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FINAL REPORT

Start date: Dec. 03 **Duration: 36 month**

Title : Reducing mortality and long-term disability of TBI victims through research into treatment procedures used in Bosnia-Herzegovina, Macedonia and Croatia. RESEARCH TREAT TBI

Project homepage : http://www.igeh.org/project4_1_1.php

Keywords : (5 maximum) Balkans, CEEC, Brain Injuries, Evidence Based Medicine, Guidelines

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CONTENTS

1 Abstract

Number of death from injuries in Bosnia-Hercegovina, Macedonia and Croatia as reported by the WHO in 1998 is very high. Injuries rank number one, number two and number three killer in young population of the region (ages 5 to 44). The broad objectives of RESEARCH-TREAT-TBI project are to save the lives of traumatic brain injury (TBI) victims and to improve the quality of life of survivors through research in factors determining health outcomes of hospital care and through changing current clinical practices to provide better care. The project builds up on experiences with the research in determinants of health outcomes and in implementation of scientific based guidelines for good clinical practice. Planned Project facilitates the research and subsequent guidelines implementation in concrete clinical settings, and reflecting local situation both clinical and public health.

The Project focused on the research into factors determining the quality of care for victims of severe Traumatic Brain Injuries (TBI) (Glasgow Coma Scale less then 9), accentuating the quality of life after recovery. Dissemination of state-of-the-art knowledge on quality care of Traumatic Brain Injury patients; practical and participative implementing programs for the introduction into clinical care procedures of Scientific Evidence Based Guidelines (elaborating protocols, practice modification taking local conditions fully into consideration, behavioral change of the staff involved, collecting data on patients in order to monitor the progress so that participants can see the results of their work, and can check and revisit the assumptions on best clinical practice). The implementation of Scientific Evidence Based procedures is followed by a research in efficacy of changed medical practice. This was facilitated by developing a guidelines compliance measurement tool, which evaluates how closely the guidelines are followed in the treatment of individual case. When evaluating the compliance and when discussing the guidelines implementation one of the major problems surfaced is lack of support from the management of hospitals. This could be overcome through creation of public awareness campaign. A draft of a policy to deal with the situation was delineated.

One of the goals of the endeavor was to help the countries in preserving and developing their research excellence in the field of public health. This has materialized in visits and presentations given by project participants at meetings, conferences, symposia and in individual departments. Joint publications were submitted to national and international conferences and symposia. Several PhD studies were initiated, too.

1 SUMMARY OF THE FINAL REPORT

Objectives:

General objective of the project is to research main factors of traumatic brain injury (TBI) in Bosnia-Herzegovina, Macedonia and Croatia. The objectives of the 1st year of the project were to introduce scientific evidence-based guidelines in participating centers, install database for entering patient data, implement the guidelines, monitor TBI management, analyze interim results of patient data and disseminate the interim outcomes. The second year was focused on the implementation of scientific evidence-based guidelines on severe TBI management in the participating centers and monitoring the process of guidelines implementation. The specific accent was put on identification of barriers to implementation and how to be overcome. The third year had two major focus areas, one was developing a method to measure guidelines compliance and the second was developing a policy approach to facilitate guidelines implementation.

Materials and Methods:

For the launching up of the project an introductory workshop and local workshops in individual centers were organized. Centers were equipped with necessary hardware. As software ITCP database was installed in all the centers. At least 2 people per each center were trained in using the database. New version of the database was installed in all the centers in March 2003. Since that time another modification was introduced towards the ed of the project, not influencing the data collection.

Interim analyses of collected data were performed. The data set was transferred to Excel format. As the first step basic data cleaning was performed. The second step was to convert all measurements to common SI units. Data were analyzed using built in Excel functions as well as XLSTAT statistical package.

Retrospective patients' data for 2000 and 2001 were entered into the ITCP database. The year 2004-05 was busy with development and testing of scores used to measure the compliance to TBI guidelines at individual patient. In order to monitor guidelines implementation and to discuss the results of the data quality assurance, a workshop was organized in Rijeka (Croatia) in June 2004. The scores were successfully tested on all patients entered into the database. The results were discussed at the meeting in Wien, October 2005.

Data analysis started with formulating hypothesis for the final data analysis to be performed during the next phase of the project (meeting in Rijeka). The first step in securing the study's design was to assure that only patients satisfying the selection criteria were included into this study. The criteria of severe TBI were used according to the National Traumatic Coma Database[1] established in the US:

- Glasgow Coma Scale (GCS) score of 8 or less following resuscitation, which may include endotracheal intubation; or
- GCS score deteriorating to 8 or less within 48 hours of injury.

Patients who died at the scene, during transport to the hospital, or immediately after admission to the emergency room were excluded. Data from patients who fulfilled these

[1] Marshall, L. F., Becker, D. P., Bowers, S. A et al. (1983) The National Traumatic Coma Data Bank. Part 1: design, purpose, goals, and results. Journal of Neurosurgery 59:276–284

criteria were collected using the ITCP database accessible via internet. The data set comprises a total of 592 records from the 5 participating hospitals.

By using a standardized, structured questionnaire, we recorded information three months, half a year and one year after the injury from the patients, or their relatives, or their carers by a telephone interview or mail. About one quarter of surviving patients were lost to follow up. In many cases there was a positive personal note added to written or oral contact with either TBI patient or a relative. The outcomes were recorded in two ways. The ICU outcome was based on Glasgow Coma Scale (GCS). If a patient died, details on circumstances of death were recorded (primary cause of death and facility). For survivors specifications of the facility to which the patient was discharged, as well as characteristics of general ICU treatment process, complications and specific diagnostic and treatment procedures were recorded. For those who survived 90 days information on Glasgow Outcome Score (GOS [2]) and actual location were recorded. In addition to that, the follow-up questionnaire for 180 and 360 days contained information on the percentage of permanent disability (if available) and characteristics of rehabilitation.

All data were collected locally on laptop or desktop computers. After each session a copy of the full data set from the center (and not only the new additions) was sent in a secure format via internet to the central server located at the INRO office. Personal patient data were not transmitted to the central server; at the central server all patients received a case number, but the actual patient identities remained hidden. Data could not be retrieved from the central server via internet; to obtain copies of files the study coordinators had to contact the INRO data manager.

Statistical Methods: a combination of univariant and multivariant methods was used. In a first step correlations were tested using $\bullet^2$ and Pearson coefficient of correlation, in the second step correlating variables were tested in multivariate analysis General Linear Model (ANOVA and Regression), for group comparisons using ANOVA, to test influence factors. Predictors of death or disability were identified by using logistic regression with forward stepwise selection of variables. The calculations were done using the XLSTAT[3] statistical packages. A $p < .05$ was considered statistically significant.

Summary of results were formed into a format common in reporting the trauma care within the EUROTARN initiative for all centers involved. The patients were divided according to ISS into two groups: those with the Injury Severity Score less then 15 and over 15. Following variables were investigated: type of injury blunt and penetrating, mechanism of injury, and isolated injury versus polytrauma. Within all those variables total number of patients, survival, gender, age, age groups were reported. Further analysis was focused on clinical factors related to outcome: The analysis focused on:

- Complications and outcome of intensive care
- Monitoring of ICP: which patients had, and which did not have ICP monitoring; type of ICP devices used, periods of use, effects of ICP monitoring upon outcome
- Course of ICP and CPP in survivors and non-survivors
- Efficacy of interventions (analgesia, sedation, barbiturates, steroids, mannitol, hypertonic saline, hyperventilation, hypothermia)
- Management of haemodynamics and CPP: use of catecholamines, fluid balance
- Ventilation strategies: peak inspiratory pressure (PIP), PEEP, and pO_2/FiO_2 ratio
- Effects of hyperglycaemia

Data on clinical effects were gained from day-by-day analysis of treatment options vs. patient status. For analysis of effects upon outcome daily treatment data were re-organized

[2] Wilson JTL, Pettigrew LEL, Teasdale GT (1998) Structured interviews for the Glasgow outcome scale and the extended Glasgow outcome scale: guidelines for their use. J Neurotrauma 15:573-585

[3] XLSTAT. Addinsoft, inc. http://www.addinsoft.com/

according to each patient, so that repeated treatments in a single patient could be assessed. Daily values for data on treatment (e.g. body temperature, pCO_2) and patient status (e.g. hours of ICP>25 mmHg) were averaged over the first 10 treatment days (or less, if the patient did not survive 10 days, or was discharged before day 10). For all treatment options correlations between these averaged data and ICU outcome (survival or death), 90-day outcome (survival or death) and final outcome (based on the last available Glasgow Outcome Score) were performed. The mortality prediction made possible by TRISS[4]; a combination of Glasgow Coma Scale (CGS), Revised Trauma Score (RTS), trauma mechanism (blunt or penetrating), patient age, and Injury Severity Score (ISS) was used to correct for trauma severity and to calculate the observed vs. expected mortality ratio (O/E ratio) at day 90. Mortality at day 90 was used as surrogate for hospital mortality, as hospital outcome is not recorded in ITCP.

Specific method used to evaluate extent of compliance with the guidelines recommendations is based on a scoring system developed for the purpose. The guidelines document is comprised of fourteen topics where a recommendation or recommendations are formulated ranging from trauma systems and prehospital resuscitation to monitoring and treatment of intracranial hypertension and intensive care. In assessing the degree of certainty associated with a particular recommendation, the following terminology is used in the guidelines document based on formalization used by the American Academy of Neurology[5]

We scored recommendations according the level of evidence involved, so that a recommendation based on the strongest evidence (standard) is scored 5, the lower one (guideline) is scored 3 and the one based on the weakest evidence (option) is scored 1. Not all recommendations comprise all three levels. Actually only two recommendations out of 13 are based on the firm evidence and thus score 5. The total maximal possible score is 40. The scores within a recommendation are hierarchical, only the highest one is accepted. We scored all 13 recommendations and subsequently we have developed an algorithm, which operates on the ITCP database data producing a table of scores. The recommendation on nutrition contained within the TBI guidelines was not scored as we felt that the definition given is too complicated and we have had not enough data to base the algorithm on. Scores for the first and second recommendations are not reported in the paper, since the first one reflects the organization of trauma care and it was regarded as adequate in all areas. The second recommendation was not scored, since we were interested in treatment modalities provided intramurally.

The activity oriented towards the policy to disseminate guidelines into entire country was based on reports given by project participants and a series of focused discussions on various topics. Major points of the discussion was then summarized n a document specifying current situation and the ways to overcome it. A summary of recommendations was assembled based on comparisons among the countries of the project.

Results:

All participating centers were instructed on scientific evidence based guidelines on TBI management, had ITCP database installed and were trained in using it. They all entered their TBI patients in the database during the year.

Data set of more than 600 patients was formed until November 2003. The data were cleaned and statistical methods were applied for interim analysis.

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[4] Boyd CR, Tolson MA, Copes WS (1987) Evaluating trauma care: the TRISS method. Trauma Score and the Injury Severity Score. J Trauma 27:370-378.

[5] Walters BC. Clinical practice parameter development. In: Bean JR, ed. Neurosurgery in Transition. Baltimore: Williams & Wilkins; 1998:99–111.

All the centers started implementing scientific evidence based guidelines on TBI management and continued collecting patients' data. Problems met in these two activities were identified and possible solutions were discussed.

Until November 2004, 502 records from Bosnia, Croatia, and Macedonia were entered in the database. Additional 84 cases of TBI were entered by other participants. An interim analysis provided preliminary results on the epidemiological aspects of severe TBI in the centers. A set of hypothesis to be investigated during the final data analysis was formulated.

The analysis of survival based on proportions revealed that the best proportion of survivors of blunt TBI is in Croatia, followed by Bosnia and Herzegovina and the least proportion of survivors is in Macedonia. However, Macedonia had the highest proportion of penetrating TBI followed by Croatia and Bosnia. The latter center had almost half of the proportion of survivors compared to Macedonia. Age and ISS differences could hardly be responsible for such a pattern of survivals. Males are more frequently represented than females. Among the causes of TBI the transportation plays the primary role. In Bosnia and Herzegovina as well as in Macedonia guns contribute significantly. Falls are almost equally represented.

Policy for quality improvement in management of TBI patient

It has been agreed, that full guidelines implementation requires a system on national level, which will prepare general conditions for quality processes and in this respect the process of TBI guidelines implementation will be based on a firm legal basis. Such a system would also incorporate tools for External Quality Assessment, based on one or more of the following options for permitting organizations or individuals to provide health services to the general public:

As it could be seen from the results of compliance to the guidelines recommendations, increasing the number of scores achieved (or the scope of services provided) is not solely in hands of few dedicated persons. It requires the whole team to act in close cooperation with the rest of the system of care provision. Therefore sanctions for non compliance should be instituted as integral part of the system. A license or accreditation is issued for a limited period of time (e.g. 3 years). The periodic assessment for this permission provides a moment to decide whether the institution/practitioner could continue working. Between the moments of assessment there should be a system for quality control, especially when complaints are launched or when other information indicates poor performance. Specific role is there for health insurance companies who make contracts with health care providers and through their system of inspector physicians they perform quality control. However, these inspector physicians can judge whether the insurance company can contract the health institutions. In case of poor performance the insurance companies can (temporarily) stop contracts. They cannot withdraw licenses, and poor performers can continue to work for other insurance companies or private patients.

The project itself addressed one of the most important components of quality of care: standards for provision of "lege artis" health care. The first of them are Managerial and Procedural Standards, which cover general quality issues. These standards are more or less covered in ISO standards. Normally, in accreditation or licensing, having standard managerial procedures in place is part of the conditions. However, clinical practice guidelines or standards for diagnostic and therapeutic interventions such as the one on TBI management experimentally introduced into the practice in hospitals of Croatia, Macedonia and Bosnia and Herzegovina represent the cornerstone for a clinician. Unfortunately, no system to develop such guidelines exists in those countries.

Clinical practice guidelines cannot by imposed like managerial procedures, as it would turn health care into a static process. Each patient needs a personalized approach, and standards need to be adapted to medical-technical developments. Clinical practice guidelines should be developed through collaboration between professionals, health institutions and clients. The guidelines have to be scientifically sound, bringing together international experiences and local practices. Another very important part of the process is the dissemination of Clinical Guidelines. That is why this project played an important role in sensitizing the clinical society on the results and thus by creating a background for development projects of disseminating the guidelines over the country. The methodology should be converted from experimental to a daily routine.

Results dissemination and communication

The web site for the project was developed based on existing IGEH's web site (http://www.igeh.org/project4_1_1.php). The site includes relevant information on the project (plan, members and contacts) and reports. Individual teams were regularly informed on the status of the data collection and principal results in terms of survival of patients on a 3 monthly basis. During the last year of the project, there has been regular updates set to centers on how closely individual recommendations of the guidelines has been followed, using recently developed scores. This was also used as a tool to evaluate the usability of the scoring system as well as to support the usage the guidelines more extensively. Number of scientific gatherings was used to communicate preliminary results from the project. In the nearest future there is a plan to publish the results extensively in national and international conferences and journals.

Comments and Conclusions:

Few minor organizational changes took place within the implementation of the project. First workshop was organized in Vienna instead of planned Zagreb, which allowed participants to visit the Europe leading trauma centre – Lorenz Bohler Unfall Krankehaus.

The second workshop was organized in Slovakia were it was easier to obtain visa for the participants.

Use of TBI_trac™ database for data collection was originally planned. However, over time, the IGEH developed new version of this database under new label: ITCP - International Traumatic Coma Program. The ITCP is more research oriented, it allows for international cooperation (language versions), supports different measurement units, follows patients outcome up to 180 days.

The project exceeded the set of indicators stated by individual work packages in number of trauma cases collected, in quality of data and in activities of all members of the project.

In 2004 the project continued according the plan. Because of the leave of Dr. Urbansky the center in Banska Bystrica resumed his activity.

In 2005 the scores for compliance to the guidelines recommendations were introduced to measure the how closely individual treatment activities follow individual recommendations. The results were reported repeatedly to individual centres to assess the level of compliance and to improve it. This is also to start the cycle of quality of care improvement, where quantitative information on services could be used to measure if all available procedures were administered.

In this respect the major obstacles were revealed: financial burden in Skoplje did not allow for using the intraventricular catheters to measure and monitor the intracranial pressure, thus leaving the treatment to be based on the observation of clinical signs only. In spite of that, the

survival of patients was relatively good. The financial burden was an issue also in other centres; however, in most of them it was overcome by personal involvement of the team leaders. That is why all the members of the project agreed upon a fact, that without sound campaigning for resources (personal and financial) on different levels, implementation of guidelines into daily practice is limited.

In this respect a set of procedures was agreed on to foster the quality improvement in the field of TBI management as well as in general terms.

Deliverables list

Deliverable no.	Deliverable title	Delivered Yes/No
1.	Report on **WORKSHOP I** (project work plan and other modifications/fine-tuning based on Assessment of Situation)	**Yes**
2.	TBI situation analysis based on questionnaires	**Yes**
3.	Dataset of retrospective TBI patients from years 2000 – 2001 being used as the base-for further comparison.	**Yes**
4.	Report on training on TBI database use	**Yes**
5.	**Report on descriptive analysis**: descriptive statistical measures, frequencies tables, graphs	**Yes**
6.	**Report explorative analysis**: 2x2 tables mxn tables, probabilities computed	**Yes**
7.	**Summation of findings report**	**Yes**
8.	**Report on WORKSHOP II:** Report on the workshop with proposals for changing practices to improve care of Traumatic Brain Injury victims	**Yes**
9.	**Quarterly reports on TBI guidelines implementation**	**Yes**
10.	**Report** containing data set with the prospective data from TBI patients POST implementation of TBI_Guidelines;	**Yes**
11.	**Analysis of** factors enabling and reinforcing the TBI_Guidelines implementation	**Yes**
12.	**Site visit** to Lorenz-Böhler Trauma Hospital in Vienna	**Yes**
13.	**Report on Final Analysis of data**	**Yes**
14.	**Report on WORKSHOP III containing interpretation of results**	**Yes**
15.	**Final Report** giving full results of project plus participants' collected responses and experiences and their own recommendations for Health policy in the region	**Yes**
16.	**Policy Paper Report –** special report on policy and practice implications flowing from the results of this project and workshops (as a part of the Final Report)	**Yes**

Main publications:

Rusnak, M.: Traumatic Brain Injuries – EU Balkan Project. BIT conference, Wien, Jan. 2003.

Mauritz,W., Rusnak,M., and Janciak,I.: Implementing Scientific Evidence-Based Guidelines: Case Study of Severe Traumatic Brain Injuries. Clinical Research and Regulatory Affairs Vol. 20(1), 2003, 81-87

P. Brezany, A.M. Tjoa, M. Rusnak, J. Brezanyova, I. Janciak: Knowledge Grid Support for Treatment of Traumatic Brain Injury Victims. In: Computational Science and Its Applications – ICCSA 2003 International Conference Montreal, Canada, May 18-21, 2003. Proceedings, Part II Springer-Verlag Berlin Heidelberg 2003, pp. 446 – 455.

Rusnak,M., Mauritz,W., Urbansky,M.: Evidence based medicine in brain trauma care. Presentation given at the Regional Meeting of Young Anesthesiologists, Skopje, March 2003.

M.Rusnák: Evidence based medicine and neurotrauma (Medicina bazirna na činjenicama i neurotrauma) . First B&H Meeting on Neurotrauma wirth International Participation, September 20, 2003, Sarajevo

K. Dizdarevic: B&H and The International project of neurotrauma (BiH i internacionalni projekt za neurotraumu). First B&H Meeting on Neurotrauma wirth International Participation, September 20, 2003, Sarajevo

Brazinova, A., Mauritz, W., Rusnak,M., Janciak, I., I.Wilbacher, P.Dado, L.Lenartova, J.Leitgeb, F.Chmelizek, G.Clarici, K. Dizdarevic, M. Soljakova, Z. Todorova-Nikolova: Brain Trauma Risk Factors in selected Regions of Austria, Bosnia and Herzegovina and Macedonian. Abstract submitted to conference Safety 2004, June 6-9, Vienna, Austria

Soljakova M., Nikolova –Todorova Z., Stojanova S: The influence of the level of blood lactate on the outcome of trauma patients. Abstract submitted to conference Safety 2004, June 6-9, Vienna, Austria

Dizdarevic, K.: Two articles on new treatment options in head injured patients are in press (Med journal; Med Voice- Bosnian Journals). Sarajevo, Bosna-Hercegovina

M. Soljakova, Z. Todorova-Nikolova: The effects of hypotensive anaesthesia to the BTI victimes ; Ministry of science, report, Skopje, March 2004

Z. Todorova-Nikolova, M. Soljakova: Management of fluid balance in Brain trauma injuries, DIGI-print, Skopje, 2004 ISBN 9989-2188-46 (COBISS.MK-ID 57959690)

M.Soljakova, B. Kuzmanovska: Syndrom of lost of sodium, Acta anestesiologica Macedonica, :22, 2004

Z. Todorova-Nikolova, B. Kuzmanovska: Resuscitaion of brain trauma victims, I workshop of MSCCM, Skopje, 2004

J.Nanceva, M. Soljakova, E Stoickovski: Anaesthesia for geriatric patients, MSA FEEA VI, :9-18, 2004, ISBN 9989-2018-3-8 (COBISS.MK-ID 56383754)

Z. Todorova-Nikolova: TIVA, MSA FEEA VI, :117-120, 2004 ISBN 9989-2018-3-8 (COBISS.MK-ID 56383754)

Splavski B, Ivić D, Saftić R, Mužević D, Kčira-Fideršek V. Most important early predictors of outcome following severe traumatic brain injury.ations: an international focus meeting, September 19-20, 2003, Rimini, Italy, p 28.

K Dizdarevic, I.Omerhodžić, N Iblizović. B Jahić: Neurosurgical intensive care unit as a prerequisite of current approach to neuropatients. Med Journal, in press.

K. Dizdarević: Cerebral microdialysis and prevention of cerebral ischemia after neurotrauma and aneurysmal hemorrhage. Med Arch, in press

Rusnak,M., Janciak, I., Brazinova, A., Mauritz, W., Project Research Team (Dr. Miroslav Vukic, Dr. Bruno Splavski, Dr. Dean Girotto, Dr. Kemal Dizdarevic, Dr. Maria Soljakova): Epidemic and Clinical Characteristics of TBI situation in three Balkan countries: case study of Croatia, Macedonia and Bosnia. Proceedings of the 7th World Conference on Injury Prevention and Safety Promotion, Wien, June 06th – 09th, 2004.

Leitgeb J., Lenartova L., Dado P., Mauritz W., Rusnak M., Vécsei V.; Trauma systems in Middle Europe. 6th European Trauma Congress, Prague, 16-19 May, 2004

Martin Rusnak, Walter Mauritz, Ivan Janciak, Ingrid Wilbacher, Alexandra Brazinova, and Traumatic Brain Injury Study: Epidemic of Severe TBI in Selected Regions of Austria and Balkan. Proceedings of the third International Conference on Healthcare Systems, Charleston, West Virginia, USA, October 14-17, 2004

Doc. MUDr. Martin Rusnák, CSc a prof. Dr.Med. Walter Mauritz: Kvalita zdravotníckej starostlivosti a znalostná medicína. Klinická epidemiológia ťažkých úrazov mozgu. Červenkove dni preventívnej medicíny, Banska Bystrica,Slovak Republic, June 2003

Wilbacher I., Brazinova A., Janciak I., Leitgeb J., Lenartova L., Mauritz W., Rosso A., Rusnak M.: Brain Injury – a short Epidemiology of TBI and presentation of a new European database**.** Proceedings of the 11th International Mondsee Medical Meeting, Unterach, Austria, September 9–12, 2004

Rusnak M., Brazinova A., Janciak I., Leitgeb J., Lenartova L., Mauritz W., Rosso A., Wilbacher I.: Perspectives on Guidelines and Standards. Do They Make a Difference in Outcomes? Proceedings of the 11th International Mondsee Medical Meeting, Unterach, Austria, September 9–12, 2004

Splavski B, Saftić R, Radanović B, Butković-Soldo S, Mužević D. Intracranial pressure assessment by transcranial Doppler ultrasonography following severe traumatic brain injury. 13th World Congress of Neurological Surgery; 19 – 24 June 2005; Marrakech, Morocco.

Splavski B, Mužević D, Saftić R, Butković-Soldo S, Kčira-Fideršek V. Predicting outcome of severe traumatic brain injury by transcranial Doppler ultrasonography. 10th Congress of Neurosurgeons of Serbia and Montenegro; 2 – 5 October 2005; Novi Sad, Serbia and Montenegro.

