

Trauma scoring systems

*^{1,2}Oleg Arnaut, ¹Dan Croitoru, ¹Ion Grabovschi, ²Serghei Sandru

¹Department of Human Physiology and Biophysics, ²Valeriu Ghereg Department of Anesthesiology and Intensive Care Nicolae Testemițanu State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova

Authors' ORCID iDs, academic degrees and contributions are available at the end of the article

*Corresponding author: oleg.arnaut@usmf.md

Manuscript received January 31, 2020; accepted manuscript February 27, 2020; published online March 10, 2020

Abstract

Background: Worldwide, traumas represent an actual theme of discussion. The recognition and interpretation of severe traumas are essential for choosing the right treatment strategy. There are two approaches to mark the patients with a high risk of unfavorable evolution and death. First, to use the terms as "major trauma", "severe trauma" and "polytrauma", without ability to stratify the patients according the severity of lesions inside categories mentioned above. Second, to implement the trauma scoring systems (anatomical, physiological or mixed), when a doctor uses a mathematical algorithm/model to calculate the risks for each trauma patient. At the same time, according to the articles found on PubMed/Medline, Web of Science, and EBSCO databases, there is no international consensus concerning the most accurate traumatic score. This article's goal was to revise the existing trauma scoring systems to highlight the potential scoring systems that in perspective can be validated in the Moldovan medical system.

Conclusions: Different traumatic scores are used worldwide (different continents, countries or regions) to estimate the severity of trauma patients in relation to the anatomical, physiological or combined criteria. All of them could be potentially validated for the Moldovan medical system. A part of these scores could be validated and compared to identify those ones that have the best determination, calibration and discrimination abilities to predict the outcomes for the local medical system. As a result, the coefficients from the mathematical equations belonging to the scores could be adjusted to the conditions of the national medical system of the Republic of Moldova.

Key words: trauma scoring systems, severe trauma.

Cite this article

Arnaut O, Croitoru D, Grabovschi I, Sandru S. Trauma scoring systems. *Mold Med J.* 2020;63(1):64-74. doi: 10.5281/zenodo.3685673.

Introduction

Actually, traumas represent an actual subject at international scale, being the main cause of death in the world for the patients in the age category of 1-40 years [1, 2]. In the Republic of Moldova, according to the National Center for Management of the National Agency of Public Health, in the period of 2008-2017, traumas are on the 4th place in the list of causes of lethal outcome, constituting 8.1% (36889 cases) of all registered cases, being placed after the cardiovascular diseases (61%, 226195 cases), tumors (15.8%, 58518 cases) and digestive system diseases (10%, 36889 cases). The analysis of lethality structures according to the age showed that in the first year of life, traumas are placed on the 2nd place (30.3%) after the respiratory system diseases (57.9%). The lethality rate related to traumas is progressing along with the age and has its maximum incidence at the age of 18 years (81.3%), after that, it is decreasing, the lethality rate of traumas being 24.1%, and loses its predominance in the age category of 44 years and further, when the cardiovascular diseases are dominant (26.3%), being in decrease until 0% at the senile age category [3]. The recognition and interpretation of severe traumas is essential for choosing the right treatment strategy.

To describe the patients with a high risk of unfavorable evolution and also of death, there exists a series of terms like "severe trauma", "major trauma" and "polytrauma". The analysis of entries/documents in Web of Science database shows 24441, 19471 and 2813 entries for these notions, respectively. The terms "severe trauma" and "major trauma" are very similar, synonymic, but the criteria are not precise and fixed, the critical value of ISS (Injury Severity Score) or NISS (New Injury Severity Score) varies in different studies at the threshold of 16-17 points [4, 5, 6]. The polytraumas represent the most unexplored and unresearched part of traumas, being a narrow notion compared to severe trauma and major trauma. There are a lot of definitions for polytrauma. In most of the sources, the criteria for polytrauma represents the anatomical scale ISS, the value of more than 15 being the threshold. At the same time, according to other authors, this value varies from 15 up to 26 and more [7, 8, 9]. In a study made in 1996, it was proven that the medical personnel's incompetence represents one of the causes of the errors in the usage of ISS for polytrauma diagnosis [10]. Another criteria used for polytrauma definition are at least two lesions in any topographical region and at least one of them is a threat for the patient's life [9]. According to the New Berlin Definition, proposed and validated in studies

with high evidence, the polytrauma is defined as severe lesions for at least 2 body regions, appreciated by AIS (Abbreviated Injury Scale) with a score of ≥ 3 being present at least one of the 5 physiological parameters (systolic blood pressure ≤ 90 mmHg, GCS ≤ 8 , acidosis, coagulopathy and age ≥ 70 years) [11]. At the same time a series of scores and algorithms are created to assess the severity of traumas, but at the moment, as a study has shown, there is no international consensus in the articles found on PubMed/Medline, Web of Science, and EBSCO databases according the most efficient scale, many of them claiming different things [9, 11, 12], this situation being related to geographical factors and differences in the medical systems, particularities of demographic structure [10].

On the other hand, the Moldovan medical system doesn't use any trauma scoring system that was validated in order to evaluate the patient's risk of death and complications in case of trauma. Because of that, at the patient's evaluation there are disagreements on the prognostic, different scores often estimating the outcomes completely different. The solution for this problem includes a few stages as follows. First of all, we need to revise the existing trauma scoring systems that can be used in the Moldovan medical system. Secondly, to validate these scores for the Moldovan medical system and to elaborate the new trauma scoring systems. Lastly, the comparative evaluation of the trauma scoring systems is necessary in order to identify the ones that have the optimal ability (determination, calibration and discrimination) to predict the outcomes for the medical system of Moldova.

This article's goal is to accomplish the first task listed above, especially to revise the existing trauma scoring systems to highlight the potential scoring systems that in perspective can be validated in the Moldovan medical system.

Material and methods

We revised the articles in the PubMed archive using the HINARY system, overall 77 sources. For each score, we have mentioned their mathematic models and for some of them a calculation example. We did not mention the coefficients for equations because they are available in the cited sources. The information was classified in correlation with the parameters included in presented models (anatomical, physiological and mixed scales) and also with geographical distribution (different continents, different countries or regions).

Results

The scoring systems used to evaluate the severity of traumas can be classified into 3 categories: (I) the anatomical scores that take into consideration the anatomical injuries as a result of the traumatic event, (II) the physiological scores that are based on the clinical signs/measurements, (III) mixed, that enrolled both anatomical and physiological parameters.

Anatomical scores

All the scores from this category are derived from the AIS (Abbreviated Injury Scale) or ICD (International Clas-

sification of Diseases and Related Health Problems, <https://icd.codes/icd10cm>). Each lesion has its own certain score, attributed using the AIS or ICD dictionaries. Medical staff can apply the scores using the existing algorithms. For example, according to last edition of Abbreviated Injury Scale (AIS dictionary 2015), the comminuted tibial fracture is estimated by 3 points and according to ISS9.

Abbreviated Injury Scale (AIS) Derived Scores

AIS represents an anatomical score that appreciates by a scale that varies from 1 to 6 the severity of a trauma in a topographical region of the body by the following model: 1 – Minor, 2 – Moderate, 3 – Serious, 4 – Severe, 5 – Critical and 6 – Fatal [13]. The topographical regions considered in this score are: Head and neck, Face, Thorax, Abdomen, Limbs (also includes the pelvis), Exterior (burns, skin lesions etc.). More recently a term called MAIS (Maximum AIS) was introduced. It represents the highest AIS value for any body region [14]. For example, in case of traumas combination $AIS_{thorax} = 3$ and $AIS_{abdomen} = 4$, the MAIS value is 4.

Injury Severity Score (ISS) and New Injury Severity Score (NISS)

In the past decades, ISS and NISS were used widely for the evaluation of the severity of trauma. To estimate ISS, we have to use the following formula: $ISS = A^2 + B^2 + C^2$, where A, B, C are the highest AIS values present in each topographic region. It can vary from 0 up to 75. In condition if there is a topographical region with AIS = 6, ISS is automatically equal to 75 [15]. NISS in comparison with ISS, estimates trauma severity taking into account three maximal values of AIS, indifferent of the lesions localization [14]. For example, in case of trauma in 4 topographical regions $AIS_{abdomen} = 2$, $AIS_{head\ and\ neck} = 3$, $AIS_{head\ and\ neck} = 3$ and $AIS_{thorax} = 5$, the NISS value will be higher ($NISS = 5^2 + 3^2 + 3^2 = 43$) versus ISS ($ISS = 5^2 + 3^2 + 2^2 = 38$). At the same time, according to the results obtained by clinicians from China, NISS is similar to ISS in predicting the outcome of the traumatic patients [2]. We suppose that such result can be explained by insufficient determination coefficient (40%-60%) in equations that use NISS or ISS [16, 17].

Logarithm Injury Severity Score (LISS) and Exponential Injury Severity Score (EISS)

LISS uses the natural logarithm of AIS as follows: $LISS = \ln(A_1)^{5.53} \times 1.7987 + \ln(A_2)^{5.53} \times 1.7987 + \ln(A_3)^{5.53} \times 1.7987$, where A_1 - A_3 are the AIS values for the three most severe traumas. For example, a patient with $AIS_{abdomen} = 3$, $AIS_{thorax} = 2$, $AIS_{head\ and\ neck} = 4$, $AIS_{limbs} = 5$, will have $LISS = \ln(3)^{5.53} \times 1.7987 + \ln(4)^{5.53} \times 1.7987 + \ln(5)^{5.53} \times 1.7987 = 38.9716620395$. According to the results obtained by certain researches it has tendency to have better calibration and discrimination characteristics than NISS [18].

