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Review article

Prediction of critical haemorrhage following trauma: A narrative review

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ABSTRACT

Introduction: Traumatic haemorrhagic shock can be difficult to diagnose. Models for predicting critical bleeding and massive transfusion have been developed to aid clinicians. The aim of this review is to outline the various available models and report on their performance and validation.

Methods: A review of the English and non-English literature in Medline, PubMed and Google Scholar was conducted from 1990 to September 2015. We combined several terms for i) haemorrhage AND ii) prediction, in the setting of iii) trauma. We included models that had at least two data points. We extracted information about the models, their developments, performance and validation.

Results: There were 36 different models identified that diagnose critical bleeding, which included a total of 36 unique variables. All models were developed retrospectively. The models performed with variable predictive abilities – the most superior with an area under the receiver operating characteristics curve of 0.985, but included detailed findings on imaging and was based on a small cohort. The most commonly included variable was systolic blood pressure, featuring in all but five models. Pattern or mechanism of injury were used by 16 models. Pathology results were used by 15 models, of which nine included base deficit and eight models included haemoglobin. Imaging was utilised in eight models. Thirteen models were known to be validated, with only one being prospectively validated.

Conclusions: Several models for predicting critical bleeding exist, however none were deemed accurate enough to dictate treatment. Potential areas of improvement identified include measures of variability in vital signs and point of care imaging and pathology testing.

Keywords: Massive transfusion, haemorrhage, shock, haemorrhagic, severity of illness index, prediction, trauma severity indices, wounds and injuries

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INTRODUCTION

Trauma is the major cause of years of life lost.[1] Haemorrhage accounts for up to 40% of these deaths,[2] and is responsible for most of the preventable deaths.[3] The treatment of traumatic haemorrhagic shock has evolved substantially,[4] a vital component being blood transfusion. Current resuscitation of haemorrhagic shock involves replacement with components of whole blood, with some patients requiring large amounts of red blood cells in a short period of time, in the practice termed massive transfusion (MT). One in four recipients of MT following trauma dies in hospital. For survivors, the long-term outcomes are also poor, with approximately half of patients having unfavourable Glasgow Outcome Scale-Extended (GOSE) at both six and 12-months (52% and 44% respectively) following injury.[5]

A key step in improving outcomes could be early diagnosis of haemorrhagic shock. However, commonly sought physiological abnormalities such as tachycardia and hypotension are often masked until treatment is futile. There is a strong recommendation based on low level evidence (i.e. Grade 1C) that "physician clinically assess the extent of traumatic haemorrhage using a combination of mechanism of injury, patient physiology, anatomical injury pattern and the patient's response to initial resuscitation".[6] In other words, diagnosis remains largely subjective, not objective. However, gestalt of trauma surgeons for predicting MT reveals low predictive values (positive predictive value (PPV) = 34.9% and negative predictive value (NPV) = 86.2%).[7]

In an attempt to more objectively and rapidly identify occult haemorrhage in the trauma patient, prediction models have been developed. In the efforts to create these models, more than 30 independent variables have been associated with MT (Table 1).[8] The aim of this review is to outline the various models for detecting critical haemorrhage, report on their performance and validation, as well as discuss the utility of the individual variables in these models in the setting of trauma.

METHODS

Search strategy

This review searched the English and non-English literature. Subject headings (/) and key words (" ") were used in the following combinations:

1. Haemorrhage (hemorrhagic shock/ OR (Shock, Hemorrhagic)/ OR hemorrhage/ OR "haemorrhag*" OR "hemorrhag*" OR blood transfusions/ OR Erythrocyte transfusion/ OR "massive transfusion" OR "critical bleeding" OR "massive blood transfusion", AND
2. Severity of illness index/ OR "prediction" OR "risk assessment" OR hemorrhage, diagnosis/ OR "trauma severity indices", AND
3. Wounds and injuries/ OR "trauma".

Eligibility criteria

Studies proposing objective methods of identifying critical bleeding through models or prediction scores were eligible for inclusion. For inclusion, a model needed to contain more than a single variable. A single variable was therefore not eligible. Articles were excluded if they i) described MT, without suggesting prediction, or ii) predicted localised bleeding e.g., intracranial haemorrhage only, or iii) predicted outcomes such as mortality, without predicting MT. We also excluded animal studies.

Table 1. Independent variables associated with massive transfusion.

Class of variable	Reported association with MT
Patient demographics	Male, age
Vital signs	SBP, DBP, HR, GCS, RR, SaO2, admission SI, pre-hospital SI, trending SI
Pathology	BE, Hg, INR, pH, Hct, lactate, PT
Mechanism/pattern of injury	ISS, unstable long bone fracture, unstable pelvic fracture, fall, traffic related injury, penetrating injury, high risk trajectory
Imaging	FAST, haemoperitoneum
Emerging technology	ROTEM, FIBTEM, PPG Waveform analysis, StO2
Others:	Scene admit, time to ED, treatment at referring hospital

GCS = Glasgow Coma Score; MT = Massive Transfusion; RR = Respiratory Rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; SaO2 = oxygen saturations; SI = shock index; BE = base excess; Hg = haemoglobin; INR = international normalised ratio; Hct = haematocrit; PT = prothrombin time; ISS = injury severity score; FAST = Focused Assessment with Sonography in Trauma; ROTEM = rotational thromboelastometry; FIBTEM = extrinsically activated test with tissue factor and the platelet inhibitor cytochalasin D; PPG = photoplethysmogram; StO2 = tissue oxygen saturation.

