

**Executive summary:**

Post-operative pain is an inevitable consequence of surgery. Poorly managed post-operative pain causes suffering, increases costs of care and can lead to disabling chronic pain. Despite the availability of high-quality guidelines and advanced pain management techniques acute postoperative pain management is still far from being satisfactory. About 40% of patients worldwide report inadequate pain relief despite receiving treatment.

PAIN OUT is a comprehensive, concerted European effort to develop effective, evidence-based approaches to improve care of pain in patients after surgery. Launched in January 2009, with four-year funding from the European Union's (EU) 7th Framework Program, it integrates experience gained from a national initiative in Germany (QUIPS, a national acute pain database) and the expertise of world-leading, European-based groups dealing with benchmarking, health outcomes and health care utilization research. PAIN OUT has created a large, international Acute Pain Registry as a platform for research and quality improvement. A network of participating hospitals contributes data to the registry and receives web-based feedback and benchmarking of their quality of care, in return. In parallel, the registry allows analysis of the large data bank as well as additional prospective data collections by using the existing infrastructure and network of PAIN OUT hospitals.

The main objective of the PAIN OUT project was to develop and to validate a system for measurement and feedback of outcome quality and support of decision making. Therefore, a core data set to be collected in all participating sites was defined using a Delphi consenting process. Project implementation in the 11 national clinical consortium sites (NCCS) included translation of questionnaires according to the standard procedures of translation and back-translation and training of staff for data collection. Online web-based data input facilities are fully established. The central data base was established successfully and contains more than 35,000 patient cases by now. A web-based software system has been developed, allowing for internal and external benchmarking of patient outcome data and offering users continuous feedback and analyses of their quality of care. By evaluating their results, users are able to implement change management concepts and can provide their patients with better care.

In addition to the registry, PAIN OUT offers a case-based Clinical Decision Support System – a tool that will allow sending queries to the database seeking for similar cases so that physicians can check which treatment strategies were used in the past to treat specific patients. This case-based Clinical Decision Support System has been developed, and a prototype has been successfully tested by participating sites. A Point-of-Care (PoC)-application has been set up, which is ready to use in clinical routine.

The third feature of PAIN OUT is an Electronic Knowledge Library (EKL) that provides users with summaries of contemporary guidelines for postoperative pain treatment and with direct access to specific chapters in these guidelines. The Electronic Knowledge Library has been set up and accessible for PAIN OUT participants via the PAIN OUT website <http://www.pain-out.eu>. More than 30 chapters have been created, transformed into web documents, and linked to the original guideline documents used as sources.

For the issue of health economics in post-operative pain a protocol for the collection of the main cost drivers has been developed, disseminated and piloted in participating sites. Data collection has been proven to be feasible, and a health economic data base has been set up as part of the main pain registry.

All modules of the project are designed for daily use in clinical routine, continuation and international dissemination. Thus, a strategy for sustainability and co-operation with relevant stakeholders in this field are important parts of the project.

To enhance dissemination, contacts and co-operation with societies and potential project partners after the funding period have been intensified and established. PAIN OUT is collaborating with the International Association for the Study of Pain (IASP), the largest international multi-disciplinary society of pain, as well as with its European counterpart, EFIC. Both societies will help to promote PAIN OUT and its work amongst its members.

The consortium has agreed to continue the project after end of funding, contracts and the organizational structure have been agreed on, and a financing concept for continuation of the project after end of funding has been developed. Already now there is remarkable worldwide interest in the project and more than 60 clinical sites from all over the world participate in the international branch of the project on a voluntary base.

## **Project Context and Objectives:**

### **Overview**

The overall goal of the PAIN OUT project is to improve the quality of postoperative pain management of European citizens. The heart of the project is a large acute pain registry which contains clinical data (surgery, pain management, comorbidities) as well as patient-reported outcomes. So far, the patient's perspective has rarely been taken into account in medical registries. The registry is continuously fed by participating hospitals, containing currently (Nov 2012) data from more than 35.000 patients. This makes the project's database the largest international registry on postoperative pain. The two main services it provides are quality improvement and health care research.

**Quality improvement:** The registry data are used to give hospitals, physicians and nurses a feedback on their quality of care in comparison with other hospitals and over time (feedback and benchmarking). In addition, the database offers a clinical decision support system. Participants can search the registry for similar cases and benefit from their colleagues' experience. Furthermore, a guidelines library supplies the user with the most recent international therapy recommendations.

**Health care research:** The large registry data allows for analyzing epidemiology of postoperative pain, national and international differences in patient care, and the efficiency of pain management in everyday clinical routine.

### **Features of the project**

- A core data set for postoperative pain including the International Pain Outcome (IPO) Questionnaire, extensively validated in over 9.700 patients in ten languages (Workpackage 1).

- A large international pain registry including web-based data input facilities, data quality checks and data security features. An easy-to-use toolset for the acquisition and storing of data, including standard operating procedures and e-learning. (WP 2).
- A user-friendly, internet-based toolset for hospitals and clinicians, comprising the following elements:
  - A feedback and benchmark tool which provides internal and external benchmarking of patient outcome data, allowing identifying best practice and learning from each other. Furthermore, institutions are able to monitor their longitudinal performance and effects of interventions, and identify areas which require improvement.

The system will present treatment strategies of those institutions with best outcomes and facilitates benchmark discussion rounds, thereby supporting identification of deficits as well as foster change of clinical routine if needed (WP 3). The tool will be complemented by a module for comparing costs of postoperative pain management between different sites (WP 6).

- A case-based clinical decision support system (CDSS) which supports clinical decision making in the concrete, individual case. CDSS takes into account former cases similar to the current problem and attempts to use successful solutions previously employed to fit the current, new case. It will support clinicians at the point of care by responding to individual queries for the: (1) most appropriate treatment, (2) relative risk of adverse events. The CDSS may also aid the decision process by identifying similar cases/solutions with an undesired outcome (WP 4).
- An Electronic Knowledge Library (EKL), an interactive library on the base of six large international guidelines / summaries of evidence which retrieves knowledge according to 31 specific search areas, such as patient characteristics, type of surgery, type of pain management etc. It includes direct, clickable web links to the sources (WP 5).
- A protocol for the collection of the health economics data / resource requirements in post-operative pain. It will be integrated into the benchmark / feedback system (WP 6).
- Data of short-term health-related quality of life after postoperative pain management (WP 6).
- Data on gender and age differences in management and outcome of postoperative pain (WP 7).

## **Project Results:**

### **Introduction**

Every year, surgery is performed on approximately over 40 million patients in the European Union. At least half of these patients suffer from moderate to severe post-operative pain. Pain impedes recovery; overloads health care resources, and causes suffering. The field of postoperative pain is characterized by large variability in clinical care and treatment results, similar to some other fields of medicine. As is often the case in medicine, guidelines and quality assurance initiatives have changed management of pain to some extent, but across the European continent they failed to support clinical decision making and to improve pain outcomes. Lack of methods to measure and compare outcome quality are a major obstruction for clinicians to assess, and consequently, to improve the consequence of their treatment decisions.

The main objective of PAIN OUT was to develop a system for the continuous measurement, feedback and benchmarking of treatment quality in the field of postoperative pain. The system should allow comparison of quality of

postoperative care between different countries and health care settings, provide clinicians with real-time treatment recommendations based on measured patients' outcome, and foster knowledge transfer and application of evidence-based medicine. In order to achieve this, a large scale data registry needed to be created, serving not only as a source for the benchmark and case-based decision support system but also allowing us to perform a wide range of clinical and statistical analyses of this data. Furthermore, we wanted to give participating clinical sites a feedback of their own quality of postoperative pain management over time.

The main results/foregrounds of PAIN OUT are achieved in the following areas although some overlap exists:

a) Technical results. These results comprise technical processes and achievements as the core data set and development, translation and validation of the International Pain Outcomes Questionnaire (IPO) (WP 1), development and set up of the European Pain Registry (WP 2), the Feedback and Benchmark module (WP 3), the case-based Clinical Decision Support System (CDSS) (WP 4), the Electronic Knowledge Library (EKL) (WP 5), and the technical requirements for obtaining data for the health economic module (WP 6).

b) Scientific results. In this field, analyses of data obtained by the methods developed in area a) were carried out. In addition to post operative pain outcomes, our results included data on quality of life and costs (WP 6), influence of gender and age (WP 7) and other analyses of data from the Pain Registry.

c).Implementation and dissemination results (WP 8 and 9). PAIN OUT was successfully implemented not only in the 11 beneficiaries' clinical sites but also in 60 additional hospitals. Results were disseminated on 70 national and international meetings/conferences and in 9 scientific publications.

