COAGULOPATHY AND TRANSFUSION STRATEGIES IN TRAUMA
Overwhelmed by literature, supported by weak evidence

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SIMTI

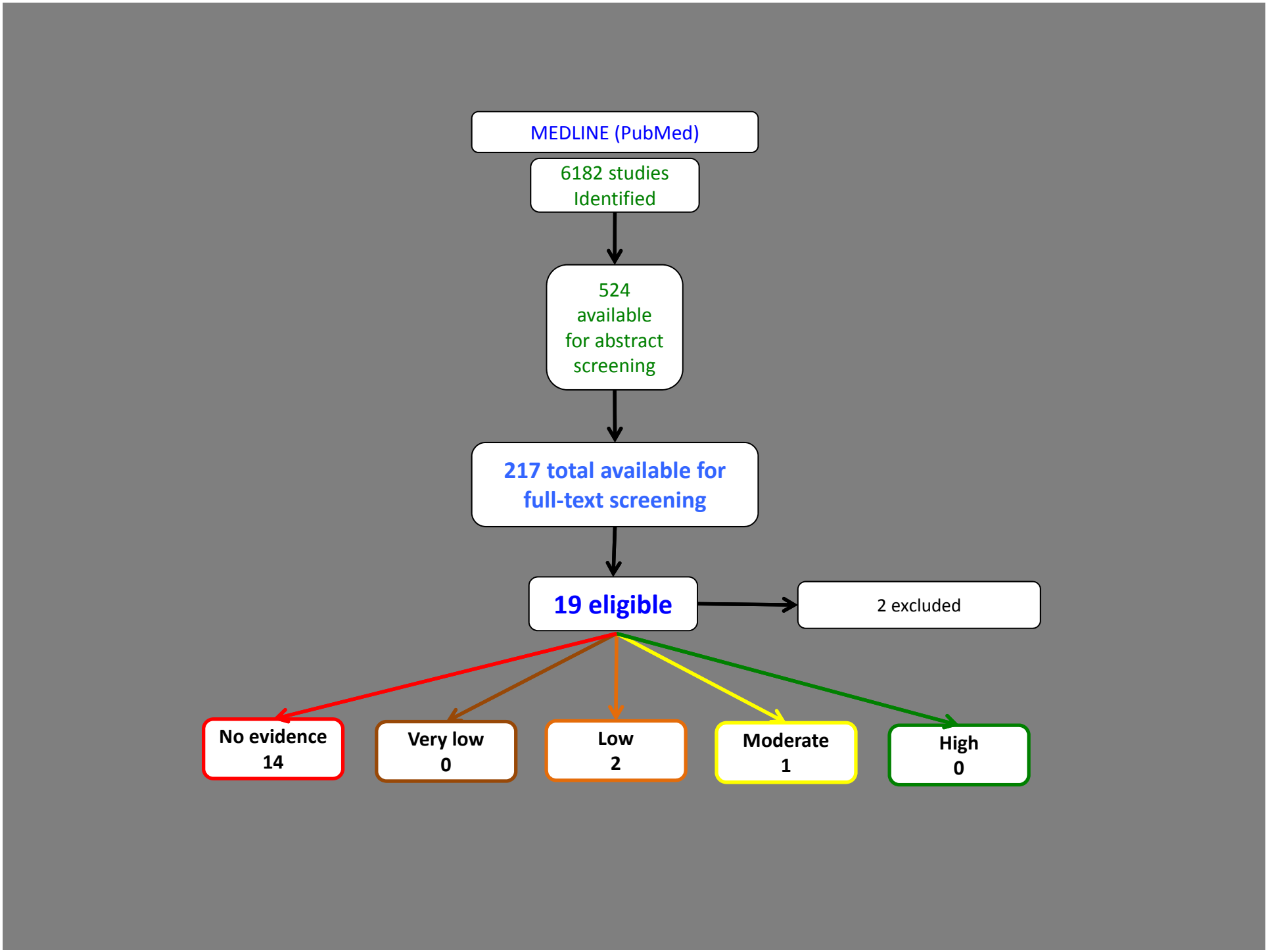
Special Conference
Il Patient Blood Management: non solo una questione di ferro e anemia
Roma, 15 ottobre 2015

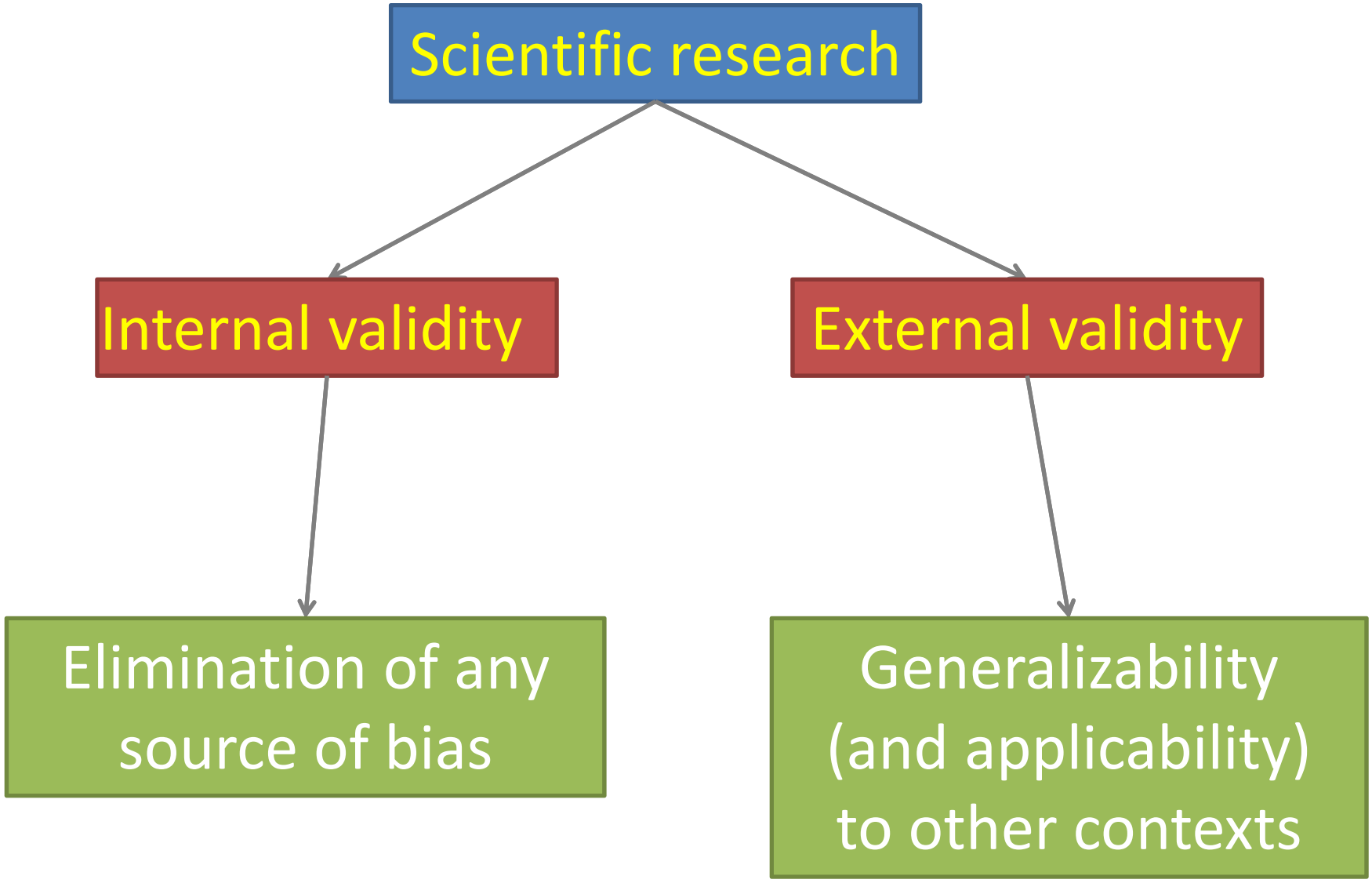
Il/La sottoscritto/a, in qualità di Relatore
dichiara che

