

# A Time Efficient Heart Attack Pre-Hospital Management Methodology Based on Collaborative Scheduling Using Constraint Optimization

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**Abstract-** The task of medical diagnosis is a complex one, considering the level vagueness and uncertainty management, especially when the disease has multiple symptoms. The management of effective diagnosis depends on factors dealing with heart attack incidents and pre-hospital service of the patient. Although heart attack has no strict medical definition it is commonly used to indicate a sudden and potentially life threatening abnormality of heart function. Important factor in a heart attack incident (with severe results sometimes) is the efficient handling of the time especially on the interval time management starting from the moment the incident is recognized up to the time the patient is in the emergency unit. Time management of the incident could be achieved by controlling the time constraints proposing a methodology where the pre-hospital service is treated as a process consisted by three stages. Best solutions of the time constrains could be calculated considering constraint optimization techniques. A case study of five of heart attack reported incidents is analyzed and the results indicate the possible contribution of the application of this methodology. This methodology appears to be very useful, thanks to its ability not only to generate an effective initial schedule as an additional guidance to all participants involved in heart attack service, but also to respond to changes occurred once the first actions have started and abrupt complications necessitate additional or updated actions.

**Keywords-** pre-hospital service; constraint optimization; process scheduling; heart attack

## I. INTRODUCTION.

Every year, '1 250 000 persons in the United States experience an acute myocardial infarction, of these > 50% die before reaching a medical facility, while they can reduce mortality by 25% if initiated within 1 hour of the onset of acute symptoms. Survival rates are improved by up to 50% if reperfusion is achieved within 1 hour of symptom onset and by 23% if it is achieved within 3 hours of symptom onset [19].

Although heart attack has no strict medical definition it is commonly used to indicate a sudden and potentially life threatening abnormality of heart function [1]. Major deaths from coronary disease occur in the pre-hospital phase and the most of the patients do not survive long enough to receive medical help [1].

The fastest possible pre-hospital process may be crucial for saving a life but might, also, lead to careless use of resources which could be useful to other patients. Factors like number of practitioners, number of ambulance vehicles, number of available emergency units, etc are crucial for the pre-hospital process management scheduling. The above factors are important for the time management leading to the effective decision especially in the early in-hospital phase. A set of health care rules are used as guidelines to constraint the problem and set permitted procedural limits for the safety of the patients.

## II. RELATED WORK

Significant contribution in the field of pre-hospital management is provided by Task Force Report [1] which remains to be the basic reference for describing procedures, standards, tactics, etc. related with heart attack incidents, reporting diagnostic factors that could be included into the evaluation process using optimization techniques. In [2] the proposed methodology emphasizes on the coordination of activities and resources in order to achieve primarily the execution of the process, carrying the patient safety in an ER and optimize the recourses according the time.

A coordination algorithm [3] based on distributed system optimization formulations shares similar characteristics with the proposed algorithm that allocates adequate resources in the right timing. Although, the proposed methodology refers to a central system, yet the pre-hospital process is separated in activities where optimization formulations evaluate feasible solutions. [4], [5], where the objective and constraint function values are outputs of a subset of analysis functions [6].

In order to increase the accuracy of the analysis multiple variables are simultaneously optimized, like in optimization for decision-making, right where optimal decisions are depended on a combination of various factors [7]-[9], [12-18].

Another important factor for making clinical decision is the patient decision time which is defined as the interval from the symptoms' appears until medical assistance. Decision time might not relate to knowledge of the heart symptoms but is one of the most important factors for the patient safety

improvement. As patient safety could be defined the prevention of medical error and adverse events. The influential report *To Err is Human* [20], suggested a list of strategies for improvement of the overall quality of patient care in the US, and several research programs were established to investigate the effects of factors on patient safety. The cost of preventable adverse events, for instance in the UK, is estimated to be £ 1000 million per year only counting lost bed days [21]. From these numbers it is clear that the patient safety via pre-hospitalise time management is one of the most important factor effecting the clinical decision of the doctors.

