Proceedings of the World Congress on New Technologies (NewTech 2015)
Barcelona, Spain – July 15 - 17, 2015
Paper No. 141

Prediction of Patient Controlled Analgesic Consumption Using Patient Demand Behaviours

Yuh-Jyh Hu
College of Computer Science, National Chiao Tung University
1001 University Rd., Hsinchu, Taiwan
yhu@cs.nctu.edu.tw

Tien-Hsiung Ku
Department of Anaesthesiology, Changhwa Christian Hospital
tienku@gmail.com

Yu-Hung Yang, Jia-Ying Shen
Institute of Biomedical Engineering, National Chiao Tung University
1001 University Rd., Hsinchu, Taiwan
daniel0318pisces@gmail.com; ingrid25109@hotmail.com

Abstract -Many factors affect individual variability in postoperative pain. Although several statistical studies have evaluated postoperative pain and analgesic consumption, previous research shows that the coefficient of determination of existing predictive models was small (e.g., R^2 = 0.17–0.59 for postoperative pain, and 0.27–0.46 for postoperative analgesic consumption). This study presents the real-world application of computational models to anaesthesiology and considers a wider variety of predictive factors, including PCA demands over time. It extends previous works by proposing a 2-stage computational strategy that combines clustering and regression to predict analgesic consumption. The results of the cross validation, and the comparison with human experts have demonstrated the feasibility of the proposed computational methods.

Keywords**:** pain management, patient-controlled-analgesia, regression, inductive inference, clustering

1. Introduction

The most common complaint that the medical staff gets from the patient is pain. It is one of the most commonly reported postoperative symptoms (Chung et al., 1996). Pain can negatively affect quality of life, and may do more harm than an illness itself when it becomes intolerable, making the patient both physically and mentally uncomfortable. Pain is a highly personal experience influenced by multiple factors, including sensitivity to pain, age, genetics, physical status, and psychological factors (Turn & Okifuji, 1999; Bisgaard et al., 2001). With the progress of medical science, people have gradually become aware of the importance of pain management. PCA (Patient Controlled Analgesia) is a delivery system for pain medication that makes effective and flexible pain treatments possible by allowing patients to adjust the dosage of analgesics. According to the research (Walder et al., 2001; Dolin et al., 2002), PCA is one of the most effective techniques for postoperative analgesia, and is widely used in hospitals for the management of postoperative pain, especially for major surgeries.

Most previous works on postoperative pain management were limited to evaluating the correlation of patient characteristics, such as demographic attributes, biomedical variables, and psychological states, with postoperative pain intensity or analgesic requirement (Gagliese et al., 2008; Chia et al., 2002; Pan et al., 2006). Although they identified several positive correlates, such as age and gender, their R^2 (coefficients of determination) were small. For example, the best predictor in an analysis of total analgesic need was the State Trait Anxiety Inventory, but its coefficient was only 0.22 (Pan et al., 2006).

This result suggests that other predictive factors are present that have not been analysed. Unlike other research, this study analysed PCA-related factors in addition to demographic and physiological attributes. We considered PCA demand behaviour patterns, and combined them with regression to construct the computational models for analgesic consumption prediction. The goal was to predict the total analgesic consumption of the patient according to his (or her) demographic features, physiological states, and the first few hours of PCA usage data. By the accurate prediction of analgesic consumption, we hope to provide an early warning for anaesthesiologists to make necessary changes in analgesic dosage or PCA control settings to improve patient satisfaction during postoperative pain management. We tested the trained models on real PCA patients, and compared them with medical doctors. The results showed that the proposed prediction models outperformed most of the human experts in accuracy, which demonstrated the feasibility of the computational methods.