Splavski B, Saftić R, Mužević D, Ivić D, Jančuljak D, Kčira-Fideršek V. Predictors of outcome in the management of severe traumatic brain injury. 3rd Pannonian Symposium on CNS injury; 28 – 30 April 2005; Pécs, Hungary. Clin Neurosci 2005;58(5-6):211.

Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Effects of traumatic brain injury guidelines on outcomes in selected hospitals of Croatia, Bosnia and Macedonia. In: Abstracts, 4th Congress of the Croatian Neurosurgical Society, November 9-12, 2005, Zagreb, Croatia, pp.

Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Implementing traumatic brain injury (TBI) guidelines in trauma centers of Bosnia, Croatia and Macedonia. In: Abstracts, 13th European conference on public health. November, 10 – 12, 2005, Graz, Austria, pp.

Dizdarević K., Selimović E., Kominlija E.: Subarachnoid hemorrhage: Neurosurgical treatment modalities and etiological analysis. Med Arh. 2006; 60(1) 33-37.

Rusnak M., Dizdarević K., Omerhodžić I., Soljakova M., Splavski B., Vukić M., Girotto D., Mašić I.: Traumatic Brain Injury (TBI) Guidelines, Acta informatica medica. March, 2006, 14 (1): 10-12.

2 CONSOLIDATED SCIENTIFIC REPORT

2.1 OBJECTIVES

2.1.1 General objective

Improvements in care of Traumatic Brain Injury victims will lead to lower health costs and lower burden on society by decreasing mortality and morbidity. The disintegration of the Balkans due to war has created a specific regional problem with regard to Traumatic Brain Injuries for two main reasons: Direct and Indirect impacts of war. Direct impacts of the war – war wounds, have created a higher than average burden on the Balkan region in terms of costs of care of victims of war-related Brain Injuries. Indirect impacts are those resulting from accidents due to undetonated mines (mostly landmines), severe state of roads leading to higher rates of car accidents, and under funded and poor public health systems leading to costs related to the higher incidence of such Traumatic Brain Injury cases, and the long-term disabilities created by the Secondary Brain Insults (which are preventable), caused by the poor state of roads, poor system of post impact and in-hospital care, and poor public health policy.

- Research into factors in the Balkan region, which determine the quality of care for victims of severe Traumatic Brain Injuries (TBI) (Glasgow Coma Scale less then 9), accentuating the quality of life after recovery.
- Dissemination of state-of-the-art knowledge on quality care of Traumatic Brain Injury patients; Practical and participative implementing programs for the introduction into clinical care procedures of Scientific Evidence Based Guidelines
- Specific scientific and technological objectives
- Research the factors determining health outcomes of Traumatic Brain Injury Victims in the three Balkan countries prior to project (Control Group 1 – quantitative and qualitative analyses)
- Implementation of Scientific Evidence Based guidelines for the treatment of Traumatic Brain Injury victims
- Research the extent of implementation of the Scientific Evidence Based guidelines in the three Balkan countries after the project (Control Group 2 – quantitative and qualitative analyses)
- Comparative analysis of results of patient outcomes for Control Group 1 VS Control Group 2
- Dissemination of results to all involved parties

2.1.2 Specific Objectives for the first year of the project

Objectives for the 1st year of the project were devoted to launch the project activities and to start monitoring clinical performance of trauma centers. In particular, following objectives were defined:

- Launch, situation assessment & Traumatic Brain Injury Assessment;
- Database set up & retrospective data collection;
- Interim analyses of collected data.

2.1.3 Specific Objectives for the second year of the project

The main objective for the 2nd year of the project was the implementation of scientific evidence-based guidelines on severe TBI management in the participating centers. In order to monitor guidelines implementation and its effect on patients' outcome, also the following objectives were defined:

- Continuous retrospective and prospective data collection with follow up of patients;
- Data quality assurance;
- Interim analysis of the TBI epidemics in the centers;
- Research hypothesis formulation.

2.1.4 Specific Objectives for the third year of the project

The third year had two major focus areas, one was to develop a method to measure guidelines compliance and the second was to develop a policy approach to facilitate guidelines implementation. The first objective is responding to the overall one concerned with the quality of provided care and there is a need for indicators. Such indicators would allow management of facilities to assess the quality. The scores of a compliance to guidelines provide indication on how closely to the guidelines recommendations the care was provided and it also indicates whether or not individual recommendations were implemented.

The second objective addresses the barriers to TBI guidelines implementation in centers. It reflects situation in individual center and offers ways to overcome it. There are many conditions, such as financial, where there is not a single easy solution.

2.2 ACTIVITIES

2.2.1 The first year

During the first year of the project activities carried out were oriented to implement the objectives.

- The project was started after the contract signed and all administrative aspects necessary for the successful implementation of the project were obtained. Among the first activities taken was to inform (via emails and letters) all the participants on the fact of the kicking off the activities. The second major effort was paid to prepare the first workshop. The decision was taken to arrange the meeting in Vienna. The web site for the project was developed based on existing IGEH's web site (http://www.igeh.org/project4_1_1.php). The site includes relevant information on the project (plan, members and contacts) and reports. Workshop meetings were held over two days from the 19th to the 20th of January 2003 in Vienna to obtain information on the current situation in the participating centers, to discuss the communication policy of the project and to demonstrate the software for the ITCP system.
- Situation Assessment & Traumatic Brain Injury Assessment were based on structured interviews with representatives of all participating centers. Collected information was recorded into an Excell file. Variables describe individual characteristics of centers, such as structures providing prehospital trauma care (ambulances, personnel, equipment); hospital care facilities (numbers of beds, personnel, available technologies) as well as the catchments area and a level of services.
- Database set up & retrospective data collection started with an introduction to the ITCP database and supplemented with hands-on training in data collection using ITCP database. Subsequently 2 MDs (neurosurgeon and intensivist) were selected to be responsible for

data collection – retrospectively from patients' records in 2000 and 2001. There were at least 2 people trained in data entry for each centre. Some centres trained more than 2, usually they involved a nurse to carry on the basic data entry and MDs then added CT images or surgery description. Since this part of the project was based on collection of historic data (retrospective from patients records) this approach was feasible. Under the project budget computers were provided to centers 5 – 9 in order to facilitate the collection of data. During the respective visits a computer meeting the specifications necessary to each center was purchased and installed. Data were punched into ITCP for years 2000-2001 (inclusion criteria for patients: assessment of the patient within 12 hours after injury and Glasgow Coma Scale bellow 9). The uniformity of the data collection is being maintained using tests on quality of data and tests on CT readings. The database was maintained by IGEH staff. The service comprises regular checking on quality of data (missing data, errors) and communication with centers to select or modify entries. Regular (monthly) reports were sent to centers informing them on current monthly figures (total patients inputted during the month, list of erroneous or missing data) and totals for the entire project. The database was installed in all centres. New hardware was purchased to support the data entry. New version of the database was sent to all centres in March and all of them have upgraded with no problems. Regular maintenance of data (back-ups, copying, antivirus protection, reporting) was carried on by IGEH IT staff. Consultations were provided on demand. Several suggestions from centres were already included into the latest version. Some more suggestions will be implemented into the one to come next year. No data were lost.

- Interim analyses of collected data. The data set was transferred to Excel format. As the first step basic data cleaning was performed. The second step was to convert all measurements to common SI units. Data were analyzed using built in Excel functions as well as XLSTAT statistical package.

2.2.2 The second year

During the second year of the project activities carried out were oriented to implement the objectives of the Project.

The second year of the project was launched after the workshop that took place in Bratislava in November 2003, where evidence based guidelines on the management of severe TBI were introduced to participating centers. The guidelines contained scientific indications for the management of severe TBI, including recommendations on Trauma Systems' structure, initial management of TBI victims, resuscitation of blood pressure and oxygenation, indications for Intracranial Pressure management, Cerebral Perfusion Pressure management, use of hyperventilation, and indications on the use of medicaments such as mannitol, barbiturates, steroids and antiseizure prophylaxis. Each participating center started implementing the guidelines, under the supervision of the project contact person. Continuous contact between the centers and the coordinator was kept in order to help the centers in adopting the new standards, and consultations were provided when needed.

In June 2004 a meeting of all participating institutions was organized in Rijeka, where difficulties met in guidelines implementation were discussed. Each center exposed local problems which limited the possibility of following the indications. Possible solutions to overcome those problems were discussed with the coordinator.

Retrospective data collection in the database was continued by the centers, covering the years 2002 and 2003. Furthermore, prospective collection of new cases admitted in 2004 was started. The collection of data regarding the long term outcome of registered cases was started; every center autonomously decided the method to use to obtain those data.

All entered material was sent to the central server, based in the coordinating organization.

Regular maintenance of data (back-ups, copying, antivirus protection, reporting) was provided by IGEH staff. Regular reports were sent to the centers informing them on the current status of data collection.

Data quality assurance of all recorded material was performed in June 2004 by IGEH staff. All information entered into the database before June 2004 was reviewed, and all erroneous and missing data were identified. The most frequent missing and errors were presented to all participants of the meeting in Rijeka. Furthermore, every representative received a detailed list of incomplete data from its center. Problems met in data collection and possible solutions were discussed with the coordinator.

Interim analyses were performed on collected data, focusing on the description of TBI epidemics in the centers. As the first step basic data cleaning was performed. The second step was to convert all measurements to common SI units. Data were analyzed using built in Excel functions as well as XLSTAT statistical package.

As an introduction to the following phase of the project, which will be the data analysis, participating centers were asked to make suggestions on the hypothesis to be tested. The goals of the analysis were defined, and research hypothesis to better understand the factors improving the outcome of TBI were formulated during the meeting of Rijeka.

2.2.3 The third year

The year 2005 was busy with development and testing of scores used to measure the compliance to TBI guidelines at individual patient. The scores were successfully tested on all the patients entered into the database. The results were discussed at the meeting in Wien, October 2005.

Data analysis started with securing that only patients satisfying the selection criteria were included into this study. The criteria of severe TBI were used according to the National Traumatic Coma Database[6] established in the US:

- Glasgow Coma Scale (GCS) score of 8 or less following resuscitation, which may include endotracheal intubation; or
- GCS score deteriorating to 8 or less within 48 hours of injury.

Patients who died at the scene, during transport to the hospital, or immediately after admission to the emergency room were excluded. Data from patients who fulfilled these criteria were collected using the ITCP database accessible via internet. The data set comprises a total of 592 records from the 5 participating hospitals.

By using a standardized, structured questionnaire, we recorded information three months, half a year and one year after the injury from the patients, or their relatives, or their carers by a telephone interview or mail. About one quarter of surviving patients were lost to follow up. In many cases there was a positive personal note added to written or oral contact with either TBI patient or a relative. The outcomes were recorded in two ways. The ICU outcome was based on Glasgow Coma Scale (GCS). If a patient died, details on circumstances of death were recorded (primary cause of death and facility). For survivors specifications of the facility to which the patient was discharged, as well as characteristics of general ICU treatment process, complications and specific diagnostic and treatment procedures were recorded. For those who survived 90 days information on Glasgow Outcome Score (GOS[7]) and actual location were recorded. In addition to that, the follow-up

[6] Marshall, L. F., Becker, D. P., Bowers, S. A et al. (1983) The National Traumatic Coma Data Bank. Part 1: design, purpose, goals, and results. Journal of Neurosurgery 59:276–284

[7] Wilson JTL, Pettigrew LEL, Teasdale GT (1998) Structured interviews for the Glasgow outcome scale and the extended Glasgow outcome scale: guidelines for their use. J Neurotrauma 15:573-585

questionnaire for 180 and 360 days contained information on the percentage of permanent disability (if available) and characteristics of rehabilitation.

All data were collected locally on laptop or desktop computers. After each session a copy of the full data set from the center (and not only the new additions) was sent in a secure format via internet to the central server located at the INRO office. Personal patient data were not transmitted to the central server; at the central server all patients received a case number, but the actual patient identities remained hidden. Data could not be retrieved from the central server via internet; to obtain copies of files the study coordinators had to contact the INRO data manager.

Statistical Methods: a combination of univariant and multivariant methods was used. In a first step correlations were tested using $\bullet^2$ and Pearson coefficient of correlation, in the second step correlating variables were tested in multivariate analysis General Linear Model (ANOVA and Regression), for group comparisons using ANOVA, to test influence factors. Predictors of death or disability were identified by using logistic regression with forward stepwise selection of variables. The calculations were done using the XLSTAT[8] statistical packages. A $p < .05$ was considered statistically significant.

Summary of results were formed into a format common in reporting the trauma care within the EUROTARN initiative for all centers involved. The patients were divided according to ISS into two groups: those with the Injury Severity Score less then 15 and over 15. Following variables were investigated: type of injury blunt and penetrating, mechanism of injury, isolated injury versus polytrauma. Within all those variables total number of patients, survival, gender, age, age groups were reported. Further analysis was focused on clinical factors related to outcome: The analysis focused on:

- complications and outcome of intensive care
- monitoring of ICP: which patients had, and which did not have ICP monitoring; type of ICP devices used, periods of use, effects of ICP monitoring upon outcome
- course of ICP and CPP in survivors and non-survivors
- efficacy of interventions (analgesia, sedation, barbiturates, steroids, mannitol, hypertonic saline, hyperventilation, hypothermia)
- management of haemodynamics and CPP: use of catecholamines, fluid balance
- ventilation strategies: peak inspiratory pressure (PIP), PEEP, and pO_2/FiO_2 ratio
- effects of hyperglycaemia

Data on clinical effects were gained from day-by-day analysis of treatment options vs. patient status. For analysis of effects upon outcome daily treatment data were re-organized according to each patient, so that repeated treatments in a single patient could be assessed. Daily values for data on treatment (e.g. body temperature, pCO_2) and patient status (e.g. hours of ICP>25 mmHg) were averaged over the first 10 treatment days (or less, if the patient did not survive 10 days, or was discharged before day 10). For all treatment options correlations between these averaged data and ICU outcome (survival or death), 90-day outcome (survival or death) and final outcome (based on the last available Glasgow Outcome Score) were performed. The mortality prediction made possible by TRISS[9]; a combination of Glasgow Coma Scale (CGS), Revised Trauma Score (RTS), trauma mechanism (blunt or penetrating), patient age, and Injury Severity Score (ISS) was used to correct for trauma severity and to calculate the observed vs. expected mortality ratio (O/E ratio) at day 90. Mortality at day 90 was used as surrogate for hospital mortality, as hospital outcome is not recorded in ITCP.

[8] XLSTAT. Addinsoft, inc. http://www.addinsoft.com/

[9] Boyd CR, Tolson MA, Copes WS (1987) Evaluating trauma care: the TRISS method. Trauma Score and the Injury Severity Score. J Trauma 27:370-378.

Specific method used to evaluate extent of compliance with the guidelines recommendations is based on a scoring system developed for the purpose. The guidelines document is comprised of fourteen topics where a recommendation or recommendations are formulated ranging from trauma systems and prehospital resuscitation to monitoring and treatment of intracranial hypertension and intensive care. In assessing the degree of certainty associated with a particular recommendation, the following terminology is used in the guidelines document based on formalization used by the American Academy of Neurology[10]

We scored recommendations according the level of evidence involved, so that a recommendation based on the strongest evidence (standard) is scored 5, the lower one (guideline) is scored 3 and the one based on the weakest evidence (option) is scored 1 (Table 1). Not all recommendations comprise all three levels. Actually only two recommendations out of 13 are based on the firm evidence and thus score 5. The total maximal possible score is 40.

Table 1Relation of clinical certainty to the evidence involved

	Definition	**Evidence Involved**	**Score Assigned**
Standards	accepted principles of patient management that reflect a high degree of clinical certainty.	generally based on Class I evidence. However, strong Class II evidence may form the basis for a standard, especially if the issue does not lend itself to testing in a randomized format. Conversely, weak or contradictory Class I evidence may not be able to support a standard.	5
Guidelines	represent a particular strategy or range of management strategies that reflect a moderate clinical certainty.	usually based on Class II evidence or a preponderance of Class III evidence.	3
Options	are the remaining strategies for patient management for which there is unclear clinical certainty.	usually based on Class III evidence and are clearly much less useful except for educational purposes and in guiding future studies.	1

The scores within a recommendation are hierarchical, only the highest one is accepted. We scored all 13 recommendations and subsequently we have developed an algorithm, which operates on the ITCP database data producing a table of scores. The recommendation on nutrition contained within the TBI guidelines was not scored as we felt that the definition given is too complicated and we have had not enough data to base the algorithm on. Scores for the first and second recommendations are not reported in the paper, since the first one reflects the organization of trauma care and it was regarded as adequate in all areas. The second recommendation was not scored, since we were interested in treatment modalities provided intramurally.

[10] Walters BC. Clinical practice parameter development. In: Bean JR, ed. Neurosurgery in Transition. Baltimore: Williams & Wilkins; 1998:99–111.

Table 2 Recommendations with assigned scores

	Evaluated Recommendations	Highest Score
3	Resuscitation of Blood Pressure and Oxygenation	3
4	Indications for Intracranial Pressure Monitoring	3
5	Intracranial Pressure Treatment Threshold	3
6	Recommendations for Intracranial Pressure Monitoring Technology	5
7	Guidelines for Cerebral Perfusion Pressure	1
8	The Use of Hyperventilation In the Acute Management of Severe TBI	5
9	The Use of Mannitol in Severe Head Injury	3
10	The Use of Barbiturates in the Control of Intracranial Hypertension	3
11	The Role of Glucocorticoids in the Treatment of Severe Head Injury	5
13	The Role of Anti-Seizure Prophylaxis Following Head Injury	5
	Maximal Possible Score	**40**

The activity oriented towards the policy to disseminate guidelines into entire country was based on reports given by project participants and a series of focused discussions on various topics. Major points of the discussion was then summarized n a document specifying current situation and the ways to overcome it. A summary of recommendations was assembled based on comparisons among the countries of the project. The recommendations were formally divided into three categories:

- Continuous improvement of the quality of care;
- Guidelines implementation;
- Specific policy options and the project sustainability.

Within the first one a set of recommendations was agreed upon, which delineates general approaches to setting up a system of continuous quality improvement. The second one deals specifically with the guidelines on national level and methods of implementation. The last one deals with specific policy issues oriented towards the identified barriers and limitations. It also deals with strategies of sustaining the results of the project.

2.3 RESULTS ACHIEVED

2.3.1 Guidelines implementation

All the participating centers started implementing scientific evidence based guidelines on severe TBI management.

2.3.2 The ITCP dataset

Through the retrospective data collection of patients admitted in 2002-2003, and the prospective collection of new patients admitted in 2004, a dataset of 502 records was formed until November 2004. Data collected with ITCP database in the second year of the Project formed the retrospective data set. This set will be used as the baseline data for further analysis. Most of the cases are from Sarajevo and Skopje, what complies with local situation.

2.3.3 Results from interim analysis

An interim analysis was provided with the aim to evaluate the characteristics of the TBI epidemics in the participating centers. It was chosen to focus on the epidemiology of TBI to describe the population of TBI patients and to analyze the most frequent risk factors associated with severe TBI , trying to identify significant differences between centers.

These results provided a background to understanding the extent and the characteristics of clinical procedures involved in managing patients with severe TBI in the centers involved. The analysis also demonstrated problems in quality of collected data. Most of the centers has had problems with following up patients after they were discharged from the hospital or once they were transferred to another treatment entity. Information system in all the countries collecting data on their patients does not allow for consistent tracing of patients once they left the hospital.

The results of the interim analysis were also used to formulate hypothesis for the final data analysis to come.

2.3.4 Hypothesis formulation

A set of hypotheses to be tested with the collected data analysis was developed. Aim of the analysis will be identifying the factors that can improve the outcome of severe TBI victims. The list of hypothesis is included into the report from the meeting in Rijeka.

2.3.5 Final data analysis

The first step was to assess the situation in individual centers where the data collection was performed. The data were cleared for missing values and most of the data input errors were corrected. The tables below display following variables divided by survival and gender:

- Type of injury blunt vs. penetrating;
- Mechanism of injury;
- Isolated vs. polytrauma;
- Injury severity by International Severity Score.

Injury Type Percentage of patients who sustained:	**Total Number**	**% Survived**	***% Male***	**Median Age**	**Median ISS**	**Interquartile Range for ISS**
Blunt Injury	106	50.9	79.3	36.5	26	21-34
Penetrating Injury	17	23.5	94.1	31	43	35.5-51
Percentage of patients involved in:						
Road Traffic Incident	53	58.5	73.6	25	29	21-43
Major Falls	28	50.0	78.6	45	26	19-29
Stabbing Assault	2	50.0	100.0	32	59	43-75
Blunt Assault	5	60.0	80.0	45	18	17.5-23.5
Gunshot Wounds	13	23.1	92.3	30	50	41-51
All Other	12	25.0	100.0	38	28.5	25.5-32.5
Not Known	10	30.0	90.0	62.5	26	18-27
Head Injuries: Patients with:						
Isolated severe head injury AIS $\geq$3	69	55.2	79.9	42	24	18-27
Polytrauma with severe head injury AIS $\geq$3	54	39.2	82.7	28.5	41.5	33-50
GCS <9 in isolated head injury	50	46.0	84.0	49.5	25	21-27
GCS <9 in polytrauma	47	31.8	84.4	30	42	33-50
Injury Severity						
Patients with ISS >15	123	47.2	81.3	35	27	21-38
Patients with ISS <15	18	55.6	66.7	34.5	10.5	6-11

Table 3 Descriptive data on Survival for Sarajevo, Bosnia and Herzegovina

Injury Type Percentage of patients who sustained:	**Total Number**	**% Survived**	**Gender *% Male***	**Median Age**	**Median ISS**	**Interquartile Range for ISS**
Blunt Injury	180	47.2	73. 9	34	27	22-34
Penetrating Injury	20	45	85.00	26.5	37.5	30.5-58
Percentage of patients involved in:						
Road Traffic Incident	110	46.4	72.7	30	27	27-41
Major Falls	57	45.6	75.4	42	27	22-34
Stabbing Assault	3	66.7	100.0	25	27	25-34
Blunt Assault	11	54.5	63.6	40	27	22-34
Gunshot Wounds	17	41.2	82.4	29	48	34-59
All Other	1	100.0	100.0	31	18	18-18
Not Known	7	14.3	100.0	42	27	22-33
Head Injuries: Patients with:						
Isolated severe head injury AIS $\geq$3	42	35.3	73.8	58	20.5	17-27
Polytrauma with severe head injury AIS $\geq$3	164	53	74.5	30.5	34	27-41
GCS <9 in isolated head injury	33	12	87.5	63	26	18-27
GCS <9 in polytrauma	124	40.4	74.2	28.5	34	27-48
Injury Severity						
Patients with ISS >15	206	45.63	75.2	33	27	22-34
Patients with ISS <15	36	83.3	77.8	38.5	10	6-11

Table 4 Descriptive data on Survival for Skoplje, Macedonia

Injury Type				**Median Age**	**Median ISS**	**Interquartile Range for ISS**
Percentage of patients who sustained:	**Total Number**	**% Survived**	**Gender *% Male***			
Blunt Injury	54	44.4	72.2	43	24	16-36
Penetrating Injury	6	33.3	100	39	29.5	25-38
Percentage of patients involved in:						
Road Traffic Incident	31	45.2	71	34	33	24-45
Major Falls	14	50	78.6	57.5	16	16-21
Stabbing Assault						
Blunt Assault	1	100	100	50	16	16-16
Gunshot Wounds	5	20	100	72	25	25-33.5
All Other	3	66.7	66.7	27	16	16-75
Not Known	6	16.7	66.7	56.5	16	16-16
Head Injuries: Patients with:						
Isolated severe head injury AIS $\geq$3	33	56	81.8	49	16	16-20.5
Polytrauma with severe head injury AIS $\geq$3	24	50	70.8	35	38	29-48
GCS <9 in isolated head injury	27	60	81.5	46	16	16-20
GCS <9 in polytrauma	21	50	81	35	37	29-48
Injury Severity						
Patients with ISS >15	60	43.3	75	43	25	16-36
Patients with ISS <15	34	41.2	82.4	56.5	1.5	1-9

Table 5 Descriptive data on Survival for Banska Bystrica, Slovak Republic

Percentage of patients who sustained:	Total Number	% Survived	Gender *% Male*	Median Age	Median ISS	Interquartile Range for ISS
Blunt Injury	80	56.3	86.3	37	33	24.5-45
Penetrating Injury	4	25	75	49	75	50.5-75
Percentage of patients involved in:						
Road Traffic Incident	52	57.7	86.5	25	34	29-46.5
Major Falls	22	45.5	81.8	59	24.5	18-50
Stabbing Assault	1	100	100	60	26	26-26
Blunt Assault	1	100	100	28	48	48-48
Gunshot Wounds	2	100	100	31.5	75	75-75
All Other	3	100	100	67	33	30-38
Not Known	3	100	100	48	17	16-24
Head Injuries: Patients with:						
Isolated severe head injury AIS ≥3	41	52.5	87.8	45	25	20.5-30
Polytrauma with severe head injury AIS ≥3	43	58.1	83.7	28	38	34-55.5
GCS <9 in isolated head injury	40	51.3	87.5	46.5	25	20.5-31.5
GCS <9 in polytrauma	43	58.1	83.2	64.5	39	34-55.5
Injury Severity						
Patients with ISS >15	84	54.8	85.7	38.5	33	25-48
Patients with ISS <15	7	85.7	71.4	45	10	9-14

Table 6 Descriptive data on Survival for Osijek, Rijeka and Zagreb, Croatia

The first insight into the scores revealed certain differences among centers.