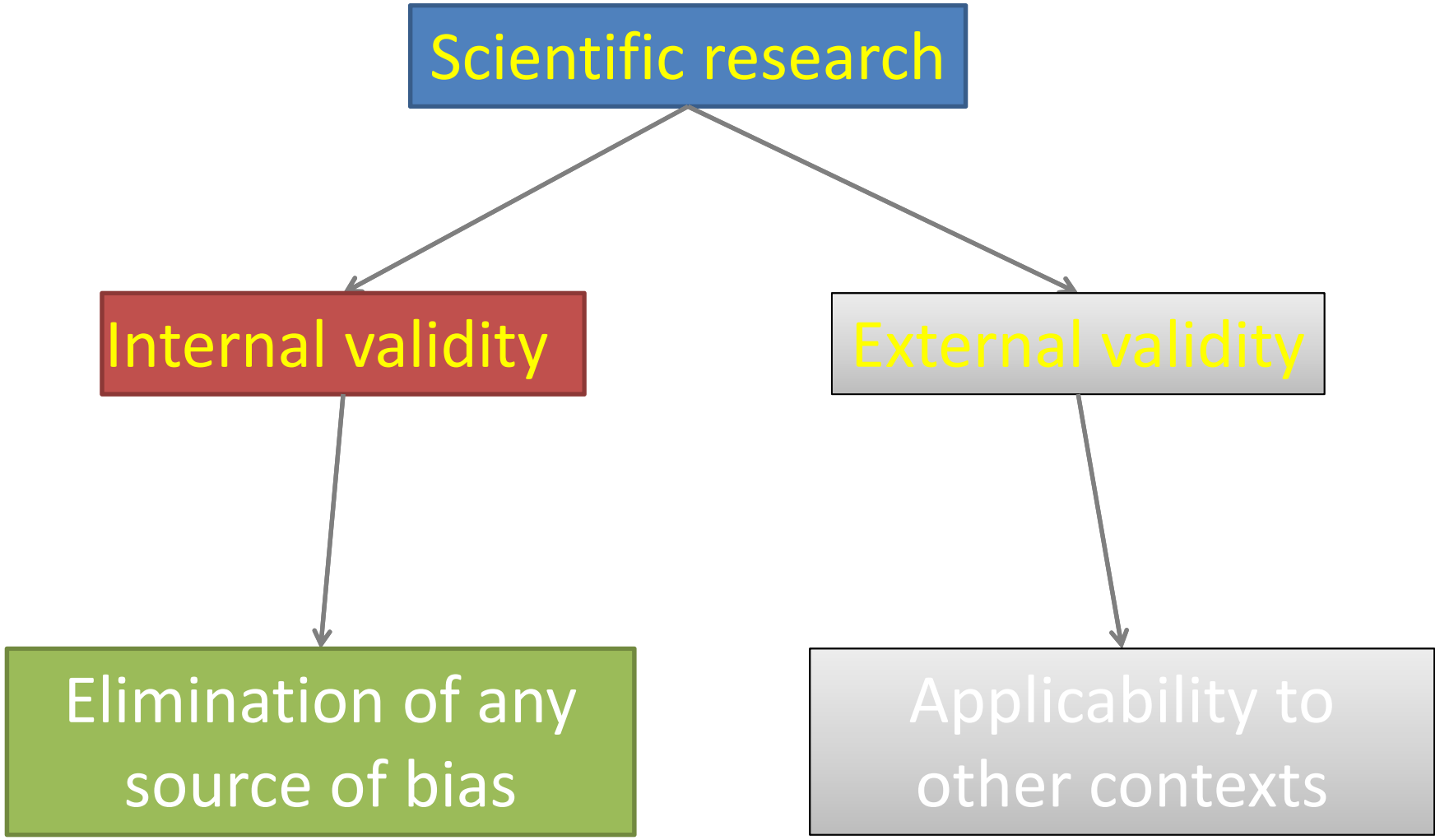
nellesercizio della Sua funzione e per l'evento in oggetto, DI NON ESSERE in alcun modo portatore di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le mie funzioni al fine di trarne vantaggio.

La coagulopatia produce di per se emorragia e aumento della mortalità?

Trattare la coagulopatia riduce la mortalità?


MEDLINE (PubMed)
6182 studies Identified
524 available for abstract screening
217 total available for full-text screening
19 eligible
2 excluded
No evidence 14
Very low 0
Low 2
Moderate 1
High 0


Scientific research
Internal validity
External validity
Elimination of any source of bias
Generalizability (and applicability) to other contexts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3 rapide regole per individuare la “cattiva” regressione logistica

1. Il numero di variabili per ogni evento (ad es. Morte) non deve essere < 10

British Journal of Anaesthesia **107** (3): 378–87 (2011)
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IF 4.8

BJA

CRITICAL CARE

Prevalence and impact of abnormal ROTEM® assays in severe blunt trauma: results of the 'Diagnosis and Treatment of Trauma-Induced Coagulopathy (DIA-TRE-TIC) study'

H. Tauber[1], P. Innerhofer[1*], R. Breitkopf[1], I. Westermann[1], R. Beer[2], R. El Attal[3], A. Strasak[4] and M. Mittermayr[1]

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Total mortality (*n*)	47 (14.1)

n. var. = 10

47/10 = 4,7

	Regression	*P*-value	Exp (*B*)	95% CI	
PT (%)		005	0.951	0.919	0.985
aPTT (s)		002	1.027	1.010	1.045
DD ratio		001	1.053	1.021	1.086
Fibrinogen (mg dl^{-1})	−0.003	0.547	0.997	0.988	1.007
Platelets (G $litre^{-1}$)	0.002	0.797	1.002	0.989	1.014
EXTEM CT (s)	0.010	0.036	1.010	1.001	1.019
EXTEM CFT (s)	0.001	0.017	1.001	1.000	1.002
EXTEM MCF (mm)	−0.61	0.022	0.940	0.892	0.991
EXTEM LI 60 (%)	−0.040	0.001	0.961	0.938	0.983
FIBTEM MCF (mm)	−0.009	0.869	0.991	0.892	1.101

British Journal of Anaesthesia **107** (7 (2011)
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SCARTATO

25 su 45 = 55%

3 rapide regole per individuare la “cattiva” regressione logistica

1. Il numero di variabili per ogni evento (ad es. Morte) non deve essere < 10

2. Il numero di variabili non deve essere “basso” per spiegare il fenomeno clinico

Journal of Thrombosis and Haemostasis, **10**: 1342–1351 DOI: 10.1111/j.1538-7836.2012.04752.x

ORIGINAL ARTICLE

Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes

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Table 3 Independent variables associated with mortality

Parameter	Odds ratio	95% CI	*P*-value
Fibrinogen level	0.22	0.10–0.47	< 0.001
Injury severity	1.03	1.00–1.06	0.07
APTT	1.05	1.01–1.09	0.02
Gender (female)	2.46	1.04–5.81	0.04
Age	1.05	1.02–1.07	< 0.001

APTT, activated partial thromboplastin time; CI, confidence interval.