## **Main S & T results per work package**

### **Work package 1 – Core data set**

**(Thomas Volk, Saarland University)**

Objectives of this work package were the establishment of a consented framework to measure the quality of acute pain management in its relevant dimensions of procedural, structural and outcome parameters; identification and establishment of a core data set of parameters for the treatment of patients with acute pain and testing of validity and reliability of the consented parameters.

In five Delphi rounds, the clinical site leaders and other experts created, modified and consented on the items for the core data set.

(Round A: Process of data collection, Round B: Demographics (= Demographics Page), Round C: Process Parameters (= Process Page), Round D: Outcome Parameters (= Outcome Page), Compilation round with version 1.0 of the core data set).

The resulting patient outcomes questionnaire, the International Pain Outcomes questionnaire (IPO) was translated in 15 languages and validated in a two-step validation process. A very strict forward and backward translation process with native speakers and independent translators was applied. The questionnaire was then administered to 9,727 patients in eight European countries and Israel. Construct validity was assessed

using factor analysis (FA). Discriminant validity assessment used U-tests to detect mean group differences between two surgical disciplines. Internal consistency reliability was calculated as Cronbach's alpha. FA resulted in a three factor structure explaining 53.6% of variance. Cronbach's alpha at overall scale level was high (0.86), and for the 3 subscales was low, moderate, or high (range 0.53 to 0.89). Significant mean group differences between general and orthopaedic surgery patients confirmed discriminant validity. The psychometric quality of the IPO can be regarded as satisfactory.

**Work package 2 - European Pain Registry and Biometry  
(Christoph Engel, Institute for Medical Informatics, Statistics and  
Epidemiology - IMISE, University of Leipzig)**

Objectives of this work package were the development of a standardized documentation concept; establishment and maintenance of a central data base (European Pain Registry, EPR); data quality management, bio-statistical analyses; providing processed data for feedback, benchmarking and the clinical decision support system (CDSS) plus validation of the questionnaires and online systems.

A standardized case report form (CRF) was developed. In an iterative process, the CRF was then reviewed by project partners for content structure, completeness and logical consistency, orthography, appropriateness of items and their answers with regard to the planned scientific data analyses. Based on the finalized CRF, an annotated CRF (aCRF) and a data dictionary were developed and made available for use by project members. The data dictionary is based on all the elements covered in the CRF and explains the database fields (plus their coding) and structure. The aCRF completes this set by visually outlining which fields in the database represent which questions.

Based on the CRF, a central data base and an electronic (internet based) remote data entry system was developed, implemented, tested and made available to end users. Together with TAKWA, who was responsible for developing the user front end of the remote data entry system, an appropriate hardware and software architecture for the EPR was chosen, obtained and integrated in the system topography of IMISE. The EPR was built using a WebObjects Java Platform and is hosted on an Apple XServe application server. An ORACLE database system is used as the central EPR database. The database structure (entity relationship model and table structure) was programmed taking into account the requirements of the user front end developed by TAKWA and requirements of the benchmarking server and researchers, regarding ease of use for future data analyses.

For managing the patient data, a concept for data management was developed and implemented. The data management concept covers data safety and quality. Regarding data safety, the following measures have been implemented:

- User access to the data entry system is restricted to registered project participants.
- All patient data are stored using uniquely generated identification codes, which do not allow the recognition of the patients. No patient names or personal identification items are stored in the central database.
- The central database can only be accessed by WP2 staff.
- Data will be shared with project partners only in an anonymized form.
- The central database sits behind the secure firewalls of the IMISE and the University of Leipzig.

Regarding data quality, the database is monitored regularly. Scripts for automated data quality reports were created, which produce data quality reports quarterly. These are sent to the Project Management team in Jena for review and appropriate distribution. There are two reports exclusively for the management team, one of which groups every outcome item plus the demographic and screening information of patients over quarters since project start, while the other compares participating centres with one another considering the same data items over the total project period. This allows detection of possible data quality changes over time or between participating centres.

One report is also generated for each centre, which collates and compares the items on a quarterly basis on the centre's own data. The centre reports are provided to the management team who then review and distribute them accordingly. All reports display tables and charts on each data item.

Biostatistical analyses on several topics were carried out and the results are at various stages of being collated in a number of articles for submission to journals relevant in this research area. The analyses include:

- Validation analysis - It validated the questionnaires and produced new versions for both. The article describing this work has been submitted and reviewed. It is in the post-review stage, ready for re-submission.
- Baseline analysis - this work reports the project baseline. It describes the data registry (EPR), its data items and some fundamental observations from these. It is in the final stages of the preparation of its first draft.
- Quality measurement scores - this work constructs, analyses and compares several indexes with the aim of measuring the quality of postoperative pain management or treatment. It analyses the associations between the suggested indexes and their predictors and with patient outcome items respectively, drawing conclusions on the advantages and usability of these indexes. This paper is in its first draft form.
- Analysis of predictors of pain - this work identifies risk factors for several patient outcome items, such as worst pain, time spent in severe pain, interference with in bed activities and pain relief. Based on these a risk profile or score is built, which could aid surgeons and anaesthesiologists adapt treatment to lower the risk of higher levels of acute post-operative pain and interference for patients. The analysis for this work is finalized, and the paper is currently being collated.

### **Additional analyses**

IMISE (ULEI) worked closely with CPM Basel on the analysis to identify drivers of patient outcomes. The focus was patient satisfaction, as analysed across centres and countries, for different patient groups. The resulting article is in its final draft prior to being submitted for publishing.

Provision of processed data for the benchmarkserver was automated in that it and the EPR both run off the same database tables, integrity, plausibility and completeness checks being the job of the EPR installation. The CDSS received processed data on a manual basis, as it was not designed to run on live data. IMISE helped define the interface for the CDSS, provided data as needed and tested the first version of the system for robustness and integrity.

### **Work package 3 - Benchmark Module**

**(Winfried Meissner, Jena University Hospital)**

Objectives of this work package were the setup of a password protected, secure, interactive feedback website for outcome data that allows internal benchmarking (comparison of own performance over time) as well as external benchmarking (comparison between participating sites) of pain management quality; the integration of a 'learning from the best' approach and the development of a template for moderated benchmark rounds where clinicians exchange their clinical experience.

The feedback server depends strongly on a working database and interactive data entry mask (WP2). After these had been finished, the feedback server was programmed and finished in month 18. It is continuously updated and improved. New filters are incorporated and the user handling is made more intuitive. It makes it possible for participating wards to compare their outcome results with other wards of their specialty (plastics, urology, traumatology, etc) and to investigate their development over time. Further, different filters like, e.g., gender, age, operation code, can be used to make the results more detailed and the statistical cohorts more comparable. The feedback server can be found under <http://painout.imise.uni-leipzig.de/cgi-bin/WebObjects/Benchmarkserver.woa/wa/PainOut>.

After logging in, hospitals can choose the specialty they want feedback for. They select the outcome parameter (least pain, worst pain, side effects, etc) and choose the graphical layout or descriptive statistics they wish (bar graph comparison to other wards, own development over time, box-whisker-plot comparison to other wards). They then get a diagram and a text box with the corresponding results on-screen and can print them.

In order to learn from the best sites, participants of PAIN OUT can access the articles in the restricted part of the PAIN OUT website.

The template for moderated benchmark rounds is available in the restricted part of the PAIN OUT website.

**Work package 4 - Clinical Decision Support System (CDSS)**

**(Peter Funk, Mälardalens Högskola)**

The objective of this work package was the setup of an interactive, case-based Clinical Decision Support System (CDSS) which uses the PAIN OUT registry to provide support in clinical decision making and uses the PAIN OUT registry as a knowledge resource of past experience enabling physicians to make more informed and personalized decisions.

A literature study was performed on CDSS to investigate recent advancements and trends. The work has resulted in a survey paper "Case-Based Reasoning Systems in the Health Sciences: A Survey on Recent Trends and Developments" published in IEEE Transactions on Systems, Man, and Cybernetics - Part C: Applications and Reviews.

A number of selected clinical decision support systems (CDSS) available in the market were examined before the design of a clinical decision support system for post operative pain. The aim and purpose of the included systems in context of their application domains were explored together with different characteristics and functionalities, methods and techniques applied to develop the systems. Also different types of cases depend on their nature and uses in case-based clinical decision support systems (CDSS) were investigated.