Center	Guidelines Compliance Scores		
	Mean	Standard Dev.	CI 95%
Osijek, HR	55.2	18.1	48.3-62.0
Rijeka, HR	71.7	20.5	64.3-79.2
Sarajevo, BH	33.4	8.9	34.8-31.9
Skoplje, MK	31.5	11.4	33.1-30.0
Zagreb, HR	36.5	30.4	45.4-27.5
Banska Bystrica, SK	57.5	15.6	61.1-53.9

Table 7 Guidelines compliance scores by centres

The lowest average scores were found in Skoplje, what corresponds to the fact, that they are not able to monitor intracranial pressures because of financial constraints. On the other hand their approach is rather consistent, what is indicated by a narrow confidence interval and SD. The center with the highest mean scores is Rijeka, what corresponds to reported personal involvement of the team, which was able to secure that all the staff follow the guidelines. High variation in care is visible in Zagreb (SD = 30.4).

Descriptive analysis of relations among variables (Figures 2 to 30)

Following relations were described in graphical and tabular forms:

- Hours of abnormal Central Perfusion Pressure CPP versus hours of Mean Arterial Pressure MAP
- Hours of abnormal ICP vs hours of MAP<70

- Relation of CPP to fluid balance (amount of fluids input versus output)
- Abnormal CPP versus fluid balance
- Abnormal ICP versus fluid balance
- Mean lowest daily SAP vs final outcome
- Hours of abnormal CPP (<70) vs serum glucose
- Hours of abnormal CPP<50 vs serum glucose
- Mean pCO2 vs ICU outcome
- Hours of abnormal CPP (<70) vs manitol dose
- Hours of abnormal CPP (<50) vs manitol dose
- Hours of abnormal ICP>25 vs manitol dose
- Mean daily hours MAP<70 vs. ICU Outcome
- Mean daily mannitol dose vs. ICU Outcome
- Hours of CPP<50 vs. fluid balance
- Mean daily hours of MAP < 70 vs. final outcome
- Mean lowest daily SAP vs. ICU outcome
- Mean daily fluid balance vs. ICU Outcome
- Mean serum glucose vs. final outcome
- Mean insulin vs. mean glucose
- Body temperature vs. ICU outcome
- Barbiturate vs. ICU outcome
- Barbiturate vs. final outcome
- Effects of barbiturate use (CPP<70)
- Effects of barbiturate use (CPP<50)
- Effects of barbiturate use (ICP>25)
- Effects of barbiturate use (MAP<70)

Estimations of Odds Ratios and Control for Confounding using logistic regression

We have used following variables to control for confounding:

- ISS Injury Severity Score to control for the severity of an injury (also for polytrauma) at admission to the hospital;
- GCS Glasgow Coma Scale to control for the extent of brain injury (coma);
- Age because this is well documented confounder in all studies.

Table 8 Relation of the center to ICU outcome

Standardized coefficients (Variable OUTCOME Alive 1 Death 0):

Source	Value	Standard error	Wald Chi-Square	Pr > Chi²	Wald Lower bound (95%)	Wald Upper bound (95%)	OR	95% CI_low	95% CI_up
AGE	-1.356	0.179	57.573	< 0.0001	-1.706	-1.006	0.26	0.18	0.37
ISS	-1.164	0.201	33.417	< 0.0001	-1.559	-0.769	0.31	0.21	0.46
T_AMBULANCE.GCS	2.368	0.274	74.596	< 0.0001	1.831	2.905	10.67	6.24	18.27
CENTERNAME-Osijek	0.000	0.000					1.00	1.00	1.00
CENTERNAME-Skopje	-0.717	0.270	7.069	0.008	-1.246	-0.188	0.49	0.29	0.83
CENTERNAME-Rijeka	0.237	0.196	1.462	0.227	-0.147	0.620	1.27	0.86	1.86
CENTERNAME-Sarajevo	-0.330	0.239	1.897	0.168	-0.799	0.140	0.72	0.45	1.15
CENTERNAME-Zagreb	0.263	0.185	2.033	0.154	-0.099	0.625	1.30	0.91	1.87

Only center in Skopje was related to the outcome from ICU (negative correlation) on a significant level.

Standardized coefficients (Variable OUTCOME Alive 1 Death 0)

Source	Value	Standard error	Wald Chi-Square	Pr > Chi²	Wald Lower bound (95%)	Wald Upper bound (95%)	OR	95% CI_low	95% CI_up
AGE	-1.332	0.175	57.744	< 0.0001	-1.675	-0.988	0.26	0.19	0.37
ISS	-1.153	0.201	32.968	< 0.0001	-1.547	-0.760	0.32	0.21	0.47
T_AMBULANCE.GCS	2.360	0.272	75.336	< 0.0001	1.827	2.893	10.59	6.22	18.04
Country-Croatia	0.000	0.000					1.00	1.00	1.00
Country-Macedonia	-1.015	0.194	27.255	< 0.0001	-1.396	-0.634	0.36	0.25	0.53
Country-Bosna	-0.590	0.174	11.536	0.001	-0.931	-0.250	0.55	0.39	0.78

Table 9 Relation of ICU outcome to the country of patients' origin

When country differences were encountered, then both Macedonia and Bosna came out with significant but negative relation to the ICU outcome.

When investigating individual guidelines recommendations and their relation to outcome, we used the same approach: controlling for confounders: Age, ISS, GCS.

The first recommendation on procedures to be administered during the transportation no significant relation was find with the ICU outcome. One could speculate that this is because of inadequate documentation received from ambulances staff.

Standardized coefficients (Variable OUTCOME Alive 1 Death 0)

Source	Value	Standard error	Wald Chi-Square	Pr > Chi²	Wald Lower bound (95%)	Wald Upper bound (95%)	OR	95% CI_low	95% CI_up
AGE	-1.226	0.165	55.303	< 0.0001	-1.549	-0.903	0.29	0.21	0.41
ISS	-1.041	0.200	27.149	< 0.0001	-1.433	-0.650	0.35	0.24	0.52
T_AMBULANCE.GCS	2.239	0.256	76.501	< 0.0001	1.738	2.741	9.39	5.68	15.50
SCORE_3	0.609	0.143	18.093	< 0.0001	0.329	0.890	1.84	1.39	2.44

Table 10 Recommendation 3: initial resuscitation and the ICU outcome

The odds of survival beyond the ICU stay in case of proper initial resuscitation was administered are significantly high (between 1.4 and 2.4).

Next table document how important it is to follow the recommendation on Indications for Intracranial Pressure Monitoring. By adhering to this one, the odds of survival are significantly increased almost two times (1.46 – 2.57). This is one of the recommendations, which is very much dependent on decisions of hospital managers on resources allocation. That is why; in some centers relatively not expensive tools were not available.

Standardized coefficients (Variable OUTCOME Alive 1 Death 0)

Source	Value	Standard error	Wald Chi-Square	Pr > Chi²	Wald Lower bound (95%)	Wald Upper bound (95%)	OR	95% CI_low	95% CI_up
AGE	-1.286	0.171	56.521	< 0.0001	-1.622	-0.951	0.28	0.20	0.39
ISS	-1.188	0.201	34.775	< 0.0001	-1.583	-0.793	0.30	0.21	0.45
T_AMBULANCE.GCS	2.188	0.257	72.474	< 0.0001	1.684	2.692	8.92	5.39	14.75
SCORE_4	0.659	0.145	20.763	< 0.0001	0.376	0.943	1.93	1.46	2.57

Table 11 ICU Survival and score 4: Indications for Intracranial Pressure Monitoring

This fact is probably related to the next observation, where the relation between score 5: Intracranial Pressure Treatment Threshold and the ICU survival was not statistically significant.

Score 6 Recommendations for Intracranial Pressure Monitoring Technology was related to increased odds of survival. It indicates, that the least costly method of intraventricular catheter is also the most effective in preventing death in the first days of acute treatment.

Standardized coefficients (Variable OUTCOME Alive 1 Death 0)

Source	Value	Standard error	Wald Chi-Square	Pr > Chi²	Wald Lower bound (95%)	Wald Upper bound (95%)	OR	95% CI_low	95% CI_up
AGE	-1.249	0.168	55.271	< 0.0001	-1.578	-0.920	0.29	0.21	0.40
ISS	-1.181	0.200	34.861	< 0.0001	-1.574	-0.789	0.31	0.21	0.45
T_AMBULANCE.GCS	2.187	0.257	72.486	< 0.0001	1.683	2.690	8.91	5.38	14.73
SCORE_6	0.620	0.144	18.503	< 0.0001	0.338	0.903	1.86	1.40	2.47

Table 12 Score 6 Recommendations for Intracranial Pressure Monitoring Technology and ICU survival

Standardized coefficients (Variable OUTCOME Alive 1 Death 0)

Source	Value	Standard error	Wald Chi-Square	Pr > Chi²	Wald Lower bound (95%)	Wald Upper bound (95%)	OR	95% CI_low	95% CI_up
AGE	-1.250	0.169	54.949	< 0.0001	-1.580	-0.919	0.29	0.21	0.40
ISS	-1.193	0.200	35.518	< 0.0001	-1.585	-0.800	0.30	0.20	0.45
T_AMBULANCE.GCS	2.149	0.253	72.316	< 0.0001	1.654	2.644	8.58	5.23	14.08
SCORE_7	-0.548	0.137	16.082	< 0.0001	-0.816	-0.280	0.58	0.44	0.76

Table 13 Guidelines for Cerebral Perfusion Pressure and ICU survival

To our surprise the Cerebral Perfusion Pressure management was negatively correlated with survival. It is hard to interpret this finding, since most of literature sources report different situation.

Recommendation 8 on The Use of Hyperventilation in the Acute Management of Severe TBI was not significantly related to the outcome from ICU. Nor was the Recommendation 9 on The Use of Mannitol in Severe Head Injury as well as the one on The Use of Barbiturates in the Control of Intracranial Hypertension. Also the Recommendation 11 on The Role of Glucocorticoids and Recommendation 12 on Barbiturates were not confirmed. These findings support findings from univariant analysis (see above) and also some new evidence.

Standardized coefficients (Variable OUTCOME Alive 1 Death 0)

Source	Value	Standard error	Wald Chi-Square	Pr > Chi²	Wald Lower bound (95%)	Wald Upper bound (95%)	OR	95% CI_low	95% CI_up
AGE	-1.180	0.161	53.624	< 0.0001	-1.495	-0.864	0.31	0.22	0.42
ISS	-1.132	0.196	33.406	< 0.0001	-1.516	-0.748	0.32	0.22	0.47
T_AMBULANCE.GCS	2.161	0.251	74.041	< 0.0001	1.669	2.654	8.68	5.31	14.20
TOTAL	0.424	0.136	9.701	0.002	0.157	0.690	1.53	1.17	1.99

Table 14 Total Score and the ICU outcome

When summary effects of guidelines adherence was investigated, then firm positive relation between total sum of scores and the ICU outcome was confirmed. That stipulates holistic role of the guidelines in improving outcomes from acute treatment.

2.3.6 Policy for quality improvement in management of TBI patient

The process of guidelines implementation was gradual over the years of the project. Linear regression was used to demonstrate the increase in total score over time.

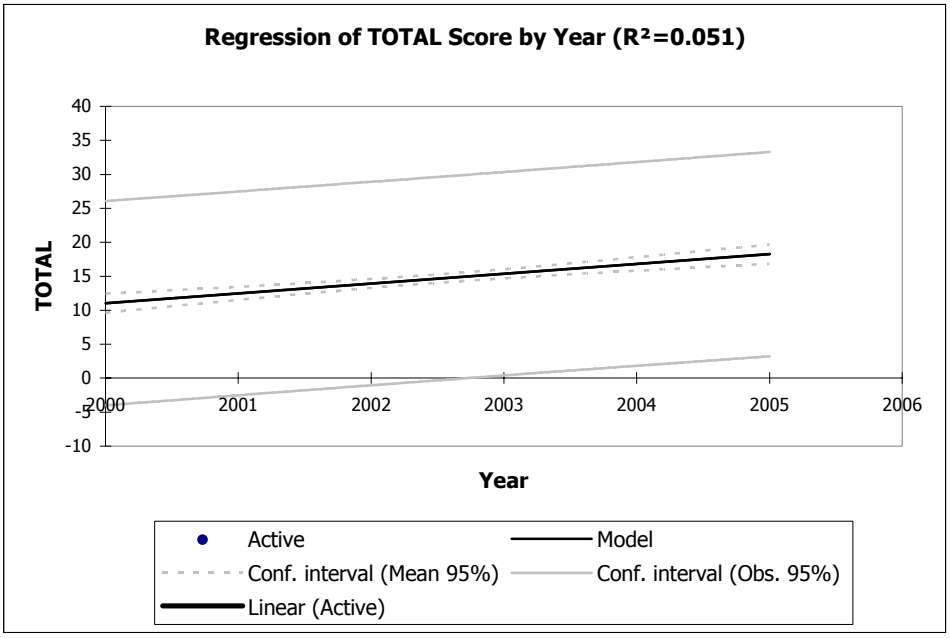
Observations	592.000
Sum of weights	592.000
DF	590.000
R^2	0.051
Adjusted R^2	0.049
MSE	58.052
RMSE	7.619
MAPE	57.352
DW	1.775
Cp	2.000
AIC	2406.314
SBC	2415.081
PC	0.956

Table 15 Linear Regression of Total Score vs Year: Goodness of fit statistics

Source	Value	Standard error	t	Pr > |t|	Lower bound (95%)	Upper bound (95%)
Intercept	-2885.125	516.789	-5.583	< 0.0001	-3900.096	-1870.154
Year	1.448	0.258	5.611	< 0.0001	0.941	1.955

Table 16 Linear Regression of Total Score vs Year: Model parameters

As it could be seen, the increase in total scores achieved was slow in spite all the efforts of teams. That is why the project members agreed on common policies to be applied in individual countries.



It has been agreed, that full guidelines implementation requires a system on national level, which will prepare general conditions for quality processes and in this respect the process of TBI guidelines implementation will be based on a firm legal basis. Such a system would also incorporate tools for External Quality Assessment, based on one or more of the

following options for permitting organizations or individuals to provide health services to the general public:
Licensure. Licensure is a process by which a governmental authority grants permission to an individual practitioner or health care organization to operate or to engage in an occupation or profession. Licensure generally focuses on minimum standards to protect public health and safety.
Accreditation. Accreditation is a formal process by which a recognized body, usually a NGO, assesses and recognizes that a health care organization meets applicable pre-determined and published standards. Accreditation addresses organizational rather than individual practitioner quality.
Certification. Certification is a process by which an authorized body, either NGO or governmental, evaluates and recognizes an individual or an organization as meeting pre-determined requirements or criteria. Accreditation and certification are often used interchangeably. However, one of the most distinctive differences is that, unlike accreditation, certification can also apply to individuals.

As it could be seen from the results of compliance to the guidelines recommendations, increasing the number of scores achieved (or the scope of services provided) is not solely in hands of few dedicated persons. It requires the whole team to act in close cooperation with the rest of the system of care provision. Therefore sanctions for non compliance should be instituted as integral part of the system. A license or accreditation is issued for a limited period of time (e.g. 3 years). The periodic assessment for this permission provides a moment to decide whether the institution/practitioner could continue working. Between the moments of assessment there should be a system for quality control, especially when complaints are launched or when other information indicates poor performance. There should be a range of sanctions, from advice, warning, temporary withdrawal of permission to operate, to permanent withdrawal of permission to operate.

Specific role is there for health insurance companies who make contracts with health care providers and through their system of inspector physicians they perform quality control. However, these inspector physicians can judge whether the insurance company can contract the health institutions. In case of poor performance the insurance companies can (temporarily) stop contracts. They cannot withdraw licenses, and poor performers can continue to work for other insurance companies or private patients.

The project itself addressed one of the most important components of quality of care: standards for provision of "lege artis" health care. The first of them are Managerial and Procedural Standards, which cover general quality issues. These standards are more or less covered in ISO standards. The model developed by the European Foundation for Quality Management is another approach for improving general management according to international standards. Normally, in accreditation or licensing, having standard managerial procedures in place is part of the conditions. However, clinical practice guidelines or standards for diagnostic and therapeutic interventions such as the one on TBI management experimentally introduced into the practice in hospitals of Croatia, Macedonia and Bosnia and Herzegovina represent the cornerstone for a clinician. Unfortunately, no system to develop such guidelines exists in those countries. Most European countries have a system in place to develop such standards, like the United Kingdom (NICE), Scotland (SIGN), New Zealand (NZGG) and the Netherlands (CBO).

Clinical practice guidelines cannot by imposed like managerial procedures, as it would turn health care into a static process. Each patient needs a personalized approach, and standards need to be adapted to medical-technical developments. Clinical practice guidelines should be developed through collaboration between professionals, health institutions and

clients. The guidelines have to be scientifically sound, bringing together international experiences and local practices. Another very important part of the process is the dissemination of Clinical Guidelines. That is why this project played an important role in sensitizing the clinical society on the results and thus by creating a background for development projects of disseminating the guidelines over the country. The methodology should be converted from experimental to a daily routine.

In all the meetings of the team the role of an individual as a leader of change was visible. While TBI is a "silent" disease, it is mostly on clinicians to advocate the need for changes to be implemented in hospitals. Public voice could be of significant support to these efforts. However, as it was clearly visible, the strictly hierarchical system of care in many centers does not stimulate clinicians in various stages in their careers to take this rather insecure road and to speak out their minds. It is also closely related to enumeration and general economic situation of staff and hospitals. In many countries which made the leap from strictly centralized system to more opened ones, that has led to more public involvement and especially more pronounced individual activities in the field.

Deliverable no.	Deliverable title	Delivered Yes/No
17.	Report on **WORKSHOP I** (project work plan and other modifications/fine-tuning based on Assessment of Situation)	**Yes**
18.	TBI situation analysis based on questionnaires	**Yes**
19.	Dataset of retrospective TBI patients from years 2000 – 2001 being used as the base-for further comparison.	**Yes**
20.	Report on training on TBI database use	**Yes**
21.	**Report on descriptive analysis**: descriptive statistical measures, frequencies tables, graphs	**Yes**
22.	**Report explorative analysis**: 2x2 tables mxn tables, probabilities computed	**Yes**
23.	**Summation of findings report**	**Yes**
24.	**Report on WORKSHOP II:** Report on the workshop with proposals for changing practices to improve care of Traumatic Brain Injury victims	**Yes**
25.	**Quarterly reports on TBI guidelines implementation**	**Yes**
26.	**Report** containing data set with the prospective data from TBI patients POST implementation of TBI_Guidelines;	**Yes**
27.	**Analysis of** factors enabling and reinforcing the TBI_Guidelines implementation	**Yes**
28.	**Site visit** to Lorenz-Böhler Trauma Hospital in Vienna	**Yes**
29.	**Report on Final Analysis of data**	**Yes**
30.	**Report on WORKSHOP III containing interpretation of results**	**Yes**
31.	**Final Report** giving full results of project plus participants' collected responses and experiences and their own recommendations for Health policy in the region	**Yes**

Deliverable no.	Deliverable title	Delivered Yes/No
32.	**Policy Paper Report –** special report on policy and practice implications flowing from the results of this project and workshops (as a part of the Final Report)	**Yes**

Table 17 Deliverables

2.4 PROBLEMS ENCOUNTERED

There were no major problems encountered during the execution of activities in three years of the project.

The timing of work packages was not significantly changed. Surprisingly more data was collected then it has been expected.

Resource Schedule - there were no changes to the resources schedule as it applies to the entire duration of the project.

Work packages - there were no changes to work packages required.

2.5 TECHNOLOGY IMPLEMENTATION PLAN

The technology developed during the project could be implemented in health systems under a reform in all countries. The plan for implementation is immensely dependent on policy decisions during the reform process. However, on national level, one could foresee several steps in order to realize the vision:

- Increase public awareness on quality of health care, particularly in the case of TBI;
- Stimulate a creation of association of critical amount of stakeholders to develop a pressure on government to implement changes;
- Institutionalize guidelines development and monitoring of effect either on an NGO or SME or other basis using examples from The Netherlands, UK, Scotland or New Zealand.
- Individual participants will start disseminating their experiences with guidelines and quality improvement in areas of their responsibilities.

2.6 PUBLICATIONS AND PAPERS

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M. Soljakova, Z. Todorova-Nikolova: The effects of hypotensive anaesthesia to the BTI victimes ; Ministry of science, report, Skopje, March 2004

Z. Todorova-Nikolova, M. Soljakova: Management of fluid balance in Brain trauma injuries, DIGI-print, Skopje, 2004 ISBN 9989-2188-46 (COBISS.MK-ID 57959690)

M.Soljakova, B. Kuzmanovska: Syndrom of lost of sodium, Acta anestesiologica Macedonica, :22, 2004

Z. Todorova-Nikolova, B. Kuzmanovska: Resuscitaion of brain trauma victims, I workshop of MSCCM, Skopje, 2004

J.Nanceva, M. Soljakova, E Stoickovski: Anaesthesia for geriatric patients, MSA FEEA VI, :9-18, 2004, ISBN 9989-2018-3-8 (COBISS.MK-ID 56383754)

Z. Todorova-Nikolova: TIVA, MSA FEEA VI, :117-120, 2004 ISBN 9989-2018-3-8 (COBISS.MK-ID 56383754)

Splavski B, Ivić D, Saftić R, Mužević D, Kčira-Fideršek V. Most important early predictors of outcome following severe traumatic brain injury.ations: an international focus meeting, September 19-20, 2003, Rimini, Italy, p 28.

K Dizdarevic, I.Omerhodžić, N Iblizović. B Jahić: Neurosurgical intensive care unit as a prerequisite of current approach to neuropatients. Med Journal, in press.

K. Dizdarević: Cerebral microdialysis and prevention of cerebral ischemia after neurotrauma and aneurysmal hemorrhage. Med Arch, in press

Rusnak,M., Janciak, I., Brazinova, A., Mauritz, W., Project Research Team (Dr. Miroslav Vukic, Dr. Bruno Splavski, Dr. Dean Girotto, Dr. Kemal Dizdarevic, Dr. Maria Soljakova): Epidemic and Clinical Characteristics of TBI situation in three Balkan countries: case study of Croatia, Macedonia and Bosnia. Proceedings of the 7th World Conference on Injury Prevention and Safety Promotion, Wien, June 06th – 09th, 2004.

Leitgeb J., Lenartova L., Dado P., Mauritz W., Rusnak M., Vécsei V.; Trauma systems in Middle Europe. 6th European Trauma Congress, Prague, 16-19 May, 2004

Martin Rusnak, Walter Mauritz, Ivan Janciak, Ingrid Wilbacher, Alexandra Brazinova, and Traumatic Brain Injury Study: Epidemic of Severe TBI in Selected Regions of Austria and Balkan. Proceedings of the third International Conference on Healthcare Systems, Charleston, West Virginia, USA, October 14-17, 2004

Doc. MUDr. Martin Rusnák, CSc a prof. Dr.Med. Walter Mauritz: Kvalita zdravotníckej starostlivosti a znalostná medicína. Klinická epidemiológia ťažkých úrazov mozgu. Červenkove dni preventívnej medicíny, Banska Bystrica,Slovak Republic, June 2003

Wilbacher I., Brazinova A., Janciak I., Leitgeb J., Lenartova L., Mauritz W., Rosso A., Rusnak M.: Brain Injury – a short Epidemiology of TBI and presentation of a new European database. Proceedings of the 11th International Mondsee Medical Meeting, Unterach, Austria, September 9–12, 2004

Rusnak M., Brazinova A., Janciak I., Leitgeb J., Lenartova L., Mauritz W., Rosso A., Wilbacher I.: Perspectives on Guidelines and Standards. Do They Make a Difference in Outcomes? Proceedings of the 11th International Mondsee Medical Meeting, Unterach, Austria, September 9–12, 2004

Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Effects of traumatic brain injury guidelines on outcomes in selected hospitals of Croatia, Bosnia and Macedonia. In: Abstracts, 4th Congress of the Croatian Neurosurgical Society, November 9-12, 2005, Zagreb, Croatia, pp.

Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Implementing traumatic brain injury

(TBI) guidelines in trauma centers of Bosnia, Croatia and Macedonia. In: Abstracts, 13th European conference on public health. November, 10 – 12, 2005, Graz, Austria, pp.

D. Girotto; N. Eškinja: Clinical Analysis And Prognosis of the Treatment Severe Head Injury (SHI) - Croatian Neurosurgical Congress – Zagreb,2005;

D. Girotto; N. Eškinja: Clinical Evaluation Of Polytrauma to the Outcome in Severe Head Injury (SHI) – Croatian Trauma Congress – Zagreb, 2005;

Splavski B, Saftić R, Mužević D, Ivić D, Jančuljak D, Kčira-Fideršek V. Predictors of outcome in the management of severe traumatic brain injury. 3rd Pannonian Symposium on CNS injury; 28 – 30 April 2005; Pécs, Hungary. Clin Neurosci 2005;58(5-6):211.

Splavski B, Saftić R, Radanović B, Butković-Soldo S, Mužević D. Intracranial pressure assessment by transcranial Doppler ultrasonography following severe traumatic brain injury. 13th World Congress of Neurological Surgery; 19 – 24 June 2005; Marrakech, Morocco.

Splavski B, Mužević D, Saftić R, Butković-Soldo S, Kčira-Fideršek V. Predicting outcome of severe traumatic brain injury by transcranial Doppler ultrasonography. 10th Congress of Neurosurgeons of Serbia and Montenegro; 2 – 5 October 2005; Novi Sad, Serbia and Montenegro.

Splavski B, Mužević D, Saftić R, Radanović B, Butković-Soldo S, Jančuljak D. Estimating intracranial pressure after severe traumatic brain injury by transcranial Doppler ultrasonography. 4th Congress of the Croatian Neurosurgical Society; 9 – 12 November 2005; Zagreb, Croatia.

Dizdarević K., Selimović E., Kominlija E.: Subarachnoid hemorrhage: Neurosurgical treatment modalities and etiological analysis. Med Arh. 2006; 60(1) 33-37.

Rusnak M., Dizdarević K., Omerhodžić I., Soljakova M., Splavski B., Vukić M., Girotto D., Mašić I.: Traumatic Brain Injury (TBI) Guidelines, Acta informatica medica. March, 2006, 14 (1): 10-12.

Dizdarević K, Rusnak M, Omerhodžić I, Gavrankapetanović F, Mašić I: Severe traumatic brain injury: Clinical research into management used in Bosnia-Herzegovina. In press.

Dizdarević K., Rusnak M., Mauritz W., Omerhodžić I., Hasanagić A., Girroto D., Soljakova M., Splavski B., Vukić M., Wilbacher I., Brazinova A., Piribauer F.: Implementation of severe traumatic brain injury guidelines. Abstract book. 2005. Surgical Congress of Bosnia and Herzegovina.

Dizdarević K., Koso M., Omerhodžić I.: Neuropsychological appraisal of cognitive function after subarachnoid hemorrhage. Randomized prospective study. 2005.

Dizdarević K., Iblizović N, Omerhodžić I, Al Qoud H.: Presentation of Neurosurgery in Sarajevo through personal serires of operated patients. Abstract book. Surgical Congress of Bosnia and Herzegovina 2006.

Dizdarević K., Omerhodžić I., Iblizović N., Jahić B: Neurosurgical intensive care unit and computerized technology as a prerequisite of contemporary approach to the neuropatients Medical journal 2005, 11 (1-2): 18-23.

Dizdarević K., Omerhodžić I., Omerhodžić M., Iblizović N: Declaration of brain death. Voice of Medics. 2005; 30(2) (2): 104-106.

2.7 CONCLUSION

The project exceeded the set of indicators stated by individual work packages in number of trauma cases collected, in quality of data and in activities of all members of the project. The project succeeded to address the main objective of the project: to improve the quality of care for severe TBI patients by implementing evidence based guidelines into clinical process with following additional effects:

- Significant number of participants from the target region was introduced into practical guidelines implementation and into policy development processes;
- Number of professionals were trained in specific procedures required to provide up to date care for TBI patients;
- There are several scientific studies in preparation with an involvement of participants from different countries taking part in a project (e.g. epidemiology of brain tumor);
- Contacts established during the project execution will remain and will continue;
- There is a proposal being under development for a development project in Croatia, exploiting the results of this project and with a broader scope of quality of care in trauma care.
- Some participants already included results from this project into their teaching materials.

3. MANAGEMENT REPORT

3.1. ORGANIZATION OF THE COLLABORATION

The cooperation among partners was kept on very good level by combination of frequent electronic contacts, web based sharing of information, newsletters, and regular circulation of information on the data set. Naturally the best results were achieved through direct personal communication arranged during the meeting in Rieka and other mostly bilateral meetings. Also conferences proved to be useful for exchange of experiences and results. The major problem observed was in delivering cost statements and annual reports due to certain misunderstandings. However, partners worked hard to overcome the problems with mutual respect.

3.2. MEETINGS

3.2.1. The 4th Workshop

Minutes of the Project's Meeting on October 29th, 2005, Vienna, Austria

Present:
Dr. Kemal Dizdarevic, Dr. Dean Girotto, Dipl. Ing. Ivan Janciak, Dr. Lucia Lenartova, prof. Walter Mauritz, Dr. Dario Muzevic, Dr. Ibrahim Omerhodzic, Dr. Martin Rusnak, Dr. Robert Saftic, Dr. Maria Soljakova, Dr. Bruno Splavski, Dr. Zorka Todorova, Dr. Miroslav Vukic, Dr. Peter Wendsche, Dr.
Zeidler,

Agenda

1. Review of the project results
    a. Assessment from Brussels
    b. Guidelines compliance methodology
    c. EUROTARN
    d. AGREE evaluation
    e. Results general
2. Results from centers
3. Analysis of Austrian data
4. Discussion
5. How to make the results sustainable
6. Lunch break
7. How to design health policies to support EBM based TBI on national basis
8. Publication of results
9. Next steps

Details

Dr. Rusnak opened the seminar and welcomed all participants.
Ing. Janciak informed all on new data installation with the relevant explanations.
Dr. Rusnak promised to send all new data during next week; to enable participants to provide individual reports for final report for Brussels.

He informed on new version of website and the opportunity for next year to write a project for international grant to EU funding promote EUROTARN in Europe.
Dr. Rusnak presented the results from the assessment TBI guidelines with Agree Instrument from individual centers.
Dr. Rusnak directed the participants, where to check the updated information: Itcp.igeh.org/info.
Dr. Rusnak reviewed the results of the project evaluation from Brussels, and opened a discussion to the following issues:

1. the scoring system,
2. whether this guidelines' approach on nursing can be used for nursing treatment,
3. the suggestion to use descriptive statistics and not explorative for final report.

prof. Mauritz stressed the important role of the nursing part of guidelines how to handle the patient (minimal handling, positioning), the process is managed by nurse and written by physician on patient sheet, but also stressed the missing evidence for construction the nursing guidelines.

The scoring system already exists and it is used to assess the compliance to guidelines recommendations at individual patient.

The multivariate statistics was performed using the logistic regression and controlling for confounding variables: age, ISS, GCS at admission. The results will be included into the final report.

prof. Mauritz presented the Austrian data from ICU paper:

- 415 patients from 7 centers
- Duration of the project was 2 and half years
- 50 centers in Austria treat TBI patients
- ICP monitored patients' with good outcome
- Overall ICU mortality is 30%
- Body temperature - high body temperature bad sign
- If hypothermia causes brain death, analyses needed
- Ventilation – to measure mean airway pressure
- Higher mortality - always hyperventilation
- Medication - barbiturates use proved slightly better outcome
- Steroids negative fluid balance – not important for ICP and CPP comparing
- Role of treatment days
- Well-controlled blood glucose level - best outcome

Discussion

Dr. Zeidler suggested using no steroids but crystalloids if the level is over 90.
Prof. Mauritz presented that first resuscitation fluids should be used to stabilize the pressure, as proved that the outcome data showed 37% total mortality after year.
Prof. Mauritz suggested to publish summarized data and to email to each center suggestions for publications.

Suggestions for topics to be described in publications:

- Osteoclastic / osteoplastic surgery

- Effect of treatment on adherence to guidelines

Dr. Rusnak underlined what can be used for publications from existing database in IGEH - good data in database, 4000 cases for analyses to be used for (PhD paper publishing, fellowships), scientific approach is required and opportunity for young scientist to start the research.

Dr. Rusnak informed on conclusions from congress organized in USA, one of the main topics were discussions on situation in Iraq and the tremendous number of victims with TBI injury (30000), Guidelines on TBI treatment published in 1995 were discussed and series of recommendations were pulled together.
Conclusions from this congress were to: nationalize the guidelines, evaluate the quality of the guidelines; consider what parameters to look at, assess the guidelines with Agree Instrument, revise the existing guidelines on national level, create group of countries interested in solving these problems, use these conclusions and ideas in cooperation with EU council for health care and start development of center dealing with research in trauma and quality of health care problems.

Dr. Zeidler shared the experiences from Croatia, where they have lack of education and legislation for EMS.
Prof. Mauritz explained how does it work in Austria, in Graz there are medical students working as volunteers for EMS and provide trainings for physicians and in Vienna it is categorized as full time profession.

Dr. Rusnak informed the project participants on last day of the program, which is October 31st 2005, and suggested to keep the database for future activities for improvement the situation in TBI treatment and publishing the results.

Representatives from Rijeka center explained their system, where training center is linked with university, which assures the education of physicians in EMS, what requires adequate human resources in training centers and qualified instructors for trauma courses.

Skopje center - still need to finalize completing the database with relevant data, they had problems with viruses in their computers, lack of outcome data and difficulties to collect the data from patients, because of low number responds in their forms. Another problem they had with establishment of measurement of ICP, because of lacking basic equipment required for this measurement.
Prof. Mauritz suggested writing publication comparing data on ICP monitoring from LBR and Skopje, with the aim of achieving missing local support, to include data on therapeutical method, what is the influence of ICP on results outcome and what are the results of not being equipped for monitoring ICP and to show to Ministry of health the arguments out of the data available, introduce monitoring and treatment based on these results to the institution dealing with quality of medical care, for official policy, guidelines development to initiate the process and find groups for supporting or try it via public, education, politics.

He informed also in TIS – therapeutic intervention score, which is controlled by MoH Austria, consisting of data on ICU patients, ventilation, intubation, with the aim to justify certain number of points to get required finances.

Dr. Rusnak challenged the participants from Croatia, Bosnia, Macedonia to re - submit for the project funded by NIH. In Croatia they can call for cooperation in projects within their pre – accession to EU.

Next steps:
Dr. Rusnak asked all participants to think of cooperation (based on conclusions from congress held in USA), to join Trauma center of excellence in cooperation with Hospital Pittsburg, creating system of education for courses, doctors, researches, to contribute to research on TBI on different level.
Suggested structure for Consortium was:
2 US universities (Scranton, Pittsburg) and 2 Austrian institutions (University of Vienna, IGEH + participating organizations.

Other suggestions for future cooperation and assuring the sustainability of improving the TBI situation:

- PhD trainings with active involvement of interested,
- Approach members of EU parliament for cooperation and to create the focus groups in EU parliament for TBI Europe wide,
- Write White paper, defining the main objectives.

Final Report
Dr.Rusnak asked all participants to contribute to the final report which will be sent to Brussels. Apart of the annual reporting scheme, he asked them to prepare numbers of PhDs, MSCs who finished their studies on topics of the project and other relevant events, such as patents.

Reported by: Dr. Lucia Lenartova

3.3. EXCHANGES

No exchanges were planned and/or realized during this phase

3.4. PROBLEMS

Give details of any problems with management, administrative and financial aspects of the contract.

The project execution was in some extent influenced by the delay in resolving reimbursement of claims from the centers by the Commission. More efforts then originally expected was needed to deal with this problem and in some cases it originally led to misunderstandings between the coordinator and the center. However, those issues were discussed to the satisfaction of all parties involved.

Similar obstacle stemmed from differences in understanding the need for precise and timely communication between the participants and the coordinator. In many cases (including the final report) the coordinator has to put in more then expected effort to receive a response or a report. It is also that there is a language problem in some participants which probably led to delays.

4. INDIVIDUAL PARTNER FINAL REPORT

Participant 2 AU Vienna Epidemiology

Dr. Franz Piribauer, MD, MPH, The Centre for Applied Epidemiology and Health Policy, Wien, Austria

Activities

The role for the center planned for the whole project was to support the project in data processing and preliminary statistical analysis of collected data. The interim analysis of data with a focus on quality of collected data was carried out by Dr. Brazinova. Data analysis was supported at repeated meeting at the Vienna site of the principal contractor.The results were presented at the 3rd meeting of the project. During the meeting in Rijeka, Dr. Brazinova took an active role in facilitating a discussion among centers preparing a background for further policy development. Participation and presentations at scientific conferences and the following discussion gave further opportunity for improving the data anylsis methods (see publications below).

Results Achieved

Updated descriptive statistical analysis (tabulations, frequencies, descriptive statistical parameters and charts) of collected data from centers was performed and results were discussed during the meeting along with indicators of data quality. The results were also displayed at the web site of the project.

Problems encountered

There were no major problems encountered during this activity. Data collected were in sufficient quality and export the ITCP database to an Excel file was performed with no major difficulties. Statistical analysis could be done as planned.

Technology implementation plan

Not relevant for this activity

Publications and papers

Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Effects of traumatic brain injury guidelines on outcomes in selected hospitals of Croatia, Bosnia and Macedonia. In: Abstracts, 4th Congress of the Croatian Neurosurgical Society, November 9-12, 2005, Zagreb, Croatia, pp.

Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Implementing traumatic brain injury (TBI) guidelines in trauma centers of Bosnia, Croatia and Macedonia. In: Abstracts, 13th European conference on public health. (EUPHA) November, 10 – 12, 2005, Graz, Austria, pp.

Internet publication (abstract)

http://www.pico.at/references/pico/eupha2005/eupha2005Posters-Contents.html

Conclusion

The project proved feasibility of the project approach. Data analysis demonstrated existing differences among centers. The final analysis considered advanced statistical methods as logistic regression and multilevel analysis. This was also proposed during the scientific discussion after presentations of the project approach and findings at scientific conferences. These advanced statistics should be applied in future projects. The missing link for long term outcome data with routine registers, like mortality registers, should be tried to be closed by future research.

Participant 3 CZ Brno

Prof. MUDr. Peter Wendsche, CSc, Urazova nemocnice Brno, Spinalni Jednotka, Brno, Czech Republic

Activities

Prof. Wendsche and Dr. Hude took an active role in communicating their experiences with intensive care of TBI patients within their hospital. They also facilitated active participation of the Project members at the conference in Prague. Dr. Hude actively participated at the meeting in Rijeka contributing to general debate about outcomes and indicators. Prof. Wendshe shared his experiences with his activities in Brno Trauma Hospital.

Results Achieved

Results were consistent with planning.

Problems encountered

There were no major problems encountered during this activity.

Technology implementation plan

Not relevant for this activity

Publications and papers

Please add any papers or publications which might be relevant

Conclusion

The project proved feasibility of the project approach and could be used of an example for other projects dealing with improvement of trauma care.

Participant 4 SK Nove Zamky/Banska Bystrica

Dr. Milan Urbansky, President of Obcianske zdruzenie pre urazy hlavy (Civic Association for Head Trauma), Nove Zamky, Slovak Republic
Dr. Milan Kaniansky, Obcianske zdruzenie Hippocrates, Banska Bystrica, Slovak Republic

Activities

M.Kaniansky put into effect a new experiences of TBI patients care in trauma Centrum and anesthesiology department in the hospital. Applied guidelines of TBI patients treatment.
M Kaniansky took part in the meeting in Rijeka and actively participated in meeting in Vienna about ICP monitoring.
M.Kaniansky took part actively in meeting at Bratislava with presentation about TBI and at Brno with presentation TBI in child age.

The improvement was achieved in TBI treatment with applications of guidelines and new methods of ICP monitoring.

Problems encountered

We didn't meet any significant problems with applications of TBI guidelines.

Technology implementation plan

Not relevant for this activity

Publications and papers

There is a paper under development intended for a publication in Czechoslovak Journal of Trauma.

Conclusions

Project is suitable for
1. Applications to intensive care of TBI patients to improve treatment and monitoring
2. To reduce mortality of TBI patients. Results Achieved

The achieved results are compliant with the results of other centers.

Dr. Milan Kaniansky
Traumasurgeon
Obcianske zdruzenie Hippocrates
Banska Bystrica, Slovak Republic

Participant 5 FYROM Skopje

Work team:

Prof. d-r. Marija Soljakova
Prof. d-r. Zorka Nikolova-Todorova
d-r. Ivica Stefanovski
d-r. Nikola Sikov

Skopje, 24.01.2006

ACTIVITIES (December 2004-December 2005)

This period of time was focused on the final collection of the data, analyses of the data and the activities that correlate with the main objectives of the project. The activities were divided in several phases:

- Collection of data
- Review of collected data
- Analyses of the data with the critical review how it meet the guide lines
- Impact of the obtained results in Public health in the Country
- Impact of the obtained results in traffics regulations of the Country.

The collection of the data was established and in this period of time we have not problem with the collection. The second step of this activity was the review of the collected data. The main activity was to collect the data of the discharged patient, this was necessary to follow up of the outcomes. An evidence of the treatment protocols of the new coming patients according the evidence base treatment of TBI was done.

We performed a meeting with the colleagues from the EMS and the anesthesiologists from Ohrid and Bitola. The task of the meeting was the first care of the patients with traumatic brain injuries. We discussed the guidelines and the necessary steps to improve the prehospital care of brain trauma patients. The implementation of the guidelines and protocols for the management of Trauma Brain Injury patients is a process that will improve the quality of patients' outcomes. The meeting with the section of the neurosurgeons that had place in Skopje was very successful. The data were presented to the Ministry of Health.

The insertion and transfer of the data were performed.

To accept the updated guidelines for the treatment of the traumatic brain injuries, the team was obliged to work in the library and using the Web. Every member was forced to work on one problem connected with the brain trauma. So, the problem of sodium and electrolytes changes in brain trauma patients was solved. We made guidelines for pre-hospital and peri-operative fluid therapy.

The results of the research for brain trauma patients were referred on the III-th Congress of the Anesthesiologists of Macedonia that had held in Ohrid (14-18 septemeber 2005). A representative from the Ministry of the Health was present. The second topic as an oral presentation was dedicated to the electrolytes balance and Sodium in brain trauma patients. The third topic was dedicated to the sepsis in a neurosurgical ICU. The research was done by a young fellow. She analyzed the brain trauma patients as well, she used the SOFA scores. In the concurs of the young fellows she gains the first prize.

The practical work with the nurses for minimal nursing of the TBI patients was performed. A workshop about the TBI guide lines in Ohrid was organized by the team and the neurosurgeons; the team of our Project attended this workshop. The novelties in the therapeutic approach in the therapy of TBI were discussed. A representative of our team joints the meeting in Vienna.

The first meeting of the Association for Critical Care Medicine this year was dedicated to the surgical bleedings. An oral presentation about the prevention of the second bleeding in brain injury patients was presented. Prof Soljakova speech was dedicated to the managements of the bleeding in an ICU settings.

RESULTS ACHIEVED

No	Sex		Age	Weight		Hight	
60	M	F		M	F	M	F
Total	55	5	43±24,9	77,3±6,4	64±1,2	168±7	156±9
%	91,66	8,33					

Table 18 Demographics of the patients with TBI (n=60) (M±SD) %

During this analysis of the data about the age and the genders, was found that the majority of the victims are from 23-58 years old. The 3 of them were children from 0-10 years old. 27 of the patients (45%) in the most active ages are victims of brain injuries.

Mechanism of injury	Number of patients	% in R of Macedonia	% of the average in the Region
Road traffic accidents	25	41,66%	32.04%
Pedestrians	11	18.33%	17.48%
Falls	9	15%	26.92%
Blunt	6	10%	4.21
Penetration wound	4	6,66%	1.62
Others	5	8,33%	11.67
Total	60	100%	96%

Table 19 Mechanism of injury

AMBULACE TRANSPORTATION

The data obtained for the purpose in this project, show that 25 (41.66%) out of 60 patients are directly transported from the field of the accidents to our center. The EMS performs 50 % of all direct transports and the rest are performed by the other traffic participants. 34 victims (56,66%) received prime resuscitation in other medical centers, where they were given first aid (intubation and other elements of the resuscitation) and indirectly transported to our center. The possibility for resuscitation in the field is very low. The main reason for such situation is the poor conditions of the EMS. They respond very fast but the first aid provided by the first responder is inappropriate. The ambulances are very old, uncomfortable for the patients and for the doctors to do the reanimation during the transport. The data implicate for very basic monitoring during the transportation, (only observation and the measurement of the arterial blood pressure). Also the equipment of the ambulances is poor; they have not the accessories for resuscitation.

The results in following tables show that the majority of the accepted patients in our series were with very severe injuries. Most of the death appeared from the 3rd to the 10th day of the admission and were victims of the developed second brain injury. We were not able to collect the data of the majority of discharged patients. The main reason of that is that on the data of histories from the archives of the discharged patients the addresses and telephone number for contact missed. All those rest as patients with unknown outcome.

	GCS >9	GCS 6-9	GCS 3-5	Alive	Death	Unknown
On admission	5	28	27	60	/	
3-th day	15	18	17	50	10	
10-th day	25	18	7	40	10	
30 days	37	3	/	/	/	/
90 days	/	/	/	/	/	/
180 days	/	/	/	/	/	/
360 days	/	/	/	/	/	/

Table 20 correlation between the BEST GCS on admission and the outcome

Scores	ISS	RTS	TRISS
M	23,80	5,08	69,21
SD	16,24	1,205	31,35

Table 21 The severity of trauma in the TBI cases

On the next table are discussed the main predictor factors for poor outcome. It is shown that 30 patients in the series of 60 patients gain more than 65 scores. The main reason for that was the severe shock that was developed to the patients (in 24 cases the MAP was <70 mmHg).

factors	range	Number of cases
The severity of trauma TRISS	>65 (65±…)	30
Haemo-dynamics changes	MAP <70	24
Co-morbidity (CVD, DM I/II, COPD, kidney diseases, alcoholism)	>1	(13+4+5+4+6):5=6,4
Spinal injury	complete	2
Aspiration	X-ray approved	20

Table 22 Incidence of predictor factors for poor out come in our series

Co-morbidity is a very serious problem that influences the outcome of the injured patients. In our 60 patients, in 32 of them more than one concomitant disease was found. The majority of the patients were with CVD (13 patients), 4 with diabetes mellitus and 5 with chronic obstructive pulmonary disease. One third of the patients on admission were with developed pneumonitis as a result of the aspiration. This is an addition problem that is a result of the poor conditions during the transportation of the patients.
The use of alcohol as a risk factor and the reason for traffic accident and head injury was found in admission at 22 of the patients in our series that is 36,66 of all treated patients. The comparative analyzes and the cross analyzes with other partners in this research study shows that this figure in Macedonia is higher. We could speculate, but one of the possible reasons is the weak regulation by the law about the use of alcohol during driving.
The low Mean arterial blood pressure less than 85 mm Hg more than tree days was found in 4 cases.

The definitive diagnoses and the type of brain injury was confirm by CT SCAN in all investigated patients. All of the accepted patients were scanned more than one time, (first on admission and on the following days according to the condition of the patients). Any worsening of the consciousness, acute development of tachycardia or increase of the blood pressure was documented by a CT scan. The average numbers of the performed CT Scans was 1,29 in our 60 patients.

According to the specific treatment, analgesia with fentanyl or tramadol was performed approximately during 5 days. It is very well documented that one of the reason of the development of the brain swelling in brain trauma patients, is the pain. It was very important to relief the pain from the very beginning. The second precaution was to permit good oxygen supply to the patients; they were intubated and artificially ventilated. The average duration of the assisted ventilation was 6 days; the duration of the persistence of the intubation with endotracheal tube was 7 days. On most of the severe injured patient a tracheotomy was performed. The average of the days spend in the ICU were 12 days.

According the final goal: to reduce the mortality, we found that in our series of 60 patients, 40 patients (66,66%) were alive after 10 days from the injury and 20 died or 33,33%. The long-term disability after 90, 180 and 360 days of the injury was checked. The modified GOS for this purpose was used. The data obtained was 4 for all interviewed patients in the noted day's term. Those data are similar in all centres included in this project.
The results in the third year show the improvement in the survival compared with the retrospective data.