National report for general ICUs - Year 2014
Prognostic models - Adult patients with LOS>=to 24 hours

Model: Logistic regression.
Dependent variable: Hospital mortality°.
Sample used for model development: Patients with LOS>=24 hours from general Italian ICUs.
Sample size: 34832 patients.

Independent variables	Coefficients (95% CI)	Odds Ratio (95% CI)	p
Intercept	-5.68 (-5.86;-5.49)	/	/
Miscellanea			
Max(Age - 41 , 0) in decades	0.41 (0.38;0.43)	/	×
Min((BMI - 33)/10, 0)^2	0.21 (0.16;0.26)	1.24 (1.18;1.3)	<0.001
Max((BMI - 33)/10, 0)^2	0.06 (0.02;0.09)	1.06 (1.03;1.1)	
Surgical status (Non surgical vs. Elective surgical)	0.76 (0.62;0.89)	/	×
Surgical status (Emergency surgical vs. Elective surgical)	0.38 (0.25;0.5)	/	
Stay before ICU (days) (logarithm)	0.26 (0.22;0.31)	1.3 (1.25;1.36)	<0.001
Admitted in hospital the same day of ICU admission (Yes vs. No)	0.08 (-0.02;0.18)	1.09 (0.98;1.2)	0.10
Ward of admission: Medical ward, High dependency care unit, Long-term chronic care hospital vs. Surgical ward, Other ICU	0.27 (0.18;0.36)	/	×
Ward of admission: Emergency room vs. Surgical ward, Other ICU	0.09 (-0.02;0.2)	/	
Physiopatological components			
Bilirubin (mg/100ml) (1.2-5.9 vs. <1.2)	0.2 (0.12;0.28)	1.22 (1.13;1.32)	<0.001
Bilirubin (mg/100ml) (>=6 vs. <1.2)	0.76 (0.52;1)	2.14 (1.68;2.73)	
WBC (10^9/L) (<1 vs. 1-20)	0.3 (0.06;0.53)	1.35 (1.07;1.71)	0.007
WBC (10^9/L) (>20 vs. 1-20)	0.09 (0.01;0.18)	1.1 (1.01;1.2)	
Sodium (mEq/L) (<125 vs. 125-145)	0.31 (0.07;0.56)	1.37 (1.07;1.74)	<0.001
Sodium (mEq/L) (>=145 vs. 125-145)	0.15 (0.06;0.24)	1.17 (1.07;1.27)	
Platelets (10^5/mm3) (20-99 vs. >=100)	0.32 (0.22;0.41)	1.37 (1.25;1.51)	<0.001
Platelets (10^5/mm3) (<20 vs. >=100)	0.73 (0.45;1.01)	2.07 (1.56;2.74)	
Urine Output (L/24h) (<0,2 vs. >=1)	0.77 (0.59;0.95)	2.16 (1.81;2.59)	<0.001
Urine Output (L/24h) (0.2-0.49 vs. >=1)	0.48 (0.34;0.63)	1.62 (1.4;1.87)	
Urine Output (L/24h) (0,5-0,99 vs. >=1)	0.3 (0.21;0.4)	1.36 (1.24;1.49)	
Serum urea (mg/100 ml) (60-179 vs. <60)	0.2 (0.11;0.28)	/	×
Serum urea (mg/100 ml) (>=180 vs. <60)	0.43 (0.28;0.59)	/	
PaO2/FiO2 (100*mmHg/%) (200-299 vs. >=300)	0.14 (0.05;0.23)	/	×
PaO2/FiO2 (100*mmHg/%) (100-199 vs. >=300)	0.46 (0.36;0.56)	/	
PaO2/FiO2 (100*mmHg/%) (<100 vs. >=300)	1.1 (0.9;1.3)	/	
Heart rate (bpm) (<70 vs. 70-119)	-0.16 (-0.24;-0.08)	/	×
Heart rate (bpm) (>=120 vs. 70-119)	0.28 (0.19;0.37)	/	
MAP (mmHg) (<70 vs. >=70)	0.31 (0.24;0.39)	/	×
Potassium (mEq/L) (>=5 vs. <5)	0.22 (0.13;0.32)	1.25 (1.13;1.37)	<0.001
Creatinine (mg/dl) (1.2-4.9 vs. <1.2)	0.15 (0.06;0.24)	1.16 (1.06;1.27)	<0.001
Creatinine (mg/dl) (>5 vs. <1.2)	-0.48 (-0.68;-0.28)	0.62 (0.5;0.76)	
Clinical conditions on admission			
Acute intoxication (Yes vs. No)	-0.76 (-1.09;-0.43)	0.47 (0.33;0.65)	<0.001
Spontaneous Intraparenchymal bleeding (Yes vs. No)	0.78 (0.6;0.96)	/	×
ARDS (Yes vs. No)	0.57 (0.38;0.77)	/	×
Haematological disease (Yes vs. No)	0.74 (0.38;1.09)	2.09 (1.46;2.98)	<0.001
Ascites (Yes vs. No)	0.71 (0.36;1.06)	2.03 (1.43;2.89)	<0.001
Lung cancer (Yes vs. No)	0.8 (0.5;1.09)	2.22 (1.65;2.99)	<0.001
Acute pancreatitis (Yes vs. No)	0.45 (0.18;0.73)	1.57 (1.19;2.07)	0.002
Seizures (Yes vs. No)	-0.45 (-0.65;-0.25)	0.64 (0.52;0.78)	<0.001
Bowel ischaemia (Yes vs. No)	0.63 (0.4;0.86)	1.88 (1.5;2.37)	<0.001
Spontaneous Subarachnoid haemorrhage (Yes vs. No)	0.79 (0.58;1.01)	2.21 (1.78;2.75)	<0.001
Cardiac arrest (Yes vs. No)	0.49 (0.29;0.69)	/	×
Cerebral artery stroke (Yes vs. No)	0.3 (0.12;0.48)	1.35 (1.13;1.62)	0.001
Left heart failure with pulmonary edema (Yes vs. No)	-0.37 (-0.5;-0.23)	0.69 (0.6;0.8)	<0.001
Metabolic disorder (Yes vs. No)	-0.17 (-0.3;-0.04)	0.84 (0.74;0.96)	0.008
Nephro-urologic disease (Yes vs. No)	-0.29 (-0.45;-0.13)	0.75 (0.64;0.88)	<0.001
Gastrointestinal bleeding: upper tract (Yes vs. No)	0.8 (0.49;1.1)	/	×
Acute on chronic liver disease (Yes vs. No)	0.67 (0.22;1.12)	1.95 (1.24;3.07)	0.003
Vertebral basilar ischemic stroke (Yes vs. No)	0.8 (0.35;1.24)	2.22 (1.42;3.46)	<0.001
Pneumothorax/Pneumomediastinum (Yes vs. No)	0.59 (0.25;0.93)	1.8 (1.28;2.54)	<0.001
Brain tumour (Yes vs. No)	0.77 (0.48;1.06)	2.16 (1.62;2.88)	<0.001
Post transplantation (Yes vs. No)	-0.92 (-1.29;-0.55)	0.4 (0.28;0.58)	<0.001
Systemic hypertensive crisis (Yes vs. No)	-0.49 (-0.85;-0.13)	0.61 (0.43;0.88)	0.006
Ruptured or fissured aneurysm (Yes vs. No)	0.41 (0.13;0.69)	1.51 (1.14;1.99)	0.004
Pneumonia (Yes vs. No)	0.34 (0.21;0.47)	/	×
Urinary tract infection (Yes vs. No)	-0.27 (-0.45;-0.08)	0.77 (0.64;0.92)	0.005
Skin or soft tissue infection (Yes vs. No)	0.6 (0.37;0.82)	1.82 (1.45;2.28)	<0.001
Cholecystitis/cholangitis (Yes vs. No)	-0.44 (-0.71;-0.16)	0.65 (0.49;0.85)	0.001
Peritonites (Yes vs. No)	0.32 (0.15;0.49)	1.38 (1.16;1.64)	<0.001
Infection severity on admission (Infection with or without SIRS vs. None)	-0.12 (-0.26;0.01)	/	×
Infection severity on admission (Severe sepsis vs. None)	0.84 (0.34;1.35)	/	
Infection severity on admission (Septic shock vs. None)	0.05 (-0.1;0.2)	/	
Multiple trauma (Yes vs. No)	-0.4 (-0.6;-0.2)	0.67 (0.55;0.82)	<0.001
Traumatic Subdural haematoma (Yes vs. No)	0.58 (0.29;0.88)	1.79 (1.33;2.41)	<0.001
Traumatic intraparenchymal bleeding (Yes vs. No)	0.52 (0.11;0.93)	1.69 (1.12;2.54)	0.013
Spine trauma (Trauma with deficit vs. No trauma or Trauma without deficit)	0.88 (0.45;1.32)	2.42 (1.56;3.76)	<0.001
Post-traumatic diffuse injury (Yes vs. No)	0.64 (0.18;1.1)	1.9 (1.2;3.01)	0.007
Head trauma (Head trauma without skull fracture vs. No head trauma)	-0.4 (-0.79;-0.02)	/	×
Head trauma (Head trauma with skull fracture vs. No head trauma)	-0.03 (-0.4;0.35)	/	

