

THE OXYTRIP STUDY

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H.U.B

Hôpital Erasme

ULB

INSTITUT JULES BORDET INSTITUUT

Hôpital Universitaire des Enfants Reine Fabiola
Universitair Kinderziekenhuis Koningin Fabiola



NIHON KOHDEN

NEUROPTICS

EUROSETS™
MEDICAL DEVICES

INTEGRA
LIMIT UNCERTAINTY

werfen

BD

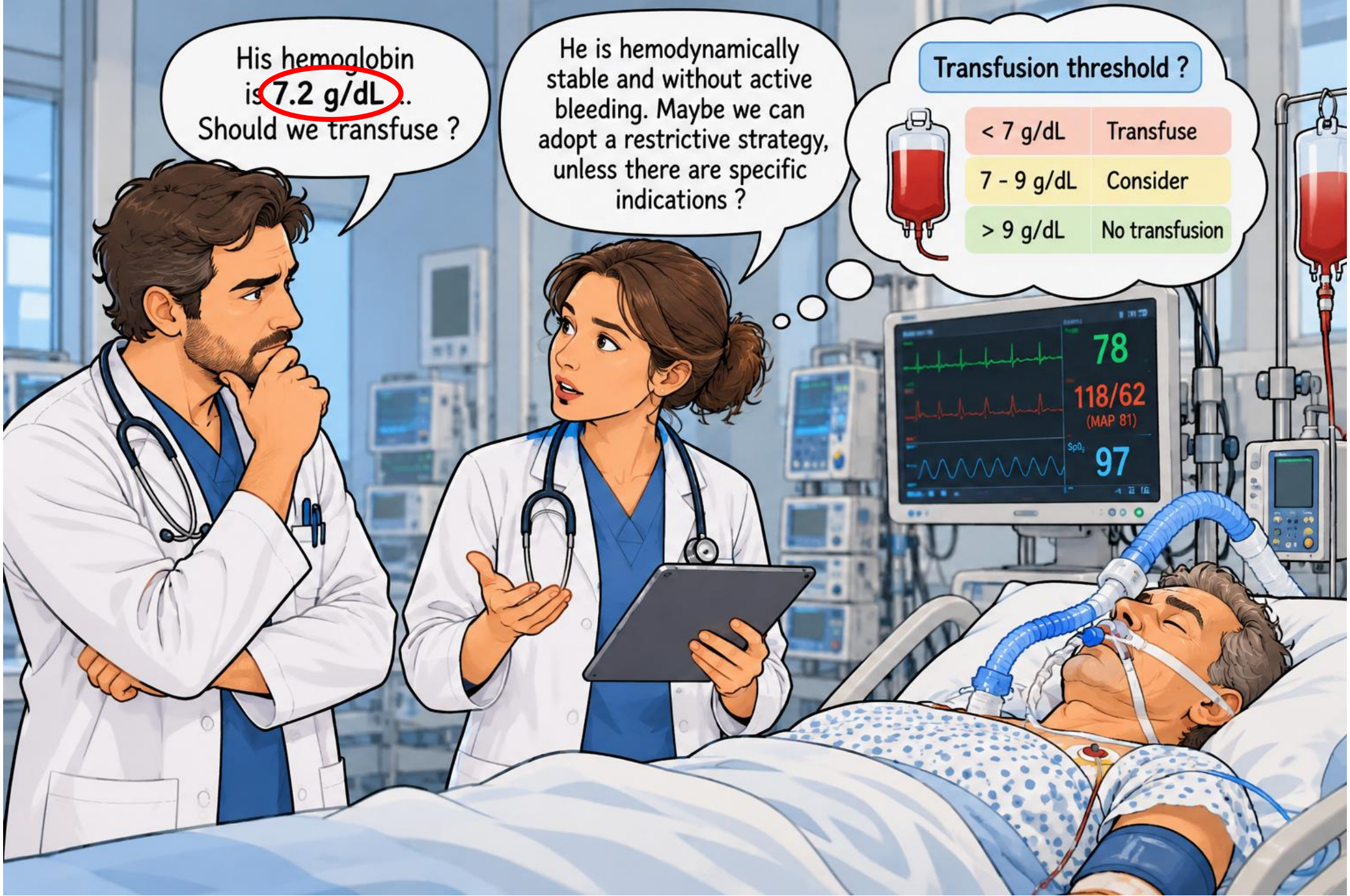
ZOLL®

CytoSorbents™

XENIOS

Medtronic




His hemoglobin is 7.2 g/dL ..
Should we transfuse ?
