Raccomandazioni 25-26 della Linea Guida per la gestione integrata del trauma maggiore dalla scena dell'evento alla cura definitiva

Questo documento rappresenta la versione finale delle raccomandazioni cliniche che hanno completato l'intero processo previsto dal Manuale metodologico per la produzione di linee guida dell'Istituto Superiore di Sanità, inclusa la consultazione pubblica e la revisione esterna indipendente.

Il documento finale della presente Linea Guida sarà pubblicato quando il processo di elaborazione di tutte le raccomandazioni relative ai quesiti clinici sarà ultimato.

Febbraio 2022

INDICE

Lista delle raccomandazioni formulate

Quesito 13: Qual è lo strumento più accurato per predire il rischio di sanguinamento critico e la necessità di trasfusioni massive in pazienti con trauma maggiore (pre-ospedaliero e ospedaliero)?

Raccomandazione 25. Per individuare in fase pre-ospedaliera i pazienti con emorragia critica conseguente a trauma, si suggerisce l'utilizzo dello Shock Index per l'interpretazione dei dati clinici e l'ABC score in caso di disponibilità dell'ecografia extended-fast, considerando in entrambi i casi l'andamento evolutivo degli indici. [Raccomandazione condizionata, qualità delle prove moderata].

Raccomandazione 26. Per individuare dopo l'accettazione in ospedale i pazienti con emorragia critica conseguente a trauma, si suggerisce l'utilizzo del TASH score. [Raccomandazione condizionata, qualità delle prove moderata].

Il panel di esperti ha formulato le due raccomandazioni seguendo un processo metodologicamente rigoroso che, in conformità a quanto previsto dal Manuale metodologico dell'ISS, ha utilizzato il GRADE Evidence to Decision (EtD) framework per procedere in modo strutturato e trasparente dalle prove alla raccomandazione.

La valutazione degli interessi dichiarati dai membri del panel non ha rilevato nessun potenziale o rilevante conflitto di interesse rispetto alla tematica oggetto del quesito clinico.

Di seguito si riportano l'**EtD framework** e le appendici per le raccomandazioni 25 e 26:

- Appendice A – Quesito clinico e Strategia di ricerca
- Appendice B – Caratteristiche degli studi inclusi ed elenco degli studi esclusi con motivazione
- Appendici C – Sintesi delle evidenze: popolazione adulta
- Appendici C – Sintesi delle evidenze: popolazione pediatrica
- Appendice D – Valutazione della qualità metodologica degli studi inclusi
- Appendice E – Tabelle delle evidenze: popolazione adulta
- Appendice E – Tabelle delle evidenze: popolazione pediatrica
- Appendice F – Bibliografia degli studi inclusi
- Appendice G – Metodi e criteri per la valutazione delle evidenze
- Appendice H – Costi e valutazioni economiche.

Per i dettagli su: Gruppo di sviluppo della LG, Policy per la gestione del Conflitto di Interesse (CdI), Scope e Metodologia fare riferimento al documento **LGTM_Racc1_4_def** scaricabile dal link: https://www.iss.it/documents/20126/8404212/LGTM_Racc1_4_def.

EtD framework – Quesito clinico n.13: Strumenti per predire l'emorragia critica

Qual è lo strumento più accurato per predire il rischio di sanguinamento critico e la necessità di trasfusioni massive in pazienti con trauma maggiore (pre-ospedaliero e ospedaliero)?	
POPOLAZIONE:	Bambini, giovani e adulti che hanno subito un trauma. Esclusi: Persone con un trauma maggiore derivante da ustioni.
TEST INDICE:	Pre-ospedaliero e ospedaliero: *Clinical risk scores* (esempi) ABC score TASH score PWH score McLaughlin score Emergency Transfusion Score (ETS) Shock Index Classificazione dello Shock (protocolli *Advanced Trauma Life Support*-ATLS) …
FINALITÀ DEL TEST:	Identificare la modalità ottimale per predire un sanguinamento critico in pazienti con trauma maggiore (pre-ospedaliero e ospedaliero). Prevedere un'emorragia grave in fase precoce attraverso un test diagnostico è fondamentale in quanto consente di preparare i componenti ematici da utilizzare eventualmente in seguito. Sebbene i trattamenti non possano essere somministrati in modo proattivo in risposta a un rischio maggiore, tuttavia, saranno prontamente disponibili al bisogno.
RUOLO DEL TEST:	Supportare i professionisti sanitari nello screening pre-ospedaliero e ospedaliero dei soggetti con trauma maggiore.
STANDARD DI RIFERIMENTO:	Necessità di trasfusione massiva diagnosticata sulla base di adeguati esami ematochimici o dei segni clinici.
ESITI ATTESI:	Accuratezza diagnostica. Esiti relativi a undertriage od overtriage.
SETTING:	Pre-ospedaliero e ospedaliero.
PROSPETTIVA:	Popolazione, SSN: • organizzazione ed erogazione dei servizi per la gestione dei pazienti con trauma; • rete regionale per il trauma; • personale sanitario dei servizi di emergenza territoriale.
SOTTOGRUPPI:	Trattamenti adottati per controllare il sanguinamento critico PRIMA della diagnosi di sanguinamento critico (cioè di test o segni clinici che indichino la necessità di una trasfusione).
CONFLITTI DI INTERESSE	La policy ISS relativa alla dichiarazione e gestione del conflitto di interessi è stata applicata e non è stato identificato nessun interesse rilevante o potenzialmente rilevante. Tutti i membri del panel presenti alla riunione hanno votato, determinando la direzione e forza della raccomandazione.

Problema Il problema è una priorità?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ No ○ Probabilmente no ○ Probabilmente si ● **Si** ○ Varia ○ Non so	Sono stati proposti numerosi sistemi di scoring pre- e intraospedaliero per attivare protocolli di trasfusione massiva (MTP); tuttavia, ad oggi, i sistemi di scoring pre-ospedaliero non sono stati validati con dati significativi. Molti centri trauma non dispongono di sangue o plasma pre-scongelato in sala di emergenza, con conseguenti ritardi nella trasfusione bilanciata. L'obiettivo è valutare in sede pre-ospedaliera l'entità del danno e i parametri fisiologici per individuare un sistema di scoring pre-ospedaliero predittivo della necessità di trasfusioni massive (MT) prima dell'arrivo del paziente (Kovar, Carmichael et al. 2019).	In Italia, la disponibilità immediata di emazie concentrate, fibrinogeno e acido tranexamico nei Pronto Soccorso non è quantificabile con esattezza e non è ubiquitaria.
Accuratezza del test Quanto è accurato il test?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Molto inaccurato ○ Inaccurato ○ Accurato ○ Molto accurato ● **Variabile** ○ Non so	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline e Cochrane Library (**Appendice A**). Sono stati identificati 80 records, di cui 5 revisioni sistematiche, 66 studi primari e 9 studi derivanti dal NICE. Considerando anche le referenze degli studi primari inclusi nelle 4 revisioni sistematiche e rispondenti ai criteri di inclusione abbiamo identificato: • **12 studi per popolazione pediatrica:** 1 revisione sistematica (2 studi primari), 10 studi primari • **89 studi primari per la popolazione adulta**: 3 revisioni sistematiche (37 studi primari), 50 studi primari **Appendice F** raccoglie le referenze degli studi inclusi. **Appendice C** fornisce il flow diagram e tutte le analisi. **Appendice C** –Studi adulti: Per gli studi sugli Adulti, sono stati identificati 24 strumenti validati e 28 non validati (indipendentemente dalle soglie) per **coagulopatia indotta da trauma (TIC)** o **trasfusione massiva (MT).** **Appendice C** –Studi pediatrici: Per gli studi pediatrici, sono stati identificati 3 strumenti validati e 5 non validati (indipendentemente dalle soglie) per **coagulopatia indotta da trauma (TIC)** o **trasfusione massiva (MT)**. Tutti gli studi primari sono osservazionali retrospettivi/ prospettici e **non ci sono studi randomizzati controllati**. Perciò non è stato possibile confrontare tutti gli strumenti ma è stato possibile soltanto analizzare ogni singolo strumento. Ad ogni modo l'eterogeneità degli strumenti e della soglia di implementazione per lo stesso strumento limita la generalizzabilità dell'accuratezza diagnostica riportata.	

Effetti desiderabili

Quanto considerevoli sono gli effetti desiderabili attesi?

GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Irrilevanti ○ Piccoli ● **Moderati** ○ Grandi ○ Variano ○ Non so	La scarsa sensibilità indica che le persone con emorragia potenzialmente grave non vengono diagnosticate e, quindi, trattate. Al contrario, una bassa specificità, che porta a diagnosi positive errate, identifica trattamenti non necessari (trasfusioni di sangue).	I benefici attesi scontano la imperfetta sensibilità e specificità dei test e la possibilità di disporre comunque, eventualmente, di risorse trasfusionali tempestive (emazie concentrate, fibrinogeno e acido tranexamico) indipendentemente dal test predittivo utilizzato.

Effetti indesiderabili

Quanto considerevoli sono gli effetti indesiderabili attesi?

GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Grandi ● **Moderati** ○ Piccoli ○ Irrilevanti ○ Variano ○ Non so	Inappropriato uso o preparazione di risorse scarse e critiche (segnatamente la preparazione di emocomponenti che restano inutilizzati, ad es plasma scongelato inutilmente) per effetto dei falsi positivi segnalati dal test predittivo prescelto.	

Qualità delle prove relative all'accuratezza diagnostica

Qual è la qualità complessiva delle prove relative all'accuratezza diagnostica?

GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Molto bassa ○ Bassa ● **Moderata** ○ Alta ○ Nessuno studio incluso	La valutazione del Risk of Bias degli studi **(Appendice D**) e la valutazione di alcuni determinanti dell'accuratezza diagnostica (**Appendice C**), necessari per la valutazione della certezza dell'evidenza sono sintetizzati nelle relative Summary of Findings con giudizio GRADE in **Appendice E**-Studi Adulti e Studi Pediatrici**.** Qui sotto si riporta un estratto della sintesi (prove che variano da molto bassa a moderata certezza delle evidenze). **Tabella dei tools utilizzati nella popolazione adulti**	Si ritiene indispensabile la disponibilità di un'ecografia Extended FAST nel Pronto Soccorso di qualsiasi ospedale che accoglie il trauma maggiore. L'E-FAST è, infatti, utilizzata in tutti gli score ospedalieri per predire un'emorragia critica. Per quanto riguarda il **setting pre ospedaliero** si ritiene preferibile lo **shock index,** in quanto di semplice calcolo e ampiamente validato. Un valore >1 è associato a emorragia critica in oltre l'80% dei casi. Un incremento progressivo dello

Index test	Threshold		Sensibilità	Specificità	Qualità evidenza - SE	Qualità evidenza - SP
Validated scores requiring clinical assessment, laboratory values, and ultrasound assessments						
Prince of Wales/Rainer	cut off ≥6	MT	0.03 - 0.37	0.97 - 0.99	VERY LOW	LOW
Prince of Wales/Rainer	cut off ≥ 2.5	MT	0.81	0.78	MODERATE	MODERATE
Prince of Wales/Rainer	cut off > 2	MT	0.68 - 0.80	0.52 - 0.80	LOW	VERY LOW
Prince of Wales/Rainer	cut off >1.5	MT	0.94	0.59	LOW	VERY LOW
TASH score (SBP [≤100 MM Hg = 4, < 120 = 1], HR ≥ 120 bpm =2, FAST +ve = 3, Hb [<7=8, <9=6, <10=4, <11=3, <12=2], Base excess [<-10=4, <-6=3, <-2=1], clinically instable pelvioc fracture =3, open/dislocated femur fracture, Male =1						
TASH score	not specified	MT	0.03 - 0.45	0.97-1	VERY LOW	LOW
TASH score	cut off >6	MT	0.55 - 0.80	0.76 - 0.80	VERY LOW	MODERATE
TASH score	cut off ≥6.5	MT	0.94	0.63	LOW	VERY LOW
TASH score	cut off >7	MT	0.87	0.84	LOW	MODERATE
TASH score	cut off ≥ 8	MT	0.68 - 0.82	0.79 - 0.82	LOW	MODERATE
TASH score	cut off ≥ 16	MT	0.13 - 0.26	0.99 - 1	VERY LOW	LOW
TASH score	cut off ≥10	MT	0.87	0.86	LOW	MODERATE
TASH score	cut off ≥18	MT	0.25	1	LOW	MODERATE
TASH score	cut off ≥8.5	MT	0.84	0.78	MODERATE	MODERATE
TASH score	cut off >5	MT	0.77	0.77	VERY LOW	LOW
MTS (massive tranfsusion score) (SBp <90, Hb <11, INR > 1.5, Base deficiti ≥6, Positive FAST, penetrating mechanism)	cut off ≥ 2	MT			NA	NA
TBSS						
TBSS	cut off ≥10	MT	0.96	0.70	MODERATE	LOW
TBSS	cut off ≥17	MT	0.80	0.98	VERY LOW	LOW
TBSS	cut off ≥14	MT	0.93	0.93	LOW	MODERATE
Milano score (max score 9 points)	Cornero et al.	MT	0.04	1	LOW	MODERATE

shock index aumenta la specificità del test. In caso di disponibilità di E-FAST nel pre-ospedaliero è suggerito l'utilizzo di **ABC score (con un cut-off di 1).** Tali considerazioni derivano dalla moderata qualità delle prove in termini di specificità e dal sample size che ha generato le stime.

Il **TASH** è lo score suggerito a livello ospedaliero in quanto è quello più validato in letteratura con una specificità per lo più moderata: un valore di 16 è associato ad oltre il 60% di pazienti che subiscono un'emorragia critica.

In età pediatrica **non c'è un sufficiente numero di studi per indicare con certezza un test preospedaliero.** Lo Shock index, qualora prescelto, va utilizzato con valori soglia variabili per le fasce di età (SIPA, Shock Index Pediatric Adjusted)

Index test	Threshold		Sensibilità	Specificità	Qualità evidenza - SE	Qualità evidenza - SP
Validated scores requiring clinical assessment and laboratory values						
Larson score Any 2 or more of the following: Hemoglobin <11 g/dL, SBP < 110 mm Hg, HR > 110 bpm, Base Deficit ≤6 mmol/L						
Larson score	cut off = 1.5	MT	0.71 - 0.77	0.77 - 0.80	MODERATE	MODERATE
Larson score	cut off > 1	MT	0.55	0.79	MODERATE	MODERATE
McLaughlin score		MT	0.16	0.98	VERY LOW	LOW
Schreiber score (Hb ≤ 11, International normalized ratio > 1.5, penetrating trauma)						
Schreiber score	cut off ≥ 0.5	MT	0.86	0.62	MODERATE	MODERATE
Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)						
Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)	cut off ≥ 3	MT	-	-	NA	NA
Vandromme score	cut off ≥ 1.5	MT	0.79	0.76	MODERATE	MODERATE
Cincinnati individual tansfusion trigget (CITT) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C) 6 hours)						
revised MTS (massive transfusion score) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C)	cut off ≥ 2	MT	-	-	NA	NA
MTS (massive tranfsusion score 6 hours) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6)	cut off ≥ 1	MT	-	-	NA	NA
Prediction scoring scheme (0-8 points) - type of trauma, injury severity score, heart rate, hemoglobin, prothrombin time, fibrinogen, and base excess						
Prediction scoring scheme	cut off = 4 points	MT	0.80	0.90	VERY LOW	VERY LOW

Index test	Threshold		Sensibilità	Specificità	Qualità evidenza - SE	Qualità evidenza - SP
Validated scores requiring clinical assessment and ultrasound assessment						

ABC score (Penetrating mechanism (0 = no, 1 = yes), ED SBP of 90 mm Hg or less (0 = no, 1 = yes), ED HR of 120 bpm or greater (0 = no, 1 = yes), Positive FAST (0 = no, 1 = yes)						
ABC score	cut off ≥ 0.5	MT	0.76 - 0.79	0.43 - 0.70	MODERATE	VERY LOW
ABC score	cuf off ≥ 2	MT	0.33 - 0.89	0.68 - 0.98	VERY LOW	VERY LOW
ABC score	cut off >1	MT	0.47 - 0.79	0.78 - 0.83	VERY LOW	MODERATE
ABC score	cut off >0	MT	0.60	0.74	VERY LOW	MODERATE
ETS score						
ETS score	cut off ≥ 3	MT	0.97-0.98	0.14-0.68	MODERATE	VERY LOW
ETS score	cut off ≥ 2.5	MT	0.80	0.53	VERY LOW	MODERATE
ETS score	cut off > 4.8	MT	0.96	0.61	LOW	LOW
Revised assessment of Bleeding and Transfusion (RABT) Score (FAST result (positive = 1), SI ([1 = 1), pelvic fracture (present = 1), and MOI (penetrating = 1)						
Revised assessment of Bleeding and Transfusion (RABT) Score	cut off ≥ 2	MT	0.78	0.91	VERY LOW	LOW

Index test	**Threshold**		**Sensibilità**	**Specificità**	**Qualità evidenza - SE**	**Qualità evidenza - SP**
Validated scores requiring clinical assessment only						
Shock Index (heart rate divided by systolic blood pressure)						
Shock Index	cut off >0.9	MT	0.62-0.95	0.66-0.86	VERY LOW	VERY LOW
Shock Index	not specified	TIC	0.48-0.85	0.54-0.86	VERY LOW	VERY LOW
Shock Index	cut off > 1.0	MT	0.62-0.77	0.79-0.87	VERY LOW	LOW
Shock Index	cut off >0.967	MT	0.765	0.74	LOW	MODERATE
Shock Index	cut off >0.933	MT	0.75	0.62	LOW	MODERATE
Shock Index	cut off >0.95	MT	0.57	0.88	VERY LOW	MODERATE
Shock Index (age adjusted)	cut off <36.95	MT	0.55	0.72	VERY LOW	MODERATE
Shock Index	cut off ≥ 0.81	MT	0.85	0.64	LOW	MODERATE
Shock Index	cut off ≥ 0.8	MT	0.67-0.96	0.36-84	VERY LOW	VERY LOW
Shock Index	cut off >	TIC	0.65	0.76	LOW	MODERATE

	0.9					
Shock Index	cut off 0.84	TIC	0.54	0.85	LOW	MODERATE
Shock Index	cut off 1.11	MT	0.92	0.80	VERY LOW	LOW
Shock Index	cut off 0.06	MT ≥ 10 U	0.41	-	VERY LOW	NA
Shock Index (Prehospital)	cut off 0.91	MT	0.65	0.67	VERY LOW	LOW
Modified Shock Index						
Modified Shock Index	cut off not reported	MT	-	-	NA	NA
Modified Shock Index	cut off 1.46	MT	0.96	0.76	VERY LOW	LOW
Modified Shock Index	cut off >1.15	MT	0.62	0.82	VERY LOW	MODERATE
Modified Shock Index (Prehospital)	cut off 1.28	MT	0.60	0.82	VERY LOW	MODERATE
ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)						
ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)	cut off ≥ 3	MT	-	-	NA	NA
EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS - obvious extremity injuries = 1 point, penetrating mechanism =2 points, shock index ≥ 0.9=2 points, GCS≤ 8 =3 points)						
EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS)	cut off ≥2	MT	0.81-0.96	0.65-0.76	LOW	LOW
TICCS Trauma induced coagulopathy clinical score (Severity [ED resuscitation room 2 points*, extent of body injury (torso, abddominal or the pelvic ring region = 2, head =1, each extremity = 1), SBP < 90 = 5)						
Trauma-Induced Coagulopathy Clinical Score (TICCS)	cut off ≥ 12	TIC	-	-	NA	NA
Trauma-Induced Coagulopathy Clinical Score (TICCS)	cut off ≥ 10	TIC	-	-	NA	NA
Early Blood Transfusion Needs Score- (age, type of injury, pulse, systolic blood pressure, GCS)						
Early Blood Transfusion Needs Score (age, type of injury, pulse, systolic	cut off > 5	MT	0.82	0.80	MODERATE	MODERATE

blood pressure, GCS)						
COAST (Coagulopathy of Severe Trauma Score - acute traumatic coagulopathy entrapment (1 point); body temperature (< 358C: 1 point, < 328C: 2 points); SBP (< 100 mm Hg: 1 point, < 90 mm Hg: 2 points); pelvic content or abdominal injury (1 point), and chest decompression (1 point).						
COAST - Coagulopathy of Severe Trauma Score	cut off ≥ 3	TIC	0.27-0.80	0.86-0.96	VERY LOW	MODERATE
PACT 1 (Prediction of Acute Traumatic Coagulopathy) (Shock index, Injury-to-ED time, White race, Age, First GCS,First RR)		TIC	0.73	0.74	VERY LOW	LOW
PACT 2 (Prediction of Acute Traumatic Coagulopathy) (Shock index, Age, GCS, Mechanism of injury, Intubation, CPR)		TIC	0.74	0.74	VERY LOW	VERY LOW

Tabella dei tools utilizzati nella popolazione pediatrica

Index test	**Threshold**	**Outcome**	**Sensibilità**	**Specificità**	**Qualità evidenza - SE**	**Qualità evidenza - SP**
Validated scores						
Shock Index (SI) - Calculated as the ratio of heart rate to systolic blood pressure.						
SI	cut off ≥ 0.9	MT	0.57 - 0.96	0.21 – 0.63	VERY LOW	LOW
SI	cut off ≥ 0.8	MT	0.82	0.27	MODERATE	MODERATE
SI	<1 year: SI>2.7, 1-2 years: SI>2.1, 2-5 years: SI>1.9, 5-12 years: SI>1.5, 12-15 years: SI>1.1	MT	0.13	0.98	MODERATE	MODERATE
Shock Index, pediatric age-adjusted (SIPA) - Calculated as the ratio of heart rate to systolic blood pressure and adjusted by age						

SIPA	ED thresholds used: 4-6 yr: SIPA >1.22, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	MT	0.58 – 0.95	0.35 – 0.83	VERY LOW	VERY LOW
SIPA	ED thresholds used: 1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	MT	0.46 – 0.80	0.35 – 0.85	VERY LOW	VERY LOW
SIPA	ED thresholds used: 0-3, 4-6 yr: SIPA >1.2, 7-12, 13-17 yr: SIPA>0.9	MT	0.61	0.66	MODERATE	MODERATE
Assessment of blood consumption (ABC-SCORE) - Penetrating mechanism, positive focused assessment sonography for trauma (FAST), arrival systolic blood pressure of 90 mmHg or less, and arrival heart rate (HR) ≥ 120 bpm.						
ABC-SCORE	cut off ≥ 1	MT	0.71 – 0.85	0.38 – 0.80	VERY LOW	VERY LOW
ABC-SCORE	cut off ≥ 2	MT	0.29 – 0.77	0.55 – 1.00	VERY LOW	VERY LOW
ABC-SCORE	cut off ≥ 3	MT	0.06 – 0.70	0.54 – 1.00	VERY LOW	VERY LOW
ABC-SCORE	Not specified	MT	0.47	0.85	LOW	MODERATE

Qualità delle prove relative agli effetti del test Qual è la certezza relativa a qualsiasi beneficio diretto critico o importante, effetto avverso o peso (burden) del test?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Molto bassa ○ Bassa ○ Moderata ○ Alta ● **Nessuno studio incluso**	Non ci sono studi test & treat che abbiano valutato gli effetti clinici derivati dalla applicazione dei test predittivi sopra analizzati.	
Qualità delle prove relative agli effetti del management della condizione Qual è la qualità delle prove relative agli effetti dal management della condizione derivante dai risultati del test?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Molto bassa ○ Bassa ○Moderata ○ Alta ● **Nessuno studio incluso**	Il trattamento del trauma maggiore in un trauma center, per effetto dell'utilizzo di uno strumento fra quelli studiati, è associato ad un aumento dell'appropriatezza dell'uso della trasfusione massiva ed una riduzione della coagulopatia indotta dal trauma, con prove di qualità molto bassa e moderata. L'assenza di studi test & treat non consente tuttavia di stabilire un legame diretto fra test ed effetto del management conseguente.	
Qualità delle prove relative al legame tra risultati del test e management che ne consegue Quanto certo è il legame tra i risultati del test e le decisioni sulla gestione?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Molto bassa ○ Bassa ○ Moderata ○ Alta ● **Nessuno studio incluso**	L'assenza di studi test & treat non consente di stabilire un legame diretto fra test ed effetto del management conseguente.	
Qualità complessiva delle prove relative agli effetti Qual è la qualità complessiva delle prove relative agli effetti sui pazienti degli interventi connessi alle indicazioni dei test?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Molto bassa ○ Bassa ● **Moderata**	Complessivamente vi è una eterogenea qualità sull'accuratezza diagnostica degli strumenti predittori degli interventi di trasfusione massiva o coagulopatia indotta da trauma.	La qualità è stata definita moderata in base ai test che il panel di esperti ha prescelto.

○ Alta ○ Nessuno studio incluso		
Valori C'è incertezza o variabilità nel valore attribuito agli esiti principali?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Importante incertezza o variabilità ○ Possibile importante incertezza o variabilità • **Probabilmente nessuna incertezza o variabilità importante** ○ Nessuna incertezza o variabilità importante	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline. Sono stati individuati 8 record. Nessuno studio incluso.	Non vi sono ragioni per ritenere che i soggetti traumatizzati abbiano incertezze o esprimano giudizi discordanti sugli esiti principali considerati.
Bilancio degli effetti Il bilancio tra effetti desiderabili ed indesiderabili favorisce l'intervento o il confronto?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ E' in favore del confronto ○ Probabilmente è in favore del confronto ○ Non è in favore né dell'intervento né del confronto • **Probabilmente è in favore dell'intervento** ○ E' in favore dell'intervento ○ Varia ○ Non lo so	In generale gli strumenti identificati hanno rilevato una bassa sensibilità e specificità variabile. In particolare i test prescelti mostrano una specificità accettabile con una qualità delle prove moderata.	Una valutazione evolutiva dell'andamento temporale dei test può essere di utilità nel migliorarne la sensibilità e specificità complessiva.
Risorse necessarie Qual è l'entità delle risorse necessarie (costi)?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Costi elevati	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline. Sono	Non ci sono certezze in merito a causa della limitata

○ Costi moderati ○ Costi e risparmi irrilevanti ○ Risparmi moderati ○ Risparmi elevati ○ Varia • **Non so**	stati individuati 9 record. Di questi sono stati esclusi 8 record ed inclusa una revisione sistematica. In mancanza di prove dirette, per argomentare il presente dominio è stata valutata questa revisione anche se: • si focalizza su una popolazione sottoposta a cardiochirurgia/trapianti e non su una popolazione di pazienti con trauma • prende in esame uno strumento utilizzato come point-of-care (POC) e non gli strumenti di tools in esame che richiedono valutazione clinica, di laboratorio e strumentazione diagnostica come ad esempio ultrasound assessment. Di conseguenza, l'evidenza riportata ha una forte limitazione per quanto riguarda la generalizzabilità (-2 gradi di indirectness) (**Appendice H**). **Costo dell'applicazione di uno strumento di predizione di trasfusione massiva o coagulopatia indotta da trauma in setting pre-ospedaliero o ospedaliero:** nessuna evidenza diretta. **Costo degli effetti indesiderabili quali a complicanze dovute a infezioni post trasfusione durante i 12 mesi successivi all'ospedalizzazione**:	generalizzabilità delle prove, dipende dalla condizione di background del territorio preso in considerazione, della rete ospedaliera relativa e soprattutto dal livello di utilizzo di risorse diagnostiche strumentali in sede pre-ospedaliera.

Health states		Mean (SD[a]) LoS	Mean (SD[a]) cost (£) per day
vCJD		0	NA
HAV	Acute hospitalisation (×2)	5.10 (0.52)	475 (48.47)
	Outpatient visit (×3)	1.00 (0.10)	266 (27.14)
Malaria	Hospitalisation (×2)	3.40 (0.34)	475 (48.47)
	Outpatient visit (×0)	1.00 (0.10)	266 (27.14)
HTLV	Hospitalisation (×2)	1.00 (0.10)	598 (61.02)
	Outpatient visit (×0)	1.00 (0.10)	266 (27.14)
HIV	Hospitalisation (×2)	6.97 (0.71)	598 (61.02)
	Outpatient visit (×3)	1.00 (0.10)	966 (98.57)
HBV	Chronic hospitalisation (×2)	7.40 (0.75)	475 (48.47)
	Outpatient visit (×3)	1.00 (0.10)	266 (27.14)
HCV	Chronic hospitalisation (×2)	3.50 (0.35)	341 (34.79)
	Outpatient visit (×3)	1.00 (0.10)	266 (27.14)

NA, not applicable.
a SDs were derived assuming a 95% CI with limits deviating 20% from the mean.

Qualità delle prove relative alle risorse necessarie Qual è la qualità delle prove relativamente alle risorse necessarie (costi)?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Molto bassa ○ Bassa ○ Moderata ○ Alta ● Nessuno studio incluso	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline. Sono stati individuati 9 records. Di questi sono stati esclusi 8 records ed inclusa una revisione sistematica. In mancanza di prove dirette, per poter argomentare il presente dominio è stata valutata questa revisione anche se: • si focalizza su una popolazione sottoposta a cardiochirurgia/trapianti e non su una popolazione di pazienti con trauma • prende in esame uno strumento utilizzato come point-of-care (POC) e non gli strumenti di tools in esame che richiedono valutazione clinica, di laboratorio e strumentazione diagnostica come ad esempio ultrasound assessment. Di conseguenza, l'evidenza riportata ha una forte limitazione per quanto riguarda la generalizzabilità (-2 gradi di indirectness).	Non si sono certezze in merito, dipende dalla condizione di background del territorio preso in considerazione e della rete ospedaliera relativa.
Costo-efficacia L'analisi di costo efficacia favorisce l'intervento o il confronto?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ È in favore del confronto ○ Probabilmente è in favore del confronto ○ Non è in favore né del confronto né dell'intervento ○ Probabilmente è in favore dell'intervento ○ È in favore dell'intervento ○ Varia **● Nessuno studio incluso**	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline. Sono stati individuati 9 record e nessuno studio pertinente. ito	

Equità Quale sarebbe l'impatto in termini di equità?		
GIUDIZI	RICERCA DELLE PROVE	CONSIDERAZIONI AGGIUNTIVE
○ Riduce l'equità ○ Probabilmente riduce l'equità ○ Probabilmente nessun impatto • **Probabilmente migliora l'equità** ○ Migliora l'equità ○ Varia ○ Non so	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline ma non sono stati identificati studi.	L'utilizzo di uno strumento di predizione di emorragia critica in sede preospedaliera/ospedaliera potrebbe contribuire ad aumentare l'equità del servizio di emergenza per l'adozione di criteri più omogenei per l'utilizzo appropriato di risorse trasfusionali critiche anche rispetto ad altre fasce di pazienti non traumatizzati.
Accettabilità L'intervento è accettabile per i principali stakeholder?		
GIUDIZI	RICERCA DELLE PROVE DI EVIDENZA	CONSIDERAZIONI AGGIUNTIVE
○ No ○ Probabilmente no • **Probabilmente si** ○ Si ○ Varia ○ Non so	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline. Sono stati valutati 146 studi ma nessuno studio risponde ai criteri di eleggibilità per cui non sono stati identificati lavori per rispondere al quesito.	Mancano evidenze dirette al contesto italiano. Con i limiti dovuti, si può ipotizzare un moderato livello di accettabilità, considerando per l'organizzazione il vantaggio di disporre di criteri oggettivi, verificabili e possibilmente migliorabili; per gli operatori vale il medesimo concetto, considerando il bilancio fra la possibilità di disporre di un tool di supporto decisionale e l'eventuale percezione di limitazione alla autonomia di scelta.
Fattibilità È fattibile l'implementazione dell'intervento?		
GIUDIZI	RICERCA DELLE PROVE DI EVIDENZA	CONSIDERAZIONI AGGIUNTIVE
○ No ○ Probabilmente no • **Probabilmente si** ○ Si	E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline. Sono stati valutati 146 studi ma nessuno studio risponde ai criteri di eleggibilità per cui non sono stati identificati studi.	Il panel ha discusso sulle barriere nell'adozione di strumenti volti a predire la necessità di trasfusione massiva o coagulopatia indotta da trauma. Alcune considerazioni nella implementazione dovrebbero riguardare:

○ Varia ○ Non so		• l'esperienza e la competenza del personale pre-ospedaliero e ospedaliero che possono influire sull'interpretazione dello strumento di triage • Formazione continua e audit sugli strumenti di triage.

RIASSUNTO DEI GIUDIZI

PROBLEMA	No	Probabilmente no	Probabilmente si	**Si**		Varia	Non so
ACCURATEZZA DEI TEST	Molto inaccurato	Inaccurato	Accurato	Molto accurato		**Varia**	Non so
EFFETTI DESIDERABILI	Irrilevanti	Piccoli	**Moderati**	Grandi		Varia	Non so
EFFETTI INDESIDERABILI	Grandi	**Moderati**	Piccoli	Irrilevanti		Varia	Non so
QUALITA' DELLE PROVE RELATIVE ALL'ACCURATEZZA DIAGNOSTICA	Molto bassa	Bassa	**Moderata**	Alta			Nessuno studio incluso
QUALITA' DELLE PROVE RELATIVE AGLI EFFETTI DEL TEST	Molto bassa	Bassa	Moderata	Alta			**Nessuno studio incluso**
QUALITA' DELLE PROVE RELATIVE AGLI EFFETTI DELLA GESTIONE	Molto bassa	Bassa	Moderata	Alta			**Nessuno studio incluso**
QUALITA' DELLE PROVE RELATIVE AL LEGAME TRA I RISULTATI DEL TEST E LA GESTIONE CHE NE CONSEGUE	Molto bassa	Bassa	Moderata	Alta			**Nessuno studio incluso**
QUALITA' COMPLESSIVA DELLE PROVE RELATIVE AGLI EFFETTI	Molto bassa	Bassa	**Moderata**	Alta			
VALORI	Importante incertezza o variabilità	Probabilmente importante incertezza o variabilità	**Probabilmente nessuna importante incertezza o variabilità**	Nessuna importante incertezza o variabilità			
BILANCIO DEGLI EFFETTI	A favore del confronto	Probabilmente a favore del confronto	Non è favorevole né al confronto né all'intervento	**Probabilmente a favore dell'intervento**	A favore dell'intervento	Varia	Non so

RISORSE NECESSARIE	Costi elevati	Costi moderati	Costi e risparmi irrilevanti	Risparmi moderati	Grandi risparmi	Varia	**Non so**
QUALITA' DELLE PROVE RELATIVE ALLE RISORSE NECESSARIE	Molto bassa	Bassa	Moderata	Alta			**Nessuno studio incluso**
COSTO EFFICACIA	A favore del confronto	Probabilmente a favore del confronto	Non è favorevole né al confronto né all'intervento	Probabilmente a favore dell'intervento	A favore dell'intervento	Varia	**Nessuno studio incluso**
EQUITA'	Riduce l'equità	Probabilmente riduce l'equità	Probabilmente nessun impatto sull'equità	**Probabilmente aumenta l'equità**	Aumenta l'equità	Varia	Non so
ACCETTABILITÀ	No	Probabilmente no	**Probabilmente si**	Si		Varia	Non so
FATTIBILITÀ	No	Probabilmente no	**Probabilmente si**	Si		Varia	Non so

TIPO DI RACCOMANDAZIONE

N. 25

Raccomandazione forte contro l'intervento	Raccomandazione condizionata contro l'intervento	Raccomandazione condizionata per l'intervento o per il confronto	**Raccomandazione condizionata a favore dell'intervento**	Raccomandazione forte a favore dell'intervento
○	○	○	●	○

N. 26

Raccomandazione forte contro l'intervento	Raccomandazione condizionata contro l'intervento	Raccomandazione condizionata per l'intervento o per il confronto	**Raccomandazione condizionata a favore dell'intervento**	Raccomandazione forte a favore dell'intervento
○	○	○	●	○

CONCLUSIONI

Raccomandazione

Racc. 25. Per individuare in fase pre-ospedaliera i pazienti con emorragia critica conseguente a trauma, si suggerisce l'utilizzo dello Shock Index per l'interpretazione dei dati clinici e l'ABC score in caso di disponibilità dell'ecografia extended-fast, considerando in entrambi i casi l'andamento evolutivo degli indici. [Raccomandazione condizionata, qualità delle prove moderata]

Racc. 26. Per individuare dopo l'accettazione in ospedale i pazienti con emorragia critica conseguente a trauma, si suggerisce l'utilizzo del TASH score. [Raccomandazione condizionata, qualità delle prove moderata]

Giustificazione

Le raccomandazioni scaturiscono dalla qualità complessiva delle prove dei test prescelti, validati da numerosi studi in letteratura e dalla necessità di ottimizzare le risorse trasfusionali disponibili.

Considerazioni relative ai sottogruppi

In età pediatrica sono diversi i cut-off da utilizzare per lo Shock Index (SIPA) e l'ABC score in relazione alla fascia di età.

Considerazioni per l'implementazione

Nessuna.

Monitoraggio e valutazione

Necessario audit su effetti dell'implementazione degli strumenti di predizione, incidenza di veri positivi e veri negativi e relative ricadute cliniche e organizzative, e benchmarking di confronto dei diversi sistemi regionali.

Priorità della ricerca

Studi sugli esiti dell'applicazione degli strumenti di predizione di trasfusione massiva o coagulopatia indotta da trauma nella realtà territoriale italiana e valutazione della performance diagnostica e degli esiti; registro nazionale.

Riferimenti bibliografici

Kovar, A., H. Carmichael, R. C. McIntyre, Jr., J. Mago, A. H. Gladden, E. D. Peltz and F. L. Wright (2019). "The Extremity/Mechanism/Shock Index/GCS (EMS-G) score: A novel pre-hospital scoring system for early and appropriate MTP activation." Am J Surg **218**(6): 1195-1200.

CQ13. Strumenti per predire l'emorragia critica

Appendice A. Quesito clinico e strategia di ricerca

Review question: What is the most accurate risk tool to predict critical bleeding and the need for massive transfusion in patients with major trauma (pre-hospital and hospital)?	
Objective: To determine the optimal strategy to predict later haemorrhagic shock in patients with major trauma (pre-hospital and hospital). Early prediction of later severe shock is vital as it allows blood components to be prepared and set up for use if required later, as shown by a diagnostic test for shock. Although treatments may not be given proactively in response to greater risk, they will be available more readily at the point of need. Hence treatment is REACTIVE to the diagnosis of shock, and therefore will not influence the gold standard (which is, of course, the diagnosis of shock).	
Population	Children, young people and adults who have experienced a traumatic incident.
Index tests	Pre-hospital and hospital: Clinical risk scores (examples) ABC score TASH score PWH score McLaughlin score Emergency Transfusion Score (ETS) Shock Index Shock Classification (part of ATLS protocols)
Reference standard	Need for massive transfusion, as diagnosed by a suitable blood test or clinical signs.
Outcomes	Diagnostic accuracy Outcomes related to under or over triage
Exclusion	People with a major trauma resulting from burns. Treatments applied for shock BEFORE diagnosis of shock (ie, test or clinical sign indicating the need for transfusion).
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English, French, Spanish, German, Italian Study designs: External validation studies. Internal validation studies (using different samples to those used to derive the risk tool) may be used if a test has no external validation studies.

POPULATION trauma
Standard major trauma population

Medline search terms

1.	(trauma* or polytrauma*).ti,ab.
2.	((serious* or severe* or major or life threaten*) adj3 (accident* or injur* or fall*)).ti,ab.
3.	multiple trauma/

4.	wounds, gunshot/ or wounds, stab/ or accidents, traffic/ or accidental falls/ or blast injuries/ or accidents, aviation/
5.	((motor* or motorbike* or vehicle* or road or traffic or car or cars or cycling or bicycle* or automobile* or bike* or head on or pile up) adj3 (accident* or crash* or collision* or smash*)).ti,ab.
6.	(mvas or mva or rtas or rta).ti,ab.
7.	(stabbed or stabbing or stab or gunshot* or gun or gunfire or firearm* or bullet* or knife* or knives or dagger).ti,ab.
8.	or/1-7

Embase search terms

1.	(trauma* or polytrauma*).ti,ab.
2.	((serious* or severe* or major or life threaten*) adj3 (accident* or injur* or fall*)).ti,ab.
3.	multiple trauma/
4.	gunshot injury/ or stab wound/ or traffic accident/ or falling/ or blast injury/ or aircraft accident/
5.	((motor* or motorbike* or vehicle* or road or traffic or car or cars or cycling or bicycle* or automobile* or bike* or head on or pile up) adj3 (accident* or crash* or collision* or smash*)).ti,ab.
6.	(mvas or mva or rtas or rta).ti,ab.
7.	(stabbed or stabbing or stab or gunshot* or gun or gunfire or firearm* or bullet* or knife* or knives or dagger).ti,ab.
8.	or/1-7

Cochrane search terms

#1.	MeSH descriptor: [multiple trauma] this term only
#2.	(trauma* or polytrauma*):ti,ab
#3.	((serious* or severe* or major) near/3 (accident* or injur* or fall*)):ti,ab
#4.	MeSH descriptor: [wounds, gunshot] this term only
#5.	MeSH descriptor: [wounds, stab] this term only
#6.	MeSH descriptor: [accidents, traffic] this term only
#7.	MeSH descriptor: [accidental falls] this term only
#8.	MeSH descriptor: [blast injuries] this term only
#9.	MeSH descriptor: [accidents, aviation] this term only
#10.	((motor* or motorbike* or vehicle* or road or traffic or car or cars or cycling or bicycle* or automobile* or bike*) near/3 (accident* or crash* or collision* or smash*)):ti,ab

#11.	(mvas or mva or rtas or rta):ti,ab
#12.	(stabbed or stabbing or stab or gunshot or gun or gunfire or firearm* or bullet or knife* or knives or dagger or shot):ti,ab
#13.	{or #1-#12}
S13.	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12

Haemorrhage AND Shock prediction tools

Medline search terms

1.	hemorrhage/ or exsanguination/ or shock/ or shock, hemorrhagic/ or shock, traumatic/ or hypovolemia/ or hypotension/
2.	(h?emorrhag* or hypovol?em* or shock or exsanguin* or olig?em* or hypoperfus* or hypotensi* or low blood pressure).ti,ab.
3.	(bleed* or bloodloss*).ti,ab.
4.	(blood* adj3 loss*).ti,ab.
5.	(coagulopath* or (abnormal* adj2 coagulation) or hyperfibrinolysis).ti,ab.
6.	blood transfusion/
7.	transfusion.ti,ab.
8.	or/1-7
9.	((transfusion or shock) adj3 (scor* or index* or classif* or predict* or tool* or risk*)).ti,ab.
10.	(risk adj3 (tool* or scor* or index* or predict*)).ti,ab.
11.	abc.ti,ab.
12.	assessment of blood consumption.ti,ab.
13.	nunez.ti,ab.
14.	tash.ti,ab.
15.	trauma-associated severe h?emorrhage.ti,ab.
16.	pwh.ti,ab.
17.	prince of wales hospital.ti,ab.
18.	rainer.ti,ab.
19.	mclaughlin.ti,ab.
20.	emergency transfusion score.ti,ab.
21.	ets.ti,ab.
22.	vandromme.ti,ab.
23.	schreiber.ti,ab.

24.	lars?n.ti,ab.
25.	revised trauma score.ti,ab.
26.	rts.ti,ab.
27.	field triage score.ti,ab.
28.	fts.ti,ab.
29.	*risk/
30.	*risk assessment/
31.	*risk factors/
32.	or/9-31
33.	8 and 32

Embase search terms

1.	exp *hypovolemia/ or *hemorrhagic shock/ or *traumatic shock/ or exp *bleeding/ or *exsanguination/
2.	*hypotension/
3.	(h?emorrhag* or hypovol?em* or shock or exsanguin* or olig?em* or hypoperfus* or hypotensi* or low blood pressure).ti,ab.
4.	(bleed* or bloodloss*).ti,ab.
5.	(blood* adj3 loss*).ti,ab.
6.	(coagulopath* or (abnormal* adj2 coagulation) or hyperfibrinolysis).ti,ab.
7.	*blood transfusion/
8.	transfusion.ti,ab.
9.	or/1-8
10.	((transfusion or shock) adj3 (scor* or index* or classif* or predict* or tool* or risk*)).ti,ab.
11.	(risk adj3 (tool* or scor* or index* or predict*)).ti,ab.
12.	abc.ti,ab.
13.	assessment of blood consumption.ti,ab.
14.	nunez.ti,ab.
15.	tash.ti,ab.
16.	trauma-associated severe h?emorrhage.ti,ab.
17.	pwh.ti,ab.