2. Materials and Methods

2. 1. Analgesic Consumption Prediction as Inductive Inference

Unlike previous works that focused on the analysis of the correlation between correlates and postoperative pain or analgesic requirement (Pan et al., 2006; Chang et al., 2006; Bellville et al., 1971), we considered PCA analgesic consumption prediction as an inductive inference problem. When addressing an inductive inference problem by representing each example by a set of descriptive attributes, its target attribute, and the attribute values, an inductive inference task can be defined as follows.

Given:
$E = \{e_1, e_2, \ldots, e_n\}$ is a set of training examples.
$X = \{x_1, x_2, \ldots, x_m\}$ is a set of descriptive attributes, and c is the target attribute.
Each training example e_i is represented by a vector $<v_1, v_2, \ldots, v_m, t_i>$,
where $v_1, v_2, \ldots, v_m$ denotes a legal value, and t_i is the target value.
Assuming:
F:: $X \rightarrow c$ is the target function, which maps an example represented by a vector of Descriptive attribute values to its target attribute value.
Output:
H:: $X \rightarrow c$ is a hypothesis that approximates the target function, i.e. $H(X) \approx F(X)$.
We learn the hypothesis H that is closest to the target function F.
For a test example j, its target value is predicted as $H(j)$.

When provided a set of patients with known analgesic requirements t_i, the initial goal is to learn a hypothesis H from a set of patients E, each of which is described by a set of patient attributes X, and then apply the hypothesis H to new PCA patients N for analgesic consumption prediction. Because the predicted target values are numeric and continuous, the inductive inference task in this study is regression. The learned hypothesis H is a regression model, and its performance is measured by the accuracy of its predictions of the target values of the new patients in N.

2. 2. Subjects in Study

This study was conducted with the approval of the Institutional Review Board at Changhua Christian Hospital (CCH). PCA usage profiles from 2009 to 2014 were collected for analysis. The Abbott Pain Management Provider (Abbott Lab, Chicago, IL, USA) was used for PCA treatment. Instructions were reviewed with patients before receiving PCA therapy. With the assistance of the Acute Pain Service, more than 5,696 patient records dated from 2009 were retrospectively collected. After discarding incomplete PCA log files and patient records with missing demographic, biomedical, or surgery-related attributes, we obtained 2,676 patient records. Of these patients, 716 were excluded from the sample if their PCA medication was administered for less than 24 h. This is because this study focused on patients that received at least 24 h of PCA treatment. Thus, the final sample included 1,960 participants after data pre-processing.

2. 3. Attributes of Subjects

Each patient record contained attributes such as basic health status, age, gender, weight, department code, doctor ID, Patient ID, PCA control parameters, and amount of anaesthetic used during different time intervals. Because not all the attributes are relevant to our study or have correct values, after consulting the anaesthetists, we discarded irrelevant attributes such as doctor ID and department code before further investigation.

Table. 1. Summary of Patient Attributes

Attribute Name	Description
Demographic: Age	patient age
Gender	patient gender
weight	patient weight
Biomedical: pulse	heart rate
sbp	systolic blood pressue
dbp	diastolic blood pressure
ASA_CLASS*	1: healthy 2: mild systemic disease 3: major systemic disease 4: life-threatening disease or condition
OP-related: OP_CLASS	1: intrathoracic 2: upper intra-abdominal 3: lower intra-abdominal 4: laminectomy 5: major joints 6: limbs 7: head & neck
OP_TIME	surgical duration
OP_PAIN	1: extreme 2: moderate 3: mild
APS	Y : received PCA before surgery N : not receive PCA before surgery
URGENCY	E: emergency surgery R: regular surgery
ANS_WAY	SA: spinal anesthesia GA: general anesthesia
PCA treatment: total _p 1hr~24hr	number of total PCA demands in 1^{st}–24^{th} h
sucess_p 1hr~24hr	number of successful PCA demands in 1^{st}–24^{th} h
failure_p 1hr~24hr	number of PCA demands that fail in 1^{st}–24^{th} h
pcadose 1hr~24hr	total PCA dose in 1^{st}–24^{th} h
pcadose_wt 1hr~24hr	PCA dose/patient weight in 1^{st}–24^{th} h
pcadose set	PCA dose setting
lockout set	minimum time gap between adjacent PCA demands
4hrlimit set	Y : have reached maximum dosage allowed for every 4 h N : not reached maximum dosage allowed for every 4 h
conti dose	continuous dose setting
PCA demand pattern: patt_pcadose_12hrs	pattern of the PCA dose profile for the first 12 hrs
patt_success_12hrs	pattern of the PCA profile of successful demands for the first 12 hrs
patt_ failure _12hrs	pattern of the PCA profile of demands that fail for the first 12 hrs
patt_total_12hrs	pattern of the PCA profile of total demands for the first 12 hrs
patt_pcadose_wt_12hrs	pattern of the PCA dose/patient weight profile for the first 12 hrs