PROBLEM ENCOUTERED

1. The transportation from the high distance posts leads to the losing time for proper treatment of the TBI. The patients are not treated or operated very quickly.
2. The ICP measurement and its' use as routine is still missing.
3. Next problem was with the computer, we finally fixed it.
4. The completion of the outcome of the patients was very difficult. We were not able to collect the data of the majority of discharged patients. Even that we made a directory with the addresses and telephone numbers of discharged patients, they are not responded. All those patients rest with unknown outcome so the severity of the disability could not be accounting.

TECHNOLOGY IMPLEMENTATION PLAN

According to the results achieved from the project the implementation should be stratified on three divisions: development of the human resources, improvement of the health care and the improvement of the community policies.
1. Potentials- development of the human resources: M1, M2, M3
M1 The results of the TBI project will be presented to the qualified doctors-neurosurgeons, EMS professionals and anesthesiologists.
M2 A workshop: Evidence based Medicine - the implementation of the TBI guidelines.
M3 Spread of the knowledge to three main centers in the country- Visit with lectures
All the participants will be encouraged to visit the IGEH web site. An interactive learning will be provide
2. Second action to improve the health care:
Technology: improvement of the health care: M4, M5, M6, M7
Volunteers to use the TBI-Trac database
Education on evidence based treatment of the TBI
Introduction of the invasive methods of monitoring, ICP measurement
The results to be presented to the health Authorities
3. Third Action
Community policies: M8, M9, M10, M11, M12
Improvement of the regulations on the roads/ improvement of the quality of the driving.
Policies for driving under alcohol.
Presenting the data to the NGO-as to the organization: save the children
Involvement of the local WHO organization for support of short schedules
Information's in mass media
CME Courses for Staff employed in the EMS
Promotion of the use of generic technology and IGEH web side for self education

PUBLICATIONS AND PAPERS

1. Soljakova M., Todorova-Nikolova Z., Sikov N., Stefanovski I.: Sodium metabolism and brain trauma injury; III -rd Congress of Anesthesiology, Book of abstracts:34, Ohrid, September 2005.
2. Todorova-Nikolova Z., Soljakova M.: Management of VIP in brain trauma patients, III -rd Congress of Anesthesiology, Book of abstracts:22, Ohrid, September 2005.
3. Soljakova M., Todorova-Nikolova Z., Stefanovski I., Sikov N.: Preliminary results of the Project on BTI, Book of abstracts:24, Ohrid, September 2005.
4. M.Soljakova,: Management of the bleeding in an ICU settings: Workshop of MSCCM, February, Skopje, 2006

CONCLUSION

TBI causes significant mortality, morbidity, and contributes substantially health care costs. Accepting of the guidelines is essential for the improvement of the treatment of the victims of the traumatic brain injuries. To force and improve the normal cerebral physiology is essential to alter the track of the poor out come. Despite acute reductions in ICP and improvements in CBF with mannitol therapy, there are insufficient data to preclude either a harmful or beneficial effect on mortality. Hyperventilation may acutely control ICP; Anticonvulsant prophylaxis has been shown to prevent early seizures after TBI. Evidence based medicine have failed to show a beneficial effect on mortality or neurological outcome in TBI patients treated with corticosteroids; however, a small but important beneficial effect of corticosteroids cannot be ruled out.

According the TBI guidelines we will use the following recommendations:

- to control the ICP less than 20-25 mm Hg;
- in the absence of an ICP monitor we will maintain the CPP ≤ 70 mm Hg; MAP above 90 mm
- to optimize the cerebral oxygenation we will provide a normocapnia

The improvement of the social and economic conditions of the country will improve the state of the roads in the country that will decrease the number of the victim injured in the road traffics.
The policies of the country would be to improve the health care and to decrease the number of the accidents that lead to brain injuries.
The obtained results at the end of the first year, that the severity of the brain injuries are due to traffic accidents, made an Impact in the Country traffics regulations. The low to use the seats belt and to drive with the lights-on is appreciated by the drivers.

Report prepared by Marija Soljakova

Participant 6 HR Osijek

Activities

During the project, data for 34 patients suffering severe traumatic brain injury were gathered. All patients' data were entered into the database designed by IGEH and on a weekly basis sent over the Internet to the IGEH, Vienna, for further statistical and technical processing. As the project developed and quality of data improved, entire database was revised and possible mistakes corrected. The database was updated daily.
According to the project plan established at the project start, we all met in Vienna in October 2005 for final review of our work.

Results achieved

Overall results showed improvement in the management outcome, as well as reduction of morbidity and significant advance in Guidelines compliance when compared to our results achieved in the previous years which were gathered and analyzed in comparable fashion.

Problems encountered

Problem related to the quality of ambulance data persisted, due to organization of emergency care system in Croatia.

Technology implementation plan

According to the Guidelines for the management of severe head injury, a state-of-the-art treatment for patients suffering severe traumatic brain injury was successfully implemented at our Department as a daily routine due to cooperation between the neurosurgeons and the anesthesiologists involved. At the end of the project, we are confident that our institution meets all prerequisites for successful treatment of patients sustaining severe traumatic brain injury.

Publications and papers

- Splavski B, Saftić R, Mužević D, Ivić D, Jančuljak D, Kčira-Fideršek V. Predictors of outcome in the management of severe traumatic brain injury. 3rd Pannonian Symposium on CNS injury; 28 – 30 April 2005; Pécs, Hungary. Clin Neurosci 2005;58(5-6):211.
- Splavski B, Saftić R, Radanović B, Butković-Soldo S, Mužević D. Intracranial pressure assessment by transcranial Doppler ultrasonography following severe traumatic brain injury. 13th World Congress of Neurological Surgery; 19 – 24 June 2005; Marrakech, Morocco.
- Splavski B, Mužević D, Saftić R, Butković-Soldo S, Kčira-Fideršek V. Predicting outcome of severe traumatic brain injury by transcranial Doppler ultrasonography. 10th Congress of Neurosurgeons of Serbia and Montenegro; 2 – 5 October 2005; Novi Sad, Serbia and Montenegro.
- Splavski B, Mužević D, Saftić R, Radanović B, Butković-Soldo S, Jančuljak D. Estimating intracranial pressure after severe traumatic brain injury by transcranial Doppler ultrasonography. 4th Congress of the Croatian Neurosurgical Society; 9 – 12 November 2005; Zagreb, Croatia.

Conclusion

As far as our experiences are concerned, this project has met the expectations regarding the benefit of the treatment of severe head injured patients according to the Guidelines for the management of severe head injury.

We believe that this project has determined the main problems facing the management of severe brain injury and offered variety of solutions in overcoming the encountered problems.

Bruno Splavski, MD, PhD

Head, Department of Neurosurgery,
Osijek Clinical Hospital

Participant 7 HR Rijeka

In the period of the 3rd year of the project we were collecting data of the patients with TBI continued with new entries of 26 patients.
The data were exported to the project centere.

In this period we were no major problems encountered during this activity. Data collected were in good quality and export the ITCP database. Problem with „alcoholisms“ in TBI patients in this period missing . In this period with all Croatian participant meet in Zagreb /1x/, Osijek /2x/ and finally at Wien. We reviewed montly and annual problems and project plans. In all participants we were happy to participate in such research for better results in outcome of patients with TBI.

Very good cooperation with intesivist in our institution are results for good outcome and based on continuity of neuromonitoring according the Guidelines for the management of TBI, because all colllected data we was strictly followed the management protocol in accordance with the Guidelines for management of BTI.
Publications and paper:

- D. Girotto; N. Eškinja: CLINICAL ANALYSIS AND PROGNOSIS OF THE TREATMENT SEVERE HEAD INJURY (SHI) - Croatian Neurosurgical Congress – Zagreb,2005;
- D. Girotto; N. Eškinja: CLINICAL EVALUATION OF POLYTRAUMA TO THE OUTCOME IN SEVERE HEAD INJURY (SHI) – Croatian Trauma Congress – Zagreb, 2005;

Conclusion:

At finally we regarding ther benefit of treatment of severe head injured patients according to Guidelines for management of TBI and we were happy to participate in this project.

Mr sc Dean Girotto. MD – Dept of Neurosurgery, Clinical Hospital Rijeka;

Participant 8 – HR Zagreb

Zagreb, January 10th , 2006

Activities

In the year 2005 we gathered another 33 patients who sustained severe head injury and who were treated either surgically or medically in our Neurosurgical department. According to project's goal, all patients' demographic and clinical data have been entered into the database designed by International Brain Trauma Foundation (IGEH, Vienna). Clinical course was then monitored and data regarding medical treatment and clinical condition was evaluated and entered in the ITCP database. Database was weekly reviewed for updates und after updating electronically sent to Vienna.

There were also two meeting organized in 2005 with regards to project. First meeting was organized in Zagreb, May 2005, with local (regional i.e. .Croatian) participants. Some problems with ambulance data were discussed and couples of solutions for overcoming those problems were proposed. All of that was later used in project as useful adjuncts.

Second meeting was organized in Vienna, last week of October, where all international participants gathered together for project evaluation. Patient's outcome and treatment modalities were discussed and further direction of investigation was suggested. Some criticism existed over one center results, but all in all participants were happy to participate in such research hoping for better results in outcome of patients with severe head injury.

Results achieved

In the year 2005 we treated 33 patients with severe brain injury in our Neurosurgical Department. Overall outcome showed much better results as compared to the year before. The most important reason for that was the number of transferred patients which was significantly lower as compared to previous year. We achieved a six months mortality rate of 36%. Out of 64% of patients who survived severe brain injury, 62 % had good and moderate outcome. The incidence of ICP monitoring was 72% and both intraventricular and intraparenchimal catheters were used.

Problems encountered

There were some minor problems related to the quality of ambulance data and missing data of the transferred patients, but after a meeting organized in Zagreb, May 2005, with all Croatian participants in this project and with the chef of Zagreb and Osijek ambulance service, that problem was significantly diminished.

Technology implementation plan

The treatment of severely head injured patients in our institution, is, in particular, based on continuity of neuromonitoring.

According to the Guidelines for the management of severe head injury, we have implemented a state-of-the-art treatment for patients with severe head injury as a daily routine. With a good cooperation between the neurosurgeons and intensivist's at our Department, current "state of the art" treatment of severe head injury, was in general, very successful.

Publications and papers

Last year we continued to publish papers about the topic of the project as well as to inform the public about our continuous effort in improving the outcome in severe head injury.

1. Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Effects of traumatic brain injury guidelines on outcomes in selected hospitals of Croatia, Bosnia and Macedonia.

In: Abstracts, 4th Congress of the Croatian Neurosurgical Society, November 9-12, 2005, Zagreb, Croatia, pp.

2. Rusnak M, Mauritz W, Janciak I, Dizdarević K, Girotto D, Šoljakova M, Splavski B, Vukić M, Wilbacher I, Brazinova A, Rosso A, Piribauer F. Implementing traumatic brain injury (TBI) guidelines in trauma centers of Bosnia, Croatia and Macedonia. In: Abstracts, 13th European conference on public health. November, 10 – 12, 2005, Graz, Austria, pp.

Assistant Professor Miroslav Vukic was invited speaker at the Fifth Croatian Congress of Neurology (held in Osijek, September 2005) reporting the current concept of pharmacological therapy of severe head injury and neuroprotection. He was also reporting about this particular project and it's perspectives in the future.

Conclusion

This project met all our expectations regarding the benefit of treatment of severely head injured patients according to the Guidelines for the management of severe head injury. In order to continue the project activities on local level, and with support of Ministry of Health, I wrote the letter and my proposal of supporting continuity of that project to Croatian Ministry of Health, explaining the benefit of treatment of severely head injured patients according to evidence - based medicine literature.

It was a general conclusion of all participants at our last meeting in Vienna that project like this should be continued and based on international participants and their personal and team-like experience.

Assistant Professor Miroslav Vukic, MD, PhD
National Project Coordinator

Participant 9 - BH Sarajevo

Dr. Kemal Dizdarevic Department of Neurosurgery, Clinical Centre University of Sarejevo, Bosnia and Herzegovina

Activities

During 2005 we collected 45 patients sustaining severe traumatic brain injury. The patients were treated in our Neurosurgical intensive care unit and all relevant data were entered in the International Brain Trauma Foundation database. Database was updated regularly and data were sent to Vienna. We have organized the neurosurgical meeting in September 2005 in Sarajevo with international participation. All aspects of neurotrauma intensive care treatment are discussed on the meeting.

Additional meeting was organized in Vienna in October 2005. During this meeting the international participants have evaluated and discussed patient's outcome and treatment modalities.

Results Achieved

The patients overall outcome showed better results than last year. The most important reason for this was the fact the standardized protocols were introduced in our Neurosurgical intensive care unit.

Problems encountered

There were some problems connected with the lack of resources and number of doctors. Also, we have chronic problems with ambulance service and primary level of medical care which have significant impact on overall outcome of our patients.

Technology implementation plan

The new technology was introduced in our Neurosurgical Intensive care unit. The monitoring of intrinsic brain biochemistry using cerebral microdialysis method was established in September 2005. Also we have continued with physiological, morphological and clinical monitoring of our patients.

We have implemented the guidelines for treatment of traumatic severe brain injury according AANS. We also stated with implementation of "Lund Concept" in December 2005 which represents a different approach to brain injury compared with AANS approach. This concept points out an importance of volume targeted therapy and reduction of ICP through reduction of brain volume.

Publications and papers

- Dizdarević K., Selimović E., Kominlija E.: Subarachnoid hemorrhage: Neurosurgical treatment modalities and etiological analysis. Med Arh. 2006; 60(1) 33-37.
- Rusnak M., Dizdarević K., Omerhodžić I., Soljakova M., Splavski B., Vukić M., Girotto D., Mašić I.: Traumatic Brain Injury (TBI) Guidelines, Acta informatica medica. March, 2006, 14 (1): 10-12.
- Dizdarević K, Rusnak M, Omerhodžić I, Gavrankapetanović F, Mašić I: Severe traumatic brain injury: Clinical research into management used in Bosnia-Herzegovina. In press.
- Dizdarević K., Rusnak M., Mauritz W., Omerhodžić I., Hasanagić A., Girroto D., Soljakova M., Splavski B., Vukić M., Wilbacher I., Brazinova A., Piribauer F.: Implementation of severe traumatic brain injury guidelines. Abstract book. 2005. Surgical Congress of Bosnia and Herzegovina.
- Dizdarević K., Koso M., Omerhodžić I.: Neuropsychological appraisal of cognitive function after subarachnoid hemorrhage. Randomized prospective study. 2005.
- Dizdarević K., Iblizović N, Omerhodžić I, Al Qoud H.: Presentation of Neurosurgery in Sarajevo through personal serires of operated patients. Abstract book. Surgical Congress of Bosnia and Herzegovina 2006.
- Dizdarević K., Omerhodžić I., Iblizović N., Jahić B: Neurosurgical intensive care unit and computerized technology as a prerequisite of contemporary approach to the neuropatients Medical journal 2005, 11 (1-2): 18-23.
- Dizdarević K., Omerhodžić I., Omerhodžić M., Iblizović N: Declaration of brain death. Voice of Medics. 2005; 30(2) (2): 104-106.

Conclusion

We found this project as a very important effort in our intention to establish the standardized and scientific based approach to the problem of severe traumatic brain injury.

We have modified our everyday practice and published our results in local Bosnian medical journals. At the moment we are preparing to start the dissemination of the scientific evidence based knowledge to all Hospitals in Bosnia & Herzegovina which deal with severe traumatic brain injury. In the near future, we will try to overcome some obstacles through creation of public awareness campaign.

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Chairman, Department of Neurosurgery, Clinical Centre University of Sarajevo
Bosnia & Herzegovina

5. DATA SHEET FOR FINAL REPORT

Contract number : ICA2-CT-2002-10005 **Year** : 2005

Data sheet
for final report
(to be completed by the co-ordinator for the whole project)

1. Dissemination activities	Published	Submitted
Number of communications in conferences	16	
Number of communications in other media (internet, video, …)	1	-
Number of publications in refereed journals	5	3
Number of articles/books	-	-
Number of other publications	-	-

2. Training	
Number of PhDs	5
Number of MScs	3 -
Number of visiting scientists	-
Number of exchanges of scientists (stay longer than 3 months)	-

3. Achieved results	
Number of patent applications	-
Number of patents granted	-
Number of companies created	-
Number of new prototypes/products developed	-
Number of new tests/methods developed	-
Number of new norms/standards developed	-
Number of new softwares/codes developed	1 -
Number of production processes	-
Number of new services	-
Number of licenses issued	-

4. Industrial aspects				
Industrial contacts	yes	☐	no	☒
Financial contribution by industry	yes	☐	no	☒

Industrial partners : - Large	yes ☐	no ☒
- SME[11]	yes ☐	no ☒

6. COMMENTS

Other achievements (use separate page if necessary)

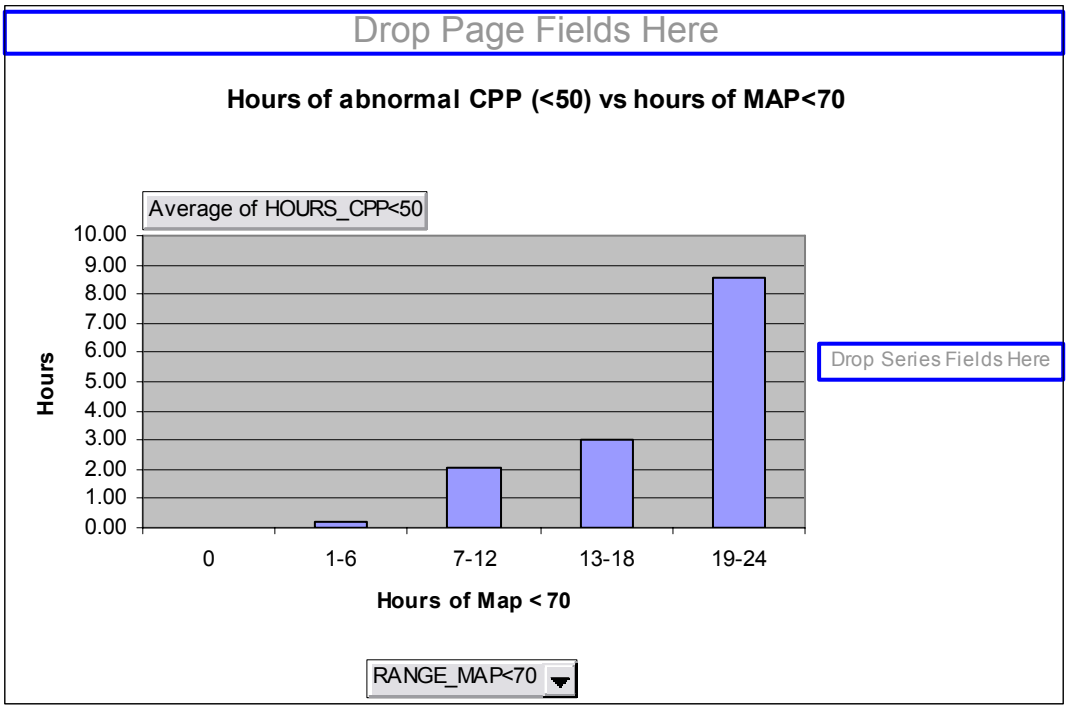
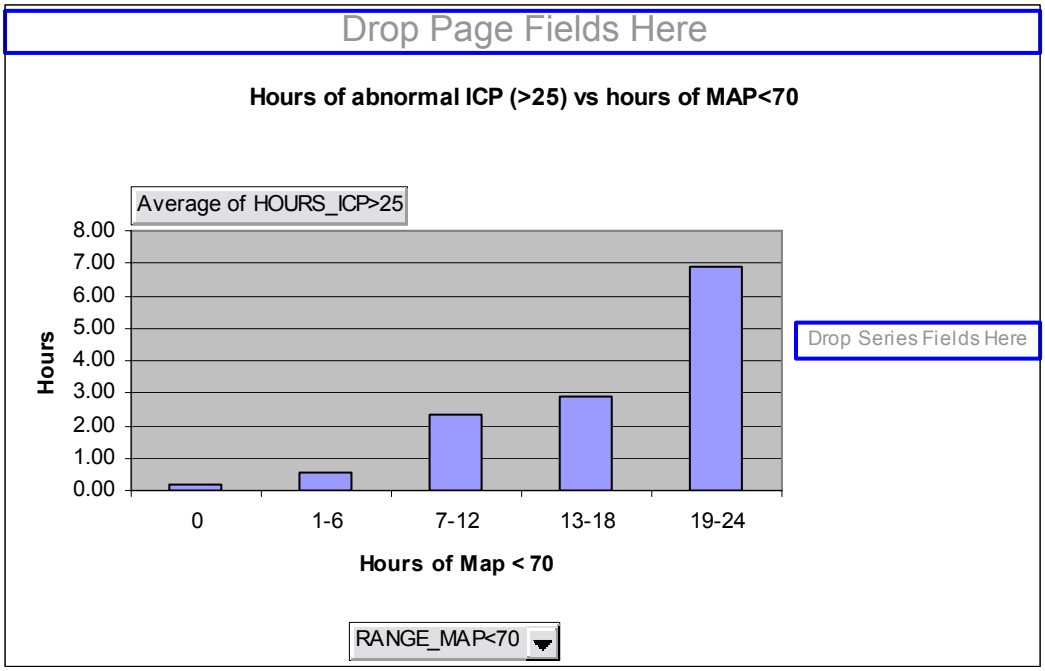


Figure 1 Hours of abnormal Central Perfusion Pressure CPP versus hours of Mean Arterial Pressure MAP

Average of HOURS_CPP<50	
RANGE_MAP<70	Total
0	0.02
1-6	0.19
7-12	2.06
13-18	3.00
19-24	8.59
Grand Total	0.36

Figure 2 Hours of abnormal ICP vs hours of low MAP



Average of HOURS_ICP>25	
RANGE_MAP<70	Total
0	0.21
1-6	0.53
7-12	2.33
13-18	2.88
19-24	6.89
Grand Total	0.52

Figure 3 Hours of abnormal ICP vs hours of MAP<70

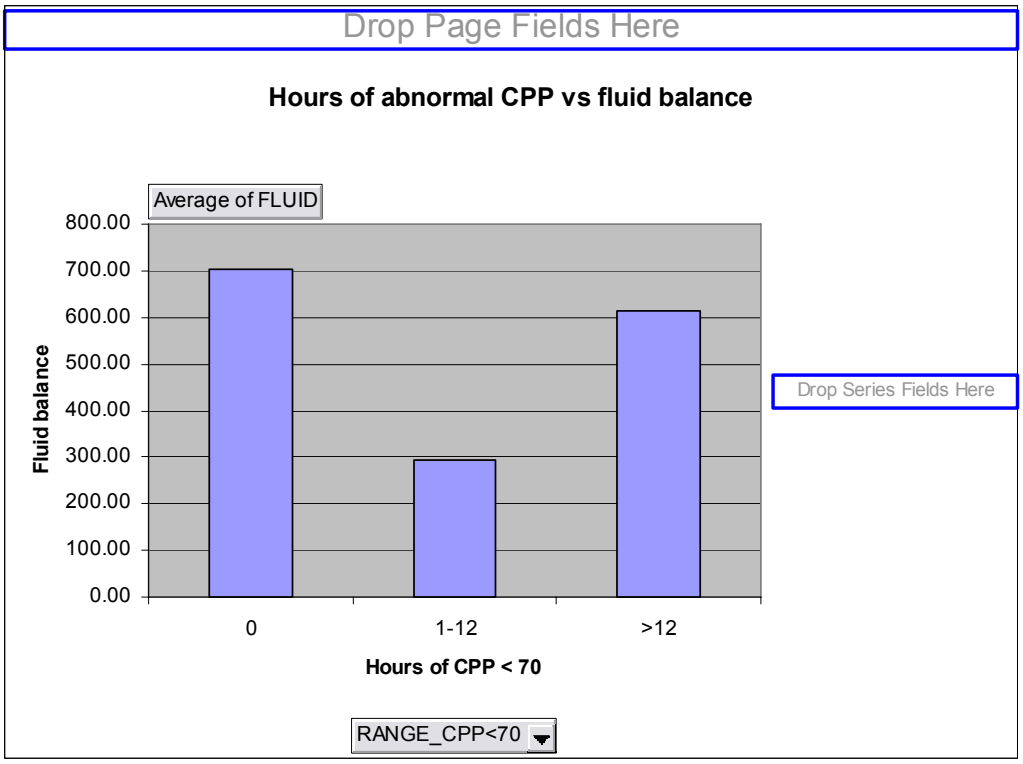


Figure 4 Relation of CPP to fluid balance (amount of fluids input versus output)

Average of FLUID	
RANGE_CPP<70	Total
0	703.47
1-12	292.44
>12	614.61
Grand Total	678.35