EISS is based as LISS on the most severe AIS scores that are used in the following formula: $EISS = 3^{A-2} + 3^{B-2} + 3^{C-2}$, where A, B and C are the highest values of AIS [19]. For example, a patient has $AIS_{head\ and\ neck} = 3$, $AIS_{thorax} = 4$, $AIS_{abdomen} = 2$ and $AIS_{limbs} = 5$, in this case $EISS = 3^{5-2} + 3^{4-2} + 3^{3-2} = 27 + 9 + 3 = 39$.

Anatomic Profile Characterization (APC)

APC is a scale that was proposed by Copes et al. According to APC algorithm a doctor has to take into consideration only the 3 most severe lesions according to AIS. The AIS scores are grouped in relation to region – A (AIS = 3-5 head, neck, brain and the spinal cord), B (AIS = 3-5 thorax), C (the anterior region of the neck with AIS = 3-5, the abdomen and pelvis with AIS = 3-5, the spine with or without the spinal column with AIS = 3, pelvic fractures with AIS = 4-5), D (the femoral artery with AIS = 4-5, collapse above the knee with AIS = 4-5, amputation above the knee with AIS = 4-5, the popliteal artery with AIS = 4, the face with AIS = 1-4, other traumas with AIS = 1-2). All of the conditions described above being classified based on ICD-9-CM, APC will be further on calculated using the following formula: $APC = M_0 + M_1 \times A + M_2 \times B + M_3 \times B^2 + M_4 \times C^2$, the used coefficients are: $M_0 = 4.0801$; $M_1 = -0.4914$; $M_2 = -0.2066$; $M_3 = 0.0161$; $M_4 = -0.0351$. D was excluded because in this case it wasn't influencing the survival predictability, but in some geographical regions it may be useful. The obtained value (APC) is considered in logistic regression formula as b and $P(\text{survival}) = e^b / (1 + e^b)$ [20]. For example, we have a patient with $AIS_{\text{abdomen}} = 2$, $AIS_{\text{Head and neck}} = 3$, $AIS_{\text{Upper limb}} = 4$ and $AIS_{\text{thorax}} = 5$, in this case $APC = 4.0801 - 0.4914 \times 3 - 0.2066 \times 5 + 0.0161 \times 5^2 - 0.0351 \times 0 = 1.9754$, further on, $P(\text{survival}) = e^{1.9754} / (1 + e^{1.9754}) = 0.8781$, respectively, the chance for survival in this case is equal to approximately 87.81%.

International Classification of Diseases (ICD) Derived Scales.

Trauma Mortality Prediction Model (TMPM)

TMPM is an algorithm that takes into consideration the 5 most severe traumas ordered from the least severe to the most severe and also includes a binary variable that reflects the presence of the 2 most severe traumas in the same body region [46]. The survival probability is calculated using the following formula: $TMPM = C_0 + \sum_{i=1}^5 (C_i I_i) + \eta S + \sigma I_1 I_2$ where I_1 - I_5 are the MARC values (Model-Averaged Regression Coefficient) for the lesions described in ICD-10-CM, written from the least severe to the most severe (I_1 being the most severe), the MARC values must be calculated *de novo* or extracted from a database, they are divided depending on gender, age and trauma mechanism, by the way, these 3 criteria determine the necessity to create $3 \times 3 = 9$ groups of MARC values (for example, MARC values senile patients of male gender with penetrant traumas will differ from the MARC values attributed to the pediatric patients of female gender with blunt traumas), the method used to calculate MARC values is exposed in the original article that belongs to Glance L. et al., S is the binary value, equal with 1 if the 2 most severe traumas are present in the same body region, $C_0 - C_5$ are coefficients that have the following values: $C_1 = 1.4298$, $C_2 = 1.3942$, $C_3 = 0.5190$, $C_4 = 0.3981$, $C_5 = 0.8278$, $C_0 = -2.2104$, $\eta = -0.1059$, $\sigma = -0.7835$, $P(\text{survival}) = 1 / \sqrt{(2\pi)} \int_{-\infty}^x (e^{-(t^2/2)}) dt$, where $t = TEMPT$ [21].

Injury mortality prediction (IMP)

The IMP derives from ICD-9-CM and is used to predict

the probability of survival for a traumatic patient. The score considers the 5 most severe traumas and is calculated using the following algorithm:

$IMP = C_0 + \sum_{i=1}^5 (C_i I_i) + C_6 S + C_7 I_1 I_2 + C_8 \ln(NBR) + C_9 NBR^{0.382}$, where I_1 - I_5 are the WADP values (Weighted Average Death Probability) for the 5 most severe traumas, the WADP values pot can be derived using a database or can be extracted from an existing one, S is a binary variable that is equal to 1 if 2 of the most severe traumas are located in the same topographical region, NBR is the number of topographical regions with traumas in a patient, $C_0 - C_9$ are the coefficients that have the following – $C_1 = 2.6352$, $C_2 = 2.3540$, $C_3 = 0.3164$, $C_4 = 0.2047$, $C_5 = 0.3681$, $C_6 = -0.3080$, $C_7 = -0.6582$, $C_8 = -1.7419$, $C_9 = 1.6154$, $C_0 = 9.0177$, $P(\text{survival}) = 1 / \sqrt{(2\pi)} \int_{-\infty}^x (e^{-(t^2/2)}) dt$, where $t = IMP$ [22].

ICD Derived Injury Severity Score (ICISS)

ICISS is an ISS derived score. It was formulated based on ICD-9 [23]. It can be calculated using the following formula: $ICISS = SRR_1 \times SRR_2 \times \dots \times SRR_n$ where SRR is Survival Rate Ratio, n – the number of lesions. Every lesion has a specific SRR value that varies from 0 to 1. Also, it varies depending on age groups, gender and trauma mechanism. Accuracy of this prediction model is based on the number of patients that were used to derive the SRR values [24]. As an example, we will show an ICISS calculated using SRR values designated for ICD-9 derived from the Florida AHCA database for the 1991-2009 period (<http://personal.health.usf.edu/epracht/ICISS/>) for a senile patient with closed clavicle fracture (code 810.00, SRR = 0.9075), open skull base fracture with laceration and contusion (code 801.6, SRR = 0.7000), closed mandible fracture (code 802.2, SRR = 0.8713). The ICISS (chances for survival) in this case = $0.9075 \times 0.7000 \times 0.8713 = 0.5534$ (55.34%).

Physiological Scores

There are used different algorithms for functional reserves estimation that can serve as scores in case of severe trauma: GCS, MODS, RTS, SOFA, SAPS II, APACHE II, MPM II [25].

Trauma Early Mortality Prediction Tool (TEMPT)

This is a scale used to predict the survival chances using the following variables: Age (≥ 59.5 years), Systolic blood pressure (≥ 163.5 mm Hg), Creatinine (≥ 1.35 mg/dl), International Normalized Ratio (≥ 1.25), Partial thromboplastin time (≥ 31.40 seconds), Hemoglobin (≤ 12.75 g/dl), Platelets (≤ 224.5 103/ μ L), Base excess (≤ -4.35 mmol/l), Temperature (≤ 36.25 °C). Each of these criteria has a coefficient that is included in the formula: $TEMPT = \sum(\text{Variables} \times \text{Coefficients})$. If $b = TEMPT$, then $P(\text{survival}) = e^b / (1 + e^b)$ [26].

MGAP and GAP scores

MGAP estimates the chances for survival considering the mechanism of trauma (blunt/penetrating), GCS (Glasgow Coma Scale), age, systolic blood pressure. It is calculated using the following model: GCS (the value of GCS), systolic blood pressure (>120 mm Hg – 5 points, $60-120$ mm Hg – 3 points, <60 mm Hg – 0 points), the mechanism of trauma (blunt – 0 points, penetrant – 4 points), age

(when <60 years – 5 points). $MGAP = \Sigma(\text{Variables})$. As a result, the patients are divided in three groups. High chances of survival ($MGAP = 23-29$), medium chances of survival ($MGAP = 18-22$) and small chances of survival ($MGAP = 3-17$) [27]. For example, a patient with penetrant trauma (4 pts), age of 49 years (5 pts), systolic blood pressure of 87 mm Hg (3 pts) and GCS = 13 has $MGAP = 4+5+3+13=25$ a respectively high chances for survival.

GAP derives from MGAP and is calculated similarly, but the mechanism of trauma is ignored. $GAP = \Sigma(\text{Variables})$ we define here: high probability of death group ($GAP = 3-10$ points), moderate probability of death group ($GAP = 11-18$ points), low probability of death group ($GAP = 19-24$ points) [28].

Kampala Trauma Score (KTS)

It is a score that was developed in Uganda to appreciate the severity of traumas, the main components are – age, systolic blood pressure, respiration rate, neurologic status (based on the AVPU scale), presence or absence of severe lesions. KTS can vary limits from 5 up to 16, to calculate the survival probability, it is necessary to create a local database based on the following model: $P(\text{survival}) = (\text{Number of deaths with the following score}) / (\text{Total number of deaths})$, that must be made for each score individually, it will appreciate the survival probability percentage, the conclusion being made based on the previous cases [29]. An example for the KTS calculation – a patient with SBP of 107 mm Hg, respiration rate – 6/min, AVPU – Pain and a severe lesion will have $KTS = 4+1+2+2=9$.