He is hemodynamically stable and without active bleeding. Maybe we can adopt a restrictive strategy, unless there are specific indications ?
Transfusion threshold ?
< 7 g/dL
Transfuse
7 - 9 g/dL
Consider
> 9 g/dL
No transfusion
78
118/62
(MAP 81)
SpO2
97

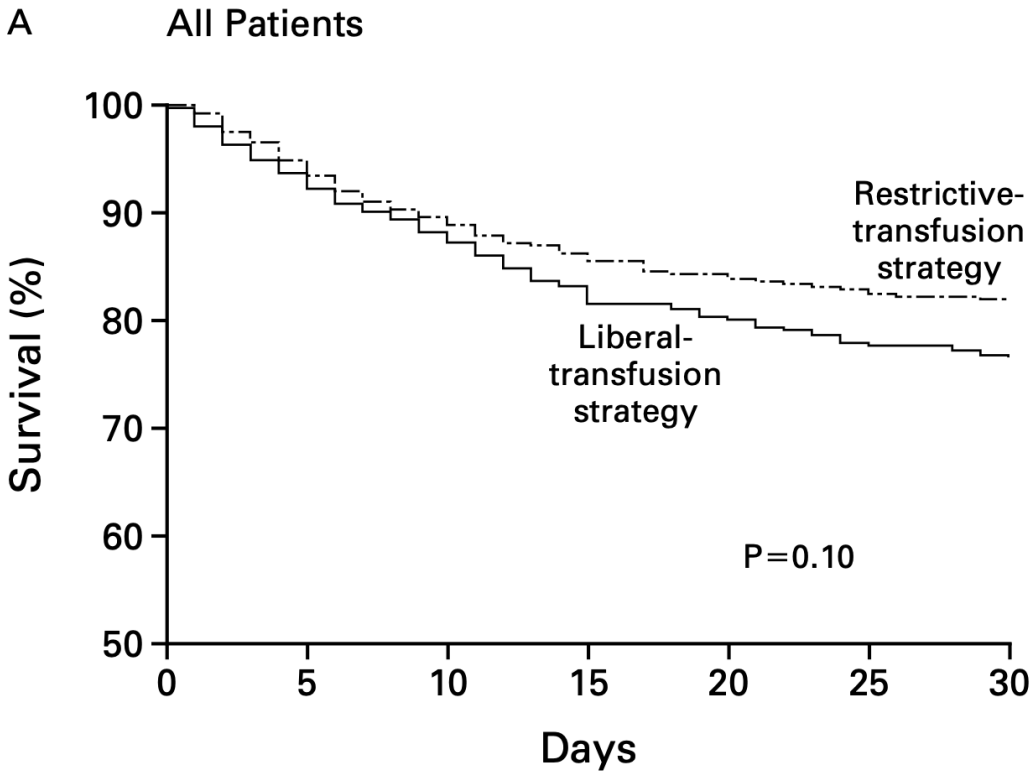


A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D., CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D., PH.D., IRWIN SCHWEITZER, M.SC., ELIZABETH YETISIR, M.SC., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS FOR THE CANADIAN CRITICAL CARE TRIALS GROUP*