*ASA class is the commonly used preoperative index of physical status defined by the American Society of Anaesthesiologists.

In addition to the commonly studied demographic and physiological factors, PCA-related attributes, such as the number of demands of PCA per hour, have been shown to correlate with analgesic consumption prediction significantly (Hu et al., 2012a). The cluster analysis of PCA demand behaviour identified significant demand patterns from the postoperative patients. These findings suggest a significant correlation between demand behaviour and analgesic consumption (Hu et al., 2012b). We considered various types of time series data from PCA demand profiles, including the number of successful PCA demands in an hour, the number of failure PCA demands in an hour, the total number of PCA demands in an hour, the PCA dose in an hour, and the PCA dose in an hour divided by patient weight. To characterize the PCA demand behaviours, from the series data of PCA demands over time, we derived and compared different PCA behaviour-based attributes by applying clustering methods to PCA demand profiles.

Table 1 presents the attributes of a patient, which were divided into five types: (a) patient demographic attributes, (b) biomedical attributes, (c) operation-related attributes, (d) PCA treatment attributes, and (e) PCA demand pattern attributes. Their values are either categorical or numeric.

2. 4. Prediction Performance Evaluation

Most previous regression studies of postoperative pain and PCA analgesic consumption used R^2 (coefficient of determination) to evaluate the learned regression model without testing it on an exclusive test data set (Chung et al., 1996; Turn & Okifuji, 1999; Bisgaard et al., 2001; Walder et al., 2001; Pan et al., 2006; Chang et al., 2006). Unlike other works, given the physical states of the patients, and their first few hours of PCA treatment profiles, we developed a predictive model to predict the total anaesthetic dose taken in subsequent hours. By addressing the analgesic consumption prediction in analogy to an inductive inference problem, we evaluated the performance of the predictive model trained from the training data by its root mean squared errors (RMSE) in the test data set N, as defined below.

$$\text{RMSE} = \sqrt{\frac{\sum_{i=1}^{|N|}(p_i - q_i)^2}{|N|}} \tag{1}$$

Where $|N|$ is the total number of test examples, p_i and q_i are the true target value and the predicted value, respectively. In our study, p_i is the actual analgesic consumption, and q_i is the predicted amount.

To evaluate the performance, we conducted a k-fold cross validation (CV). We randomly divided an initial data set of patients into k disjoint folds (i.e., subsets), each of approximately equal size. We used one fold of data for testing prediction performance, and used the remaining (k-1) folds for training. We repeated the same training-testing process on each fold iteratively. Each run produced a result based on the fold selected for testing. The overall performance was measured as the average of the results obtained from all iterations of the k-fold CVs.

2. 5. Construction of Prediction Models

The purpose of a prediction model is to predict the analgesic consumption of a PCA patient based on his (or her) observable attributes. Applying the regression methods, we constructed the computational prediction models from a set of patients as the training examples.