Acute Physiology Score (APS)

APS is used in order to estimate APACHE II. $APS = \Sigma(\text{Variables})$ [30]. For example, a patient with rectal temperature of 40°C, systolic blood pressure of 140 mm Hg, heart rate of 90/min, 13 respirations/min, $FiO_2 = 0.3$ and $PaO_2 = 81$, the arterial pH of 7.40, sodium concentration in serum of 156 mmol/l, potassium concentration in serum of 6.5 mmol/l, creatinine level in serum of 3.6 mg/100 ml, hematocrit of 55%, 43 leucocytes/mm³ GCS = 8 and bicarbonate ion concentration of 33 mmol/l will have an $APS = 3 + 3 + 0 + 0 + 0 + 0 + 2 + 3 + 4 + 2 + 4 + (15-8) + 1 = 29$.

Simplified Acute Physiology Score (SAPS)

The algorithm derived from APS (Acute Physiology Score) is used to determine the severity of a pathological condition, not necessarily for a traumatism, the parameters that are taken into consideration are: age, heart rate, systolic blood pressure, temperature, GCS, mechanical ventilation, PaO_2 , FiO_2 , urine output, level of blood urea, plasmatic concentrations of sodium, potassium, bicarbonate, bilirubin, leucocytes, chronic pathological conditions, each one of them has a specific score and is calculated using a specific formula [31]. The most recent model is the 3d model (SAPS III), the points that are given for each of the criteria are listed below: age (years): <40 (0 pts); ≥40 and <60 (5 pts); ≥60 and <70 (0 pts); ≥70 and <75 (13 pts); ≥75 and <80 years (15 pts); ≥80 (18 pts); comorbidities: cancer therapy (3 pts); Chron's disease, cardiopathies, hematologic cancer (6 pts); cirrhosis, AIDS (8 pts); metastatic cancer (11 pts). Length of stay

before ICU admission period (days): <14 (0 pts); ≥14 and <28 (6 pts); ≥28 (7 pts). Intra-hospital location before ICU admission: emergency room (5 pts), another ICU (7 pts), another department (8 pts). Use of major therapeutic options before ICU admission: vasoactive drugs (3 pts). ICU admission: unplanned (3 pts), planned (0 pts); reason for ICU admission: rhythm disturbances (-5 pts); seizures (-4 pts); hypovolemic hemorrhagic shock, hypovolemic non-hemorrhagic shock, digestive tract pathological conditions (acute abdomen for example) (3 pts); coma, stupor, obtunded patient, vigilance disturbances, confusion, agitation, delirium (4 pts); septic shock, anaphylactic shock, mixed and undefined shock (5 pts); liver failure (6 pts); focal neurological deficit (7 pts); severe pancreatitis (9 pts); intracranial mass effect (10 pts); surgical status at ICU admission: scheduled surgery (0 pts); no surgery (5 pts); emergency surgery (6 pts). Anatomical site of surgery: transplantation surgery (liver, kidney, pancreas etc.) (-11 pts); trauma – isolated, multiple (-8 pts); cardiac surgery (-6 pts); neurosurgery (5 pts). Acute infection at ICU admission – nosocomial (4 pts); respiratory (5 pts). GCS: 3-4 (15 pts); 5 (10 pts); 6 (7 pts); 7-12 (2 pts); ≥13 (0 pts). Total bilirubin – highest (in mg/dl): <2 mg/dl (0 pts); ≥2 and <6 mg/dl (4 pts); ≥6 mg/dl (5 pts). Total bilirubin – highest (in μmol/l): <34.2 μmol/l (0 pts); ≥34.2 and <102.6 μmol/l (4 pts); ≥102.6 μmol/l (5 pts). Body temperature – highest (in °C): <35 °C (7 pts); ≥35 °C (0 pts). Creatinine – highest (in mg/dl): <1.2 mg/dl (0 pts); ≥1.2 mg/dl and <2 mg/dl (2 pts); ≥2 and <3.5 mg/dl (7 pts); ≥3.5 mg/dl (8 pts). Creatinine – highest (in μmol/l): 3-4 μmol/l (15 pts); 5 μmol/l (10 pts); 6 μmol/l (7 pts) <106.1 μmol/l (0 pts); ≥106.1 and <176.8 μmol/l (2 pts); ≥176.8 and <309.4 μmol/l (7 pts); ≥309.4 μmol/l (8 pts). Heart rate: <120 /min (0 pts); ≥120 and <160 /min (5 pts); ≥160 /min (7 pts). Leucocytes – highest: <15 g/l (0 pts); ≥15 g/l (2 pts). Hydrogen ion concentration – lowest: ≤7.25 (3 pts); >7.25 (0 pts). Platelets – lowest: <20 g/l (13 pts); ≥20 and <50 g/l (8 pts); ≥50 and <100 g/l (5 pts); ≥100 g/l (0 pts). Systolic blood pressure – lowest: <40 mm Hg (11 pts); ≥40 and <70 mm Hg (8 pts); ≥70 and <120 mm Hg (3 pts); ≥120 mm Hg (0 pts). Oxygenation: PaO_2/FiO_2 <100 and VM (11 pts); PaO_2/FiO_2 ≥100 and MV (7 pts); PaO_2 <60 without MV (5 pts); PaO_2 ≥60 without MV (0 pts).

Afterwards, we calculate SAPS III. To include it in the general formula for chance of survival, we must first calculate $b = -32.6659 + \ln(\text{SAPS III} + 20.5958) \times 7.3068$, and then $P(\text{survival}) = e^b / (1 + e^b)$ [32].

For example, a 33-year old patient, without comorbidities, was admitted for 5 days, the admission in ICU was planned, the reason for admission – seizures, he had undergone an emergency surgery of liver transplantation, without acute infections, GCS = 8, bilirubin – 5 mg/dl, creatinine – 6 μmol/l, heart beats – 170/min, leucocytes highest level – 13 g/l, lowest blood pH level – 7.23, lowest platelets level of 19 g/l, minimum systolic blood pressure of 73 mm Hg, $PaO_2 = 61$ without need of intubation. The patient will have $SAPS = 0 + 0 + 0 + 0 - 4 + 6 - 11 + 0 + 2 + 4 + 8 + 7 + 0 + 3 + 13 + 3 + 0 = 31$, after that $b = -32.6659 + \ln(31 +$

+ 20.5958) x 7.3068 = -3.85197, and then we introduce it in the general formula $P(\text{survival}) = e^{-3.85197}/(1+e^{-3.85197}) = 0.0207$, in this case the chance for survival is approximately 2.07%.

Therapeutic Intervention Scoring System (TISS)

TISS is useful in assessing the best treatment strategy for the patients that are admitted in the ICU. Its criteria are grouped into 4 categories (each of them is contributing with 1, 2, 3 and respectively 4 points to the overall score in the 1983 version).

After we calculate $TISS = \sum(\text{Conditions})$ we can classify the patients in 4 categories – Class IV (≥ 40 points); Class III (20-39 points); Class II (10-19 points); Class I (< 10 points). Class III and Class IV patients require an experienced nurse, Class III patients that are relatively stable can be placed together with Class II patients, a nurse can take care of 4 Class II patients, Class I patients do not require admission in the ICU and observation, except the cases when there is present a myocardial infarction [33]. For example, a patient with peritoneal dialysis (4 points), that requires platelet transfusion (4 points) and blind intratracheal suctioning (3 points) will have $TISS = 4 + 4 + 3 = 11$ and will be categorized as a Class II patient.

Sequential Organ Failure Assessment score (SOFA) and qSOFA (quick-SOFA)

SOFA is used to determine the number and severity (quantity and quality) of a multi-organ dysfunction, the criteria used for this score are: PaO_2/FiO_2 , platelets level, GCS, bilirubin level, systolic blood pressure, creatinine level and the urine output. $SOFA = \sum(\text{Variables})$.

Also, SOFA can be used to predict the chance of death. In condition if $\Delta SOFA \geq 2$, the patient has a chance of survival two times less and when $\Delta SOFA \leq -2$ the same patient has a double chance of survival. Jones A. et al. reported that $\Delta SOFA \geq 2$ (42% chance of death); $\Delta SOFA = 1$ (23% chance of death); $\Delta SOFA = 0$ (19% chance of death); $\Delta SOFA = -1$ (11% chance of death); $\Delta SOFA \leq -2$ (9% chance of death) [34]. For example, a patient with PaO_2/FiO_2 of 50, SaO_2/FiO_2 of 253, blood platelets level of $140 \times 10^3/\text{mm}^3$, bilirubin level of 1.5 mg/dl, systolic blood pressure of 90 mm Hg and the dopamine level of 4 pg/ml, GCS = 13, creatinine level of 1.3 mg/dl, urine output 400 ml/d will have $SOFA_1 = 4 + 1 + 1 + 1 + (0+2) + 1 + 1 + 3 = 11$, afterwards the value of PaO_2/FiO_2 modified to 250, respectively $SOFA_2 = 2 + 1 + 1 + 1 + (0+2) + 1 + 1 + 3 = 9$, respectively $\Delta SOFA = SOFA_2 - SOFA_1 = 9 - 11 = -2$, the chances of death for this patient are estimated to approximately 9%.