Information sources

We searched for articles from PubMed and Medline from 1990 to September 2015. Google and Google Scholar were used for grey literature searching. Reference lists of included papers were reviewed for additional references.

Study selection

Following the search, duplicates were removed and titles subsequently appraised for eligibility by two authors independently. The abstracts of selected titles were reviewed for relevance, and full-texts were sought for articles meeting the inclusion criteria. Reference lists of relevant articles were checked for additional studies.

Data extraction

From the included papers, we extracted data on the models' development, setting and performance. Performance was assessed by reported variables and included sensitivity, specificity, positive and negative predictive values and the area under the receiver operating characteristic curve (AUROC). The AUROC is a graph combining both sensitivity and specificity representing all available cut-offs for the suggested test.[9] Variables used for prediction of critical bleeding were divided into five different groups (i.e., demographics, vital signs, injury details, pathology, and imaging). Combinations of variables, for example the shock index (i.e., heart rate divided by systolic blood pressure) were also included. Lastly, we sought to determine whether the models had been formally validated.

RESULTS

The search yielded 32 studies containing 36 unique models (Table 2).[10–41] The models included 36 different variables (Table 3). Four models used seven or more variables, three of which were published since 2011. All models were developed retrospectively, the majority of which relied on prospectively collected data. The models have been developed since 1989 with a recent spike as seen in Figure 1.

The models performed with variable predictive abilities as shown in Table 4. Ogura et al.,[42] reported the highest AUROC of 0.985 with their Traumatic Bleeding Severity Score (TBSS).

Patient demographics

Patient demographics were included in six of the models. Yucel et al.,[41] detected that males were more likely to bleed (adjusted odds ratio 1.5). Age was included in four models. Demuro et al.,[17] researched the shock index (SI) and found that when using the ≥ 0.9 beats per minute/mm Hg cut-off, the sensitivity in the elderly population (≥ 65 years old) was 41.2%, compared to 57.5% in the younger subgroup (< 65 years old). However, this cut-off increased specificity (95.7% in the elderly v. 91.6% in the non-elderly). A cut-off of 0.8 in older patients yielded similar predictability to 0.9 in younger patients. Other models used a lower age cut-off. The Emergency Transfusion Score (ETS),[34] Mechanism, Glasgow coma scale, Age, Arterial Pressure (MGAP) score,[33] and TBSS[29] used 60 years, whilst Yuan et al.'s[40] model of traumatic brain injury used 57 years.

Vital signs

Vital signs were included in all models with the exception of two (Schreiber[35] and Yuan[40]). The most commonly included variable was systolic blood pressure (SBP), featuring in all but five models. The most common combination was the heart rate (HR) and SBP to derive the shock index (SI).[43] In the TBSS by Ogura et al.,[29] the SBP entered into the formula was after one litre of rapidly infused crystalloid fluids. Heart rate was included in 19 models. Other vital signs included different measures of perfusion and respiration, but were less frequently used and sometimes based on subjective assessment.

Injury details

Injury details (i.e., pattern and mechanism of injury) were included in 16 models. Unstable pelvic fracture was most often included, featuring in four models. Penetrating trauma was the most frequent mechanism of injury, used in five models. For the remainder, considerable differences existed between the models. Whilst most models included injury details as one of several variables in their prediction model, some studies only predicted in a particular subset of patients with a particular pattern or mechanism of injury (e.g., gunshot wound or traumatic brain injury).

Table 2. The models, their formula, development setting and definition of critical haemorrhage.

