E. General complementary treatments: 2 indicators
   - Physical therapy: 1 indicator
   - Cannabinoids use: 1 indicator

F. Perceived quality/patient report: 2 indicators
   - Perceived quality of treatment: 1 indicator
   - Effectiveness of educational activities: 1 indicator

TOTAL: 22 indicators

* These indicators could be considered applicable to an immediate implementation of management of CCP due to its usual application in our environment.
### A. PATIENT ASSESSMENT

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Feasibility</th>
<th>Hospital Care</th>
<th>Primary Care</th>
<th>All settings</th>
<th>Kappa Index (hospital care)</th>
<th>Kappa Index (Primary care)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pain assessment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td>Percentage of patients with CCP and pain assessment through validated scales</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2. Psychological/Emotional distress assessment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1</td>
<td>Percentage of patients with CCP and explicit psychological distress assessment through validated scales</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

### B. PHARMA COLOGIC TREATMENT OF PAIN

1. NSAIDs. Side effects prevention

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Feasibility</th>
<th>Hospital Care</th>
<th>Primary Care</th>
<th>All settings</th>
<th>Kappa Index (hospital care)</th>
<th>Kappa Index (Primary care)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Percentage of patients with CCP and treated with NSAIDs in which gastric protection was prescribed</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>0.71</td>
<td>0.73</td>
<td></td>
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</tbody>
</table>

2. Opioids. Side effects prevention

<table>
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<tr>
<th>Indicator</th>
<th>Description</th>
<th>Feasibility</th>
<th>Hospital Care</th>
<th>Primary Care</th>
<th>All settings</th>
<th>Kappa Index (hospital care)</th>
<th>Kappa Index (Primary care)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Existence of equianalgesic doses charts to limit side effects through opioid rotation*</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>100%*</td>
<td>100%*</td>
<td></td>
</tr>
<tr>
<td>2.2</td>
<td>Percentage of patients with CCP in which opioid rotation is carried out using adopted an equianalgesic doses chart</td>
<td>✓</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3</td>
<td>Percentage of older patients with CCP in which initial dose of short-acting oral morphine is adequately adjusted to age</td>
<td>✓</td>
<td>0.93</td>
<td>0.93</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>Percentage of patients with CCP and strong opioids treatment in which constipation prophylaxis is prescribed</td>
<td>✓</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2.5</td>
<td>Percentage of patients with CCP and opioids treatment in which emetic side effects prophylaxis was prescribed</td>
<td>✓</td>
<td>0.93</td>
<td></td>
<td></td>
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</tbody>
</table>

3. General

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Feasibility</th>
<th>Hospital Care</th>
<th>Primary Care</th>
<th>All settings</th>
<th>Kappa Index (hospital care)</th>
<th>Kappa Index (Primary care)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1</td>
<td>Percentage of patients with CCP and pain assessment in which adequate treatment is prescribed according to WHO analgesic ladder</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>0.71</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>3.2</td>
<td>Percentage of patients with CCP and opioid treatment in which adequate breakthrough pain treatment was prescribed (composite indicator including: 1. treatment plan including anticipated prescription for breakthrough pain, and 2. Adequate drug and dosage)</td>
<td>✓</td>
<td>0.85/0.65*</td>
<td>0.85/0.65*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.3</td>
<td>Percentage of patients with severe CCP in which adequate initial I.V. or S.C. morphine pain management is established</td>
<td></td>
<td></td>
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</tbody>
</table>

4. Specific complementary treatment
| B.4.1 | Percentage of patients with bone metastatic CCP in which bisphosphonate treatment is prescribed (composite indicator including: 1. bisphosphonate prescription, and 2. Adequate dosage) | ✓ | ✓ | ✓ | 1 | 0.80/0.86³ |
| B.4.2 | Percentage of patients with chronic neuropathic cancer-related pain in which anticonvulsant or tricyclic antidepressant medication is prescribed |
| B.4.3 | Percentage of patients with pancreatic cancer and uncontrolled CCP in which blockade plexus coeliacus or spinal opioids were used |

C. PSYCHOLOGICAL TREATMENT

1. Psychological/Emotional distress treatment

| C.1.1 | Percentage of patients with CCP in which psychological distress treatment is established | ✓ | ✓ | ✓ | 1 | 0.93 |

D. PATIENT EDUCATION

1. Treatment education needs care

| D.1.1 | Existence of pharmacological treatment education materials for patients with CCP* | ✓ | ✓ | ✓ | 100%‖ | 100%‡ |
| D.1.2 | Existence of pharmacological treatment education protocols for patients with CCP* | ✓ | ✓ | ✓ | 100%‖ | 100%‡ |
| D.1.3 | Percentage of patients with CCP in which pharmacological treatment education activities are carried out | ✓ | ✓ | ✓ | 1 |

E. GENERAL COMPLEMENTARY TREATMENTS

1. Physical therapy

| E.1.1 | Percentage of patients with CCP in which complementary physical therapy programs are established | ✓ | ✓ | ✓ | 1 | 1 |