2. 5. 1. One-Stage Regression

For 1-stage regression, we took four types of patient attributes, except the PCA behaviour-based attributes, as the candidate predictors (i.e. independent variables) in regression. The PCA behaviour-based attributes were excluded because they have categorical values. The regression model was trained from the training examples, and then used to predict the analgesic consumption of a new patent.

In a preliminary test for R^2 and RMSE on a sample patient data set, four regression tools were evaluated: libSVM (hang & Lin, 2011), REPTree (Weka 3, 2015), and SMOreg (Weka 3, 2015), and stepwise multiple linear regression LR (Weka 3, 2015). The results show that LR outperformed REPTree and SMOreg significantly, and there was no significant difference in prediction performance between LR and libSVM. For the remaining experiments in the study, we only used LR because compared with LR, libSVM requires markedly more computational time.

2. 5. 2. Two-Stage Regression

PCA demand patterns show significant correlation with analgesic consumption (Hu et al., 2012a, 2012b). Unlike 1-stage regression that produces a single regression model without considering the patient demand behaviours, the 2-stage regression strategy constructed different regression models from the patients with different PCA demand patterns, respectively. We identified the demand patterns by applying the k-medoids (Reynolds et al., 2004) clustering algorithm to the PCA demand profiles of the patients in the training data set. We used the k-medoids algorithm because it mitigates the effects of outliers on the resulting cluster prototypes, and ensures that all the resulting clusters are non-empty. To find the appropriate number of patterns, we performed a series of k-medoids clustering on bootstrap samples with the value of k varying from 2 to *K*, a user-specified maximum number of clusters. Following (Dolnicar & Leisch, 2010), by conducting the sequential *t* tests on the adjusted Rand index (Hu et al., 2012b; Hubert & Arabie, 1985), we selected the value of k that produced the most stable clustering result.

To predict the analgesic consumption of a new patient, firstly we determined the demand pattern of this patient according to his (or her) observable PCA demand profiles, such as the PCA demands per hour for the first 12 hours of the PCA medication. Secondly, we used the regression model trained from the patients with the same demand pattern to predict the total analgesic consumption. Figure 1 shows the control flows of the 1-stage and 2-stage regression strategies.

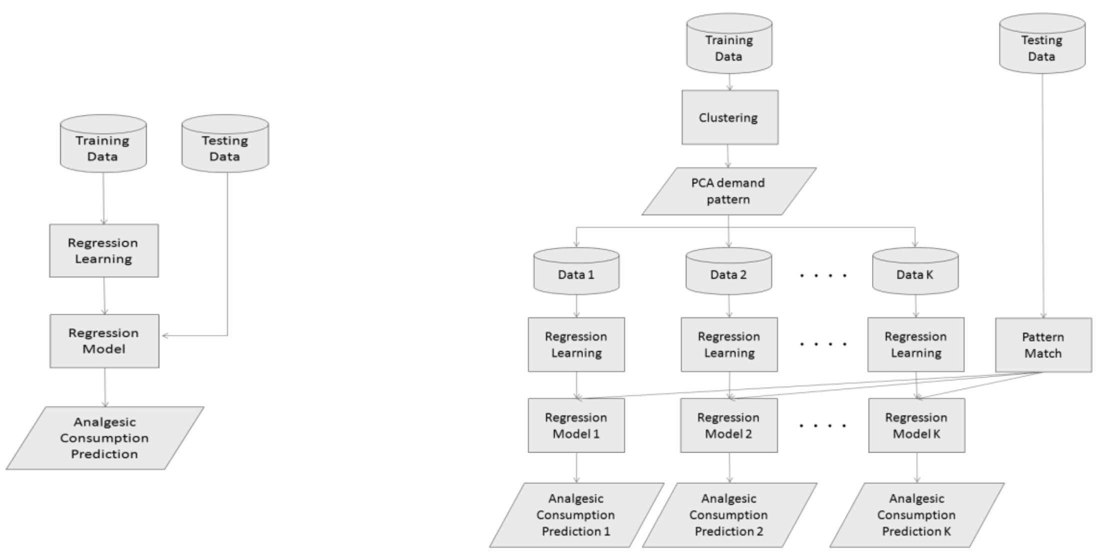

Fig. 1. Construction of regression models. (a) control flow of 1-stage regression, (b) control flow of 2-stage regression