The core methods selected for the CDSS system for post operative pain management was a hybrid case-based reasoning approach including different methods and techniques from artificial intelligence and from statistics. The main design is based on the in-depth literature study and previous research carried out in the research group. Also, a number of user scenarios that have been discussed with clinicians within both the PAIN OUT project and other clinical experts. The result has been published in computer science and artificial intelligence context.

The CDSS has been implemented and has been used for evaluation by physicians in Europe (not used on real patient). In the work we have involved a number of senior researchers, post docs and PhD students (one PhD degree was produced during the project partly based on the work carried out in PAIN OUT) to develop the system. The first prototype of the intelligent dynamic case-based system for post-operative pain treatment was in operation in 2011 and has been continuously developed and improved until the end of the project.

The ambition is to make it available for hospitals within and outside Europe

A basic user interface for the case-based decision support system has been implemented enabling the addition of new cases and editing of patient data. A case-based retrieval algorithm has been implemented into the system to search similar cases.

A framework for the CDSS has been designed and developed in a server with secure https access, MySQL database and the core implementation is made in the programming language PHP enabling faster development time. The framework enables physicians to log in and use the system. All physicians in the PAIN OUT project that have requested login have received an account in the PAIN OUT CDSS tool with the condition that they take part in the evaluation (a questionnaire).

A case based retrieval system is based on case-based retrieval approach has been developed. The work has resulted in the published paper entitled "A Computer Aided System for Post-operative Pain Treatment Combining Knowledge Discovery and Case-Based Reasoning", M.U. Ahmed, P. Funk, International Conference on Case-Based Reasoning, Lyon, France, September, 2012, Springer Verlag. Here, the vision of the system together with a novel case representation by applying two-layer case structure is presented.

The first layer is the context including patient data and the selected treatment. The second layer connects the context and treatment to the outcome. The outcome is both clinical outcome and patient's self-assessment of pain, nausea and dizziness. The cases are formulated by using number of extracted features through a feature abstraction approach. Moreover, different types of cases namely regular and rare cases are proposed where the system provides the option to authorize and tag a case.

An automatic approach has been implemented to identify and separate rare (i.e. unusual) cases in post-operative pain treatment domain. The work has resulted in a paper "Mining Rare Cases in Post-Operative Pain by Means of Outlier Detection" and the paper is published in the IEEE International Symposium on Signal Processing and Information Technology, 2011. Here, the system applies a 2nd order clustering approach by



combining the Fuzzy C-means algorithm with the Hierarchical one. The approach was used to identify rare cases from 1572 patient cases in the domain of post-operative pain treatment. The results show that the approach enables the identification of rare cases in the domain of post-operative pain treatment and 18% of cases were identified as rare. The results shows that with the given dataset the proposed approach allows identification of "rare cases" that often cause high level of pain (57% compared with 23.6%) without including the pain level i.e. outcome in the clustering.

Combining case-based retrieval with knowledge discovery, in terms of clustering and outlier detection, enables experience reuse by identifying rare cases. The identified rare cases are incorporated into the CBR system in order to provide better decision support in a medical domain where it is essential that the physician also is aware of rare cases, especially with a less desirable outcome. The work has been presented in chapter 4.2 in a doctoral thesis report titled "A MULTIMODAL APPROACH FOR CLINICAL DIAGNOSIS AND TREATMENT" and thesis no "113". Here, two-step retrieval has been conducted where in the first step a new case is compared with the center of each clusters, a similarity value is calculated and all the clusters are sorted according to the similarity value. Then, in the second step, the new case is compared to only the cases that belong to the selected clusters. Moreover, the retrieved cases are presented (as regular and rare) together with their clusters.

The interface for "the bedside point of care use" presents results and statistical information on treatments and outcome for patients similar to the current patient. The interface and presentation has been developed in close collaboration with physicians testing the tool. The decision support system has been implemented as a tool and evaluated by physicians in a number of hospitals (se WP 8). The system runs and is tested in PC/MAC computers, IPADs and Mobile phones, <https://www.pain-out.se> gives bank security. The system uses the full Pain-out registry (currently 35 000 records).

Every patient is a model and the system identifies similar models by using domain knowledge to find relevant similar patients, used to provide the clinician with relevant and valuable information on this group of patient, transferring the relevant experience from the Pain-Out Registry to the physician providing knowledge valuable in the decision process in how to treat the patient at hand. The system also gives an overview over what medication similar patients have received.

#### **Work package 5 – Electronic Knowledge Library (Narinder Rawal, Universitetssjukhuset Örebro)**

The objective of this work package was to setup an Electronic Knowledge Library (EKL) on management of pain after surgery. The EKL provides users with summaries of contemporary national and international guidelines about major issues related to management of postoperative pain, with direct access to the source citations.

The first step in setting up the library was to decide on criteria according to which sources will be included in the EKL. Sources were included if they addressed management of postoperative pain; were evidence-based, written by an authoritative body, i.e. national or international society of anaesthesia or pain or surgery, were published during the last 8 years and were publicly available.

The EKL was piloted by asking potential users to provide feedback about content and format of three sample chapters. Feedback was given by an international audience, consisting chiefly of anaesthetists but also nurses and a surgeon. The majority of readers found the content useful and would consider using the EKL once more chapters were available. Readers requested that the chapters would be written according to a uniform format. In response, templates were created for the three major sections of the EKL. The templates promoted uniformity in the writing of the chapters and also served as guide to authors while they were writing up a particular chapter.

The current version of the EKL includes 4 sections. General aspects in management of post-operative pain; Treatment specific topics; Patient or condition specific topics Procedure specific topics and 32 chapters.

The EKL is accessed via the PAIN OUT homepage. Chapters are web documents that include direct, hyperlinks links to the sources. To make the EKL easier to use the documents were converted from WORD documents to HTML format (conforming to the HTML5 standard). This allows that multiple windows can be accessed and open at once. For example, the chapter being read, hyperlinks to the various sources that the chapter is based on and also to one or more EKL chapters which are referred to in this particular chapter. Documents can be resized so that they can be accessed by mobile devices (e.g. tablet -PC or 'Smartphone'). We aim that the EKL will be updated periodically, to include updates of the guidelines we are currently using and new guidelines that will be created over time.

#### **Work package 6 - Health Economics (Rod Taylor, University of Exeter)**

Objectives of this work package were to assess healthcare utilization costs associated with management of postoperative pain and to explore the variation in these costs across healthcare systems in Europe.

#### **Pilot study**

Between March and September 2010, a pilot study was performed in the Bart and The London Hospital in United Kingdom. This pilot sought to assess the feasibility and acceptability of data tool to collect healthcare resource utilisation and health-related quality of life (HRQoL) outcomes associated with post operative pain management.

Whilst we were able to successfully collect a large quantity of health care utilisation and quality of life (SF-36 and EQ-5D) data (in 228 patients), aspects of the data collection were found to be challenging. First, the time demands on research and clinical staff to collect this level of healthcare utilisation data were high. Furthermore, whilst possible to collect and reliably estimate the specialist pain team time associated with post-operative pain management of patients, it did prove feasible to obtain such timings data from general medical staff.

Our experience indicated that the application of this pilot study data too and level of healthcare resource utilisation data collection would not be feasible to roll out across PAIN OUT centres. As a consequence, following discussion with the central PAIN OUT coordinating team in Jena, it was decided that a reduced ('cut down') health care resource cost data tool needed to be developed and that we needed to test this tool within a more constrained data collection exercise across PAIN OUT sites. This multi-centre data collection exercise is described below.

Results of our single centre pilot study showed that:

- (1) a proportion of patients continue to experience severe pain at 7 days post-operatively, even after minor surgery;
- (2) quality of life is strongly associated a patient's level of post-operative pain; and
- (3) quality of life assessment provides additional data on the impact of post surgery pain on patient's function and well-being.

An analysis of the cost data from the pilot study is currently in process.

#### **PAIN OUT multicentre study**

Based on the experiences of the pilot study, a modified and shorter 'cut down' health care utilisation data tool was developed that could be rolled out to PAIN OUT centres to allow comparison of health care utilisation for selected high maintenance pain management techniques between centres that use specialist pain teams.

To maximise the acceptability and likely success of this multicentre data collection exercise it was decided that the PAIN OUT core questionnaire would not be applied to patients during the period of healthcare utilisation data collection.