III. PROPOSED METHODOLOGY.

The proposed methodology includes constrained optimization programming to evaluate optimal, or close to optimal values for the variables of the defined pre-hospital activities. The main contribution of this methodology lies in the synchronous evaluation of all variables for all three defined activities, both at the stage of initial scheduling and most importantly during the carrying out of the activities. The produced rules are related to:

i) The diagnosis stage. The aim is to perform and handle the diagnosis as efficiently as possible. Emphasis is given on the timing and the communication of the diagnosis report supported by advanced collaborative technology. The results of the diagnosis, at any stage, are used to set the safety limits and constraint the problem.

ii) The coordination stage. The aim is to manage synchronously patients in compliance to safety standards and involved resources in relevance to time

Constrained Optimization Programming has been considered as the most suitable technique to evaluate simultaneously multiple variables, aiming to obtain, in combination, feasible and optimal, if possible, values. This methodology is used when the designer needs to find a solution to an optimization problem that includes a number of contradicting criteria. In mathematical analysis, the method is defined as nonlinear vector optimization with constraints.

Assuming that there are N design variables to be found. A design space  $\mathbf{X} \subset \mathbb{R}^N$  can be introduced. Each element in the design space is represented by a design vector  $\mathbf{x} = (x_1, x_2, \dots, x_N)^T$ :  $\mathbf{x} \in \mathbf{X}$ . Suppose that the quality of each combination of design variables is characterized by M objectives functions. Along with the design space  $\mathbf{X}$ , the space of the objective functions  $\mathbf{Y} \subset \mathbb{R}^M$  is introduced. Each element in the objective space  $\mathbf{Y}$  is represented by a vector  $\mathbf{y} = (y_1, y_2, \dots, y_M)^T$ , where  $y_i = f_i(\mathbf{x})$ ,  $f_i: \mathbb{R}^N \rightarrow \mathbb{R}^1$ ,  $i=1,2,\dots,M$ . Thus  $\mathbf{X}$  is mapped onto  $\mathbf{Y}$  by  $\mathbf{f} \in \mathbb{R}^M$ :  $\mathbf{X} \rightarrow \mathbf{Y}$ . Suppose that there are constraints which are formulated as inequalities. Then, the following multiobjective optimization problem under constraints could be defined as:

$$\text{Min } \mathbf{y}(\mathbf{x})$$

subject to K inequality constrains

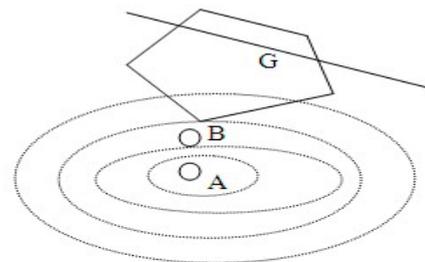
$$g_i(\mathbf{x}) \leq 0, i=1,2,\dots,K$$

The design space  $\mathbf{X}^*$  is defined as the set of design variables satisfying all the constraints g. The criterion space  $\mathbf{Y}^*$  is defined as the set  $\{\mathbf{Y}(\mathbf{x}): \mathbf{x} \in \mathbf{X}^*\}$ .

The following graph explains the above idea, The constraints  $g_i(\mathbf{x}) \leq 0$  carve out a region G where the optimum has to lie. A line indicates in which are the first constraints is satisfied ( $g_i(\mathbf{x}) \leq 0$ ) and where it is violated ( $g_i(\mathbf{x}) > 0$ ). The unconstrained optimum would be at the point A while constrained to the region G the optimum is at the point B.

$$g_i(\mathbf{x}) \geq 0$$

$$g_i(\mathbf{x}) \leq 0$$



Multiobjective optimization requires a decision making process as there is not a single solution but a set of non-dominated solutions out of which the best must be chosen. Three strategies can be used:

1. An a priori method, where the decision making is specified in terms of a scalar function and an optimization function is used to obtain to appropriate solution
2. An a posteriori method, where an optimization function exists and a final solution could be reached by that function. Decision making is applied manually at the end of the optimization. A new decision is possible without any repeat ion of the optimization process.
3. Mixture method, where during the optimization process periodically information can be used which may be used to reformulate the results.