3. Experimental Results

3. 1. Comparison between One-Stage and Two-Stage Regressions

We conducted a 10-fold CV to evaluate the performances of the 1-stage and 2-stage regression methods. The goal was to predict the 24-h total analgesic consumption (PCA dose) based on the patient's first 12 h of physical states, surgery-related attributes, and PCA treatment data. The PCA demand patterns were considered when 2-stage regression was applied. We ran the k-medoids algorithm, varying k from 2 to 5, and found k=3 to result in the most stable clustering results. For 2-stage regression in the study, we identified 3 marked patterns of the PCA profile of total demands for the first 12 hrs. Although we also identified other PCA demand patterns from different PCA profiles, such as the PCA successful demands, the experimental results showed that the 2-stage regression produced the highest performances when the patterns of total PCA demands were considered, and the patterns were more distinguishing than the others. Figure 2 shows the patterns of PCA total demands for the first 12 hrs of the patients.

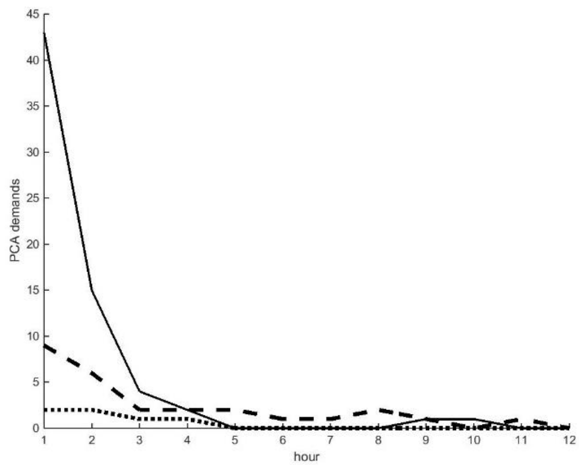

Fig. 2. PCA total demand patterns for the first 12 hrs. The x-axis is the time, and the y-axis is the number of PCA demands.

In each run of the CV, one fold of patients were selected iteratively to test the regression models, and the remaining nine folds were used to train the regression models. Unlike 1-stage regression that does not consider the patterns, the 2-stage regression models were trained separately from the patients with the specific PCA demand patterns. To make a fair and consistent comparison, the 1-stage regression model was trained from the same number of patients without specific patterns to avoid the variance caused by the different training data sizes. Furthermore, the RMSE for 1-stage regression was averaged over ten 1-stage regression models trained from ten patient sets randomly selected from the 9-fold training data to mitigate the effect of sample variance.

Table. 2. RMSE of analgesic consumption predictions

Model Test	1-stage (mg)	2-stage (mg)
Fold 1	2.442 5	2.397 3
Fold 2	2.236 36	2.209 2
Fold 3	2.582 38	2.479
Fold 4	2.502 86	2.469 5
Fold 5	2.469 14	2.396 9
Fold 6	2.530 44	2.363 7
Fold 7	2.046 88	2.024 9
Fold 8	2.354 08	2.278 8
Fold 9	2.830 91	2.476 7
Fold 10	2.728 37	2.575 3
Average	**2.472 39**	**2.367 1**

Table 2 presents the prediction results of the 1-stage regression method, and the 2-stage regression strategy that employed the PCA total demand patterns. The paired *t* test shows that 2-stage regression that exploits the PCA demand patterns outperformed 1-stage regression significantly ($p << 0.05$). The results suggest that the information of demand behaviours can improve the accuracy of analgesic consumption prediction.