Model	Author, et al./Year	Formula	Range	Suggested cut-off	Number of components	Country	Setting	CH definition	Study sample size (n)
SI	Demuro 2013[17]	HR/SBP	Indefinite (0.5–0.7 normal range)	≥0.8	2	USA	Tertiary care facility and a regional trauma center	≥2 U PRBC within 24 hrs of admission, or requiring operation/ intervenational radiology within 24 hrs	4277
Pre-hospital SI	Vandromme 2011[36]	HR/SBP	Indefinite (0.5–0.7 normal range)	≥0.9	2	USA	Level 1 Trauma Centre	≥10 U in 24 hrs	8111
Pre-hospital SI post >1 L crystalloid	Mitra 2014[26]	HR/SBP	Indefinite (0.5–0.7 normal range)	≥1.0	2	Australia	Pre-hospital	≥5 U in 4 hrs	1419
SI 'dichotomised'	Olaussen 2014[30]	phSI AND tcSI ≥1	Indefinite (0.5–0.7 normal range)	≥1	4	Australia	Pre-hospital and Level 1 Trauma Centre	≥5 U in 4 hrs	6990
SI 'formulaic'		log Odds (MT) = 2.16*tcSI +0.89*phSI-5.42		-	4				
SI 'combination'		0.5*phSI + tcSI		≥1.32	4				
SI 'upward trending'		tcSI-phSI		≥0.17	4				
Pulse Rate Over Pressure Evaluation (ROPE)	Ardagh 2001[10]	HR/(SBP-DBP)	n/a	>3	3	NZ	Regional ED	Shock defined as SBP drop below 100 mm Hg or requiring ≥4 L of infused fluid	184
Pre-hospital index	Jones 1993[19]	SBP >100 mm Hg = 0, 86–100 mm Hg = 1, 75–85 mm Hg = 2, 0–74 mm Hg = 5; HR: ≥120 = 3, 51–119 = 0, <50 = 5; resp: normal = 0, laboured/shallow = 3, <10 breaths per min OR needs intubation = 5; consciousness: normal = 0, confused/combative = 3, no intelligent words = 5, 4 points to be added for penetrating MOI or abdominal injuries	0–24	>3 (for any transfusion)	4	USA	Trauma Registry	>3 U of blood transfused (no time frame)	217
Baker	Baker 2001[11]	SBP <90 mm Hg = 1; GCS <9 = 1; HR >120 = 1; MOI/POI: High risk injuries (trauma to the chest between the midclavicular lines, abdominal injury with diffuse tenderness, survival of a fatal vehicular crash, ejection from a vehicle, or stab or gunshot wound to the trunk) = 1	0–4	None suggested	4	USA	Level 1 Trauma Centre	Any transfusion within the first 24 hrs	654
Assessment of Blood Consumption (ABC)	Nunez 2009[28]	Penetrating MOI = 1; SBP ≤ 90 mm Hg = 1; HR ≥120 bpm = 1; positive FAST = 1	0–4	≥2	4	USA	Level 1 Trauma Centre	≥10 U in 24 hrs	596
Trauma Associated Severe Hemorrhage (TASH)	Yucel 2006[41]	Hgb criteria: <7 g/dL = 8 pts, <9 = 6 pts, <10 = 4 pts, <11 = 3 pts, <12 = 2 pts. Base deficit criteria: <−10 = 4 pts, <−6 = 3 pts, <−2 = 1 pts. SBP <100 mm Hg = 4 pts, <120 mm Hg = 1 pt; HR >120 = 2 pts; free abdominal fluid = 3 pts, extremities: (clinically unstable pelvis 6 or open or dislocated femur # = 3 pt) male = 1	0–28	≥18	7	Germany	The Trauma Registry of the German Trauma Society (DGU)	≥10 U in 24 hrs	6044
Prince of Wales Hospital (PWH)	Rainer 2011[32]	SBP ≤ 90 mm Hg = 3; GCS ≤ 8 = 1; HR ≥120 = 1; displaced pelvic fracture = 1; CT scan or FAST positive = 2; BD >5 mmol/L = 1; Hgb <7 g/dL = 10, Hgb 7–10 g/dL = 1	0–10	≥6	7	Hong Kong	A regional trauma centre	≥10 U in 24 hrs	1891

Table 2. *Continued*.