18.	prince of wales hospital.ti,ab.
19.	rainer.ti,ab.
20.	emergency transfusion score.ti,ab.
21.	ets.ti,ab.
22.	vandromme.ti,ab.
23.	schreiber.ti,ab.
24.	lars?n.ti,ab.
25.	revised trauma score.ti,ab.
26.	rts.ti,ab.
27.	field triage score.ti,ab.
28.	fts.ti,ab.
29.	*risk assessment/ or *risk/ or *risk factor/
30.	or/10-29
31.	9 and 30

Cochrane search terms

#1.	MeSH descriptor: [hemorrhage] this term only
#2.	MeSH descriptor: [exsanguination] this term only
#3.	MeSH descriptor: [shock] this term only
#4.	shock, hemorrhagic
#5.	MeSH descriptor: [shock, traumatic] this term only
#6.	MeSH descriptor: [hypovolemia] this term only
#7.	(h?emorrhag* or hypovol?em* or shock or exsanguin* or olig?em* or hypoperfus*):ti,ab
#8.	(bleed* or bloodloss* or blood loss*):ti,ab
#9.	(coagulopath* or (abnormal* near/2 coagulation) or hyperfibrinolysis):ti,ab
#10.	{or #1-#9}
#11.	((transfusion or shock) near/3 (scor* or index* or classif* or predict* or tool* or risk*)):ti,ab
#12.	(risk near/3 (tool* or scor* or index* or predict*)):ti,ab
#13.	abc:ti,ab
#14.	assessment of blood consumption:ti,ab
#15.	nunez:ti,ab
#16.	tash:ti,ab
#17.	trauma associated severe h?emorrhage:ti,ab

#18.	pwh:ti,ab
#19.	prince of wales hospital:ti,ab
#20.	rainer:ti,ab
#21.	mclaughlin:ti,ab
#22.	emergency transfusion score:ti,ab
#23.	ets:ti,ab
#24.	vandromme:ti,ab
#25.	schreiber:ti,ab
#26.	lars?n:ti,ab
#27.	revised trauma score:ti,ab
#28.	rts:ti,ab
#29.	field triage score:ti,ab
#30.	fts:ti,ab
#31.	MeSH descriptor: [risk] this term only
#32.	MeSH descriptor: [risk assessment] this term only
#33.	MeSH descriptor: [risk factors] this term only
#34.	{or #11-#33}
#35.	#10 and #34

CQ13. Strumenti per predire l'emorragia critica

Appendice B. Tabelle delle caratteristiche degli studi inclusi in adulti.

	Study Author	Year	Validated test	Unvalidated test	Study Design	Number of participants	MT/TIC	Population/ condition
1	Afshari	2019	TASH score		Retrospective	200	MT	
2	Alimohammadi	2017	ETS score		Retrospective	793	MT	
3	Ardegh	2001	ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)		Retrospective	184	MT	
4	Arlsan	2015	Shock index		Retrospective	373	MT	
5	Barnes	2018	Modified Schok Index		Retrospective	7623	MT	
6	Belanger-Quintana	2019	ABC score		Retrospective	NA	MT	
			TASH score					
7	Baker	2011		Baker model (SBp <90=1, HR>120=1, GCS < 9=1, High risk injury =1,(ventral chest trauma, abdominal trauma, MVC, penetrating torso trauma)	Retrospective	654	MT	
8	Brockamp	2012	ABC score		Retrospective	5147	MT	
			Larson score					
			Schreiber score					
			Vandromme score					
			Prince of Wales/Rainer					
			TASH score					
9	Calcutt	2011	Cincinnati individual tansfusion trigget (CITT) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C) 6 hours	prince of Walse + lactate (max score 11 pts); Prince of Walse (base deficit replaced by lactate) (max score 10 pts)	Prospective	170	MT	
10	Calcutt	2016	MTS (massive tranfsusion score 6 hours) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6)		Prospective	NA	MT	
			revised MTS (massive transfusion score) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C)					
11	Calcutt	2013	MTS (massive tranfsusion score) (SBp <90, Hb <11, INR > 1.5, Base deficiti ≥6, Positive FAST, penetrating mechanism)		Prospective	1245	MT	

12	Campos-Serra	2018	ABC score		Retrospective	1402	MT	
			Shock Index					
			ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)					
13	Cancio	2008		RTS (SBP, Respiratory Rate, GCS)	Retrospective	536	MT	
14	Chaochankit	2018	ABC score	ABC score + lactate	Retrospective	165	MT	
15	Choi	2017	Prince of Wales/Rainer	Prince of Walse + lactate (max score 11 pts); Prince of Walse (base deficit replaced by lactate) (max score 10 pts)	Retrospective	305	MT	
16	Cornero	2020	Milano score (max score 9 points)		Prospective	905+139=1044	MT	
17	Cotton	2010	ABC score		Retrospective	513+133+372=1018	MT	
18	David .	2017	Shock Index		Retrospective	485	TIC	
			Shock Index					
			TASH score					
			TASH score					
19	De Jong	2016	TASH score		Retrospective	910	MT	obese
20	Eastridge	2010		Modified field triage score (SBP < 100, GCS <8)	Retrospective	536	MT	
21	El Menyar	2019a		FASYLA score (FAST (0=negative, 1=positive), Shock Index (SI) (0= 0.50-0.69, 1 =0.70-0.79, 2 = 0.80-0.89, 3=> 0.90), and initial serumLActate (0= <2.0, 1=2.0-4.0, 2>=4.0mmol/l).)	Retrospective	1199	MT	
			Revised assessment of Bleeding and Transfusion (RABT) Score			1127	MT	solid organ failure
22	El Menyar	2019b	Shock Index, ABC score		Retrospective	572	MT	solid organ failure
23	El Menyar	2019c	Shock Index		Retrospective	966	MT	pelivic fracture
24	El Menyar	2018	Shock Index		Retrospective	8710	MT	
25	Figueiredo	2018	Shock Index		Prospective	6402	MT	
26	Fligor	2016	Shock Index		Retrospective	194	MT	geriatric
27	Frohlich	2016	Shock Index		Retrospective	16760+24128=40888	MT	TBI and not TBI
28	Galvagno	2015		Algorithm including age, sex, prehospital shock index, admission HR, SpHb and SpO	Retrospective	711	MT	
29	Hanna	2020	ABC score		Retrospective	1018	MT	

			Revised assessment of Bleeding and Transfusion (RABT) Score					
30	Horst	2020	ABC score	modified TICCS	Prospective	479	MT	
			Larson score					
			Prince of Wales/Rainer					
			ETS score					
			TASH score				MT	
31	Hsu	2013		Hsu score (Base deficit greater than 5 and either INR of 1.5 or greater or hemoperitoneum)	Retrospective	479	MT	
32	Jenkins	2017	Shock Index		Retrospective	81	MT	pregnant
			ROPE Pulse Rate Over Pressure					
33	Joseph	2018	ABC score		Retrospective	380	MT	
			Revised assessment of Bleeding and Transfusion (RABT) Score (FAST result (positive = 1), SI ([1 = 1), pelvic fracture (present = 1), and MOI (penetrating = 1)				MT	
34	Juste	2021	Shock index		Retrospective	184	MT	
35	Kovar	2019	Shock Index	ABC score (without FAST)	Retrospective	764	MT	
			EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS)					
36	Krumrei.	2012	TASH score		Retrospective	373	MT	rural population
			McLaughlin score				MT	
			ABC score				MT	
37	Kuhne	2008	ETS score		Retrospective	481	MT	
38	Larson	2010	Larson score Any 2 or more of the following: Hemoglobin <11 g/dL, SBP < 110 mm Hg, HR > 110 bpm, Base Deficit ≤6 mmol/L		Retrospective	1024	MT	
39	Lee young	2020	Shock Index	SIA (Shock Index*age)	Retrospective	1627	TIC	
				QSOFA score (qSOFA score was calculated as the sum of 1 point each for SBP ≤100 mmHg, GCS ≤14, and RR ≥22 breaths/min)				
				Reverse shock index multiplied by the Glasgow Coma Scale score (rSIG) (BP/HR* GCS)				
40	Lui Chun	2018	TASH score	DMBT dynamic MBT score (similar to TASH and PHW, plus hemoglobin drop as a predictor variable)	Retrospective	2945	MT	
			Prince of Wales/Rainer					

41	Maegele	2011	TASH score		Retrospective	5834+6444=11878	MT
			TASH score				MT
42	McLaughlin	2008	McLaughlin score		Retrospective	301+396=698	MT
43	McKinley	2016		Shock volume (Initially incremental SV measurements (SVi) were made by calculating average SIth(i) values between two adjacent time points, and by multiplying the incrementally averaged SIth(i) by the duration of the corresponding time interval)	Retrospective	467	MT
44	Mitra	2011	COAST (Coagulopathy of Severe Trauma Score - acute traumatic coagulopathy entrapment (1 point); body temperature (< 358C: 1 point, < 328C: 2 points); SBP (< 100 mm Hg: 1 point, < 90 mm Hg: 2 points); pelvic content or abdominal injury (1 point), and chest decompression (1 point).		Prospective	1680+1225=2905	TIC
45	Mitra	2012	TASH score		Retrospective	1234	MT
			ABC score				
			Prince of Wales/Rainer				
46	Mina	2013		Mobile application modeling (mechanism of injury, HR, SBP, and BD)	Retrospective	13961	MT
47	Moore	2007		Moore model (SBP in first hour, pH min during 1st hour, ISS ≤ 25=0, > 25 = 1)	Retrospective	383	MT
48	Moore	2017	Shock Index		Prospective	324	MT
			ABC score				MT
49	Mutschler	2013	Shock Index		Retrospective	21853	MT
50	Nunez	2009	McLaughlin score		Retrospective	586	MT
			TASH score				
			ABC score (Penetrating mechanism (0 = no, 1 = yes), ED SBP of 90 mm Hg or less (0 = no, 1 = yes), ED HR of 120 bpm or greater (0 = no, 1 = yes), Positive FAST (0 = no, 1 = yes)				
51	Ogura	2014	TBSS		Retrospective	119	MT
			ABC score				
			TASH score				

52	Ogura	2015	TBSS		Retrospective	264	MT	
			TASH score					
53	Ogura	2016	TBSS	Modified TBSS (age, sonography, pelvic fracture, serum lactate and systolic blood pressure on arrival)	Retrospective	300	MT	
			TASH score					
54	Ogura	2018	TBSS		Retrospective	1025	MT	
			ABC score					
			Shock Index					
55	Ohmori	2017	ABC score		Prospective	334+380=714	MT	<65 years old and > years old
			Prince of Wales/Rainer					
			TASH score					
56	Parimi	2016	Shock Index		Retrospective	10636	MT	
57	Park	2019		Injury Severity Score	Retrospective	553 (294+309)	MT	TBI and non TBI
				RTS (SBP, Respiratory Rate, GCS)				
58	Pommerening	2015	Mclaughlin score	Clinical gestalt	Prospective	966	MT	
			ABC score				MT	
			TASH score				MT	
59	Poon	2012	TASH score		Retrospective	1030	MT	
			ABC score				MT	
			Prince of Wales/Rainer				MT	
60	Pottecher	2016	Shock Index		Retrospective	2557	MT	
61	Prichayudh	2020	ABC score	Class-4 Hemorrhage Unresponsive to Lactated Ringer's (CHULA) - 1) a patient with clinical sign of class-4 hemorrhage; 2)not responding to one to two liters of Lactated Ringer's bolus; 3) had suspected ongoing bleeding.	Retrospective	358	MT	
62	Rainer	2011	Prince of Wales/Rainer		Retrospective	1891	MT	
63	Rau	2016	Shock Index		Retrospective	2490	MT	
64	Ruchholtz.	2006	ETS score		Prospective	1103	MT	
65	Schreiber	2007	Schreiber score (Hb ≤ 11, International normilized ratio > 1.5, penetrating trauma)		Retrospective	558	MT	military truama
66	Schroll	2018	ABC score		Retrospective	644	MT	
			Shock Index					
67	Shackelford	2015		Algorithm including triage vital signs, pulse oximetry features, and laboratory values (C1, Cartridge 1 (hematocrit, glucose, potassium,	Retrospective	852	MT	

				chloride, and bicarbonate); C2, Cartridge 2 (PT, INR); C3, Cartridge 3 (lactate); pulse oximetry features for 15 minutes)			
68	Sharma.	2019	Modified Shock Index	Pulse Pressur/ Heart rate	Retrospective	254	MT
			Shock Index				
69	Swerts	2020	Trauma-Induced Coagulopathy Clinical Score (TICCS)	Trauma-Induced Coagulopathy Clinical Score (TICCS). BE - (+ 3 points if BE < − 5 and + 3 points in case of a positive FAST)	Retrospective	328	MT
			TASH score				
70	Terceros-Almanza	2019	ABC score		Retrospective	183	MT
			ETS score			189	
			Prince of Wales/Rainer			129	
			Larson score			392	
			TASH score			131	
			Shock Index			535	
71	Terceros-Almanza	2017	Shock Index		Retrospective	279	MT
			Modified Shock Index				
72	Thorn	2019	COAST - Coagulopathy of Severe Trauma Score		Retrospective	133	TIC
73	Tonglet.	2017	Trauma-Induced Coagulopathy Clinical Score (TICCS)		Prospective	33385	MT
74	Tonglet.	2014	TICCS Trauma induced coagulopathy clinical score (Severity [ED resuscitation room 2 points*, extent of body injury (torso, abddominal or the pelvic ring region = 2, head =1, each extremity = 1), SBP < 90 = 5)		Prospective	82	MT
75	Umemura	2016	TASH score		Retrospective	153	MT
			ABC score				
76	Vandromme	2011a	Shock Index (heart rate divided by systolic blood pressure) (original J Trauma. 2011)		Prospective	8111	MT
77	Vandromme	2011b	Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)			306+208=514	MT
78	Wade	2008		Wade model (SBP, HR, Ph, Hematocrit)	Retrospective	838	MT

79	Weaver	2016		Code red attivation (SBP < 90, Blood pressure failure to repsond to bolus intraveneous fluid)	Prospective	129	MT
80	Wang	2019	Shock Index (Prehospital)		Retrospective	1007	MT
			Modified Shock Index (Prehospital)				MT
81	Wang	2016	Early Blood Transfusion Needs Score- (age, type of injury, pulse, systolic blood pressure, GCS)		Retrospective	24303	MT
82	Wei	2017	Prediction scoring scheme		Retrospective	265	MT
83	Wei	2020	Prediction scoring scheme (0-8 points) - type of trauma, injury severity score, heart rate, hemoglobin, prothrombin time, fibrinogen, and base excess		Retrospective	332+146=478	MT
84	Wu	2019	Shock Index		Retrospective	7957	MT
85	Yang	2021	Shock Index	Bleeding risk idnex BRI (PPG, ECG waveforms, oximetry SpO2, SBP)	Retrospective	1396	MT
			ABC score	RTS (SBP, Respiratory Rate, GCS)			MT
86	Yucel	2006	TASH score		Retrospective	4527+1517=6044	MT
87	Yumoto	2014	ABC score	Yumoto New screening method (schok index ≥ 1, Base Excess ≤ 3, positive FAST results)	Retrospective	259	MT
88	Peltan	2015	PACT1 score		Prospective	324	TIC
89	Peltan	2016	PACT2 score COAST		Retrospective	Derivation cohort (n = 1963) Validation cohort (n = 285)	TIC

Appendice B. Tabelle delle caratteristiche degli studi pediatrici.

Study	**Adult-Based Massive Transfusion Protocol Activation Criteria Do Not Work in Children Acker 2016**
Study type	A retrospective review of the medical records
Number of studies/ number of participants	N=50 (early transfusion: n=31; late transfusion: n=19)
Countries and Settings	Colorado, United States
Funding	Not reported
Duration of study	Between January 2008 and December 2014.
Age, gender, ethnicity	Age [mean (IQR)]: Group 1: 10 (4.5-12.75), Group 2: 8 (6-12) Gender (% M): Group 1: 74%, group 2: 63% Ethnicity: not reported
Patient characteristics	All children age 4 to 15 years admitted to either of two pediatric trauma centers (PTCs), Children's Hospital Colorado (Level I PTC), and Denver Health Medical Center (Level II PTC). Children who received any packed red blood cell (PRBC) transfusion during an inpatient admission following traumatic injury between January 2008 and December 2014 were included. Children less than 4 years of age were excluded as we have not yet defined SIPA in this population. Data collected include demographic information, mechanism of injury, vital signs on presentation, and injury severity score (ISS). The authors also recorded which children required early PRBC transfusion (within 6 hours of presentation; defined as the early group) and which required delayed transfusion (late group).
Intervention	The authors calculated the ABC and ABC-S scores for each child in both the early (Group 1, n=31) and late (Group 2: n=19) transfusion groups. The authors evaluated the sensitivity, specificity, positive predictive value (PPV), and accuracy of ABC and ABC-S scores of 1, 2, and 3 in predicting the need for early PRBC transfusion as a marker of MTP activation. They also calculated the sensitivity, specificity, PPV, and accuracy of elevated SIPA alone at the time of presentation to predict the need for early blood transfusion.

Outcomes	Prediction of the need for early PRBC transfusion as a marker of MTP activation

Study	**Validation of the age-adjusted shock index for pediatric casualties in Iraq and Afghanistan Cuenca 2020**
Study type	A secondary analysis of a previously published dataset: retrospective review of prospectively collected data within the registry.
Number of studies/ number of participants	N=3145 (massive transfusion: n=502)
Countries and Settings	USA, military
Funding	The authors received no external funding for this study.
Duration of study	From January 2007 to January 2016
Age, gender, ethnicity	Age [n (%)]: < 1 year: 50 (1.59%); 1-3 years: 396 (12.59%); 4-6 years: 576 (18.31%); 7-12 years: 1356 (43.12%); 13-17 years: 767 (24.39%) Gender (% M): < 1 year: 64%; 1-3 years: 64.4%; 4-6 years: 69.3%; 7-12 years: 80.7%; 13-17 years: 86.3% Ethnicity: not reported
Patient characteristics	The authors queried the Department of Defense Trauma Registry (DODTR) for all pediatric (age < 18 years) encounters from January 2007 to January 2016. The DODTR comprises all patients admitted to a Role 3 (fixed-facility) or forward surgical team (FST) with an injury diagnosis using the International Classification of Disease 9th Edition (ICD-9) between 800.0–959.9, near-drowning/drowning with associated injury (ICD-9994.1) or inhalational injury (ICD-9987.9) and trauma occurring within 72 h from presentation.
Intervention	We used nominal logistic regression analyses for receiver operating characteristic (ROC) thresholds and analyses with areas under the curve (AUC) for model fit. We used nominal logistic regression analyses for receiver operating characteristic (ROC) thresholds and analyses with areas under the curve (AUC) for model fit.
Outcomes	Prediction of massive transfusion and mortality

Study	Evaluation of a Pediatric Assessment of Blood Consumption Score to Predict Blood Transfusion in Pediatric Trauma El-Shafy 2016
Study type	Retrospective review of pediatric trauma patients
Number of studies/ number of participants	N=6030 (received blood: n=185)
Countries and Settings	National Trauma Data Bank (NTDB)
Funding	Not reported
Duration of study	2012
Age, gender, ethnicity	Age: < 14 years Gender (% M): not reported Ethnicity: not reported
Patient characteristics	pediatric trauma patients (age<14) with Injury Severity Score (ISS)>15 in the 2012 National Trauma Data Bank (NTDB).
Intervention	ABC score criteria was modified by excluding FAST and adding temperature.
Outcomes	Blood transfusions within 48 hours were identified using ICD-9 codes.

Study	Admission lactate and base deficit in predicting outcomes of pediatric trauma Huh 2020
Study type	A planned secondary analysis of a pediatric trauma dataset-based study

Number of studies/ number of participants	N=545 (transfusion: n=237)
Countries and Settings	Korean academic hospital trauma center, equivalent to level 1 trauma centers in the United States
Funding	The authors declare they have no conflicts of interest or funding sources.
Duration of study	From 2010 through 2018
Age, gender, ethnicity	Age [median (IQR)]: 13 (7-16) Gender (% M): 77.8% Ethnicity: not reported
Patient characteristics	All consecutive children (<18 years) with trauma who visited the center and underwent assays for admission lactate and BD values from 2010 through 2018 were included in this study. The exclusion criteria were unavailability of data on lactate or BD, environmental injury or poisoning, being dead on arrival, transfer to outside hospitals, and transfer from outside hospitals after transfusion or surgical interventions.
Intervention	As a marker of shock or indication for surgical interventions, lactate and BD are usually measured using venous blood gas analysis within several hours of the initial presentation. Using receiver operating characteristic curves for the primary outcomes, the authors compared the areas under the curve (AUCs) and cutoffs of lactate and BD. Based on such cutoffs, the sensitivity, specificity, and likelihood ratios were calculated.
Outcomes	The primary outcomes included in-hospital mortality, early transfusion, and early surgical interventions (surgery or angioembolization) for the torso or major vessels. Early transfusion and surgical interventions were defined as the procedures performed within 24 hours of the initial presentation. These two outcomes reflect the need for hemorrhage-related procedures. The secondary outcomes were early use of blood products (unit), early brain surgery, intubation, intensive care unit hospitalization, and ventilator days.

Study	**Prospective validation of the shock index pediatric-adjusted (SIPA) in blunt liver and spleen trauma: An ATOMAC+ study** **Linnaus 2016**
Study type	A planned secondary analysis of a prospective observational study

Number of studies/ number of participants	N=386 (transfusion: n=97)
Countries and Settings	Participating centers were part of the Arizona-Texas-Oklahoma-Memphis-Arkansas + Consortium (ATOMAC+) and include: Phoenix Children's Hospital (Phoenix, AZ), Dell Children's Medical Center (Austin, TX), Children's Medical Center Dallas, part of Children's HealthSM(Dallas, TX), Arkansas Children's Hospital (Little Rock, AR), The Children's Hospital at OU Medical Center (Oklahoma City, OK), LeBonheur Children's Hospital (Memphis, TN), American Family Children's Hospital (Madison, WI), Akron Children's Hospital (Akron, OH), Children's Mercy Hospital (Kansas City, MO), and Children's Healthcare of Atlanta (Atlanta, GA).
Funding	Not reported
Duration of study	From April 2013 through January 2016
Age, gender, ethnicity	Age [n (%)]: 4-6 years: 76 (19.69%); 7-12 years: 156 (40.41%); 13-16 years: 154 (39.9%) Gender (% M): 4-6 years: 49%; 7-12 years: 47%; 13-16 years: 66% Ethnicity: not reported
Patient characteristics	Patients 18 years of age or younger, presenting to any of ten level 1 pediatric trauma centers (PTC) from April 2013 through January 2016 with a grade 3 or higher blunt liver and/or spleen injury (BLSI). Children with an injury severity score (ISS) ≤15 were excluded from analysis to be consistent with Acker et al.
Intervention	Vitals collected during evaluation in the trauma bay were used to calculate SIPA (maximum heart rate/minimum systolic blood pressure (SBP)). Based on the Acker et al. paper, SIPA was considered elevated at >1.22 for 4–6.9 year olds, >1.0 for 7–12.9 year olds, and >0.9 for 13–16.9 year olds. SI (not age-adjusted) was considered elevated if >0.9. Patients were dichotomized to elevated or non-elevated SI and elevated or non-elevated SIPA.
Outcomes	Outcomes included the need for blood transfusion within 24 hours of injury, having an ISS N 24, having a grade 3 or greater BLSI requiring transfusion, inhospital mortality, need for laparotomy or laparoscopy, or requiring ICU admission.

Study	**Identifying potential predictive indicators of massive transfusion in pediatric trauma Hwu 2018**
Study type	A retrospective case–control study of children

Number of studies/ number of participants	N= 303 (massive transfusion: n=44)
Countries and Settings	American College of Surgeons pediatric level 1 trauma center
Funding	The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was funded by the Training of the Pediatric Emergency Physician-Scientist Grant (NIH Grant#T32HD049338) and Washington University Institute of Clinical and Translational Sciences which is, in part, supported by the NIH/National Center for Advancing Translational Sciences (NCATS) (CTSA grant #UL1TR000448).
Duration of study	From 1 May 2005 to 28 February 2014
Age, gender, ethnicity	Age [n (%)]: Group 1: 0-4 y: 18 (40.9%), 5-12 y: 13 (29.5%), 13-18 y: 13 (29.5%); Group 2: 0-4 y: 32 (24.2%), 5-12 y: 62 (47%), 13-18 y: 38 (28.8%); Group 3: 0-4 y: 51 (40.2%), 5-12 y: 38 (29.9%), 13-18 y: 38 (29.9%); Gender (% M): Group 1: 70.5%; Group 2: 62.9%; Group 3: 65.4% Ethnicity: not reported
Patient characteristics	All children who presented before their 18th birthday to our American College of Surgeons verified level-1 pediatric trauma center during the study period were eligible for review. Patients who never achieved a perfusing heart rhythm, died within 1 h of presentation to our emergency department (ED), presented or were transferred to the ED ≥24 h after injury, were transferred out of our institution within the first 24 h of injury, or had injuries not related to blunt or penetrating trauma such as burns, hangings, or drownings were excluded. The authors identified potential eligible children through query of our electronic medical record database and trauma registry using ICD-9 E-codes for blunt and penetrating trauma.
Intervention	'Cases' (Group 1, n=44) were children who received massive blood transfusion defined as ≥40 ml/kg of RBCs or ≥80 ml/kg total blood products in the first 24 h following injury. 'Controls' were children who received <40 ml/kg of RBCs and <80 ml/kg total blood products or were not transfused. Two control groups for comparison were used: (1) unmatched (random) (Group 2, n=132) and (2) matched (Group 3, n=127) for age and injury severity score (ISS) (matched).
Outcomes	Predictive indicators of massive transfusion in injured children

Study	**Assessment of blood consumption score for pediatrics predicts transfusion requirements for children with trauma Komori 2021**

Study type	A case–control study
Number of studies/ number of participants	N=5943 (transfusion: n=540)
Countries and Settings	A nationwide registry of patients with trauma in Japan: Japan Trauma Data Bank (JTDB).
Funding	There is no funding.
Duration of study	Between 2004 and 2015
Age, gender, ethnicity	Age [mean (SD)]: Transfusion group: 8.6 (4.6); Non-transfusion group: 9.2 (4) Gender (% M): Transfusion group: 67.4%; Non-transfusion group: 69.8% Ethnicity: not reported
Patient characteristics	All patients aged <16years of age with blunt trauma were included. The exclusion criteria were as follows: patients who had missing data of age; patients who had trauma mechanisms other than blunt trauma or patients with missing data of the trauma mechanism; patients who had no information about transfusion; patients who experienced cardiorespiratory arrest upon arrival at the hospital; or patients with an abbreviated injury scale (AIS) score of ≤2 or 6 (i.e., nonsurvivable injury) for any reason. Patients for whom focused assessment with sonography for trauma (FAST) scan was not conducted or data were missing; patients with missing data of systolic blood pressure (SBP), heart rate (HR), and Glasgow coma scale (GCS) scores in the ED were also excluded. Thus, the data of patients who represented complete datasets for score predictors of SBP, HR, GCS, and FAST were included in the analysis.
Intervention	The assessment of blood consumption score for pediatrics (ped-ABC score) was developed based on previous literatures and clinical relevance. It comprises some components of the ABC score, which was developed to predict massive transfusion for adult patients with trauma, as well as disturbance of consciousness, which we defined as GCS score <15. One point was scored for each of the following criteria: SBP≤90mm Hg; HR≥120/min; GCS score <15; and positive FAST scan.
Outcomes	The objective of this study was to develop a scoring system to predict the requirements for transfusion in children with trauma.

Study	**Validation of Shock Index Pediatric-Adjusted for children injured in warzones Marenco 2020**

Study type	A retrospective review of all pediatric trauma patients
Number of studies/ number of participants	N=2121 (need for blood product transfusion: n=753)
Countries and Settings	the Department of Defense Trauma Registry, USA
Funding	There are no sources of funding related to this work to disclose.
Duration of study	From 2008 to 2015
Age, gender, ethnicity	Age [n (%)]: 0-3 yr: 250 (11.8%); 4-6 yr: 379 (17.9%); 7-12 yr: 1013 (47.8%); 13-17 yr: 479 (22.6%) Gender (% M): 79.2% Ethnicity: not reported
Patient characteristics	All patients with records in the database younger than 18 years that received care for traumatic injuries during the specified period were included. Patients without vital signs recorded upon arrival to the initial level of care and patients whose only records were from tertiary care centers (defined as Role IV center or above) were excluded. Patients were then assigned to a predefined age category (0–3, 4–6, 7–12, 13–17 years).
Intervention	Shock Index was first calculated using the HR and SBP recorded upon arrival to the initial level of care. Lastly, utilizing threshold values for SIPA based on age categories previously validated by Nordin et al. in the civilian pediatric trauma population, patients were classified as having either a “normal” or “elevated” SIPA.
Outcomes	The primary outcomes of our study were need for BPT or emergent surgical procedure (ESP) within the first 24 hours of care. Blood product transfusion included the receipt of either packed red blood cells, whole blood (WB), fresh frozen plasma, cryoprecipitate, platelets, or some combination of these products. Secondary outcomes included intensive care unit (ICU) admission, Injury Severity Score (ISS), severe injury (defined as ISS > 15), need for mechanical ventilation (≥3 days), need for advanced imaging (computed tomography), and mortality.

Study	**Validation of the age-adjusted shock index using pediatric trauma quality improvement program data Nordin 2018**
Study type	A retrospective study

Number of studies/ number of participants	N=22957 (transfusion: n=534)
Countries and Settings	Pediatric Trauma Quality Improvement Program (TQIP) database
Funding	Not reported
Duration of study	Year 2014
Age, gender, ethnicity	Age [n (%)]: 1-3 yr: 2980 (13%); 4-6 yr: 5897 (25.7%); 7-12 yr: 8851 (38.5%); 13-16 yr: 5229 (22.8%) Gender (% M): 63.8% Ethnicity [n (%)]: White: 14843 (64.7%); Black: 3623 (15.8%); Other: 4491 (19.6%)
Patient characteristics	All children 1–16 years old who sustained either blunt or penetrating traumatic injuries in 2014 were included. Children under 1 year of age were excluded since their ages were not reliably recorded and their SIPA cut-offs could not be reliably calculated. The dataset is limited to patients with an Abbreviated Injury Scale ≥2.
Intervention	The authors calculated SI and SIPA, and applied the same SIPA cut-off values as previously reported by Acker et al., which are based on published normal vital sign ranges. For binary variables, they also calculated and compared test characteristics including sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for both SI and SIPA.
Outcomes	Outcome measures included ICU and total hospital LOS, ventilator usage, number of ventilator days, transfusion requirement within 24 h of admission, discharge to rehab and mortality.

Study	**The ABC-D score improves the sensitivity in predicting need for massive transfusion in pediatric trauma patients Phillips 2019**
Study type	A retrospective study

Number of studies/ number of participants	N=211 (massive transfusion: n=66)
Countries and Settings	Trauma registry at Children's Hospital Colorado (CHCO)
Funding	Not reported
Duration of study	Between January 2008 to December 2018
Age, gender, ethnicity	Age [mean (SD)]: MT: 8.0 (5.1); No MT: 9.1 (5.0) Gender (% M): MT: 67%; No MT: 68% Ethnicity: not reported
Patient characteristics	Pediatric patients (18 years old) who received at least one blood product transfusion within the first 24 hours after their injury were included. Children who died in the emergency department and children <1-year-old were excluded because SIPA scores have not been validated in this age group.
Intervention	ABC scores were calculated based on: penetrating mechanism, positive FAST, systolic blood pressure (SBP) <90, and heart rate (HR) >120. Age-adjusted ABC scores (ABC-S) were calculated by substituting SIPA for HR and SBP. Using a ROC, the authors simultaneously maximized sensitivity and specificity and defined optimal cut-offs for lactate at >3.5 and base deficit (BD) >−8.8. ABCD scores were calculated by combining penetrating mechanism, positive FAST, SIPA, lactate, and BD. The sensitivity, specificity, and accuracy of each score were calculated based on the need for MT
Outcomes	Need for massive transfusion

Study	**The shock index, pediatric age-adjusted (SIPA) enhanced: Prehospital and emergency department SIPA values forecast transfusion needs for blunt solid organ injured children Phillips 2020**

Study type	A retrospective review of two cohorts
Number of studies/ number of participants	N=477 (massive transfusion: n=31)
Countries and Settings	Children's Hospital Colorado (CHCO), American College of Surgeons verified level-1 pediatric trauma center in Colorado
Funding	No grant funding was used to support this research.
Duration of study	Between 2009 and 2019
Age, gender, ethnicity	Age [median (IQR)]: blood transfused: 9 (4-13); no blood transfusion 11 (7-14) Gender (% M): not reported Ethnicity: not reported
Patient characteristics	All children ages 1 to 18 years who were admitted to Children's Hospital Colorado (CHCO) between 2009 and 2019 with a diagnosis of BLSI. Children who did not require inpatient admission and those who died within 6 hours of their injury were excluded.
Intervention	The authors calculated SIPA in the prehospital setting and on ED arrival. They performed a univariable logistic regression for SIPA predicting the need for blood transfusion, and a multivariable logistic regression analysis adjusting for ISS, GCS, intubation in the field, positive FAST, and elevated SIPA. Using a receiver operator characteristic (ROC) curve, the authors defined optimal cut points for change in SIPA for stratified age groups (1e6 years, 7e12 years, and >13 years old) and performed a linear regression analysis to determine whether a significant association between SIPA and blood transfusion exists. Following the findings from the SIPA analysis, ROC curve cutoffs with area under the curve (AUC) calculations were generated for each stratified age group to determine the optimal prehospital and ED SIPA values that could alert clinicians of a BLSI at risk for both blood transfusion and mortality.
Outcomes	The need for blood transfusion

Study	**Shock Index as a Predictor of Morbidity and Mortality in Pediatric Trauma Patients Strutt 2019**
Study type	A cohort study

Number of studies/ number of participants	N=28741 (blood transfusion: n=397)
Countries and Settings	National Trauma Data Bank (NTDB), American College of Surgeons (Chicago, Ill).
Funding	This study was granted exemption status of Children's Hospitals and Clinics of Minnesota Institution Review Board because the data set contained deidentified patient information
Duration of study	Year 2010
Age, gender, ethnicity	Age [median (IQR)]: 9 (4-12) Gender (% M): 64.4% Ethnicity (%): White: (53.54%); African American: 18.34%; Hispanic: 17.39%; Asian: 2.19% ; Other: 8.54%
Patient characteristics	The inclusion criteria were traumatically injured patients younger than 15 years. Patients transferred from another institution, patients dead on arrival, patients with burn injuries, patients with missing data on presentation (HR, SBP, GCS, and Injury Severity Score [ISS]), and patients with data that were considered inconsistent with signs of life (HR <30 beats/min and SBP <60mmHg) were excluded.
Intervention	The aim was evaluate the utility of age-adjusted SI to predict negative outcomes in pediatric trauma. Elevated SI was defined as high normal heart rate divided by low-normal blood pressure for age.
Outcomes	The primary outcome was mortality in the ED or hospital. Secondary outcomes were need for a blood transfusion, ventilation, any OR/IR procedures, and ICU stay.

Esclusi

1	Hu GW, Lang HL, Guo H, Wu L, Zhang P, Kuang W, Zhu XG. A risk score based on admission characteristics to predict progressive hemorrhagic injury from traumatic brain injury in children. Eur J Pediatr. 2017 Jun;176(6):689-696. doi: 10.1007/s00431-017-2897-9. Epub 2017 Mar 25. PMID: 28343321.	OUT OF SCOPE

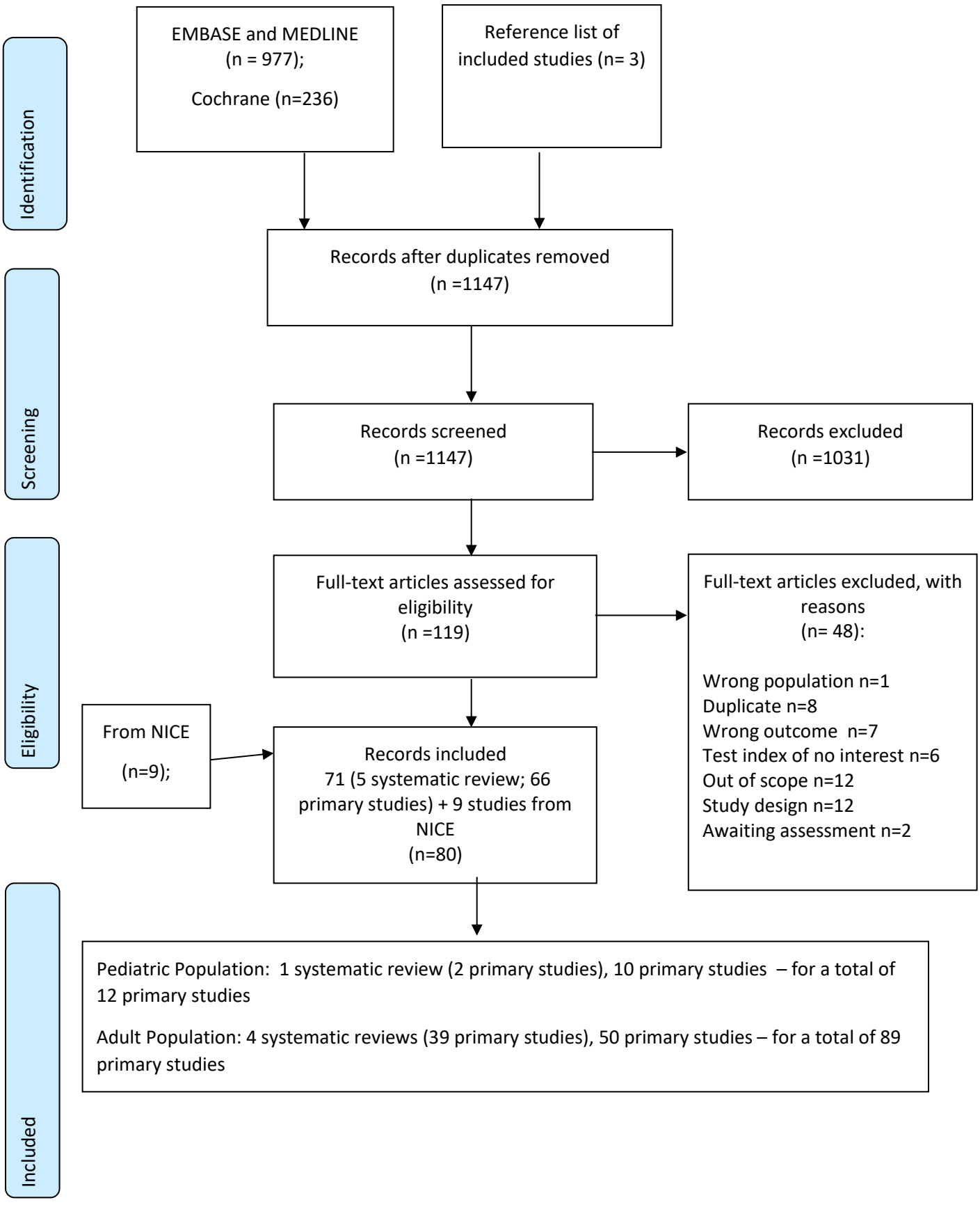
CQ13. Strumenti per predire l'emorragia critica

Appendice C – Sintesi dell'evidenza

Popolazione Adulta

Selezione Degli Studi

Figure 1. Flow Chart of study selection



Score inclusi predittivi per MT o TIC

E' stata effettuata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline e Cochrane CENTRAL. Sono stati individuati 87 primary studies nella popolazione adulta (3 systematic reviews (37 primary studies), 50 primary studies). Nella popolazione adulta, sono stati individuati 28 score non validati e 24 score validati comprensivi di tutte le varianti (i.e., cut offs), di cui 19 per indentificare la trasfusione massiva trasfusioni massive (MT- Massive Transfusion or need for blood trasfusion) e 5 per identificare la coagulopatia (TIC- Trauma Induced Coagulopathy) (**Tabella 1**). Le caratteristiche dei principali score sono ripprtate in **Tabella 2** e un sommario di tutti gli score validati per numero di studi e partecipanti è riportato in **Tabella 3**.