3. 2. Comparison between Computational Methods and Human Experts

In addition to the 10-fold CV between 1-stage and 2-stage regressions, we also compared the regression models with the human experts. Ten anaesthesiologists or medical specialists at CCH participated in the comparative study.

We first trained the 2-stage regression models on 1,900 patient records selected randomly from the data set, and compared the models with the human experts on an independent test set of the remaining 60 patients. To ensure the consistency in comparison, we presented the same patient attributes used to train the regression models to the human experts. We also represented the PCA demand behaviours in the form of a time course, as shown in Figure 3, to make the data more comprehensible to human.

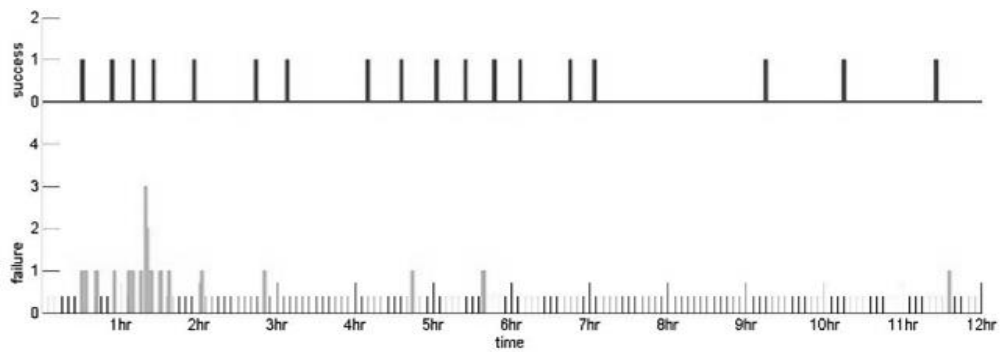

Fig. 3. Sample PCA demand profiles, where the x-axis is the time scale, and the y-axis is the number of PCA demands. The successful and failure demand profiles are represented by the histograms, respectively

Table 3 presents the RMSEs of the 2-stage regression models and the human experts. They were averaged over the test patients. The final row of Table 3 shows the ranks of the predictions according to the RMSE. The results indicate that the 2-stage regression strategy outperformed the human experts on the test patient set, which demonstrates the feasibility of the computational models for analgesic consumption prediction.

Table. 3. Prediction results of the computational models and the human experts

	2-stage	E_1	E_2	E_3	E_4	E_5	E_6	E_7	E_8	E_9	E_{10}
RMSE (mg)	3.36	4.08	4.10	3.94	4.02	4.03	12.91	4.55	4.28	3.88	3.77
Rank	1	7	8	4	5	6	11	10	9	3	2

4. Conclusion

PCA is one of the most effective techniques for postoperative analgesia, and is now widely used in hospitals for the management of postoperative pain. To improve patient satisfaction, this study attempts to predict analgesic consumption based on the first few hours of PCA treatment. Accurate predictions can assist anaesthesiologists in PCA administration. Several studies have discovered a number of significant correlates, e.g. age, with the dose of opioid required in the postoperative period (Gagliese et al., 2008; Chang et al., 2006), while a systematic review shows that the R^2 were small (Abrishami et al., 2011). These findings indicate that most of the variability in prediction models is unexplained, and that factors other than demographic or physiological attributes may contribute to the complexity of postoperative outcomes. By clustering analysis, we identified significant patterns in the demand behaviours of the PCA patients, and showed how to utilize the patterns to develop the computational models for analgesia consumption prediction. The experimental results suggest the feasibility of the strategy proposed in the study, and demonstrate that the computational models can outperform the human experts in pain management.

Acknowledgements

This study was partially supported by the Ministry of Science and Technology in Taiwan (MOST 103-2221-E-009-145).

References

Abrishami, A., Chan, J., Chung, F., & Wong, J. (2011). Preoperative Pain Sensitivity and Its Correlations with Postoperative Pain and Analgesic Consumption. *Anesthesiology*, 114, 445-457.