The qSOFA is the simplified version of SOFA, it contains only 3 clinical criteria that can be very easily appreciated: A – Altered mental status (GCS < 15); R – Respiratory rate (≥ 22 respirations/minute) and S – Systolic blood pressure (≤ 100 mm Hg). It is calculated using the formula:

$qSOFA = A + R + S$, the criteria listed above are binary. If the expressed conditions are true, then they are equal with 1. In condition if $qSOFA \geq 2$, then there is a high change of poor outcome [35]. For example, a patient with GCS = 13; respiratory rate of 25 respirations/min and systolic blood

pressure of 63 mm Hg will have a $qSOFA = 1 + 1 + 1 = 3$.

Acute Physiology, Age, Chronic Health Evaluation II (APACHE II)

APACHE II is a score used to determine the severity of a pathological condition, it is derived from the following criteria: APS, AS and PSI (APS – Acute Physiology Score; AS – Age Score; PSI – Points for surgical interventions), the points that are given in this case are:

APS – the exact value (see above); age (AS): ≤ 44 (0 pts); 45-54 (2 pts); 55-64 (3 pts); 65-74 (5 pts); ≥ 75 (6 pts). Points for surgical interventions (PSI): for nonsurgical or postoperative patients that had undergone an emergency surgery (5 pts); for postoperative patients that had undergone a planned surgery (2 pts). $APACHE II = APS + SV + PIC$, $b = -3.517 + (0.146 \times APACHEII) + 0.603 \times S + Y$ [30]. Where S is a binary value equal to 1 when the patient has undergone an emergency surgery, Y is a constant that is attached to chronic diseases. Afterwards b is introduced in the formula $P(\text{survival}) = e^b/(1+e^b)$ [36]. As an example, we will take a patient with APS = 29, 33 years old, with multiple traumas and emergency surgical intervention ($y = -1.081$). $APACHE II = 29 + 0 - 5 = 24$, $x = -3.517 + (0.146 \times 24) + 0.603 \times 1 - 1.081 = -0.491$, and then we calculate $P(\text{survival}) = e^{-0.491}/(1+e^{-0.491}) = 0.3796$, in this case the chance for survival is equal to approximately 37.96%.

Revised Trauma Score (RTS)

RTS has inversely proportional value with the severity of trauma, it is calculated using the following model: $RTS = b_0 + b_1 \times GCS + b_2 \times SBP + b_3 \times RR$, where SBP – systolic blood pressure; RR – respiration rate, the constants – $b_0 = -3.5718$; $b_1 = 0.9368$; $b_2 = 0.7326$; $b_3 = 0.2908$. After that, the chances for survival are calculated using the standard formula $P(\text{survival}) = e^b/(1+e^b)$ if we consider that $RTS = b$ [37]. For example, a patient with GCS = 7, systolic blood pressure of 120 mm Hg, and the respiration rate of 6/min has $RTS = -3.5718 + 0.9368 \times 7 + 0.7326 \times 120 + 0.2908 \times 6 = 1.8134$, $P(\text{survival}) = e^{1.8134}/(1+e^{1.8134}) = 0.8597$, respectively in this case the patient has a chance of survival equal to approximately 85.97%.

Triage RTS (T-RTS)

T-RTS is used to assess the dynamics in the state of a trauma patient using the same criteria as RTS, but in the case of T-RTS we calculate the Δ values in order to appreciate how the patient's state has changed according to the following formula: $\Delta T-RTS = TRTS_{\text{at hospital}} - TRTS_{\text{on scene}}$.

There are three variants – $\Delta T-RTS = 0$ (No Change); $\Delta T-RTS \geq 1$ (Improving); $\Delta T-RTS < 0$ (Deteriorating) [38]. For example, a patient with a respiratory rate of 23 respirations/min, systolic blood pressure of 63 mm Hg and GCS = 12 will have a $TRTS_{\text{on scene}} = 4 + 2 + 3 = 9$, systolic blood pressure raised at 79 mm Hg and GCS = 13 in hospital, $TRTS_{\text{at hospital}} = 4 + 3 + 4 = 11$, $\Delta T-RTS = 11 - 9 = 2$, we conclude that this patient's state is improving, whereas his initial state was poor.

Glasgow Coma Score (GCS)

This is a score widely used by neurologists, neurosurgeons, anesthesiologist etc. It takes into consideration eye

opening, verbal response and motor response. The value can be directly proportional to the patient's consciousness. The spontaneous eye opening is characterized by opening without stimulating the patient, the patient is doing it consciously, the eye opening on verbal stimulus is when the patient is opening his eyes when is verbally called, the eye opening on pain stimulus is when the patient is opening his eyes after causing him physical pain sensations, and not reacting on verbal stimuli. The oriented verbal response is the response given by an auto- and allopsychically oriented patient, the confused verbal response is a logic bond order of words that cannot be understood, with the patient being oriented on the circumstances, the abstract verbal response is a verbal response that doesn't have a logical continuity and is not oriented on the circumstances, the incomprehensible verbal response is a continuity of words that cannot be understood. The obeying motor response is the response in which the patient is following the doctor's commands, the pain localized motor response is the response in which the patient is trying to palpate the topographical region in which the pain is localized, the avoiding pain motor response is the response in which the patient is avoiding the topographical region in which the pain is localized, the abnormal flexion motor response is the response in which a body part is flexed spontaneously and usually accompanied by abduction, the abnormal extension motor response is the response in which the patient has a body part that is spontaneously extending and it is usually accompanied by adduction.

A patient that is opening eyes on a pain stimulus, has confused verbal response and pain localized, his motor response will have a GCS = 2 + 4 + 5 = 11. After a craniocerebral trauma, in the case of GCS = 13-15, we can suspect a mild traumatic brain injury, in cases when GCS = 9-12, we can suspect a moderate traumatic brain injury, in cases when GCS = 3-8, we can suspect a severe traumatic brain injury, some researchers say that severe traumatic brain injuries do not correspond to GCS = 8 but GCS <8 [39].

Mixed scores

The mixed scores combine the anatomical, functional and other criteria, most of them there described above:

Mortality Probability Admission Model (MPMoIII)

This is a score used to determine the chances of survival based on the following criteria: physiological parameters, acute and chronic diagnoses, mechanical ventilation, reason for admission in ICU, age and other details that will be discussed afterwards [51]. The most recent model that we can use is MPMoIII, which can be calculated the following way: $MPMoIII = b_0 + b_1 + b_3 \times \text{Age} + b_4 + b_5 + b_6 \times \alpha + b_7$ where b_0 – general constant; b_2 – comorbidity constant; b_3 – age constant; b_4 – constant for other situations; b_5 – constant to identify the cardiac and respiratory arrest; $b_6 \times \alpha$ – the interaction product between 2 factors; b_7 – the physiological constant. Each of these constants has certain values that can be associated with the patient. To understand how this score must be calculated, we must take into consideration that constants in the same category can be simultaneously in the formula. For example, a patient with metastatic

neoplasm and cirrhosis will have both constants included in the formula, the factor interactions can be introduced in the formula only when the main factor is present and then the constant is multiplied to the age, afterwards to calculate the score we consider $MPMoIII = b$ and introduce it in the standard formula $P(\text{survival}) = e^b / (1 + e^b)$ [40].

A patient that is 56-year old, GCS = 4, heartbeats = 161/min, metastatic neoplasm, gastrointestinal bleeding, in which a respiratory arrest was identified, was resuscitated during the ICU stay and needed an unplanned surgical intervention will have $MPMoIII = -5.36283 + 2.050514 + 0.433188 + 3.204902 - 0.165253 + (53 \times 0.0385582) - 0.7969783 - (53 \times 0.0330237) = -0.3431288$, and $P(\text{survival}) = e^{-0.3431288} / (1 + e^{-0.3431288}) = 0.4150496549$, respectively the chance for survival in this case is equal to approximately 41.50%.

Harborview Assessment for Risk of Mortality (HARM)

HARM is a mixed score developed based on the ICD-9-CM and takes into consideration the mechanism of injury, anatomical criteria, comorbidities and age. It is calculated using the formula $b = b_0 + b_1 + \dots + b_n (\alpha \times \beta)$ where the b_1, b_2, \dots, b_n are constants that are attached to different conditions, the $\alpha \times \beta$ product is an interaction product that will be included in the formula only in the case when both of the product criteria are present. For example, the variable *head x spinal cord* will be added when both of these anatomical structures had undergone a lesion. In the case of age constants, we multiply them by the patient's age expressed in years. According to the results obtained by West T.A., HARM manifested a better performance compared to TRISS and ICISS. Also, it is important to mention comorbidity constants: congenital coagulopathy (1.494934), cirrhosis (2.954898), ischemic heart disease (0.9844608), hypertension (-0.546734), psychoses (-1.854641) and alcohol or drug dependence (-0.7681033), after calculating the b value, if we consider $HARM = b$, then we can introduce this value in the standard formula $P(\text{survival}) = e^b / (1 + e^b)$ [41]. For example, a 46-year old patient has cirrhosis and had undergone a skull fracture with incomplete spinal cord injury above the C4 segment. He has $b = -4.708587 - 0.2163938 \times 46 + 0.0109741 \times 46 + 0.0019716 \times 46 + 2.954898 + 0.6120652 + 1.879599 + 0.7507725 = 1.8678561$, and respectively $P(\text{survival}) = e^{1.8678561} / (1 + e^{1.8678561}) = 0.8662$, respectively, in this case, the chances for survival are equal to approximately 86.62%.