(to be continued)

° *For patients transferred to other ICU or to rehabilitation/high dependency care unit in other hospital, it is considered the outcome at the last hospital discharge.*
× *See interaction significance.*

Comorbidities			
Metastatic cancer (Yes vs. No)	0.96 (0.82;1.1)	2.61 (2.27;3)	<0.001
NYHA class II-III (Yes vs. None)	0.21 (0.12;0.3)	1.23 (1.13;1.35)	<0.001
NYHA class IV (Yes vs. None)	0.5 (0.31;0.68)	1.65 (1.37;1.98)	
Malignant haematological disease (Yes vs. No)	0.69 (0.49;0.89)	1.99 (1.64;2.43)	<0.001
Moderate or severe liver disease (Yes vs. No)	0.56 (0.37;0.75)	1.75 (1.45;2.12)	<0.001
Severe COPD (Yes vs. No)	0.4 (0.3;0.51)	1.5 (1.35;1.67)	<0.001
Severe malnutrition (Yes vs. No)	0.5 (0.24;0.76)	1.64 (1.27;2.13)	<0.001
Dementia (Yes vs. No)	0.43 (0.29;0.58)	/	×
Immunosuppression or AIDS (Yes vs. No)	0.3 (0.1;0.5)	1.35 (1.11;1.64)	0.003
Restrictive lung disease (Yes vs. No)	0.46 (0.29;0.63)	1.58 (1.34;1.87)	<0.001
Hypertension (Yes vs. No)	-0.13 (-0.2;-0.07)	0.88 (0.82;0.94)	<0.001
Cerebrovascular disease (Yes vs. No)	0.13 (0.04;0.21)	1.14 (1.04;1.24)	0.003
Peripheral vascular disease (Yes vs. No)	0.23 (0.13;0.33)	1.26 (1.14;1.38)	<0.001
Diabetes Type II with insulin treatment (Yes vs. No)	0.19 (0.08;0.3)	1.21 (1.09;1.35)	<0.001
Organ failures			
GCS (3,4 vs. 15)	2.43 (2.17;2.7)	/	×
GCS (5 vs. 15)	1.64 (1.37;1.91)	/	
GCS (6 vs. 15)	1.41 (1.17;1.65)	/	
GCS (7,8,9 vs. 15)	0.94 (0.79;1.1)	/	
GCS (10,11,12 vs. 15)	0.48 (0.35;0.62)	/	
GCS (13,14 vs. 15)	0.29 (0.18;0.4)	/	
GCS (Not evaluable in the first 24 hours in neurological patient* vs. 15)	1.24 (1.04;1.44)	/	
GCS (Not evaluable in the first 24 hours in NON-neurological patient* vs. 15)	0.57 (0.44;0.7)	/	
Neurologic failure (Cerebral coma vs. None or Not evaluable in the first 24 hours)	0.25 (0.09;0.42)	/	×
Neurologic failure (Metabolic coma vs. None or Not evaluable in the first 24 hours)	-0.56 (-0.77;-0.36)	/	
Neurologic failure (Postanoxic coma vs. None or Not evaluable in the first 24 hours)	0.38 (0.04;0.71)	/	
Neurologic failure (Toxic coma vs. None or Not evaluable in the first 24 hours)	-0.95 (-1.46;-0.43)	/	
Cardiogenic shock (Yes vs. No)	0.35 (0.23;0.47)	1.42 (1.26;1.6)	<0.001
Neurogenic shock (Yes vs. No)	0.94 (0.62;1.27)	2.57 (1.85;3.56)	<0.001
Non shock (Yes vs. No)	0.17 (0.05;0.29)	1.19 (1.05;1.34)	0.005
Haemorrhagic-Hypovolemic shock (Yes vs. No)	0.14 (-0.01;0.29)	1.15 (0.99;1.34)	0.069
Hypovolemic (non-haemorrhagic) shock (Yes vs. No)	0.05 (-0.14;0.23)	/	×
Renal failure (AKIN) (Mild vs. None)	0.09 (-0.01;0.19)	/	
Renal failure (AKIN) (Moderate vs. None)	0.48 (0.33;0.63)	/	×
Renal failure (AKIN) (Severe vs. None)	0.78 (0.59;0.97)	/	
Respiratory failure (Only hypoxic failure vs. None)	0.32 (0.22;0.41)	/	
Respiratory failure (Only hypercapnic failure vs. None)	0.26 (0.1;0.41)	/	×
Respiratory failure (Intubation for airway maint. vs. None)	0.42 (0.32;0.51)	/	
Metabolic failure (pH <= 7.3, PaCO2 < 45 mmHg vs. None)	0.44 (0.33;0.55)	/	×
Metabolic failure (gsub("*",*",formato("metabolicFail","baseMetaFail")) vs. None)	0.23 (0.14;0.32)	/	
Surgical and non surgical procedures			
Peripheral vascular surgery (Yes vs. No)	0.35 (0.09;0.61)	1.42 (1.1;1.84)	0.009
Gastrointestinal surgery (Yes vs. No)	0.31 (0.19;0.43)	1.36 (1.2;1.53)	<0.001
Pancreatic surgery (Yes vs. No)	0.54 (0.19;0.88)	1.71 (1.21;2.41)	0.003
Interactions among independent variables			
GCS (10,11,12,Not evaluable in the first 24 hours in NON-neurological patient*) × Heart rate (bpm) (>120)	-0.35 (-0.52;-0.17)	/	<0.001
GCS (Not evaluable in the first 24 hours in neurological patient*) × Heart rate (bpm) (<70)	0.49 (0.19;0.78)	/	
GCS (3,4) × Serum urea (mg/100 ml) (60-180)	-0.27 (-0.49;-0.04)	/	<0.001
GCS (3,4) × Serum urea (mg/100 ml) (>180)	-1.05 (-1.56;-0.55)	/	
GCS (3,4) × PaO2/FiO2 (100*mmHg/%) (200-300)	-0.33 (-0.58;-0.08)	/	
GCS (10,11,12,Not evaluable in the first 24 hours in NON-neurological patient*) × PaO2/FiO2 (100*mmHg/%) (200-300)	0.21 (0.05;0.36)	/	
GCS (3,4) × PaO2/FiO2 (100*mmHg/%) (100-200)	-0.76 (-1.02;-0.5)	/	
GCS (5,6,7,8,9,Not evaluable in the first 24 hours in neurological patient*) × PaO2/FiO2 (100*mmHg/%) (100-200)	-0.28 (-0.45;-0.11)	/	<0.001
GCS (3,4,5,6,Not evaluable in the first 24 hours in neurological patient*) × PaO2/FiO2 (100*mmHg/%) (<100)	-1.15 (-1.51;-0.79)	/	
GCS (7,8,9,13,14) × PaO2/FiO2 (100*mmHg/%) (<100)	-0.63 (-0.93;-0.32)	/	
GCS (10,11,12,Not evaluable in the first 24 hours in NON-neurological patient*) × PaO2/FiO2 (100*mmHg/%) (<100)	-0.32 (-0.59;-0.05)	/	
Pneumonia × Renal failure (AKIN) (Severe)	-0.42 (-0.7;-0.15)	/	0.002
GCS (3,4,5,6) × Dementia	-0.53 (-0.9;-0.16)	/	0.005
ARDS × Infection severity on admission (Septic shock)	-0.57 (-0.94;-0.2)	/	0.003
Infection severity on admission (Infection with or without SIRS) × Renal failure (AKIN) (Severe)	-0.36 (-0.72;0.01)	/	0.002
Infection severity on admission (Severe sepsis,Septic shock) × Renal failure (AKIN) (Moderate)	-0.27 (-0.46;-0.07)	/	
Respiratory failure (Only hypercapnic failure) × Neurologic failure (Cerebral coma)	-0.82 (-1.51;-0.14)	/	0.016
GCS (3,4,5,6) × Head trauma with skull fracture	0.75 (0.23;1.26)	/	0,004
Max(Age - 41 , 0) in decades × Head trauma without skull fracture	0.14 (0.03;0.24)	/	0.008
Max(Age - 41 , 0) in decades × Neurologic failure (Postanoxic coma)	-0.15 (-0.25;-0.06)	/	0.002
GCS (3,4,Not evaluable in the first 24 hours in neurological patient*) × Infection severity on admission (Infection with or without SIRS)	-0.47 (-0.8;-0.15)	/	0.004
MAP (mmHg) (<70) × Gastrointestinal bleeding: upper tract	-0.79 (-1.25;-0.32)	/	<0.001
GCS (3,4) × Spontaneous Intraparenchymal bleeding	0.76 (0.42;1.11)	/	<0.001
Surgical status (Non surgical) × Infection severity on admission (Severe sepsis)	-0.93 (-1.44;-0.42)	/	0.002
Surgical status (Emergency surgical) × Infection severity on admission (Severe sepsis)	-0.84 (-1.38;-0.3)	/	
Hypovolemic (non-haemorrhagic) shock × Metabolic failure (pH <= 7.3, PaCO2 < 45 mmHg)	-0.48 (-0.91;-0.04)	/	0.032
MAP (mmHg) (<70) × Cardiac arrest	-0.45 (-0.69;-0.2)	/	<0.001
GCS (3,4,Not evaluable in the first 24 hours in neurological patient*,Not evaluable in the first 24 hours in NON-neurological patient*) × Ward of admission (Emergency room)	0.28 (0.15;0.42)	/	<0.001