#### **Methods**

##### **Centre and patient inclusion criteria**

To be included centres had to meet the following criteria:

- have an acute pain service (APS) undertake at least one of the following postoperative analgesia techniques: intravenous patient controlled analgesia (PCA), epidural infusions/patient controlled epidural analgesia (PCEA), or continuous/catheter peripheral nerve block
- be able to collect data on all patients the above analgesia techniques for a period of at least 2 weeks aiming for a minimum of 30 complete data sets (on consecutive patients) per hospital. If all 3 techniques are audited a minimum of 45 complete datasets should be the target.
- have a specialist pain team (anaesthesia led or pain nurse led) involved in the care of patients with these analgesia techniques.
- that the study falls within centre local ethics committee's rules on collection of audit data and does not require patients' consent.

For patients to be entered in eligible centres they had to meet the following additional criteria:

- undergoing surgery requiring regional or general anaesthesia in an operative department included in the cost data collection.
- started on either an intravenous PCA, an epidural infusion or PCEA, or a continuous or catheter delivered peripheral nerve block for postoperative analgesia during or directly after this operation.

##### **Data collection tool**

The tool required details of staff time, drugs and materials used in theatre and recovery associated with post-operative pain management for each patient.

#### **Results and conclusions**

The cut down tool was applied across three post-operative pain procedures (epidurals, PCA, blocks) in 7 PAIN OUT centres. The multicentre study demonstrated that it was feasible to collect data on healthcare utilisation during the post-operative period including pain team time and physical resources, as assessed by the number of bags used for each

procedure. Post-operative healthcare utilisation data was collected on a total of 323 post-surgery patients.

The results of the multi-centre study showed considerable variation in the level of healthcare utilisation across centres for each of the three post-operative pain procedures. For example, for epidurals, the level of pain team activity associated with the management of post-operative varied some 4-fold in terms of patient visits, i.e., median of 2 patient visits (Barcelona and London) versus 8.5 visits (Homburg) and pain time team time per patient varied some 5-fold, i.e., median of 17.5 mins (Barcelona) versus 88.5 mins (Homburg). Large differences across centres were also seen in the average amount of staff time associated with a procedure-related injection and procedure setup time. Finally, there was considerable variation across centres in the proportion of time associated with different health professional groups. For example, for epidurals, the percentage of pain team doctor time involvement varied in one centre from 0% (Barcelona), i.e., the procedure was entirely undertaken by a pain team nurse, to 100% in another (Jena), i.e., the procedure was entirely undertaken by pain team doctors.

Whilst, we were only able to collect data from a sub sample of PAIN OUT centres and limited number of pain procedures, results indicate that different centres have established contrasting models of service delivery. Future studies show investigate whether these contrasting models of post-operative care (and healthcare costs) can lead to important differences in patient's pain and quality of life experience following surgery.

#### **Work package 7 – Age and Gender: Bridge inequalities (Esther Pogatzki-Zahn, University Hospital Münster)**

Objectives of this work package were to identify and possibly reduce differences in treatment and outcome of postoperative pain between genders and age groups.

The first steps in order to meet the objectives were two analyses:

1. One analysis was related to pain data sets from University Hospital Münster to identify gender differences in patients receiving epidural analgesia after surgery
2. The second analysis used a broader approach aiming to identify gender and age related differences in treatment and outcome of postoperative pain after a different orthopedic surgeries and pain management techniques.

Data from patients undergoing orthopedic surgery at the University Hospital of Muenster between March 2010 and June 2011 were analyzed. The PAIN OUT questionnaire was used to assess postoperative pain, pain related psychological variables, opioid consumption, satisfaction, and side effects on the first day after surgery. Additionally, preoperative, operative and anesthetic parameters were recorded. Data were compared with SPSS Statistics 19.0 between women and men. A stepwise multivariate analysis of variances (ANOVA) was used to investigate possible influencing factors on sex differences. We analyzed data from 980 patients (403 females, 487 males). Women reported higher postoperative pain scores ( $p=0.000$ ) and a higher cumulative opioid consumption ( $p=0.012$ ). Adverse events, like nausea ( $p=0.002$ ) and dizziness ( $p=0.012$ ), were more often reported by women compared to men. Gender differences were more pronounced in older patients, patients not receiving regional

analgesia techniques and patients with preoperative chronic pain. The multivariate ANOVA revealed that age was the most important factor influencing these sex differences.

Based on these results we analysed the whole pain out dataset (international, 50 centers, appr. 26000 data sets) for risk factors predicting postoperative pain outcome including gender and age. We have chosen the following variables as outcome criteria: worst pain in the first 24h postop, duration of severe time in pain, in bed activities, amount of pain relief. All analyses were performed with SPSS 21.0.

Our data indicate that the factors "preoperative pain greater than 3" (Odds ratio (OR): 1.84, p less than 0.001), "younger age less than 20" (OR: 1.86, p=0.015) and "use of preoperative opioids" (OR: 1.9, p less than 0.001) were higher risk factors than female gender (OR: 1.51, p less than 0.001) and surgery duration (OR: 1.5; p less than 0.001) for the prediction of worst pain. Interestingly the OR for worst pain in the different age decades decreased almost linearly from the youngest to the oldest age group; furthermore only in the youngest group this result was significant. Similar results were calculated for the prediction of the other pain outcomes (percentage of time in severe pain, amount of pain relief, level of interference of pain with in bed activities (data not shown)).

We would advise caregivers to be aware of these risk factors and treat patients with one or more of these risks with special care.

#### **Work package 8 - National project implementation (Ruth Zaslansky, University Hospital Jena)**

Objectives of this work package were to prepare the necessary groundwork in each National Clinical Consortium Site (NCCS) for data collection and implementation of the feedback technology; to assure proper data collection and transmission from each NCCS to the registry; to assure proper use of the feedback, CDSS and EKL in each NCCS and to find new sites for implementation of the project.

During Year 1 and half of year 2 of the project, NCCS leaders assisted in establishing the groundwork for the project, namely, participating in the consent process which was the basis for devising the questionnaires (outcomes and process) for the project; applied and received approval from local ethics committees, appointed Research Assistants (RAs), participated in the process of translation and back-translation of the patient questionnaire into the local language of participating sites. Following this, RAs were trained about the objectives of the project and methodology of data collection. For this, standard operating procedures were set up. RAs in each site have been collecting data, inputting it into the web-based mask and assessing the process.

We have used the same methodology to train RAs in new sites which have joined the project, as part of a preliminary process of dissemination. An e-learning module to train data collecting RAs in additional sites has been developed (see <http://www.cognomedic.de/painout/> online).

The tools for collecting patient outcomes and processes were evaluated by the research assistants.

A paper has been submitted to a scientific journal (PAIN) describing the results of the work developing and testing PAIN OUT in the NCCS, use of

the data collection instruments, the feasibility of continuous data collection to constantly update the registry and illustrate site-specific information feedback. We have carried out analyses of the data to illustrate the potential informational value of a multi-center, international, acute pain registry for clinicians, researchers and healthcare policy makers.

By end of 2012, more than 35,000 datasets have been collected in 11 PAIN OUT clinical sites and 39 additional PAIN OUT International sites.

The EKL (WP5) was assessed by clinicians internationally using a web-based feedback form. The prototype of the CDSS was also assessed by the NCCS site leaders.

Dissemination of the project to new clinical sites is described in work package 9.

#### **Work package 9: Dissemination**

**(Margarita Puig, Parc de Salut Mar, Hospital del Mar, Barcelona)**

Objectives of this work package were the dissemination of the project to new sites within and outside Europe; setup of a sustainable financing of the project; rise of public awareness and dissemination to other fields of medicine.

**PAIN OUT International:** In the early stages of the project, clinical sites within and outside Europe have expressed interest to join PAIN OUT. Therefore, a framework to make this possible was developed. After evaluating if a new hospital meets the requirements for joining (i.e. sufficient number of procedures, English speaking staff), an agreement is signed that rules data security and privacy issues, publication rights, data use, liability and duty of care. After which, the new participant has to make sure that the standard operating procedures for the data collection are followed. More than 60 hospitals from both Europe and outside Europe have signed this PAIN OUT International Agreement. By end of 2012, 37 of these hospitals actually contributed to the data collection.