Model	Author, et al./Year	Formula	Range	Suggested cut-off	Number of components	Country	Setting	CH definition	Study sample size (n)
Schreiber score	Schreiber 2007[35]	Hgb ≤ 11 = 1; penetrating MOI = 1; INR ≥1.5 = 1	0–3	None suggested	3	Iraq	Combat hospital	≥10 U in 24 hrs	558
Cincinnati Individual Transfusion Trigger (CITT)	Callcut 2012[13]	SBP <90 mm Hg = 1, Hgb <11 = 1; INR >1.5 = 1; Base deficit ≥6 = 1; + ve FAST = 1	0–5	≥2	5	USA	Level 1 Trauma Centre	>10 U PRBCs in 6 hrs	170
Vandromme score	Vandromme 2011[37]	HR >105 = 1; SBP <110 mm Hg; Hgb ≤ 11 = 1; INR >1.5 = 1; lactate ≥5 = 1	0–5	≥3	5	USA	Level 1 Trauma Centre	≥10 U in 24 hrs	6638
Larson score	Larson 2010[20]	HR >110 = 1; SBP <110 mm Hg = 1; Hgb <11 = 1; base excess ≤ −6 = 1	0–4	≥2	4	Combat areas	Joint Theater Trauma Registry	≥10 U in 24 hrs	1124
McLaughlin score	McLaughlin 2008[24]	HR >105 = 1 or 0; SBP <110 mm Hg = 1 or 0; pH <7.25 = 1 or 0; haematocrit <32.0% = 1 or 0	0–4	None suggested	4	Combat	Joint Theater Trauma Registry	≥10 U in 24 hrs	3442
Massive Transfusion Score (MTS)	Callcut 2013[13]	INR >1.5; SBP <90 mm Hg; Hgb <11 g/dL; BD ≥6; dFAST + ve HR ≥120 bpm; penetrating MOI temperature <35.5°C	0–8	>2	8	USA	PROMMTT (10 Level 1 trauma centers)	≥10 U in 24 hrs + Haemorrhagic death	1245
Emergency Transfusion Score (ETS)	Ruchholtz 2006[34]	Age between 20–60 = 0.5; >60 yrs = 1.5; admission from scene of accident = 1; from other hospital = 0. Injury mechanism (traffic accident = 1, fall >3 m = 1; blood pressure (0–90 mm Hg = 2.5, 90–120 mm Hg = 1.5) pelvic ring disruption = 1.5, abdominal ultrasound with free fluid = 2	0–9.5	>3	6	Germany	Trauma ER	Emergency Room Transfusion (average 7.3 ± 7.6 PRBC)	1103
Blackmore	Blackmore 2006[12]	Displaced obturator ring fracture: >1 cm = 1, displaced pubic symphysis: >1 cm = 1; hematocrit <30% = 1; HR >130 bpm = 1	0–4	≥2	4	USA	Level 1 Trauma Centre	Pelvic haemorrhage volume ≥600 ml OR ≥6 U transfused	783
Torso Gunshot	Dente 2010[18]	A hierarchical algorithm: MOI: high risk (multicavitary or transpelvic) = 1, initial SBP <90 mm Hg = 1, if not, the next initial base deficit <10 = 1	-	None suggested	3	USA	Level 1 Trauma Centre	≥10 U in 24 hrs	215 MTP activations
Traumatic Bleeding Severity Score (TBSS)	Ogura 2012[29]	Age (>60 years old = 6 pts), SBP after 1 L of crystalloid (<110 mm Hg = 4pts, <100 mm Hg = 8 pts, <90 mm Hg = 12 pts), + ve FAST ([the number of regions with positive FAST] × 3 pts), severity of pelvic # (stable # = 3 pts, incomplete unstable # = 6 pts, complete unstable # = 9pts), lactate (>2.5 mmol/L = 4 pts, >5.0 mmol/L = 8 pts, >7.5 mmol/L = 12 pts)	0–57	>15	5	Japan	Single institution which cares for approximately 250 severely injured patients per year	≥10 U in 24 hrs	119 development-113 validation
Moore	Moore 2007[27]	$\text{Log}(p/(1-p)) = -0.1263 + 0.6832$ (if ISS >25) $- 1.3316$ (if treated at referring hospital) $- 0.0296 \times$ (min SBP 1st 1/2 h) $+1.2685 \times$ (max INR 1st 1/2 h)	n/a	None suggested	3	USA	7 Level 1 Trauma Centres	≥10 U in 24 hrs	383
Wade	Wade 2011[38]	$\log[\pi/(1-\pi)] = \beta 1 \times \text{SBP} + \beta 2 \times \text{HR} + \beta 3 \times \text{pH} + \beta 4 \times \text{HCT} + \beta 0$ ß1 = −0.0113, ß2 = 0.0158, ß3 = 0.0932, ß4 = −0.0395, and ß0 = 32.8738	n/a	$\pi > 0.5$	4	USA	17 Level 1 Trauma Centres	≥10 U in 24 hrs	1574
Automated prediction	Mackenzie 2014[23]	HR + photoplethysmograph + SpO2/HR features	n/a	n/a	3	USA	Level 1 Trauma Centre	>4 U in <4 hrs	556
Advanced Trauma Life Support (ATLS)	Lawton 2014[21]	Class 1 = normal vitals; no further IV fluids required; EBL <750 ml, Class 2 = HR >100 & SBP >90 mm Hg; no further IV fluids required; EBL 750–1500 ml, Class 3 = SBP <90 mm Hg; requires recurrent IV bolus; EBL 1500–2000 ml, Class 4 = SBP <90 mm Hg and/or imminent arrest; declining SBP despite recurrent IV bolus; EBL >2000 ml	n/a	n/a	4	Australia	Major Trauma Centre, Sydney	Major haemorrhage based on composite endpoints	715
Mobile Application	Mina 2013[25]	Algorithm: MOI: Gunshot/blunt/stab BD HR SBP	n/a	n/a	4	USA	Trauma Centre	10 U in 24 hrs	10900

Table 2. *Continued*.

Model	Author, et al./Year	Formula	Range	Suggested cut-off	Number of components	Country	Setting	CH definition	Study sample size (n)
Linear and non-linear pre-hospital Vital Signs	Chen 2007[16]	Various linear and non-linear combinations of: HR, RR, SaO2, SBP, DBP	n/a	n/a	5	USA	Level-I unit at the Memorial Hermann Hospital	≥1 U of red cells and an explicit haemorrhagic injury	898
Progressive hemorrhagic injury in traumatic brain injury (PHI in TBI)	Yuan 2012[40]	Age ≥57 = 5; intra-axial bleed/contusion = 4; midline shift ≥5 mm = 6; PLT count <100 × 10^9 = 10; PLT count 100–150 = 4; PT >14 sec = 4; D-dimer ≥5 mg/L = 12; glucose ≥10 mmol/L = 10	0–54	Low; intermediate; high risk	7	China	Shanghai Sixth People's Hospital	Appearance of new lesions or ≥25% increase compared to the first post-injury CT	468
West	West 1989[39]	SBP, GCS, cap refill, RR, resp quality	0–16	>14	5	USA	Level 1 Trauma Centre	>3 U of blood required. No time frame	250
Field Triage Score 07 (FTS07)	Cancio 2008[15]	p = e^k/(1 + e^k), where k = − 0.740–0.376 × FTS07–0.011 × DAP. FTS07 = [GCS total (<8) = 1, SBP <100 mm Hg = 1]	n/a	n/a	3	Combat, mainly in Iraq	Mainly level 1	>10 U of WB in 24 hrs	536
Revised Trauma Score (RTS), Diastolic Arterial Pressure, SI	Cancio 2008[15]	p = e^k/(1 + e^k), where k = 0.638–0.115 × RTS–0.011 × diastolic arterial pressure +0.358 × SI	n/a	n/a	4				
Acidosis, Blood loss, Cold, Damage (ABCD)	Ordonez 2012[31]	(A) acidosis (base deficit ≥8); (B) blood loss (hemoperitoneum ≥1,500 mL); (C) cold (temperature <35 C); (D) damage (New Injury Severity Score ≥35)	n/a	n/a	4	USA	Regional Level 1 Trauma Centre Gunshot victims	DCR	331
MGAP (Mechanism, Glasgow coma scale, Age, arterial Pressure)	Raux 2011[33]	MGAP score: Glasgow Coma Scale (from 3–15 points), blunt trauma (4 points), systolic arterial blood pressure (>120 mm Hg: 5 points, 60 to 120 mm Hg: 3 points), and age <60 yrs (5 points)	n/a	n/a	4	France	Prehospital	6 U PRBC or death or both from haemorrhagic shock	2363
APPRAISE (Automated Processing of the Physiological Registry for Assessment of Injury Severity)	Liu 2015[22]	Computational real-time algorithms of: heart rate (HR), respiratory rate (RR), oscillometric SBP, and pulse pressure ([PP])	n/a	n/a	4	USA	HEMS to Level 1 Trauma Centre	≥9 U in 24 hrs	209