Dependent variable explained		Goodness-of-fit	
Likelihood Ratio Test:	11570	Area under the ROC curve:	0.851
Degree of freedom:	139	GiViTI Calibration Test:	1.71
p-value:	<0.0001	p-value:	0.191
		Polynomial Degree:	2

** A neurological patient is a one with an altered consciousness, probably due to a direct brain injury. It is defined by the presence of at least one of these clinical conditions on admission: Cerebral artery stroke, Vertebral basilar ischemic stroke, Intracranial hypertension, Spontaneous Hydrocephalus, Non traumatic cerebral oedema, Metabolic/postanoxic encephalopathy, Seizures, Brain tumour, Cerebral Aneurysm, AVM (ArterioVenous Malformation), Chronic Subdural haematoma, Spontaneous Subarachnoid haemorrhage, Spontaneous Intraparenchymal bleeding, CNS degenerative disease, Brain and skull malformations, Cerebral contusion/laceration, Traumatic diffuse injury without oedema, Traumatic diffuse injury with oedema, Extradural/epidural haematoma, Traumatic Subdural haematoma, Traumatic intraparenchymal bleeding, Traumatic subarachnoid haemorrhage, Skull fracture, NON-surgical CNS infection, Post-surgical CNS infection, Ventriculostomy-related CNS infection.*
× *See interaction significance.*