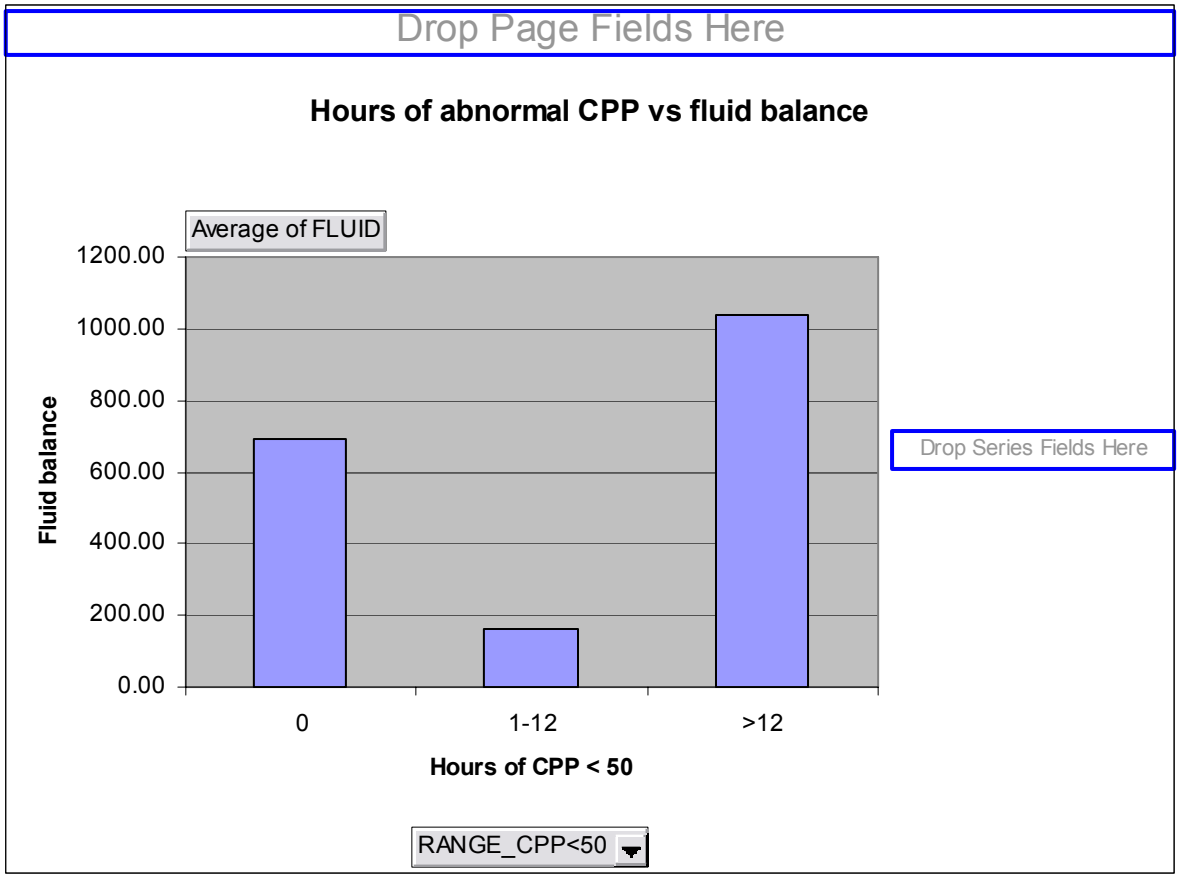


Figure 5 Abnormal CPP versus fluid balance

Average of FLUID	
RANGE_CPP<50	Total
0	690.23
1-12	162.30
>12	1037.22
Grand Total	678.35

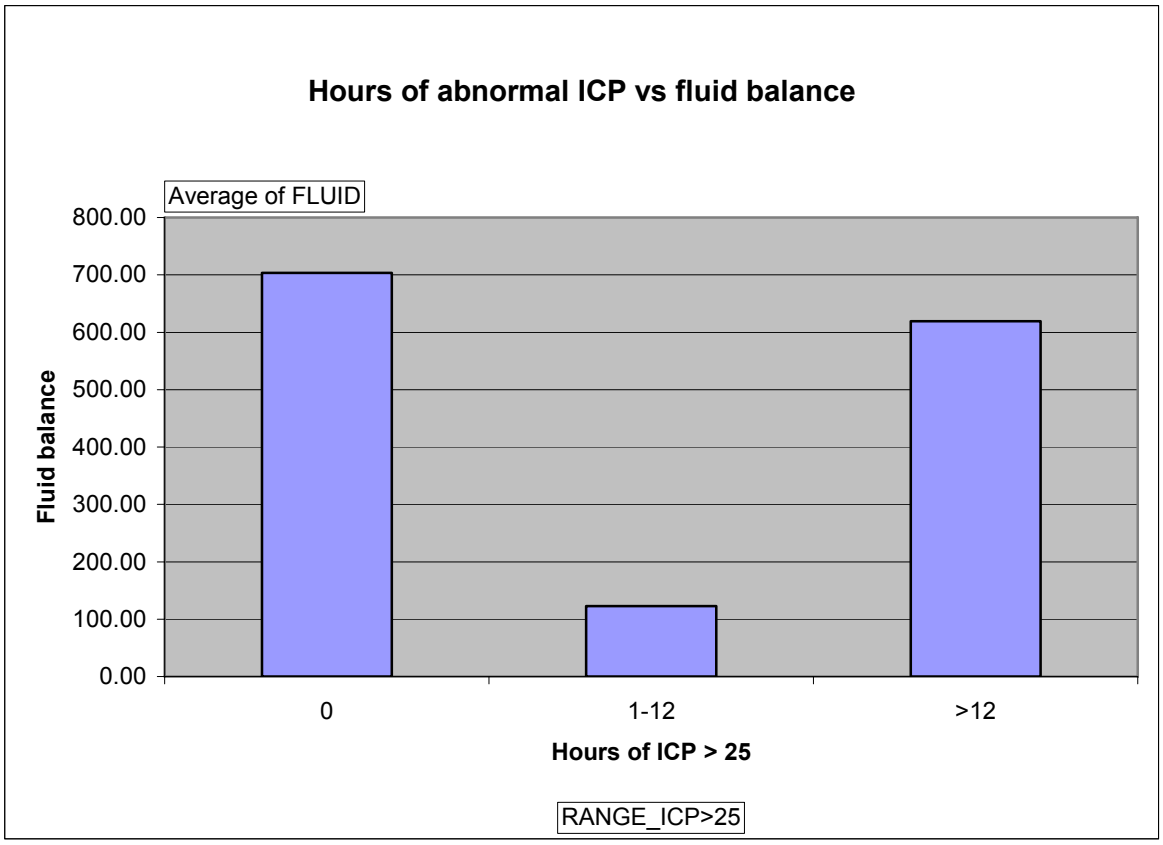


Figure 6 Abnormal ICP versus fluid balance

Average of FLUID	
RANGE_ICP>25	Total
0	703.45
1-12	122.86
>12	618.97
Grand Total	678.35

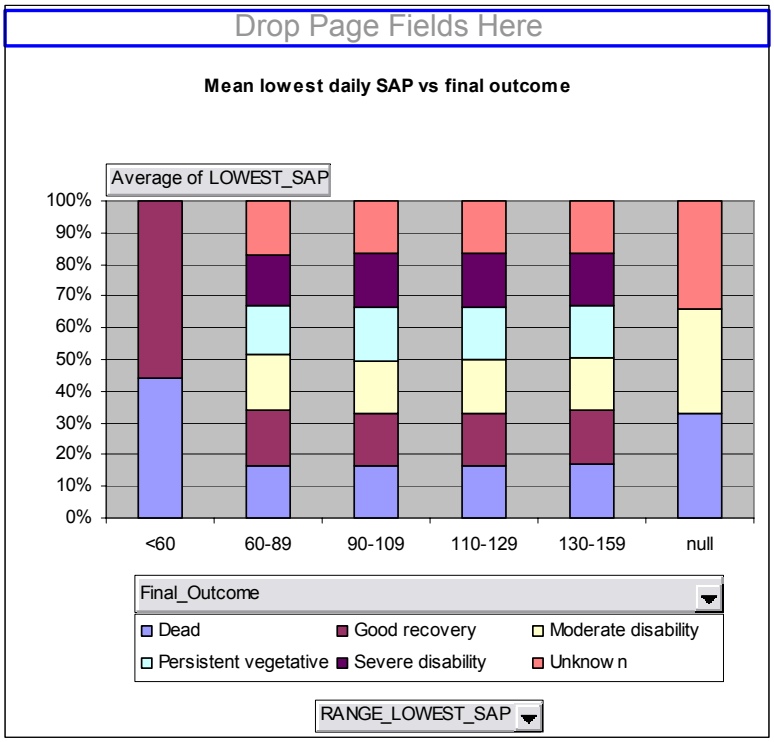


Figure 7 Mean lowest daily SAP vs final outcome

Average of LOWEST_SAP	Final_Outcome						
RANGE_LOWEST_SAP	Dead	Good recovery	Moderate disability	Persistent vegetative	Severe disability	Unknown	Grand Total
<60	39.84	50.00					40.00
60-89	73.45	79.53	81.33	70.00	72.50	75.88	74.03
90-109	96.94	98.10	97.92	98.89	99.09	98.59	97.67
110-129	115.69	116.89	116.89	117.42	117.52	115.94	116.45
130-159	140.17	134.48	135.31	136.50	131.35	135.33	136.95
null	165.75	#DIV/0!	165.78	#DIV/0!		170.00	165.86
Grand Total	**103.11**	**114.22**	**114.07**	**116.89**	**114.55**	**114.24**	**109.73**

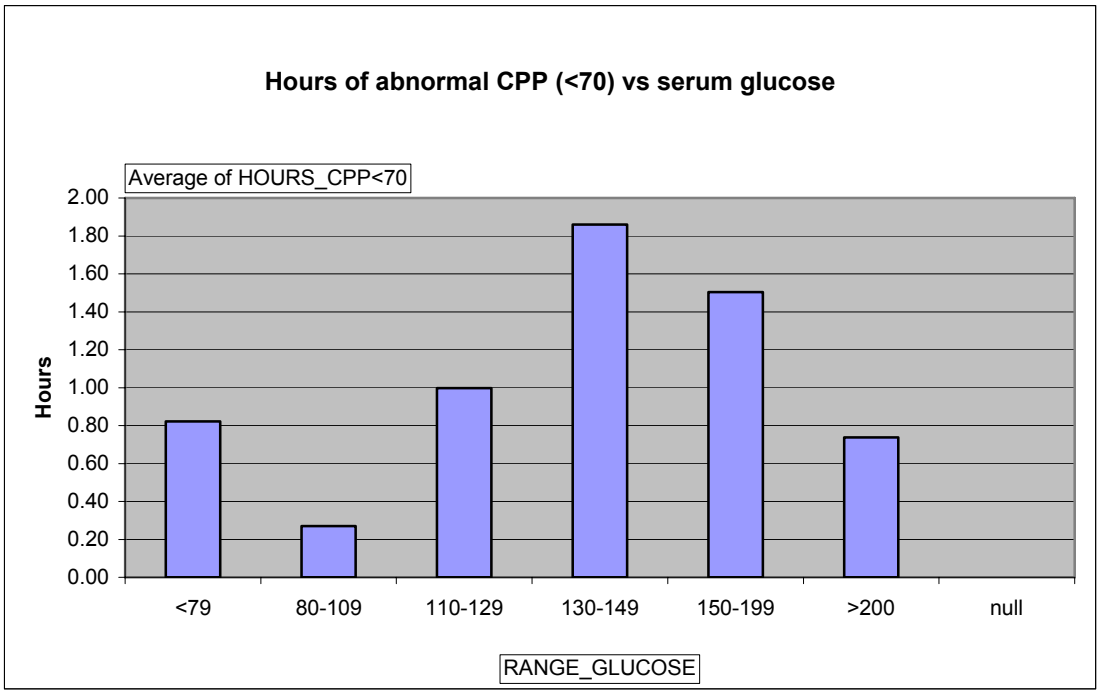


Figure 7 Hours of abnormal CPP (<70) vs serum glucose

Average of HOURS_CPP<70	
RANGE_GLUCOSE	Total
<79	0.82
80-109	0.27
110-129	1.00
130-149	1.86
150-199	1.50
>200	0.74
null	0.00
Grand Total	0.85

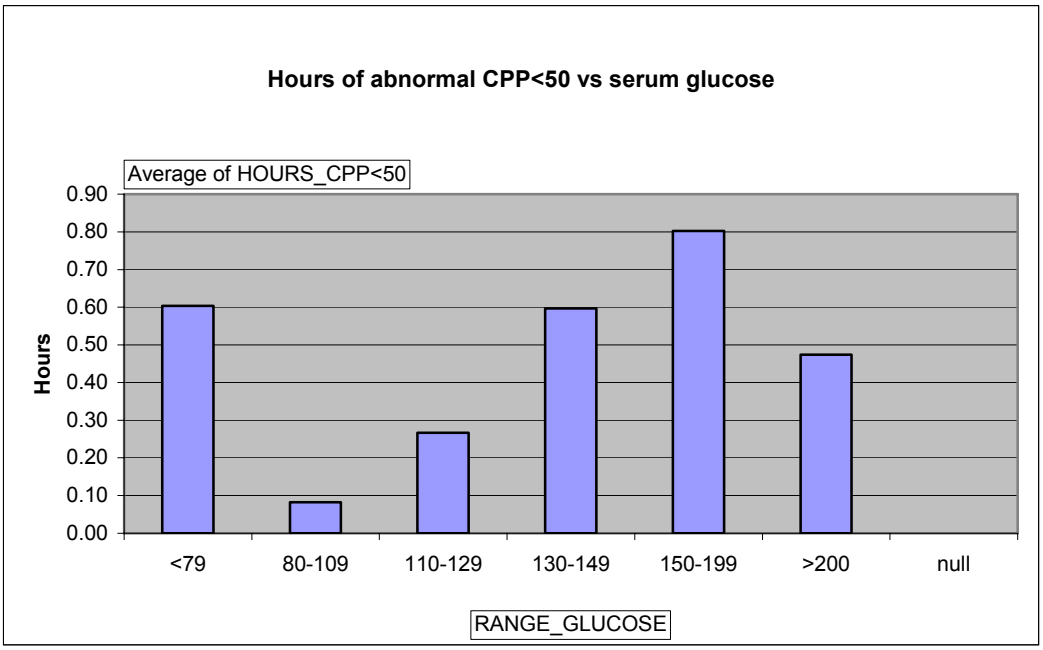


Figure 8 Hours of abnormal CPP<50 vs serum glucose

Average of HOURS_CPP<50	
RANGE_GLUCOSE	Total
<79	0.60
80-109	0.08
110-129	0.27
130-149	0.60
150-199	0.80
>200	0.47
null	0.00
Grand Total	0.36

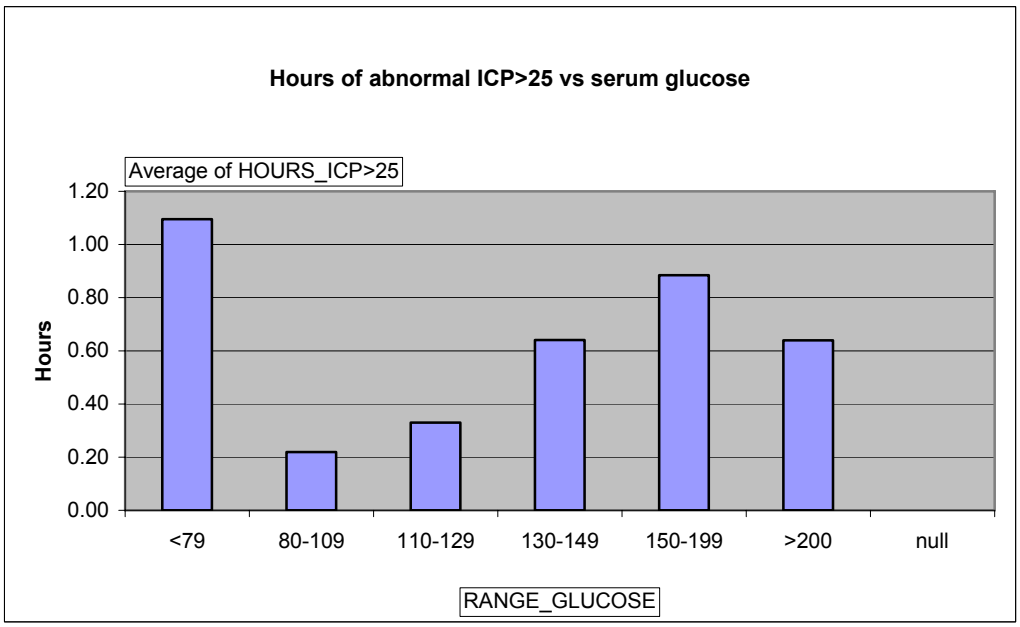


Figure 9 Hours of abnormal ICP>25 vs serum glucose

Average of HOURS_ICP>25	
RANGE_GLUCOSE	Total
<79	1.09
80-109	0.22
110-129	0.33
130-149	0.64
150-199	0.88
>200	0.64
null	0.00
Grand Total	0.52

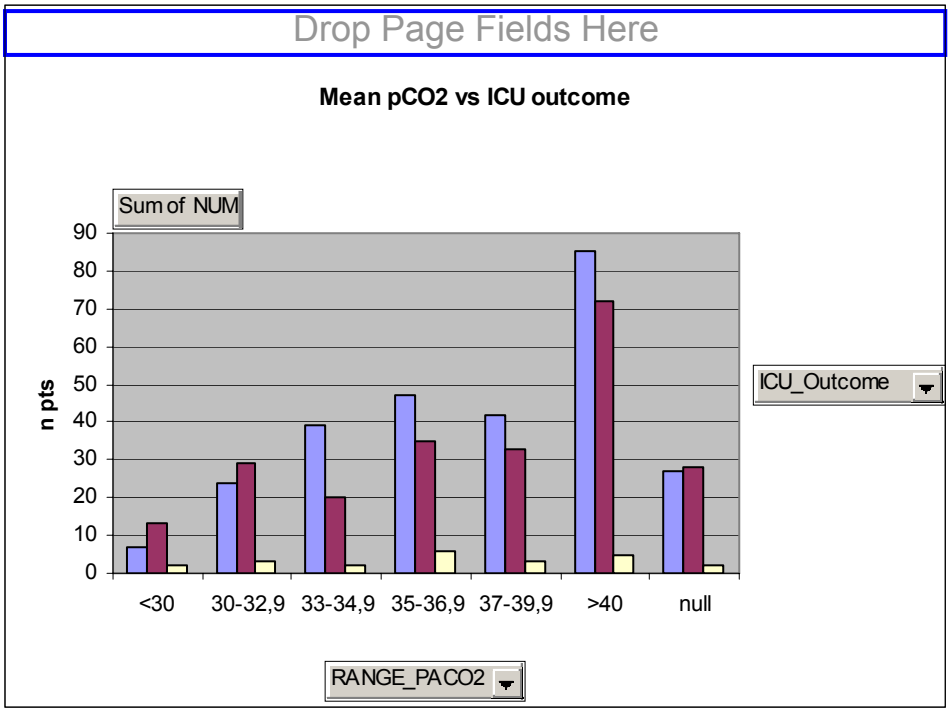


Figure 10 Mean pCO2 vs ICU outcome

Sum of NUM	ICU_Outcome			
RANGE_PACO2	Alive	Dead	Unknown	Grand Total
<30	7	13	2	22
30-32,9	24	29	3	56
33-34,9	39	20	2	61
35-36,9	47	35	6	88
37-39,9	42	33	3	78
>40	85	72	5	162
null	27	28	2	57
Grand Total	271	230	23	524

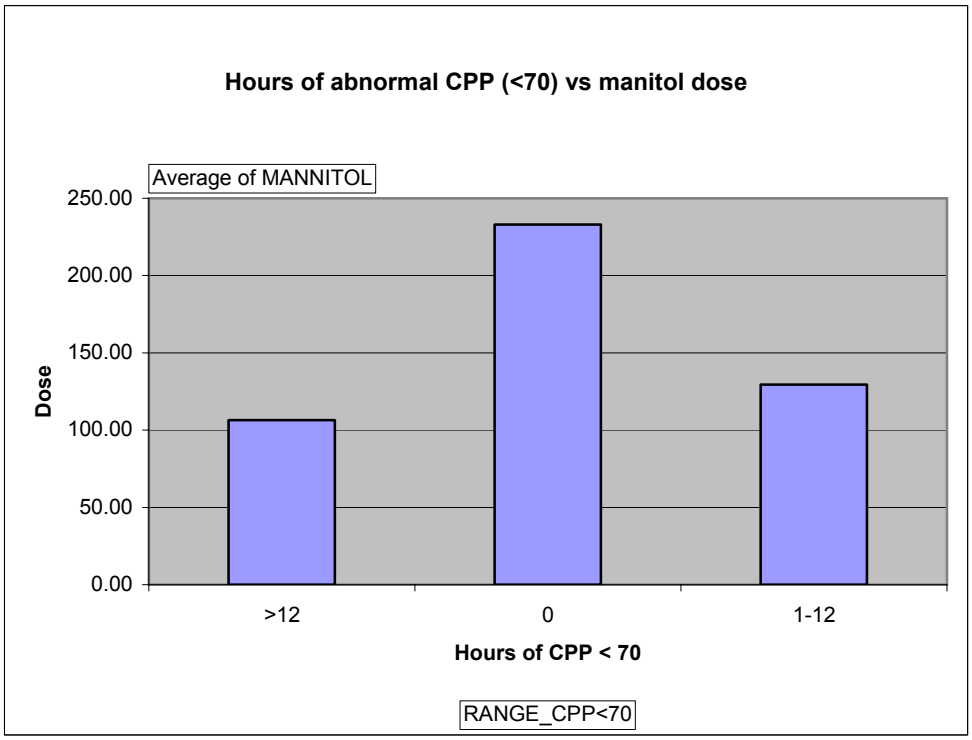


Figure 11 Hours of abnormal CPP (<70) vs manitol dose

Average of MANNITOL	
RANGE_CPP<70	Total
>12	106.41
0	233.02
1-12	129.50
Grand Total	223.83

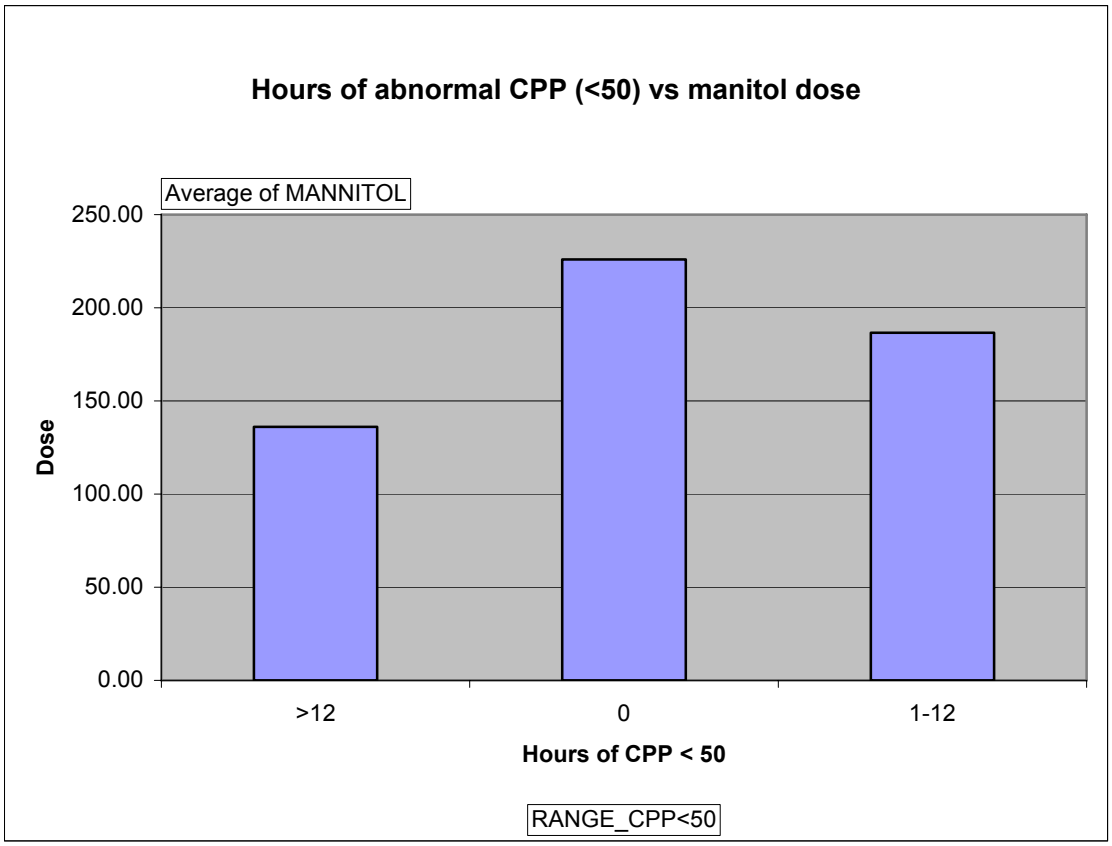


Figure 12 Hours of abnormal CPP (<50) vs manitol dose

Average of MANNITOL	
RANGE_CPP<50	Total
>12	136.11
0	225.89
1-12	186.52
Grand Total	223.83