Trauma and Injury Severity Score (TRISS)

TRISS is a score used to predict the consequences of a trauma. It is derived from RTS and ISS, ISS is calculated using the usual formula, and then we calculate $b = b_0 + b_1 \times \text{RTS} + b_2 \times \text{ISS} + b_3 \times \text{AgeConst}$, where $b_0 = -1.29803310$, $b_1 = 0.89538700$, $b_2 = -0.09521947$ and $b_3 = -1.27540759$ in case of penetrating traumas and $b_0 = -1.64790049$, $b_1 = 0.90535734$, $b_2 = -0.07845091$, $b_3 = -1.38013670$ for blunt traumas, where AgeConst is a binary value (0 if Age < 55, 1 if Age ≥ 55). The chance of survival can be further calculated using the standard formula $P(\text{survival}) = e^b / (1 + e^b)$ [42]. For example, a patient with RTS = 1.8134,

ISS = 16, penetrant traumas, age of 31 years will have TRISS = $-1.29803310 + 0.89538700 \times 1.8134 - 0.09521947 \times 16 + 0 = -1.1978498342$, after that $P(\text{survival}) = e^{-1.1978498342} / (1 + e^{-1.1978498342}) = 0.2318579399$, the chance for survival in this case is approximately 23.18%.

New Trauma and Injury Severity Score (NTRISS)

This score is a NISS, RTS and GCS derived scale. It is calculated using the $b = b_0 + b_1 \times MR + b_2 \times SBP + b_3 \times NISS + b_4 \times \text{AgeConst}$, where SBP – systolic blood pressure in RTS, MR – motor response in GCS, AgeConst is a binary value (0 if Age < 55, 1 if Age ≥ 55), its constants are – for penetrating traumas – $b_0 = -1.58632944$, $b_1 = 0.58883203$, $b_2 = 0.96952677$, $b_3 = -0.06659814$, $b_4 = -1.00582810$, for blunt traumas – $b_0 = -1.67602650$, $b_1 = 0.61944706$, $b_2 = 0.89539814$, $b_3 = -0.07289039$, $b_4 = -1.33088941$, then, the b value is introduced in the standard formula $P(\text{survival}) = e^b / (1 + e^b)$ [42]. For example, a 57-year old patient with MR = 4 in GCS, SBP = 2 in the RTS scale; NISS = 27 and blunt traumas has a NTRISS = $-1.67602650 + 0.61944706 \times 4 + 0.8953814 \times 2 - 0.07289039 \times 27 - 1.33088941 \times 1 = -0.7064054$, afterwards $P(\text{survival}) = e^{-0.7064054} / (1 + e^{-0.7064054}) = 0.3303936013$, in this case, the chances for survival are equal to approximately 33.03%.

Trauma and Injury Severity Score with SpO₂ (TRISS SpO₂)

It is a recently developed score that takes into consideration the SpO₂ (Peripheral oxygen saturation). It is calculated using the following model – $b = b_0 + b_1 \times \text{GCS} + b_2 \times \text{SBP} + b_3 \times \text{SpO}_2 + b_4 \times \text{ISS} + b_5 \times \text{AgeConst}$, where GCS – Glasgow Coma Scale, points being accorded from RTS, SBP – systolic blood pressure calculated based on RTS, ISS – Injury Severity Score, AgeConst is a binary value (0 if Age < 55, 1 if Age ≥ 55), SpO₂ (0 if it can't be measured; 1-80% = 1; 81-90% = 2; 91-95% = 3; 96-100% = 4), the constants for this score are: in case of penetrant trauma – $b_0 = -3.5166820$, $b_1 = 0.8515884$, $b_2 = 0.3453793$, $b_3 = 1.3098071$, $b_4 = -0.1955984$, $b_5 = -4.0353761$, in case of blunt trauma – $b_0 = -2.97523446$, $b_1 = 0.75773826$, $b_2 = 0.58321377$, $b_3 = 0.38492625$, $b_4 = 0.08441861$, $b_5 = -1.59455370$, after that, the chances for survival are calculated using the following formula: $P(\text{survival}) = e^b / (1 + e^b)$ [42]. For example, a 43-year old patient with GCS – 3 points in RTS scale, SBP = 2 points in RTS scale, SpO₂ = 3 points, ISS = 18 and blunt trauma will have TRISS SpO₂ = $-2.97523446 + 0.75773826 \times 3 + 0.58321377 \times 2 + 0.38492625 \times 3 + 0.08441861 \times 18 + 0 = 2.36886909$, and then $P(\text{survival}) = e^{2.36886909} / (1 + e^{2.36886909}) = 0.9144224937$, respectively, in this case, the chances for survival will be approximately 91.44%.

New Trauma and Injury Severity Score with SpO₂ (NTRISS SpO₂)

NTRISS SpO₂ is also a recently developed scale that takes into consideration the peripheral oxygen saturation. It is calculated using the following formula – $b = b_0 + b_1 \times \text{MR} + b_2 \times \text{SBP} + b_3 \times \text{SpO}_2 + b_4 \times \text{NISS} + b_5 \times \text{AgeConst}$, where MR – motor response points according to GCS, SBP – systolic blood pressure according to RTS, AgeConst is a binary value (0 if Age < 55, 1 if Age ≥ 55), SpO₂ (0 if it can't

be measured; 1-80% = 1; 81-90% = 2; 91-95% = 3; 96-100% = 4), the constants are: in case of penetrating trauma – $b_0 = -1.5156694$, $b_1 = 0.1832071$, $b_2 = 1.0209288$, $b_3 = 1.1288631$, $b_4 = -0.1138697$, $b_5 = -1.7286860$, in case of blunt traumas – $b_0 = -2.73634921$, $b_1 = 0.59396868$, $b_2 = 0.66226833$, $b_3 = 0.56405908$, $b_4 = -0.06841853$, $b_5 = -1.43274160$, afterwards, the chance of survival is calculated using the standard formula $P(\text{survival}) = e^b / (1 + e^b)$ [42]. For example, a 56-year old patient with MR = 3 points according to GCS, SBP = 3 points according to RTS, SpO₂ = 2 points, NISS = 31, and penetrating trauma will have NTRISS SpO₂ = $-1.5156694 + 0.1832071 \times 3 + 1.0209288 \times 3 + 1.1288631 \times 2 - 0.1138697 \times 31 - 1.7286860 \times 1 = -0.9041822$, then $P(\text{survival}) = e^{-0.9041822} / (1 + e^{-0.9041822}) = 0.2881918128$, respectively, patient's survival chance is approximately 28.81%.

A Severity Characterization of Trauma (ASCOT)

ASCOT takes into account – AgeConst which is a binary value (0 if Age < 55, 1 if Age ≥ 55), GCS value, systolic blood pressure and respiration rate based on RTS, ISS calculated based on AIS85, which is more effective in the opinion of the authors, similarly with TRISS, it has specific constants that take into consideration the mechanism of trauma: in case of penetrant trauma – $b_0 = -1.1350$, $b_1 = 1.0626$, $b_2 = 0.3638$, $b_3 = 0.3332$, $b_4 = -0.3702$, $b_5 = -0.2053$, $b_6 = -0.3188$, $b_7 = 0.8365$, in case of blunt trauma – $b_0 = -1.1570$, $b_1 = 0.7705$, $b_2 = 0.6583$, $b_3 = 0.2810$, $b_4 = -0.3002$, $b_5 = -0.1961$, $b_6 = -0.2086$, $b_7 = -0.6355$ [43], the variables considered are part of APC (Anatomical Profile Characterization) – A (severe traumas with AIS ≥ 3 in the head region, brain and spinal column), B (thorax and the anterior portion of neck), C (severe traumas in other body regions) and D (lesions with AIS = 1 and 2 that are present in any body region), they are further included in the following formula $b = b_0 + b_1 \times \text{GCS} + b_2 \times \text{SBP} + b_3 \times \text{RR} + b_4 \times \text{A} + b_5 \times \text{B} + b_6 \times \text{C} + b_7 \times \text{AgeConst}$, where SBP – systolic blood pressure according to RTS, GCS – Glasgow Coma Score and RR – respiratory rate according to RTS, AgeConst – The age constant. The survival chances are then appreciated using the standard formula $P(\text{survival}) = e^b / (1 + e^b)$ [44]. For example, a 34-year old patient with a blunt trauma GCS = 3 points, SBP = 2 points according to RTS; RR = 3 points according to RTS, $\text{AIS}_{\text{Head and neck}} = 3$; $\text{AIS}_{\text{Thorax}} = 4$; $\text{AIS}_{\text{Lower limb}} = 4$ will have an ASCOT = $-1.1570 + 0.7705 \times 3 + 0.6583 \times 2 + 0.2810 \times 3 - 0.3002 \times 3 - 0.1961 \times 4 - 0.2086 \times 4 + 0 = 0.7947$, and then $P(\text{survival}) = e^{0.7947} / (1 + e^{0.7947}) = 0.6888396197$, respectively, in this case, survival chances are equal to approximately 68.83%. We should mention that, in case of ASCOT, TRISS and NTRISS, the mechanism of trauma is taken into consideration (blunt or penetrating) [43].

Revised Injury Severity Classification (RISC)

RISC is used to evaluate the survival chances considering the following variables: age, NISS, AIS for head, AIS for extremities, GCS, thromboplastin action time, base excess, preclinical cardiac arrest presence, preclinical systolic blood pressure, the most recent version of this score is the II edition [45]. After that, we calculate it in the following way –

the initial variable is equal to 5, we then add the points from the table depending on the patient's condition, $RISC = 5.0 + \Sigma(\text{Variables})$, and then we consider $RISC = b$, and introduce it in the standard formula $P(\text{survival}) = e^b / (1 + e^b)$ [46]. For example, a 40-year old patient with $NISS = 27$, $GCS = 12$; $TT = 45$ s; without base excess, $SBP = 85$ mm Hg, without cardiac arrest will have a $RISC = 5.0 - 0 - 0.03 \times 27 - 0 - 1 - 0 - 0.8 - 0 - 0.4 - 0 = 1.99$, and then $P(\text{survival}) = e^{1.99} / (1 + e^{1.99}) = 0.8797431375$, respectively, this patient has an approximately survival chance equal to 87.97%.