There are three decision variables evaluated simultaneously, in order to increase the accuracy of the combinatorial analysis and turn into an advantage the complexity of the problem, irrespectively the size of it. As far as the search of the optimal time values concerned, this is performed, instantly, considering all the future states of the possible clinical conditions of a patient and avoiding future disturbances caused by data updates.

The advantage of the proposed methodology lies in the presence of various constraints that define the problem from multiple perspectives, but at the same time allow many opportunities to relax the defined limits and obtain a solution. We use the analytical term "solution" for a rather qualitative problem, to define the safe and efficient in time and resources transition of the patient to the hospital. Having predefined every activity of the process the transition of the patient can either be achieved within the desired limits or not, meaning that provided that all set standards are satisfied a *solution* is

reached. If one and one only condition is not satisfied, then there is no solution for this qualitative problem.

We usually meet weights and priorities used for the evaluation or relaxation of constraints. In other cases, constraints responsible for leading to non feasible solution are identified and then relaxed. Although, such an algorithm could be adopted and lead to solutions, the intention is not to generally optimize the pre-hospital process, but instead focus, primary, on the satisfaction of all safety standards for the patients and then obtain close to optimal conditions for timing and resources, where possible. This is achieved through continuous relaxation of resources and time constraints until the necessary conditions in table 1 are satisfied. While the values determination is running, the algorithm relaxes the resources constraints by 10% each time, until the safety standards are met.

The pre-hospital process is separated into three discrete stages; home, ambulance and hospital stages, where each of them is defined by certain variables. Each activity is further separated in operations as described in Fig. 1 [22].

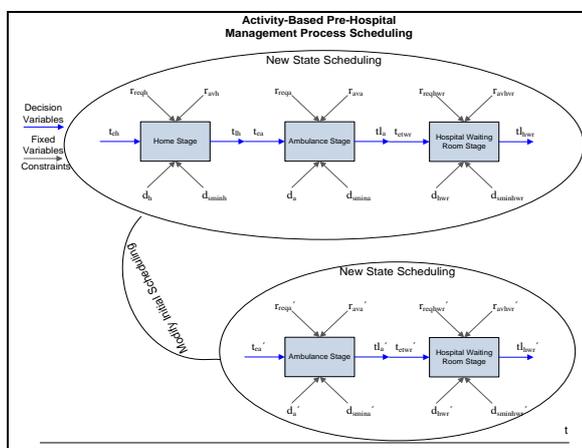


Fig.1 Representation of the pre-hospital process

The very first action of a medical crew is to arrive at the location of the patient in need and proceed with the initial examination followed by the first aids. The ambulance activity consists of the placing and removing of the patient into and out of the ambulance and most importantly in terms of time, the driving up to the hospital. The last activity starts with the Treatment preparation, i.e. preparing the patient bed, or the surgical tools, etc. followed by the final examination. The queuing period although it cannot be characterized as an operation it still consumes time and needs to be regarded in the process. It is not necessary for all these operations to be sequential, but they can be performed in parallel. The schematic representation in Fig. 1, provides a basic understanding of the characteristics of the process management for heart attack incidents.

This time management problem is treated as Constraint Optimization Programming Problem which consists of [22]:

1. DV= {d<sub>v1</sub>, d<sub>v2</sub> ...d<sub>vn</sub>} is a set of decision variables and FV= {d<sub>f1</sub>, d<sub>f2</sub> ...d<sub>fn</sub>} is a set of fixed variables as described in Table 1.

2. F(v). An objective function (sum of all objective functions of all involved activities of each tier), which is optimized simultaneously aiming to give optimal or close to optimal values by minimizing the total time and

3. C a set of constraints upon which the objective function is subject to. Those constraints define the permitted limits within which the values can vary until a solution is determined.