2. Cannabinoids use

| E.2.1 | Percentage of patients with CCP in which cannabinoid treatment is NOT prescribed as initial treatment | ✓ | ✓ | ✓ | 1 | 1 |

F. PERCEIVED QUALITY/PATIENT REPORT

1. Perceived quality of treatment

| F.1.1 | Existence of survey or questionnaire of perceived CCP management quality, and its results* | ✓ | ✓ | ✓ | 100%‖ | 100%‡ |

2. Effectiveness of educational activities

| F.2.1 | Existence of survey, questionnaire or structured interview about major treatment concerns in CCP, and its results* | ✓ | ✓ | ✓ | 100%‖ | 100%‡ |

✓ Feasible indicators
* Inspection-based indicators
‖ General Agreement index
‡ Kappa of the two components of the Composite indicator
TABLE 3. Quality problem identification with LQAS and compliance estimates of feasible percentage-based indicators

<table>
<thead>
<tr>
<th>INDICATOR</th>
<th>Centers with acceptable quality (LQAS 75/40)</th>
<th>Centers with acceptable quality (LQAS 95/70)*</th>
<th>Compliance estimate in hospital care</th>
<th>Compliance estimate in primary care</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. PATIENT ASSESSMENT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.1.1 Percentage of patients with CCP and pain assessment through validated scales</td>
<td>0 of 3</td>
<td>0 of 3</td>
<td>0 ± 0</td>
<td>6.7 ± 8.9</td>
</tr>
<tr>
<td>A.2.1 Percentage of patients with CCP and explicit psychological distress assessment through validated scales</td>
<td>0 of 3</td>
<td>0 of 3</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>B. PHARMACOLOGIC TREATMENT OF PAIN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.1.1 Percentage of patients with CCP and treated with NSAIDs in which gastric protection was prescribed</td>
<td>3 of 3</td>
<td>2 of 3</td>
<td>91.7 ± 10.7</td>
<td>53.3 ± 17.8</td>
</tr>
<tr>
<td>B.2.4 Percentage of patients with CCP and strong opioids treatment in which constipation prophylaxis is prescribed</td>
<td>0 of 2</td>
<td>0 of 2</td>
<td>33.3 ± 19.9</td>
<td>Not feasible</td>
</tr>
<tr>
<td>B.2.5 Percentage of patients with CCP and opioids treatment in which emetic side effects prophylaxis was prescribed</td>
<td>0 of 2</td>
<td>0 of 2</td>
<td>38.6 ± 20.7</td>
<td>Not feasible</td>
</tr>
<tr>
<td>B.3.1 Percentage of patients with CCP and pain assessment in which adequate treatment is prescribed according to WHO analgesic ladder</td>
<td>1 of 3</td>
<td>0 of 3</td>
<td>1.6 ± 3.1</td>
<td>73.3 ± 15.8</td>
</tr>
<tr>
<td>B.3.2 Percentage of patients with CCP and opioid treatment in which adequate breakthrough pain treatment was prescribed (composite indicator including: 1. treatment plan including anticipated prescription for breakthrough pain, and 2. Adequate drug and dosage)</td>
<td>0 of 2</td>
<td>0 of 2</td>
<td>11.9 ± 14.2</td>
<td>Not feasible</td>
</tr>
<tr>
<td>B.4.1 Percentage of patients with bone metastatic CCP in which bisphosphonate treatment is prescribed (composite indicator including: 1. bisphosphonate prescription, and 2. Adequate dosage)</td>
<td>1 of 2</td>
<td>0 of 2</td>
<td>51.4 ± 21.7</td>
<td>Not feasible</td>
</tr>
<tr>
<td>C. PSYCHOLOGICAL TREATMENT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.1.1 Percentage of patients with CCP in which psychological distress treatment is established</td>
<td>0 of 3</td>
<td>0 of 3</td>
<td>0 ± 0</td>
<td>6.7 ± 8.9</td>
</tr>
<tr>
<td>D. PATIENT EDUCATION</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.1.3 Percentage of patients with CCP in which pharmacological treatment education activities are carried out</td>
<td>0 of 2</td>
<td>0 of 2</td>
<td>0 ± 0</td>
<td>Not feasible</td>
</tr>
<tr>
<td>E. GENERAL COMPLEMENTARY TREATMENTS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.1.1 Percentage of patients with CCP in which complementary physical therapy programs are established</td>
<td>0 of 3</td>
<td>0 of 3</td>
<td>3.2 ± 4.3</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>E.2.1 Percentage of patients with CCP in which cannabinoid treatment is NOT prescribed as initial treatment</td>
<td>3 of 3</td>
<td>3 of 3</td>
<td>100 ± 0</td>
<td>100 ± 0</td>
</tr>
</tbody>
</table>

*Centers with LQAS 95/70 accomplishment take into account of LQAS 70/45 accomplishment too.

¶Percentage Estimation ± binomial exact 95% Confidence Interval, no proportional stratified sampling.