CH = Critical Haemorrhage; DCR = Damage Control Resuscitation; U = units; WB = whole blood; PRBC = Packed Red Blood Cells; HEMS = Helicopter Emergency Medical Service.
Suggested cut-off is that which the study used to predict critical haemorrhage. Number of components relates to how many different components the prediction models contain. Formula is the actual prediction rule.

Table 3. The models and their included variables.

	SI	ROPE	Pre-hospital Index	Baker	ABC	TASH	PWH	Schreiber	CITT	Vandromme	Larson score	McLaughlin	MTS	ETS	Blackmore	Torson Gunshot	TBSS	Moore	Wade	Automated prediction	ATLS	Mobile Application	Linear and non-linear pre-hospital VSS	PHI in TBI	West	FTS07	ABCD	MGAP	RTS, DAP, SI	APPRAISE
Demographics																														
Age														✓			✓							✓				✓		
Gender						✓																								
Admission (from scene or hospital)														✓				✓												
Vital signs																														
SBP	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓	✓	✓		✓	✓		✓	✓	✓
HR	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓		✓				✓	✓	✓	✓	✓						✓	✓
GCS				✓			✓																		✓	✓		✓	✓	
Diastolic Arterial Pressure																													✓	
DBP		✓																					✓							✓
RR			✓																				✓		✓*				✓	✓
Oxygen Saturations																				✓			✓							
Cap refill																									✓					
Temperature													✓														✓			
Pattern of injury																														
Clinically unstable/ displaced pelvis						✓	✓							✓			✓													
Stable pelvic #																	✓													
Displaced obturator ring #															✓															
Displaced pubic symphysis															✓															
Transpelvic/multicavitary																✓														
Abdominal injuries			✓	✓																										
Chest trauma between MC lines				✓																										
Chest decompression																														
Open or dislocated femur #						✓																								
Injury Severity Score																		✓									✓	(NISS)		
Response to initial fluid bolus																					✓									
Estimated blood loss																					✓						✓			
Mechanism of injury																														
Penetrating			✓		✓			✓					✓									✓								
Blunt																												✓		
Traffic accident														✓																
Survival of a fatal vehicular crash				✓																										
Ejection from a vehicle				✓																										
Fall from > 3 meters														✓																
Stab or gunshot to the chest				✓												✓						✓								
Pathology																														
Hameoglobin						✓	✓	✓	✓	✓	✓		✓																	
Base deficity						✓	✓		✓		✓		✓			✓						✓					✓			
INR								✓	✓	✓			✓					✓												
pH												✓							✓											
Haematocrit												✓			✓				✓											
Lactate										✓							✓													
Imaging																														
+ ve FAST					✓	✓	✓		✓				✓	✓			✓													
PPG																				✓										
CT scan							✓																							

*includes details on respiratory quality.
Abbreviations in the top row relate to the models and is defined in Table 2; DBP = Diastolic Blood Pressure; RR = Respiratory Rate; # = fracture; INR = International Normalized Ratio; NISS = New Injury Severity Score; FAST = Focused Assessment with Sonography in Trauma; PPG = photoplethysmogram.

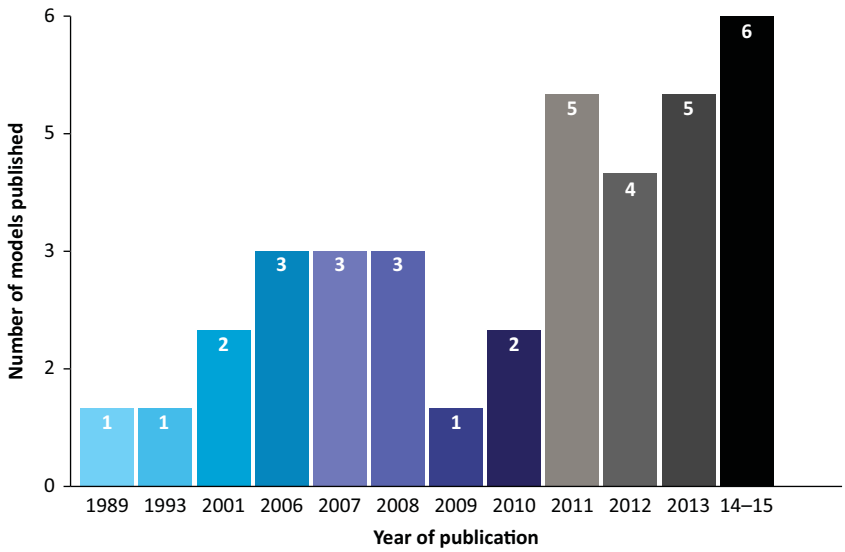

Figure 1. The number of models published in any given year.