3 rapide regole per individuare la “cattiva” regressione logistica

1. Il numero di variabili per ogni evento (ad es. Morte) non deve essere < 10

2. Il numero di variabili non deve essere “basso” per spiegare il fenomeno clinico

3. Risultati paradossali o quantitativamente “eccessivi”

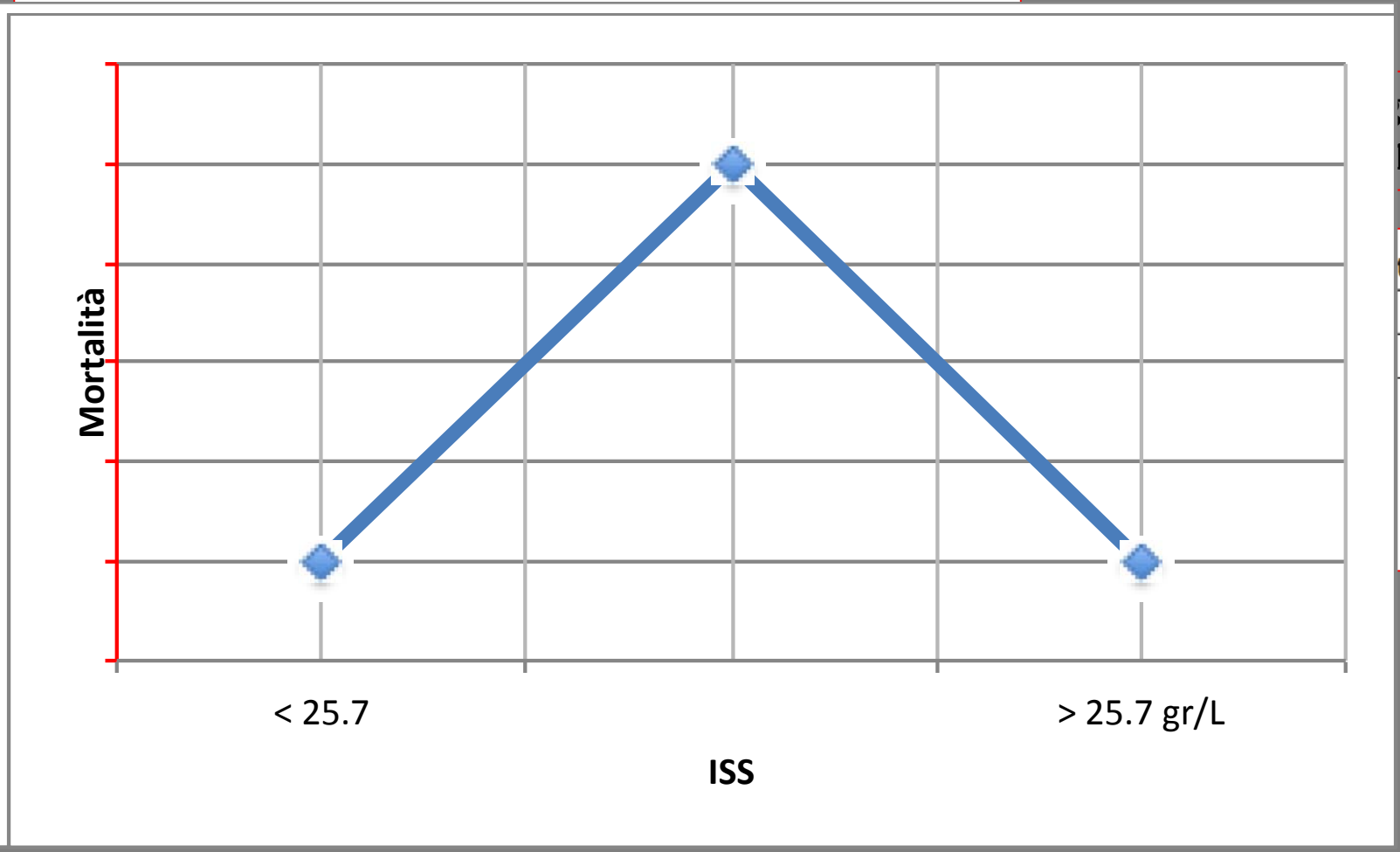
Hagemo *et al. Critical Care* 2014, **18**:R52
http://ccforum.com/content/18/2/R52

CRITICAL CARE

IF 4.4

RESEARCH Open Access

Prevalence, predictors and outcome of



gr/L
100 ml)

Tab

t variable

P value

Fibr

< 0.001

0.076

Hagemo *et al. Critical Care* 2014, **18**:R52
http://ccforum.com/content/18/2/R52

CRITICAL CARE

RESEARCH Open Access

Prevalence, predictors and outcome of hypofibrinogenaemia in trauma: a multicentre observational study

Jostein S Hagemo[1,2*], Simon Stanworth[3], Nicole P Juffermans[4,5], Karim Brohi[6], Mitchell Jay Cohen[7], Pär I Johansson[8,9], Jo Røislien[1,10], Torsten Eken[11], Paal A Næss[12] and Christine Gaarder[12]

2.29 gr/L
(229 mg/100 ml)

Table 2 Linear and piecewise linear multiple logistic regression models with 28-day mortality as the dependent variable

	Linear model		Piecewise linear model		
	Odds ratio v	***P* value**	**Segment**	**Odds ratio (95% CI)**	***P* value**
Fibrinogen (g/l)[a]	0.46	< 0.001	Lower	0.08	< 0.001
	(0.31, 0.67)			(0.03, 0.20)	
			Upper	1.77	0.076
				(0.94, 3.32)	

Il Survival Bias

Survival in Academy Award–Winning Actors and Actresses

Donald A. Redelmeier, MD, and Sheldon M. Singh, BSc

Ann Intern Med. 2001;134:955-962.

Annals of Internal Medicine | ACADEMIA AND CLINIC

Do Oscar Winners Live Longer than Less Successful Peers? A Reanalysis of the Evidence

Marie-Pierre Sylvestre, MSc; Ella Huszti, MSc; and James A. Hanley, PhD

Ann Intern Med. 2006;145:361-363.

JAMA Surg. 2013 February ; 148(2): 127–136. doi:10.1001/2013.jamasurg.387.

The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study: Comparative Effectiveness of a Time-varying Treatment with Competing Risks

Multivariable Cox regression models examining the association of plasma and platelet transfusion ratios with in-hospital mortality

A. Time Interval 1: Minute 31 to hour 6 post ED admission[a] (N=876)[b]

	Continuous transfusion ratio variables				*Categorical transfusion ratio variables*					
					Low <1:2		Moderate ≥ 1:2–<1:1		High ≥1:1	
	HR	95% CI		P value	HR	P value	HR	P value	HR	P value
Early initial and time-varying plasma:RBC ratios	0.31	0.16	0.58	<.001	1.00	Ref	0.42	<.001	0.23	<.001
Early initial and time-varying platelet:RBC ratios	0.55	0.31	0.98	.04	1.00	Ref	0.66	0.16	0.37	0.04
Sum of blood product transfusions	1.05	1.04	1.06	<.001	*c*					
Age	1.01	1.00	1.02	.03						
Injury Severity Score	1.02	1.01	1.04	.001						
Time interval at cohort entry	0.73	0.63	0.86	<.001						
Bleeding from the head	3.73	2.15	6.45	<.001						
Bleeding from the chest	1.52	0.96	2.39	.07						
Bleeding from a limb	0.54	0.32	0.89	.02						

Confounding by indication

Il Propensity Score

Confounding by indication

Journal of Thrombosis and Haemostasis, **10**: 1342–1351 DOI: 10.1111/j.1538-7836.2012.04752.x

ORIGINAL ARTICLE

Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes

C. ROURKE,*[1] N. CURRY,†[1] S. KHAN,* R. TAYLOR,† I. RAZA,* R. DAVENPORT,* S. STANWORTH† and K. BROHI*

**Trauma Sciences, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London; and † National Health Service Blood & Transplant/Haematology, John Radcliffe Hospital, Oxford, UK*

Table 4 Effect of fibrinogen administration on 28-day mortality (conditional on 12-h survival)

Parameter	Odds ratio	95% CI	*P*-value
Fibrinogen given in first 12 h	0.91	0.81–1.01	0.08
Injury severity	1.06	1.03–1.10	< 0.001
APTT	1.10	1.04–1.16	0.001
Age	1.03	1.01–1.05	0.005
Gender (female)	3.03	1.24–7.39	0.01

APTT, activated partial thromboplastin time; CI, confidence interval.