Tabella 1. Score validati e non validati

	Study Author	**Year**	**Validated test**	**Unvalidated test**
1	Afshari et al.	2019	TASH score	
2	Alimohammadi et al.	2017	ETS score	
3	Ardegh et al.	2001	ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)	
4	Arlsan et al.	2015	Shock index	
5	Barnes et al.	2018	Modified Schok Index	
6	Belanger-Quintana 2019	2019	ABC score	
			TASH score	
7	Baker et al.	2011		Baker model (SBp <90=1, HR>120=1, GCS < 9=1, High risk injury =1,(ventral chest trauma, abdominal trauma, MVC, penetrating torso trauma)
8	Brockamp et al.	2012	ABC score	
			Larson score	
			Schreiber score	
			Vandromme score	
			Prince of Wales/Rainer	
			TASH score	
9	Calcutt et al.	2011	Cincinnati individual tansfusion trigget (CITT) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C) 6 hours	prince of Walse + lactate (max score 11 pts); Prince of Walse (base deficit replaced by lactate) (max score 10 pts)
10	Calcutt et al.	2016	MTS (massive tranfsusion score 6 hours) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6)	
			revised MTS (massive transfusion score) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C)	
11	Calcutt et al.	2013	MTS (massive tranfsusion score) (SBp <90, Hb <11, INR > 1.5, Base deficiti ≥6, Positive FAST, penetrating mechanism)	
12	Campos-Serra et al.	2018	ABC score	
			Shock Index	
			ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic	

	Study Author	Year	Validated test	Unvalidated test
			blood pressure and the diastolic blood pressure.)	
13	Cancio et al.	2008		RTS (SBP, Respiratory Rate, GCS)
14	Chaochankit et al.	2018	ABC score	ABC score + lactate
15	Choi et al.	2017	Prince of Wales/Rainer	Prince of Walse + lactate (max score 11 pts); Prince of Walse (base deficit replaced by lactate) (max score 10 pts)
16	Cornero et al.	2020	Milano score (max score 9 points)	
17	Cotton et al.	2010	ABC score	
18	David et al.	2017	Shock Index	
			Shock Index	
			TASH score	
			TASH score	
19	De Jong	2016	TASH score	
20	Eastridge et al.	2010		Modified field triage score (SBP < 100, GCS <8)
21	El Menyar et al.	2019a		FASYLA score (FAST(0=negative, 1=positive), Shock Index (SI) (0= 0.50-0.69, 1 =0.70-0.79, 2 = 0.80-0.89, 3=> 0.90), and initial serumLActate (0= <2.0, 1=2.0-4.0, 2>=4.0mmol/l).)
			Revised assessment of Bleeding and Transfusion (RABT) Score	
22	El Menyar et al.	2019b	Shock Index, ABC score	
23	El Menyar et al.	2019c	Shock Index	
24	El Menyar ey al.	2018	Shock Index	
25	Figueiredo et al.	2018	Shock Index	
26	Fligor et al.	2016	Shock Index	
27	Frohlich et al.	2016	Shock Index	
28	Galvagno et al.	2015		Algorithm including age, sex, prehospital shock index, admission HR, SpHb and SpO
29	Hanna et al.	2020	ABC score	
			Revised assessment of Bleeding and Transfusion (RABT) Score	
30	Horst et al.	2020	ABC score	modified TICCS
			Larson score	
			Prince of Wales/Rainer	
			ETS score	
			TASH score	
31	Hsu et al.[28]	2013		Hsu score (Base deficit greater than 5 and either INR of 1.5 or greater or hemoperitoneum)
32	jenkins et al.	2017	Shock Index	
			ROPE Pulse Rate Over Pressure	
33	Joseph et al.	2018	ABC score	
			Revised assessment of Bleeding and Transfusion (RABT) Score (FAST result (positive = 1), SI ([1 = 1), pelvic fracture (present = 1), and MOI (penetrating = 1)	
34	Juste 2020	2021	Shock index	
35	Kovar 2019	2019	Shock Index	ABC score (without FAST)

	Study Author	Year	Validated test	Unvalidated test
			EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS)	
36	Krumrei et al.	2012	TASH score	
			McLaughlin score	
			ABC score	
37	Kuhne et al.	2008	ETS score	
38	Larson et al.	2010	Larson score Any 2 or more of the following: Hemoglobin <11 g/dL, SBP < 110 mm Hg, HR > 110 bpm, Base Deficit ≤6 mmol/L	
39	Lee young et al.	2020	Shock Index	SIA (Shock Index*age)
				QSOFA score (qSOFA score was calculated as the sum of 1 point each for SBP ≤100 mmHg, GCS ≤14, and RR ≥22 breaths/min)
				Reverse shock index multiplied by the Glasgow Coma Scale score (rSIG) (BP/HR* GCS)
40	Lui Chun et al.	2018	TASH score	DMBT dynamic MBT score (similar to TASH and PHW, plus hemoglobin drop as a predictor variable)
			Prince of Wales/Rainer	
41	Maegele et al.	2011	TASH score	
			TASH score	
42	McLaughlin et al.	2008	McLaughlin score	
43	McKinley et al.	2016		Shock volume (Initially incremental SV measurements (SVi) were made by calculating average SIth(i) values between two adjacent time points, and by multiplying the incrementally averaged SIth(i) by the duration of the corresponding time interval)
44	Mitra et al	2011	COAST (Coagulopathy of Severe Trauma Score - acute traumatic coagulopathy entrapment (1 point); body temperature (< 358C: 1 point, < 328C: 2 points); SBP (< 100 mm Hg: 1 point, < 90 mm Hg: 2 points); pelvic content or abdominal injury (1 point), and chest decompression (1 point).	
45	Mitra et al.	2012	TASH score	
			ABC score	
			Prince of Wales/Rainer	
46	Mina et al.	2013		Mobile application modeling (mechanism of injury, HR, SBP, and BD)
47	Moore et al.	2007		Moore model (SBP in first hour, pH min during 1st hour, ISS ≤ 25=0, > 25 = 1)
48	Moore et al.	2017	Shock Index	
			ABC score	
49	Mutschler et al.	2013	Shock Index	
50	Nunez et al.	2009	McLaughlin score	
			TASH score	
			ABC score (Penetrating mechanism (0 = no, 1 = yes), ED SBP of 90	

	Study Author	Year	Validated test	Unvalidated test
			mm Hg or less (0 = no, 1 = yes), ED HR of 120 bpm or greater (0 = no, 1 = yes), Positive FAST (0 = no, 1 = yes)	
51	Ogura et al.	2014	TBSS	
			ABC score	
			TASH score	
52	Ogura et al.	2015	TBSS	
			TASH score	
53	Ogura et al.	2016	TBSS	Modified TBSS (age, sonography, pelvic fracture, serum lactate and systolic blood pressure on arrival)
			TASH score	
54	Ogura et al.	2018	TBSS	
			ABC score	
			Shock Index	
55	Ohmori et al.	2017	ABC score	
			Prince of Wales/Rainer	
			TASH score	
56	Parimi et al.	2016	Shock Index	
57	Park et al.	2019		Injury Severity Score
				RTS (SBP, Respiratory Rate, GCS)
58	Pommerening et al.	2015	Mclaughlin score	Clinical gestalt
			ABC score	
			TASH score	
59	Poon et al.	2012	TASH score	
			ABC score	
			Prince of Wales/Rainer	
60	Pottecher et al.	2016	Shock Index	
61	Prichayudh et al.	2020	ABC score	Class-4 Hemorrhage Unresponsive to Lactated Ringer's (CHULA) - 1) a patient with clinical sign of class-4 hemorrhage; 2)not responding to one to two liters of Lactated Ringer's bolus; 3) had suspected ongoing bleeding.
62	Rainer et al.	2011	Prince of Wales/Rainer	
63	Rau et al.	2016	Shock Index	
64	Ruchholtz et al.	2006	ETS score	
65	Schreiber et al.	2007	Schreiber score (Hb ≤ 11, International normilized ratio > 1.5, penetrating trauma)	
66	Schroll et al.	2018	ABC score	
			Shock Index	
67	Shackelford et al.	2015		Algorithm including triage vital signs, pulse oximetry features, and laboratory values (C1, Cartridge 1 (hematocrit, glucose, potassium, chloride, and bicarbonate); C2, Cartridge 2 (PT, INR); C3, Cartridge 3 (lactate); pulse oximetry features for 15 minutes)
68	Sharma et al.	2019	Modified Shock Index	Pulse Pressur/ Heart rate
			Shock Index	

	Study Author	Year	Validated test	Unvalidated test
69	Swerts et al.	2020	Trauma-Induced Coagulopathy Clinical Score (TICCS)	Trauma-Induced Coagulopathy Clinical Score (TICCS). BE - (+ 3 points if BE < − 5 and + 3 points in case of a positive FAST)
			TASH score	
70	Terceros-Almanza et al.	2019	ABC score	
			ETS score	
			Prince of Wales/Rainer	
			Larson score	
			TASH score	
			Shock Index	
71	Terceros-Almanza et al.	2017	Shock Index	
			Modified Shock Index	
72	Thorn et al.	2019	COAST - Coagulopathy of Severe Trauma Score	
73	Tonglet et al.	2017	Trauma-Induced Coagulopathy Clinical Score (TICCS)	
74	Tonglet et al.	2014	TICCS Trauma induced coagulopathy clinical score (Severity [ED resuscitation room 2 points*, extent of body injury (torso, abddominal or the pelvic ring region = 2, head =1, each extremity = 1), SBP < 90 = 5)	
75	Umemura et al.	2016	TASH score	
			ABC score	
76	Vandromme et al. (J Trauma. 2011)	2011a	Shock Index (heart rate divided by systolic blood pressure) (original J Trauma. 2011)	
77	Vandromme et al.	2011b	Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)	
78	Wade et al.	2008		Wade model (SBP, HR, Ph, Hematocrit)
79	Weaver et al.	2016		Code red attivation (SBP < 90, Blood pressure failure to repsond to bolus intraveneous fluid)
80	Wang et al.	2019	Shock Index (Prehospital)	
			Modified Shock Index (Prehospital)	
81	Wang et al.	2016	Early Blood Transfusion Needs Score- (age, type of injury, pulse, systolic blood pressure, GCS)	
82	Wei et al.	2017	Prediction scoring scheme	
83	Wei et al.	2020	Prediction scoring scheme (0-8 points) - type of trauma, injury severity score, heart rate, hemoglobin, prothrombin time, fibrinogen, and base excess	
84	Wu et al.	2019	Shock Index	
85	Yang et al.	2021	Shock Index	Bleeding risk idnex BRI (PPG, ECG waveforms, oximetry SpO2, SBP)
			ABC score	RTS (SBP, Respiratory Rate, GCS)
86	Yucel et al.	2006	TASH score	
87	Yumoto et al.	2014	ABC score	Yumoto New screening method (schok index ≥ 1, Base Excess ≤ 3, positive FAST results)

	Study Author	Year	Validated test	Unvalidated test
88	Peltan et al.	2015	PACT 1 - (Prediction of Acute Traumatic Coagulopathy)	
89	Peltan et al.	2016	PACT 2- (Prediction of Acute Traumatic Coagulopathy) COAST - Coagulopathy of Severe Trauma Score	

Tabella 2. Componenti dei principali Score validati

	TASH	ABC (ED 1st value)	CITT (ED 1st value)	Original MTS (ED 1st value)	Revised MTS (ED 1st value)	MTS_{3hour} (at 3 hours)	MTS_{6hour} (at 6 hours)	Shock Index	Prince of Wales/Rainer**	TBSS***	Larson Score	McLaughlin****	ETS score	Schreiber	Vandromme	COAST- Coagulopathy of Severe Trauma Score	ROPE Pulse Rate Over Pressure Evaluation	EMS-G scoring system	TICCS Trauma induced coagulopathy clinical score	Early Blood Transfusion Needs Score-	Milano score
total score	max 28 points	any two or more of the following:						different cutoffs used - typically >0.9–1	Score of ≥6 (maximum value 20)	Score of >14 (original study >15, maximum value 57)	any two or more of the following:	log (p / [1 − p]) = 1.576 + (0.825*SBP) + (0.826 * HR) + (1.044* Hct) +	Score of≥3 (maximum value, 9.5)	**0.5**	Score of≥3 (maximum value 5)			cut off = 3	Cut off 10 - 14		Max score = 9
SBP (mm Hg)	<100 (4 pts); 100 to <120 (1 pt)	<90	<90	<90	<90	<90	<90	HR/SBP	<90 =3 pts	after 1 L Cristalloid: < 90 (11 pts); 90-99 (8 pts); 100-109 (4 pts)	<110	< 110	90–120 (1.5 pts); SBP: 0–90 (2.5 pts)		< 110 = 1	< 100 mm Hg (1 pt); < 90 mm Hg (2 pts)	HR / (SBP - DBP)	shock index ≥ 0.9=	SBP < 90 = 5)		SBP ≤ 70 mmHg SR (0-1 points)
HR (bpm)	>120 (3 pts)	>=120		>=120				HR/SBP	>=120 =1pt		>110	> 105 bpm			> 105 = 1		HR / (SBP - DBP)	shock index ≥ 0.9=2 points,			HR ≥ 120 bpm SR (0-1 points)
Positive FAST	included (3 pts)	included		included					included (2 pts)	included (3 pts per region, 6 regions total)			Free fluid in abdominal ultrasound (2 pts)								Included (0-1 points)
Accident/Penetrating Mechanism		included		included									Admission from scene of accident (1 pt)	penetrating trauma				extremity injurye = 1 point, penetrating mechanism =2 points,			Penetrating trauma - present
Base Deficit (mmol/L)	6 to 10 (4 pts) 2 to 6 (3 pts) < 2 (1 pt)		>=6	>=6	>=6	>=6	>=6		>5		<=6										
INR			>1.5	> 1.5	> 1.5	> 1.5	> 1.5							> 1.5	> 1.5 =1						
Hemoglobin (g/dL)	<7 (8 pts); 7 to <9 (6 pts); 9 to <10 (4 pts); 10 to <11 (3 pts); 11 to <12 (2 pts)		< 11	< 11	< 11	< 11	< 11		< = 7 (10 pts) 7.1-10 (1 pt)		<11			Hb ≤ 11	≤ 11=1						
Temperature (°C)			<35.5		<35.5	<35.5	<35.5									< 358C (1 pt); < 328C (2 pts)					
Long Bone Fracture or Complex Pelvis Fracture / Body injury	included (AIS 3/4 (3 pts); AIS 5 (6 pts)								dislaced pelivic fracture =1 pt	pelvic fracture: Type C (9 pts), Type B (6 pts), Type A (3 pts)			Pelvic ring disruption (1.5 pts)						torso, abddominal or the pelvic ring region = 2, head =1, each extremity = 1)		Pelvic fractire (0-1 points)
Male	included (1 point)																				
PH												< 7.25									
Hct												< 32%									
Age (years)										>=60 (6points)			20–60 (0.5 pts); >60 (1.5 pts)								
Lactate mmol/L										>=7.5 (12 pts); 5-7.4 (8 pts); 2.5-4.9 (4 pts)					Lactate ≥5=1						
Coagulopathy																acute traumatic coagulopathy entrapment (1 pt)					PTT Partial Thromboplastin Time ≥ 40.0 sec) (0-1 points)
Abdominal interventions or others																pelvic content or abdominal injury (1 pt), and chest decompression (1 pt).			ED resuscitation room 2 points*,		Hemothorax (0-1 points); tranex (0-1 points); limb amputation (0-1 points)
GCS																		GCS≤ 8 =3 points			GCS 3 pre hospital (points 0-1)

Tabella 3. Sommario degli score validati per numero di studi e partecipanti (MT, TIC)

Test	Studies	Participants
1 Larson score (cut off > 1)	1	479
2 Larson score (cut off = 1.5)	2	5539
3 ABC score (cut off > 0)	1	479
4 ABC score (cut off ≥ 0.5)	2	5330
5 ABC score (cut off > 1)	4	986
6 ABC score (cut off ≥ 2)	19	8607
7 Prince of Wales/Reiner (cut off > 1.5)	1	129
8 Prince of Wales/Rainer (cut off > 2)	3	1193
9 Prince of Wales/Rainer (cut off ≥ 2.5)	1	5147
10 Prince of Wales/Rainer (cut off ≥ 6)	4	5209
11 TBSS score (cut off ≥ 10)	1	264
12 TBSS score (cut off ≥14)	1	300
13 TBSS score (cut off ≥ 17)	2	264
14 TASH score (cut off not reported)	4	6417
15 TASH score (cut off >5)	1	153
16 TASH score (cut off ≥ 6)	2	714
17 TASH score (cut off ≥ 6.5)	1	131
18 TASH score (cut off > 7)	1	300
19 TASH score (cut off ≥ 8)	2	598
20 TASH score (cut off ≥ 8.5)	1	5147
21 TASH score (cut off ≥10)	1	910
22 TASH score (cut off >16)	7	3975
23 TASH score (cut off ≥18)	1	1234
24 McLaughlin score	4	373
25 Schreiber score (cut off ≥ 0.5)	1	5147
26 Vandromme score (cut off ≥1.5)	1	5147
27 Vandromme score (cut off ≥ 3)	1	0
28 Prediction scoring scheme (cut off = 4)	2	146
29 ETS score (cuf off ≥ 2.5)	1	479

30 ETS score (cut off ≥ 3)	2	1274
31 ETS score (cut off ≥ 4.8)	1	189
32 RABT	2	1018
33 ROPE Pulse Rate Over Pressure Evaluation (cut off ≥ 3)	2	0
34 EMS-G scoring system (cut off ≥2)	2	153354
35 TICCS Trauma induced coagulopathy clinical score (cut off ≥ 10) for Damage Control Resuscitation	1	0
36 TICCS Trauma induced coagulopathy clinical score (cut off ≥ 12) for Damage Control Resuscitation	1	0
37 Early Blood Transfusion Needs Score (cut off >5)	1	24303
38 Modified Shock Index (cut off <1.15)	1	2490
39 Modified Shock Index (cut off 1.28)	1	1007
40 Modified Shock Index (cut off 1.46)	1	279
41 Modified Shock Index (cut off not reported)	1	0
42 Shock Index (cut off 0.06)	1	82
43 Shock Index (cut off > 0.8)	4	2734
44 Shock Index (cut off 0.81)	1	8710
45 Shock Index (cut off > 0.9)	6	7828
46 Shock Index (cut off 0.91)	1	1007
47 Shock Index (cut off >0.933, prehospital)	1	2557
48 Shock Index (cut off <0.95)	1	2490
49 Shock Index (cut off >0.967, prehospital)	1	2557
50 Shock Index (cut off>1)	9	50162
51 Shock Index (cut off 1.11)	1	279
52 Shock Index, age adjusted (cut off <36.95)	1	2490
53 Shock Index (cut off not reported)	9	2857
54 PACT1	1	324
55 PACT 2	1	285
56 Milano score (cut off ≥ 6))	1	139
57 Shock Index (cutoff >0.9) for TIC	1	485
58 Shock Index (cut off 0.84) for TIC	1	1627
59 COAST (cut off ≥ 3) for TIC	3	1644

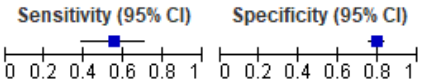
Sensibilità e specificità dei test predittivi per la MT

Score validati

1- Larson score

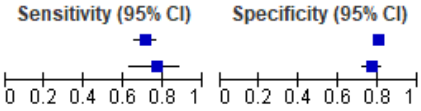
Larson score (cut off > 1)

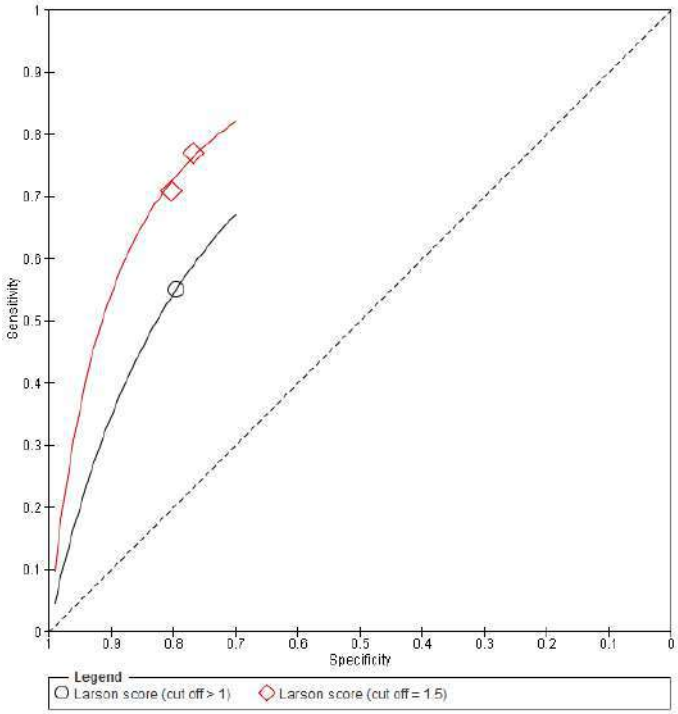
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Horst 2020	22	90	18	349	0.55 [0.38, 0.71]	0.79 [0.75, 0.83]



Larson score (cut off = 1.5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brockamp 2012	205	952	84	3906	0.71 [0.65, 0.76]	0.80 [0.79, 0.82]
Terceros-Almanza 2019	37	79	11	265	0.77 [0.63, 0.88]	0.77 [0.72, 0.81]

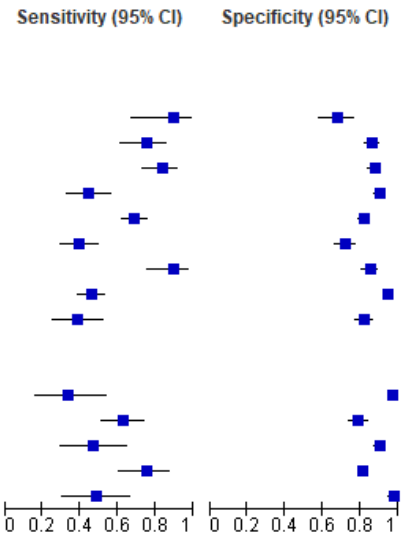




2- ABC score

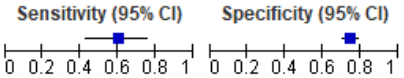
ABC score (cut off ≥ 2)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Belanger-Quintana 2019	0	0	0	0	Not estimable	Not estimable
Campos-serra 2018	0	0	0	0	Not estimable	Not estimable
Chaochankit 2018	0	0	0	0	Not estimable	Not estimable
Cotton 2010 (JHH cohort)	17	37	2	77	0.89 [0.67, 0.99]	0.68 [0.58, 0.76]
Cotton 2010 (PMH cohort)	42	44	14	272	0.75 [0.62, 0.86]	0.86 [0.82, 0.90]
Cotton 2010 (VUMC cohort)	60	55	12	386	0.83 [0.73, 0.91]	0.88 [0.84, 0.90]
El Menyar 2019	33	49	41	449	0.45 [0.33, 0.57]	0.90 [0.87, 0.93]
Hanna 2020	133	149	60	677	0.69 [0.62, 0.75]	0.82 [0.79, 0.85]
Joseph 2018	40	78	62	200	0.39 [0.30, 0.49]	0.72 [0.66, 0.77]
Krumrei 2012	34	50	4	285	0.89 [0.75, 0.97]	0.85 [0.81, 0.89]
Mitra 2012	89	60	106	979	0.46 [0.39, 0.53]	0.94 [0.93, 0.96]
Moore 2017	21	48	34	221	0.38 [0.25, 0.52]	0.82 [0.77, 0.87]
Ogura 2018	0	0	0	0	Not estimable	Not estimable
Pommerening 2015	0	0	0	0	Not estimable	Not estimable
Poon 2012	9	32	18	971	0.33 [0.17, 0.54]	0.97 [0.96, 0.98]
Prichayudh 2020	49	59	29	221	0.63 [0.51, 0.74]	0.79 [0.74, 0.84]
Schroll 2018	16	62	18	548	0.47 [0.30, 0.65]	0.90 [0.87, 0.92]
Yang 2021	34	257	11	1094	0.76 [0.60, 0.87]	0.81 [0.79, 0.83]
Yumoto 2014	16	5	17	221	0.48 [0.31, 0.66]	0.98 [0.95, 0.99]



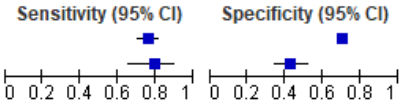
ABC score (cut off > 0)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Horst 2020	24	112	16	327	0.60 [0.43, 0.75]	0.74 [0.70, 0.79]



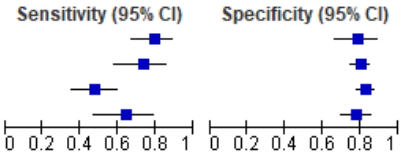
ABC score (cut off ≥ 0.5)

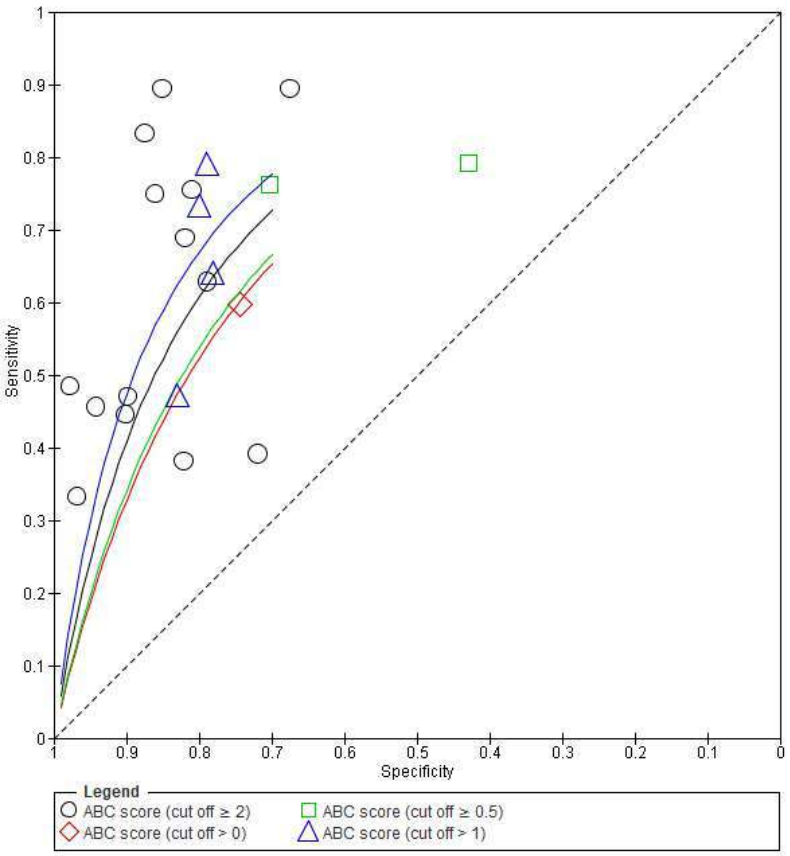
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brockamp 2012	220	1443	69	3415	0.76 [0.71, 0.81]	0.70 [0.69, 0.72]
Terceros-Almanza 2019	38	77	10	58	0.79 [0.65, 0.90]	0.43 [0.34, 0.52]



ABC score (cut off > 1)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ogura 2014	49	12	13	45	0.79 [0.67, 0.88]	0.79 [0.66, 0.89]
Ohmori 2017 (less than 65 year)	33	58	12	231	0.73 [0.58, 0.85]	0.80 [0.75, 0.84]
Ohmori 2017 (more than 65 years)	35	52	39	254	0.47 [0.36, 0.59]	0.83 [0.78, 0.87]
Umemura 2016	25	25	14	89	0.64 [0.47, 0.79]	0.78 [0.69, 0.85]

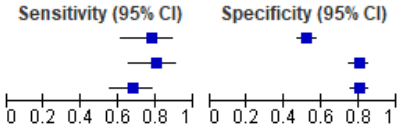



Sensitivity
Specificity
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Legend
ABC score (cut off ≥ 2)
ABC score (cut off ≥ 0.5)
ABC score (cut off > 0)
ABC score (cut off > 1)

3- Prince of Wales/Rainer

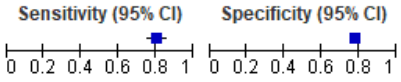
Prince of Wales/Rainer (cut off > 2)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Horst 2020	31	211	9	228	0.78 [0.62, 0.89]	0.52 [0.47, 0.57]
Ohmori 2017 (less than 65 year)	36	58	9	231	0.80 [0.65, 0.90]	0.80 [0.75, 0.84]
Ohmori 2017 (more than 65 years)	50	61	24	245	0.68 [0.56, 0.78]	0.80 [0.75, 0.84]



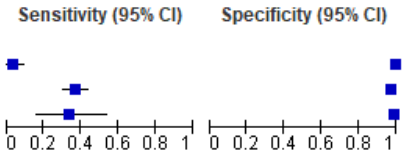
Prince of Wales/Rainer (cut off ≥ 2.5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brockamp 2012	233	1083	56	3775	0.81 [0.76, 0.85]	0.78 [0.77, 0.79]



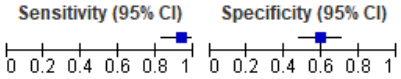
Prince of Wales/Rainer (cut off ≥ 6)

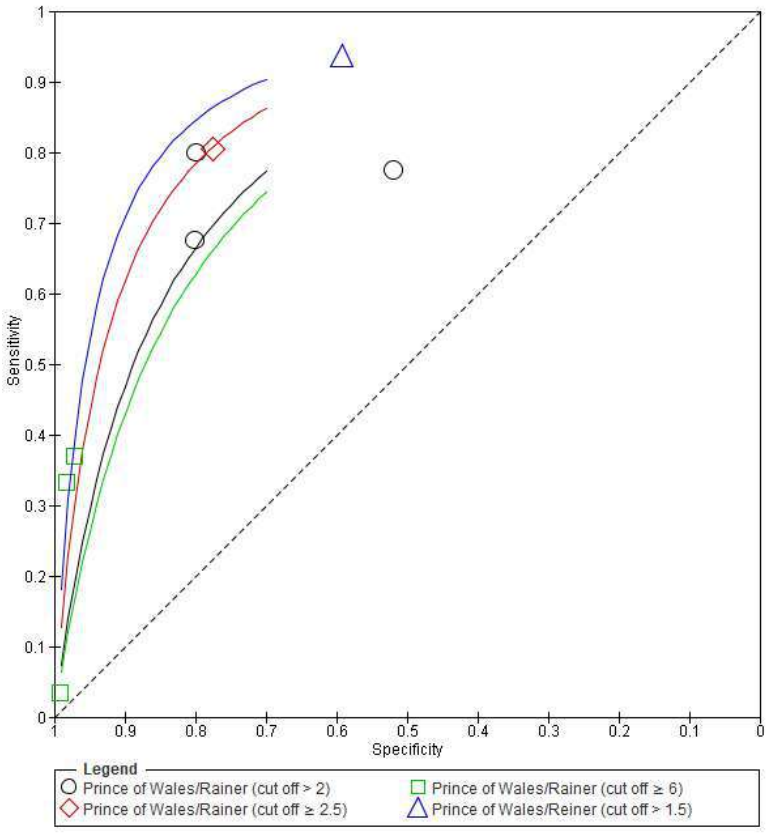
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Choi 2017	0	0	0	0	Not estimable	Not estimable
Lui Chun 2018	3	26	85	2831	0.03 [0.01, 0.10]	0.99 [0.99, 0.99]
Mitra 2012	72	30	123	1009	0.37 [0.30, 0.44]	0.97 [0.96, 0.98]
Poon 2012	9	18	18	985	0.33 [0.17, 0.54]	0.98 [0.97, 0.99]



Prince of Wales/Reiner (cut off > 1.5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Terceros-Almanza 2019	45	33	3	48	0.94 [0.83, 0.99]	0.59 [0.48, 0.70]

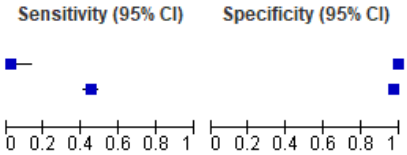




4- TASH

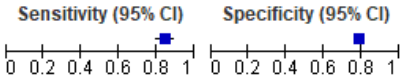
TASH score (cut off not reported)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Afshari 2019	0	0	0	0	Not estimable	Not estimable
Krumrei 2012	1	1	37	334	0.03 [0.00, 0.14]	1.00 [0.98, 1.00]
Maegele 2011	385	156	470	5033	0.45 [0.42, 0.48]	0.97 [0.96, 0.97]
Nunez 2009	0	0	0	0	Not estimable	Not estimable



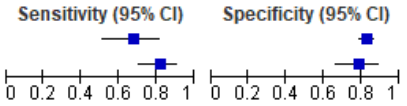
TASH score (cut off ≥ 8.5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brockamp 2012	244	1049	45	3809	0.84 [0.80, 0.88]	0.78 [0.77, 0.80]



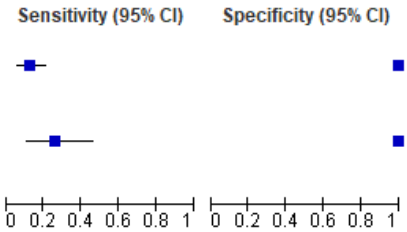
TASH score (cut off ≥ 8)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Horst 2020	27	77	13	362	0.68 [0.51, 0.81]	0.82 [0.79, 0.86]
Ogura 2014	51	12	11	45	0.82 [0.70, 0.91]	0.79 [0.66, 0.89]



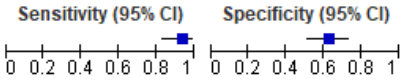
TASH score (cut off >16)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Belanger-Quintana 2019	0	0	0	0	Not estimable	Not estimable
Lui Chun 2018	11	11	77	2846	0.13 [0.06, 0.21]	1.00 [0.99, 1.00]
Ogura 2015	0	0	0	0	Not estimable	Not estimable
Pommerening 2015	0	0	0	0	Not estimable	Not estimable
Poon 2012	7	8	20	995	0.26 [0.11, 0.46]	0.99 [0.98, 1.00]
Swerts 2020	0	0	0	0	Not estimable	Not estimable
Yucel 2006	0	0	0	0	Not estimable	Not estimable



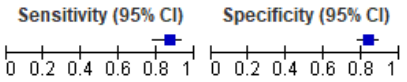
TASH score (cut off ≥ 6.5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Terceros-Almanza 2019	45	31	3	52	0.94 [0.83, 0.99]	0.63 [0.51, 0.73]



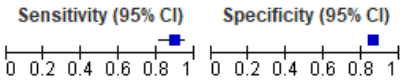
TASH score (cut off > 7)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ogura 2016	73	35	11	181	0.87 [0.78, 0.93]	0.84 [0.78, 0.88]



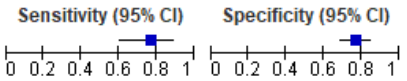
TASH score (cut off ≥ 10)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
De Jong 2016	84	114	10	702	0.89 [0.81, 0.95]	0.86 [0.83, 0.88]



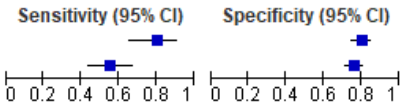
TASH score (cut off >5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Umemura 2016	30	26	9	88	0.77 [0.61, 0.89]	0.77 [0.68, 0.85]



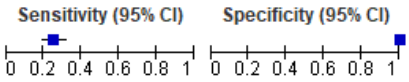
TASH score (cut off ≥ 6)

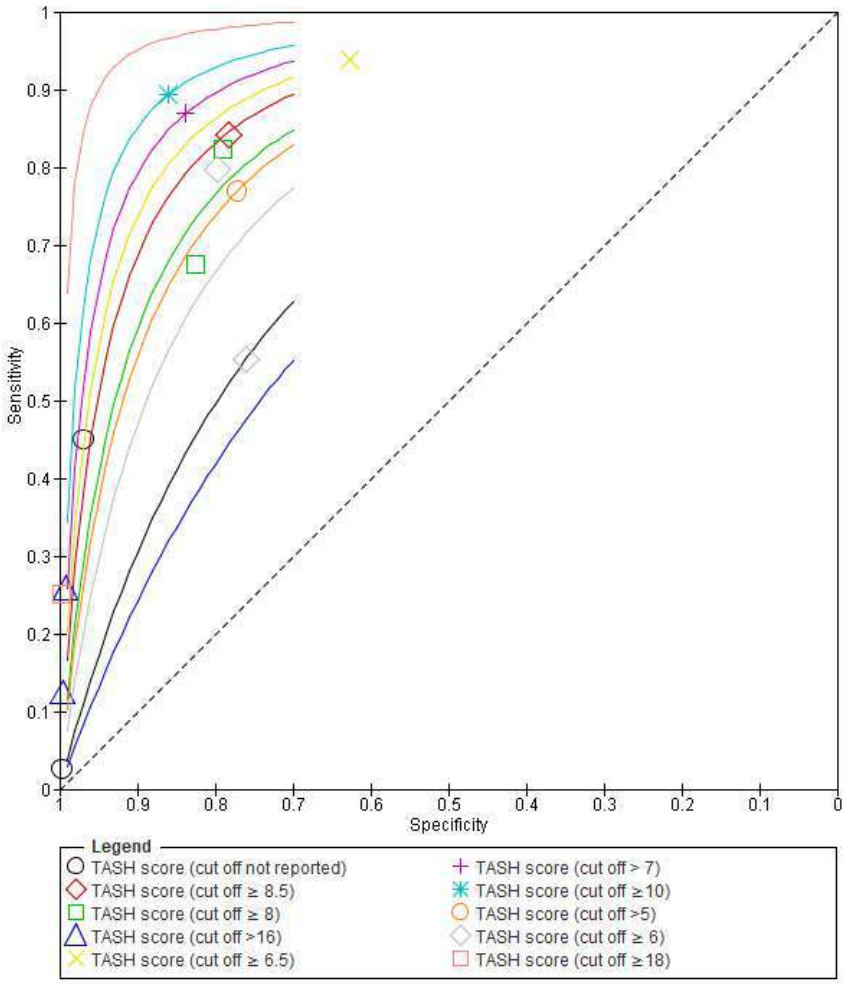
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ohmori 2017 (less than 65 year)	36	58	9	231	0.80 [0.65, 0.90]	0.80 [0.75, 0.84]
Ohmori 2017 (more than 65 years)	41	73	33	233	0.55 [0.43, 0.67]	0.76 [0.71, 0.81]



TASH score (cut off ≥ 18)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mitra 2012	49	2	146	1037	0.25 [0.19, 0.32]	1.00 [0.99, 1.00]

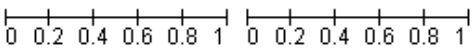




5- TBSS score

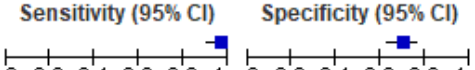
TBSS score (cut off ≥ 17)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ogura 2015	68	4	17	175	0.80 [0.70, 0.88]	0.98 [0.94, 0.99]		
Ogura 2018	0	0	0	0	Not estimable	Not estimable		



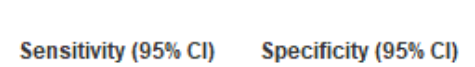
TBSS score (cut off ≥ 10)

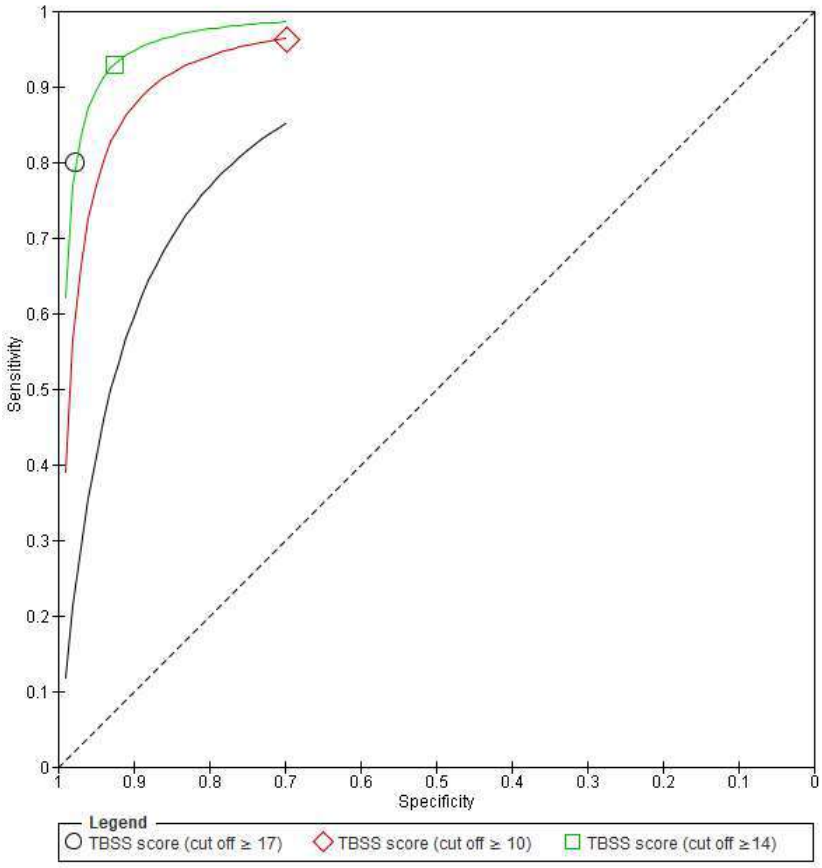
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ogura 2015	82	54	3	125	0.96 [0.90, 0.99]	0.70 [0.63, 0.76]		



TBSS score (cut off ≥ 14)

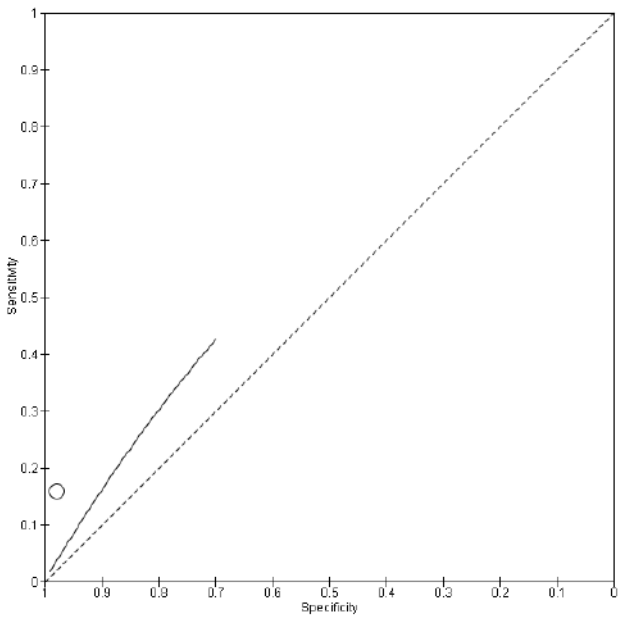
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ogura 2016	78	16	6	200	0.93 [0.85, 0.97]	0.93 [0.88, 0.96]		





6- McLaughlin score

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Krumrei 2012	6	7	32	328	0.16 [0.06, 0.31]	0.98 [0.96, 0.99]
McLaughlin 2008	0	0	0	0	Not estimable	Not estimable
Nunez 2009	0	0	0	0	Not estimable	Not estimable
Pommerening 2015	0	0	0	0	Not estimable	Not estimable



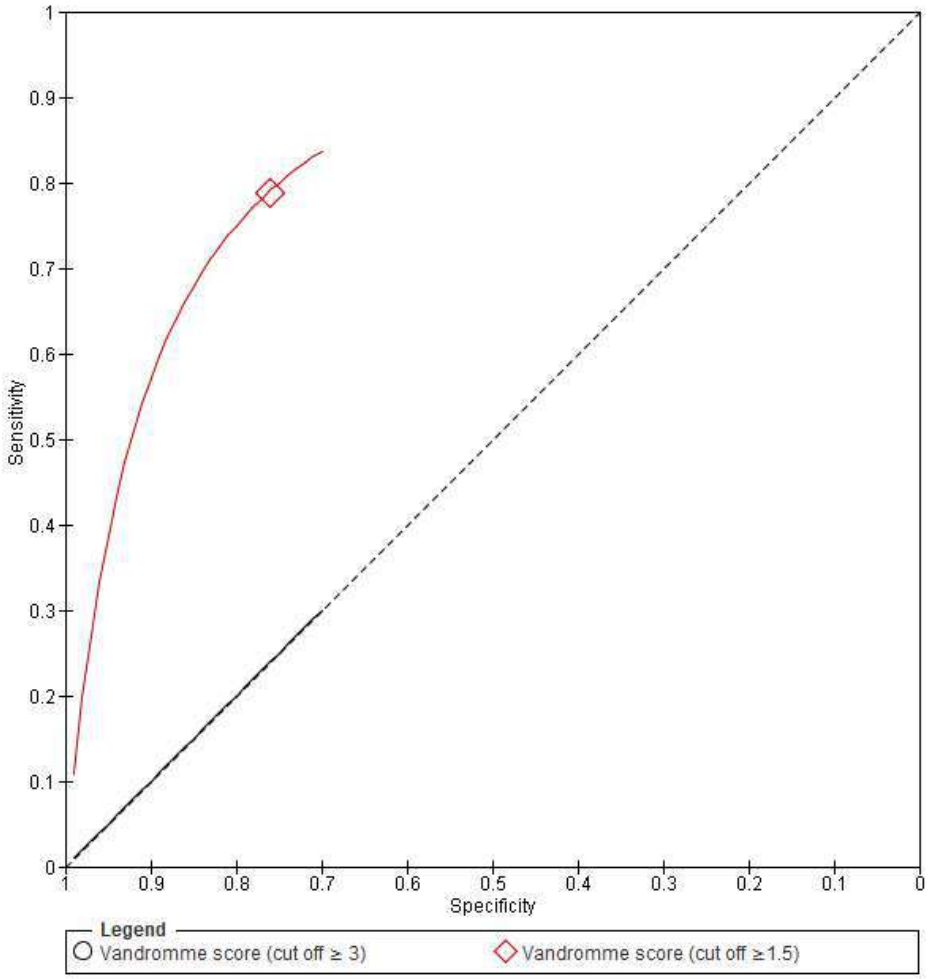
7- Vandromme score

Vandromme score (cut off ≥ 3)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Vandromme 2011	0	0	0	0	Not estimable	Not estimable	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

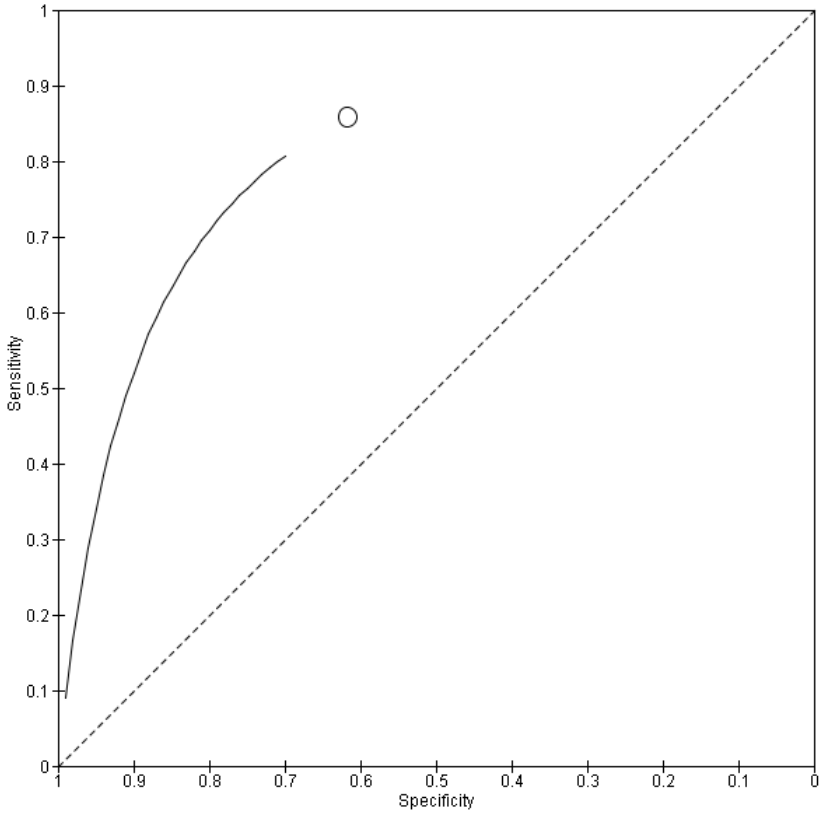
Vandromme score (cut off ≥ 1.5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Brockamp 2012	228	1156	61	3702	0.79 [0.74, 0.83]	0.76 [0.75, 0.77]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1



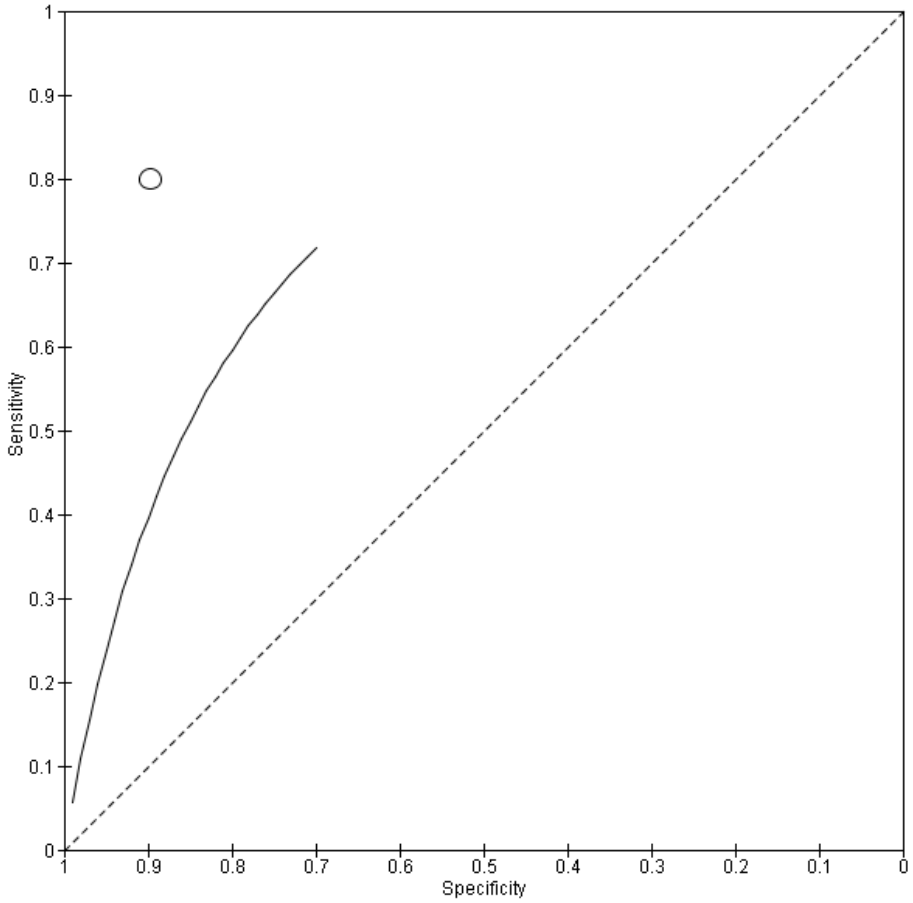
8- Schreiber score

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Brockamp 2012	248	1861	41	2997	0.86 [0.81, 0.90]	0.62 [0.60, 0.63]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1