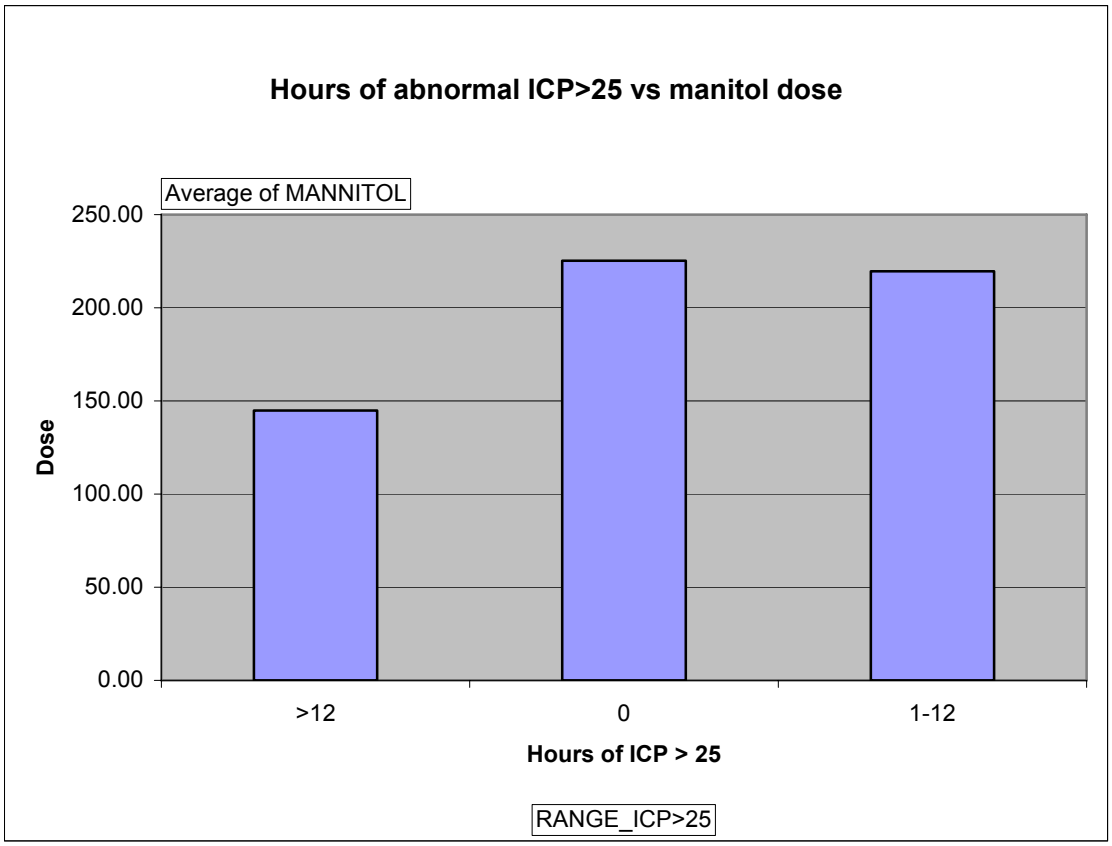


Figure 13 Hours of abnormal ICP>25 vs manitol dose

Average of MANNITOL	
RANGE_ICP>25	Total
>12	144.87
0	225.23
1-12	219.60
Grand Total	223.83

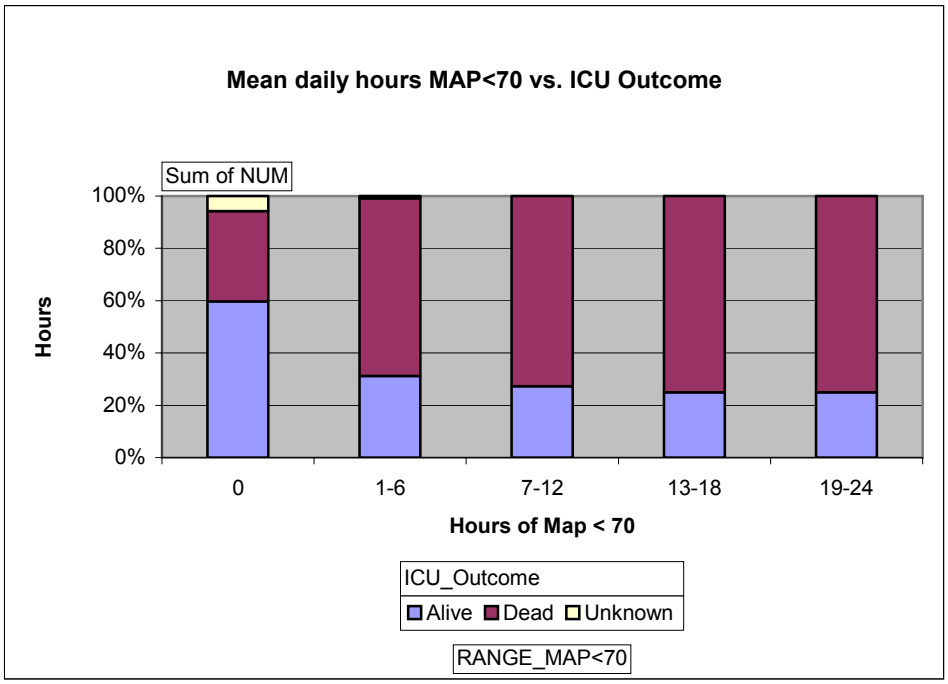


Figure 84 Mean daily hours MAP<70 vs. ICU Outcome

Sum of NUM	ICU_Outcome			
RANGE_MAP<70	Alive	Dead	Unknown	Grand Total
0	228.00	132.00	22.00	382.00
1-6	35.00	76.00	1.00	112.00
7-12	6.00	16.00		22.00
13-18	1.00	3.00		4.00
19-24	1.00	3.00		4.00
Grand Total	271.00	230.00	23.00	524.00

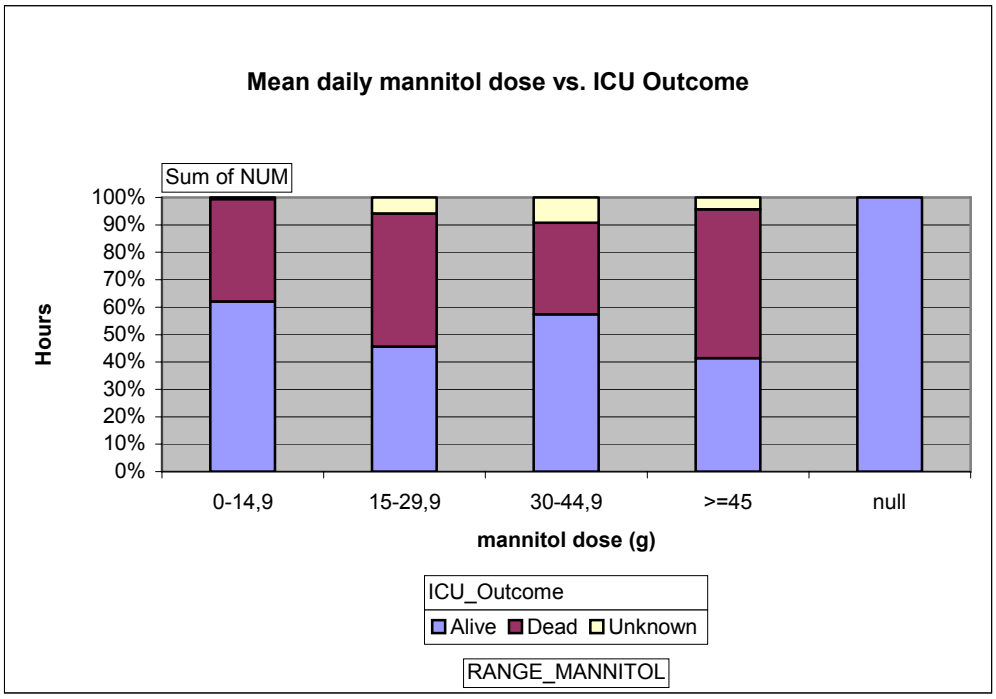


Figure 15 Mean daily mannitol dose vs. ICU Outcome

Sum of NUM	ICU_Outcome			
RANGE_MANNITOL	Alive	Dead	Unknown	Grand Total
0-14,9	100	60	1	161
15-29,9	31	33	4	68
30-44,9	62	36	10	108
>=45	77	101	8	186
null	1	0	0	1
Grand Total	271	230	23	524

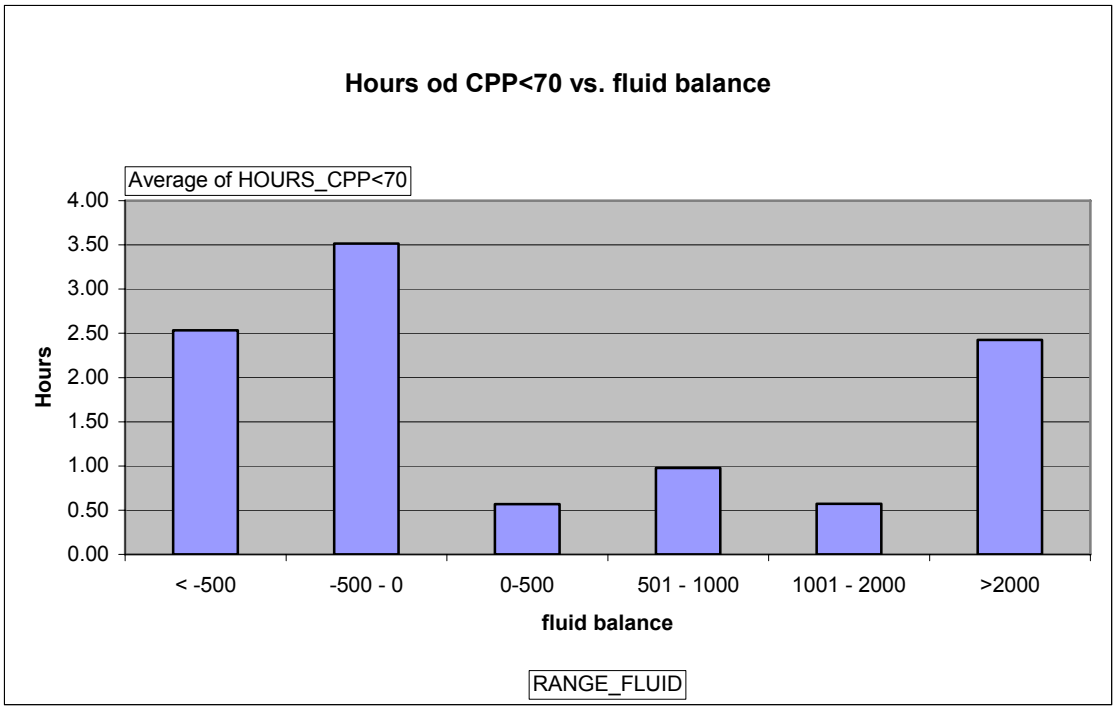


Figure 16 Hours od CPP<70 vs. fluid balance

Average of HOURS_CPP<70	
RANGE_FLUID	Total
< -500	2.53
-500 - 0	3.51
0-500	0.57
501 - 1000	0.98
1001 - 2000	0.57
>2000	2.43
Grand Total	0.85

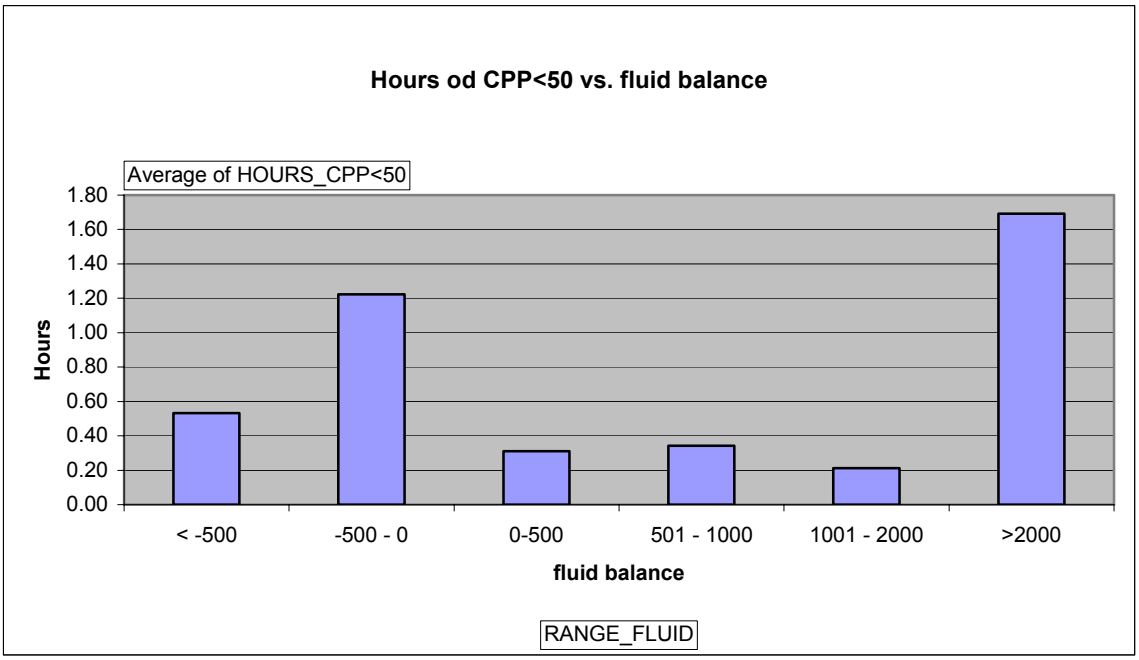


Figure 17 Hours of CPP<50 vs. fluid balance

Average of HOURS_CPP<50	
RANGE_FLUID	Total
< -500	0.53
-500 - 0	1.22
0-500	0.31
501 - 1000	0.34
1001 - 2000	0.21
>2000	1.69
Grand Total	0.36

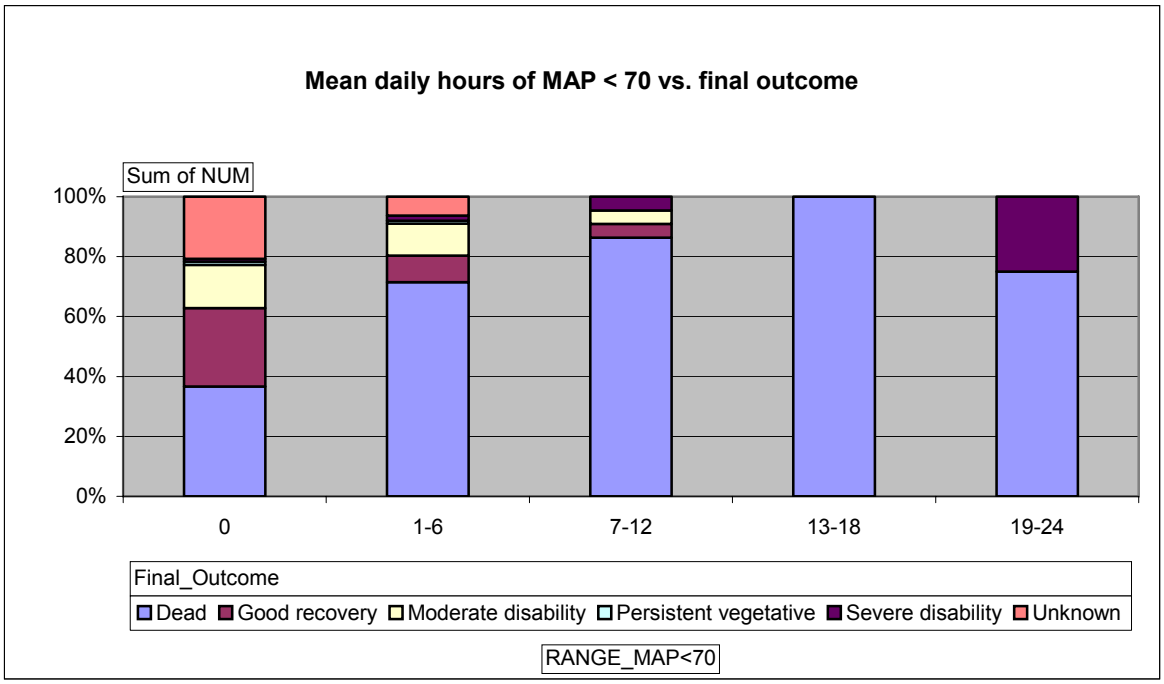


Figure 18 Mean daily hours of MAP < 70 vs. final outcome

Sum of NUM	Final_Outcome				
RANGE_MAP<70	Dead	Good recovery	Moderate disability	Persistent vegetative	Severe
0	140	100	55	4	
1-6	80	10	12	1	
7-12	19	1	1		
13-18	4	0	0		
19-24	3		0		
Grand Total	246	111	68	5	

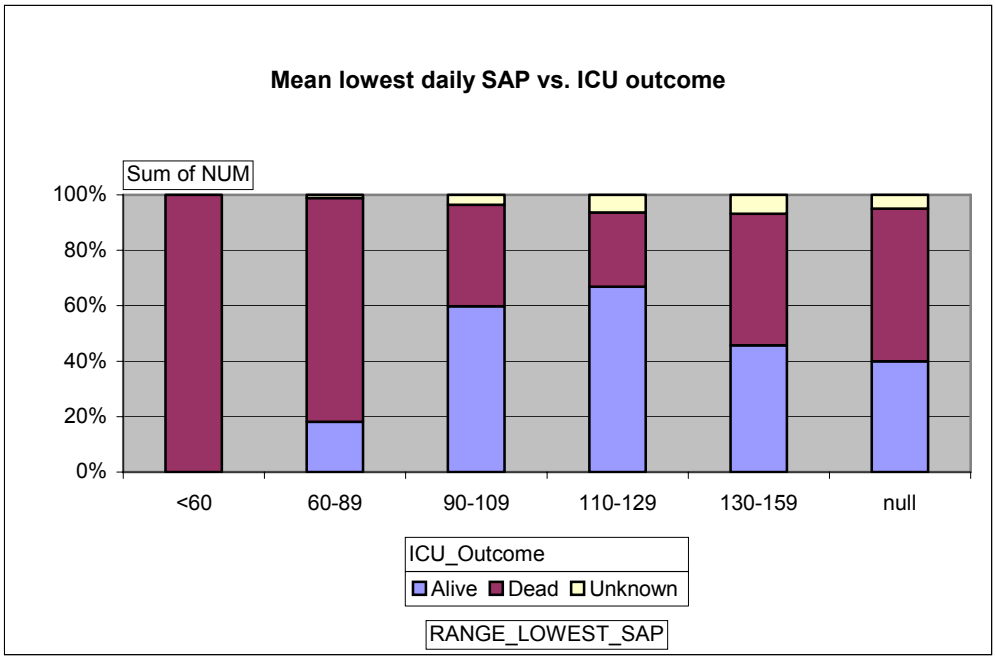


Figure 19 Mean lowest daily SAP vs. ICU outcome

Sum of NUM	ICU_Outcome			
RANGE_LOWEST_SAP	Alive	Dead	Unknown	Grand Total
<60	0	11		11
60-89	15	67	1	83
90-109	116	71	7	194
110-129	105	42	10	157
130-159	27	28	4	59
null	8	11	1	20
Grand Total	271	230	23	524

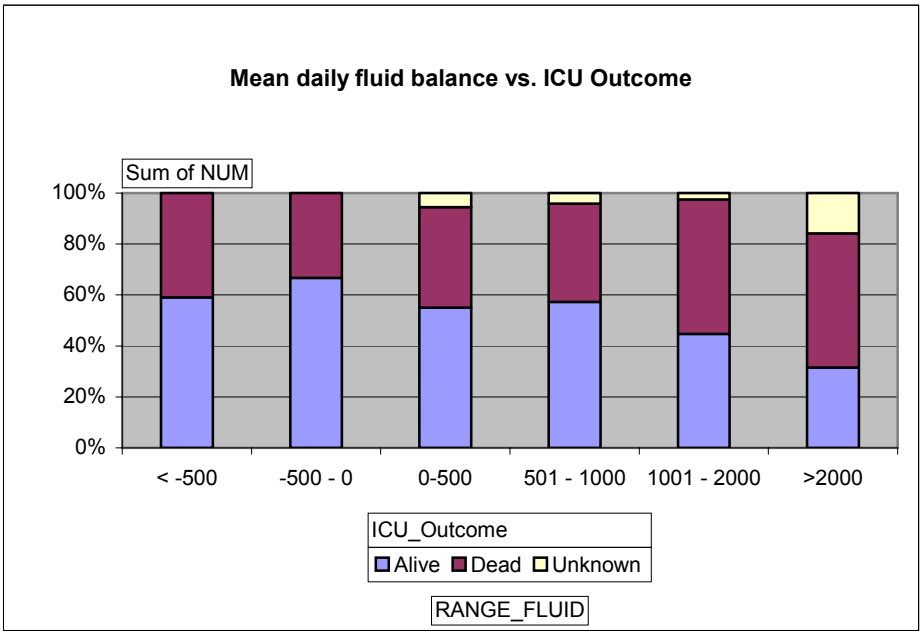


Figure 20 Mean daily fluid balance vs. ICU Outcome

Sum of NUM	ICU_Outcome			
RANGE_FLUID	Alive	Dead	Unknown	Grand Total
< -500	13	9		22
-500 - 0	4	2		6
0-500	120	86	12	218
501 - 1000	55	37	4	96
1001 - 2000	73	86	4	163
>2000	6	10	3	19
Grand Total	271	230	23	524

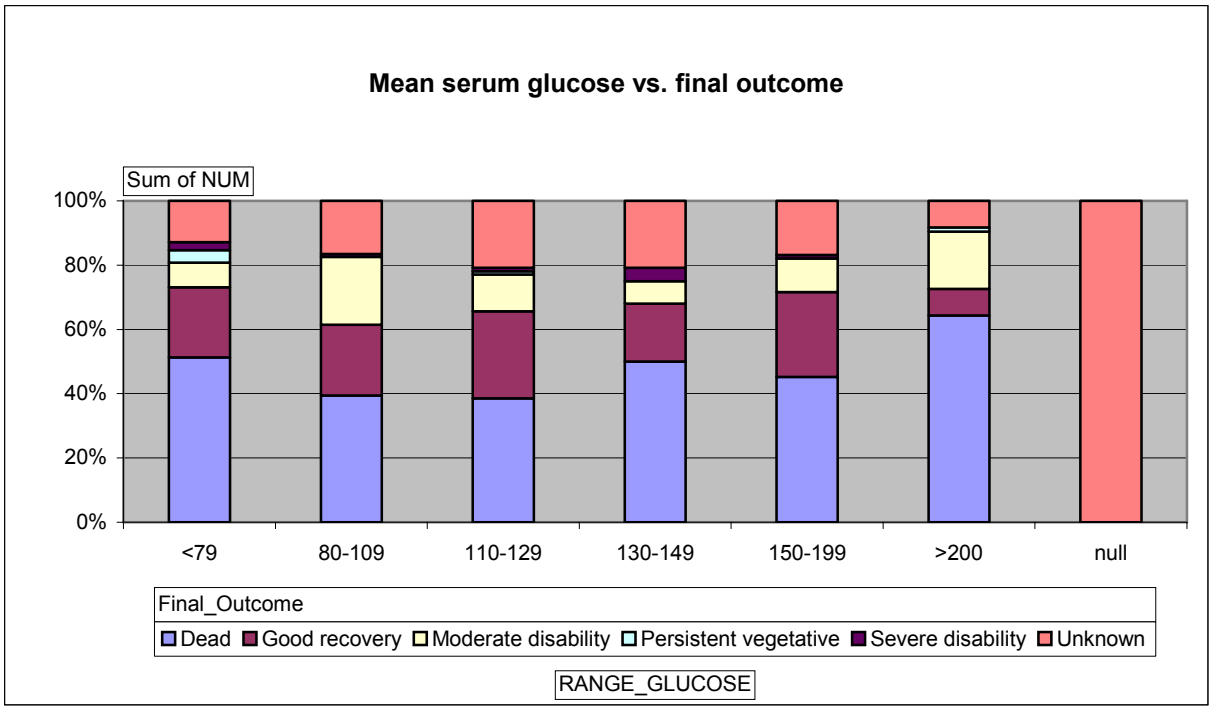


Figure 21 Mean serum glucose vs. final outcome

Sum of NUM	Final_Outcome						
RANGE GLUCOSE	Dead	Good recovery	Moderate disability	Persistent vegetative	Severe disability	Unknown	Grand Total
<79	40	17	6	3	2	10	78
80-109	43	24	23	0	1	18	109
110-129	37	26	11	1	1	20	96
130-149	36	13	5	0	3	15	72
150-199	43	25	10	0	1	16	95
>200	47	6	13	1	0	6	73
null	0	0	0			1	1
Grand Total	**246**	**111**	**68**	**5**	**8**	**86**	**524**