Pediatric Trauma Score (PTS)

This is a score used exclusively for pediatric patients. It includes the following variables: body weight, airway status, systolic blood pressure, central nervous system status, skeletal traumas, skin lesions.

We differentiate 5 groups of risk in this case, for $PTS = 9-12$, the death risk is equal to 0%, for $PTS = 7-8$, the death risk is equal to 3%, for $PTS = 5-6$, the death risk is equal to 15%, for $PTS = 3-4$, the death risk is equal to 36%, for $PTS = 1-2$, the death risk is equal to 45%, for $PTS \leq 0$, the death risk is equal to 100% according to the original article [47]. For example, a patient with a body weight of 15 kg, normal airway status, systolic blood pressure of 80 mm Hg, alert CNS status, a closed fracture and without skin lesions will have a $PTS = 1+2+1+2+1+2=9$ and 0% risk of death.

Norwegian Prediction Model in Trauma 2 (NORMIT2)

It was developed in Norway. Its coefficients are derived from AIS98. NORMIT2 can be calculated using T-RTS, NISS, age and ASA-PS attached coefficients by introducing them in the following formula: $NORMIT2 = (0.5562 \times T-RTS) - 4.3234 \times [(Age + 1)/100]^3 + ASA$, where ASA is the individual American Society of Anesthesiologists physical status classification system (ASA-PS) categories estimated before the injury ($ASA1 = (-0.0713 \times NISS) + 0.6266$, $ASA2 = (-0.0565 \times NISS) - 0.2142$, $ASA3 = (-0.0487 \times NISS) - 0.8971$, $ASA4 = (-0.0081 \times NISS) - 3.8748$). The result of NORMIT2 score is considered as coefficient b in standard logistic regression equation - $P(\text{survival}) = e^b / (1 + e^b)$ [48]. For example, a 41-year old ASA1 patient with a T-RTS = 3 and NISS = 31 will have a $NORMIT2 = (0.5562 \times 3) - 4.3234 \times [(41+1)/100]^3 + (-0.0713 \times 31) + 0.6266 = -0.213073$, afterwards $P(\text{survival}) = e^{-0.213073} / (1 + e^{-0.213073}) = 0.4469$, the chances for survival are equal to 44.69% in this case.

Trauma Audit and Research Network (TARN) Probability of survival model

This model was developed in 2019 and is constantly updated by the Trauma Audit and Research Network using its own institutional database of trauma patients. It takes into consideration the following criteria: ISS, GCS, modified Charlson Comorbidity Index (mCCI), age, gender, intubation necessity and the interactions between these factors using the following formula $b = \text{GenConst} + \text{AgeVar} + \text{GenderVar} + \sqrt{(10/ISS)} - 0.8618 + \log_e(ISS/10) - 0.2974 + \text{GCS}_{\text{var}} + \text{mCCI}_{\text{var}} + \text{Interactions}$, where GenConst – general constant, Age_{var} – age variable + Gender_{var} – gender variable, ISS – Injury Severity Score, mCCI_{var} – modified Charlson Comor-

bidity Index. Afterwards we use the formula: $P(\text{survival}) = e^b / (1 + e^b)$ [49].

The Sequential Trauma Score (STS)

STS is a scale that takes into consideration the patient's data (P), preclinical measured physiological variables (A), early clinical physiological variables (B1) and late clinical physiological variables (B2) of a traumatic patient. The coefficients for equation may vary for different regions where the score was validated. The survival chance is calculated depending on the information that is available at the 4 different periods of contact with the patient:

For Model P - $P(\text{survival}) = 1 - (1 / (1 + \text{EXP}(2.268 - 1.234 \times \text{AgeConst})))$.

For Model P+A - $P(\text{survival}) = 1 - (1 / (1 + \text{EXP}(3.566 - 1.653 \times \text{AgeConst} - 1.353 \times \text{GCS} - 1.311 \times \text{PreclinicalAnisocoria} - 0.983 \times \text{SBP} - 0.78 \times \text{HR})))$.

For Model P+A+B1 - $P(\text{survival}) = 1 - (1 / (1 + \text{EXP}(3.901 - 1.663 \times \text{AgeConst} - 0.602 \times \text{SBP} - 0.7 \times \text{PreclinicalAnisocoria} - 1.11 \times \text{GCS} - 1.294 \times \text{ClinicalAnisocoria} - 1.316 \times \text{BE} - 0.756 \times \text{SpO}_2 - 0.947 \times \text{TT})))$.

For Model P+A+B1+B2 - $P(\text{survival}) = 1 - (1 / (1 + \text{EXP}(4.857 - 1.333 \times \text{CCCC} - 0.772 \times \text{MT} - 0.345 \times \text{MAIS}(=4) - 2.199 \times \text{MAIS}(=5) - 1.73 \times \text{AgeConst} - 0.752 \times \text{GCS} - 0.647 \times \text{PreclinicalAnisocoria} - 1.251 \times \text{ClinicalAnisocoria} - 0.98 \times \text{BE} - 0.711 \times \text{TT})))$.

Where AgeConst – age constant; GCS – Glasgow Coma Scale; SBP – systolic blood pressure; HR – heart rate; BE – base excess; TT – Thromboplastin action time; CCCC – closed chest cardiac compressions; MT – massive transfusion; MAIS – maximum AIS. In the model P+A+B1+B2, MAIS is considered only in the cases when it is equal to 4 or 5, in case when it is equal to 4, only one of the variables listed above is considered, this means that the product -2.199 x MAIS (=5) is not included in the formula. The authors of the original article note that this score is not efficient to evaluate blunt trauma patients [50].

As an example, we will review a 62-year old patient at the late clinical period – no necessity for CCCC, necessity for massive transfusion, MAIS = 4, GCS = 13, without clinical or preclinical anisocoria, base excess = -9, thromboplastin action time reduced by 61%, respectively $P(\text{survival}) = 1 - (1 / (1 + \text{EXP}(4.857 - 1.333 \times 0 - 0.772 \times 1 - 0.345 \times 4 \times (-4) - 2.199 \times 0 - 1.73 \times 1 - 0.752 \times 0 - 0.647 \times 0 - 1.251 \times 0 - 0.98 \times 1 - 0.711 \times 1))) = 0.3282744176$, respectively, in this case, the chances for survival are equal to approximately 32.82%.

World Dispersion

Europe

In Germany, the AIS, ISS, NISS, GCS and RISCII in association with wbCT (whole body computer tomography) are used [51, 52, 53, 54, 55]. In France, T-RTS, TRISS, MGAP are widely used [56, 57]. The Scandinavian countries widely exploit the ISS [58]. In Norway, TRISS, TARN and NORMIT2 are introduced in daily practice. Taking into account that NORMIT 2 was developed in Norway's population, it has the best characteristics to predict the outcomes in local medical system. TARN was proposed by UK scientific team [48]. For Spain population, the implementation of ASCOT,

ICISS and TRISS was discussed [59]. APACHE II, RTS and GCS are widely used in Romania without any validation [60]. ASCOT or TRISS were compared by the Bucharest clinicians with no significant difference in their usage for the Romanian population [61].

Asia and Oceania

In China, there are implemented the ISS, TRISS, RTS algorithms and to appreciate the severity of traumas, instead of wbCT, the ultrasonography is recommended [62]. NISS methodology wasn't accepted, because a study has proven that it has similar efficiency with ISS in this zone. Also, this study proves that ISS74 and ISS97 have a similar accuracy [2]. LISS score was proposed for the first time in Hangzhou in 2012 [18]. In Korea, doctors consider the RTS and value of the serum albumin [63]. In Australia, AIS, ISS and TRISS methodology is accepted [64, 65, 66]. Taiwan's medical system benefits by GCS, AIS, ISS and RTS scores [7, 67].

South America

The clinicians from Brazil have developed a new score – NTRISS, that shows similar performance with TRISS [42]. Also in Brazil, the independent diagnostic criteria as peripheral oxygen saturation, lactate concentration, GCS, infused crystalloid volume, presence of TBI (Traumatic Brain Injury) are considered in patient's trauma assessment [69]. In Colombia, the ISS, RTS and TRISS are used for severity trauma characterization [68].

North America

With no matter that TRISS is originary from USA, there is used a series of scales in order to evaluate the severity of trauma as follows: ISS, NISS, TRISS, ICISS MGAP, GAP HARM and KTS [41, 72, 73, 74].

Republic of Moldova

In the Republic of Moldova, there have been used TS, RTS, AIS and ISS scores. The majority of traumatic scores haven't statistical validation [75]. We also have identified that in the ICU, the APACHE II score was used by the anesthesiologists to predict mortality rate for critical patients without any validation as well [76]. For the patients with associated trauma and TBI (Traumatic Brain Injury), the clinicians from the Republic of Moldova use MGAP and ASCOT, because they include the SBP (Systolic Blood Pressure) and GCS (Glasgow Coma Score). In the opinion of these authors, SBP and GCS are good predictors of survival in case of TBI, but there is no evidence that these scores are able to predict the evolution of trauma patients better than other scores mentioned before [77].