9- Prediction scoring scheme

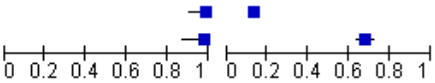
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Wei 2017	0	0	0	0	Not estimable	Not estimable		
Wei 2020	8	14	2	122	0.80 [0.44, 0.97]	0.90 [0.83, 0.94]		



10- ETS score

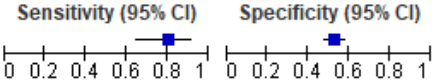
ETS score (cut off ≥ 3)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Alimohammadi 2017	53	637	1	102	0.98 [0.90, 1.00]	0.14 [0.11, 0.17]
Kuhne 2008	39	141	1	300	0.97 [0.87, 1.00]	0.68 [0.63, 0.72]



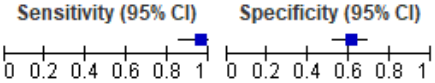
ETS score (cuf off ≥ 2.5)

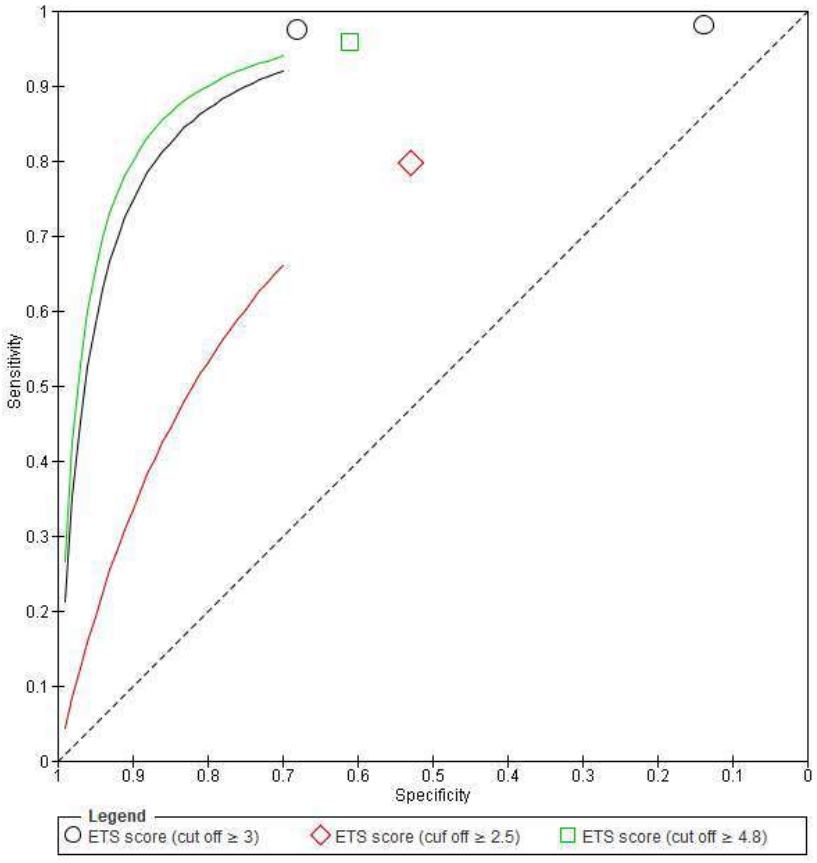
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Horst 2020	32	206	8	233	0.80 [0.64, 0.91]	0.53 [0.48, 0.58]



ETS score (cut off ≥ 4.8)

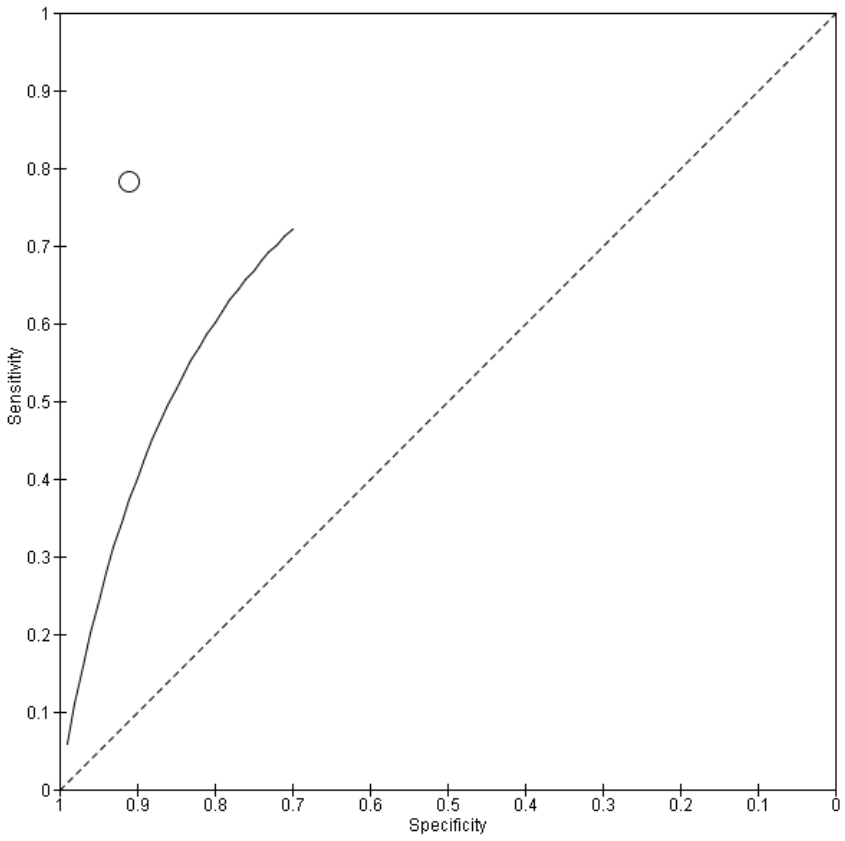
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Terceros-Almanza 2019	46	55	2	86	0.96 [0.86, 0.99]	0.61 [0.52, 0.69]





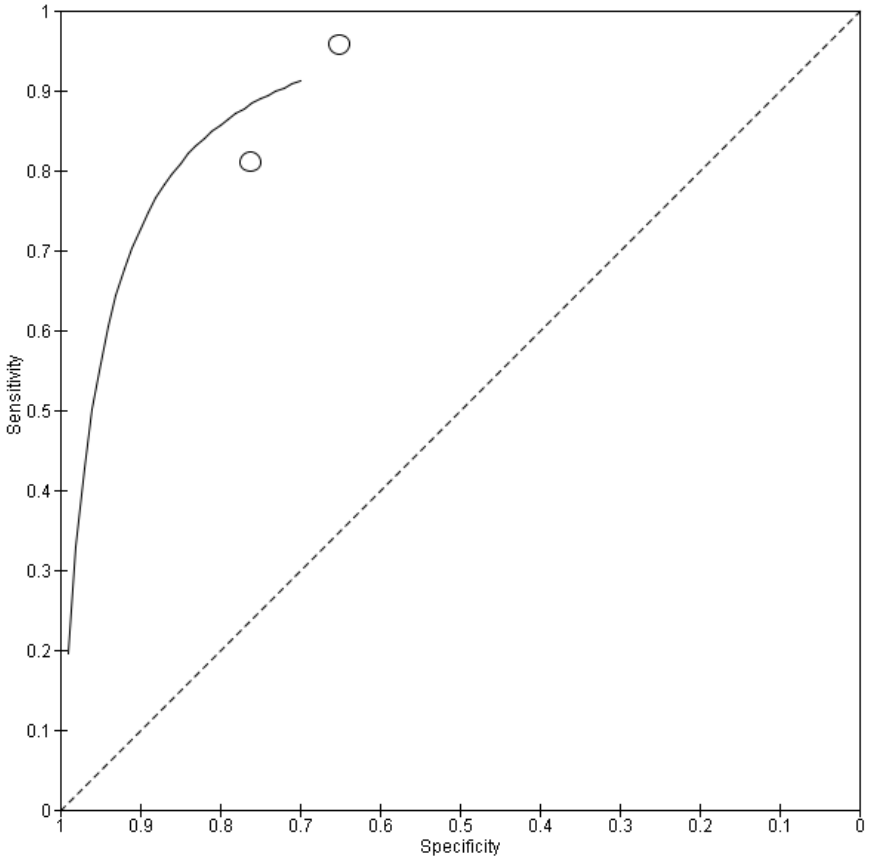
11- RABT

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
El Menyar 2019	0	0	0	0	Not estimable	Not estimable		
Hanna 2020	151	74	42	751	0.78 [0.72, 0.84]	0.91 [0.89, 0.93]		



12- EMS-G scoring system

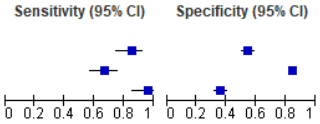
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kovar 2019 a	90	234	4	436	0.96 [0.89, 0.99]	0.65 [0.61, 0.69]		
Kovar 2019 b	7425	34138	1730	109297	0.81 [0.80, 0.82]	0.76 [0.76, 0.76]		



13- Shock index

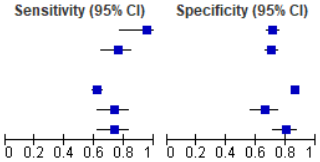
Shock Index (cut off > 0.8)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Campos-serra 2018	0	0	0	0	Not estimable	Not estimable
El Menyar et al. (id 27)	63	226	11	272	0.85 [0.75, 0.92]	0.55 [0.50, 0.59]
Lee Young 2020	78	242	39	1268	0.67 [0.57, 0.75]	0.84 [0.82, 0.86]
Terceros-Almanza 2019	46	311	2	176	0.96 [0.86, 0.99]	0.36 [0.32, 0.41]



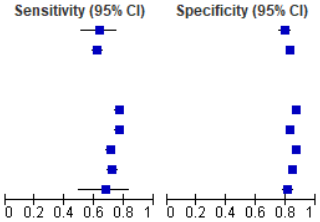
Shock Index (cut off > 0.9)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
David 2017	21	134	1	329	0.95 [0.77, 1.00]	0.71 [0.67, 0.75]
El Menyar et al. (id 27)	56	147	18	351	0.76 [0.64, 0.85]	0.70 [0.66, 0.74]
El Menyar et al. (id 30)	0	0	0	0	Not estimable	Not estimable
Figueiredo 2018	468	791	287	4856	0.62 [0.58, 0.65]	0.86 [0.85, 0.87]
Juste 2021	55	37	20	72	0.73 [0.62, 0.83]	0.66 [0.56, 0.75]
Juste 2021 in hospital	56	22	20	87	0.74 [0.62, 0.83]	0.80 [0.71, 0.87]



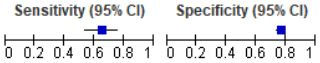
Shock Index (cut off>1)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
El Menyar et al. (id 27)	47	104	27	394	0.64 [0.52, 0.74]	0.79 [0.75, 0.83]
Figueiredo 2018	468	960	287	4687	0.62 [0.58, 0.65]	0.83 [0.82, 0.84]
Jenkins 2017	0	0	0	0	Not estimable	Not estimable
Mutschler 2013	0	0	0	0	Not estimable	Not estimable
Parimi et al. (≥10 U pRBCs/24 h; admission SI)	622	1278	186	8550	0.77 [0.74, 0.80]	0.87 [0.86, 0.88]
Parimi et al. (≥10 U pRBCs/24 h; prehospital SI)	622	1671	186	8157	0.77 [0.74, 0.80]	0.83 [0.82, 0.84]
Parimi et al. (≥4 U pRBCs/4 h; admission SI)	574	1278	234	8550	0.71 [0.68, 0.74]	0.87 [0.86, 0.88]
Parimi et al. (≥4 U pRBCs/4 h; prehospital SI)	582	1572	226	8256	0.72 [0.69, 0.75]	0.84 [0.83, 0.85]
Schroll 2018	23	114	11	496	0.68 [0.49, 0.83]	0.81 [0.78, 0.84]



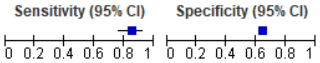
Shock Index (cut off 0.91)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Wang 2019	51	214	27	715	0.65 [0.54, 0.76]	0.77 [0.74, 0.80]



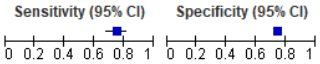
Shock Index (cut off 0.81)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
El Menyar 2018	76	3104	13	5517	0.85 [0.76, 0.92]	0.64 [0.63, 0.65]



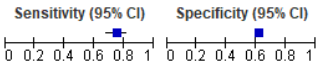
Shock Index (cut off >0.967, prehospital)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Pottecher 2016	132	619	44	1762	0.75 [0.68, 0.81]	0.74 [0.72, 0.76]



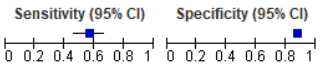
Shock Index (cut off >0.933, prehospital)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Pottecher 2016	132	905	44	1476	0.75 [0.68, 0.81]	0.62 [0.60, 0.64]



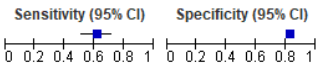
Shock Index (cut off <0.95)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rau 2016	56	296	43	2095	0.57 [0.46, 0.67]	0.88 [0.86, 0.89]



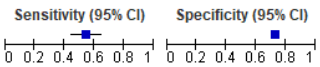
Modified Shock Index (cut off <1.15)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rau 2016	61	423	38	1968	0.62 [0.51, 0.71]	0.82 [0.81, 0.84]



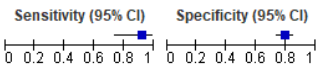
Shock Index, age adjusted (cut off <36.95)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rau 2016	54	662	45	1729	0.55 [0.44, 0.65]	0.72 [0.70, 0.74]



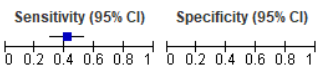
Shock Index (cut off 1.11)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Terceros-Almanza 2019	23	52	2	202	0.92 [0.74, 0.99]	0.80 [0.74, 0.84]



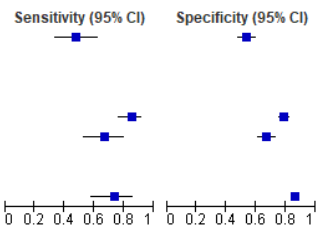
Shock Index (cut off 0.06)

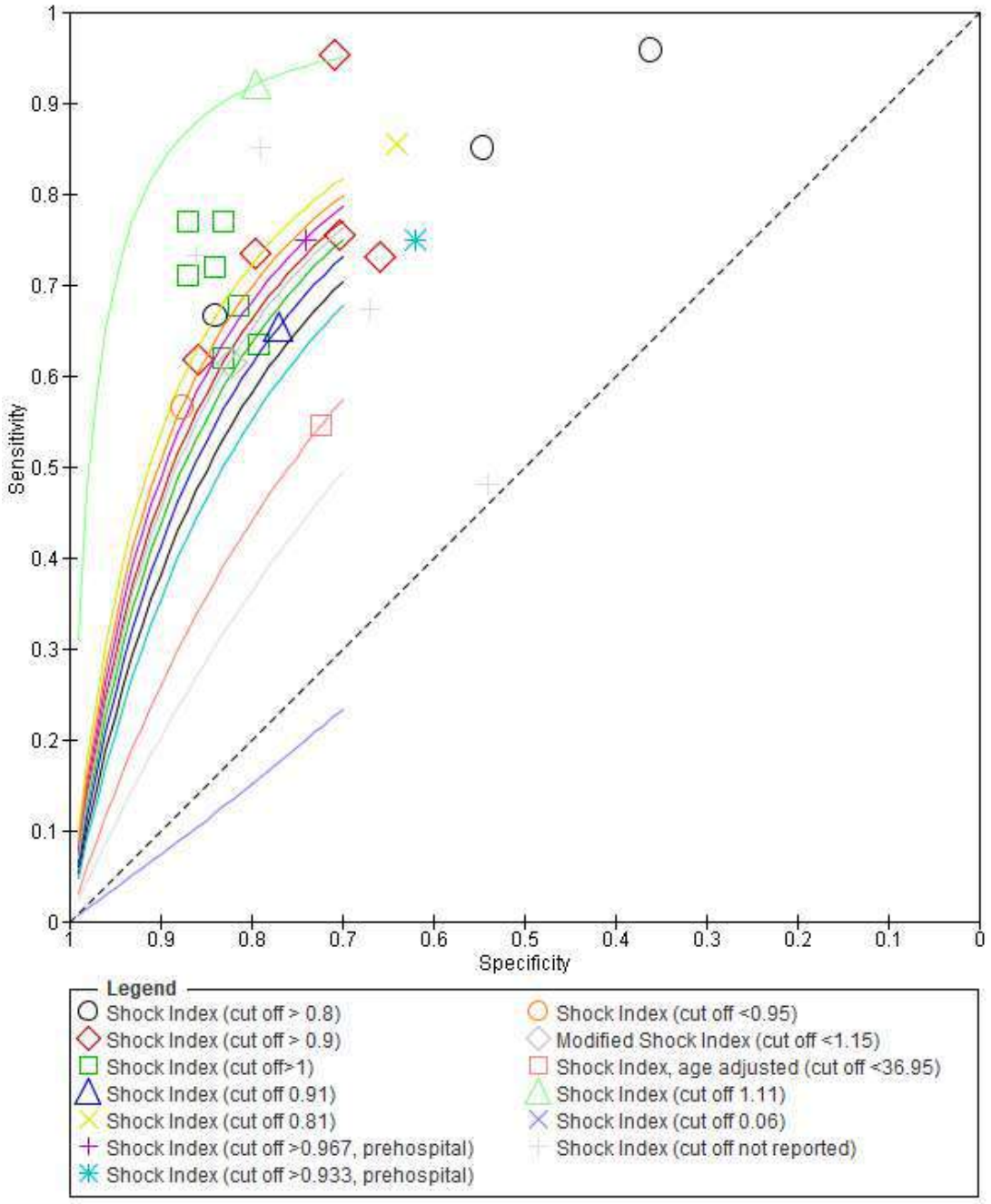
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Wu 2019	34	0	48	0	0.41 [0.31, 0.53]	Not estimable



Shock Index (cut off not reported)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arlsan 2015	25	148	27	173	0.48 [0.34, 0.62]	0.54 [0.48, 0.59]
Fligor 2016	0	0	0	0	Not estimable	Not estimable
Frohlich 2016 (non TBI population)	0	0	0	0	Not estimable	Not estimable
Frohlich 2016 (TBI population)	0	0	0	0	Not estimable	Not estimable
Kovar 2019	80	141	14	529	0.85 [0.76, 0.92]	0.79 [0.76, 0.82]
Moore 2017	37	89	18	180	0.67 [0.53, 0.79]	0.67 [0.61, 0.73]
Ogura 2018	0	0	0	0	Not estimable	Not estimable
Sharma 2019	0	0	0	0	Not estimable	Not estimable
Yang 2021	33	189	12	1162	0.73 [0.58, 0.85]	0.86 [0.84, 0.88]




Sensitivity
Specificity
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Legend
Shock Index (cut off > 0.8)
Shock Index (cut off > 0.9)
Shock Index (cut off>1)
Shock Index (cut off 0.91)
Shock Index (cut off 0.81)
Shock Index (cut off >0.967, prehospital)
Shock Index (cut off >0.933, prehospital)
Shock Index (cut off <0.95)
Modified Shock Index (cut off <1.15)
Shock Index, age adjusted (cut off <36.95)
Shock Index (cut off 1.11)
Shock Index (cut off 0.06)
Shock Index (cut off not reported)

14- Modified Shock Index

Modified Shock Index (cut off not reported)

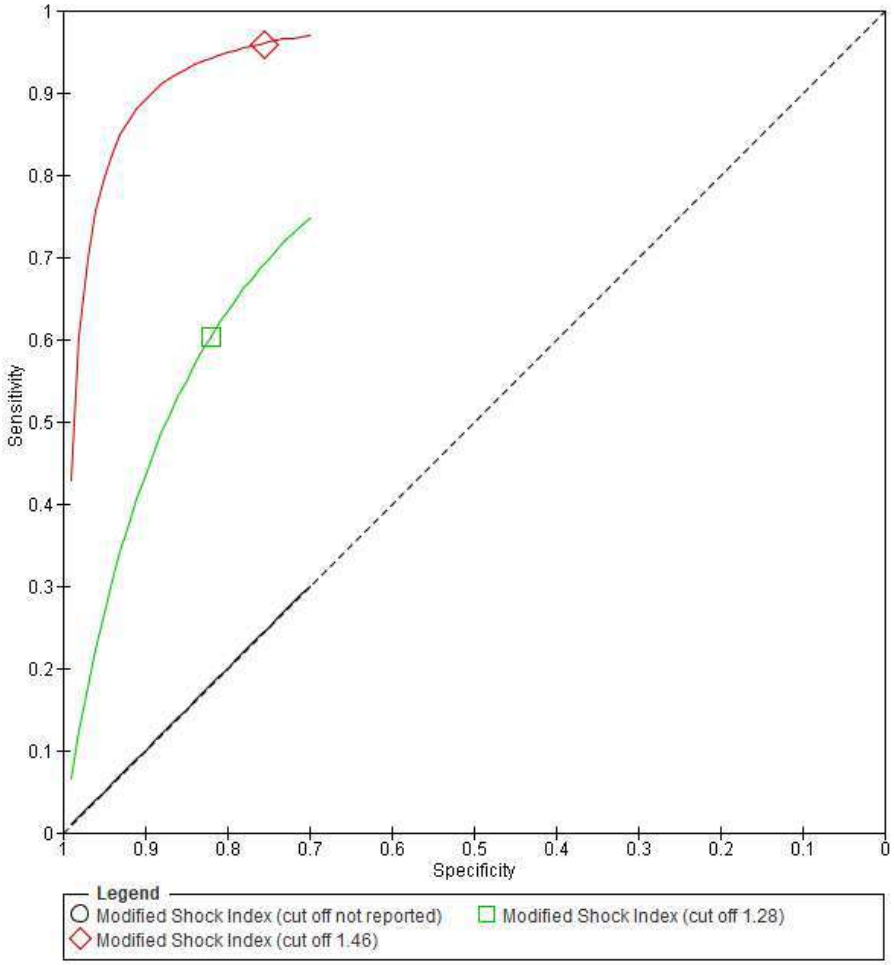
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Sharma 2019	0	0	0	0	Not estimable	Not estimable

Modified Shock Index (cut off 1.46)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Terceros-Almanza 2019	24	62	1	192	0.96 [0.80, 1.00]	0.76 [0.70, 0.81]

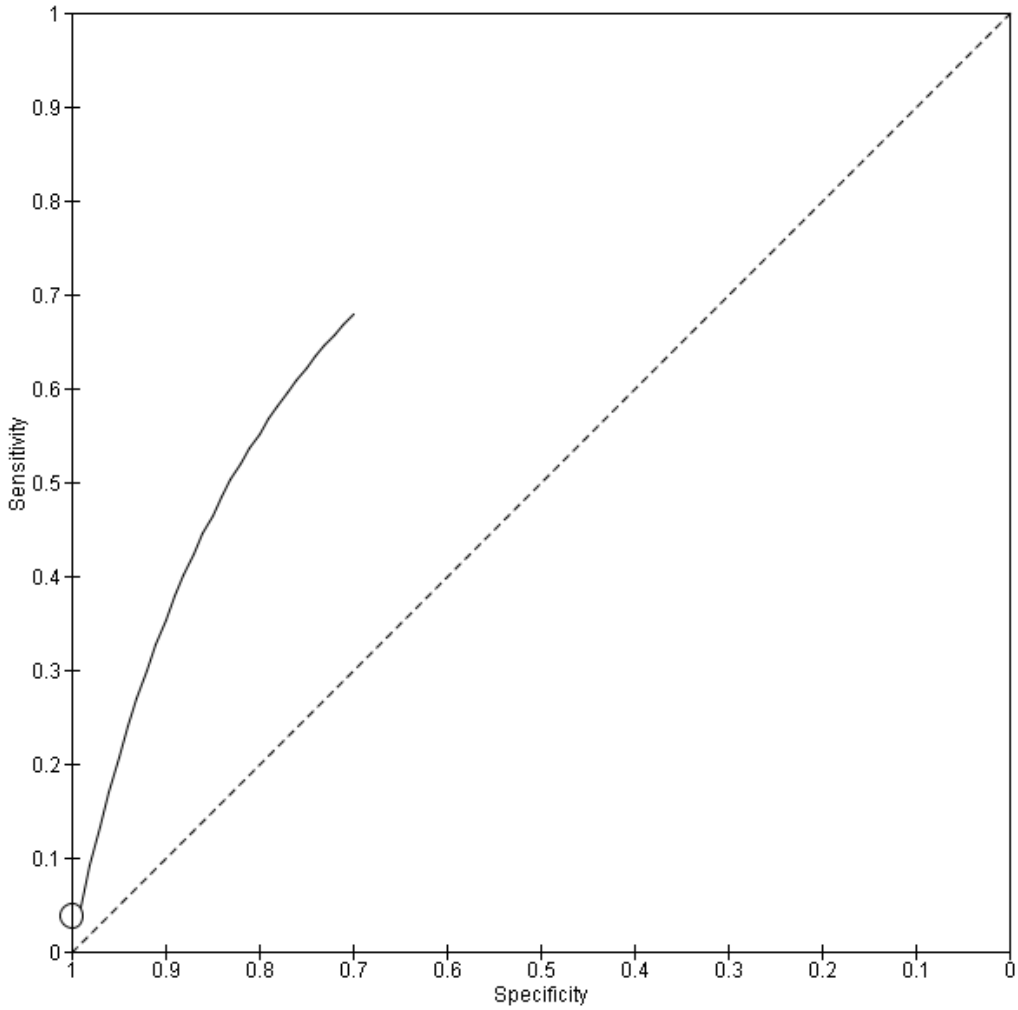
Modified Shock Index (cut off 1.28)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Wang 2019	47	167	31	762	0.60 [0.49, 0.71]	0.82 [0.79, 0.84]



15-Milano score (cut off ≥6)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cornero 2020	3	0	75	61	0.04 [0.01, 0.11]	1.00 [0.94, 1.00]

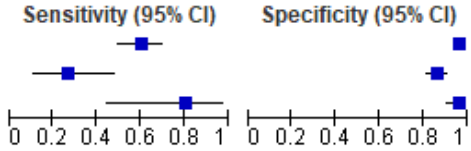


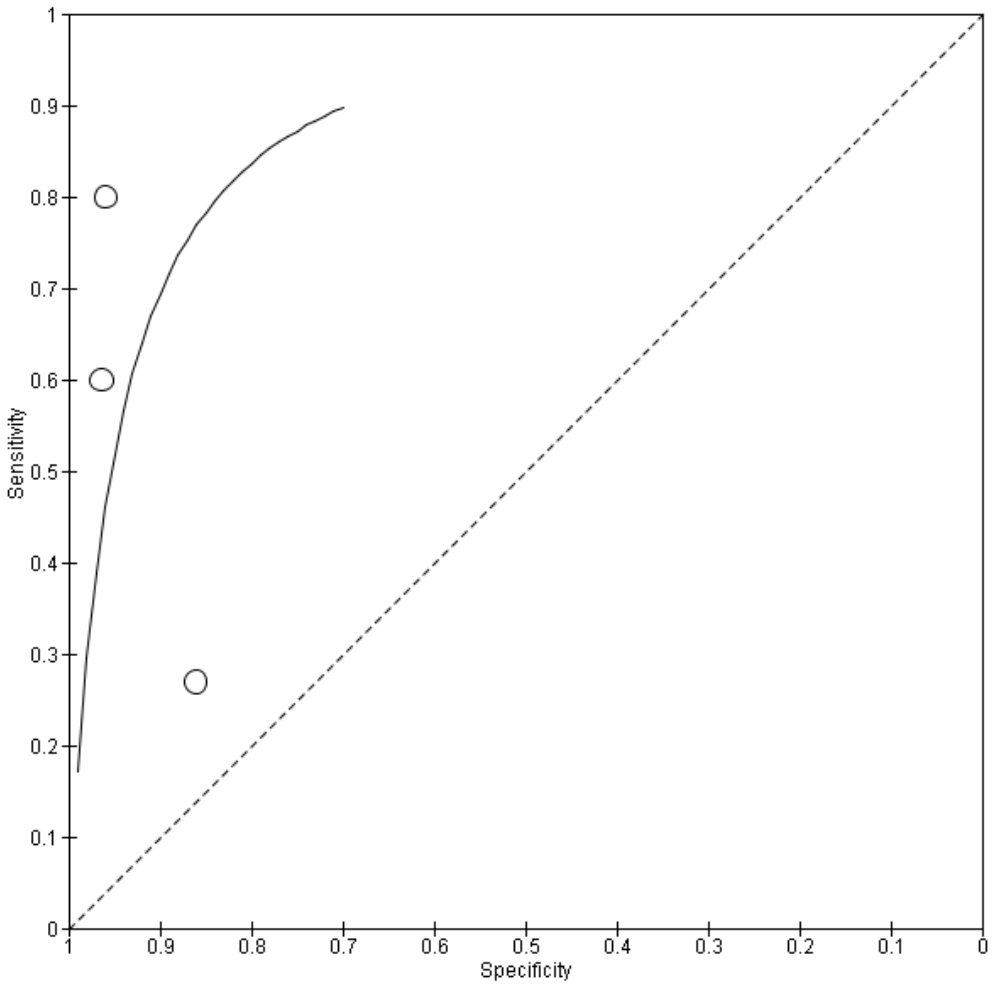
Sensibilità e specificità dei test predittivi per TIC (trauma induced coagulopathy)

Score validati

1- COAST

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mitra 2011	60	41	40	1085	0.60 [0.50, 0.70]	0.96 [0.95, 0.97]
Peltan 2016	7	36	19	223	0.27 [0.12, 0.48]	0.86 [0.81, 0.90]
Thorn 2019	8	5	2	118	0.80 [0.44, 0.97]	0.96 [0.91, 0.99]





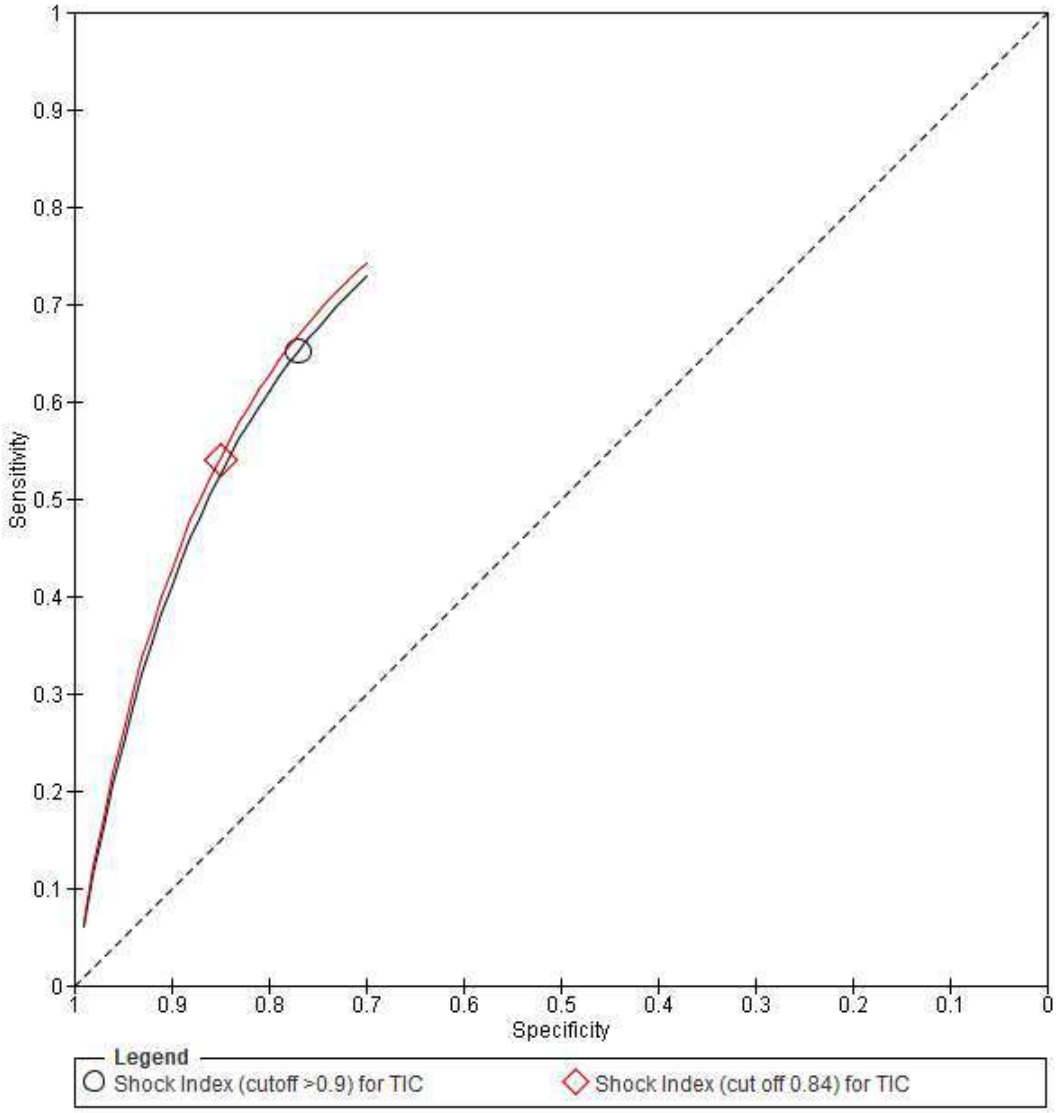
2- Shock Index

Shock Index (cutoff >0.9) for TIC

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
David 2017	73	86	39	287	0.65 [0.56, 0.74]	0.77 [0.72, 0.81]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

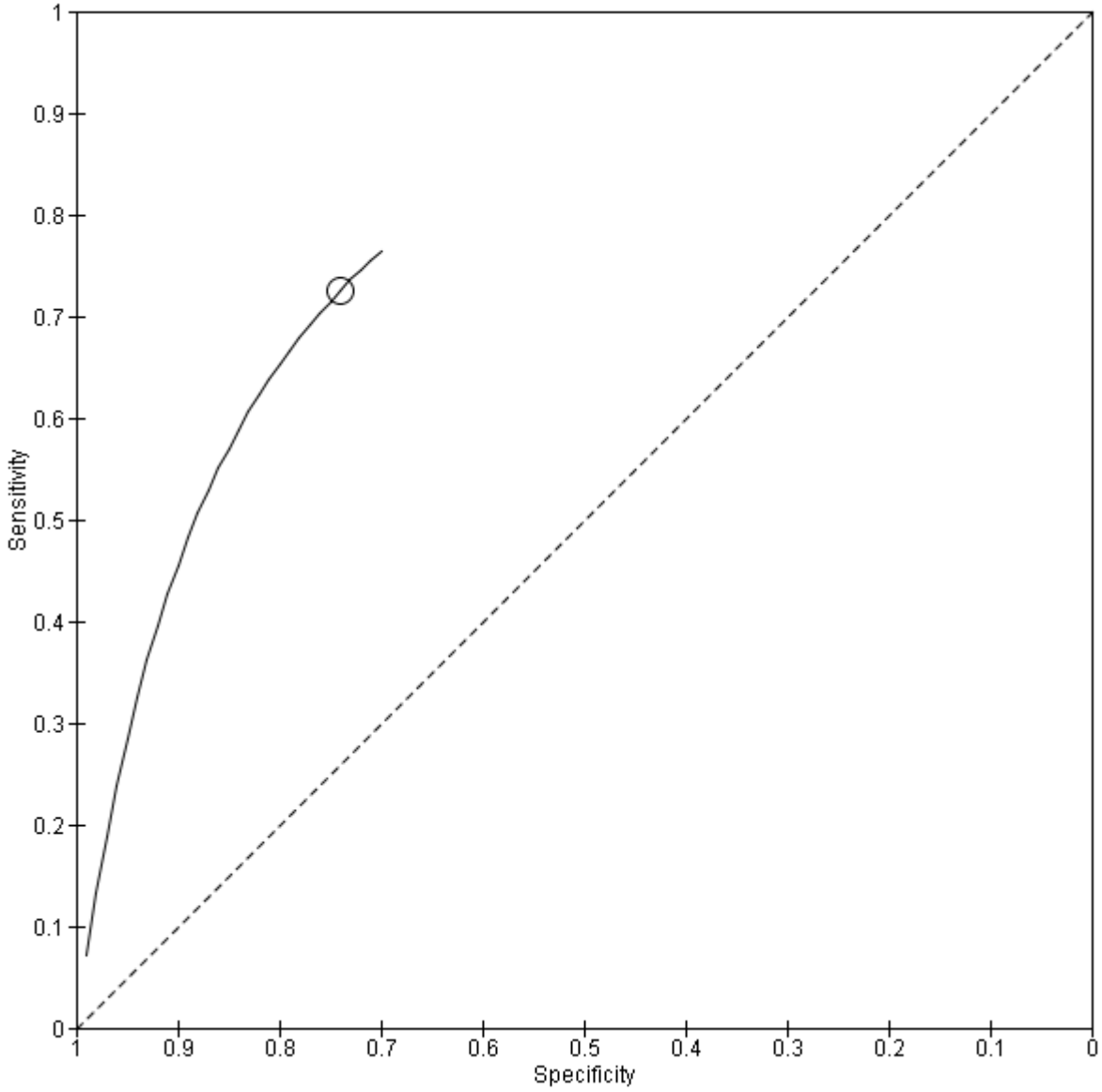
Shock Index (cut off 0.84) for TIC

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Lee Young 2020	97	217	82	1231	0.54 [0.47, 0.62]	0.85 [0.83, 0.87]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1



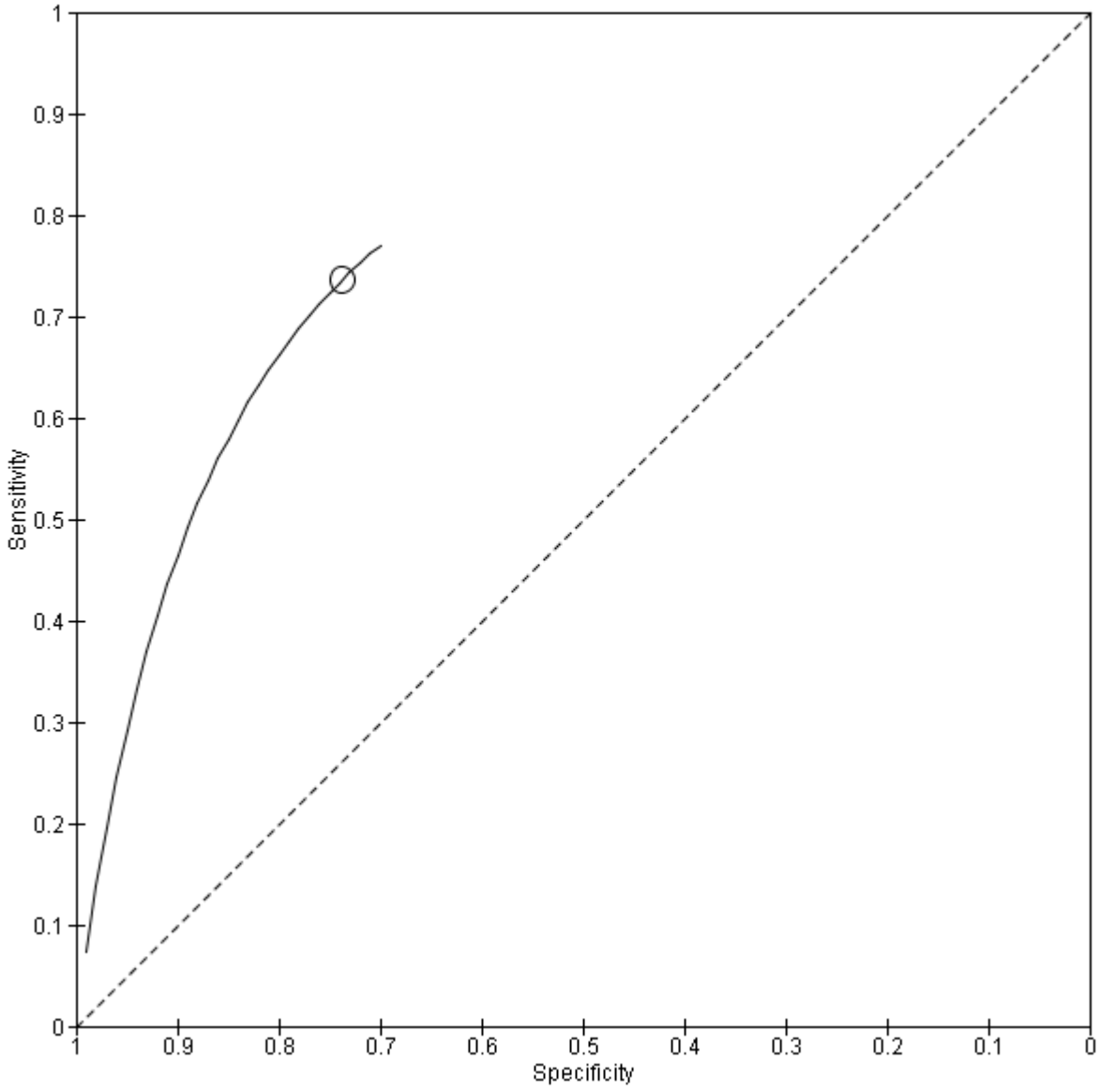
3- PACT 1

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Peltan 2015	37	71	14	202	0.73 [0.58, 0.84]	0.74 [0.68, 0.79]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1



4- PACT 2

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Peltan 2016	64	52	23	146	0.74 [0.63, 0.82]	0.74 [0.67, 0.80]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1



AUC dei test validati predittivi per MT e TIC

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
Validated scores requiring clinical assessment, laboratory values, and ultrasound assessments						
Prince of Wales/Rainer	Original Study	Rainer et al.[13] (cut off ≥6)	2011	MT	0.889	1891
Prince of Wales/Rainer	Validation Studies	Brockamp et al.[45] (cut off ≥ 2.5)	2012	MT	0.86	5147
Prince of Wales/Rainer		Mitra et al.[46 (cut off ≥6)]	2012	MT	0.8419	1234
Prince of Wales/Rainer		Ohmori et al. (age, <65 y)[47 (cut off >2)]	2017	MT	0.858	334
Prince of Wales/Rainer		Ohmori et al. (age, ≥65 y) (cut off >2)	2017	MT	0.764	380
Prince of Wales/Rainer		Poon et al.[48 (cut off ≥ 6)]	2012	MT	0.886	1030
Prince of Wales/Rainer		Choi et al. (cut off ≥6)	2017	MT	0.866	305
Prince of Wales/Rainer		Lui Chun et al. (cut off ≥ 6)	2018	MT	0.844	2945
Prince of Wales/Rainer		Horst et al. (cut off > 2)	2020	MT	0.648	479
Prince of Wales/Rainer		Terceros-Almanza et al. (cut off >1.5)	2019	MT	0.82	129
TASH score (SBP [≤100 MM Hg = 4, < 120 = 1], HR ≥ 120 bpm =2, FAST +ve = 3, Hb [<7=8, <9=6, <10=4, <11=3, <12=2], Base excess [<-10=4, <-6=3, <-2=1], clinically instable pelvioc fracture =3, open/dislocated femur fracture, Male =1	Original Study	Yucel et al.[19] (> 16) (development set)	2006	MT	0.892	4527
TASH score		Yucel et al.[19] (> 16) (validation study set)	2006	MT	0.887	1517
TASH score	Validation Studies	Brockamp et al.[45] (cut off ≥8.5)	2012	MT	0.889	5147
TASH score		De Jong et al.[49 (cut off ≥10)]	2016	MT	0.94	910
TASH score		De Jong et al. (obese patients)(cut off ≥11)	2016	MT	0.93	119
TASH score		De Jong et al. (nonobese patients)(cut off ≥10)	2016	MT	0.94	791
TASH score		Krumrei et al. (rural)[50]	2012	MT	0.51	373
TASH score		Maegele et al. (premodification)[11]	2011	MT	0.905	6044
TASH score		Maegele et al. (postmodification)	2011	MT	0.905	5834
TASH score		Mitra et al.[46 (cut off ≥18)]	2012	MT	0.7822	1234
TASH score		Nunez et al.[12 (cut off >16)]	2009	MT	0.842	586