Pathology

Pathology results were included in 15 models with nine models including base deficit, eight models haemoglobin, and six models INR. Haematocrit was included in three models, while pH and lactate were included in two models.

Imaging

Imaging was included in eight models, seven of which included a positive FAST (Focused Assessment with Sonography in Trauma) with varying weighting, ranging from a binary finding (i.e., positive/negative) to the number of regions positive.

Validation

Formal validation efforts have been mainly undertaken retrospectively and often during the development of new models. Thirteen of the models have been validated, including four that were only validated internally at the time of development (Table 5). The Trauma Associated Severe Hemorrhage (TASH) score[41] has been validated six times, including during the development, and five years later in the same population with a different cohort, to update their coefficients. The Assessment of Blood Consumption (ABC)[28] has been validated five times. Only the ETS has been prospectively validated.[44] With a cut-off of ≥3, the sensitivity and specificity were 97.5% and 68%, respectively. Although this had good NPV of 0.997, the PPV of 0.222 provides minimal clinical utility. The chosen cut-off to validate differed among the validation studies (e.g., the TASH has been validated for ≥8, ≥8.5, ≥18, and for 80% MT probability).

DISCUSSION

Numerous prediction models have been developed towards the goal of early identification of the potential need for MT and critical bleeding in trauma patients. Although the number of models has gradually increased over time, a spike has been noticed since 2010, with 19 models published since 2011. This may have been triggered by the work of Guly et al.,[45] which retrospectively validated the Advanced Trauma Life Support (ATLS)[21] guidelines and concluded that the traditionally taught values for abnormality for grading haemorrhagic shock were overstated. In addition to the available evidence, it has also been suggested that several of the prediction models struggle to survive,[46] and never make it to publication.[47] The reasoning behind this may be their lack of utility beyond the institutions that developed them.[48] Moreover, lack of external and prospective validation may threaten the survival of the models.

Inclusion of age was commonly observed and may be subject to bias when included retrospectively, since some clinicians regard blood transfusion in the elderly as futile,[49] and may not resuscitate as

Table 4. The predictive value of the various models.

Model	Author, et al.	Sensitivity %	Specificity %	Area under the receiver operating characteristic curve
Shock Index (SI)	Demuro[17]	76.1	87.4	NR
Pre-hospital SI	Vandromme[36]	Not provided. Just mean pRBC for several SI cut-off compared to normal SI (0.5–0.7). SI >0.9–1.1 RR = 1.61 (1.13–2.31) SI >1.1–1.3 RR = 5.57 (3.74–8.30) SI >1.3 RR = 8.13 (4.60–14.36)		NR
Pre-hospital SI post >1 L crystalloid	Mitra[26]	47.9	90.5	NR
SI 'dichotomised'	Olaussen[30]	37.6	96	NR
SI 'formulaic'	Olaussen[30]	NR	NR	0.83
SI 'combination'	Olaussen[30]	72.4	83.5	0.83
SI 'upward trending'	Olaussen[30]	74.8	72.2	0.79
Pulse Rate Over Pressure Evaluation (ROPE)	Ardagh[10]	26	95	NR
Pre-hospital index	Jones[19]	94.4 [calculated based on available data]	71.2 [calculated based on available data]	NR
Baker	Baker[11]	NR	NR	NR
Assessment of Blood Consumption (ABC)	Nunez[28]	75	86	0.842
Trauma Associated Severe Hemorrhage (TASH)	Yucel[41]	NR	NR	0.892–0.887 (in development and validation setting of the original cohort)
Prince of Wales Hospital (PWH)	Rainer[32]	31.5	99.7	0.889
Schreiber score	Schreiber[34]	NR	NR	0.804
Cincinnati Individual Transfusion Trigger (CITT)	Callcut[13]	NR	NR	0.83
Vandromme score	Vandromme[37]	53.4	97.6	0,90%
Larson score	Larson[20]	69	65	NR
McLaughlin score	McLaughlin[24]	59.4	77.4	0.839 - but 0.747 in their validation group
Massive Transfusion Score (MTS)	Callcut[14]	85	41	0.69
Emergency Transfusion Score (ETS)	Ruchholtz[34]	-	-	-
Blackmore	Blackmore[12]	75	83	0.85
Torso Gunshot	Dente[18]	NR	NR	NR
Traumatic Bleeding Severity Score (TBSS)	Ogura[29]	97.4	96.2	0.985
Moore	Moore[3]	NR	NR	0.78
Wade	Wade[38]	87	53	-