At present, there is only one validated trauma score – NISS. Also, MPMoIII was used in a pilot research with relatively reduced number of respondents and the accuracy of coefficient needs improvement. The ability of NISS to predict the probability of survival rate was estimated in the retrospective study that enrolled 467 severe trauma patients and 225 critical trauma patients admitted in Emergency Medicine Institute (EMI). The modelling for critical trauma patients had a good fit in comparison with severe trauma patients [16]. Both, the MPMoIII or/and NISS were tested for survival prediction in severe trauma patients (NISS>15)

transferred from regional hospitals to EMI. According to these results, the NISS has a better prediction power than MPMoIII (Nagelkerke R square was 64.1% vs 51%, mixed model having it equal to 81%). In comparison with patients admitted directly in EMI, the determination coefficient increased by more than 20% (40% and 64.1%, respectively) [17], being a serious argument to continue studies in this direction.

Conclusions

Different traumatic scores are used worldwide (different continents, countries or regions) to estimate the severity of trauma patients in relation to the anatomical, physiological or combined criteria. All of them have a potential to be validated for the Moldovan medical system.

In perspective, a part of these scores will be validated and compared to identify those ones that have the best determination, calibration and discrimination abilities to predict the outcomes for the local medical system. As a result, the coefficients from the mathematical equations belonging to the scores will be adjusted to the conditions of the national medical system of the Republic of Moldova.

References

1. Keel M, Trentz O. Pathophysiology of polytrauma. *Injury*. 2005;36(6):691-709.
2. Deng Q, Tang B, Xue C, et al. Comparison of the ability to predict mortality between the injury severity score and the new injury severity score: a meta-analysis. *Int J Environ Res Public Health*. 2016;13(8):1-12.
3. National Bureau of Statistics of the Republic of Moldova. Statistical databank: Health protection [Internet]. Chisinau: The Bureau; c2019 [cited 2019 Nov 10]. Available from: <https://statbank.statistica.md/>.
4. Femling JK, West SD, Hauswald EK, et al. Nosocomial infections after severe trauma are associated with lower apolipoproteins B and AII. *J Trauma Acute Care Surg*. 2013 Apr;74(4):1067-73.
5. McCullough AL, Haycock JC, Forward DP, Moran CG. Early management of the severely injured major trauma patient. *Br J Anaesth*. 2014;113(2):234-241.
6. Winfield RD, Delano MJ, Lottenberg L, et al. Traditional resuscitative practices fail to resolve metabolic acidosis in morbidly obese patients following severe blunt trauma. *J Trauma*. 2010;68(2):317-30.
7. Hsieh CH, Chen YC, Hsu SY, Hsieh HY, Chien PC. Defining polytrauma by abbreviated injury scale ≥ 3 for at least two body regions is insufficient in terms of short-term outcome: a cross-sectional study at a level I trauma center. *Biomed J*. 2018;41(5):321-327.
8. Rau CS, Wu SC, Kuo PJ, et al. Polytrauma defined by the new Berlin definition: a validation test based on propensity-score matching approach. *Int J Environ Res Public Health*. 2017;14(9):4-13.
9. Butcher NE, Enninghorst N, Sisak K, Balogh ZJ. The definition of polytrauma: variable interrater versus interrater agreement – a prospective international study among trauma surgeons. *J Trauma Acute Care Surg*. 2013;74(3):884-889.
10. Rutledge R. The Injury Severity Score is unable to differentiate between poor care and severe injury. *J Trauma*. 1996;40(6):944-50.
11. Pape HC, Lefering R, Butcher N, et al. The definition of polytrauma revisited: an international consensus process and proposal of the new "Berlin definition". *J Trauma Acute Care Surg*. 2014;77(5):780-786.
12. Butcher N, Balogh ZJ. The definition of polytrauma: the need for international consensus. *Injury*. 2009;40 Suppl 4:S12-22.
13. Champion HR. Trauma scoring. *Scand J Surg*. 2002;91(1):12-22.
14. Association for the Advancement of Automotive Medicine (AAAM). ISS, NISS and MAIS Mapping with AAAM's ICD ISS Map [Internet].

- Chicago: AAAM; c2016-2010 [cited 12 Dec 2019]. Available from: <https://www.aaam.org/abbreviated-injury-scale-ais/ais-icd-iss-map/>
15. Lefering R. Trauma scoring systems. *Curr Opin Crit Care*. 2012;18(6):637-640.
 16. Arnaut O, Rojnovanu G, Sandru S, Saulea A. Validation of New Injury Severity Score in severe trauma from autochthonous medical system. *Arta Medica (Chisinau)*. 2019;3(72):8-9.
 17. Arnaut O. Survival predictive models in severe trauma patients' transportation within Moldovan medical system. *Mold Med J*. 2019;62(4):39-44.
 18. Wang X, Gu X, Zhang Z, QIU F, Zhang K. The natural logarithm transforms the abbreviated injury scale and improves accuracy scoring. *Turkish J Trauma Emerg Surg*. 2012;18(6):483-489.
 19. Kuo SCH, Kuo PJ, Chen YC, Chien PC, Hsieh HY, Hsieh CH. Comparison of the new Exponential Injury Severity Score with the Injury Severity Score and the New Injury Severity Score in trauma patients: a cross-sectional study. *PLoS One*. 2017;12(11):1-12.
 20. Copes WS, Champion HR, Sacco WJ, Lawnick MM, Gann DS, Gennarelli T, MacKenzie E. Progress in characterizing anatomic injury. *J Trauma*. 1990;30(10):1200-7.
 21. Glance LG, Osler TM, Mukamel DB, Meredith W, Wagner J, Dick AW. TMPM-ICD9: a trauma mortality prediction model based on ICD-9-CM codes. *Ann Surg*. 2009;249(6):1032-9.
 22. Wang M, Wu D, Qiu W, Wang W, Zeng Y, Shen Y. An injury mortality prediction based on the anatomic injury scale. *Medicine (Baltimore)*. 2017;96(35):e7945.
 23. Osler T, Rutledge R, Deis J. ICISS: an international classification of disease-9 based injury severity score. *J Trauma*. 1996;41(3):380-6.
 24. Davie G, Cryer C, Langley J. Improving the predictive ability of the ICD-based Injury Severity Score. *Inj Prev*. 2008;14(4):250-255.
 25. Seliverstov PA, Shapkin YG. Assessment of severity and prognosis of polytrauma outcome: the current state of the problem. *Sovrem Tekhnologii Med*. 2017;9(2):207-216.
 26. Kunitake RC, Kornblith LZ, Cohen MJ, Callcut RA. Trauma early mortality prediction tool (TEMPT) for assessing 28-day mortality. *Trauma Surg Acute Care Open*. 2018;3(1):1-6.
 27. Sartorius D, Le Manach Y, David JS, et al. Mechanism, Glasgow Coma Scale, Age, and Arterial Pressure (MGAP): a new simple prehospital triage score to predict mortality in trauma patients. *Crit Care Med*. 2010;38(3):831-837.
 28. Kondo Y, Abe T, Kohshi K, Tokuda Y, Cook EF, Kukita I. Revised trauma scoring system to predict in-hospital mortality in the emergency department: Glasgow Coma Scale, Age, and Systolic Blood Pressure score. *Crit Care*. 2011;15(4):R191.
 29. Weeks SR, Juillard CJ, Monono ME, et al. Is the Kampala Trauma Score an effective predictor of mortality in low-resource settings? A comparison of multiple trauma severity scores. *World J Surg*. 2014;38(8):1905-1911.
 30. Wagner DP, Draper EA. Acute physiology and chronic health evaluation (APACHE II) and Medicare reimbursement. *Health Care Financ Rev*. 1984;Suppl:91-105.
 31. Le Gall Jr, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA*. 1993;270(24):2957-63.
 32. Moreno RP, Metnitz PG, Almeida E, et al. SAPS 3 – From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med*. 2005;31(10):1345-1355.
 33. Keene AR, Cullen DJ. Therapeutic Intervention Scoring System: update 1983. *Crit Care Med*. 1983;11(1):1-3.
 34. Jones AE, Trzeciak S, Kline JA. The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. *Crit Care Med*. 2009;37(5):1649-54.
 35. Medlej K. Calculated decisions: Sequential Organ Failure Assessment (SOFA) Score. *Emerg Med Pract*. 2018;20(Suppl 10):1-6.
 36. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13(10):818-29.
 37. Champion HR, Sacco WJ, Copes WS, Gann DS, Gennarelli TA, Flanagan ME. A revision of the trauma score. *J Trauma*. 1989;29(5):623-9.
 38. Lichtveld RA, Spijkers AT, Hoogendoorn JM, Panhuizen IF, van der Werken C. Triage Revised Trauma Score change between first assessment and arrival at the hospital to predict mortality. *Int J Emerg Med*. 2008;1(1):21-26.
 39. Reith FCM, Lingsma HF, Gabbe BJ, Lecky FE, Roberts I, Maas AIR. Differential effects of the Glasgow Coma Scale Score and its Components: an analysis of 54,069 patients with traumatic brain injury. *Injury*. 2017;48(9):1932-1943.
 40. Higgins TL, Teres D, Copes WS, Nathanson BH, Stark M, Kramer AA. Assessing contemporary intensive care unit outcome: An updated Mortality Probability Admission Model (MPM0-III). *Crit Care Med*. 2007;35(3):827-835.
 41. West TA, Rivara FP, Cummings P, Jurkovich GJ, Maier RV. Harborview assessment for risk of mortality: an improved measure of injury severity on the basis of ICD-9-CM. *J Trauma*. 2000;49(3):530-541.
 42. Domingues CA, Coimbra R, Poggetti RS, Nogueira LS, de Sousa RMC. New Trauma and Injury Severity Score (TRISS) adjustments for survival prediction. *World J Emerg Surg*. 2018;13(1):1-6.
 43. Champion HR, Copes WS, Sacco WJ, Lawnick MM, Bain LW, Gann DS, Gennarelli T, Mackenzie E. A new characterization of injury severity. *J Trauma*. 1990;30(5):539-45.
 44. Kim YJ. Injury severity scoring systems: a review of application to practice. *Nurs Crit Care*. 2012;17(3):138-150.
 45. Raj R, Brinck T, Skrifvars MB, et al. Validation of the revised injury severity classification score in patients with moderate-to-severe traumatic brain injury. *Injury*. 2015;46(1):86-93.
 46. Lefering R. Development and validation of the Revised injury severity classification score for severely injured patients. *Eur J Trauma Emerg Surg*. 2009;35(5):437-47.
 47. Tepas JJ 3rd, Ramenofsky MI, Mollitt DL, Gans BM, et al. The Pediatric Trauma Score as a predictor of injury severity: an objective assessment. *J Trauma*. 1988;28(4):425-9.
 48. Skaga NO, Eken T, Søvik S. Validating performance of TRISS, TARN and NORMIT survival prediction models in a Norwegian trauma population. *Acta Anaesthesiol Scand*. 2018;62(2):253-266.
 49. Trauma Audit & Research Network (TARN). The TARN Probability of Survival Model. August 2019 [Internet]. Salford: TARN; 2019 [cited 2019 Dec 19]. Available from: <https://www.tarn.ac.uk/Content.aspx?c=3515>
 50. Huber-Wagner S, Stegmaier J, Mathonia P, et al. The sequential trauma score – a new instrument for the sequential mortality prediction in major trauma. *Eur J Med Res*. 2010;15(5):185-195.
 51. Gnass I, Ritschel M, Andrich S, et al. Assessment of patient-reported outcomes after polytrauma: protocol for a systematic review. *BMJ Open*. 2018;8(3):1-4.
 52. Reske SU, Braunschweig R, Reske AW, Loose R, Wucherer M. Whole-body CT in multiple trauma patients: clinically adapted usage of differently weighted CT protocols. *RoFo*. 2018;190(12):1141-51.
 53. Frellesen C, Klein D, Tischendorf P, et al. Indication of whole body computed tomography in pediatric polytrauma patients – Diagnostic potential of the Glasgow Coma Scale, the mechanism of injury and clinical examination. *Eur J Radiol*. 2018;105:32-40.
 54. de Vries R, Reininga IHF, Pieske O, Lefering R, El Moumni M, Wendt K. Injury mechanisms, patterns and outcomes of older polytrauma patients – an analysis of the Dutch trauma registry. *PLoS One*. 2018;13(1):1-10.
 55. Stoica B, Paun S, Tanase I, Negoii I, Chiotoroiu A, Beuran M. Probability of survival scores in different trauma registries: a systematic review. *Chirurgia (Bucharest)*. 2016;111(2):115-119.
 56. Bouzat P, Legrand R, Gillois P, et al. Prediction of intra-hospital mortality after severe trauma: which pre-hospital score is the most accurate? *Injury*. 2016;47(1):14-18.
 57. Vivien B, Raux M, Riou B. Évaluation préhospitalière de la gravité des traumatisés [Pre-hospital assessment of the severity of the traumatized]. *Ann Fr Med d'urgence*. 2011;1(1):33-42. French.
 58. Grubmüller M, Kerschbaum M, Diepold E, Angerpointner K, Nerlich M, Ernstberger A. Severe thoracic trauma – still an independent predictor for death in multiple injured patients? *Scand J Trauma Resusc Emerg Med*. 2018;26(1):1-8.