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
TASH score		Ogura et al.[23] (cut off >8)	2014	MT	0.892	119
TASH score		Ogura et al.[51](cut off > 16)	2015	MT	0.889	264
TASH score		Ogura et al.[22] (cut off >7)	2016	MT	0.912	300
TASH score		Ohmori et al. (age, <65 y)[47] (cut off >6)	2017	MT	0.881	334
TASH score		Ohmori et al. (age, ≥65 y)(cut off >6)	2017	MT	0.793	380
TASH score		Poon et al.[48] (cut off >16 or more)	2012	MT	0.911	1030
TASH score		Pommerening et al. (cut off > 16)	2015	MT	0.72	966
TASH score		Umemura et al.[52] (cutt off >5)	2016	MT	0.833	153
TASH score		Afshari et al.	2019	MT	0.93	200
TASH score		Belanger-Quintana 2019 (cut off >16 or more)	2019	MT		NA
TASH score		Horst et al. (cut off > 8)	2020	MT	0.782	479
TASH score		Lui Chun et al. (cut off ≥ 16)	2018	MT	0.869	2945
TASH score		Swerts et al. (cut off>16)	2020	Damage Control Resuscitation	0.89	328
TASH score		Terceros-Almanza et al. (cut off >6.5)	2019	MT	0.82	131
MTS (massive tranfsusion score) (SBp <90, Hb <11, INR > 1.5, Base deficiti ≥6, Positive FAST, penetrating mechanism)	Original study	Calcutt et al. (Cut off ≥ 2)	2013	MT	N/A	1245
TBSS	Original Study	Ogura et al. (cutoff >15)[23]	2014	MT	0.985	119
TBSS	Validation Studies	Ogura et al. (cutoff ≥10)[51]	2015	MT	0.967	264
TBSS		Ogura et al. (cutoff ≥17)[51]	2015	MT	0.967	264
TBSS		Ogura et al. (cutoff ≥14)[22]	2016	MT	0.956	300
TBSS		Ogura et al. (pre hospital) (cutoff >16)	2018	MT	0.97	1025
Milano score (max score 9 points)	Original study	Cornero et al. (german population)	2020	MT	0.738	905
Milano score		Cornero et al. (italian population)	2020	MT	0.854	139
Validated scores requiring clinical assessment and laboratory values						
Larson score Any 2 or more of the following: Hemoglobin <11 g/dL, SBP < 110 mm Hg, HR > 110 bpm, Base Deficit ≤6 mmol/L	Original study	Larson et al.	2010	MT	N/A	1124 (military trauma)
Larson score		Brockamp et al.[45] (cut off ≥ 1.5)	2012	MT	0.823	5147

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
Larson score		Horst et al. (cut off > 1)	2020	MT	0.740	479
Larson score		Terceros-Almanza et al. (cut off >1.5)	2019	MT	0.81	392
McLaughlin score	Original study	McLaughlin et al.[21] (development set)	2008	MT	0.839	302 (military trauma)
McLaughlin score		McLaughlin et al. (internal validation set)	2008	MT	0.747	396 (military trauma)
McLaughlin score	Validation studies	Krumrei et al. (rural)[50]	2012	MT	0.56	373
Mclaughlin score		Pommerening et al.	2015	MT	0.66	966
McLaughlin score		Nunez et al.[12]	2009	MT	0.767	586
Schreiber score (Hb ≤ 11, International normilized ratio > 1.5, penetrating trauma)	Original study	Schreiber et al.[24]	2007	MT	0.8	558 (military trauma)
Schreiber score	Validation studies	Brockamp et al.[45] (cut off ≥ 0.5)	2012	MT	0.8	5147
Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)	Original study	Vandromme et al. (cut off ≥ 3) [25] (development set)	2011	MT	0.9	306
Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)		Vandromme et al. (cut off ≥ 3) [25](internal validation set)	2011	MT	NA	208
Vandromme score	Validation studies	Brockamp et al.[45] (cut off ≥ 1.5)	2012	MT	0.84	5147
Cincinnati individual tansfusion trigget (CITT) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C) 6 hours	Original study	Calcutt et al.	2011	MT	NA	170
revised MTS (massive transfusion score) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C)	Validation studies	Calcutt et al. (cut off ≥ 2)	2016	MT	0.69	NA
MTS (massive tranfsusion score 6 hours) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6)		Calcutt et al. (cut off ≥ 1)	2016	MT by 6 hours	0.68	NA
Prediction scoring scheme (0-8 points) - type of trauma, injury severity score, heart rate, hemoglobin, prothrombin time, fibrinogen, and base excess	Original study	Wei et al. (cut off 4 points) set derivation/training pop	2020	MT	0.85	332
Prediction scoring scheme	Original study	Wei et al. (cut off 4 points) set validation/testing pop	2020	MT	0.86	146

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
Prediction scoring scheme		Wei et al. (cut off 4 points)	2017	MT	0.914	265
Validated scores requiring clinical assessment and ultrasound assessment						
ABC score (Penetrating mechanism (0 = no, 1 = yes), ED SBP of 90 mm Hg or less (0 = no, 1 = yes), ED HR of 120 bpm or greater (0 = no, 1 = yes), Positive FAST (0 = no, 1 = yes)	Original study	Nunez et al.[12] (cut off ≥ 2)	2009	MT	0.895	586
ABC score	Validation studies	Brockamp et al.[45] (cut ≥ off 0.5)	2012	MT	0.763	5147
ABC score		Cotton et al. (VUMC cohort)[53 (cuf off ≥ 2)]	2010	MT	0.903	513
ABC score		Cotton et al. (PMH cohort)(cuf off ≥ 2)	2010	MT	0.833	372
ABC score		Cotton et al. (JHH cohort)(cuf off ≥ 2)	2010	MT	0.883	133
ABC score		Krumrei et al. (rural)[50 (cut off ≥ 2)]	2012	MT	0.86	373
ABC score		Mitra et al.[46 (cut off ≥2)]	2012	MT	0.8986	1234
ABC score		Moore et al.[43(cuf off ≥ 2)]	2017	MT	0.66	324
ABC score		Ogura et al.[23 (cut off >1)]	2014	MT	0.813	119
ABC score		Ohmori et al. (age, <65 y)[47 (cut off >1)]	2017	MT	0.792	334
ABC score		Ohmori et al. (age, ≥65 y) (cut off >1)	2017	MT	0.655	380
ABC score		Poon et al.48 (cut off ≥ 2)	2012	MT	0.809	1030
ABC score		Umemura et al.52 (cut off >1)	2016	MT	0.724	153
ABC score		Pommerening et al. (cut off ≥ 2)	2015	MT	0.64	966
ABC score		Yumoto et al.31(cuf off ≥ 2)	2014	MT	0.934	259
ABC score		Joseph et al. (cut off ≥ 2)	2018	MT	0.617	380
ABC score		El Menyar et al. (id 27) (cuf off ≥ 2)	2019	MT	NA	572 (solid organ injury)
ABC score		Campos-Serra et al. (cuf off ≥ 2)	2018	MT	0.733	1402
ABC score		Belanger-Quintana 2019 (cuf off ≥ 2)	2019	MT	NA	NA
ABC score		Chaochankit et al. (cut off ≥ 2)	2018	MT	0.587	165
ABC score		Hanna et al. (cut off ≥ 2)	2020	MT	NA	1018
ABC score		Horst et al. (cut off > 0)	2020	MT	0.684	479
ABC score		Prichayudh et al. (cuf off ≥ 2)	2020	MT	NA	358
ABC score		Schroll et al. (cuf off ≥ 2)	2018	MT	0.74	644
ABC score		Ogura et al.	2018	MT	0.83	1025
ABC score		Terceros-Almanza et al. (cuf off > 0.5)	2019	MT	0.68	183

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
ABC score		Yang et al. (cuf off ≥ 2)	2021	MT	0.8	1396
ETS score	Original Study	Ruchholtz et al. (cut off ≥ 3)	2006	MT	N/A	1103
ETS score	Validation Studies	Kuhne et al.44 (cut off ≥ 3)	2008	MT	N/A	481
ETS score		Alimohammadi et al. (cut off ≥ 3)	2017	MT	0.84	793
ETS score		Horst et al. (cut off > 2.5)	2020	MT	0.713	479
ETS score		Terceros-Almanza et al. (cut off > 4.8)	2019	MT	0.85	189
Revised assessment of Bleeding and Transfusion (RABT) Score (FAST result (positive = 1), SI ([1 = 1), pelvic fracture (present = 1), and MOI (penetrating = 1)	Original Study	Joseph et al. (cut off ≥ 2)	2018	MT	0.828	380
Revised assessment of Bleeding and Transfusion (RABT) Score	Validation Study	El Menyar et al. (cut off ≥ 2) id 27	2019	MT	0.84	1199
Revised assessment of Bleeding and Transfusion (RABT) Score		Hanna et al. (cut off ≥ 2)	2020	MT	NA	1018
Validated scores requiring clinical assessment only						
Shock Index (heart rate divided by systolic blood pressure)	Original Study	Vandromme et al.	2011	MT	N/A	8111
Shock Index	Validation Studies	David et al. (cutoff >0.9)36	2017	MT	0.859	485 (444)
Shock Index		David et al. (cutoff >0.9)36	2017	TIC	0.721	485(444)
Shock Index		Moore et al.43	2017	MT	0.7	324
Shock Index		Mutschler et al. (SI > 1.0)54	2013	MT	0.719	21853
Shock Index		Parimi et al. (≥10 U pRBCs/24 h; prehospital SI)55 (cut off 1)	2016	MT	0.82	10636
Shock Index		Parimi et al. (≥10 U pRBCs/24 h; admission SI)(cut off 1)	2016	MT	0.85	10636
Shock Index		Parimi et al. (≥4 U pRBCs/4 h; prehospital SI)(cut off 1)	2016	MT	0.81	10636
Shock Index		Parimi et al. (≥4 U pRBCs/4 h; admission SI)(cut off 1)	2016	MT	0.82	10636
Shock Index		Pottecher et al. (≥10 U pRBCs/24 h; prehospital SI >0.967)56	2016	MT	0.77	2557
Shock Index		Pottecher et al. (≥3 U pRBCs/1 h; prehospital SI >0.933)	2016	MT	0.71	2557
Shock Index		Rau et al. (cutoff <0.95)57	2016	MT	0.76	2490

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
Shock Index		Rau et al. (age adjusted SI: cutoff <36.95)	2016	MT	0.627	2490
Shock Index		El Menyar ey al. (cut off ≥ 0.81) (nostro id 26)	2018	MT	0.820	8710
Shock index		Arlsan et al.	2015	MT (greater then 2 units of packed red blood cells)	NA	373
Shock Index		El Menyar et al. (id 27) (cut off ≥ 0.8)	2019	MT	0.71	572 (solid organ injury)
Shock Index		El Menyar et al. (id 27) (cut off ≥ 0.9)	2019	MT	NA	572 (solid organ injury)
Shock Index		El Menyar et al. (id 27) (cut off ≥ 1.0)	2019	MT	NA	572 (solid organ injury)
Shock Index		El Menyar et al. (id 30) (cut off ≥ 0.9)	2019	MT	NA	966 (pelvic fracture)
Shock Index		Campos-Serra et al. (cut off ≥ 0.8)	2018	MT	0.749	1402
Shock Index		Figueiredo et al. (cut off > 1) pre hospital	2018	MT	0.71	6402
Shock Index		Figueiredo et al. (cut off > 0.9) in hospital	2018	MT	0.77	6402
Shock Index		Fligor et al. (geriatric population)	2016	MT	0.8573	194
Shock Index		Frohlich et al. (TBI population)	2016	MT	0.756	16760
Shock Index		Frohlich et al. (non TBI population)	2016	MT	0.764	24128
Shock Index		jenkins et al. (cut off > 1) (pregnant population)	2017	MT	0.68	81
Shock index		Juste 2020 pre hospital (cut off ≥ 0.9)	2021	MT	0.68	184
Shock Index		Kovar 2019 (id 56)	2019	MT	0.822	764
Shock index		Juste 2020 in hospital (cut off ≥ 0.9)	2021	MT	0.72	184
Shock Index		Lee young et al. (cut off 0.80)	2020	MT	0.796	1627
Shock Index		Lee young et al. (cut off 0.84	2020	TIC	0.704	1627
Shock Index		Schroll et al. (cut off ≥1)	2018	MT	0.83	644
Shock Index		Ogura et al. Cut off not reported	2018	MT	0.89	1025
Shock Index		Sharma et al. Cut off not reported	2019	MT	0.798	254
Shock Index		Terceros-Almanza et al. (cut off 0.8)	2019	MT	0.77	535

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
Shock Index		Terceros-Almanza et al. (cut off 1.11)	2017	MT	0.89	279
Shock Index		Wu et al. (cut off 0.06)	2019	MT ≥ 10 U	0.61	7957
Shock Index		Yang et al.	2021	MT	0.83	1396
Shock Index (Prehospital)		Wang et al. (cut off 0.91)	2019	MT	0.773	1007
Modified Schok Index	Original Study	Barnes et al.	2018	MT	0.794	7623
Modified Shock Index		Sharma et al.	2019	MT	0.787	254
Modified Shock Index		Terceros-Almanza et al. (cut off 1.46)	2017	MT	0.90	279
Shock Index		Rau et al. (modified SI: cutoff <1.15)	2016	MT	0.756	2490
Modified Shock Index (Prehospital)		Wang et al. (cut off 1.28)	2019	MT	0.765	1007
ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)	Original study	Ardegh et al. (cut off ≥ 3)	2001	MT	NA	184
ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)	Validation study	Campos-Serra et al. (cut off ≥ 3)	2018	MT	0.700	1402
ROPE Pulse Rate Over Pressure		Jenkins et al. (Cut off > 3)(pregnant population)	2017	MT	0.54	81
COAST (Coagulopathy of Severe Trauma Score - acute traumatic coagulopathy entrapment (1 point); body temperature (< 358C: 1 point, < 328C: 2 points); SBP (< 100 mm Hg: 1 point, < 90 mm Hg: 2 points); pelvic content or abdominal injury (1 point), and chest decompression (1 point).	Original Study	Mitra et al (cut off ≥ 3) (development set)	2011	TIC	0.77	1680 (151 patients were coaugolopathic)
COAST - Coagulopathy of Severe Trauma Score		Mitra et al (cut off ≥ 3) (internal validation set)	2011	TIC	0.83	1225

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
COAST - Coagulopathy of Severe Trauma Score	Validation study	Thorn et al. (cut off ≥ 3)	2019	TIC	0.941	133
COAST - Coagulopathy of Severe Trauma Score	validation study	Peltan et al. (cut off ≥ 3)	2016	TIC	0,68	285
EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS - obvious extremity injurye = 1 point, penetrating mechanism =2 points, shock index ≥ 0.9=2 points, GCS≤ 8 =3 points.	Original study	Kovar 2019 (id 56) (cut off ≥3)	2019	MT	0.866	764
EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS)	Original study	Kovar 2019 (id 56) (cut off ≥2)	2019	MT	0.81	764
EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS)	Validation study	Kovar 2019 (id 57) (cut off ≥2)	2019	MT	0.786	152590
TICCS Trauma induced coagulopathy clinical score (Severity [ED resuscitation room 2 points*, extent of body injury (torso, abddominal or the pelvic ring region = 2, head =1, each extremity = 1), SBP < 90 = 5)	Original Study	Tonglet et al. (cut off: 10)	2014	TIC	NA	82
Trauma-Induced Coagulopathy Clinical Score (TICCS)	Validation study	Tonglet et al. (cut off ≥ 12)	2017	TIC	0.7	33385
Trauma-Induced Coagulopathy Clinical Score (TICCS)		Swerts et al. (cut off ≥ 10)	2020	TIC	0.73	328
Early Blood Transfusion Needs Score- (age, type of injury, pulse, systolic blood pressure, GCS)	Original study	Wang et al. (set Derivation) (cut off >5)	2016	MT	0.8729	24303
Early Blood Transfusion Needs Score (age, type of injury, pulse, systolic blood pressure, GCS)		Wang et al. (set validation) (cut off 5)	2016	MT	0.8593	24303
PACT 1 (Prediction of Acute Traumatic Coagulopathy) (Shock index, Injury-to-ED time, White race, Age, First GCS, First RR)	Original study	Peltan et al.	2015	TIC	0.79	324
PACT 2 (Prediction of Acute Traumatic Coagulopathy) (Shock index, Age, GCS)	Original study	Peltan et al.	2016	TIC	NA	1963

Validated tool						
		Study Author	**Year**	**MT/TIC**	**AUROC**	**N civilians trauma**
PACT 2 (Prediction of Acute Traumatic Coagulopathy) (Shock index, Age, GCS)	Original study	Peltan et al. (set derivation) (cut off >196)	2016	TIC	0.74	285

Test non validati

Unvalidated scores							
Test index	**Study Author, Year**		**Prediction**	**Sensitivity**	**Specificity**	**AUROC**	**n civilian trauma**
Validated scores requiring clinical assessment, laboratory values, and ultrasound assessments							
Hsu score (Base deficit greater than 5 and either INR of 1.5 or greater or hemoperitoneum)	Hsu et al.[28]	2013	MT	89,7%	73,9%	0,859	479
FASYLA score (FAST(0=negative, 1=positive), Shock Index (SI) (0= 0.50-0.69, 1 =0.70-0.79, 2 = 0.80-0.89, 3=> 0.90), and initial serumLActate (0= <2.0, 1=2.0-4.0, 2>=4.0mmol/l).)	El Menyar et al. (id 29)	2019	MT	42%	97%	0,87	1199
Modified TBSS (age, sonography, pelvic fracture, serum lactate and systolic blood pressure on arrival)	Ogura et al. (cutoff ≥14)[22]	2016	MT	80%	91,1%	0,915	300
Trauma-Induced Coagulopathy Clinical Score (TICCS). BE - (+ 3 points if BE < − 5 and + 3 points in case of a positive FAST)	Swerts et al. (cut off ≥ 14)	2020	Damage Control Resuscitation	NA	NA	0.76	328
Yumoto New screening method (schok index ≥ 1, Base Excess ≤ 3, positive FAST results)	Yumoto et al.[31] (cut off ≥ 1)	2014	MT	97%	81%	0,934	259
Bleeding risk idnex BRI (PPG, ECG waveforms, oximetry SpO2, SBP)	Yang et al.	2021	MT	87%	85%	0.92	1396
Validated scores requiring clinical assessment and laboratory values							
Moore model (SBP in first hour, pH min during 1st hour, ISS ≤ 25=0, > 25 = 1)	Moore et al.	2007	MT	N/A	N/A	0.80	383
Wade model (SBP, HR, Ph, Hematocrit)	Wade et al. ($\pi > 0.05$)	2008	MT	87%	53%	NA	838
Algorithm including triage vital signs, pulse oximetry features, and laboratory values (C1, Cartridge 1 (hematocrit, glucose, potassium, chloride, and bicarbonate); C2, Cartridge 2 (PT, INR); C3, Cartridge 3 (lactate); pulse oximetry features for 15 minutes)	Shackelford et al.	2015	MT	NA	NA	0.91	852
ABC score + lactate	Chaochankit et al.	2018	MT	NA	NA	0.749	165
Prince of Walse + lactate (max score 11 pts)	Choi et al.	2017	MT	NA	NA	0,862	305
Prince of Walse (base deficit replaced by lactate) (max score 10 pts)	Choi et al.	2017	MT	NA	NA	0,86	305
Validated scores requiring clinical assessment and ultrasound assessment							
None							
Validated scores requiring clinical assessment only							

Unvalidated scores							
Test index	**Study Author, Year**		**Prediction**	**Sensitivity**	**Specificity**	**AUROC**	**n civilian trauma**
ABC score (without FAST)	Kovar 2019 (id 56) (cut off ≥2)	2019	MT (requiring >4 units of packed red blood cells (pRBCs) within 4 h of arrival13,14	46%	94%	0.827	764
Algorithm including age, sex, prehospital shock index, admission HR, SpHb and SpO	Galvagno et al.	2015	>4 units of packed red blood cells in <4 h	NA	NA	0.93	711
Baker model (SBp <90=1, HR>120=1, GCS < 9=1, High risk injury =1,(ventral chest trauma, abdominal trauma, MVC, penetrating torso trauma)	Baker et al.	2011	MT	NA	NA	NA	654
Class-4 Hemorrhage Unresponsive to Lactated Ringer's (CHULA) - 1) a patient with clinical sign of class-4 hemorrhage; 2)not responding to one to two liters of Lactated Ringer's bolus; 3) had suspected ongoing bleeding.	Prichayudh et al.	2020	MT	93,60%	90,40%	NA	358
Clinical gestalt	Pommerening et al.	2015	MT	65.6%	63.8%	0.65	966
Code red attivation (SBP < 90, Blood pressure failure to repsond to bolus intraveneous fluid)	Weaver et al. (91% of the code red activation in pre hospital setting received MT at trauma center)	2016	MT	NA	NA	NA	129
DMBT dynamic MBT score (similar to TASH and PHW, plus hemoglobin drop as a predictor variable)	Lui Chun et al. (cut off ≥ 6)	2018	MT	78,40%	88,10%	NA	2945
DMBT dynamic MBT score (similar to TASH and PHW, plus hemoglobin drop as a predictor variable)	Lui Chun et al. (cut off ≥ 12)	2018	MT	17%	99.3%	NA	2945
Injury Severity Score	Park et al. Overall population	2019	MT	NA	NA	0.651	553
Injury Severity Score	Park et al. Subrgroup: TBI patients	2019	MT	NA	NA	0.649	294
Injury Severity Score	Park et al. Subgroup: nonTBI patients	2019	MT	NA	NA	0.666	309
Mobile application modeling (mechanism of injury, HR, SBP, and BD)	Mina et al.[30]	2013	MT	N/A	N/A	0,96	13,961
Modified field triage score (SBP < 100, GCS <8)	Eastridge et al.	2010	MT	N/A	N/A	0.62	536 (military trauma)
modified TICCS	Horst et al. (cut off > 5)	2020	MT	77.5%	74.03%	0.776	
Pulse Pressur/ Heart rate	Sharma et al.	2019	MT	NA	NA	0.744	254

Unvalidated scores							
Test index	**Study Author, Year**		**Prediction**	**Sensitivity**	**Specificity**	**AUROC**	**n civilian trauma**
QSOFA score (qSOFA score was calculated as the sum of 1 point each for SBP ≤100 mmHg, GCS ≤14, and RR ≥22 breaths/min)	Lee young et al. (cut off 1.50)	2020	MT	80%	70%	0.791	1627
Reverse shock index multiplied by the Glasgow Coma Scale score (rSIG) (BP/HR* GCS)	Lee young et al. (cut off 9.52)	2020	MT	79%	77%	0.842	1627
RTS (SBP, Respiratory Rate, GCS)	Cancio et al.	2008	MT	N/A	N/A	0.64	536 (military trauma)
RTS (SBP, Respiratory Rate, GCS)	Park et al. Overall population	2019	MT	NA	NA	0.717	553
RTS (SBP, Respiratory Rate, GCS)	Park et al. Subrgroup: TBI patients	2019	MT	NA	NA	0.731	294
RTS (SBP, Respiratory Rate, GCS)	Park et al. Subgroup: nonTBI patients	2019	MT	NA	NA	0.745	309
RTS (SBP, Respiratory Rate, GCS)	Yang et al.	2021	MT	78%	69%	0.78	1396
Shock volume (. Initially incremental SV measurements (SVi) were made by calculating average SIth(i) values between two adjacent time points, and by multiplying the incrementally averaged SIth(i) by the duration of the corresponding time interval)	McKinley et al. (6 h)[29]	2016	MT	85%	82%	0,902	467
Shock volume (Initially incremental SV measurements (SVi) were made by calculating average SIth(i) values between two adjacent time points, and by multiplying the incrementally averaged SIth(i) by the duration of the corresponding time interval)	McKinley et al. (12 h)	2016	MT	92%	84%	0,924	467
SIA (Shock Index*age)	Lee young et al. (cut off 45.47)	2020	MT	70%	78%	0.792	1627
QSOFA score (qSOFA score was calculated as the sum of 1 point each for SBP ≤100 mmHg, GCS ≤14, and RR ≥22 breaths/min)	Lee young et al. (cut off 1.50)	2020	TIC	65%	70%	0.716	1627
Reverse shock index multiplied by the Glasgow Coma Scale score (rSIG) (BP/HR* GCS)	Lee young et al. (cut off 10.3)	2020	TIC	69%	77%	0.769	1627
SIA (Shock Index*age)	Lee young et al. (cut off 40.81)	2020	TIC	56%	77%	0.693	1627

CQ13. Strumenti per predire l'emorragia critica

Appendice C – Sintesi dell'evidenza

Popolazione Pediatrica

Caratteristiche degli Score per la previsione di trasfusioni massive (MT)

E' stata effettutata una revisione sistematica con ricerca della letteratura sulle banche dati Embase, Medline e Cochrane CENTRAL. Sono stati individuati 80 records: sono state selezionate 11 referenze che soddisfano i criteri per rispondere al quesito clinico proposto relative alla popolazione pediatrica, di cui 10 studi primari e una SR da cui si sono considerati eleggibili 2 studi, per un totale di 12 pubblicazioni.

Nella popolazione pediatrica, si sono individuati 8 score, di cui 3 validati (SI, SIPA, ABC) e 5 non validati (ABC-S, ABCD, Pre-arrival model, ED model, PED-ABC). Di seguito le principali caratteristiche.

SCORE		**Characteristics**
Validated		
Shock Index	SI	Calculated as the ratio of heart rate to systolic blood pressure.
Shock index, pediatric age-adjusted	SIPA	Calculated as the ratio of heart rate to systolic blood pressure and adjusted by age.
Assessment of blood consumption	ABC	Penetrating mechanism, positive focused assessment sonography for trauma (FAST), arrival systolic blood pressure of 90 mmHg or less, and arrival heart rate (HR) ≥ 120 bpm.
Not validated		
Age-adjusted ABC score	ABC-S	The replacement of HR and BP cut-offs in the ABC score with the age-adjusted shock index (SIPA). Penetrating mechanism, positive FAST, and elevated SIPA on presentation.
Adult-based ABC score with the inclusion of base deficit and lactate	ABCD	Combination of penetrating mechanism, positive FAST, SIPA, lactate, and BD.
Pre-arrival model		Without laboratory test, only physical examination variables included HR, GCS, temperature, and penetrating injury mechanism.
ED model		Laboratory test including GCS, hemoglobin, and presence of penetrating injury.
Assessment of Blood Consumption score for pediatrics	PED-ABC	One point was assigned for each of the following criteria: systolic blood pressure ≤ 90 mmHg; heart rate ≥ 120/min; Glasgow Coma Scale < 15; and positive result on focused assessment with sonography for trauma (FAST) scan
	BIG score	Base Deficit + [2.5*International Normalized Ratio] + [15-GCS].
Admission lactate		Marker of shock or indication for surgical interventions.
Base deficit		Marker of shock or indication for surgical interventions.

Table 1. Characteristics of massive transfusion predictive score.

Sensibilità e specificità dei test predittivi per la MT (massive transfusion or need for blood trasfusion)

Score validati

- *SI*

Per lo score SI, considerato per valori più elevati, si sono trovate 4 pubblicazioni, di cui, 2 (Linnaus 2016, Nordin 2018) relative a pazienti con trauma contusivo, 1 (Nordin 2018) a pazienti con trauma penetrante, e 2 (Marenco 2020, Strutt 2019) sulla popolazione generale con trauma.

Author, year	Setting	Population	Outcome	Cut-off	SE	SP
Blunt trauma patient						
Linnaus 2016 [a]	Civilian	4-16 years	The need for blood transfusions within 24 hours of injury	SI ≥ 0.9	0.959	0.215
Nordin 2018	Civilian	1-16 years	Transfusion requirement within 24 h of admission	SI ≥ 0.9	0.697	0.591
Penetrating trauma patient						
Nordin 2018	Civilian	1-16 years	Transfusion requirement within 24 h of admission	SI ≥ 0.9	0.569	0.631
Trauma patient						
Marenco 2020	Military	< 18 years	The need for blood product transfusion within the first 24 hours of care	SI ≥ 0.8	0.823	0.274
Strutt 2019	Civilian	< 15 years	The need for a blood transfusion (ICD-9 procedures codes 99.00-99.09)	<1 year: SI>2.7, 1-2 years: SI>2.1, 2-5 years: SI>1.9, 5-12 years: SI>1.5, 12-15 years: SI>1.1	0.126	0.984

a patients with a grade 3 or higher blunt liver and/or spleen injury (BLSI)

Table 2. Diagnostic accuracy (sensitivity and specificity) of Shock Index (SI) score.

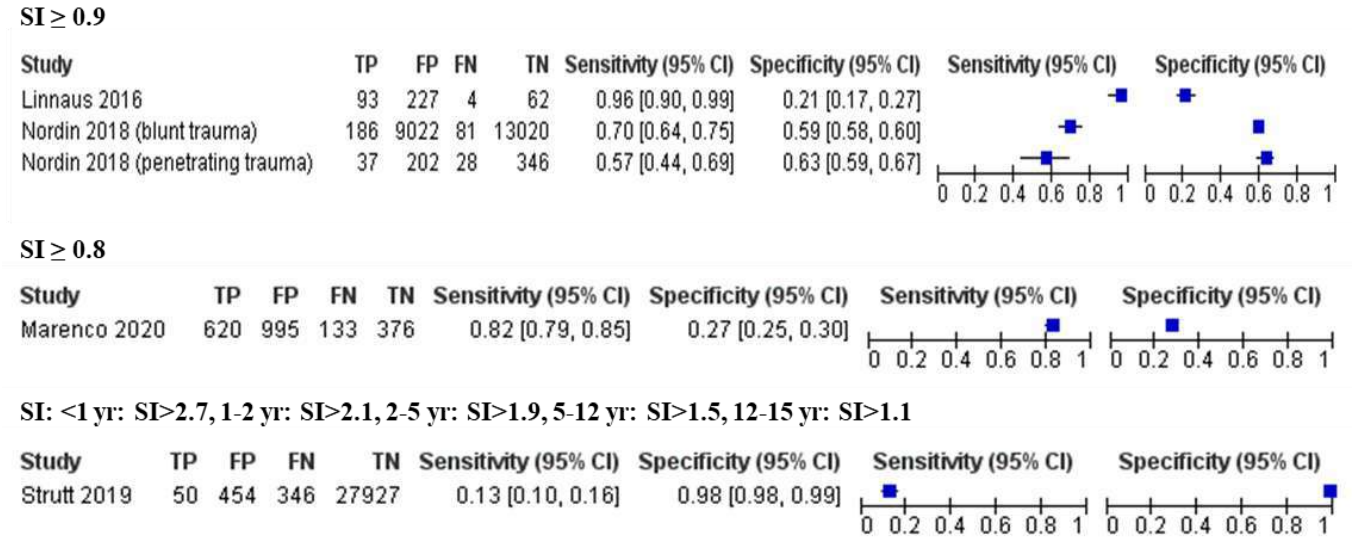


Figure 1. Diagnostic accuracy (sensitivity and specificity) of Shock Index (SI) score

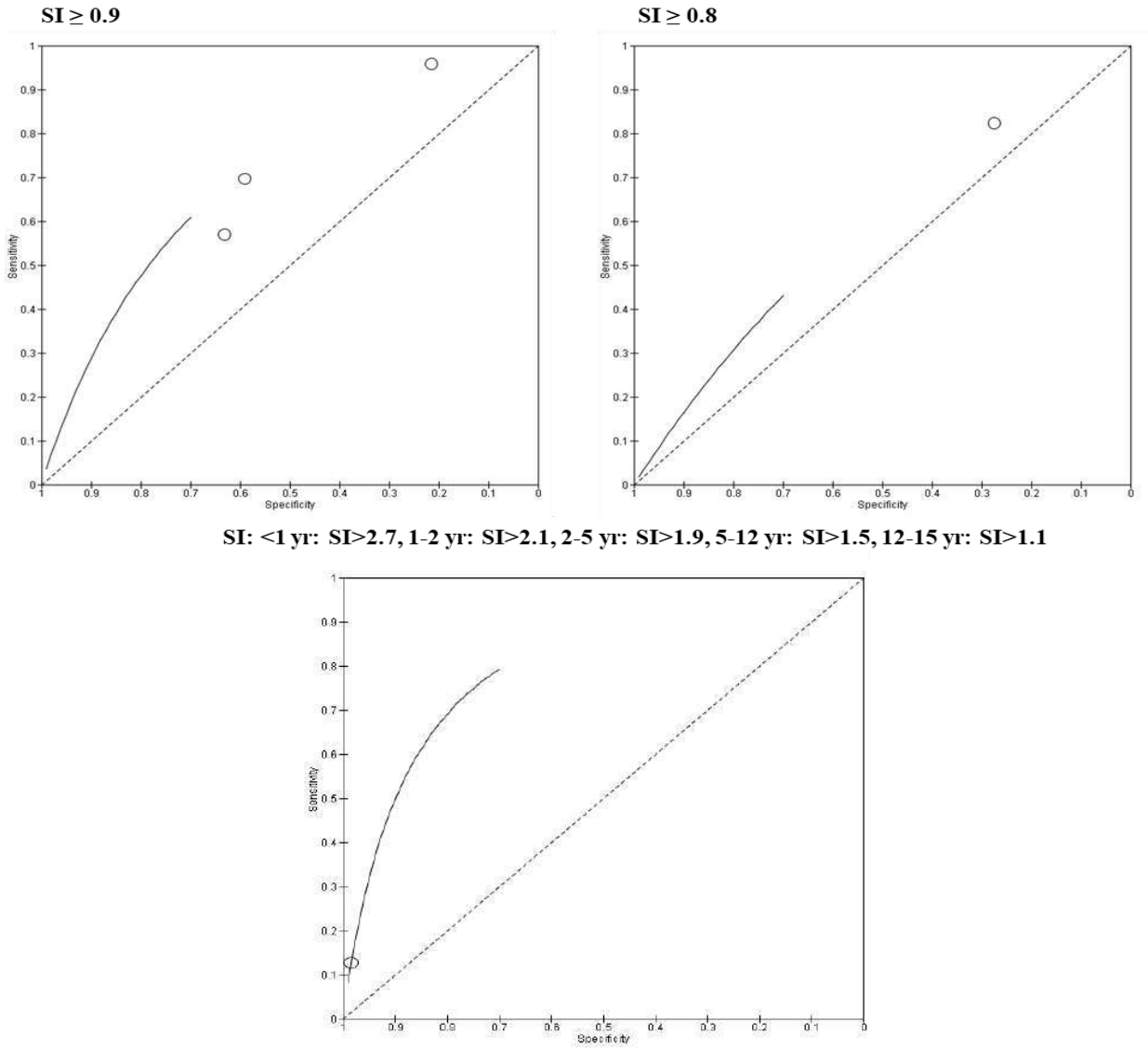


Figure 2. SROC accuracy plot for Shock Index (SI) score.

- *SIPA*

Per lo score SIPA, considerato per valori più elevati, si sono trovate 5 pubblicazioni, di cui, 3 (Acker 2017, Linnaus 2016, Nordin 2018) relative a pazienti con trauma contusivo, 1 (Nordin 2018) a pazienti con trauma penetrante, e 2 (Cuenca 2020, Marenco 2020) sulla popolazione generale con trauma. Per Cuenca 2020 si sono riportati i livelli di accuratezza del test divisi per fascia d'età.

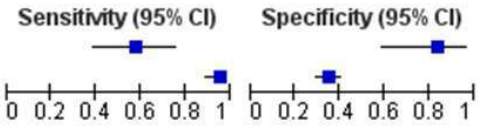
Author, year	Setting	Population	Outcome	Cut-off	SE	SP
Blunt trauma patient						
Acker 2017 (original study)	Civilian	4-15 years	The need for PRBC transfusion in the first 6 hours as a marker of MTP activation	ED thresholds used: 4-6 yr: SIPA >1.22, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	0.58	0.84
Linnaus 2016 [a]	Civilian	4-16 years	The need for blood transfusions within 24 hours of injury	ED thresholds used: 4-6 yr: SIPA >1.22, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	0.948	0.351
Nordin 2018	Civilian	1-16 years	Transfusion requirement within 24 h of admission	ED thresholds used: 1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	0.524	0.849
Penetrating trauma patient						
Nordin 2018	Civilian	1-16 years	Transfusion requirement within 24 h of admission	ED thresholds used: 1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	0.462	0.838
Trauma patient						
Cuenca 2020	Military	1-3 years	Massive transfusion defined as a threshold of 40 mL/kg of all blood products given within the first 24 h	ED thresholds used: 1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-17 yr: SIPA>0.9	0.73	0.35
		4-6 years			0.63	0.60
		7-12 years			0.80	0.57
		13-17 years			0.77	0.62
Marenco 2020	Military	< 18 years	The need for blood product transfusion within the first 24 hours of care	ED thresholds used: 0-3, 4-6 yr: SIPA >1.2, 7-12, 13-17 yr: SIPA>0.9	0.606	0.658

a patients with a grade 3 or higher blunt liver and/or spleen injury (BLSI)

Table 3. Diagnostic accuracy (sensitivity and specificity) of Shock index, pediatric age-adjusted (SIPA) score.

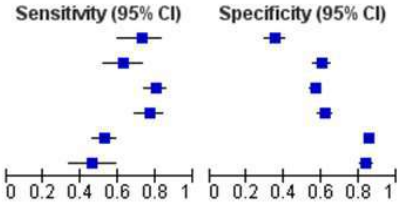
SIPA: 4-6 yr: SIPA >1.22, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Acker 2017	18	3	13	15	0.58 [0.39, 0.75]	0.83 [0.59, 0.96]
Linnaus 2016	92	188	5	101	0.95 [0.88, 0.98]	0.35 [0.29, 0.41]



SIPA: 1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
a Cuenca 2020_ 1-3 yr	47	216	18	116	0.72 [0.60, 0.83]	0.35 [0.30, 0.40]
b Cuenca 2020_ 4-6 yr	57	192	34	288	0.63 [0.52, 0.73]	0.60 [0.55, 0.64]
c Cuenca 2020_ 7-12 yr	169	506	42	671	0.80 [0.74, 0.85]	0.57 [0.54, 0.60]
d Cuenca 2020_ 13-17 yr	97	238	29	388	0.77 [0.69, 0.84]	0.62 [0.58, 0.66]
Nordin 2018 (blunt trauma)	140	3343	127	18721	0.52 [0.46, 0.59]	0.85 [0.84, 0.85]
Nordin 2018 (penetrating trauma)	30	89	35	459	0.46 [0.34, 0.59]	0.84 [0.80, 0.87]



SIPA: 0-3, 4-6 yr: SIPA >1.2, 7-12, 13-17 yr: SIPA>0.9

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Marenco 2020	453	468	295	900	0.61 [0.57, 0.64]	0.66 [0.63, 0.68]

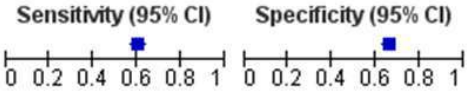
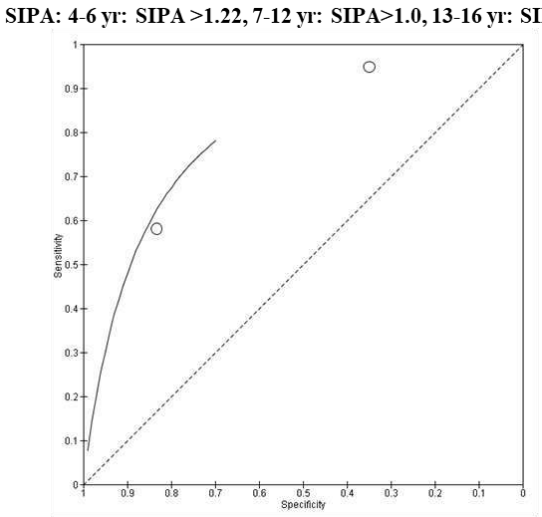
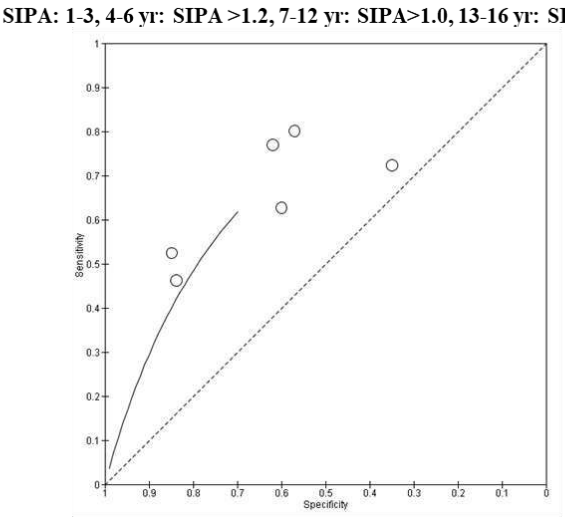


Figure 3. Diagnostic accuracy (sensitivity and specificity) of Shock index, pediatric age-adjusted (SIPA) score.





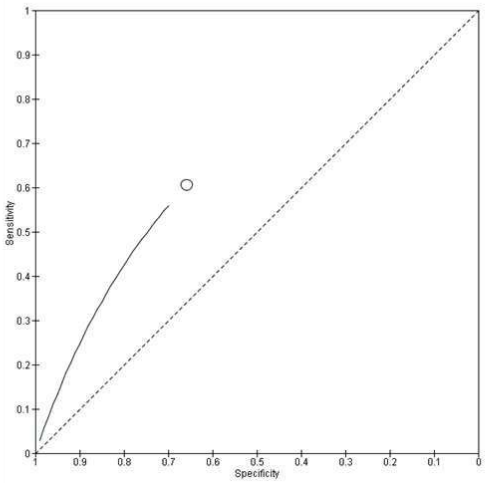


Figure 4. SROC accuracy plot for Shock index, pediatric age-adjusted (SIPA) score.

- *ABC score*

Per lo score ABC si sono trovate 3 pubblicazioni, di cui, 2 (Acker 2017, Phillips 2019) per cut-off rispettivamente uguali o superiori a 1,2 o 3, e 1 (El-Shafy 2018) generale.

Author, year	Setting	Population	Outcome	SE	SP
ABC score ≥ 1					
Acker 2017	Civilian	4-15 years	The need for PRBC transfusion in the first 6 hours as a marker of MTP activation	0.71	0.79
Phillips 2019*	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.852	0.372
ABC score ≥ 2					
Acker 2017	Civilian	4-15 years	The need for PRBC transfusion in the first 6 hours as a marker of MTP activation	0.29	1.00
Phillips 2019*	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.78	0.55
ABC score ≥ 3					
Acker 2017	Civilian	4-15 years	The need for PRBC transfusion in the first 6 hours as a marker of MTP activation	0.07	1.00
Phillips 2019*	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.69	0.545
ABC score					
El-Shafy 2016	Civilian	< 14 years	The need for blood transfusions within 48 hours	0.47	0.85

*Phillips 2019 included part of the population considered by Acker 2017.

Table 4. Diagnostic accuracy (sensitivity and specificity) of Assessment of blood consumption (ABC) score.

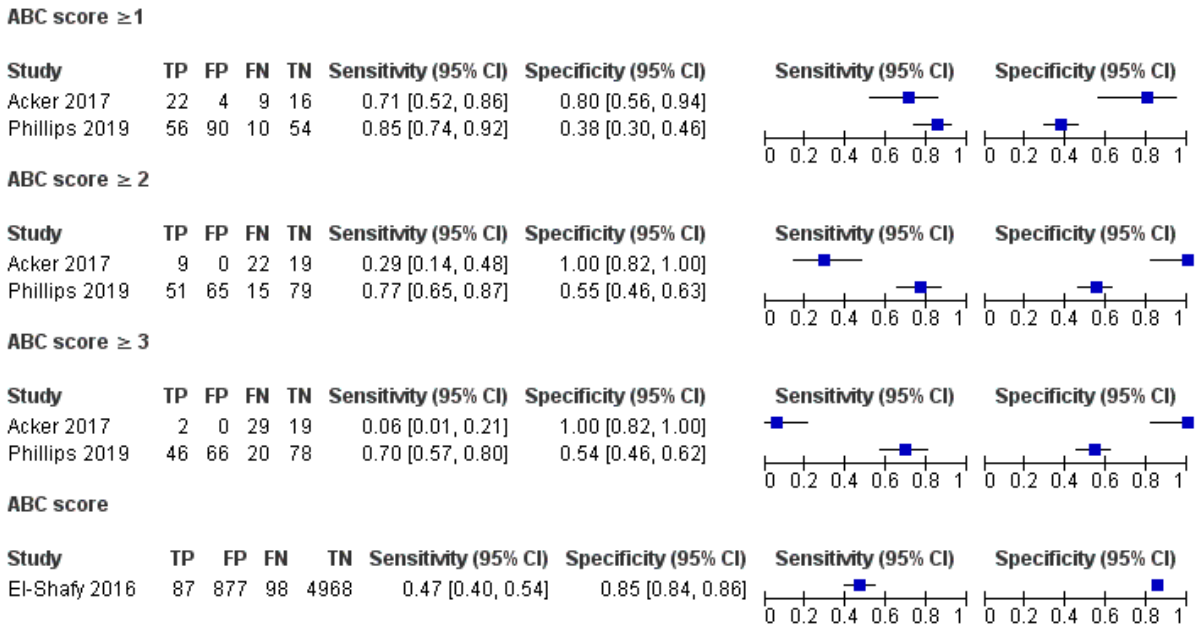


Figure 5. Diagnostic accuracy (sensitivity and specificity) of Assessment of blood consumption (ABC) score.