Bellville, J.W., Forest, W.H. Jr, Miller, E., & Brown, B.W. Jr. (1971). Influence of Age on Pain Relief from Analgesics. A Study of Postoperative Patients. *JAMA*, 217, 1835-1841.

Bisgaard, T., Klarskov, B., Rosenberg, J., & Kehlet, H. (2001). Characteristics and Prediction of Early Pain after Laparoscopic Cholecystectomy. *Pain*, 90, 261-269.

Chang, C., & Lin, C. (2011). LIBSVM: A Library for Support Vector Machines. *ACM Trans. Intelligent Systems and Technology*, 2(27), 1–27.

Chang, K.Y., Tsou, M.Y., Chiou, C.S., & Chan, K.H. (2006). Correlations between Patient-Controlled Epidural Analgesia Requirements and Individual Characteristics among Gynecologic Patients. *Acta Anaesthesiol Taiwan*, 44, 135-140.

Chia, Y., Chow, L., Hung, C., Liu, K., Ger, L., & Wang, P. (2002). Gender And Pain Upon Movement Are Associated With The Requirement For Postoperative Patient-Controlled IV Analgesia: A Prospective Survey Of 2298 Chinese Patients. *Can J Anaesth*, 49, 249-55.

Chung, F., Un, V., & Su, J. (1996). Postoperative Symptoms 24 Hours after Ambulatory Anaesthesia. *Canadian Journal of Anesthesia*, 43, 1121-1127.

Dolin, S.J., Cashman, J.N., & Bland, J.M. (2002). Effectiveness of Acute Postoperative Pain Management: Evidence from Published Data. *Br J Anaesth*, 89, 409-423.

Dolnicar, S., & Leisch, F. (2010). Evaluation of Structure and Reproducibility of Cluster Solutions Using the Bootstrap. *Market Letters*, 21, 83.

Gagliese, L., Gauthier, L.R., Macpherson, A.K., Jovellanos, M., & Chan, V. (2008). Correlates of Postoperative Pain and Intravenous Patient-Controlled Analgesia Use in Younger and Older Surgical Patients. *Pain Med*, 9, 299-314.

Hu. Y., Ku, T., Jan, R., Wang, K., Tseng, Y., & Yang, S. (2012a). Decision Tree-Based Learning to Predict Patient Controlled Analgesia Consumption and Readjustment. *BMC Medical Informatics and Decision Making*, 12, 131.

Hu, Y., & Ku, T. (2012b). Pattern Discovery from Patient Controlled Analgesia Demand Behavior. *Computers in Biology and Medicine*, 42, 1005-1011.

Hubert, L., & Arabie, P. (1985). Comparing Partitions. *Journal of Classification*, 2, 193.

Pan, P.H., Coghill, R., Houle, T.T., Seid, M.H., Lindel, W.M., & Parker, R.L. (2006). Multifactorial Preoperative Predictors for Post-Cesarean Section Pain and Analgesic Requirement. *Anesthesiology*, 104, 417-425.

Reynolds, A.P., Richards, G., & Rayward-Smith, V.J. (2004). The Application of K-medoids and PAM to the Clustering of Rules. *Proceedings of the Fifth International Conference on Intelligent Data E ngineering and Automated Learning*, 173.

Turk, D.C., & Okifuji, A. (1999). Assessment of Patients' Reporting Of Pain: An Integrated Perspective. *Lancet*, 352, 1784-1788.

Walder, B., Schafer, M., Henzi, I., & Tramer, M.R. (2001). Efficacy and Safety Of Patient-Controlled Opioid Analgesia For Acute Postoperative Pain. A Quantitative Systematic Review. *Acta Anaesthesiologica Scandinavica*, 45, 795-804.

Web sites:
Web-1: http://www.cs.waikato.ac.nz/ml/weka/, consulted 10 Feb. 2015.