**Addressing needs of less developed countries:** Data is being collected as part of POI in one hospital in Malaysia (for over 2 years). We gained experience about the feasibility of implementing the project in Serbia, Rwanda and Gaza. The main problems these sites face are difficulties with finding personnel for data collection, training the research assistants at a distance, and obtaining basic resources such as access to internet or paper for printing the questionnaires. We are also in the process of developing an 'International Pain School'. This consists of a series of talks about pain management written by experts associated with IASP and EFIC. The talks will be piloted in two low resource countries (Albania and Kenya), after which they will be available in the websites of organizations such as the IASP so that physicians in low resource countries can download them and present the information to their colleagues. We anticipate that teaching staff about pain (=Pain School), together with data collection and feedback of the results (=benchmarking), will be more effective strategies for improving patient outcomes than either activity on its own.

**Cooperations:** In order to encourage dissemination to hospitals outside Europe, the International Association for the Study of Pain (IASP) was

approached. The governing body of IASP agreed to establish close cooperation with PAIN OUT. A Working Group dedicated to the International Pain Registry will jointly promote and support research, education and improved management in the PAIN OUT project. IASP provided funds to test feasibility of implementing PAIN OUT in 5 hospitals in low resource countries over one year. The results of the testing will be used to develop a broader plan of implementation.

A grant application to the European Society of Anaesthesiologists (ESA) Clinical / Translational Research Network (ESA-CTN) was awarded to Prof. D Fletcher (PI, NCCS leader, Paris), to study possible factors leading to chronic pain after surgery using PAIN OUT methodology to follow-up the patients. Dr Fletcher's was one of the five applications granted (June 2010). The ESA-CTN was created to provide infrastructure for trans-national European collaborations to improve patient care in fields related to anaesthesia and pain. The ESA-CTN grant for trans-national, multi center studies is an excellent opportunity to initiate a group effort where PAIN OUT members and the ESA will closely collaborate.

In order to raise public awareness, the PAIN OUT project was presented on more than 60 meetings/conferences by end of 2012, among them all the important international and European congresses on pain, initiated by societies such as IASP, EFIC, ESA, ESRA.

We are currently assessing the application of the methodology of PAIN OUT to be used in Emergency Departments (ED). The dissemination to EDs is justified on the basis of the high prevalence of acute pain in patients admitted to EDs, the inconsistency of analgesic treatments provided, and the need to properly treat acute pain in order to prevent pain chronification.

Consent on a publication plan and schedule: The project's publication committee prepared a document outlining the strategy and guidelines of how collaborators will have access to data from the PAIN OUT registry, carry out studies and publish the results. Consent for the document was given by all collaborators. A similar document was prepared for PAIN OUT International members. The document was updated for use when PAIN OUT continues after the end of funding.

Financing the project after end of EC funding: UKJ developed a financing plan for the time after funding. Participating clinical sites will have to pay a yearly fee for participation in PAIN OUT. In the German QUIPS project, this concept has already been proven to be working so that we are optimistic to be able to finance the continuation of PAIN OUT. The legal basis for this concept is a continuation agreement that has been signed by the PAIN OUT beneficiaries who want to continue after end of funding.

## **Discussion**

### **a) Technical results.**

The achievements and tools of this area are characterized by the fact that all "front end" tools are designed to provide a concrete clinical benefit for care givers and their institutions. The Feedback and Benchmark module as well as the EKL are in routine use by project partners as well as more than 40 additional PAIN OUT international sites. Feedback and benchmark features have been continuously improved according

to needs of users who report an immediate clinical benefit for their daily work (strengths, weaknesses and variability of clinical care is immediately mirrored and set into perspective by comparison to data from other hospitals). Additional, "best practice" and "learning from the best" approaches further increased attractiveness of this project. This benefit is the main reason of the outstanding acceptance of both individuals as well as institutions, and thus facilitates dissemination of PAIN OUT. Often registries have the problem to get data on a voluntary base because data collectors don't get anything "back". Traditionally, this problem is overcome by a "money-for-data" policy or by legal obligation. Both solutions do not result in "endogenous" motivation, they are costly and/or cumbersome. Our approach, in contrast, motivates sites not only to obtain high quality data (because it is the prerequisite for their high-quality feedback), but allows to offer participation on a voluntary base (as proven by the unexpected high number of additional PAIN OUT int. sites - see WP 8,9) or even charge them moderately, thus facilitating project continuation on a self-sustainable base.

Moreover, front-end tools are shaped for use in every day practice. The relatively high number of clinical project partners permitted to test the systems under daily life conditions in different European countries, in different settings, and by different professions (e.g., nurses, physicians, administrators). Their advice, comments and formal feedback lead to continuous improvements of user friendliness of data collection, inputting, and feedback features.

A major achievement of PAIN OUT is the development and validation of a multi-lingual questionnaire to obtain patient-reported outcomes (PRO) in the postoperative setting. During this process, it turned out that an American group worked on a similar project (American Pain Society Quality of Care Committee, developing the APS-POQ-R questionnaire). Thus, although not previously planned, a close co-operation with this group was established which not only led to participation of five large US sites on a voluntary base but will "open" the North American "market" for the project. Translation in up to now 17 languages makes PAIN OUT's IPO to best validated multi-lingual instrument in the field of postoperative PROs.

The case-based Clinical Decision Support System is perhaps the most "experimental" tool of all front-end features of the project. It should be highlighted that the developed prototype is one of the first case-based CDSS electronically linked with a routinely used data base containing real patient cases from everyday clinical routine, which has been established and tested in the field of pain medicine, if not the whole area of medicine. It has been repeatedly shown that most physicians and nurses prefer to receive support for clinical decision making from other colleagues than from published evidence and scientific research. Thus, the CDSS developed by PAIN OUT does not only mimic this attitude but makes the cumulated experience usable for other caregivers. This "hidden" information would otherwise not be accessible for daily practice. Moreover, the clinical value of the case-based CDSS grows with increase of the database without need of frequent updating of the CDSS itself. CDSS piloting made obvious that such an "electronic" approach of exchange of clinical experience is still unfamiliar for nurses and physicians, and front-end features, search algorithms and feedback formats may be further improved. However, feedback was very encouraging, specifically in uncommon clinical situations (e.g., rare surgeries, very old and morbid patients, use of uncommon or very new drugs) which are



hardly studied by RCTs or other forms of EBM. Thus, the case-based CDSS differs substantially from conventional rule-based, knowledge-based or expert CDSS, and it is a clearly innovation in the field of decision support. From all technical results, it bears the largest potential for further commercial use and is able to give added value to the PAIN OUT registry and there is effort on-going to bring it out to clinicians as a product offered to hospitals by the PAIN OUT consortium (under construction).

The CDSS is complemented by the Electronic Knowledge Library. While the CDSS provides physicians, via the registry, with experience and information obtained from other clinical settings and colleagues, the EKL provides evidence-based information derived from guidelines based on randomized controlled studies. Although this information is globally available, it is perceived as less helpful in everyday clinical practice for a variety of reasons. These include the limited transferability of RCT-derived results into clinical practice and that the evidence-based information can conflict with established, local practices resulting in 'clinical inertia', meaning, slowness to updated practices in light of evolving evidence.

Again, it is a unique feature of PAIN OUT to combine both "worlds" of clinical evidence, namely results from experimental research as well as data from real life, in one project. Thus, this approach will help to bridge the gap between experimental efficacy and every day effectiveness which has been claimed so often in the field of evidence-based medicine. Furthermore, both sources of support for clinical decision are provided online, realtime, and at point of care.

Data collection of health economic data faced the group with some challenges. Whilst it was possible to collect detailed post-operative healthcare utilisation data including specialist pain team time and data on patient quality of life, the demands of this data collection process were high and, therefore, judged not to be feasible in the context of the PAIN OUT registry. Based on the experience of the pilot study, a shorter/less detailed data collection tool to collect healthcare utilisation data was developed. This tool was applied across three post-operative pain procedures (epidurals, PCA, blocks) in 7 PAIN OUT centres. This multicentre study demonstrated that it was feasible to collect data on healthcare utilisation during the post-operative period including pain team time and physical resources, as assessed by the number of bags used for each procedure. Post-operative healthcare utilisation data was collected on a total of 323 post-surgery patients. This 'cut down' health economic data collection was still informative and indentified some important variations across centres.

#### b) Scientific results.

In-depth analysis of registry data took place so far related to the topics

- health economics;
- gender and age issues; and
- patient satisfaction.

Results of the health economics single centre pilot study showed that:

- (1) a proportion of patients continue to experience severe pain at 7 days post-operatively, even after minor surgery;

(2) quality of life is strongly associated a patient's level of post-operative pain; and  
(3) quality of life assessment provides additional data on the impact of post surgery pain on patient's function and well-being. An analysis of the cost data from the pilot study is currently in process.