High Ratios of Plasma and Platelets to Packed Red Blood Cells Do Not Affect Mortality in Nonmassively Transfused Patients

Chitra N. Sambasivan, MD, Nicholas R. Kunio, MD, Prakash V. Nair, MS, Karen A. Zink, MD, Joel E. Michalek, PhD, John B. Holcomb, MD, Martin A. Schreiber, MD, and the Trauma Outcomes Group

(*J Trauma.* 2011;71: S329–S336)

TABLE 3. Proportional Hazards Analysis of In-Hospital Mortality in Terms of FFP:PRBC Ratio Category (<1:1, ≥1:1)

Independent Variable*	RR	95% CI	*p*
FFP:PRBC ratio†	0.872	0.551–1.378	0.56
ISS	1.031	1.016–1.046	<0.001
GCS	0.877	0.838–0.917	<0.001
PTT	1.015	1.010–1.019	<0.001
Propensity Score‡	0.938	0.901–0.977	0.002

* Multivariate propensity-adjusted proportional hazards model of time to death in terms of FFP:PRBC ratio category, ISS, GCS, PTT, and propensity score (n = 618 used in the model).

<1:1 (referent) or ≥1:1.

Score = 17.44 − 0.12 × (age) − 1.10 × (admission hemoglobin) + 0.82 × (admission base deficit).

High Ratios of Plasma and Platelets to Packed Red Blood Cells Do Not Affect Mortality in Nonmassively Transfused Patients

Chitra N. Sambasivan, MD, Nicholas R. Kunio, MD, Prakash V. Nair, MS, Karen A. Zink, MD, Joel E. Michalek, PhD, John B. Holcomb, MD, Martin A. Schreiber, MD, and the Trauma Outcomes Group

(*J Trauma.* 2011;71: S329–S336)

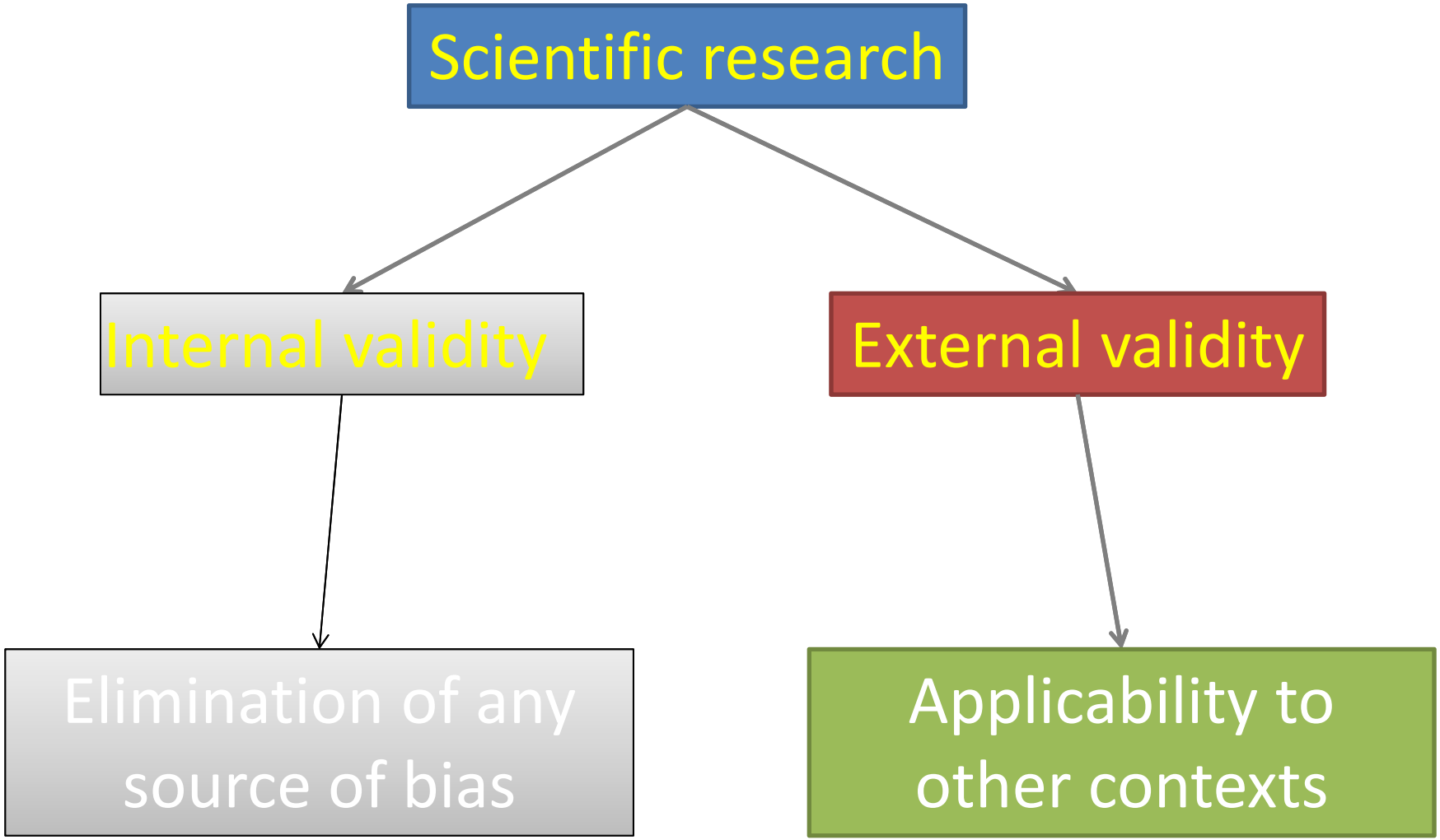
TABLE 4. Proportional Hazards Analysis of In-Hospital Mortality in Terms of PLT:PRBC Ratio Category (<1:1, ≥1:1)