TABLE 1 PROBLEM VARIABLES

Decision Variables	Fixed Variables
t <sub>ei</sub> : earliest time of an activity i	r <sub>rec</sub> : recommended resources for activity i
t <sub>li</sub> : latest time of an activity i	r <sub>avi,j</sub> : available resources at activity/operation i
r <sub>i</sub> : resources of an activity i	d <sub>reci</sub> : recommended duration of activity i
d <sub>j</sub> : duration of each operation j	d <sub>maxi</sub> : the maximum permitted duration before a patient passes away without any action taken at the activity i
	d <sub>wj</sub> : waiting duration of each operation j
	v <sub>a</sub> : driving velocity of ambulance
	s : distance form the location of the patient up to the hospital
	d <sub>mini</sub> : the minimum necessary duration for activity i to be executed within safety standards
	t <sub>i</sub> : total time consumed at activity i
	d <sub>wi</sub> : waiting duration at activity i

$$\text{Suppose a function } T(p) = \sum_{i=1}^n t_i = \sum_{(sb_{pl}, sb_a, sb_{hp}) \in p} t \min$$

defined on a set  $S \in \mathbb{R}$ . Where T is the total time consumed during process p, consisted of the sub-processes sp<sub>pl</sub>, sp<sub>a</sub>, and sp<sub>hp</sub>, where n the No of variables and i the No of activities:

$$T(p) = \sum_{i=t_{pl}}^n t_i + \sum_{i=t_a}^n t_i + \sum_{i=t_{hp}}^n t_i . \text{ Where } t_{pl}, t_a, \text{ and } t_{hp} \text{ are the time periods (including delays) consumed at each sub-process:}$$

$$T(p) = \sum_{i \in t_{pl}} \sum_{i \in t_a} \sum_{i \in t_{hp}} t_i$$

$\in \mathbb{R}$ . The multivariable constrained optimization problem is defined by equation 1 as [22]: min T(p)= min f(t<sub>li</sub>, t<sub>ei</sub>, r<sub>i</sub>) subject to

$$\left\{ \begin{array}{l} t_{li} - t_{ei} < d_{max i} \\ t_{li} - t_{ei} \geq d_{min i} \\ t_{ei} > t_{li-1} \\ t_{ei} + d_i < t_{li} \\ t_{ei} > 0 \\ r_i \geq r_{reci} \\ r_i \leq r_{avi} \end{array} \right. \quad (1)$$

We are interested in global time minimization, since local targets are satisfied through local constraints. Time objective functions are defined for the three activities of the process. The time consumed at each activity i.e.  $t_h$  is again the sum of all durations i.e. for each operation within the specific activity:

- Home Stage

$$t_h = d_{wh} + d_h = (t_{lwh} - t_{ewh}) + \frac{t_{lh} - t_{eh}}{r_{avh}} \quad (2)$$

Where  $d_{wj} = t_{ij} - t_{ej}$  and  $d_j = \frac{(t_{1j} - t_{ej})}{r_{avj}}$

- Ambulance Stage

$$t_a = d_{tr} + d_l + d_{um} = \frac{v_a}{s} + \frac{t_{ll} - t_{el}}{r_{ava}} + \frac{t_{lum} - t_{eum}}{r_{ava}} \quad (3)$$

Where  $t_{tr} = \frac{v_a}{s}$

- Hospital Waiting Stage

$$t_{hp} = d_{whp} + d_{pr} = (t_{lwhp} - t_{ewhp}) + \frac{t_{lpr} - t_{epr}}{r_{avpr}} \quad (4)$$

Thus the final expression to be optimized is the total of all activities time consumption and delays:

$$T(p) = \sum_{i=1}^n \left( (t_{lwi} - t_{ewi}) + \frac{t_{li} - t_{ei}}{r_{avi}} + \frac{v_a}{s} \right) \quad (5)$$

Where n = number of variables and i= number of activities

#### IV. RESULTS.

The case study presented is taken from a medical study where three decision variables are evaluated and six fixed variables are used to constraint the problem. Provided that there is a certain number of available resources for each stage, every time the availability and the timing changes the central database updates the new information and the activities are scheduled by allocating the new available resources effectively among activities. Due to qualitative constraints in sharing common medical resources, the major operation lies in shifting the starting and the end time of activities forward or backwards. Moreover resources can be added or substituted by others. This model that can be expanded as much as we need vertically (number of patients) is programmed in *Mathematica* (Wolfram).