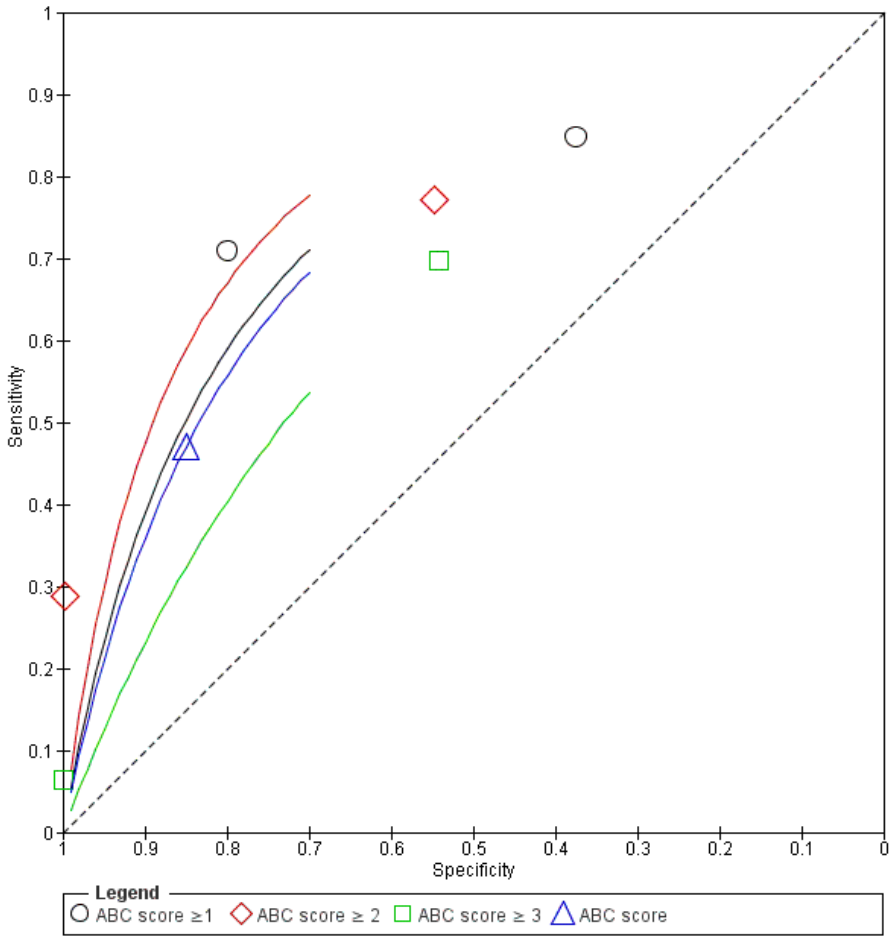


Figure 6. SROC accuracy plot for Assessment of blood consumption (ABC) score.

Score non validati

Oltre agli score validati, si sono trovati altri 5 score: ABC-S (Acker 2017, Phillips 2019), ABCD (Acker 2017, Phillips 2019), Pre-arrival model (Hwu 2015), ED model (Hwu 2015) e PED-ABC (Komori 2019), di cui l'ultimo è stato analizzato a diversi cut-off.

- *ABC-S score*

Per lo score ABC-S si sono trovate 2 pubblicazioni (Acker 2017, Phillips 2019) per cut-off rispettivamente uguali o superiori a 1,2 o 3.

Author, year	Setting	Population	Outcome	SE	SP
ABC-S score ≥ 1					
Acker 2017 (original study)	Civilian	4-15 years	The need for PRBC transfusion in the first 6 hours as a marker of MTP activation	0.65	0.84
Phillips 2019*	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.845	0.396
ABC-S score ≥ 2					
Acker 2017	Civilian	4-15 years	The need for PRBC transfusion in the first 6 hours as a marker of MTP activation	0.23	1.00
Phillips 2019*	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.716	0.471
ABC-S score ≥ 3					
Acker 2017	Civilian	4-15 years	The need for PRBC transfusion in the first 6 hours as a marker of MTP activation	0.03	1.00
Phillips 2019*	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.683	0.0

*Phillips 2019 included part of the population considered by Acker 2017.

Table 5. Diagnostic accuracy (sensitivity and specificity) of Age-adjusted ABC score (ABC-S) score.

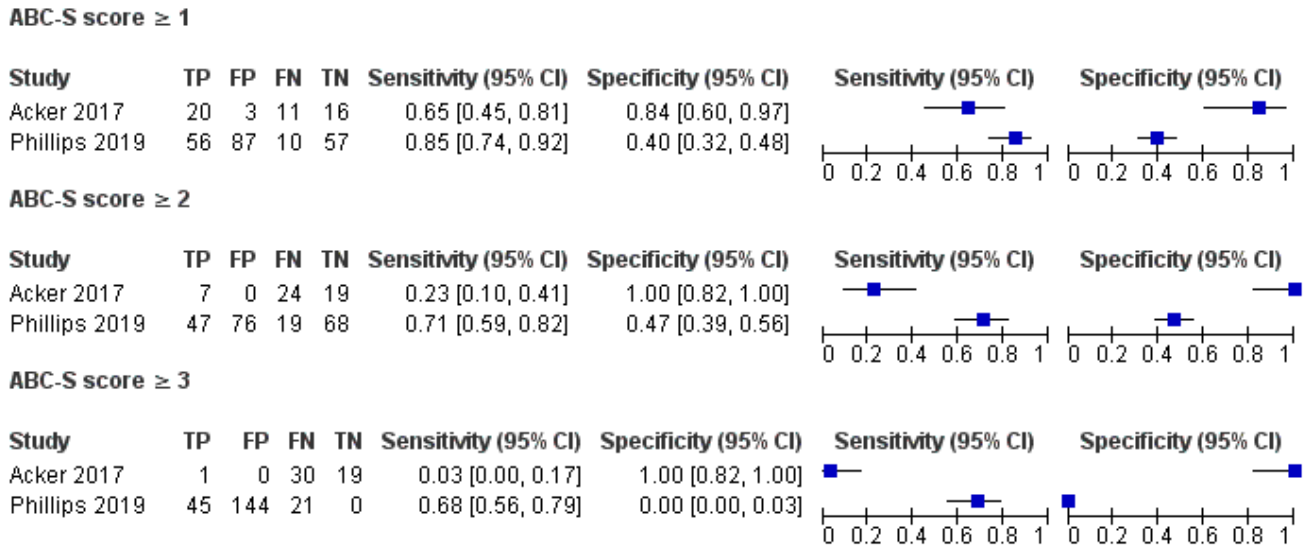


Figure 7. Diagnostic accuracy (sensitivity and specificity) of Age-adjusted ABC score (ABC-S) score.

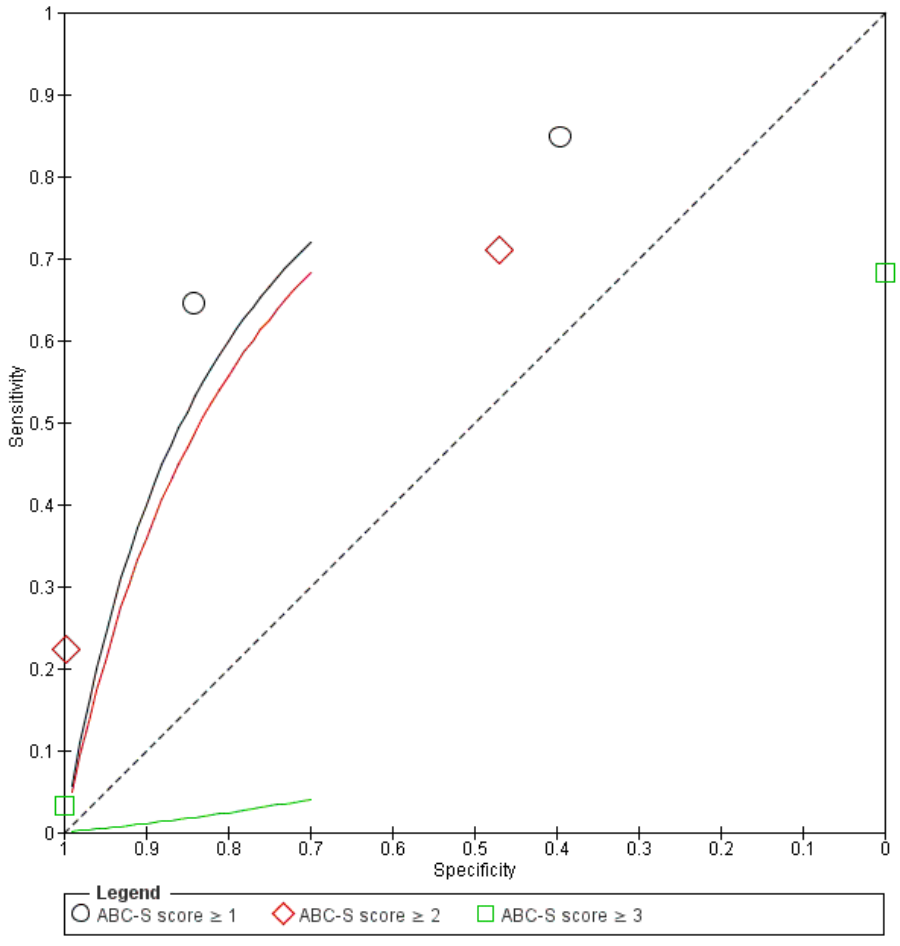


Figure 8. SROC accuracy plot for Assessment of Age-adjusted ABC score (ABC-S) score.

- *ABCD score*

Per lo score ABCD si sono trovate 2 pubblicazioni (Acker 2017, Phillips 2019) per cut-off rispettivamente uguali o superiori a 1,2 o 3.

Author, year	Setting	Population	Outcome	SE	SP
ABCD + base deficit					
Phillips 2019, score ≥ 1	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.964	0.413
Phillips 2019, score ≥ 2				0.839	0.569
Phillips 2019, score ≥ 3				0.732	0.75
ABCD + lactate					
Phillips 2019, score ≥ 1	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.877	0.386
Phillips 2019, score ≥ 2				0.765	0.526
Phillips 2019, score ≥ 3				0.695	0.50
ABCD + base deficit and lactate					
Phillips 2019, score ≥ 1	Civilian	1-18 years	MT determined by ≥40 cc/kg of total blood product within the first 6 hours following the injury.	0.979	0.404
Phillips 2019, score ≥ 2				0.874	0.525
Phillips 2019, score ≥ 3				0.774	0.788

Table 6. Diagnostic accuracy (sensitivity and specificity) of Adult-based ABC score with the inclusion of base deficit and lactate (ABCD) score

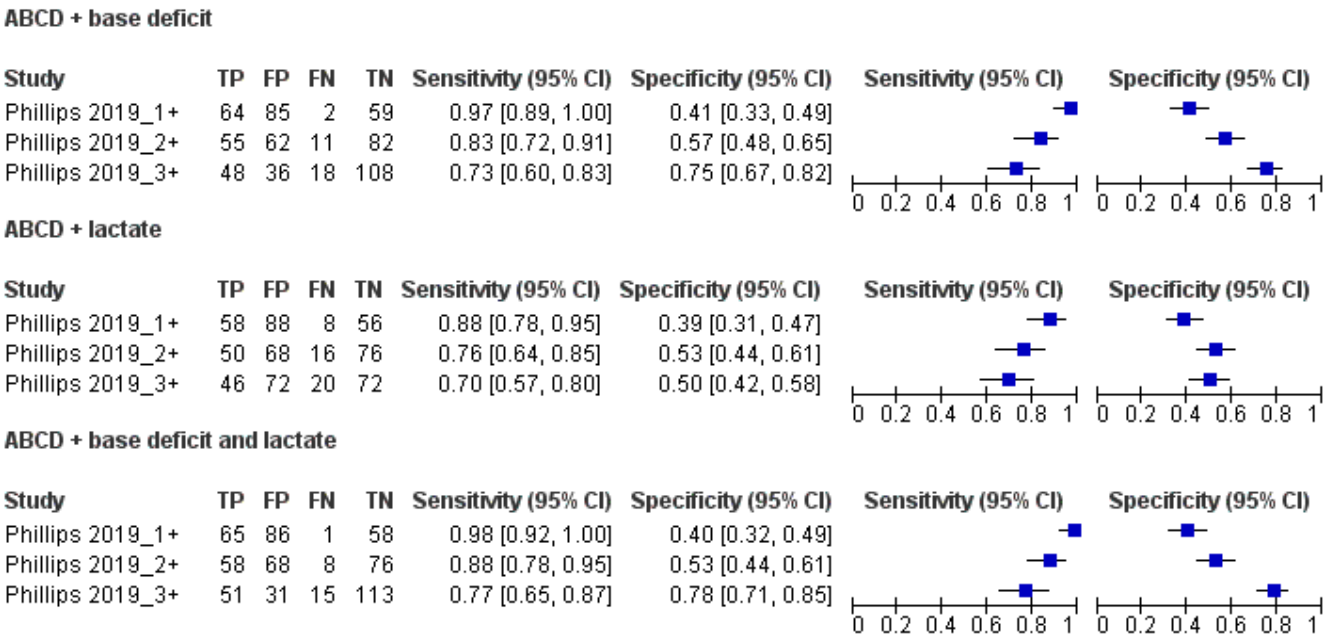


Figure 9. Diagnostic accuracy (sensitivity and specificity) of Adult-based ABC score with the inclusion of base deficit and lactate (ABCD) score.

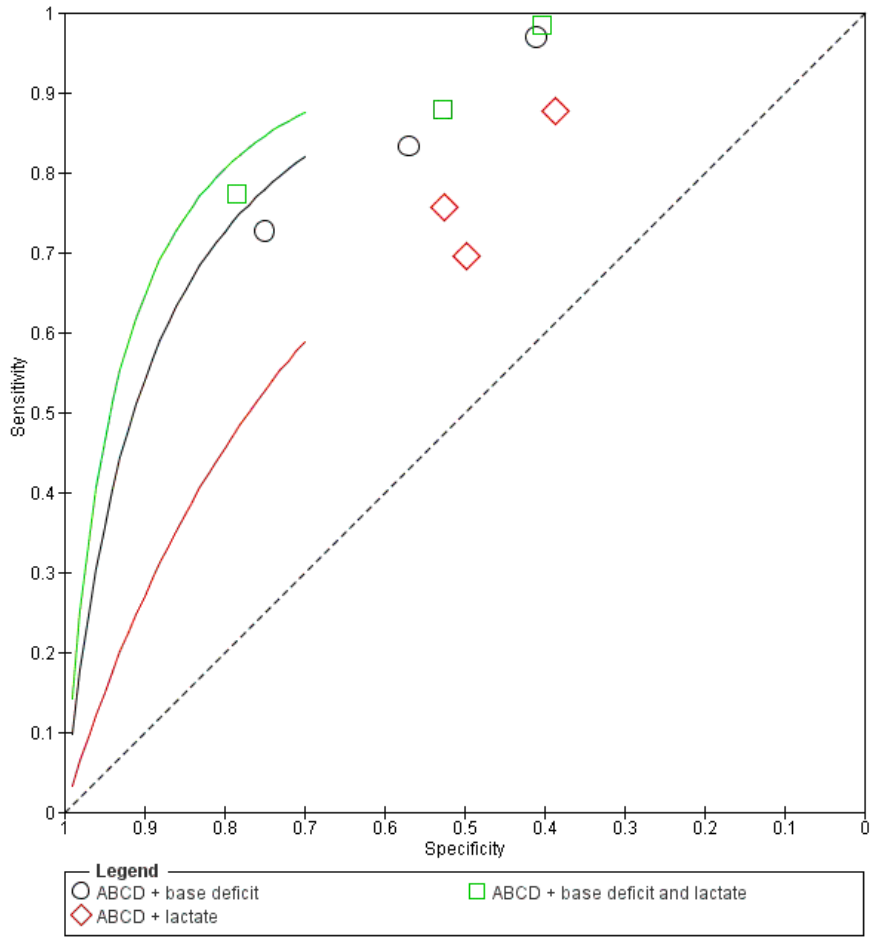


Figure 10. SROC accuracy plot for Assessment of Adult-based ABC score with the inclusion of base deficit and lactate (ABCD) score.

- *Pre-arrival model, ED model e PED-ABC*

Author, year	Setting	Population	Outcome	SE	SP
Pre-arrival model					
Hwu 2015	Civilian	< 18 years	Massive blood transfusion defined as 40 ml/kg of RBCs or 80 ml/kg total blood products in the first 24 h following injury	0.865	0.947
ED model					
Hwu 2015	Civilian	< 18 years	massive blood transfusion defined as 40 ml/kg of RBCs or 80 ml/kg total blood products in the first 24 h following injury	0.795	0.641
PED-ABC					
Komori 2019, score ≥ 1	Civilian	< 16 years	Transfusion within 24 hours	0.911	0.40
Komori 2019, score ≥ 2				0.544	0.85
Komori 2019, score ≥ 3				0.209	0.985
Komori 2019, score ≥ 4				0.046	0.999

Table 7. Diagnostic accuracy (sensitivity and specificity) of non-validated score

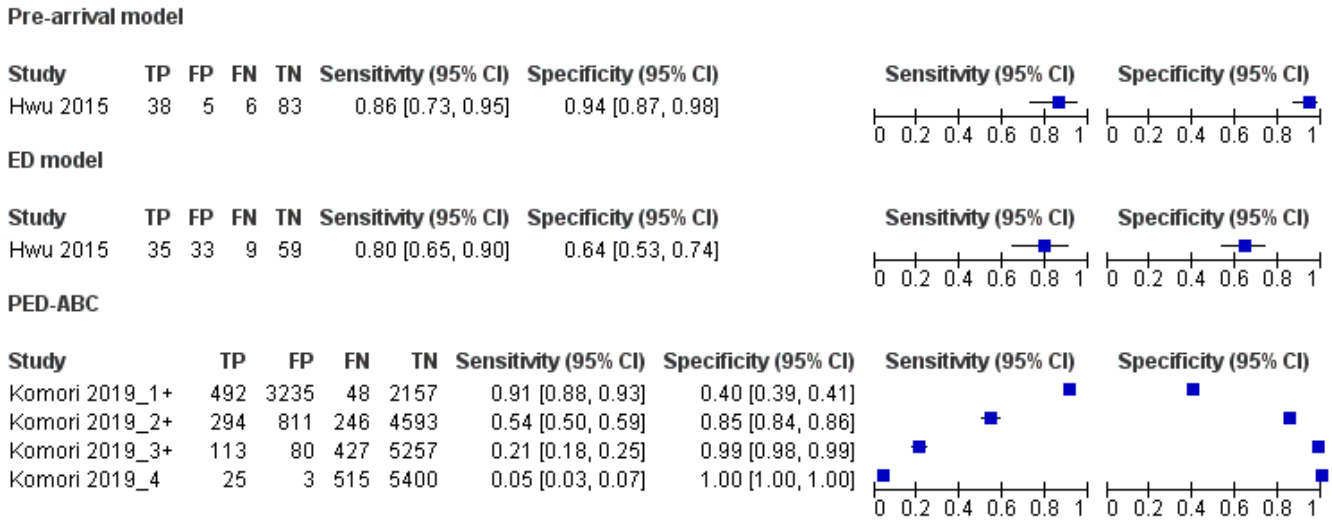


Figure 11. Diagnostic accuracy (sensitivity and specificity) of non-validated score.

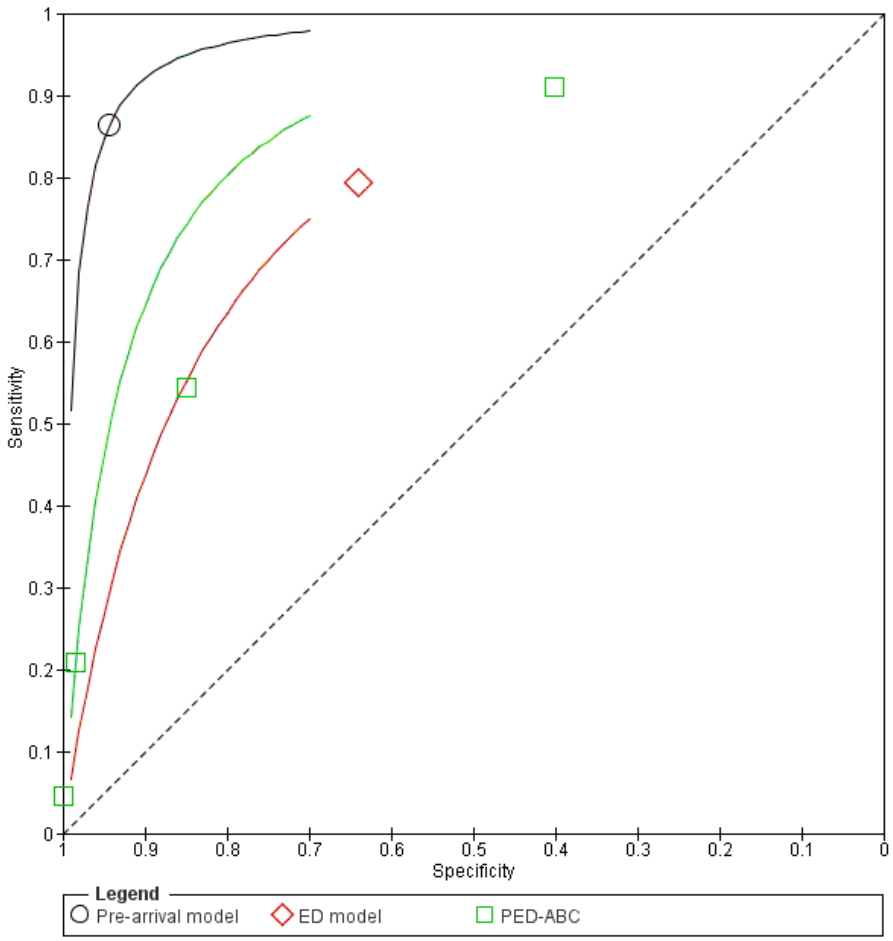


Figure 12. SROC accuracy plot for Assessment of non-validated score.

AUC dei test predittivi per la MT (massive transfusion or need for blood trasfusion)

Score validati

- *SI*

Per lo score SI è stata trovata una pubblicazione (Cuenca 2020), per cui si riporta l'AUC calcolato a diverse fasce d'età, a cui corrispondono i seguenti cut-off: 1-3 e 4-6 anni SI>1.2, 7-12 anni SI>1.0.

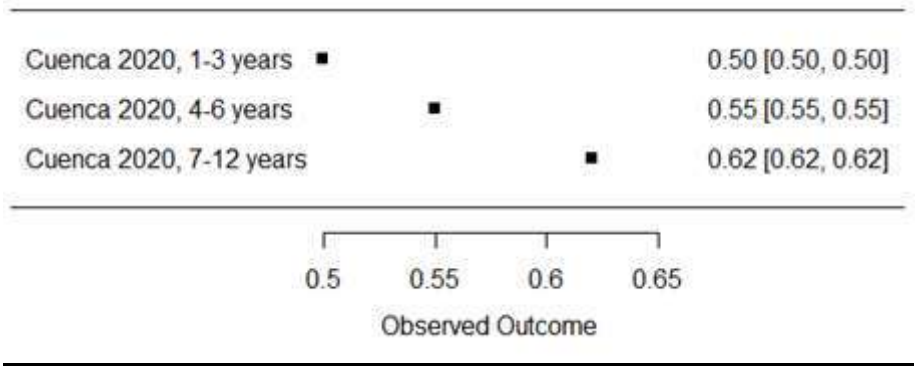
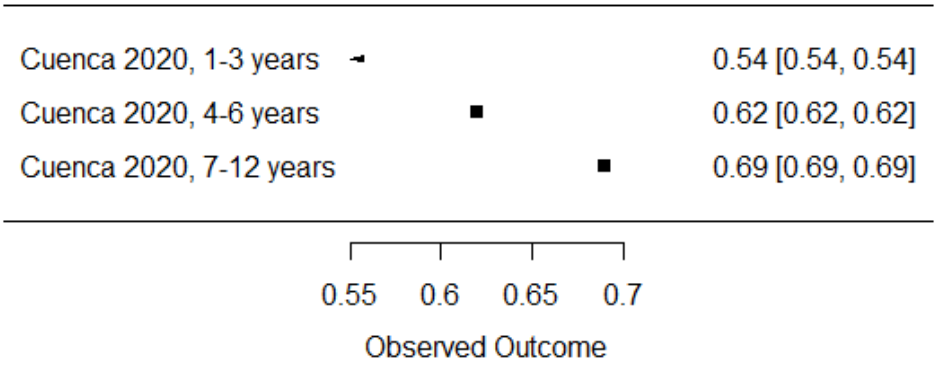


Figure 13. AUC of Shock Index (SI) score.

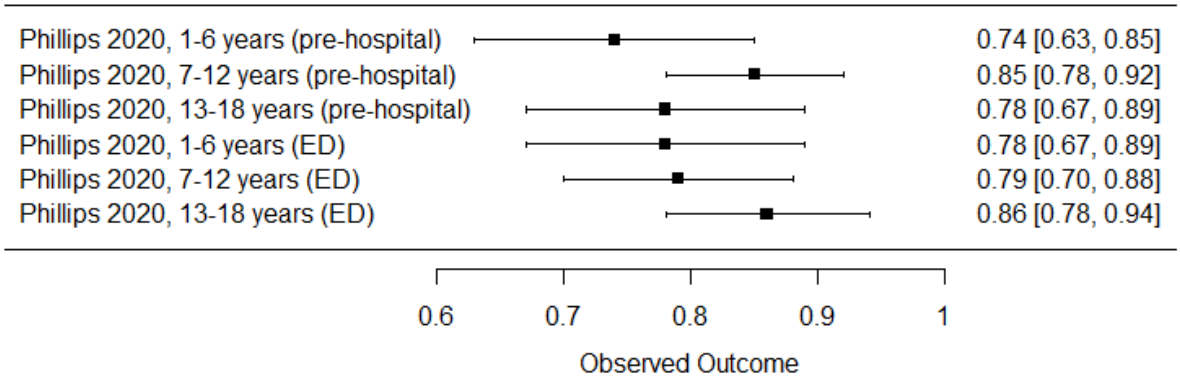
- *SIPA*

Per lo score SIPA, considerato per valori più elevati, si sono trovate 3 pubblicazioni, di cui, 1 (Acker 2017) relativa a pazienti con trauma contusivo, e 2 (Cuenca 2020, Phillips 2020) sulla popolazione generale con trauma. Per Cuenca 2020 e Phillips 2020 si sono riportati gli AUC per fascia d'età.

1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-17 yr: SIPA>0.9



1-6 years: SIPA> 1.52 (pre-hospital) or 1.27 (ED), 7-12 years: SIPA> 1.17 (pre-hospital) or 1.20 (ED), >13 years: SIPA> 0.99 (pre-hospital) or 0.86 (ED)



4-6 yr: SIPA >1.22, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9

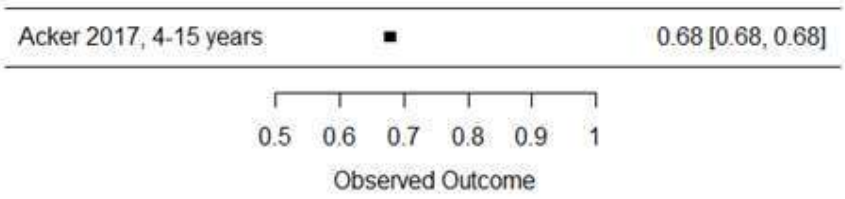


Figure 14. AUC of Shock index, pediatric age-adjusted (SIPA) score.

- *ABC score*

Per lo score ABC si sono trovate 2 pubblicazioni (Acker 2017, Phillips 2019) per cut-off rispettivamente uguali o superiori a 1,2 o 3.

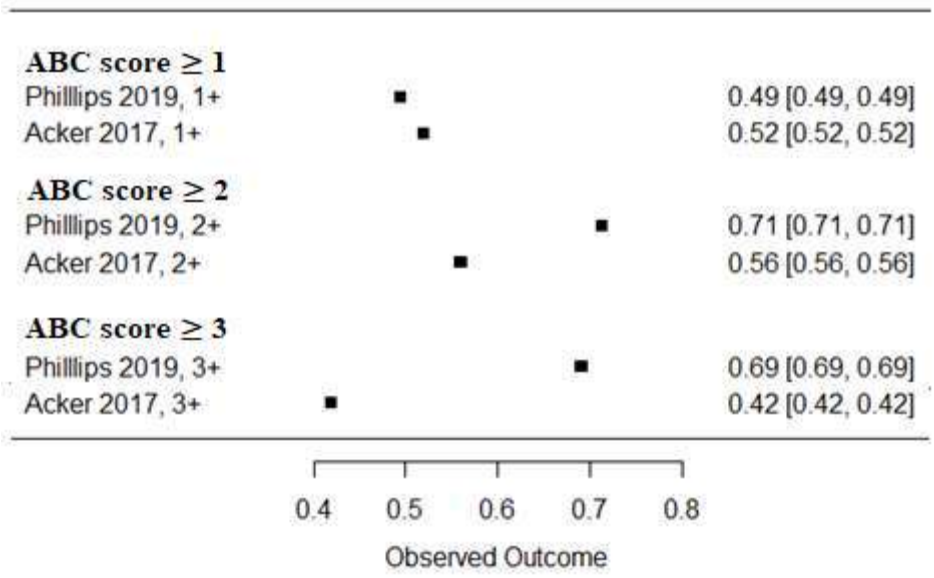


Figure 15. AUC of Assessment of blood consumption (ABC) score.

Score non validati

Oltre agli score validati, si sono trovati altri 7 score: ABC-S score, ABCD score, Pre-arrival model (Hwu 2015), ED model (Hwu 2015), BIG score (Hwu 2015), Admission lactate (Huh 2020) e Base deficit (Hwu 2020).

- *ABC-S score*

Per lo score ABC-S si sono trovate 2 pubblicazioni (Acker 2017, Phillips 2019) per cut-off rispettivamente uguali o superiori a 1,2 o 3.

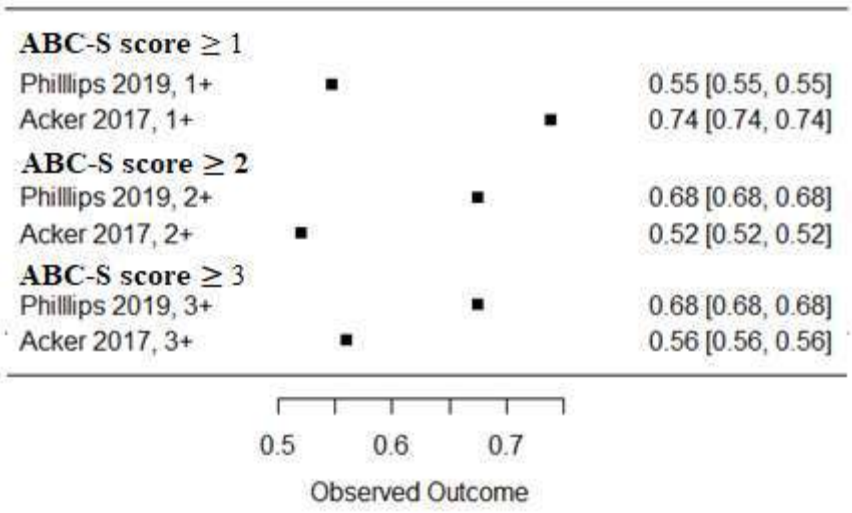


Figure 16. AUC of Age-adjusted ABC score (ABC-S) score.

- *ABCD score*

Per lo score ABCD è stata trovata una pubblicazione (Phillips 2019) per cut-off rispettivamente uguali o superiori a 1,2 o 3

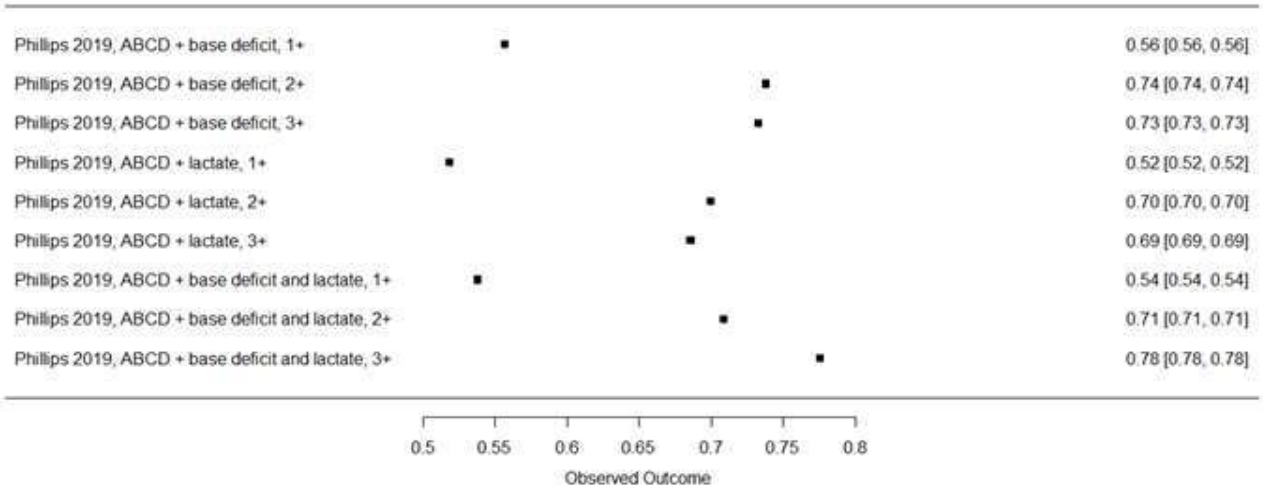
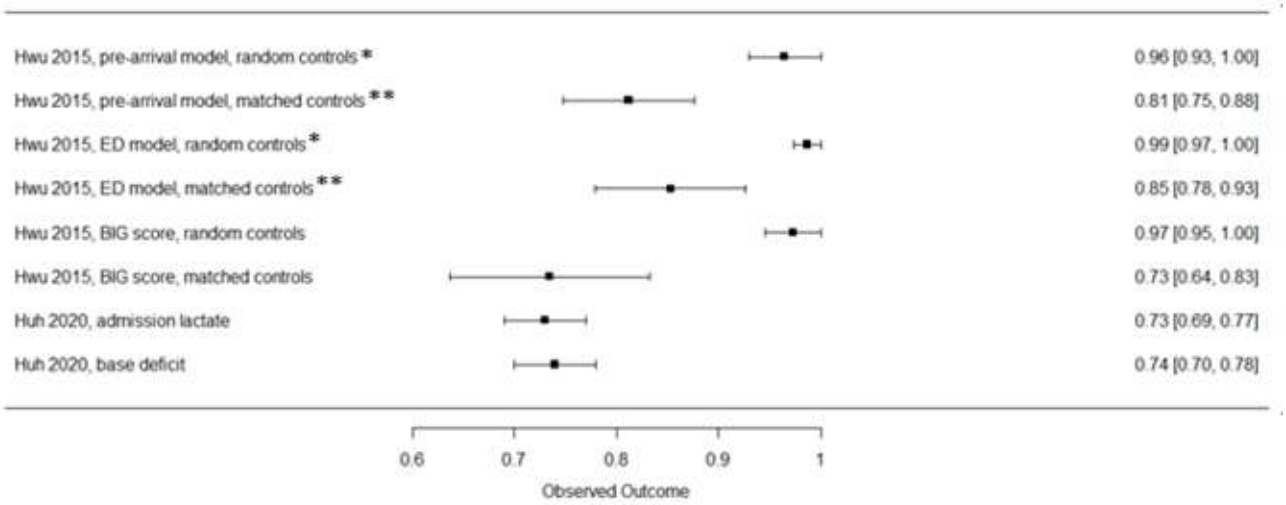


Figure 17. AUC of Adult-based ABC score with the inclusion of base deficit and lactate (ABCD) score.

- *Pre-arrival model, ED model, BIG score, Admission lactate and Base deficit*



* The pre-arrival model using random controls included HR, GCS, temperature, and penetrating injury mechanism and when using age and ISS-matched controls included GCS, penetrating injury, and active bleeding. The ED model using random controls included GCS, hemoglobin, and presence of penetrating injury and the age and ISS-matched controls model included hemoglobin, temperature, PTT, and active bleeding on arrival.
** Matched for age and injury severity score (ISS)

Figure 18. AUC of Pre-arrival model, ED model, BIG score, Admission lactate and Base deficit.

Analisi per sottogruppi: trauma contusivo e/o penetrante

- *SI*

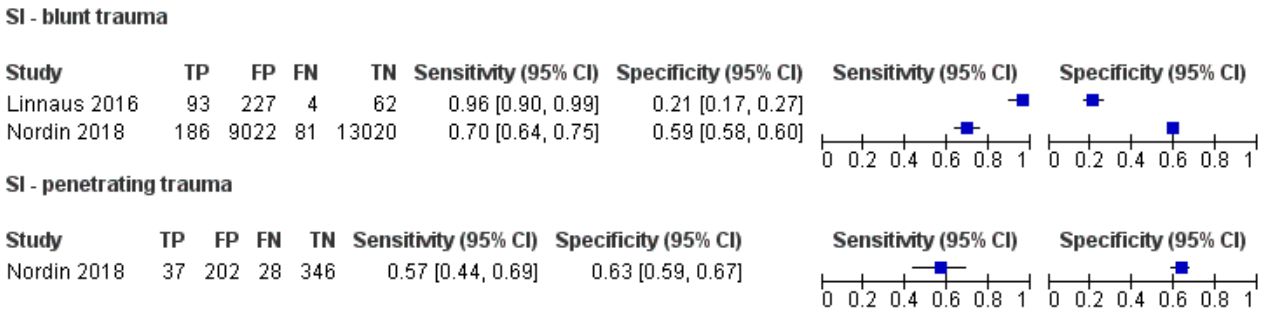


Figure 19. Diagnostic accuracy (sensitivity and specificity) of Shock Index (SI) score for blunt and penetrating trauma.

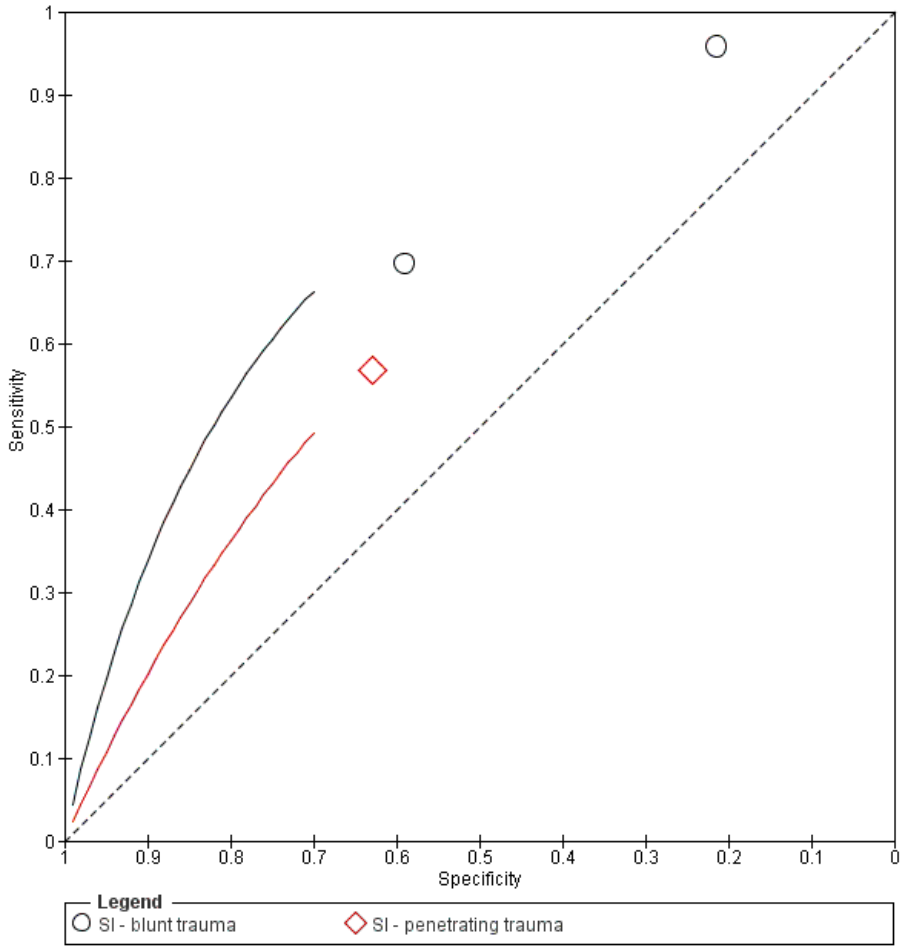
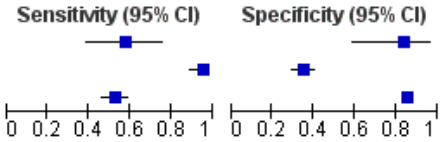


Figure 20. SROC accuracy plot for Shock Index (SI) score.

- *SIPA*

SIPA - blunt trauma

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Acker 2017	18	3	13	15	0.58 [0.39, 0.75]	0.83 [0.59, 0.96]
Linnaus 2016	92	188	5	101	0.95 [0.88, 0.98]	0.35 [0.29, 0.41]
Nordin 2018	140	3343	127	18721	0.52 [0.46, 0.59]	0.85 [0.84, 0.85]



SIPA - penetrating trauma

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Nordin 2018	30	89	35	459	0.46 [0.34, 0.59]	0.84 [0.80, 0.87]

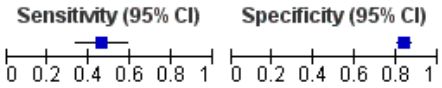


Figure 21. Diagnostic accuracy (sensitivity and specificity) of Shock index, pediatric age-adjusted (SIPA) score for blunt and penetrating trauma.

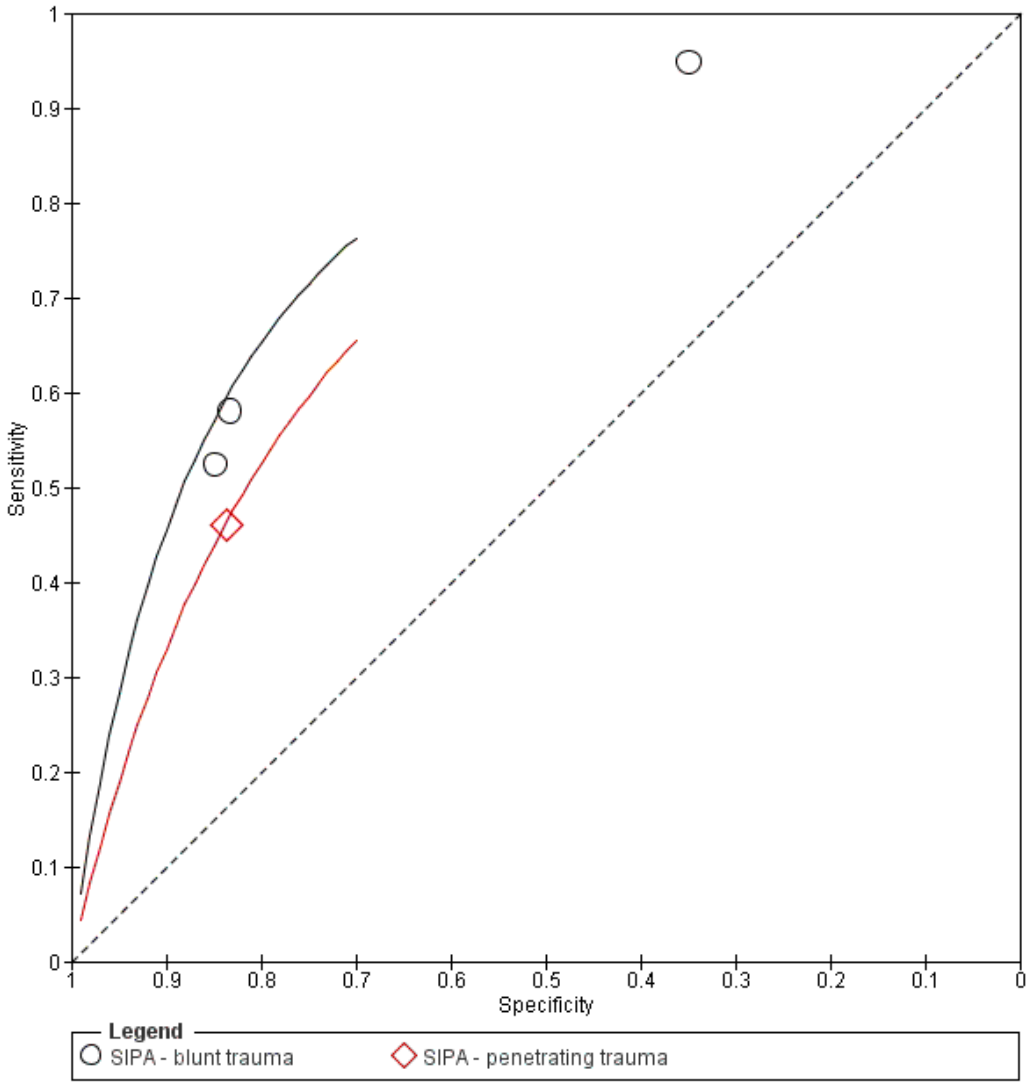


Figure 22. SROC accuracy plot for Shock index, pediatric age-adjusted (SIPA) score.