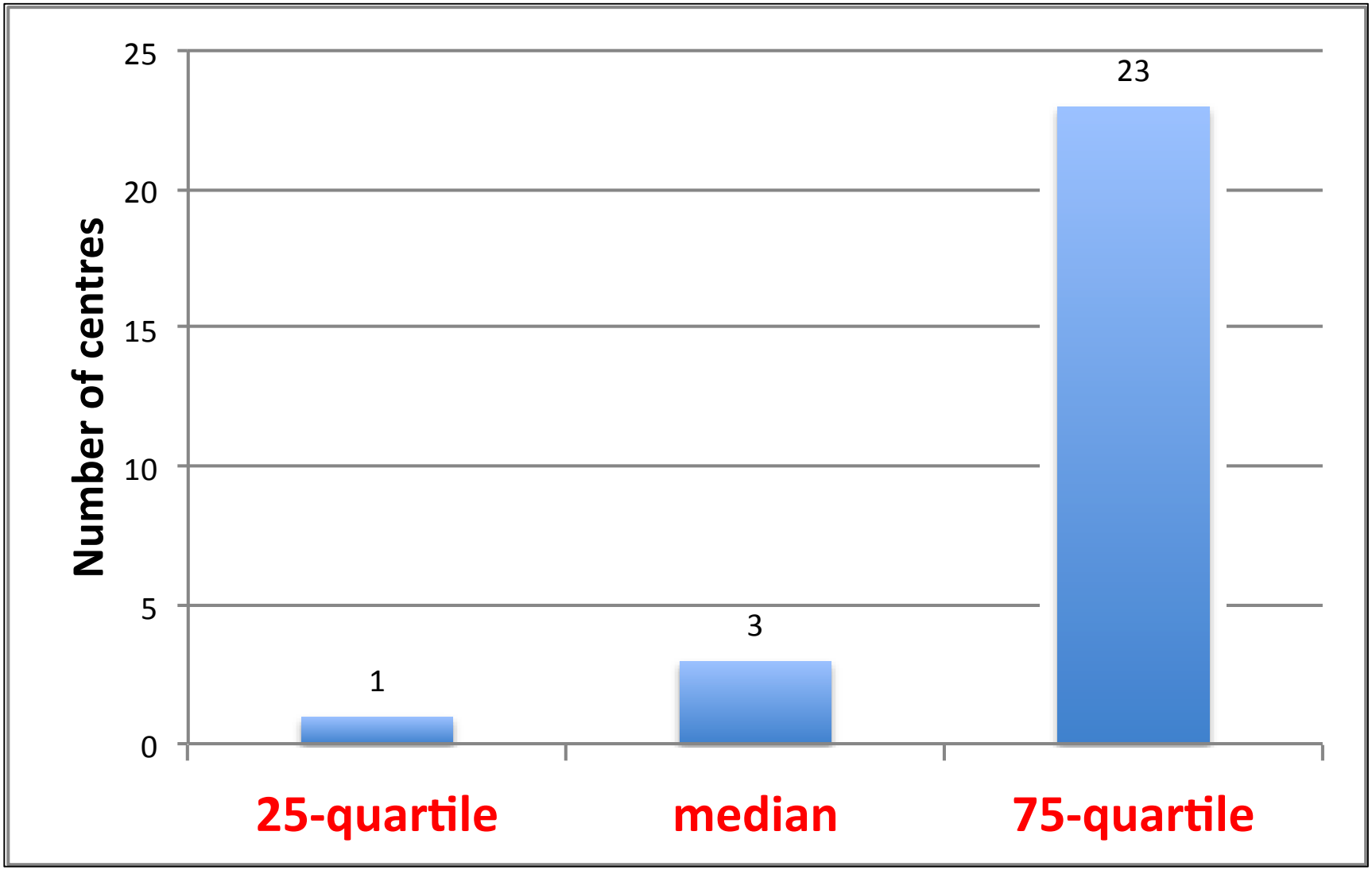
Independent Variable*	RR	95% CI	*p*
PLT:PRBC ratio†	1.031	0.555–1.918	0.92
Age	1.027	1.019–1.035	<0.001
ISS	1.051	1.039–1.062	<0.001
Propensity score‡	1.058	1.017–1.100	0.005

* Multivariate propensity-adjusted proportional hazards model of time to death in terms of PLT:PRBC ratio, age, ISS, and propensity score (n = 1,051 used in the model).

<1:1 (referent) or ≥1:1.

Score = −7.37 − 0.049 × (admission platelets) + 1.07 × (admission hemoglobin).


Scientific research
Internal validity
External validity
Elimination of any source of bias
Applicability to other contexts


Number of centres
25
20
15
10
5
0
1
3
23
25-quartile
median
75-quartile

The Ratio of Blood Products Transfused Affects Mortality in Patients Receiving Massive Transfusions at a Combat Support Hospital

Matthew A. Borgman, MD, Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD, Thomas Repine, MD, Alec C. Beekley, MD, James Sebesta, MD, Donald Jenkins, MD, Charles E. Wade, PhD, and John B. Holcomb, MD

J Trauma. 2007;63:805–813.

- Condotto a Bagdad
- 246 pazienti, 3 di sesso femminile
- Età media 24
- 94% di ferite penetranti
- Durata degenza mediana = 1 giorno

Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

Lancet 2010; 376: 23–32

CRASH-2 trial collaborators*

Dead	1463 (14·5%)	1613 (16·0%)	0·91 (0·85–0·97)	0·0035

Riduzione assoluta di mortalità del 1,5%

Condotto prevalentemente in paesi in via di sviluppo

Indicazione a somministrarlo in 3 ore frutto di analisi per sottogruppi che per definizione possono generare solo ipotesi

Spahn *et al. Critical Care* 2013, **17**:R76
http://ccforum.com/content/17/2/R76

RESEARCH Open Access

Management of bleeding and coagulopathy following major trauma: an updated European guideline

Donat R Spahn[1], Bertil Bouillon[2], Vladimir Cerny[3,4], Timothy J Coats[5], Jacques Duranteau[6], Enrique Fernández-Mondéjar[7], Daniela Filipescu[8], Beverley J Hunt[9], Radko Komadina[10], Giuseppe Nardi[11], Edmund Neugebauer[12], Yves Ozier[13], Louis Riddez[14], Arthur Schultz[15], Jean-Louis Vincent[16] and Rolf Rossaint[17*]

Massive bleeding = massive transfusion(?): patients receiving at least 10 U PRBC within the first 24 hours

We recommend the initial administration of plasma … (Grade 1B) … in patients with massive bleeding.

A practical guideline for the haematological management of major haemorrhage

Beverley J. Hunt,[1] Shubha Allard,[2] David Keeling,[3] Derek Norfolk,[4] Simon J. Stanworth,[5] Kate Pendry[6] and on behalf of the British Committee for Standards in Haematology

[1]Department of Haematology, GSTT, St Thomas' Hospital, [2]Department of Haematology, Royal London Hospital, London, [3]Oxford Haemophilia and Thrombosis Centre, Oxford University Hospitals, Churchill Hospital, Oxford, [4]Department of Haematology, Leeds Hospital, Leeds, [5]NHSBT/Department of Haematology, John Radcliffe Hospital, Oxford, and [6]Patients' Clinical Team, NHSBT, Manchester, UK

British Journal of Haematology, 2015, **170,** 788–803

Our arbitrary definition of major haemorrhage is bleeding which leads to a heart rate more than 110 beats/ min and/or systolic blood pressure less than 90 mmHg.

Adult trauma patients with, or at risk of, massive haemorrhage should initially be transfused empirically with a 1: 1 ratio of plasma: red blood cells (1B).

Raccomandazioni per l'implementazione del programma di *Patient Blood Management* *Applicazione in chirurgia ortopedica maggiore elettiva dell'adulto*

… pazienti con sanguinamento critico (> 40% della volemia) …

I protocolli di trasfusione massiva basati sull'impiego di schemi e rapporti fissi ed elevati tra emocomponenti … non sono attualmente supportati da evidenze solide …

SCIENCE • VOL. 257 • 31 JULY 1992

When Does Intellectual Passion Become Conflict of Interest?

Financial conflicts of interest are very much in the news it cutting-edge fi biotechnology the confusion the scientific c procedures for research and p But in talking tial financial conflicts, *Science* heard one refrain over and over again: that money problems are simple compared to the intellectual conflicts of interest that scientists have always had to deal with.

What did those researchers mean by in- proving a thesis, therefore, scientists must be sustained by something that approaches faith. And, as paleontologist-essayist-historian Stephen Jay Gould says, it is a "pervasive fact of human existence as social beings" that we find it extraordinarily difficult to step outside our own convictions and see them through the eyes of a detached observer.

Every researcher relies on personal intuition to some extent, so the important question is: When does a scientist's enthusiasm for an idea cross the line that separates passion from ogist to recog- scientists can s whom they es, no longer evenhanded ates are right. advanced by the obsessed individual, not by the doubting peers.

To examine the intertwined positive and negative aspects of commitment to one's own hypotheses, *Science* chose three cases in which researchers seemed to have an unusual per-

All researchers tend to "mythologize" their research, says Boston University's philosopher of anthropology, Misia Landau. And this isn't

Grazie