In order to assess the validity of the proposed methodology, five scenarios has been selected to be examined as of their efficiency to meet the constraints (Table 1) set. Those five scenarios refer to heart attack incidents where each of them

represents a different combination of difficulties met during the pre-hospital process. The difficulties that occurred during the process vary from unintentional delay of the involved personnel up to resources unavailability. The ultimate goal is to ensure that the patient arrives in the ER before the indicated time of 30 minutes (end time of 3<sup>rd</sup> activity), satisfying all in between time and health and safety constraints, and making at the same time reasonable use of the available resources.

#### Health Safety Constraints

- $d_{maxi} = \text{MaxDurationActivity}_i = 8, 8'$  is the maximum allowed time for a patient to wait without first aids.
- $d_{mini} = \text{MinDurationActivity}_i = 1.5$ , the minimum time for activity i to be executed within health and safety standards is 1.5 minutes.
- $\text{RecomDurationActivity}_i = 3$  the recommended duration that activity i should last
- $\text{RecomResourcesActivity}_i = 2$ , there are 2 resources recommended for the completion of activity i.

When the total of all these conditions is satisfied then a solution is obtained. An example of actual Health Safety standards [10], [11] for acute heart diseases is given below:

TABLE 2: HEALTH SAFETY STANDARDS

Safety Standard	Constraint
SR-to-drug must be < 30'	$t_{pl} < t_{epl} + 30$
SR-to-ER must be < 90'	$t_{hp} < t_a + 90$
Current Time spent at patient's location ~ 25'	$\text{RecomDurationActivity}_{pl} = 25$
Current Time spent at hospital prior to treatment ~ 14'	$\text{RecomDurationActivity}_{hp} = 14$

**Patient 1:** The available number of resources needed for the completion of the hospital activity is less than the recommended number of resources. There are four nurses and one doctor in an available bed, instead of five nurses and two doctors in an available bed.

**Indication:** Move the starting time of activity earlier in order to allow the limited personnel provide more services.

**Patient 2:** The paramedics moved the patient in the ambulance without providing the first aids, violating the necessary time needed for this stage.

**Indication:** Extend the duration of the presence of the patient in the ambulance where the necessary first aid assistance is provided.

**Patient 3:** The driving speed of the ambulance is lower and it is expected to be late by 11 minutes.

**Indication:** Start earlier the pick up of the patient and increase the number of paramedics both at activity 1 and mainly 2.

**Patient 4:** Due to late notification from the patient, 10 minutes have already passed.

**Indication:** All three activities start earlier with greater utilization of available resources where possible.

**Patient 5:** Due to complete unavailability of ambulances, the patient cannot be transferred to the hospital.

**Indication:** The ambulance is replaced by an alternative vehicle with an increase in the resources of the 3<sup>rd</sup> activity to speed up the last activity.

TABLE 2 FIVE INITIAL DATA SETS OF THE FIVE EXAMINED SCENARIOS

#	Initial End Time (min)	Initial Resources (pcs)	End Time (min)	Activity Available (pcs)	Total Resources (pcs)	Health Safety Standards Compliance
1	4.0	3.0	29.0	7.0	16.0	x
2	2.0	3.0	26.0	13.0	22.0	x
3	3.0	3.0	30.0	13.0	22.0	x
4	12.0	3.0	30.0	14.0	20.0	√
5	11.0	3.0	30.0	13.0	23.0	x

The completion time of the activities is not analogous to the number of resources, as presented in Table 1, because the values are optimally determined. However, the activities in all five cases are coordinated in such a way that they are all completed within the recommended time lines irrespectively of the resources availability.