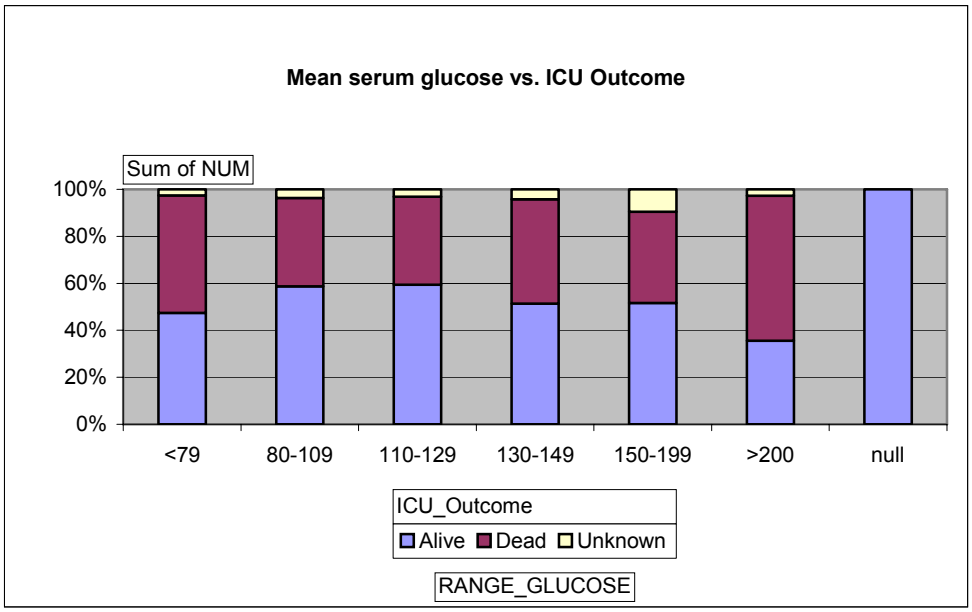


Figure 22 Mean serum glucose vs. ICU Outcome

Sum of NUM	ICU_Outcome			
RANGE_GLUCOSE	Alive	Dead	Unknown	Grand Total
<79	37	39	2	78
80-109	64	41	4	109
110-129	57	36	3	96
130-149	37	32	3	72
150-199	49	37	9	95
>200	26	45	2	73
null	1	0	0	1
Grand Total	271	230	23	524

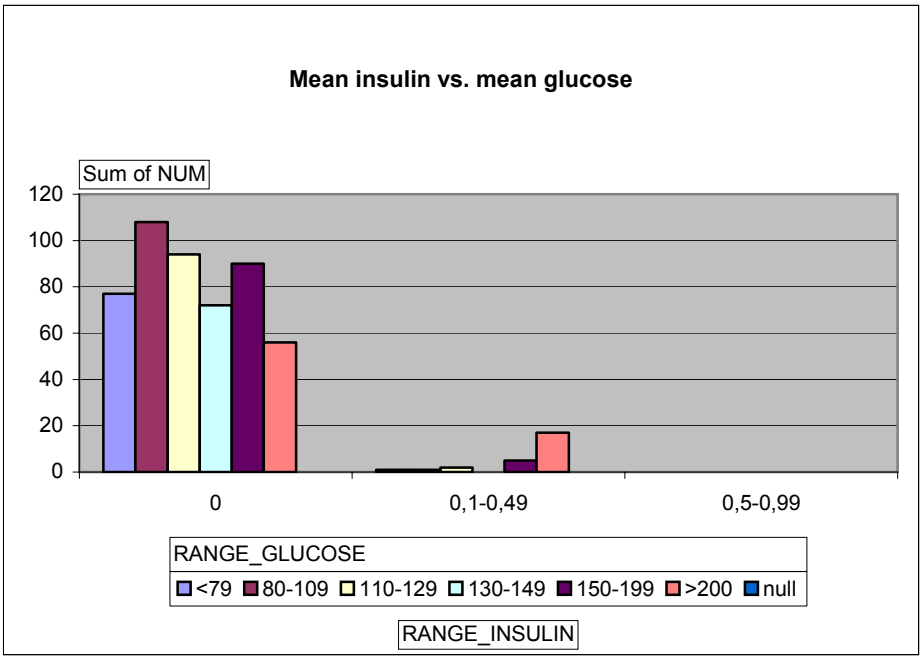


Figure 93 Mean insulin vs. mean glucose

Sum of NUM	RANGE_GLUCOSE							
RANGE_INSULIN	<79	80-109	110-129	130-149	150-199	>200	null	Grand Total
0	77	108	94	72	90	56	0	497
0,1-0,49	1	1	2	0	5	17		26
0,5-0,99			0	0	0			0
Grand Total	78	109	96	72	95	73	0	523

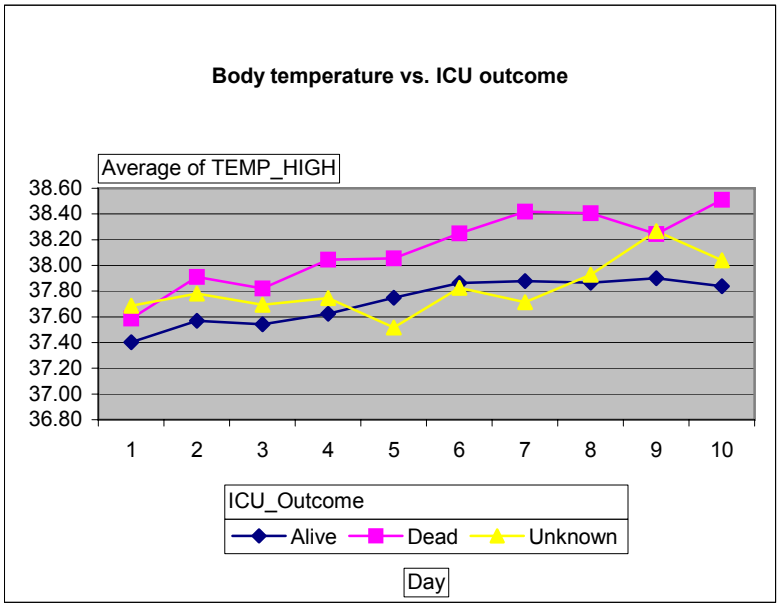


Figure 24 Body temperature vs. ICU outcome

Average of TEMP_HIGH	ICU_Outcome			
Day	Alive	Dead	Unknown	Grand Total
1	37.40	37.59	37.69	37.49
2	37.57	37.91	37.78	37.72
3	37.54	37.82	37.69	37.65
4	37.62	38.04	37.75	37.77
5	37.75	38.06	37.52	37.84
6	37.86	38.25	37.83	37.98
7	37.88	38.42	37.71	38.03
8	37.86	38.41	37.93	38.00
9	37.90	38.24	38.27	37.99
10	37.84	38.51	38.04	37.99
Grand Total	37.66	37.94	37.77	37.77

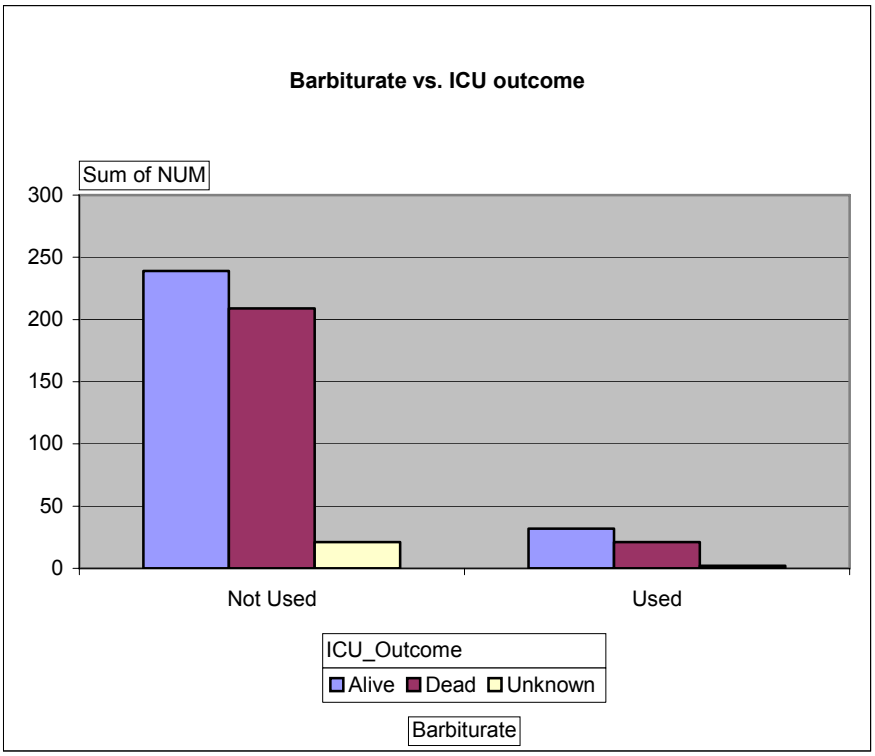


Figure 25 Barbiturate vs. ICU outcome

Sum of NUM	ICU_Outcome			
Barbiturate	Alive	Dead	Unknown	Grand Total
Not Used	239	209	21	469
Used	32	21	2	55
Grand Total	271	230	23	524

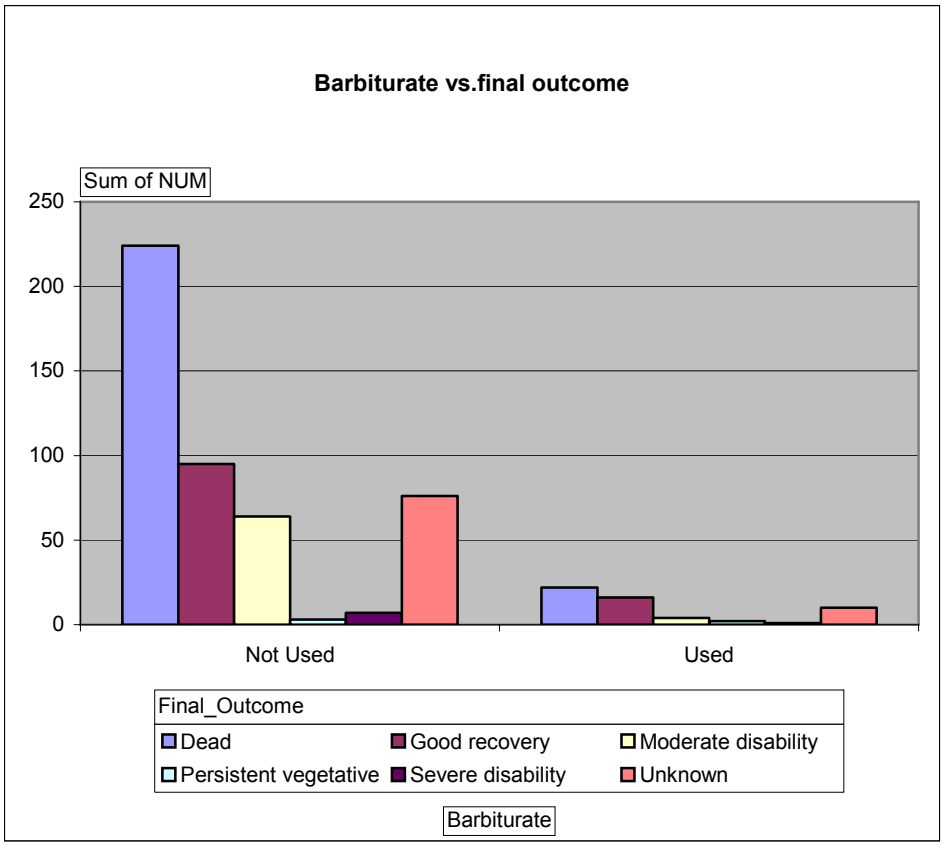


Figure 26 Barbiturate vs.final outcome

Sum of NUM	Final_Outcome						
Barbiturate	Dead	Good recovery	Moderate disability	Persistent vegetative	Severe disability	Unknown	Grand Total
Not Used	224	95	64	3	7	76	469
Used	22	16	4	2	1	10	55
Grand Total	**246**	**111**	**68**	**5**	**8**	**86**	**524**

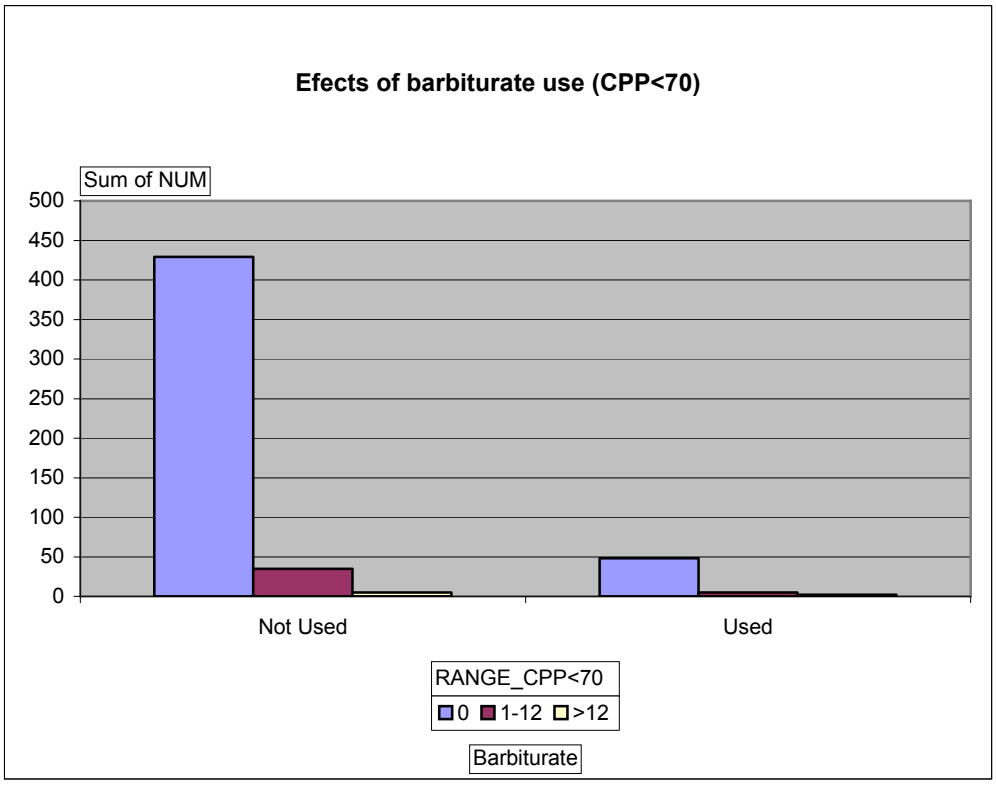


Figure 27 Effects of barbiturate use (CPP<70)

Sum of NUM	RANGE_CPP<70			
Barbiturate	0	1-12	>12	Grand Total
Not Used	429	35	5	469
Used	48	5	2	55
Grand Total	477	40	7	524

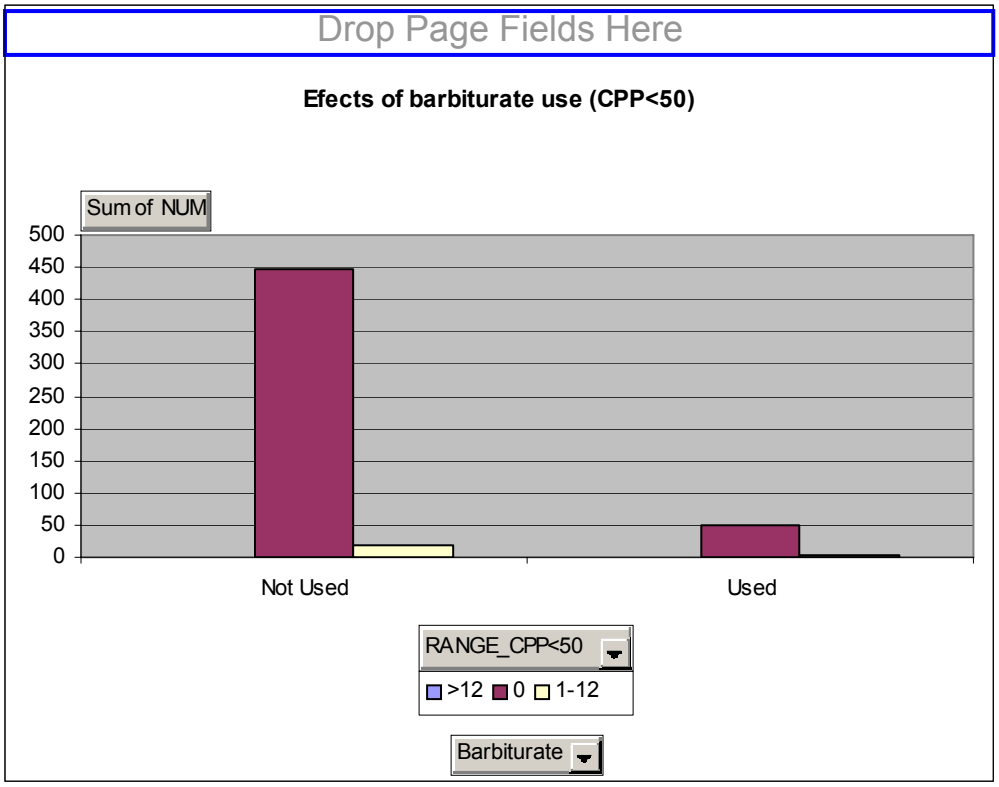


Figure 28 Effects of barbiturate use (CPP<50)

Sum of NUM	RANGE_CPP<50			
Barbiturate	>12	0	1-12	Grand Total
Not Used	1	448	20	469
Used	1	50	4	55
Grand Total	2	498	24	524

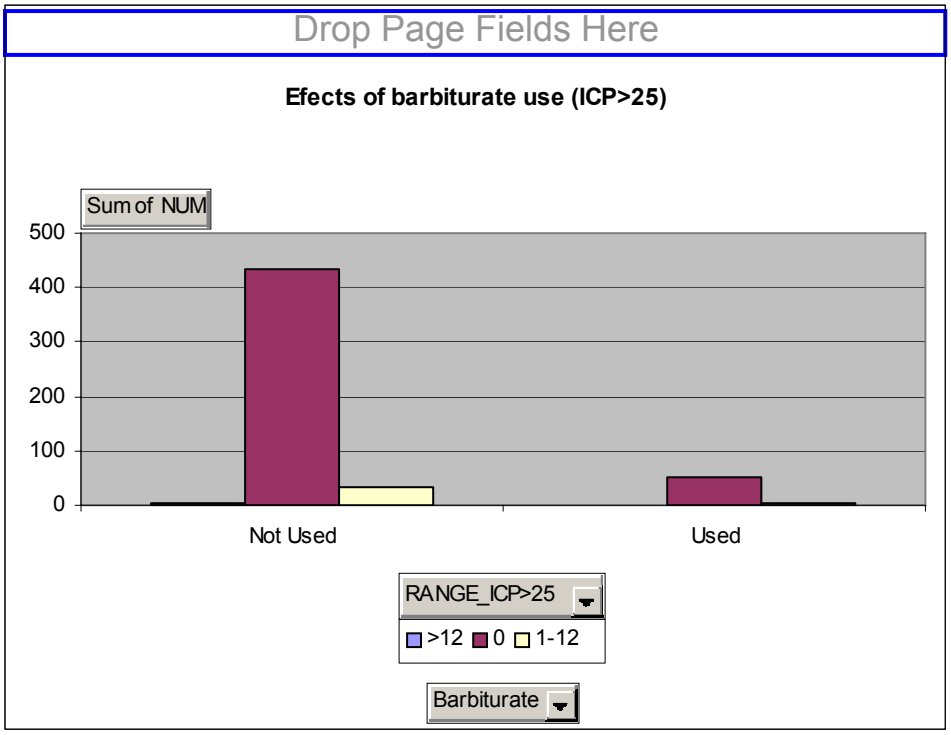


Figure 29 Effects of barbiturate use (ICP>25)

Sum of NUM	RANGE_ICP>25			
Barbiturate	>12	0	1-12	Grand Total
Not Used	2	434	33	469
Used	1	50	4	55
Grand Total	3	484	37	524

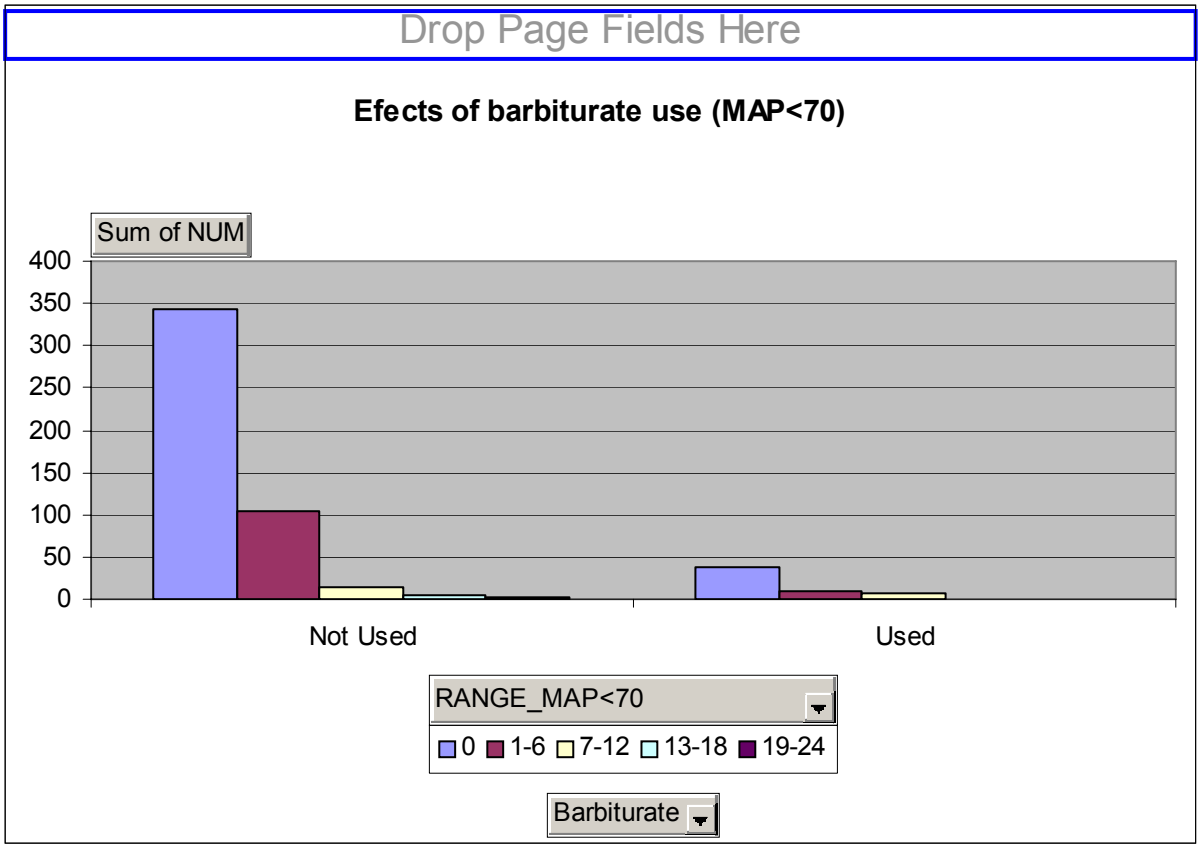


Figure 30 Effects of barbiturate use (MAP<70)

Sum of NUM	RANGE_MAP<70					
Barbiturate	0	1-6	7-12	13-18	19-24	Grand Total
Not Used	344	103	15	4	3	469
Used	38	9	7	0	1	55
Grand Total	382	112	22	4	4	524