Table 4. *Continued.*

Model	Author, et al.	Sensitivity %	Specificity %	Area under the receiver operating characteristic curve
Automated prediction	Mackenzie[23]	-	-	92% overall, based on 94% in training set and 65% in test
Advanced Trauma Life Support (ATLS)	Lawton[21]	84	83	0.86
Mobile Application	Mina[25]	-	-	0.96
Linear and non-linear pre-hospital Vital signs	Chen[16]	-	-	-
Progressive hemorrhagic injury in traumatic brain injury (PHI in TBI)	Yuan[40]	56.5	92.3	0.862
West	West[39]	91.67	78.04	NR
Field Triage Score 07 (FTS07)	Cancio[15]	NR	NR	0.618
Acidosis, Blood loss, Cold, Damage (ABCD)	Ordonez[31]	-	-	0.8745
MGAP (Mechanism, Glasgow coma scale, Age, arterial Pressure)	Raux[33]	NR	NR	0.70
Revised Trauma Score (RTS), Diastolic Arterial Pressure, SI	Cancio[15]	NR	NR	0.638
APPRAISE (Automated Processing of the Physiological Registry for Assessment of Injury Severity)	Liu[22]	76	87, for detecting 0 units of blood in 24 hrs	NR

NR = Not reported.

Table 5. Validation of the prediction models.

Model	Validation Setting	Cut-off used	Validation sensitivity	Validation specificity	Validation ROC
Assessment of Blood Consumption (ABC)	1,018 patients from 3 US Trauma Centres, retrospective[67]	≥2	75.6–90.0%	67.3–87.6%	0.83–0.90
	373 patients in rural US level 1 Trauma Centre, retrospective[59]	≥2	89%	85%	0.86
	1,234 patients from The Alfred Trauma Centre, retrospective[68]	≥2	45.6%	94.2%	0.78
	113 patients from single institution, Japan, retrospective[29]	≥1	79.0%	78.2%	0.813
	5,147 patients from the German Trauma Register DGU database, retrospective[69]	≥0.5	76.1%	70.3%	0.76
Trauma Associated Severe Hemorrhage (TASH)	Same population. Reduction in MT rates (Yucel et al.[41])	NA	45%	97%	0.905 (0.892–0.918)
	Internal re-validation and coefficient update (Maegele et al.[70])	NA	31%	98%	0.905 (0.892–0.918)
	373 patients in rural US level 1 Trauma Centre, retrospective[59]	Using 80% probability	2.6%	99.7%	0.51
	1,234 patients from The Alfred Trauma Centre, retrospective[68]	≥18	25.1%	99.8%	0.90
	113 patients from single institution, Japan, retrospective[29]	≥8	81.6%	78.2%	0.89
	5,147 patients from the German Trauma Register DGU database, retrospective[69]	≥8.5	84.4%	78.4%	0.89
Prince of Wales Hospital (PWH)	1,234 patients from The Alfred Trauma Centre, retrospective[68]	≥6	36.9%	97.1%	0.84
	5,147 patients from the German Trauma Register DGU database, retrospective[69]	≥2.5	80.6%	77.7%	0.86
Schreiber score	5,147 patients from the German Trauma Register DGU database, retrospective[69]	≥0.5	85.8%	61.7%	0.80
Vandromme score	Internal validation	NA	61.3%	96.0%	0.90
	5,147 patients from the German Trauma Register DGU database, retrospective[69]	≥1.5	78.9%	76.2%	0.84
Larson score	5,147 patients from the German Trauma Register DGU database, retrospective[69]	≥1.5	70.9%	80.4%	0.82
McLaughlin score	Internal validation	NA	59.4%	77.4%	0.747
	373 patients in rural US level 1 Trauma Centre, retrospective[59]	NA	15.8%	98%	0.56
Emergency Transfusion Score (ETS)	481 patients from University Hospital, Essen, Germany, retrospective[44]	≥3	97.5%	68%	NA
Traumatic Bleeding Severity Score (TBSS)	Internal validation	NA	97.4	96.2	0.985
Advanced Trauma Life Support (ATLS)	715 patients trauma cohort, Australia, prospective[21]	NA	84%	83%	0.86
Progressive Hemorrhagic Injury in Traumatic Brain Injury	Internal validation	NA	NA	NA	0.862 (0.776–0.949)
MGAP (Mechanism, Glasgow coma scale, Age, arterial Pressure)	2,363 patients US, retrospective[33]	NA	NA	NA	0.70
Revised Trauma Score (RTS)	2,363 patients US, retrospective[33]	NA	NA	NA	0.72

NA = Not available.

aggressively as in the younger population. Although MT in the setting of trauma in patients aged ≥65 years is infrequent, high rates (60%) of survival to hospital discharge are still observed.[50] Interestingly, the accurate TBSS[29] was developed on a relatively older cohort (mean age 57.6) compared to the TASH[41] (mean age 39.2) and the ABC[28] (mean age 40).

Limitations of traditional vital signs have long been known.[51] Pacagnella et al.'s[52] recent systematic review showed that HR and SBP are only associated with bleeding (when using heterogeneous definitions) in 91% and 74%, respectively. When dichotomising SBP as occurred in nine models,[11,13,14,18,20,21,28,32,37] variable cut-offs used to define hypotension further limit the utility of blood pressure ranging from 90 to 110 mm Hg. Moreover, hypotension is a late marker of shock[53] and in certain populations such as paediatric trauma, hypotension without volume-loosing injury or normally low blood pressure may be present.[54] It is reasonable to suggest that a change in a patient's blood pressure from their normal, pre-injury measure is a better metric of haemorrhage than the absolute value. Therefore, knowledge of the patient's pre-existing conditions and access to their latest readings become essential, but such a change was not considered in any current model.