TABLE 3 FIVE SCENARIOS OF DEFFERENT PATIENTS AFTER THE PROPOSED METHODOLOGY

#	Initial End Time (min)	Initial Resources (pcs)	End Time (min)	Activity Available (pcs)	Total No of Resources (pcs)	Health Safety Standards Compliance
1	5.7	2.8	25.0	10.3	18.6	√
2	5.7	2.8	23.7	13.6	21.9	√
3	5.7	4.2	29.3	5.4	16	√
4	5.7	2.8	29.3	13.6	21.9	√
5	13.0	1.0	27.0	6.0	9.5	√

At a first glance, there would, only, be a small improvement observed between Table 2 and 3, in terms of activity time completion performance. The most important criterion, though, to compare, prior to any quantitative comparisons, is the condition of whether the pre-hospital process complies with the health safety standards necessary to ensure the health of the patient. The last incident due to complete resources insufficiency was not feasible to be performed while within the safety standards. A further relaxation of 2 critical constraints up to 30%, allowed the 5<sup>th</sup> patient to be safely accommodated in an ER [22].

Having satisfied this primary criterion an improvement in the time completion is observed in five out of five cases. No fair comparisons can be made in terms of resources utilization, since in the first table; we can only see the available resources that could be theoretically used, while in the second table we have records of the actual resources that were used. Yet, a decrease in the number of resources used is observed again in three out of five cases.

## V. SUMMARY

The purpose of this methodology is not to assess the qualitative characteristics of the current pre-hospital methodologies and systems, but instead ensure the conforming to health standards transition of the patient from his/her location to the hospital and improve where possible the time management of this process. Result of this optimization will be a set of rules used as guidance to such incidents and the development of this methodology into a complete web-based collaborative system able to allocate resources and time events based on availability and qualitative constraints as indicated by health care regulations.

## REFERENCES

- [1] Article No. 981106, Task Force Report: The pre-hospital management of acute heart attacks Recommendations of a Task Force of the European Society of Cardiology and The European Resuscitation Council. *European Heart Journal* 19 (1998), p. 1140–1164
- [2] E.D. Adamides, N. Karacapilidis, C. Pylarinou, and D. Koumanakos: Supporting collaboration in the development and management of lean supply networks. *Production Planning and Control*. Vol 19 (2008), p. 35-52
- [3] J.T. Allison, P.Y. Papalambros: Optimal Partitioning and Coordination Decisions in System Design Using an Evolutionary Algorithm. 7th World Congress on Structural and Multidisciplinary Optimization COEX Seoul, 21 May - 25 May 2007, Korea
- [4] C. Heuberger: Inverse Combinatorial Optimization: A Survey on Problems, Methods, and Results. *Journal of Combinatorial Optimization* Vol 8 (2004), p. 329-361
- [5] S. A. Tarim, S. Manandhar and T. Walsh: Stochastic Constraint Programming: A Scenario-Based Approach. *Constraints*, Vol.11 (2006), pp.53-80
- [6] E.J. Cramer, J.E. Dennis, P.D. Frank, R.M. Lewis, and G.R. Shubin: Problem formulation for multidisciplinary optimization. *SIAM Journal of Optimization* Vol 4 (1994), p. 754–776
- [7] Hertz, M. Widmer: Guidelines for the use of meta-heuristics in combinatorial optimization. *European Journal of Operational Research* Vol 151 (2003), p. 247-252
- [8] L. Gortzis, H. Papadopoulos, T.A. Roelofs, S. Rakowsky, D. Karnabatidis, D. Siablis, C. Makropoulos, G. Nikiforidis, G. Grasczew: Collaborative Work During Interventional Radiological Procedures Based on a Multicast Satellite-Terrestrial Network. *IEEE Transactions on Information Technology in Biomedicine*, Vol 11 (2007), p. 597-599
- [9] R. Mason, C. Lalwani, R. Boughton: . *Supply Chain Management: An International Journal* Vol 12 (2007), p. 187-189
- [10] DeLuca G, Suryapranata J, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardialinfarction: every minute of delay counts. *Circulation*. 2004; 109: 1223–1225.
- [11] Debra K. Moser, Laura P. Kimble, Mark J. Alberts, Angelo Alonzo, Janet B. Croft, Kathleen Dracup, Kelly R. Evenson, Alan S. Go, Mary M. Hand, Rashmi U. Kothari, George A. Mensah, Dexter L. Morris, Arthur M. Pancioli, Barbara Riegel and Julie, Johnson Zerwic. Association Council on Cardiovascular Nursing and Stroke Council Syndrome and