CQ13. Strumenti per predire l'emorragia critica

Appendice D. Risk of bias studi inclusi

Sottogruppo Adulti

	STUDY AUTHOR	YEAR	RISK OF BIAS				APPLICABILITY CONCERNS		
			PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
1	Afshari et al.	2019	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
2	Alimohammadi et al.	2017	HIGH	HIGH	LOW	UNCLEAR	UNCLEAR	LOW	LOW
3	Ardegh et al.	2001	HIGH	HIGH	LOW	UNCLEAR	LOW	LOW	LOW
4	Arlsan et al.	2015	HIGH	HIGH	LOW	UNCLEAR	LOW	LOW	LOW
5	Barnes et al.	2018	HIGH	LOW	LOW	UNCLEAR	UNCLEAR	LOW	LOW
6	Belanger-Quintana et al.	2019	HIGH	HIGH	LOW	UNCLEAR	UNCLEAR	LOW	LOW
7	Baker et al.	2011	HIGH	HIGH	LOW	UNCLEAR	UNCLEAR	LOW	LOW
8	Brockamp et al.	2012	HIGH	HIGH	LOW	UNCLEAR	UNCLEAR	LOW	LOW
9	Calcutt et al.	2011	LOW	UNCLEAR	LOW	UNCLEAR	UNCLEAR	LOW	LOW
10	Calcutt et al.	2016	LOW	UNCLEAR	LOW	UNCLEAR	UNCLEAR	LOW	LOW
11	Calcutt et al.	2013	NA	NA	NA	NA	NA	LOW	LOW
12	Campos-Serra et al.	2018	HIGH	UNCLEAR	LOW	UNCLEAR	LOW	LOW	LOW
13	Cancio et al.	2008	HIGH	UNCLEAR	LOW	UNCLEAR	UNCLEAR	LOW	LOW
14	Chaochankit et al.	2018	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
15	Choi et al.	2017	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
16	Cornero et al.	2020	LOW	UNCLEAR	LOW	HIGH	LOW	LOW	LOW
17	Cotton et al.	2010	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
18	David et al.	2017	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
19	De Jong et al	2016	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
20	Eastridge et al.	2010	HIGH	UNCLEAR	LOW	unclear	UNCLEAR	LOW	LOW
21	El Menyar et al.	2019 a	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
22	El Menyar et al.	2019 b	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
23	El Menyar et al.	2019 c	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
24	El Menyar ey al.	2018	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW

	STUDY AUTHOR	YEAR	RISK OF BIAS				APPLICABILITY CONCERNS		
			PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
25	Figueiredo et al.	2018	LOW	UNCLEAR	LOW	HIGH	LOW	LOW	LOW
26	Fligor et al.	2016	HIGH	UNCLEAR	LOW	HIGH	LOW	LOW	LOW
27	Frohlich et al.	2016	HIGH	UNCLEAR	LOW	UNCLEAR	LOW	LOW	LOW
28	Galvagno et al.	2015	HIGH	UNCLEAR	LOW	UNCLEAR	UNCLEAR	LOW	LOW
29	Hanna et al.	2020	HIGH	LOW	LOW	HIGH	LOW	LOW	LOW
30	Horst et al.	2020	UNCLEAR	UNCLEAR	LOW	LOW	LOW	LOW	LOW
31	Hsu et al.[28]	2013	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
32	jenkins et al.	2017	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
33	Joseph et al.	2018	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
34	Juste et al.	2021	HIGH	UNCLEAR	LOW	UNCLEAR	LOW	LOW	LOW
35	Kovar et al.	2019	HIGH	UNCLEAR	LOW	HIGH	HIGH	LOW	LOW
36	Krumrei et al.	2012	HIGH	LOW	LOW	LOW	LOW	LOW	LOW
37	Kuhne et al.	2008	HIGH	LOW	LOW	UNCLEAR	UNCLEAR	LOW	LOW
38	Larson et al.	2010	HIGH	LOW	LOW	LOW	LOW	LOW	LOW
39	Lee young et al.	2020	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
40	Lui Chun et al.	2018	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
41	Maegele et al.	2011	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
42	McLaughlin et al.	2008	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
43	McKinley et al.	2016	HIGH	HIGH	LOW	UNCLEAR	LOW	LOW	LOW
44	Mitra et al	2011	LOW	UNCLEAR	LOW	LOW	LOW	LOW	LOW
45	Mitra et al.	2012	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
46	Mina et al.	2013	UNCLEAR	HIGH	LOW	LOW	LOW	LOW	LOW
47	Moore et al.	2007	NA	NA	NA	NA	NA	NA	NA
48	Moore et al.	2017	LOW	LOW	LOW	HIGH	LOW	LOW	LOW
49	Mutschler et al.	2013	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
50	Nunez et al.	2009	HIGH	HIGH	LOW	UNCLEAR	LOW	LOW	LOW
51	Ogura et al.	2014	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
52	Ogura et al.	2015	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
53	Ogura et al.	2016	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
54	Ogura et al.	2018	LOW	HIGH	LOW	UNCLEAR	LOW	LOW	LOW
55	Ohmori et al.	2017	LOW	UNCLEAR	LOW	LOW	LOW	LOW	LOW
56	Parimi et al.	2016	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW

	STUDY AUTHOR	YEAR	RISK OF BIAS				APPLICABILITY CONCERNS		
			PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
57	Park et al.	2019	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
58	Pommerening et al.	2015	LOW	LOW	LOW	HIGH	LOW	LOW	LOW
59	Poon et al.	2012	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
60	Pottecher et al.	2016	HIGH	UNCLEAR	LOW	HIGH	LOW	LOW	LOW
61	Prichayudh et al.	2020	HIGH	HIGH	LOW	HIGH	UNCLEAR	LOW	LOW
62	Rainer et al.	2011	HIGH	HIGH	LOW	HIGH	LOW	LOW	LOW
63	Rau et al.	2016	HIGH	LOW	LOW	LOW	LOW	LOW	LOW
64	Ruchholtz et al.	2006	LOW	LOW	LOW	LOW	LOW	LOW	LOW
65	Schreiber et al.	2007	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
66	Schroll et al.	2018	HIGH	HIGH	LOW	HIGH	LOW	LOW	LOW
67	Shackelford et al.	2015	UNCLEAR	HIGH	LOW	LOW	LOW	LOW	LOW
68	Sharma et al.	2019	LOW	UNCLEAR	LOW	LOW	LOW	LOW	LOW
69	Swerts	2020	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
70	Terceros-Almanza	2019	HIGH	UNCLEAR	LOW	HIGH	LOW	LOW	LOW
71	Terceros-Almanza	2017	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
72	Thorn	2019	HIGH	UNCLEAR	LOW	HIGH	LOW	LOW	LOW
73	Tonglet	2017	LOW	HIGH	LOW	LOW	LOW	LOW	LOW
74	Tonglet	2014	LOW	HIGH	LOW	LOW	LOW	LOW	LOW
75	Umemura	2016	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
76	Vandromme	2011 a	LOW	UNCLEAR	LOW	LOW	LOW	LOW	LOW
77	Vandromme	2011 b	UNCLEAR	UNCLEAR	LOW	LOW	LOW	LOW	LOW
78	Wade	2008	NA	NA	NA	NA	NA	NA	NA
79	Weaver.	2016	LOW	UNCLEAR	LOW	HIGH	LOW	LOW	LOW
80	Wang	2019	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
81	Wang	2016	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
82	Wei	2017	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
83	Wei	2020	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
84	Wu	2019	HIGH	UNCLEAR	LOW	LOW	UNCLEAR	LOW	LOW
85	Yang	2021	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW
86	Yucel	2006	HIGH	UNCLEAR	LOW	LOW	LOW	LOW	LOW

	STUDY AUTHOR	YEAR	RISK OF BIAS				APPLICABILITY CONCERNS		
			PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
87	Yumoto	2014	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW
88	Peltan	2015	LOW	HIGH	LOW	UNCLEAR	LOW	LOW	LOW
89	Peltan	2016	HIGH	HIGH	LOW	LOW	LOW	LOW	LOW

Sottogruppo Pediatrico

	RISK OF BIAS				APPLICABILITY		
STUDY ID	**Patient selection**	**Index test**	**Reference standard**	**Flow and timing**	**Patient selection**	**Index test**	**Reference standard**
Acker 2017	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Cuenca 2020	LOW	LOW	LOW	LOW	LOW	LOW	LOW
El-Shafy 2016	LOW	LOW	LOW	LOW	HIGH	LOW	LOW
Huh 2021	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Hwu 2015	HIGH	LOW	LOW	LOW	LOW	LOW	LOW
Komori 2021	HIGH	LOW	LOW	LOW	HIGH	LOW	LOW
Linnaus 2016	LOW	LOW	LOW	LOW	HIGH	LOW	LOW
Marenco 2020	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Nordin 2018	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Phillips 2019	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Phillips 2020	LOW	LOW	LOW	LOW	HIGH	LOW	LOW
Strutt 2019	LOW	LOW	LOW	LOW	LOW	LOW	LOW

CQ13. Strumenti per predire l'emorragia critica

Appendice E – Summary of findings in Adults

Sommario

Judgements criteria

Dati epidemiologici

The incidence of massive transfusion was higher in Denmark (4.5 per 10,000) than in Sweden (2.5 per 10,000). https://pubmed.ncbi.nlm.nih.gov/26901542/ While only 3 percent of civilian trauma patients will receive a massive transfusion (>10 units red blood cells [RBC] in 24 hours), these patients consume 70 percent of all blood transfused at a trauma center. https://www.facs.org/-/media/files/quality-programs/trauma/tqip/transfusion_guildelines.ashx, https://www.doh.wa.gov/Portals/1/Documents/2900/MassiveTransfusionTrauma.pdf

Our SR found 7.7 % of prevalence of need of massive transfusion.

Ragioni specifiche adottate per Downgrading

(a) downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

(b) downgrade di 1 livello per inconsistenza da ispezione visiva dei plots; downgrade di 2 livello

(c) la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli. Quando non disponibili dati di variabilità (e quindi l'imprecisione non era valutabile) gli studi sono stati abbassati di 1 livello

Summary – Certainty of the evidence of included validated risk prediciton tools

Index test	Threshold	N° studies	MT/TIC	Sensitivity	Specificity
Prince of Wales/Rainer	cut off ≥6	4	MT	VERY LOW	MODERATE
Prince of Wales/Rainer	cut off ≥ 2.5	1	MT	MODERATE	MODERATE
Prince of Wales/Rainer	cut off > 2	3	MT	LOW	VERY LOW
Prince of Wales/Rainer	cut off >1.5	1	MT	LOW	VERY LOW
TASH score (SBP [≤100 MM Hg = 4, < 120 = 1], HR ≥ 120 bpm =2, FAST +ve = 3, Hb [<7=8, <9=6, <10=4, <11=3, <12=2], Base excess [<-10=4, <-6=3, <-2=1], clinically instable pelvioc fracture =3, open/dislocated femur fracture, Male =1					
TASH score	not specified	4	MT	VERY LOW	MODERATE
TASH score	cut off ≥6	2	MT	VERY LOW	MODERATE
TASH score	cut off ≥6.5	1	MT	LOW	VERY LOW
TASH score	cut off >7	1	MT	LOW	MODERATE
TASH score	cut off ≥ 8	2	MT	LOW	MODERATE
TASH score	cut off ≥ 16	7	MT	LOW	MODERATE
TASH score	cut off ≥10	1	MT	LOW	MODERATE
TASH score	cut off ≥18	1	MT	LOW	MODERATE
TASH score	cut off ≥8.5	1	MT	MODERATE	MODERATE
TASH score	cut off >5	1	MT	VERY LOW	LOW
MTS (massive tranfsusion score) (SBp <90, Hb <11, INR > 1.5, Base deficiti ≥6, Positive FAST, penetrating mechanism)	cut off ≥ 2	1	MT	NA	NA
TBSS	cut off >15		MT		
TBSS	cut off ≥10	1	MT	MODERATE	LOW
TBSS	cut off ≥17	1	MT	LOW	MODERATE
TBSS	cut off ≥14	1	MT	LOW	MODERATE
TBSS	cut off >16	1	MT	NA	NA
Milano score (max score 9 points)	Cornero et al.	1	MT	NA	NA
Larson score Any 2 or more of the following: Hemoglobin <11 g/dL, SBP < 110 mm Hg, HR > 110 bpm, Base Deficit ≤6 mmol/L					
Larson score	cut off = 1.5	2	MT	MODERATE	MODERATE
Larson score	cut off > 1	1	MT	MODERATE	MODERATE
Larson score	cut off >1.5		MT		
McLaughlin score		4	MT	VERY LOW	MODERATE
Schreiber score (Hb ≤ 11, International normilized ratio > 1.5, penetrating trauma)					
Schreiber score	cut off ≥ 0.5	1	MT	MODERATE	MODERATE

Index test	Threshold	N° studies	MT/TIC	Sensitivity	Specificity
Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)					
Vandromme score (SBP < 110 = 1, HR > 105 = 1, Lactate ≥5=1, international normalized ratio > 1.5 =1, Hb ≤ 11=1)	cut off ≥ 3	1	MT	NA	NA
Vandromme score	cut off ≥ 1.5	1	MT	MODERATE	MODERATE
Cincinnati individual tansfusion trigget (CITT) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C) 6 hours					
revised MTS (massive transfusion score) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6. temprature < 35.5 C)	cut off ≥ 2	1	MT	NA	NA
MTS (massive tranfsusion score 6 hours) (SBp <90, Hb <11, INR > 1.5, Base deficit ≥6)	cut off ≥ 1	1	MT	NA	NA
Prediction scoring scheme (0-8 points) - type of trauma, injury severity score, heart rate, hemoglobin, prothrombin time, fibrinogen, and base excess					
Prediction scoring scheme	cut off = 4 points	2	MT	VERY LOW	LOW
ABC score (Penetrating mechanism (0 = no, 1 = yes), ED SBP of 90 mm Hg or less (0 = no, 1 = yes), ED HR of 120 bpm or greater (0 = no, 1 = yes), Positive FAST (0 = no, 1 = yes)					
ABC score	cut off ≥ 0.5	2	MT	MODERATE	VERY LOW
ABC score	cuf off ≥ 2	19	MT	VERY LOW	VERY LOW
ABC score	cut off >1	4	MT	VERY LOW	MODERATE
ABC score	cut off >0	1	MT	VERY LOW	MODERATE
ABC score	not specified		MT		
ETS score					
ETS score	cut off ≥ 3	2	MT	MODERATE	VERY LOW
ETS score	cut off > 2.5	1	MT	VERY LOW	MODERATE
ETS score	cut off > 4.8	1	MT	LOW	LOW
Revised assessment of Bleeding and Transfusion (RABT) Score (FAST result (positive = 1), SI ([1 = 1), pelvic fracture (present = 1), and MOI (penetrating = 1)					
Revised assessment of Bleeding and Transfusion (RABT) Score	cut off ≥ 2	2	MT	LOW	MODERATE
Shock Index (heart rate divided by systolic blood pressure)					
Shock Index	cut off >0.9	6	MT	VERY LOW	VERY LOW
Shock Index	not specified	9	TIC	VERY LOW	VERY LOW
Shock Index	cut off > 1.0	9	MT	LOW	MODERATE
Shock Index	cut off >0.967	1	MT	LOW	MODERATE
Shock Index	cut off SI >0.933	1	MT	LOW	MODERATE
Shock Index	cut off >0.95	1	MT	VERY LOW	MODERATE
Shock Index	cut off <36.95	1	MT	VERY LOW	MODERATE
Shock Index	cut off ≥ 0.81	1	MT	LOW	MODERATE
Shock Index	cut off ≥ 0.8	4	MT	VERY LOW	VERY LOW
Shock Index	cut off > 0.9	1	MT	LOW	MODERATE
Shock Index	cut off 0.84	1	TIC	LOW	MODERATE

Index test	Threshold	N° studies	MT/TIC	Sensitivity	Specificity
Shock Index	cut off 1.11	1	MT	VERY LOW	LOW
Shock Index	cut off 0.06	1	MT ≥ 10 U	VERY LOW	NA
Shock Index (Prehospital)	cut off 0.91	1	MT	VERY LOW	LOW
Modified Schok Index					
Modified Shock Index	cut off not reported	1	MT	NA	NA
Modified Shock Index	cut off 1.46	1	MT	VERY LOW	LOW
Shock Index	cut off <1.15	1	MT	VERY LOW	MODERATE
Modified Shock Index (Prehospital)	cut off 1.28	1	MT	VERY LOW	MODERATE
ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)					
ROPE Pulse Rate Over Pressure Evaluation (heart rate divided by the difference between the systolic blood pressure and the diastolic blood pressure.)	cut off ≥ 3	2	MT	NA	NA
COAST (Coagulopathy of Severe Trauma Score - acute traumatic coagulopathy entrapment (1 point); body temperature (< 358C: 1 point, < 328C: 2 points); SBP (< 100 mm Hg: 1 point, < 90 mm Hg: 2 points); pelvic content or abdominal injury (1 point), and chest decompression (1 point).					
COAST - Coagulopathy of Severe Trauma Score	cut off ≥ 3	3	TIC	VERY LOW	MODERATE
EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS - obvious extremity injurye = 1 point, penetrating mechanism =2 points, shock index ≥ 0.9=2 points, GCS≤ 8 =3 points.					
EMS-G scoring system (Extremity, Mechanism, Shock Index, GCS)	cut off ≥2	2	MT	LOW	LOW
TICCS Trauma induced coagulopathy clinical score (Severity [ED resuscitation room 2 points*, extent of body injury (torso, abddominal or the pelvic ring region = 2, head =1, each extremity = 1), SBP < 90 = 5)					
Trauma-Induced Coagulopathy Clinical Score (TICCS)	cut off ≥ 12	1	TIC	NA	NA
Trauma-Induced Coagulopathy Clinical Score (TICCS)	cut off ≥ 10	1	TIC	NA	NA
Early Blood Transfusion Needs Score- (age, type of injury, pulse, systolic blood pressure, GCS)					
Early Blood Transfusion Needs Score (age, type of injury, pulse, systolic blood pressure, GCS)	cut off > 5	1	MT	MODERATE	MODERATE
PACT 1 (Prediction of Acute Traumatic Coagulopathy) (Shock index, Injury-to-ED time, White race, Age, First GCS,First RR)		1	TIC	VERY LOW	LOW
PACT 2 (Prediction of Acute Traumatic Coagulopathy) (Shock index, Age, GCS Mechanism of injury, Intubation, CPR)		1	TIC	VERY LOW	VERY LOW
Milano score	Cut off ≥ 6	1	MT	LOW	MODERATE

Question 1: Should ABC score (cut off > 0) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.60 (95% CI: 0.43 to 0.75)
Specificity	0.74 (95% CI: 0.70 to 0.79)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 40 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	46 (33 to 58)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								31 (19 to 44)	
True negatives (patients without massive transusion)	1 studies 439 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	683 (646 to 729)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								240 (194 to 277)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli. Quando non disponibili dati di variabilità (e quindi l'imprecisione non era valutabile) gli studi sono stati abbassati di 1 livello

Question 2: Should ABC score (cut off > 1) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.47 to 0.79
Specificity	0.78 to 0.83

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	4 studies 220 patients	cohort & case-control type studies	serious [a]	not serious	serious [b]	very serious [c]	none	36 to 61	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								16 to 41	
True negatives (patients without massive transusion)	4 studies 766 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	720 to 766	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								157 to 203	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. downgrade di 1 livello per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 3: Should ABC score (cut off ≥ 0.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.76 to 0.79
Specificity	0.43 to 0.70

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 337 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	59 to 61	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								16 to 18	
True negatives (patients without massive transusion)	2 studies 4993 patients	cohort & case-control type studies	serious [a]	not serious	serious [b]	very serious [c]	none	397 to 646	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								277 to 526	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 1 livello per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 4: Should ABC score (cut off ≥ 2) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.33 to 0.89
Specificity	0.68 to 0.98

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	19 studies 1021 patients	cohort & case-control type studies	serious [a]	not serious	serious [b]	very serious [c]	suspected	25 to 69	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								8 to 52	
True negatives (patients without massive transusion)	19 studies 7586 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [c]	suspected	628 to 905	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								18 to 295	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 1 livello per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 5: Should Larson score (cut off >1) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.55 (95% CI: 0.38 to 0.71)
Specificity	0.79 (95% CI: 0.75 to 0.83)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 40 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	42 (29 to 55)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								35 (22 to 48)	
True negatives (patients without massive transusion)	1 studies 439 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	729 (692 to 766)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								194 (157 to 231)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

Question 6: Should Larson score (cut off = 1.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.71 to 0.77
Specificity	0.77 to 0.80

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 337 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	55 to 59	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								18 to 22	
True negatives (patients without massive transusion)	2 studies 5202 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	711 to 738	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								185 to 212	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

Question 7: Should Prince of Wales/Rainer (cut off > 2) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.68 to 0.80
Specificity	0.52 to 0.80

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	3 studies 159 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	52 to 62	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								15 to 25	
True negatives (patients without massive transusion)	3 studies 1034 patients	cohort & case-control type studies	serious [a]	not serious	serious [c]	very serious [b]	none	480 to 738	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								185 to 443	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

c. downgrade di 1 livello per inconsistenza da ispezione visiva dei plots

Question 8: Should Prince of Wales/Rainer (cut off ≥ 2.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.81 (95% CI: 0.76 to 0.85)
Specificity	0.78 (95% CI: 0.77 to 0.79)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 289 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	62 (59 to 65)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								15 (12 to 18)	
True negatives (patients without massive transusion)	1 studies 4858 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	720 (711 to 729)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								203 (194 to 212)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

Question 9: Should Prince of Wales/Rainer (cut off ≥ 6) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.03 to 0.37
Specificity	0.97 to 0.99

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	4 studies 310 patients	cohort & case-control type studies	serious [a]	not serious	very serious [b]	very serious [c]	suspected	2 to 28	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								49 to 75	
True negatives (patients without massive transusion)	4 studies 4899 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	suspected	895 to 914	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								9 to 28	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 2 livello per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 10: Should Prince of Wales/Reiner (cut off > 1.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.94 (95% CI: 0.83 to 0.99)
Specificity	0.59 (95% CI: 0.48 to 0.70)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 48 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	72 (64 to 76)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								5 (1 to 13)	
True negatives (patients without massive transusion)	1 studies 81 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	545 (443 to 646)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								378 (277 to 480)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 11: Should TBSS score (cut off ≥ 10) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.96 (95% CI: 0.90 to 0.99)
Specificity	0.70 (95% CI: 0.63 to 0.76)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 85 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	74 (69 to 76)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								3 (1 to 8)	
True negatives (patients without massive transusion)	1 studies 179 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	646 (581 to 701)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								277 (222 to 342)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 12: Should TBSS score (cut off ≥14) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.93 (95% CI: 0.85 to 0.97)
Specificity	0.93 (95% CI: 0.88 to 0.96)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 84 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	72 (65 to 75)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								5 (2 to 12)	
True negatives (patients without massive transusion)	1 studies 216 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	858 (812 to 886)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								65 (37 to 111)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 13: Should McLaughlin score be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.16 (95% CI: 0.06 to 0.31)
Specificity	0.98 (95% CI: 0.96 to 0.99)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	4 studies 38 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	suspected	12 (5 to 24)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								65 (53 to 72)	
True negatives (patients without massive transusion)	4 studies 335 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	suspected	905 (886 to 914)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								18 (9 to 37)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 14: Should TASH score (cut off > 7) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.87 (95% CI: 0.78 to 0.93)
Specificity	0.84 (95% CI: 0.78 to 0.88)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 84 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	67 (60 to 72)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								10 (5 to 17)	
True negatives (patients without massive transusion)	1 studies 216 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	775 (720 to 812)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								148 (111 to 203)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli

Question 15: Should TASH score (cut off > 16) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.13 to 0.26
Specificity	0.99 to 1.00

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	7 studies 115 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	suspected	10 to 20	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								57 to 67	
True negatives (patients without massive transusion)	7 studies 3860 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	suspected	914 to 923	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								0 to 9	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli

Question 16: Should TASH score (cut off >5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.77 (95% CI: 0.61 to 0.89)
Specificity	0.77 (95% CI: 0.68 to 0.85)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 39 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	59 (47 to 69)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								18 (8 to 30)	
True negatives (patients without massive transusion)	1 studies 114 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	711 (628 to 785)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								212 (138 to 295)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 17: Should TASH score (cut off ≥ 6) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.55 to 0.80

Prevalences	7.7%		

Specificity	0.76 to 0.80

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 119 patients	cohort & case-control type studies	serious [a]	not serious	very serious [b]	very serious [c]	none	42 to 62	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								15 to 35	
True negatives (patients without massive transusion)	2 studies 595 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	701 to 738	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								185 to 222	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 2 livelli per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 18: Should TASH score (cut off ≥ 6.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.94 (95% CI: 0.83 to 0.99)
Specificity	0.63 (95% CI: 0.51 to 0.73)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 48 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	72 (64 to 76)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								5 (1 to 13)	
True negatives (patients without massive transusion)	1 studies 83 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	581 (471 to 674)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								342 (249 to 452)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 19: Should TASH score (cut off ≥ 8) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.68 to 0.82
Specificity	0.79 to 0.82

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 102 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	52 to 63	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								14 to 25	
True negatives (patients without massive transusion)	2 studies 496 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	729 to 757	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								166 to 194	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli

Question 20: Should TASH score (cut off ≥ 8.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.84 (95% CI: 0.80 to 0.88)
Specificity	0.78 (95% CI: 0.77 to 0.80)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 289 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	65 (62 to 68)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								12 (9 to 15)	
True negatives (patients without massive transusion)	1 studies 4858 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	720 (711 to 738)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								203 (185 to 212)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

Question 21: Should TASH score (cut off ≥ 10) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.89 (95% CI: 0.81 to 0.95)

Prevalences	7.7%		

Specificity	0.86 (95% CI: 0.83 to 0.88)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 94 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	69 (62 to 73)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								8 (4 to 15)	
True negatives (patients without massive transusion)	1 studies 816 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	794 (766 to 812)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								129 (111 to 157)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli

Question 22: Should TBSS score (cut off ≥ 17) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.80 (95% CI: 0.70 to 0.88)
Specificity	0.98 (95% CI: 0.94 to 0.99)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 85 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	suspected	62 (54 to 68)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								15 (9 to 23)	
True negatives (patients without massive transusion)	2 studies 179 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	suspected	905 (868 to 914)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								18 (9 to 55)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 23: Should TASH score (cut off ≥ 18) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.25 (95% CI: 0.19 to 0.32)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 195 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	19 (15 to 25)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								58 (52 to 62)	
True negatives (patients without massive transusion)	1 studies 1039 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	923 (914 to 923)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								0 (0 to 9)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 24: Should TASH score (cut off not reported) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.03 to 0.45
Specificity	0.97 to 1.00

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	4 studies 893 patients	cohort & case-control type studies	serious [a]	not serious	very serious [b]	very serious [c]	suspected	2 to 35	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								42 to 75	
True negatives (patients without massive transusion)	4 studies 5524 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	suspected	895 to 923	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								0 to 28	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice

b. downgrade di 1 livello per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 25: Should EMS-G scoring system (cut off ≥2) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.81 to 0.96
Specificity	0.65 to 0.76

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 9249 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	62 to 74	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								3 to 15	
True negatives (patients without massive transusion)	2 studies 144105 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	600 to 701	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								222 to 323	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 26: Should ETS score (cut off ≥ 2.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.80 (95% CI: 0.64 to 0.91)
Specificity	0.53 (95% CI: 0.48 to 0.58)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 40 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	62 (49 to 70)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								15 (7 to 28)	
True negatives (patients without massive transusion)	1 studies 439 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	489 (443 to 535)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								434 (388 to 480)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 27: Should ETS score (cut off ≥ 3) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.97 to 0.98

Prevalences	7.7%		

Specificity	0.14 to 0.68

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 94 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	75 to 75	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								2 to 2	
True negatives (patients without massive transusion)	2 studies 1180 patients	cohort & case-control type studies	serious [a]	not serious	very serious [b]	very serious [c]	none	129 to 628	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								295 to 794	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 2 livelli per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 28: Should ETS score (cut off ≥ 4.8) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.96 (95% CI: 0.86 to 0.99)
Specificity	0.61 (95% CI: 0.52 to 0.69)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 48 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	74 (66 to 76)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								3 (1 to 11)	
True negatives (patients without massive transusion)	1 studies 141 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	563 (480 to 637)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								360 (286 to 443)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 29: Should Prediction scoring scheme (cut off = 4) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.80 (95% CI: 0.44 to 0.97)
Specificity	0.90 (95% CI: 0.83 to 0.94)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 10 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	suspected	62 (34 to 75)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								15 (2 to 43)	
True negatives (patients without massive transusion)	2 studies 136 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	suspected	831 (766 to 868)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								92 (55 to 157)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 30: Should RABT (cut off ≥ 2) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.78 (95% CI: 0.72 to 0.84)
Specificity	0.91 (95% CI: 0.89 to 0.93)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	2 studies 193 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	suspected	60 (55 to 65)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								17 (12 to 22)	
True negatives (patients without massive transusion)	2 studies 825 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	suspected	840 (821 to 858)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								83 (65 to 102)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 31: Should ROPE Pulse Rate Over Pressure Evaluation (cut off ≥ 3) be used to diagnose massive transfusion in trauma patients?

Sensitivity	-- (95% CI: -- to --)

Prevalences	0%		

Specificity	-- (95% CI: -- to --)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0%	
True positives (patients with massive transusion)	2 studies 0 patients							0 (0 to 0)	-
False negatives (patients incorrectly classified as not having massive transusion)								0 (0 to 0)	
True negatives (patients without massive transusion)	2 studies 0 patients							0 (0 to 0)	-
False positives (patients incorrectly classified as having massive transusion)								1000 (1000 to 1000)	

Question 32: Should Schreiber score (cut off ≥ 0.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.86 (95% CI: 0.81 to 0.90)
Specificity	0.62 (95% CI: 0.60 to 0.63)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 289 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	66 (62 to 69)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								11 (8 to 15)	
True negatives (patients without massive transusion)	1 studies 4858 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	572 (554 to 581)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								351 (342 to 369)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

Question 33: Should TICCS Trauma induced coagulopathy clinical score (cut off ≥ 10) for Damage Control Resuscitation be used to diagnose massive transfusion in trauma patients?

Sensitivity	No source of data selected

Prevalences	0%		

Specificity	No source of data selected

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0%	
True positives (patients with massive transusion)	1 studies 0 patients							0 (0 to 0)	-
False negatives (patients incorrectly classified as not having massive transusion)								0 (0 to 0)	
True negatives (patients without massive transusion)	1 studies 0 patients							0 (0 to 0)	-
False positives (patients incorrectly classified as having massive transusion)								1000 (1000 to 1000)	

Question 34: Should TICCS Trauma induced coagulopathy clinical score (cut off ≥ 12) for Damage Control Resuscitation be used to diagnose massive transfusion in trauma patients?

Sensitivity	No source of data selected
Specificity	No source of data selected

Prevalences	0%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0%	
True positives (patients with massive transusion)	1 studies 0 patients							0 (0 to 0)	-
False negatives (patients incorrectly classified as not having massive transusion)								0 (0 to 0)	
True negatives (patients without massive transusion)	1 studies 0 patients							0 (0 to 0)	-
False positives (patients incorrectly classified as having massive transusion)								1000 (1000 to 1000)	

Question 35: Should Vandromme score (cut off ≥ 3) be used to diagnose massive transfusion in trauma patients?

Sensitivity	-- (95% CI: -- to --)
Specificity	-- (95% CI: -- to --)

Prevalences	0%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0%	
True positives (patients with massive transusion)	1 studies 0 patients							0 (0 to 0)	-
False negatives (patients incorrectly classified as not having massive transusion)								0 (0 to 0)	
True negatives (patients without massive transusion)	1 studies 0 patients							0 (0 to 0)	-
False positives (patients incorrectly classified as having massive transusion)								1000 (1000 to 1000)	

Question 36: Should Vandromme score (cut off ≥1.5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.79 (95% CI: 0.74 to 0.83)
Specificity	0.76 (95% CI: 0.75 to 0.77)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 289 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	61 (57 to 64)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								16 (13 to 20)	
True negatives (patients without massive transusion)	1 studies 4858 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	701 (692 to 711)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								222 (212 to 231)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

Question 37: Should Early Blood Transfusion Needs Score (cut off >5) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.82 (95% CI: 0.79 to 0.85)
Specificity	0.80 (95% CI: 0.79 to 0.81)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 784 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	63 (61 to 65)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having massive transusion)								14 (12 to 16)	
True negatives (patients without massive transusion)	1 studies 23519 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	738 (729 to 748)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								185 (175 to 194)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

Question 38: Should Modified Shock Index (cut off >1.15) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.62 (95% CI: 0.51 to 0.71)
Specificity	0.82 (95% CI: 0.81 to 0.84)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 99 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	48 (39 to 55)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								29 (22 to 38)	
True negatives (patients without massive transusion)	1 studies 2391 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	757 (748 to 775)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								166 (148 to 175)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 39: Should Modified Shock Index (cut off 1.28) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.60 (95% CI: 0.49 to 0.71)
Specificity	0.82 (95% CI: 0.79 to 0.84)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 78 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	46 (38 to 55)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								31 (22 to 39)	
True negatives (patients without massive transusion)	1 studies 929 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	757 (729 to 775)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								166 (148 to 194)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 40: Should Modified Shock Index (cut off 1.46) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.96 (95% CI: 0.80 to 1.00)
Specificity	0.76 (95% CI: 0.70 to 0.81)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 25 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	74 (62 to 77)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								3 (0 to 15)	
True negatives (patients without massive transusion)	1 studies 254 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	701 (646 to 748)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								222 (175 to 277)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 41: Should Shock Index (cut off 0.06) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.41 (95% CI: 0.31 to 0.53)
Specificity	-- (95% CI: -- to --)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 82 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	32 (24 to 41)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								45 (36 to 53)	
True negatives (patients without massive transusion)	1 studies 0 patients							0 (0 to 0)	-
False positives (patients incorrectly classified as having massive transusion)								923 (923 to 923)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 42: Should Shock Index (cut off > 0.8) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.67 to 0.96
Specificity	0.36 to 0.84

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	4 studies 239 patients	cohort & case-control type studies	serious [a]	not serious	very serious [b]	very serious [c]	suspected	52 to 74	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								3 to 25	
True negatives (patients without massive transusion)	4 studies 2495 patients	cohort & case-control type studies	serious [a]	not serious	very serious [b]	very serious [c]	suspected	332 to 775	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								148 to 591	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 2 livelli per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 43: Should Shock Index (cut off 0.81) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.85 (95% CI: 0.76 to 0.92)
Specificity	0.64 (95% CI: 0.63 to 0.65)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 89 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	65 (59 to 71)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								12 (6 to 18)	
True negatives (patients without massive transusion)	1 studies 8621 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	591 (581 to 600)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								332 (323 to 342)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 44: Should Shock Index (cut off > 0.9) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.62 to 0.95
Specificity	0.66 to 0.86

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	6 studies 1002 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	suspected	48 to 73	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								4 to 29	
True negatives (patients without massive transusion)	6 studies 6826 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	suspected	609 to 794	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								129 to 314	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 45: Should Shock Index (cut off 0.91) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.65 (95% CI: 0.54 to 0.76)
Specificity	0.77 (95% CI: 0.74 to 0.80)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 78 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	50 (42 to 59)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								27 (18 to 35)	
True negatives (patients without massive transusion)	1 studies 929 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	711 (683 to 738)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								212 (185 to 240)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 46: Should Shock Index (cut off >0.933, prehospital) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.75 (95% CI: 0.68 to 0.81)
Specificity	0.62 (95% CI: 0.60 to 0.64)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 176 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	58 (52 to 62)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								19 (15 to 25)	
True negatives (patients without massive transusion)	1 studies 2381 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	572 (554 to 591)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								351 (332 to 369)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 47: Should Shock Index (cut off >0.95) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.57 (95% CI: 0.46 to 0.67)
Specificity	0.88 (95% CI: 0.86 to 0.89)

Prevalences	7.7%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with massive transusion)	1 studies 99 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	44 (35 to 52)	0 (0 to 0)	0 (0 to 0)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								33 (25 to 42)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without massive transusion)	1 studies 2391 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	812 (794 to 821)	880 (860 to 890)	880 (860 to 890)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								111 (102 to 129)	120 (110 to 140)	120 (110 to 140)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 48: Should Shock Index (cut off >0.967, prehospital) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.75 (95% CI: 0.68 to 0.81)
Specificity	0.74 (95% CI: 0.72 to 0.76)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 176 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	58 (52 to 62)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								19 (15 to 25)	
True negatives (patients without massive transusion)	1 studies 2381 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	683 (665 to 701)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								240 (222 to 258)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 49: Should Shock Index (cut off>1) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.62 to 0.77
Specificity	0.79 to 0.87

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	9 studies 4095 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	suspected	48 to 59	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								18 to 29	
True negatives (patients without massive transusion)	9 studies 46067 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	suspected	729 to 803	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								120 to 194	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 50: Should Shock Index (cut off 1.11) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.92 (95% CI: 0.74 to 0.99)
Specificity	0.80 (95% CI: 0.74 to 0.84)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 25 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	71 (57 to 76)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								6 (1 to 20)	
True negatives (patients without massive transusion)	1 studies 254 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	738 (683 to 775)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								185 (148 to 240)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 51: Should Shock Index, age adjusted (cut off = 36.95) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.55 (95% CI: 0.44 to 0.65)
Specificity	0.72 (95% CI: 0.70 to 0.74)

Prevalences	7.7%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with massive transusion)	1 studies 99 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	42 (34 to 50)	0 (0 to 0)	0 (0 to 0)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								35 (27 to 43)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without massive transusion)	1 studies 2391 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	665 (646 to 683)	720 (700 to 740)	720 (700 to 740)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								258 (240 to 277)	280 (260 to 300)	280 (260 to 300)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli

Question 52: Should Shock Index (cut off not reported) be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.48 to 0.85
Specificity	0.54 to 0.86

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	9 studies 246 patients	cohort & case-control type studies	serious [a]	not serious	serious [b]	very serious [c]	none	37 to 65	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								12 to 40	
True negatives (patients without massive transusion)	9 studies 2611 patients	cohort & case-control type studies	serious [a]	not serious	serious [b]	very serious [c]	none	498 to 794	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								129 to 425	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 1 livello per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli

Question 53: Should Shock Index (cut off >0.9) for TIC be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.65 (95% CI: 0.56 to 0.74)
Specificity	0.77 (95% CI: 0.72 to 0.81)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 112 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	50 (43 to 57)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								27 (20 to 34)	
True negatives (patients without massive transusion)	1 studies 373 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	711 (665 to 748)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								212 (175 to 258)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 54: Should Shock Index (cut off 0.84) for TIC be used to diagnose massive transusion in trauma patients?

Sensitivity	0.54 (95% CI: 0.47 to 0.62)
Specificity	0.85 (95% CI: 0.83 to 0.87)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 179 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	42 (36 to 48)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								35 (29 to 41)	
True negatives (patients without massive transusion)	1 studies 1448 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	785 (766 to 803)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								138 (120 to 157)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 55: Should COAST (cut off ≥ 3) for TIC be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.27 to 0.80
Specificity	0.86 to 0.96

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	3 studies 136 patients	cohort & case-control type studies	serious [a]	not serious	serious [b]	very serious [c]	none	21 to 62	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								15 to 56	
True negatives (patients without massive transusion)	3 studies 1508 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	794 to 886	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								37 to 129	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. downgrade di 1 livello per inconsistenza da ispezione visiva dei plots

c. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 57: Should PACT 1 be used to diagnose massive transfusion in trauma patients?

Sensitivity	0.73 (95% CI: 0.58 to 0.84)
Specificity	0.74 (95% CI: 0.68 to 0.79)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 51 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	56 (45 to 65)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								21 (12 to 32)	
True negatives (patients without massive transusion)	1 studies 273 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	683 (628 to 729)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having massive transusion)								240 (194 to 295)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 58: Should PACT 2 be used to diagnose massive transusion in trauma patients?

Sensitivity	0.74 (95% CI: 0.63 to 0.82)
Specificity	0.74 (95% CI: 0.67 to 0.80)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 87 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	57 (49 to 63)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having massive transusion)								20 (14 to 28)	
True negatives (patients without massive transusion)	1 studies 198 patients	cohort & case-control type studies	serious [a]	not serious	not serious	very serious [b]	none	683 (618 to 738)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having massive transusion)								240 (185 to 305)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli.

Question 59: Should Milano score (cut-off ≥6) be used to diagnose massive transusion in trauma patients?