There were 19 models that used tachycardia as predictive of MT, but similar concerns exist with the variability of the pulse rate with up to 30% of hypotensive trauma patients having relative bradycardia.[55] In a subset of patients (Injury Severity Score (ISS) ≥16, chest Abbreviated Injury Scale (AIS) score ≥3, abdominal AIS ≥3), relative bradycardia had a significantly lower adjusted mortality rate.[55] In addition, the relationship between heart rate and mortality is clearly not linear. For instance, patients with head injury may suffer from Cushing's response (i.e., bradycardia) and are more likely to die given their head injury. The multiple correlations and potential bidirectional relationship between HR and mortality requires careful adjustment. In prediction of 30-day mortality, a recent large retrospective review demonstrates how pre-existing hypertension, age and use of beta or calcium-channel-blockers weakens the association between the SI and mortality.[56]

Injury characteristics are prone to bias from diagnostic mechanisms and most patients with blunt trauma present with injuries to concurrent body regions. Models specific for defined populations such as liver injury,[57] pelvic fractures,[12,58] traumatic brain injury,[40] or gunshot wounds to the torso,[18] or to the abdomen,[31] have also been developed. Unfortunately, results from these studies have not yielded more promising predictive powers, with AUROCs ranging from 0.85–0.87 (0.85,[12] 0.86,[40] 0.87[31]). Geographic differences in injury characteristics may account for such observations.[59]

Pathology results have traditionally been regarded highly. In light of the growing desire and need for pre-hospital identification and notification,[26,30] avoiding reliance on pathology results has been used as an argument to facilitate both early and automated prediction.[23] On the contrary, technological advances have resulted in focus on early and accurate point of care testing, which also can be deployed pre-hospital. Many models considered in-hospital pathology tests,[12–14,16,18,20,24,27,29,32,35,37,38,41] but perhaps evaluation of pre-hospital point of care testing would be more appropriate to include in prediction models for MT.

Imaging in prediction of critical bleeding can only be useful if available early. The role of the FAST has been researched extensively following Rozycki et al.'s[60] landmark study in 1995. Although Verbeek et al.,[61] have suggested the obvious correlation between free fluid volume and the need for operative intervention, when Charbit et al.,[62] quantified the amount of haemoperitoneum, only a large size: not small or moderate, was associated with MT (OR 6.4, 95% CI 2.9–14). One model considered computed tomography (CT),[32] but poor levels of sensitivity for detecting internal haemorrhage in torso trauma have been reported (sensitivity = 75%), and in addition to the obvious time delays, perhaps not a useful variable for early prediction.[63]

External validation is required before adoption of any model. For instance, the most frequently cited model, the TASH score,[41] was developed on an original population of 17,200 patients. Only 35% of this population had complete data on which the model was developed. The major missing variable was base excess levels. Although no comparison between the groups was offered, it is plausible that patients who had base excess measured were sicker when compared to patients without base excess measurements; simply because the clinician is unlikely to order such tests in stable and well patients.

Predictive models of critical bleeding appear limited by selection bias. For instance, models have been developed and validated on data from the Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) study.[13] However, to be included on PROMMTT, patients must have received at least one unit of blood during their hospital stay. This limits clinical utility as detection of haemorrhage should ideally occur before the patient has received one unit, so as to enable adequate time for

planning. Similarly, McKenzie et al.,[23] only included patients with a pre-hospital SI > 0.62. Furthermore, there is often exclusion of the sickest patients. Vandromme et al.,[36] and Ardagh et al.,[10] excluded patients with a pre-hospital SBP ≤ 90 mm Hg, and ≤ 100 mm Hg respectively. This may have occurred due to the notion that these patients are obviously haemorrhaging, and as such, do not need a prediction model. However, that is not always the case, and unnecessarily lowers the predictive values.

Optimal models must trade accuracy with simplicity. Simple models are of greater benefit in resource-poor environments, can be readily calculated, can function as triage and/or stratifying tools and can be incorporated into guidelines in hospitals with limited expertise in receiving injured patients. Complex and accurate scores may be useful for resource benchmarking but become cumbersome when applied clinically. In future, combining simplicity with accuracy can be achieved by the use of technology for instance in the MT model by Mina et al.,[25] who used a mobile phone application which achieved 96% accuracy (AUROC = 0.96).

This review must be viewed in light of its limitations. The search may have missed some studies, but our wide search was aimed at reducing the likelihood of such. We relied on information from the studies, which were of varying quality. We did not search in-depth for validation studies, but are confident that relevant studies would emerge from our research strategy. Due to the heterogeneity amongst the studies, we were unable to compare the coefficients in the models. Among the reasons for the heterogeneity is the variable definition of MT. In addition, the commonest used definition of MT of 10 or more units in 24 hours excludes patients that die early prior to receiving 10 units of red blood cells and those that receive definitive management prior to receiving 10 units.[64] Using a more acute definition or latent-class modelling may improve incorporation of such patients and therefore performance of models.[65,66]

CONCLUSION

At the time of study, there were 36 models for predicting massive transfusion in trauma, but these are limited by being time-consuming, resource-intensive and scarcely sufficiently validated. Thirteen models have been validated (one prospectively), and consistently perform with modest predictive powers. Performance of these models was too poor to mandate treatment, or involved variables that are only available in an advanced period of resuscitation.

Competing interests

No competing interests.

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