- Stroke: A Scientific Statement From the American Heart Reducing Delay in Seeking Treatment by Patients With Acute Coronary. *Journal of the American Heart Association Circulation* 2006, 114:168-182: originally published online June 26, 2006, doi: 10.1161/CIRCULATIONAHA.106.176040
- [12] Allison, K. (2002). The UK pre-hospital management of burn patients: current practice and the need for a standard approach. *Burns* 28, 135–142.
- [13] Krüger AJ, Skogvoll E, Castrén M, Kurola J, Lossius HM: Scandinavian prehospital physician-manned Emergency Medical Services-Same concept across borders? *Resuscitation* 2010, 81:427-433.
- [14] Wang HE, Yealy DM: Emergency medical services system research: challenges and opportunity. *Ann Emerg Med* 2007, 50:643-644.
- [15] Smith RM, Conn AK: Prehospital care - scoop and run or stay and play? *Injury* 2009, 40(Suppl 4):S23-26.
- [16] Haut ER, Kalish BT, Cotton BA, Efron DT, Haider AH, Stevens KA, Kieninger AN, Cornwell EE, Chang DC: Prehospital intravenous fluid administration is associated with higher mortality in trauma patients: a National Trauma Data Bank analysis. *Ann Surg* 2011, 253:371-377.
- [17] Bernard SA, Nguyen V, Cameron P, Masci K, Fitzgerald M, Cooper DJ, Walker T, St. BP, Myles P, Murray L, et al: Prehospital rapid sequence intubation improves functional outcome for patients with severe traumatic brain injury: a randomized controlled trial. *Ann Surg* 2010, 252:959-965.
- [18] Davis DP: The need for standardized data reporting for prehospital airway management. *Critical care* 2011, 15:133.
- [19] George A. Mensah, Dexter L. Morris, Arthur M. Pancioli, Barbara Riegel and Julie Kathleen Dracup, Kelly R. Evenson, Alan S. Go, Mary M. Hand, Rashmi U. Kothari, Debra K. Moser, Laura P. Kimble, Mark J. Alberts, Angelo Alonzo, Janet B. Croft, Association Council on Cardiovascular Nursing and Stroke Council Syndrome and Stroke : A Scientific Statement From the American Heart Association Council on Cardiovascular Nursing and Stroke Council, *Journal of the American Heart Association* 2006, 114:168-182: originally published online June 26, 2006
- [20] Madsen, MD, Østergaard, D, Andersen, HB, Hermann, N, Schiøler, T, Freil, M. (2006). Lægers og sygeplejerskers holdninger til at rapportere og lære af utilsigtede hændelser og andre fejl. *Ugeskrift for læger*, (accepted for publication) (p.11)
- [21] Andersen, H.B.; Madsen, M.D.; Østergaard, D.; Ruhnu, B.; Freil, M.; Hermann, N., (2004). Spørgeskemaundersøgelse af patientholdninger til reaktioner efter utilsigtede hændelser. Delrapport 2 fra projekt om patientsikkerhed. *Risø-R-1498(DA)* (2004) (p.32).
- [22] Pylarinou, Ch., Gortzis, L., Zimeras, S. Coordinating effectively a heart attack pre-hospital service process using constraint optimization programming (2011) 2011 International Conference on Electrical and Control Engineering, ICECE 2011 – Proceedings, 4752 – 4755.