59. Chico-Fernández M, Llompart-Pou JA, Sánchez-Casado M, et al. Predicción de la mortalidad a través de la metodología TRISS en el Registro Español de Trauma en UCI (RETRAUCI) [Mortality prediction using TRISS methodology in the Spanish ICU Trauma Registry (RETRAUCI)]. *Med Intensiva*. 2016;40(7):395-402. Spanish.
60. Cernea D, Novac M, Drăgoescu PO, et al. Polytrauma and Multiple Severity Scores. *Curr Heal Sci J*. 2014;40(4):244-8.
61. Török A, Bancu Ș, Neagoe R, et al. The utility of the predictive scores in polytrauma with abdomino-pelvic injuries: a series of 38 patients. *Chirurgia (Bucharest)*. 2014;109(1):44-47.
62. Xu Y, Wang R, Zhu M, et al. [Diagnostic value of dynamic-extended focused assessment with sonography for trauma in patients with multiple trauma]. *Chin Crit Care Med*. 2018 Jan;30(1):61-66. Chinese.
63. Kim SC, Kim DH, Kim TY, et al. The Revised Trauma Score plus serum albumin level improves the prediction of mortality in trauma patients. *Am J Emerg Med*. 2017;35(12):1882-6.
64. Gomez D, Sarrami P, Singh H, Balogh ZJ, Dinh M, Hsu J. External benchmarking of trauma services in New South Wales: Risk-adjusted mortality after moderate to severe injury from 2012 to 2016. *Injury*. 2019;50(1):178-185.
65. Sefrioui I, Amadini R, Mauro J, El Fallahi A, Gabbrielli M. Survival prediction of trauma patients: a study on US National Trauma Data Bank. *Eur J Trauma Emerg Surg*. 2017;43(6):805-822.
66. Palmer CS, Gabbe BJ, Cameron PA. Defining major trauma using the 2008 Abbreviated Injury Scale. *Injury*. 2016;47(1):109-115.
67. Hong ZJ, Chen CJ, Chan DC, Chen TW, Yu JC, Hsu S. Experienced trauma team leaders save the lives of multiple-trauma patients with severe head injuries. *Surg Today*. 2019;49(3):261-267.
68. Valderrama-Molina CO, Giraldo N, Constain A, et al. Validation of trauma scales: ISS, NISS, RTS and TRISS for predicting mortality in a Colombian population. *Eur J Orthop Surg Traumatol*. 2017;27(2):213-220.
69. Da Costa LGV, Carmona MJC, Malbouisson LM, et al. Independent early predictors of mortality in polytrauma patients: A prospective, observational, longitudinal study. *Clinics (Sao Paulo)*. 2017;72(8):461-468.
70. Elbaih AH, Housseini AM, Khalifa ME. Accuracy and outcome of rapid ultrasound in shock and hypotension (RUSH) in Egyptian polytrauma patients. *Chinese J Traumatol*. 2018;21(3):156-162.
71. Imen Mekki, Hamed Rym, Housseini Aouni, et al. [New Berlin definition versus injury severity score in severe trauma for mortality prediction]. In: *Urgences 2018: MCO Congress; 2018 Jun 13-15, Paris*. French
72. Dijkink S, van der Wilden GM, Krijnen P, et al. Polytrauma patients in the Netherlands and the USA: a bi-institutional comparison of processes and outcomes of care. *Injury*. 2018;49(1):104-109.
73. Laytin AD, Dicker RA, Gerdin M, et al. Comparing traditional and novel injury scoring systems in a US level-I trauma center: an opportunity for improved injury surveillance in low- and middle-income countries. *J Surg Res*. 2017;215:60-66.
74. Smith BP, Goldberg AJ, Gaughan JP, Seamon MJ. A comparison of Injury Severity Score and New Injury Severity Score after penetrating trauma: a prospective analysis. *J Trauma Acute Care Surg*. 2015;79(2):269-274.
75. Pascari V. Evaluarea intraspitalicească și unele acțiuni terapeutice urgente la pacienții cu fracturi multiple de locomotor [Interhospital evaluation of urgent therapeutic actions in patients with multiple fractures]. *Curierul Medical (Chisinau)*. 2009;(4/310):23-2. Romanian.
76. Tazlavan T. Delirul în terapia intensivă [Delirium in intensive care]. *Curierul Medical (Chisinau)*. 2009;(6/324):72-74. Romanian.
77. Cojocari V, Ciobanu G, Scurtov N. [The impact of pre-hospital arterial hypo- and hypertension on clinical severity and prognosis of patients with traumatic brain injury]. *Curierul Medical (Chisinau)*. 2013;56(3):29-33. Romanian.

Authors' ORCID iDs and academic degrees

Oleg Arnaut – <https://orcid.org/0000-0002-5483-8672>, MD, PhD.

Dan Croitoru – <https://orcid.org/0000-0002-8915-0157>, MD.

Ion Grabovschi – <https://orcid.org/0000-0002-7716-9926>, MD.

Serghei Sandru – <https://orcid.org/0000-0002-2973-9154>, MD, PhD.

Authors' contributions

OA designed the trial and interpreted the data. DC drafted the first manuscript. IG interpreted the data. SS revised the manuscript critically. All the authors approved the final version of the manuscript.

Funding

This study was supported by *Nicolae Testemitsanu* State University of Medicine and Pharmacy. The trial was authors' initiative. The authors are independent and take responsibility for the integrity of the data and accuracy of the data analysis.

Ethics approval and consent to participate

No approval was required for this review study.

Conflict of Interests

No competing interests were disclosed.