The results of the second multi-centre study showed considerable variation in the level of healthcare utilisation across centres for each of the three post-operative pain procedures. For example, for epidurals, the level of pain team activity associated with the management of post-operative varied some 4-fold in terms of patient visits, i.e., median of 2 patient visits (Barcelona and London) versus 8.5 visits (Homburg) and pain team time per patient varied some 5-fold, i.e., median of 17.5 mins (Barcelona) versus 88.5 mins (Homburg). Large differences across centres were also seen in the average amount of staff time associated with a procedure-related injection and procedure setup time. Finally, there was considerable variation across centres in the proportion of time associated with different health professional groups. For example, for epidurals, the percentage of pain team doctor time involvement varied in one centre from 0% (Barcelona), i.e., the procedure was entirely undertaken by a pain team nurse, to 100% in another (Jena), i.e., the procedure was entirely undertaken by pain team doctors.

Whilst we were only able to collect data from a sub sample of PAIN OUT centres and limited number of pain procedures, results indicate that different centres have established contrasting models of service delivery. Future studies should investigate whether these contrasting models of post-operative care (and healthcare costs) can lead to important differences in patient's pain and quality of life experience following surgery.

From the results of the first Gender/Age WP analysis we conclude that clinical relevant gender differences in postoperative pain and opioid requirement are evident and increased in older patients, patients with preoperative pain and patients not receiving regional analgesia techniques. Thus, female patients with one or more of these additional factors need more awareness with respect to an optimized perioperative pain management.

The second analysis demonstrates that gender might not be the most important risk factor for postoperative pain outcome. Moreover chronic pain patients with the need for opioids undergoing surgery might be at the highest risk for severe postoperative pain, and therefore need appropriate awareness and pain treatment.

These analyses are only some examples of the scientific potential of the large and still growing data base. Several additional analyses have been already initiated which have not been part of the original DoW. Another example from the German "sister" project QUIPS is the recent landmark publication on painfulness of different surgical procedures.

Another characteristic of the project is the possibility to conduct additional prospective studies by "adding" further parameters and items to be collected for specific research questions and a specific time frame. This is only possible in continuously ongoing registry projects with existing data collection infrastructure in contrast to a completed or "closed" data bank. This potential of PAIN OUT has been proven by the successful application for funding from the European Society of

Anaesthesiologists' Translational Research Network for an add-on to study possible factors leading to chronic pain after surgery using PAIN OUT methodology to follow-up the patients. These activities show the attractiveness of a large scale data base for researchers.

Another important future field of research will address public health issues in developed and less developed countries. Right now, very few knowledge exists on quality and variation of care in many middle and low income countries of Europe (and other parts of the world). The constantly growing European Pain Registry will allow identifying areas with need of improvement in terms of availability of better EBM-derived knowledge, drugs and methods, staff skills and more.

c) Implementation and dissemination of results (WP 8 and 9).

PAIN OUT was successfully implemented in the 11 clinical sites of the project beneficiaries as well as in 39 additional hospitals from all over the world. Implementation included training of data collectors, setting up standard operating procedures to ensure standardized collection and input of data, development of an e-learning program and ongoing support of the data collecting research assistants.

The rapid dissemination of the project even before end of funding and before it's "formal" launch together with IASP is perhaps one of the most important results achieved. Moreover, not only European sites but clinicians and hospitals around whole Europe joined the project, and many more expressed their interest to do so. Feedback from these additional sites was most often indicating that PAIN OUT - although demanding moderate resources for participation - gives "something back" which is clinically useful. Benchmarking with other sites and web-based, immediate feedback (in contrast to written reports after months or later as in other registry projects), easy access to EBM sources, user-friendliness and the possibility to contact colleagues and to learn from each other were repeatedly mentioned as reasons for participation. Specifically colleagues in middle- or low-resource areas characterized the project as "giving us the feeling to be part of a network".

Patient-reported outcomes - instead of surrogate quality indicators as chart data - are more demanding to obtain but mirror "real life" and outcome much more reliable. These data helped participating staff in several sites to convince their colleagues and administrators "action is necessary", that patient care has to be improved and variability of care should be reduced.

Results were disseminated on 70 national and international meetings and conferences and by 9 publications in scientific journals; further publications are in preparation.

To enhance dissemination, contacts and co-operation with professional societies and potential project partners after the funding period have been intensified and established. PAIN OUT is collaborating with the International Association for the Study of Pain (IASP), the largest international multi-disciplinary society of pain, as well as with its European counterpart, EFIC. Both societies will help to promote PAIN OUT and its work amongst its members.

The rapid dissemination even in the US clearly demonstrated that the US-based International Association for the Study of Pain (IASP) chose PAIN

OUT and not competing North American initiatives as cooperating partners. As stated in our DoW, several similar international initiatives have been planned at the time of submitting the PAIN OUT application. Seventh Framework Programme (FP7) funding could successfully push the European initiative even on the beyond the European level, resulting in one competing project to be stopped (supported by the American Society of Regional Anesthesia), and another one being still restricted to the US.

Co-operation with scientific societies, a non-for-profit financing concept, and an academic institutional background (in contrast to commercial companies working in the field of quality improvement) turned out to be an important argument for hospitals to participate in PAIN OUT.

During the two "Societal Impact of Pain" meetings (2011 in the EU parliament in Brussels, 2012 in Kopenhagen), organized by the European Federation of IASP chapters (EFIC) in cooperation with a large number of patient organisations and other stakeholders in the field of pain, PAIN OUT was involved not only as official endorser but in several presentations and talks.

The consortium has agreed to continue the project after end of funding, contracts and the organizational structure have been agreed on, and a financing concept for continuation of the project after end of funding has been developed.

Sustainability and a realistic financing concept were important parts of the dissemination WP. Based on our experience with German "QUIPS" project and the acceptance of the developed financial concept by the current participating sites we are optimistic that PAIN OUT will soon reach a self-sustaining state. The proposed participating fee (1500 EUROS/year/hospital) is perceived as very low (although in less developed areas support may be needed, and sponsoring programs for these regions are planned by IASP). Staff resources for data collection will be more challenging in developed countries but approaches for minimizing required staff time by e-teaching, tablet-based data collection and random patient sampling will reduce this problem. In Germany and Austria, as developed countries with relatively high salaries, currently 155 hospitals are participating in the German project, collecting data, and pay a yearly fee without any legal obligation.

A small part of PAIN OUT addressed co-operation with settings in low-resource countries. Aim of these activities was studying feasibility and assessing interest concerning benchmark and feedback approaches in these areas. Even in the pilot phase before start of Seventh Framework Programme (FP7) funding, two sites in low developed regions (Gaza strip and Kenya) participated successfully in a feasibility trial. Thus, it was not surprising that a couple of low- and middle income areas are represented amongst the additional PAIN OUT participants, and both sites even presented their results in scientific meetings. Certainly, PAIN OUT will not become an essential tool in a high number of hospitals in such countries but it might help to disseminate knowledge and evidence-based information from selected sites. Moreover, even preliminary analysis of collected data indicates that developed settings do not always perform better in terms of pain management and patient-reported outcomes. In contrast, in some situations high-level institutions may learn a lot from so called low-resource sites. Thus, "learning from each other" seems not to be a one way process but a forth-and-back exchange.

Another important political argument for including a wide range of countries outside Central Europe and North America is the fact that the vast majority of RCTs is conducted in these highly developed countries. However, it is not known if its results are transferable to other regions. A large data base containing routine data from these areas allows to adjust findings from highly industrialized to other parts of Europe.

**Potential Impact:**  
**Expected impacts**

There is a variety of means according to which PAIN OUT contributes substantially towards the impacts envisaged by the European Commission in the Theme "HEALTH" work program of Seventh Framework Programme (FP7) and those specifically addressed by the topic HEALTH-2007-3.1-4, Impact on activity 3: "Optimising the Delivery of Health Care to European Citizens"

PAIN OUT provides tools to compare treatment strategies across Europe, to support health policy-driven research at the European level, in particular through benchmarking, comparisons and analysis of models, systems and use of databases.

The PAIN OUT registry, already now the largest data base in its field worldwide, is and will keep on generating knowledge from different health care settings in European countries to facilitate informed decisions on effective strategies in therapy of postoperative pain, and thus adds observational-derived information to evidence-based derived information.