Sensitivity	0.04 (95% CI: 0.01 to 0.11)
Specificity	1.00 (95% CI: 0.94 to 1.00)

Prevalences	7.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 7.7%	
True positives (patients with massive transusion)	1 studies 78 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b]	none	3 (1 to 8)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having massive transusion)								74 (69 to 76)	
True negatives (patients without massive transusion)	1 studies 61 patients	cohort & case-control type studies	serious [a]	not serious	not serious	not serious	none	923 (868 to 923)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having massive transusion)								0 (0 to 55)	

Explanations

a. downgrade di 1 livello perché gli studi presentano un rischio di bias riferito alla descrizione, modalità di somministrazione e interpretazione del test indice.

b. la valutazione della precisione per sensibilità e specificità separate è stata condotta attraverso ispezione visiva degli intervalli di confidenza della metanalisi diagnostica; in assenza di metanalisi l'imprecisione è stata giudicata sulla base degli intervalli di confidenza attorno alla mediana di sensibilità o specificità. Per gli studi che riportano solo i valori AUC la stima di precisione si è basata sui corrispondenti limiti di confidenza al 95%. Per intervalli di confidenza del 10% si è proceduto al downgrading di 1 livello e di 2 livelli per intervalli maggiori di due livelli. Quando non disponibili dati di variabilità (e quindi l'imprecisione non era valutabile) gli studi sono stati abbassati di 1 livello

CQ13. Strumenti per predire l'emorragia critica

Appendice E – Summary of findings Pediatric

Summary – Certainty of the evidence of included validated risk prediciton tools

Index test	Threshold	Outcome	Sensibilità	Specificità	Qualità evidenza - SE	Qualità evidenza - SP
Validated scores						
Shock Index (SI) - Calculated as the ratio of heart rate to systolic blood pressure.						
SI	cut off ≥ 0.9	MT	0.57 - 0.96	0.21 – 0.63	VERY LOW	LOW
SI	cut off ≥ 0.8	MT	0.82	0.27	MODERATE	MODERATE
SI	<1 year: SI>2.7, 1-2 years: SI>2.1, 2-5 years: SI>1.9, 5-12 years: SI>1.5, 12-15 years: SI>1.1	MT	0.13	0.98	MODERATE	MODERATE
Shock Index, pediatric age-adjusted (SIPA) - Calculated as the ratio of heart rate to systolic blood pressure and adjusted by age						
SIPA	ED thresholds used: 4-6 yr: SIPA >1.22, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	MT	0.58 – 0.95	0.35 – 0.83	VERY LOW	VERY LOW
SIPA	ED thresholds used: 1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9	MT	0.46 – 0.80	0.35 – 0.85	VERY LOW	VERY LOW
SIPA	ED thresholds used: 0-3, 4-6 yr: SIPA >1.2, 7-12, 13-17 yr: SIPA>0.9	MT	0.61	0.66	MODERATE	MODERATE
Assessment of blood consumption (ABC-SCORE) - Penetrating mechanism, positive focused assessment sonography for trauma (FAST), arrival systolic blood pressure of 90 mmHg or less, and arrival heart rate (HR) ≥ 120 bpm.						
ABC-SCORE	cut off ≥ 1	MT	0.71 – 0.85	0.38 – 0.80	VERY LOW	VERY LOW
ABC-SCORE	cut off ≥ 2	MT	0.29 – 0.77	0.55 – 1.00	VERY LOW	VERY LOW
ABC-SCORE	cut off ≥ 3	MT	0.06 – 0.70	0.54 – 1.00	VERY LOW	VERY LOW
ABC-SCORE	Not specified	MT	0.47	0.85	LOW	MODERATE

- **Shock Index**

- cut-off ≥ 0.9

Sensitivity (median)	0.70 (95% CI: 0.64 to 0.75)
Specificity (median)	0.59 (95% CI: 0.58 to 0.60)

Prevalences (median)	11%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 11%	
True positives (patients with [target condition(s)])	3 studies 429 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	serious [b]	serious [c]	none	77 (70 to 83)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								33 (27 to 40)	
True negatives (patients without [target condition(s)])	3 studies 22879 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	serious [b]	not serious	none	525 (516 to 534)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								365 (356 to 374)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

c. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 0.8

Sensitivity	0.82 (95% CI: 0.79 to 0.85)
Specificity	0.27 (95% CI: 0.25 to 0.30)

Prevalences	35%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 35%	
True positives (patients with [target condition(s)])	1 studies 753 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	287 (276 to 298)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								63 (52 to 74)	
True negatives (patients without [target condition(s)])	1 studies 1371 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	176 (163 to 195)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								474 (455 to 487)	

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

- cut-off: <1 yr: SI>2.7, 1-2 yr: SI >2.1, 2-5 yr: SI>1.9, 5-12 yr: SI>1.5, 12-15 yr: SI>1.1

Sensitivity	0.13 (95% CI: 0.10 to 0.16)
Specificity	0.98 (95% CI: 0.98 to 0.99)

Prevalences	1%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 1%	
True positives (patients with [target condition(s)])	1 studies 396 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	1 (1 to 2)	⊕⊕⊕◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								9 (8 to 9)	
True negatives (patients without [target condition(s)])	1 studies 28381 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	970 (970 to 980)	⊕⊕⊕◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								20 (10 to 20)	

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

- **SIPA**

- cut-off: 4-6 yr: SIPA >1.22, 7-12 yr: SIPA >1.0, 13-16 yr: SIPA >0.9

Sensitivity (median)	0.76 (95% CI: 0.63 to 0.86)
Specificity (median)	0.59 (95% CI: 0.44 to 0.68)

Prevalences (median)	44%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 44%	
True positives (patients with [target condition(s)])	2 studies 128 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	very serious [c]	none	334 (277 to 378)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								106 (62 to 163)	
True negatives (patients without [target condition(s)])	2 studies 307 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	very serious [c]	none	330 (246 to 381)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								230 (179 to 314)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

c. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%

- cut-off: 1-3, 4-6 yr: SIPA >1.2, 7-12 yr: SIPA>1.0, 13-16 yr: SIPA>0.9

Sensitivity (median)	0.67 (95% CI: 0.56 to 0.78)
Specificity (median)	0.61 (95% CI: 0.56 to 0.65)

Prevalences (median)	15%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 15%	
True positives (patients with [target condition(s)])	6 studies 825 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	serious [b]	very serious [c]	none	101 (84 to 117)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								49 (33 to 66)	
True negatives (patients without [target condition(s)])	6 studies 25227 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	not serious	none	519 (476 to 553)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								331 (297 to 374)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

c. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off: 0-3, 4-6 yr: SIPA >1.2, 7-12, 13-17 yr: SIPA>0.9

Sensitivity	0.61 (95% CI: 0.57 to 0.64)
Specificity	0.66 (95% CI: 0.63 to 0.68)

Prevalences	35%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 35%	
True positives (patients with [target condition(s)])	1 studies 748 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	214 (199 to 224)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								136 (126 to 151)	
True negatives (patients without [target condition(s)])	1 studies 1368 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	429 (410 to 442)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								221 (208 to 240)	

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

- **ABC score**

- cut-off ≥ 1

Sensitivity (median)	0.78 (95% CI: 0.63 to 0.89)
Specificity (median)	0.59 (95% CI: 0.43 to 0.70)

Prevalences (median)	46%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 46%	
True positives (patients with [target condition(s)])	2 studies 97 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	very serious [c]	none	359 (290 to 409)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								101 (51 to 170)	
True negatives (patients without [target condition(s)])	2 studies 164 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	very serious [c]	none	319 (232 to 378)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								221 (162 to 308)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

c. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

- cut-off ≥ 2

Sensitivity (median)	0.53 (95% CI: 0.39 to 0.67)
Specificity (median)	0.77 (95% CI: 0.64 to 0.81)

Prevalences (median)	46%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 46%	
True positives (patients with [target condition(s)])	2 studies 97 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	very serious [c]	none	244 (179 to 308)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								216 (152 to 281)	
True negatives (patients without [target condition(s)])	2 studies 163 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	serious [c]	none	416 (346 to 437)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								124 (103 to 194)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

c. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 3

Sensitivity (mediaN)	0.38 (95% CI: 0.29 to 0.50)
Specificity (median)	0.77 (95% CI: 0.64 to 0.81)

Prevalences (median)	46%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 46%	
True positives (patients with [target condition(s)])	2 studies 97 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	very serious [c]	none	175 (133 to 230)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								285 (230 to 327)	
True negatives (patients without [target condition(s)])	2 studies 163 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	serious [c]	none	416 (346 to 437)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								124 (103 to 194)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

c. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off not specified

Sensitivity	0.47 (95% CI: 0.40 to 0.54)
Specificity	0.85 (95% CI: 0.84 to 0.86)

Prevalences	3%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 3%	
True positives (patients with [target condition(s)])	1 studies 185 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	14 (12 to 16)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								16 (14 to 18)	
True negatives (patients without [target condition(s)])	1 studies 5845 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	825 (815 to 834)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								145 (136 to 155)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- **ABC-S score**

- cut-off ≥ 1

Sensitivity (median)	0.75 (95% CI: 0.59 to 0.86)
Specificity (median)	0.62 (95% CI: 0.46 to 0.72)

Prevalences (median)	46%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 46%	
True positives (patients with [target condition(s)])	2 studies 97 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	very serious [b]	none	345 (271 to 396)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								115 (64 to 189)	
True negatives (patients without [target condition(s)])	2 studies 163 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [c]	very serious [b]	none	335 (248 to 389)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								205 (151 to 292)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

c. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

- cut-off ≥ 2

Sensitivity (median)	0.47 (95% CI: 0.34 to 0.61)
Specificity (median)	0.73 (95% CI: 0.60 to 0.78)

Prevalences (median)	46%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 46%	
True positives (patients with [target condition(s)])	2 studies 97 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	very serious [c]	none	216 (156 to 281)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								244 (179 to 304)	
True negatives (patients without [target condition(s)])	2 studies 163 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	serious [c]	none	394 (324 to 421)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								146 (119 to 216)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

c. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 3

Sensitivity (median)	0.35 (95% CI: 0.28 to 0.48)
Specificity (median)	0.50 (95% CI: 0.41 to 0.51)

Prevalences (median)	46%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 46%	
True positives (patients with [target condition(s)])	2 studies 97 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	serious [c]	none	161 (129 to 221)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								299 (239 to 331)	
True negatives (patients without [target condition(s)])	2 studies 163 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	very serious [b]	serious [c]	none	270 (221 to 275)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								270 (265 to 319)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Studies were downgraded by one increment for inconsistency (was assessed by inspection of the sensitivity/specificity RevMan 5.4 plots).

c. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- **ABCD + base deficit**

- cut-off ≥ 1

Sensitivity	0.97 (95% CI: 0.89 to 1.00)
Specificity	0.41 (95% CI: 0.33 to 0.49)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	301 (276 to 310)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								9 (0 to 34)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	283 (228 to 338)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								407 (352 to 462)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.
b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 2

Sensitivity	0.83 (95% CI: 0.72 to 0.91)
Specificity	0.57 (95% CI: 0.48 to 0.65)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	257 (223 to 282)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								53 (28 to 87)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	393 (331 to 448)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								297 (242 to 359)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 3

Sensitivity	0.73 (95% CI: 0.60 to 0.83)
Specificity	0.75 (95% CI: 0.67 to 0.82)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	very serious [b]	none	226 (186 to 257)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								84 (53 to 124)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	518 (462 to 566)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								172 (124 to 228)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- **ABCD + lactate**

- cut-off ≥ 1

Sensitivity	0.88 (95% CI: 0.78 to 0.95)
Specificity	0.39 (95% CI: 0.31 to 0.47)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	273 (242 to 295)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								37 (15 to 68)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	269 (214 to 324)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								421 (366 to 476)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 2

Sensitivity	0.76 (95% CI: 0.64 to 0.85)
Specificity	0.53 (95% CI: 0.44 to 0.61)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	very serious [b]	none	236 (198 to 264)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								74 (46 to 112)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	366 (304 to 421)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								324 (269 to 386)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 3

Sensitivity	0.70 (95% CI: 0.57 to 0.80)
Specificity	0.50 (95% CI: 0.42 to 0.58)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	very serious [b]	none	217 (177 to 248)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								93 (62 to 133)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	345 (290 to 400)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								345 (290 to 400)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- **ABCD + base deficit and lactate**

- cut-off ≥ 1

Sensitivity	0.98 (95% CI: 0.92 to 1.00)
Specificity	0.40 (95% CI: 0.32 to 0.49)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	304 (285 to 310)	⊕⊕⊕◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								6 (0 to 25)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	276 (221 to 338)	⊕⊕◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								414 (352 to 469)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 2

Sensitivity	0.88 (95% CI: 0.78 to 0.95)
Specificity	0.53 (95% CI: 0.44 to 0.61)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	273 (242 to 295)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								37 (15 to 68)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	366 (304 to 421)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								324 (269 to 386)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.a.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- cut-off ≥ 3

Sensitivity	0.77 (95% CI: 0.65 to 0.87)
Specificity	0.78 (95% CI: 0.71 to 0.85)

Prevalences	31%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 31%	
True positives (patients with [target condition(s)])	1 studies 66 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	very serious [b]	none	239 (202 to 270)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								71 (40 to 108)	
True negatives (patients without [target condition(s)])	1 studies 144 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	538 (490 to 586)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								152 (104 to 200)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- **Pre arrival model**

Sensitivity	0.86 (95% CI: 0.73 to 0.95)
Specificity	0.94 (95% CI: 0.87 to 0.98)

Prevalences	33%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 33%	
True positives (patients with [target condition(s)])	1 studies 44 patients	case-control type accuracy study	serious [a]	not serious	not serious	very serious [b]	none	284 (241 to 314)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								46 (16 to 89)	
True negatives (patients without [target condition(s)])	1 studies 88 patients	case-control type accuracy study	serious [a]	not serious	not serious	serious [b]	none	630 (583 to 657)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having [target condition(s)])								40 (13 to 87)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

- **ED model**

Sensitivity	0.80 (95% CI: 0.65 to 0.90)
Specificity	0.64 (95% CI: 0.53 to 0.74)

Prevalences	32%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 32%	
True positives (patients with [target condition(s)])	1 studies 44 patients	case-control type accuracy study	serious [a]	not serious	not serious	very serious [b]	none	256 (208 to 288)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [target condition(s)])								64 (32 to 112)	
True negatives (patients without [target condition(s)])	1 studies 92 patients	case-control type accuracy study	serious [a]	not serious	not serious	very serious [b]	none	435 (360 to 503)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [target condition(s)])								245 (177 to 320)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

b. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%.

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- **PED-ABC**

- cut-off ≥ 1

Sensitivity	0.91 (95% CI: 0.88 to 0.93)
Specificity	0.40 (95% CI: 0.39 to 0.41)

Prevalences	9%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 9%	
True positives (patients with [target condition(s)])	1 studies 540 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	82 (79 to 84)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								8 (6 to 11)	
True negatives (patients without [target condition(s)])	1 studies 5392 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	364 (355 to 373)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								546 (537 to 555)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

- cut-off ≥ 2

Sensitivity	0.54 (95% CI: 0.50 to 0.59)
Specificity	0.85 (95% CI: 0.84 to 0.86)

Prevalences	9%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 9%	
True positives (patients with [target condition(s)])	1 studies 540 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	49 (45 to 53)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								41 (37 to 45)	
True negatives (patients without [target condition(s)])	1 studies 5404 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	774 (764 to 783)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								136 (127 to 146)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

- cut-off ≥ 3

Sensitivity	0.21 (95% CI: 0.18 to 0.25)
Specificity	0.99 (95% CI: 0.98 to 0.99)

Prevalences	9%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 9%	
True positives (patients with [target condition(s)])	1 studies 540 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	19 (16 to 23)	⊕⊕⊕◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								71 (67 to 74)	
True negatives (patients without [target condition(s)])	1 studies 5337 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	901 (892 to 901)	⊕⊕⊕◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								9 (9 to 18)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

- cut-off = 4

Sensitivity	0.05 (95% CI: 0.03 to 0.07)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	9%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1.000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 9%	
True positives (patients with [target condition(s)])	1 studies 540 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	5 (3 to 6)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having [target condition(s)])								85 (84 to 87)	
True negatives (patients without [target condition(s)])	1 studies 5403 patients	case-control type accuracy study	serious [a]	not serious	not serious	not serious	none	910 (910 to 910)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having [target condition(s)])								0 (0 to 0)	

Explanations

a. Downgrading by one increment was applied because of risk of bias regarding description, method of administration and interpretation of the index test.

CQ13. Strumenti per predire l'emorragia critica

Appendice F. Bibliografia

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- **Studi pediatrici**

Dalla review:

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CQ13. Strumenti per predire l'emorragia critica

Appendice G. Method and Criteria For Evaluating The Scientific Evidence

1 Definition of Clinical Questions

The clinical questions initially formulated by the authors of each working group and subsequently agreed were developed according to the PICOS method (Greenhalgh 1997, O'Connor 2008, Richardson 1995)
P: patients/ population characteristics
I: intervention on which the question is focused
C: comparison intervention / control /reference group
O: outcome measure relevant for the clinical question
S: study design on which to base the evidence search
The PICOS components of each prioritized question have been used by the Literature Group to define specific key words employed in comprehensive bibliographic searches.

2 Inclusion Criteria

3. Data synthesis

For diagnostic test accuracy studies, a positive result on the index test was found in two different ways, according to whether the index test was measured on a continuous scale or was bivariate.
For continuous index test measures, a positive result on the index test was found if the patient had values of the chosen measured quantity above or below a threshold value, and different thresholds could be used. The threshold of a diagnostic test is defined as the value at which the test can best differentiate between those with and without the target condition and, in practice, it varies amongst studies.

Diagnostic test accuracy measures used in the analysis were sensitivity and specificity, and, if different diagnostic thresholds were used within a single study, area under the receiver operating characteristics (ROC) curve.

Only external validation data set were used in quantitative analysis.

Diagnostic test accuracy measures used in the analysis were sensitivity and specificity. Diagnostic meta-analysis was conducted where appropriate; that is, when 5 or more studies were available per threshold. Coupled forest plots of sensitivity and specificity with their 95% CIs across studies (at various thresholds) were produced for each test, using RevMan (Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.) In order to do this, 2x2 tables (the number of true positives, false positives, true negatives and false negatives) were directly taken from the study if given, or else were derived from raw data or calculated from the set of test accuracy statistics.

For scores with less than five studies, median sensitivity and the paired specificity were reported where possible. If an even number of studies were reported the lowest value of the two middle pairs was reported. Heterogeneity or inconsistency amongst studies was visually inspected in the forest plots.

3 Risk of bias for included studies

Diagnostic accuracy studies was assessed by QUADAS-2. (Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011 Oct 18;155(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009. PMID: 22007046)

If a study is judged as “low” on all domains relating to bias or applicability, then it is appropriate to have an overall judgment of “low risk of bias” or “low concern regarding applicability” for that study. If a study is judged “high” or “unclear” in 1 or more domains, then it may be judged “at risk of bias” or as having concerns regarding applicability.”

4 Grading the quality of evidence

The overall quality of evidence will be assessed using the GRADE approach (GRADE Working Group Website, Guyatt 2008).

HIGH quality of evidence: further research is very unlikely to change our confidence in the estimate of effect.

- Several high-quality studies (RCTs for treatment, cross sectional diagnostic accuracy studies for diagnosis) with consistent results
- In special cases: one large, high-quality multi-centre trial

MODERATE quality of evidence: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

- One high-quality study
- Several studies with some limitations

LOW quality of evidence: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

- One or more studies with severe limitations

VERY LOW quality of evidence: Any estimate of effect is very uncertain.

- Expert opinion
- No direct research evidence
- One or more studies with very severe limitations

Factors that might decrease quality of evidence will be:

- Study limitations (risk of bias)
- Inconsistency of results
- Indirectness of evidence
- Imprecision
- Publication bias

Factors that might increase quality of evidence will be

- Large magnitude of effect
- Plausible confounding, which would reduce a demonstrated effect
- Dose-response gradient

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CQ13. Strumenti per predire l'emorragia critica

Appendice H. Costi e analisi economica

Sommario

Selezione degli studi

La ricerca di letteratura ha prodotto 9 lavori provenienti dalle banche dati di Embase e Medline. Di questi, ne sono stati esclusi 6 dopo aver valutato titolo ed abstract (non valutazioni economiche, abstract o atti di convegni non informativi), e 2 dopo attenta valutazione del full text, lasciando un solo studio alla valutazione di inclusione (Whithing et al., 2015) relativo al contesto Britannico. Questo lavoro è un full report di Health Technology Assessment che al capitolo 4 presenta evidenze sia relative ai costi che alla costo-efficacia della *Viscoelastic Point of Care* per la diagnosi la gestione ed il monitoraggio dell'emostasi. Tuttavia questa revisione non risponde direttamente ai criteri di inclusione prefissati (popolazione non traumatica e test point-of-care) e viene presentata solo con intento di accompagnamento al giudizio clinico. In particolare, questa revisione:

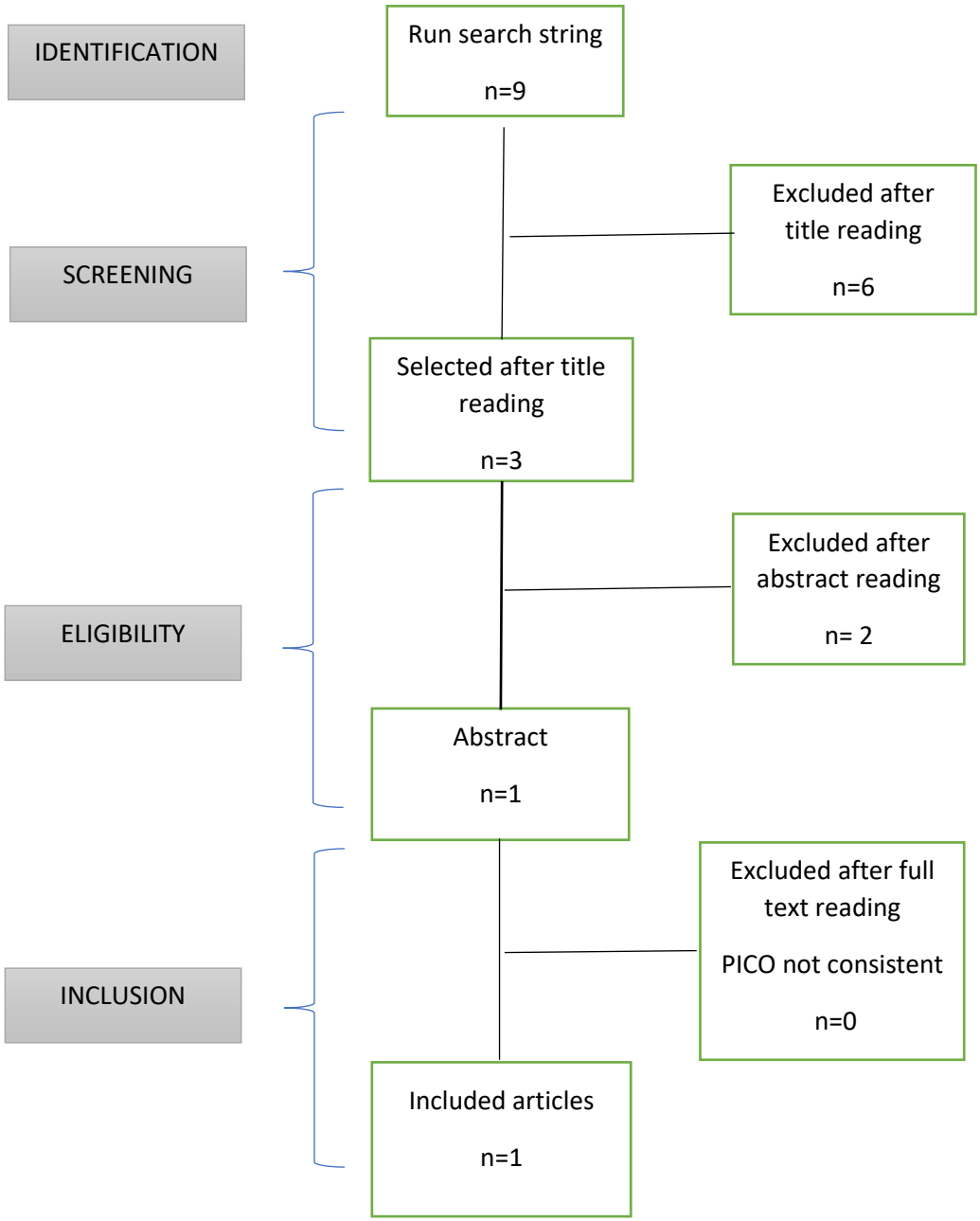
-si focalizza su una popolazione sottoposta a cardiochirurgia/trapianti e non su una popolazione di pazienti con trauma

-prende in esame uno strumento utilizzato come point-of-care (POC) e non gli strumenti di tools in esame che richiedono valutazione clinica, di laboratorio e strumentazione diagnostica come ad esempio ultrasound assessment.

Di conseguenza, l'evidenza riportata ha una forte limitazione per quanto riguarda la generalizzabilità (-2 gradi di indirectness).

La **figura 1** mostra la flow chart relativa all'estrazione delle evidenze di letteratura.

Figure 1. Flow chart revision of the literature



La revisione sistematica del lavoro selezionato (Whiting et al., 2015) non riporta evidenze inerenti il trauma, ma solo focalizzate su una popolazione sottoposta a cardiochirurgia o trapianti. Da questo gli autori hanno poi costruito un modello relativo al trauma. Infatti in questo lavoro scientifico (Whiting et al., 2015) è presente anche un modello decisionale ad hoc dove vengono riportate evidenze di costo efficacia inerenti sia una popolazione sottoposta a cardiochirurgia che a quella con trauma. Globalmente i risultati non sono direttamente trasferibili rispetto al contesto di una popolazione con trauma.

Nella presente valutazione ci si concentrerà soltanto sulla popolazione con trauma.

Struttura del modello

Il modello decisionale presentato è costruito su una struttura ad albero e vanta la costo-efficacia di: Rotational TrhomboElastroMetry (ROTEM), tormboelastografia (TEG) e Sonoclot (dispositivi Viscoeelastici - VE) in confronto con Test Laboratoristici Standard (SLT). Il modello considera un orizzonte temporale sia di un mese che di un anno al fine di considerare anche i benefici derivanti dalla riduzione delle trasfusioni di RBC. ad un mese il modello simula l'ospedalizzazione e riesce quindi a catturare l'impatto delle complicanze generati Dalla chirurgia, dalla perdita di sangue e dalle trasfusioni. Per quanto riguarda l'impatto sulla riduzione delle infezioni un orizzonte temporale di un anno passato considerato più appropriato. Dato l'orizzonte temporale che si ferma ad un anno non è stato necessario utilizzare procedure per l'attualizzazione dei costi e il loro impatto.

L' impatto economico è stato espresso in termini di costo per anno di vita guadagnati ed in termini di costo per anno di vita ponderato per la qualità- QALYs (Quality Adjusted Life Year). Le tariffe inerenti la qualità di vita sono state assegnate agli eventi avversi ed alle complicanze e si riferiscono ad una popolazione Britannica. Sono state anche condotte analisi di sensibilità di tipo probabilistico multivariate, tramite una simulazione Montecarlo che prendeva in considerazione tutti i parametri del modello (costi, mortalità ad un anno, probabilità di complicanze, probabilità di trasfusione e QALYs) ed analisi di scenario costruite sulla base delle caratteristiche di baseline della popolazione.

I dati estrapolati ed analizzati tramite una meta-analisi hanno coinvolto i seguenti outcomes:

- Probabilità di trasfusione con globuli rossi;
- Probabilità di complicanze associate al trauma e / o alla trasfusione;
- Mortalità ad un mese e ad un anno;
- Quality adjusted Life years (QALYs);
- Costi.

Costi

La **tabella 1** riporta i dati relativi alla durata della degenza espressa in giorni e i costi ad essa associata relativi a complicanze dovute a infezioni post trasfusione durante i 12 mesi successivi all'ospedalizzazione.

Tabella 1. Costi per giornata di degenza relativi alle complicanze da infezione (Whithing et al., 2015)

Health states		Mean (SD[a]) LoS	Mean (SD[a]) cost (£) per day
vCJD		0	NA
HAV	Acute hospitalisation (×2)	5.10 (0.52)	475 (48.47)
	Outpatient visit (×3)	1.00 (0.10)	266 (27.14)
Malaria	Hospitalisation (×2)	3.40 (0.34)	475 (48.47)
	Outpatient visit (×0)	1.00 (0.10)	266 (27.14)
HTLV	Hospitalisation (×2)	1.00 (0.10)	598 (61.02)
	Outpatient visit (×0)	1.00 (0.10)	266 (27.14)
HIV	Hospitalisation (×2)	6.97 (0.71)	598 (61.02)
	Outpatient visit (×3)	1.00 (0.10)	966 (98.57)
HBV	Chronic hospitalisation (×2)	7.40 (0.75)	475 (48.47)
	Outpatient visit (×3)	1.00 (0.10)	266 (27.14)
HCV	Chronic hospitalisation (×2)	3.50 (0.35)	341 (34.79)
	Outpatient visit (×3)	1.00 (0.10)	266 (27.14)

NA, not applicable.
a SDs were derived assuming a 95% CI with limits deviating 20% from the mean.

Le altre voci di costo considerate nel modello sono relative a:

- Costi di componenti ematici;
- Costi dei test per l'identificazione di pazienti a rischio di sanguinamento durante o dopo la trasfusione;
- Costi relativi a complicanze dovute alla chirurgia, alle trasfusioni ed alle infezioni sia batteriche (Durante l'ospedalizzazione) che di lungo periodo (HIV, malaria, HCV, HBV…);
- Costi dei dispositivi viscoelastici;
- Costi totali delle ospedalizzazioni;
- Costi al follow-up.

La **tabella 2** mostra le unità di componenti ematiche trasfuse in media per paziente. Le componenti ematiche sono distinte in globuli rossi, plasma fresco congelato e piastrine, così come risulta dalla estrapolazione effettuata su dati di letteratura (vedi sopra). La **tabella 3** mostra invece i costi dei dispositivi viscoelastici.

Tabella 2. Unità di componenti ematici trasfuse per paziente con trauma (Whithing et al., 2015)

Study	RBC	FFP	Platelets
Ives (2012)[72]	9.5	10.9	3.3
Nystrup (2011)[71]	3.4	2.2	1.6
Average units per patient	6.45	6.55	2.45
Average units per transfused patient SLTs group	**20.09**	**20.40**	**7.63**
Ratio of units transfused among VE-tested patients compared with SLTs-tested patients (cardiac surgery population)	1.07	0.24	0.57
Average units per transfused patient VE group	**21.50**	**4.90**	**4.35**

Tabella 3. Costi dei dispositivi viscoelastici (Whithing et al., 2015)

Basic test	Cost (£)
ROTEM INTEM	1.13
ROTEM EXTEM	1.22
ROTEM FIBTEM	2.22
Cup and pin (×3)	3.15 × 3
Equipment cost	26.67
Total cost ROTEM test	**40.69**
Rapid TEG	11.25
Plain cup and pin	5.45
Equipment cost	17.33
Total cost TEG test	**34.03**
gbACT	2.20
Equipment cost	12.33
Total cost Sonodot test	**14.53**

Costo efficacia

Risultati caso base

I risultati dell'analisi costo-efficacia sono riportati nella **tabella 4.** Tutti i dispositivi viscoelastici mostrano una dominanza rispetto a SLT. Il costo di Sonoclot risulta più basso di quello di ROTEM e TEG. Di conseguenza, nel confronto con SLT, a Sonoclot sono associati risparmi più ingenti (£818) rispetto al caso della TEG (£721) e della ROTEM (£ 688). La **tabella 5** mostra altri output intermedi prodotti dal modello di simulazione.

Tabella 4. Risultati dell'analisi costo-efficacia. (Whithing et al., 2015)

Outcome	SLTs	ROTEM	TEG	Sonoclot
LY	0.8343	0.8425	0.8425	0.8425
QALY	0.5644	0.5713	0.5713	0.5713
Cost (£)	7661	6973	6940	6842
Incremental QALYs vs. SLTs		0.0069	0.0069	0.0069
ICs vs. SLTs (£)		-688	-721	-818

IC, incremental cost.

Tabella 5. Output intermedi della analisi costo efficacia (Whithing et al., 2015)

Outcome	VE device	SLTs
1-month mortality (%)	14.9	15.7
1-year mortality (%)	17.3	18.2
Percentage trauma and/or transfusion complications	12.9	14.6
Percentage transfusion-related complications	0.02	0.02
Percentage transfusion-transmitted infections	0.00	0.00
Transfusion costs (£)	1045	1491
Hospitalisation costs (£)	5724	6040

Analisi di sensibilità

L'analisi di sensibilità probabilistica conferma che l'approccio SLT è la strategia con la probabilità più bassa di essere costo efficace (Massimo 2%) in confronto con i dispositivi viscoelastici. Tra questi Sonoclot si conferma quello in grado di generare i risparmi più ingenti. Le figure 2 e 3 mostrano i risultati dell'analisi di sensibilità probabilistica. La **tabella 6** infine mostra i risultati delle analisi di scenario.

Figura 2. Piano costo efficacia (Whithing et al., 2015)

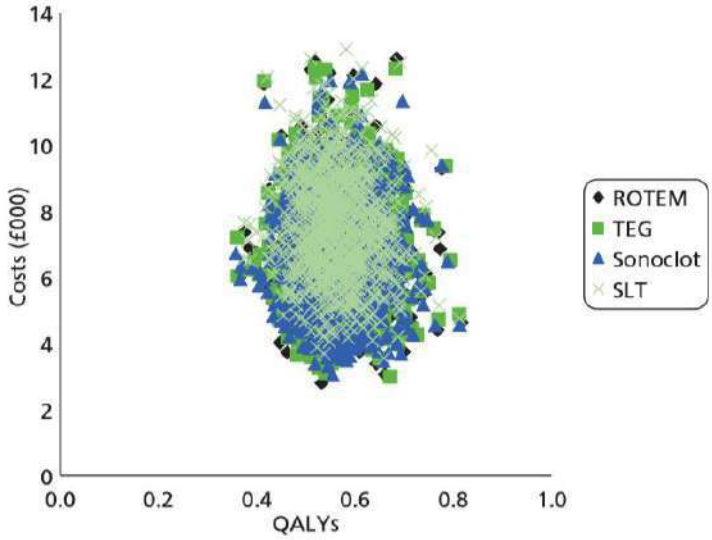


Figura 3. Curva di accettabilità del rapporto costo-efficacia (Whithing et al., 2015)

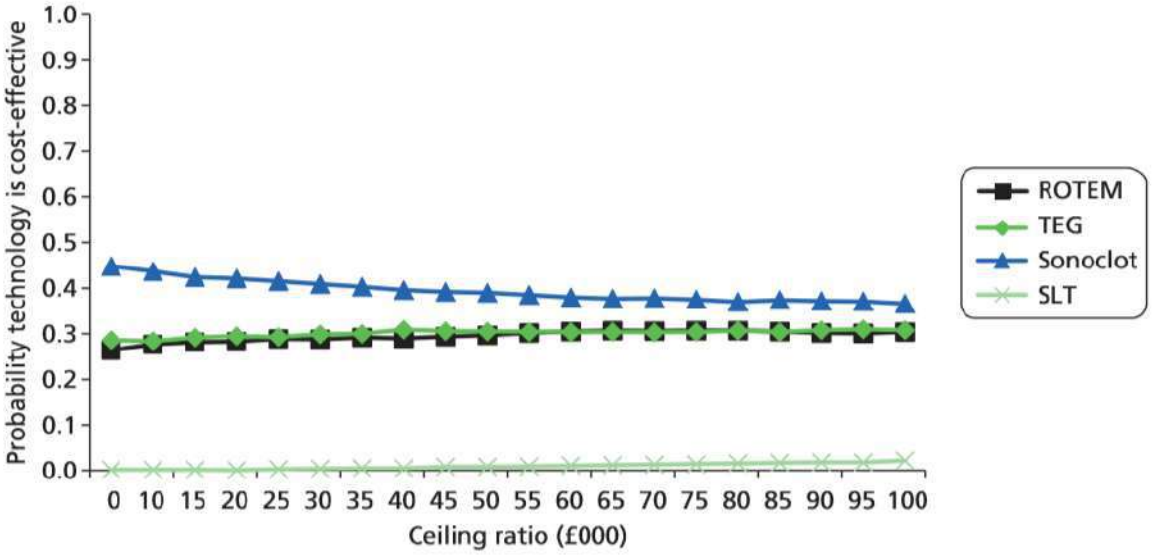


Tabella 6. Risultati delle analisi di scenario (Whithing et al., 2015)

Scenario	ROTEM			SLTs			Incremental QALY	IC	ICER
	LYs	QALYs	Cost (£)	LYs	QALYs	Cost (£)			
Base case	0.8425	0.5713	6973	0.8343	0.5644	7661	0.0069	–688	Dominance
5 years' machine usage	0.8425	0.5713	6929	0.8343	0.5644	7661	0.0069	–731	
200 tests per year	0.8425	0.5713	7173	0.8343	0.5644	7661	0.0069	–488	
No. of tests per patient decreased (2, no transfusion; 3 transfusion)	0.8425	0.5713	6862	0.8343	0.5644	7591	0.0069	–729	
VE testing add-on to SLT	0.8425	0.5713	7103	0.8343	0.5644	7661	0.0069	–558	
RR transfusion = 0.80 (lower limit)	0.8480	0.5759	6668	0.8343	0.5644	7661	0.0115	–993	
RR transfusion = 0.96 (upper limit)	0.8370	0.5667	7278	0.8343	0.5644	7661	0.0023	–383	
Lower probability of transfusion SLTs group (0.209)	0.8636	0.5889	5802	0.8582	0.5844	6224	0.0045	–422	
Higher probability of transfusion SLTs group (0.444)	0.8194	0.5520	8259	0.8080	0.5425	9238	0.0095	–979	
Equal volumes of blood components transfused	0.8425	0.5713	7240	0.8343	0.5644	7661	0.0069	–421	
Probability experiencing ARDS (0.0775) and MOF (0.15)	0.8420	0.5731	5814	0.8337	0.5665	6344	0.0066	–530	
Probability experiencing ARDS (0.2325) and MOF (0.45)	0.8430	0.5695	8132	0.8349	0.5624	8977	0.0071	–846	
Calibrated 1-month mortality (0.1483)	0.8823	0.5969	7144	0.8794	0.5935	7855	0.0034	–711	
Calibrated 1-month mortality (0.4450)	0.8028	0.5457	6801	0.7891	0.5354	7466	0.0104	–664	

IC, incremental cost.

Analisi EVPI

L'analisi EVPI (expected value for perfect information) ha la finalità di individuare il valore, espresso in misura monetaria, derivante dall'acquisizione di informazione aggiuntiva rispetto ai parametri più incerti del modello, per esempio tramite ricerca addizionale. In questo senso l'analisi presentata, mostra che considerando un valore soglia di £30.000/QALY, l'EVPI è di circa £25milioni, considerando tutti e quattro i dispositivi viscoelastici. Considerando invece i dispositivi in maniera separata, l'EVPI è di solo £1 mln.

Questa differenza può essere spiegata col fatto che esista poca incertezza sul fatto che in generale i dispositivi viscoelastici siano superiori alla SLTs, di conseguenza ricerca aggiuntiva avrebbe un valore limitato. Tuttavia, esiste un certo margine di incertezza rispetto a quale dei dispositivi viscoelastici sia ottimale punto di conseguenza l'indicazione derivante dall' EVPI è che bisognerebbe condurre studi sia clinici che di costo-efficacia volti a confrontare in maniera diretta fra loro i diversi dispositivi viscoelastici.

Valutazione della qualità delle evidenze

Nota metodologica

La valutazione della qualità delle evidenze di costo-efficacia è stata condotta a due livelli.

In prima analisi è stata applicata la checklist CHEERS - Consolidated Health Economics Evaluations Reporting Standards- (Husereau 2013) per una valutazione della qualità metodologica degli studi. In secondo luogo è stata applicata la checklist per la valutazione della generalizzabilità (Drummond, 2005; Ruggeri, 2015) dei risultati ottenuti.

L'analisi della generalizzabilità può dar luogo a tre tipi di risultati diversi:

1. Analisi context-specific: nel caso in cui lo studio non rispetti più di due requisiti richiesti dalla checklist;
2. Analisi adattabile: nel caso in cui lo studio non rispetti un requisito richiesto dalla checklist;
3. Analisi generalizzabile: nel caso in cui lo studio rispetti tutti i requisiti richiesti dalla checklist.

Nel caso in cui ci si trovi in presenza di analisi adattabili, questo adattamento può essere condotto attraverso un'analisi bayesiana che trasformi i risultati dello studio in quantili di una distribuzione stocastica. Questa analisi dà luogo ad una distribuzione probabilistica che può essere interpretata come il livello di affidabilità dello studio rispetto al contesto di riferimento.

La costruzione dell'analisi stocastica avviene considerando i valori medi dei risultati costo efficacia degli studi ritenuti adattabili e le relative deviazioni standard, che servono a popolare una distribuzione di tipo *gamma.*

Risultati

Lo studio presentato è stato valutato criticamente mediante la checklist CHEERS. la qualità generale delle evidenze è risultata essere ottima 90%) dal momento in cui il modello rispetta tutti i requisiti necessari ad un corretto reporting.

Tuttavia esistono alcuni dubbi in merito alla conduzione dell'analisi di sensibilità di tipo probabilistico. Non è chiaro infatti perché in alcuni casi per simulare le distribuzioni stocastiche inerenti i valori di qualità di vita vengano utilizzate variabili di tipo beta (coerentemente con le linee guida metodologiche) ed In altri casi vengano invece utilizzate variabili casuali normali, di cui peraltro non è chiaro se siano state standardizzati in maniera dalie da restituire solo valori in un range compreso fra 0 ed 1.

Inoltre in alcuni casi i parametri di scala e di forma così come le distribuzioni probabilistiche associate ad altri parametri come ad esempio i costi e le probabilità di complicanza o di morte non solo esplicitate.

Infine, mentre è chiaro che la struttura ad albero sia quella più appropriata rispetto a il problema decisionale delimitato in un orizzonte temporale di un anno, l'utilizzo di un approccio markoviano per lo studio dei costi

e delle conseguenze associate alle complicanze di lungo periodo, come ad esempio le infezioni trasmissibili, sarebbe stato utile per proiettare i risultati della valutazione economica oltre l'anno di riferimento. In ogni caso si denota una larga dominanza dei dispositivi viscoelastici rispetto alla SLT.

Sebbene lo studio risulti out of scope rispetto ai criteri di eleggibilità selezionati nel PICO in riferimento al quesito oggetto di analisi, è stata comunque condotta una valutazione della generalizzabilità delle evidenze economiche. Come è possibile vedere nella tabella relativa, lo studio risulta adattabile al contesto italiano. Ciò è dato dal fatto che i coefficienti di qualità di vita sono relativi ad una popolazione britannica che, se da un lato può essere assimilabile a quella italiana ed in generale europea, dall'altro esistono alcune evidenze di letteratura che dimostrano come i coefficienti di qualità di vita espressi da una popolazione italiana tendono a sottostimare gli effetti positivi di un intervento che produce guadagni di salute. In questo senso il risultato del modello inerente una popolazione Britannica è da considerarsi conservativo rispetto ad una sua eventuale applicazione ad una popolazione italiana. Rispetto ai costi, invece, quelli britannici risulterebbero essere di circa un 15% più alti rispetto a quelli italiani. Se in un caso di costi incrementali positivi ciò sarebbe andato a favore della popolazione italiana in questo caso, verificandosi dei risparmi, questi applicati ad un contesto italiano risulterebbero invece sovrastimati.

In generale, è possibile affermare come non esistano dubbi sostanziali rispetto alla conservazione di una situazione di dominanza dei dispositivi viscoelastici rispetto alla SLT anche in un contesto italiano. Tuttavia anche se lo studio risulta adattabile per contesto non è completamente aderente ai criteri di eleggibilità per quanto riguarda gli strumenti e la popolazione in esame.

Tabella 7. Checklist CHEERS

SECTION/ITEM	**WHITHING ET AL., 2015**
TITLE AND ABSTRACT	
TITLE	1
ABSTRACT	1
INTRODUCTION	
BACKGROUND AND OBJECTIVES	1
METHODS	
TARGET POPULATION AND GROUPS	1
SETTING AND LOCATION	1
STUDY PERSPECTIVE	1
COMPARATORS	1
TIME HORIZON	1

DISCOUNT RATES	0
CHOICE OF HEALTH OUTCOMES	1
MEASUREMENT OF EFFECTIVENESS	1
MEASUREMENT AND EVALUATION OF PREFERENCE BASED OUTCOMES	1
ESTIMATING RESOURCES AND COST	1
CURRENCY AND CONVERSION	1
CHOICE OF MODEL	1
ASSUMPTIONS	1
ANALYTIC METHODS	1
RESULTS	
STUDY PARAMETERS	1
INCREMENTAL COSTS AND OUTCOMES	1
CHARACTERIZING UNCERTAINTY	0
CHARACTERIZING HETEROGENEITY	1
DISCUSSION	
STUDY FINDINGS, LIMITATIONS, GENERALIZABILITY, AND CURRENT KNOWLEDGE	1
OTHER	
SOURCE OF FUNDING	1
CONFLICT OF INTEREST	1
TOTAL	90,00%

Tabella 8. Valutazione della generalizzabilità

ITEMS FOR GENERALIZABILITY	Whithing et al., 2015
multicenter study (only for trial based)	na
context and description of the alternatives	1
complete reporting of the baseline characteristics of the study sample	1
adoption of a broad study perspective	1
clinical and cost data referring to the entire population	1

preference data relevant to the study population	0
presence of quantitatiive/qualitative analyses performed to evaluate the variability of results	1
clear justification of the model structure and parameters (only for models)	1
presence of a stochastic analysis to explore uncertainty (only for models)	1
reporting of epideiology (f relevant)	na
reported source of utility data	1
separate reporting of resources and unit costs	1
RESULT	Adaptable to Italy

Adattamento al contesto Italiano

L'adattamento al contesto italiano è stato effettuato tenendo conto che:

- I costi UK risultano, in media , più alti di quelli italiani di circa il 15%;
- I coefficienti di utilità espressi dalla popolazione britannica sono sovrastimati rispetto alla popolazione italiana

Per tali motivi è stata condotta una nuova simulazione probabilistica riscalando:

- i parametri di costo (del 15%) dopo aver convertito al cambio attuale pound (£) in euro (€);
- I coefficienti di utilità diminuendoli del 5%.

In ambedue i casi, i valori di riferimento sono stati le medie e le deviazioni standard ricavate dai costi e dai QALY incrementali dell'analisi di scenario presentata nella **tabella 6.**

La **tabella 8** riporta i costi ed i QALYs incrementali derivanti dal confronto fra ROTEM ed SLT, adattati rispetto alla realtà italiana, con la relativa deviazione standard ed i parametri di scala e di forma necessari all'estrapolazione delle relative distribuzioni stocastiche.

Tabella 8. ROTEM vs SLT: parametri per l'adattamento del modello al contesto italiano

	Incremental costs	Incremental QALYs
Mean	643,93 €	0,006562
St. dev	187,67 €	0,002349
alpha	11,77	0,000015

beta	54,69	0,002333

La figura 4. Mostra infine i risultati della simulazione su dati adattati al contesto italiano.

La simulazione tiene conto dell'incertezza espressa dal modello Britannico riparametrata rispetto ai dati inerenti la realtà italiana (costi e QALYs). Come è possibile osservare, anche nel caso della realtà italiana, il 100% delle simulazioni restituisce una situazione di dominanza della tecnologia VE rispetto alla SLT, producendo un guadagno di QALYs a fronte di un risparmio di risorse per il Sistema Sanitario Nazionale(SSN).

Figura 4. ROTEM vs SLT: Piano costo – efficacia adattato alla realtà italiana