After four years of developing the methodology for the registry and continuous collection of data for 3 years, the registry consists of datasets from over 35,000 patients from 50 clinical sites, the majority of which are in Europe but also outside of Europe. The registry consists of data about patients who have undergone surgery in a variety of specialities, for example, general surgery, orthopaedics, gynaecology, plastic and thoracic surgery. This large registry and benchmark system facilitates assessment of treatment strategies across Europe and in this way can support health policy-driven research at the European level and also at national levels.

PAIN OUT collaborators regularly presented findings from the registry at scientific meetings during which they were able to compare management of patients in different healthcare centers and countries in Europe. The database is being used to generate knowledge, to facilitate informed decisions on effective strategies in therapy of postoperative pain.

On several fields, registry data revealed that everyday clinical practise may differ from evidence-based recommendations based on RCT. For example, we could show that a grade A guideline recommendation on pain management (daily pain assessment) was not associated with any clinically relevant improvement in patient-reported outcome. This was a consistent finding across all countries and sites.

The data collected in WP 6 showed that contrary to current expectations, a proportion of patients continue to experience severe pain at 7 days postoperatively, even after minor surgery. Furthermore, health-related quality of life (HRQoL) is strongly associated with the level of pain. Thus, quality of life assessment provides additional data on the impact of post surgery pain on patient's function and well-being.

As for RCTs and EBM-derived recommendation, methodological limitations of registry data have to be considered. However, these examples show that a large European database will have the impact to give additional information obtained from clinical routine to the clinician, will identify areas of improvable management of postoperative pain in Europe, and thus will lead research to fields with conflict results from registry and EBM data. This will result in better perioperative health care for citizens in Europe.

Work in PAIN OUT supports the objectives of the Community Action in the field of Health (2007-2013) Program, in particular the second and the third objectives. The second objective, Promote health for prosperity and solidarity, is being promoted by addressing inequalities in treatment and outcome between genders as well as in older patients.

In WP 7, Age and Gender: Bridge inequalities, it was found that to optimize perioperative pain management, clinicians should pay special attention to older female patients and that risk factors include having pain before surgery and lack of treatment with regional analgesia. Based on data from the whole PAIN OUT data base, a score will be created predicting development of severe pain after surgery, taking into account both the variables of patient gender and age.

Inequalities in treatment between people within Europe were further addressed by two workshops held at the International Conference on Acute Pain and organized by PAIN OUT in November 2012 in Berlin. The workshops addressed different issues related to age and gender and Ethnicity and Culture: Challenges and Opportunities for clinical management and research of acute pain. The data for both workshops was derived from the registry.

Even in a single country, differences in health care and needs of patients may exist: An analysis of the German pain data base revealed that after similar surgeries, patients in former East Germany report more pain intensity and receive less analgesics but feel more satisfied with this situation than patients in former West Germany.

A unique feature of the PAIN OUT data base is the fact that the ethical background of patients is recorded. Although no global "coding" for ethnicity exists and in some countries, national regulations impede collection of these data, PAIN OUT will be the largest data base in its field containing these data not only nationally but on an international level.

Thus, PAIN OUT will have a large impact on a better care for specific groups of patients, specifically vulnerable subgroups like very old patients or, potentially, certain ethnical groups. The prediction score will allow to translate these findings into everyday clinical practice. Furthermore, the broad area of European regions covered by PAIN OUT will allow to identify a local, regional and/or national need for improving (or changing) care. By these means, the large international data base will have an impact towards a more equal distribution of health care to patients in different regions of Europe.

The third objective, Generate and Disseminate Health Knowledge is being supported by exchange of knowledge, identification of best practice and bringing together expertise from different countries.

The Electronic Knowledge Library, with its summaries of a large number of topics related to management of postoperative pain from contemporary guidelines, is a means to disseminate current evidence-based knowledge to healthcare providers, specifically to those in non-academic settings who treat the majority of patients after surgery but not normally only have limited access to scientific sources. Having a version which can be used on handheld electronic devices is another means to facilitate dissemination of the healthcare knowledge at point of care. Thus, the EKL is a source for clinicians and administrators who intend to implement local, organizational changes and require information about the current standards.

The benchmarking facility of the registry allows identification of healthcare centers which engage in best practices with regards to different surgical procedures. This type of assessment is not possible with traditional RCT methodology. Sites providing best patient outcomes for the most commonly procedures were identified, and staff from these sites described how these were accomplished. This expertise is now available for other collaborators in the PAIN OUT website. As the database continues to grow, it will be possible to identify additional sites providing best outcomes and add to the existing library. Therefore, PAIN OUT is an example how "learning from each other" and "identification of best practice" approaches can be based on real-life outcome data (instead of surrogate items describing structures and processes), can be implemented into daily clinically routine, and reach those care givers who work on the bedside (and not only top-level management). Based on our previous experiences with the German sister project, we expect a large impact on dissemination of knowledge, improvement of clinical routine, facilitation of change management, and quality of patient care.

Impact on sub-theme 3.1: "Translating the results of clinical research outcome into clinical practice"

The International Pain Outcomes (IPO) questionnaire provides the tools for carrying out benchmarking and comparative analysis at the local, national, European and international levels and using the information as a basis for improving the quality of care provided to patients. It will take time to implement changes in the different medical centers; however, the first stage is to use tools for clinical research which allow for standardized assessment. PAIN OUT provides such tools.

The IPO questionnaire, validated and translated into 16 languages, enables assessment of a wide population of patients across Europe using standardized methodology. To date, the other validated questionnaire for assessing acute pain, developed by the American Pain Society, was available up to recently in English only.

At the local level, PAIN OUT NCCS leaders have been presenting data collected in their site to demonstrate outcomes in their hospital to their colleagues and to use this as a basis for change. Work carried out in eight PAIN OUT sites in Catania, Italy, is another example of comparative activity carried out on a local level. Data in these sites is collected by anesthesia residents and this is regarded as an integral part of their training as physicians. Consequently, over a period of two years, data was collected from 2441 patients. The anesthesia residents meet on a regular basis to review the data they collect. Their findings were presented at the IASP meeting in Milan (Minardi et al , 2012;

Sandfilippo et al, 2012). Their findings indicate that methods for provision of analgesia commonly used in large hospitals in Europe (= patient controlled analgesia (intravenous or epidural) are not used at all, and that opioids, the class of medications recommended by guidelines for severe pain, are used infrequently.

An analysis of the international database as a basis for developing quality improvement guidelines to optimize multimodal treatment in spine patients comprised over 1000 patients who underwent spine surgery in 26 hospitals. The findings will be presented at the meeting of the American Pain Society in the context of the Special Interest Group of Advancing the Science of Quality.

In WP6, the results of the multi-centre assessment of costs of healthcare utilisation across centres for three post-operative pain procedures, showed large differences across centres with regards to the average amount of staff time associated with a procedure-related injection and procedure setup time. There was considerable variation across centres in the proportion of time associated with different health professional groups. While data collection was limited to a sub sample of PAIN OUT centres and number of pain procedures, results indicate that different centres have established contrasting models of service delivery. Future studies could investigate whether these contrasting models of post-operative care (and healthcare costs) can lead to important differences in patient's pain and quality of life experience following surgery.

Moreover, the Electronic Knowledge Library (EKL) will help to translate results of existing research into daily routine by offering point-of-care access to these data.

Taken together, PAIN OUT will have impact on implementing clinical research findings into daily routine by different means and on national as well international levels. It will provide clinicians with feedback and benchmarking, allowing them to track results of clinical changes and guideline adherence. Furthermore, it will offer immediate access at point-of-care to research-derived and evidence-based recommendations via EKL.

The project supports European research in several ways. Registry data is being used as a basis for observational (epidemiological) studies. The data in the registry has been a source for several papers.

The infrastructure developed in the framework of the project allows expansion to conduct prospective studies. The study initiated by Professor Fletcher (NCCS leader in France) to assess development of chronic pain after surgery, is such an example. It is using PAIN OUT tools to assess patients in the first day of surgery but the study required additional development of software and questionnaires to enable assessment of patients 6 and 12 months after surgery. This project is facilitated and co-funded through collaboration with the European Society of Anaesthesiology (ESA) Clinical Research Network.

The PAIN OUT infrastructure was also used to set up prospective data collection in another group of patients, patients admitted to the Emergency Department (ED). This is another group of patients with considerable variation in treatment, lack of tools to assess their outcomes across Europe and little information about treatment. In Germany and Spain, a pilot project, using the PAIN OUT questionnaire as a basis,



was used to collect data from approximately 1400 patients in the EDs of three hospitals (Jena, Barcelona and Oviedo). Data from Barcelona shows that when admitted to the ED, patients have on average high levels of pain, when discharged, pain levels were lower. The most commonly used medications were non-opioid analgesics and when opioids were used, it was mostly weak opioids.

The impact of PAIN OUT on European research will be further facilitated by close co-operation with European institutions as ESA and EFIC (European Federation of IASP chapters) and the International Association for the Study of Pain (IASP). PAIN OUT was invited to present its project and to report preliminary results on both World Congresses on Pain (2010 and 2012), on both European pain meetings (2009 and 2011) as well as on the last European Anaesthesiology meeting (2012).

Based on our successful experience in Germany, such co-operation will allow members of these European scientific organisations to use PAIN OUT data and/or to conduct prospective research using PAIN OUT infrastructure. As additional resources needed for study conduction are much lower compared to a complete set up of such studies, this type of co-operation is very attractive and welcome by these organisations.

#### **Impact on topic HEALTH-2007-3.1-4: "Improving clinical decision making"**

PAIN OUT will have impact on clinical decision making on several levels. The project is using a validated patient reported outcomes questionnaire, and providing clinicians with a user-friendly tool to improve clinical decision making in different fields of medicine.

By using the benchmark server, PAIN OUT users can see the result of the interventions they administered to their patients and are able to compare them with the outcomes in patients undergoing similar procedures and treated by their colleagues in other hospitals. This facilitates clinical decision making in several ways, as illustrated below.

First, clinicians get support to decide if effectiveness of their pain management is acceptable compared to similar settings. Second, as the system is not only feeding back pain intensity but also side effects, care givers receive information on complications and potential "overtreatment", e.g. high opioid doses which reduce pain but may cause nausea and sedation. The possibility to balance effects and side effects is not often featured in decision support systems. Third, feedback of outcome over time allows support on the decision if introduction of a new treatment in a specific setting improves clinical practice and should be kept or has no impact (or even a negative one) and should be stopped. The last example is of specific interest in daily care as results derived from small randomized controlled trials may work under experimental conditions but not in the heterogeneous settings of clinical routine.

Whereas the feedback and benchmarking software assists clinicians to assess outcomes on the level of one ward, hospital, national or even international level, the case-based Clinical Decision Support Software (CDSS) helps clinicians in making decisions for treating individual patients. The complete database is used and allows clinicians to search for patients based on variables such as age, gender, weight. The output in 'B' is data about which treatments were associated with the lowest or highest levels of pain. This information can be used by the clinician to decide which treatments he would like to administer to the patient he is

seeing. These can be elderly patients or with rare conditions which will not be typically evaluated in RCTs yet, their data will be included in the registry. Thus, the cumulated "experience" of other clinicians, collected in the data bank, will be made available for decision support in daily routine.

Case-based CDSS, using a real-life database as source, is so far rarely used in medicine. Pilot feedback during development of the CDSS was very positive, as this "philosophy" of decision support mimics the one preferred by most clinicians which is asking a colleague for his or her experience.

The third element of clinical decision support is provided by the Electronic Knowledge Library (EKL) which can complement information derived from the CDSS, thus providing the clinician with information from both real life as well as evidence-based data.

Both CDSS and EKL tool has been made available at point-of-care. This will have an impact on user-friendliness in daily care.

### **Impact on principle of clinical governance**

Clinical governance addresses three key attributes:

- (1) recognizably high standards of care,
- (2) transparent responsibility and accountability for those standards, and a
- (3) constant, dynamic of improvement. These principles are being promoted and advanced by our project in several ways.

Each of the three modules in PAIN OUT aims to help clinicians provide recognizably high standards of care. The feedback and benchmarking allows people to learn from each other and 'learn from the best'; the CDSS shows which treatments arise in the best (and worst) outcomes and the EKL is a source of RCTs and guidelines, which are what is currently regarded as the highest standards of care.

The benchmarking module and Healtheconomics provide real patient information, reflecting current treatment standards and demonstrate their change over time, thereby, enabling and promoting transparency and accountability on one hand and encouraging constant, dynamic improvement. The information is accessible via the web, at different levels of detail, to clinicians, researchers, hospital administrators and through publications to the public at large.

The continuously updating Pain Registry and benchmarking tool allows beneficiaries to continuously audit the outcome quality of their clinical practice, measure the use of resources, and identify best practices at the European level.

### **Dissemination and/or exploitation of project results**

#### **Leading professional societies**

We have carried out activities to ascertain sustainability of the project as well as its comprehensive dissemination in Europe. This includes, training and education activities (SOPs and e-learning module), organization of symposia (ESA; EFIC, IASP, APS), workshops and conferences (International Conference on Acute Pain), participation in

exhibitions, scientific publications, and permanent active public relation (PR) activities.

PAIN OUT has developed close collaboration with IASP which is expected to be sustained as PAIN OUT continues into the next phase of work, after funding. IASP is the largest international, interdisciplinary professional society in the field of pain.

In response to a request from the PAIN OUT group, IASP established a Working Group dedicated to registries. Consequently, the Working Group and PAIN OUT collaborators will work together to support pain management and research in developed and developing nations. The collaboration will provide IASP members with access to standard, validated assessment tools for feedback and benchmarking. IASP will gain prominence by offering the international community an international database on acute pain.

Since inception of PAIN OUT, collaborators have been presenting findings from the project at IASP meetings in the form of abstracts or invited workshops. As the number of PAIN OUT collaborators increased and the database grew, the number of presentations at these meetings has increased. IASP also supported the one-day workshop on the topic of Ethnicity and Culture: Challenges and Opportunities for clinical management and research of acute pain.

Collaboration with the American Pain Society and the Task Force for Quality enabled PAIN OUT to use their patient outcomes questionnaire as a basis for the International Pain Outcomes questionnaire.

Within Europe, PAIN OUT has been working with EFIC and ESA. Affiliation with ESA has led to dissemination of PAIN OUT in medical centers, mainly through the project assessing development of chronic pain after surgery. PAIN OUT collaborators presented findings from the project at ESA meetings. Collaboration with EFIC will be a means of finding new sites for disseminating the project, and venue to hold workshops for presenting results from the project. It is planned that ESA and EFIC meetings can be used to hold half day workshops for training research assistants from new sites.

#### **Dissemination of the tools for feedback and benchmarking**

The majority of activities related to dissemination centered on spreading the feedback and benchmark tools to additional medical centers within Europe and internationally. This started early in the project, ahead of the planned schedule.

The project spread to medical centers in countries such as Serbia, Moldavia, Ukraine, Rwanda, that otherwise would most probably not be engaged in this sort of activity.

#### **Dissemination of the EKL**

IASP consider that disseminating the Electronic Knowledge Library will contribute to its educational goals and have expressed willingness to assist disseminating the EKL to its members through such means as the IASP website.

#### **Impact on less developed countries**

Dissemination to low resource countries took on two forms. The first comprised testing PAIN OUT and its methodology in a number of low resource countries, within Europe, Serbia and outside of Europe, Gaza and Rwanda. The second is to develop a 'Pain School' in co-operation with IASP. We have learned in the pilot phase that teaching the staff about pain (Pain School), together with data collection and feedback of the results to clinicians (benchmarking), will be more effective strategies for improving patient outcomes than either activity on its own.

### **Impact on other areas of pain medicine**

The principles of PAIN OUT - standardized collection of meaningful routine data, feedback and benchmarking, case-based Clinical Decision Support, and facilitating access to evidence-based information - can be translated to most fields of medicine. Two pilot data collection have been performed in Emergency Room Departments which deal with a large number of patients in pain. Furthermore, in the German part of the project, a module for pediatric surgery has been developed, validated, and is in use in more than 10 sites. The European Society for Pediatric Anesthesia (ESPA) has asked to translate the German version into English and to perform a feasibility study in Europe. Currently, data and experience are analysed, and it will be decided on which of these fields PAIN OUT will be spread next.

Further requests for developing PAIN OUT modules have been made for the area of chronic pain. The ESA-funded subproject on persistent pain 6 months after surgery is a first step into this direction. However, for covering areas as chronic cancer or back pain, assessment tools have to be modified and validated which is only possible with adequate resources. Nevertheless, the infrastructure developed with PAIN OUT (specifically the software, feedback technology, and case-based CDSS features) as well as the large network of experienced clinical partners and the logistic support of the scientific societies will reduce required costs substantially compared to a new development of such projects.

### **List of Websites:**

<http://www.pain-out.eu>