TABLE 2. OUTCOMES.*

OUTCOME MEASURE	RESTRICTIVE-TRANSFUSION STRATEGY (N=418)	LIBERAL-TRANSFUSION STRATEGY (N=420)	ABSOLUTE DIFFERENCE BETWEEN GROUPS	95% CONFIDENCE INTERVAL	P VALUE
			percent		
Death — no. (%)					
30-day	78 (18.7)	98 (23.3)	4.7	−0.84 to 10.2	0.11
60-day†	95 (22.7)	111 (26.5)	3.7	−2.1 to 9.5	0.23
ICU	56 (13.4)	68 (16.2)	2.3	−2.0 to 7.6	0.29
Hospital	93 (22.2)	118 (28.1)	5.8	−0.3 to 11.7	0.05
Multiple-organ-dysfunction score					
Unadjusted score	8.3±4.6	8.8±4.4	0.5	−0.1 to 1.1	0.10
Adjusted score‡	10.7±7.5	11.8±7.7	1.1	0.8 to 2.2	0.03
Change from base-line score§	3.2±7.0	4.2±7.4	1.0	0.1 to 2.0	0.04
No. of organs failing — no. (%)					
0	100 (23.9)	82 (19.5)			
1	136 (32.5)	149 (35.5)			
2	109 (26.1)	108 (26.0)			
3	51 (12.2)	63 (15.0)			
>3	22 (5.3)	18 (4.3)	1.8¶	−3.4 to 7.1¶	0.53¶
Length of stay — days					
ICU	11.0±10.7	11.5±11.3	0.5	−1.0 to 2.1	0.53
Hospital	34.8±19.5	35.5±19.4	0.7	−1.9 to 3.4	0.58



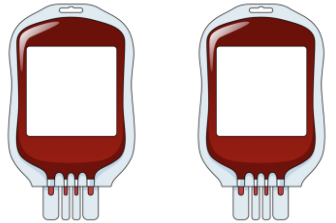


Transfusion strategies in non-bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine

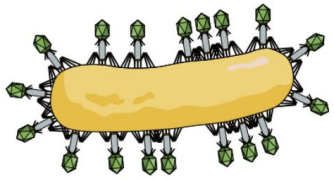




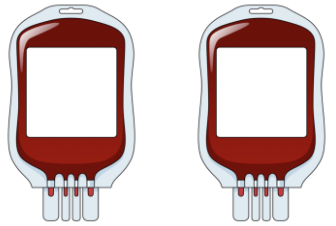
ICU



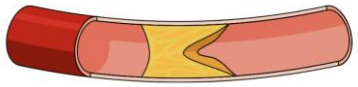
Hb < 7 g/dL



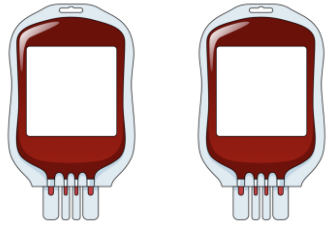
SEPSIS



Hb < 7 g/dL



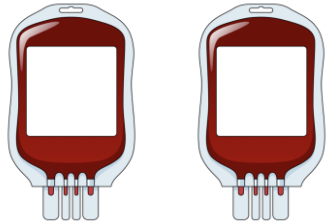
MAJOR SURGERY



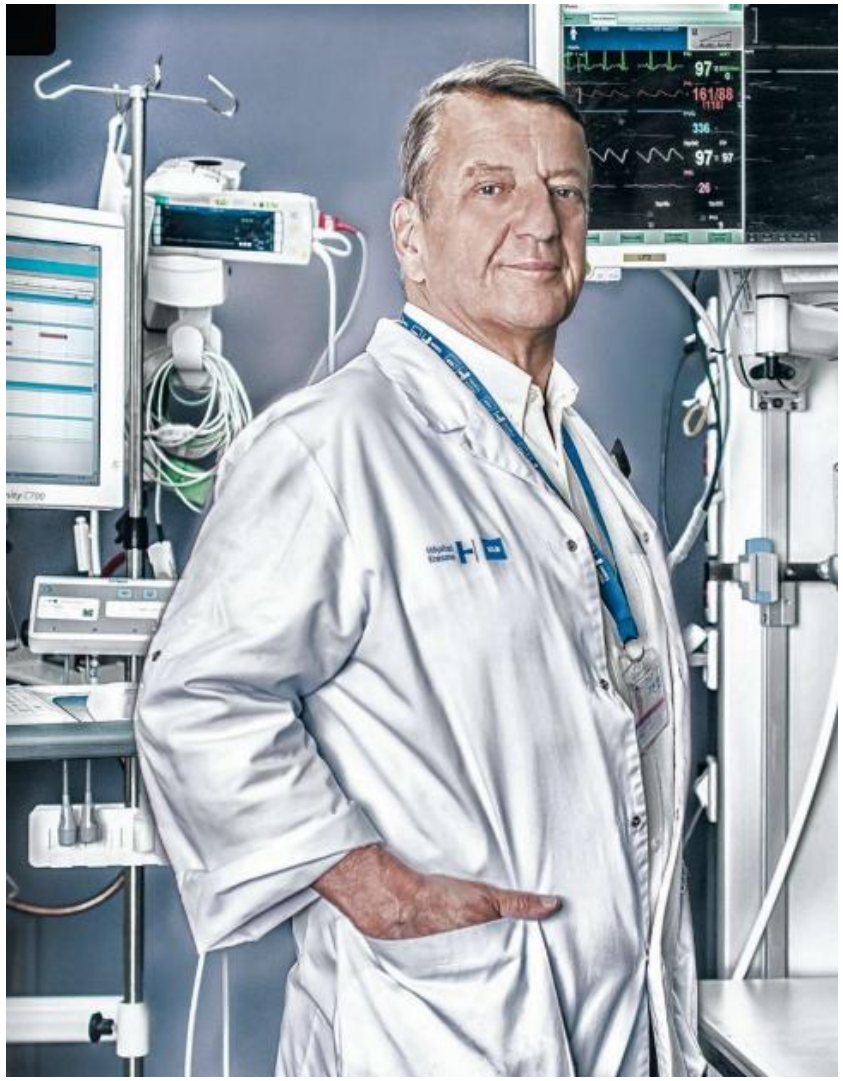
Hb < 7.5 g/dL



WEANING FROM MV



Hb < 7 g/dL

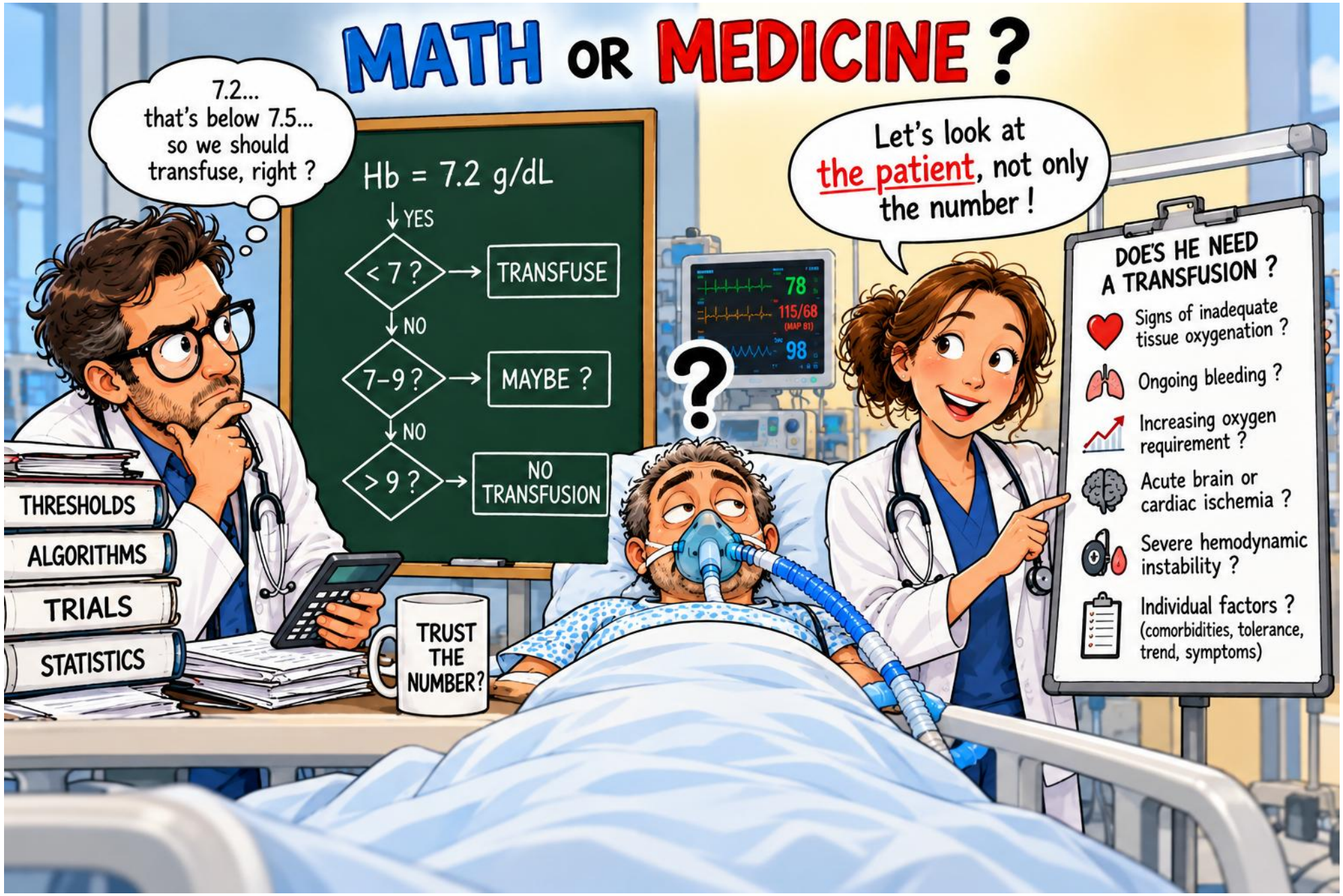


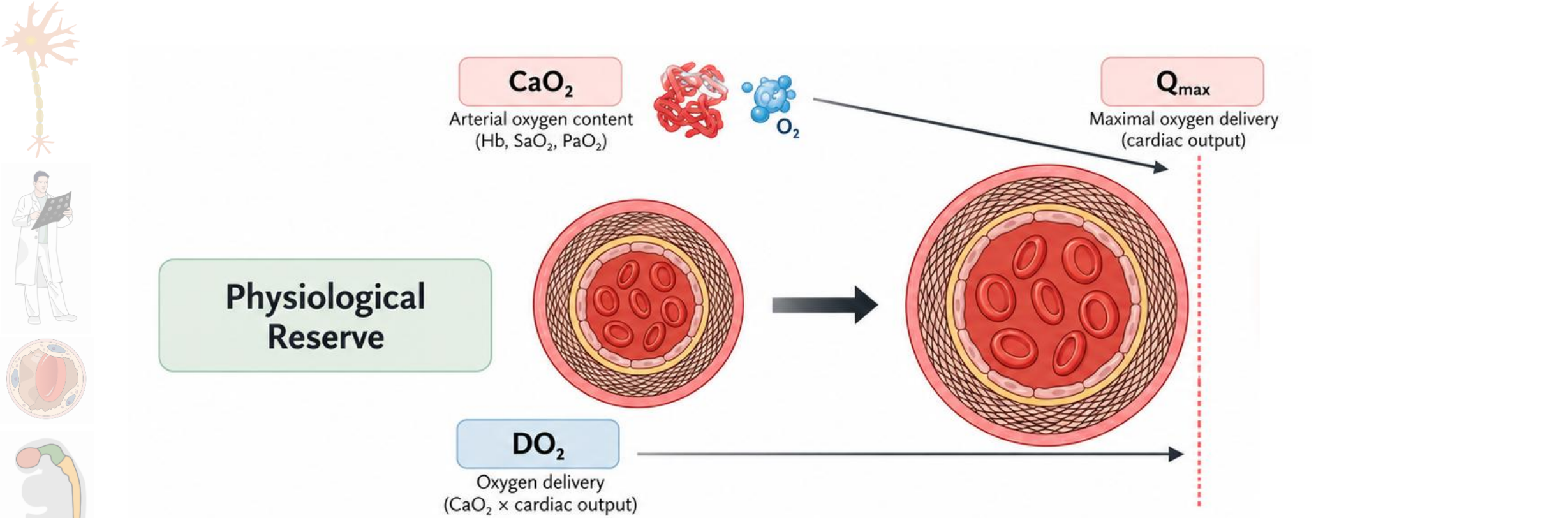
Pr. Jean-Louis VINCENT

"… This is everything but **personalized medicine** !

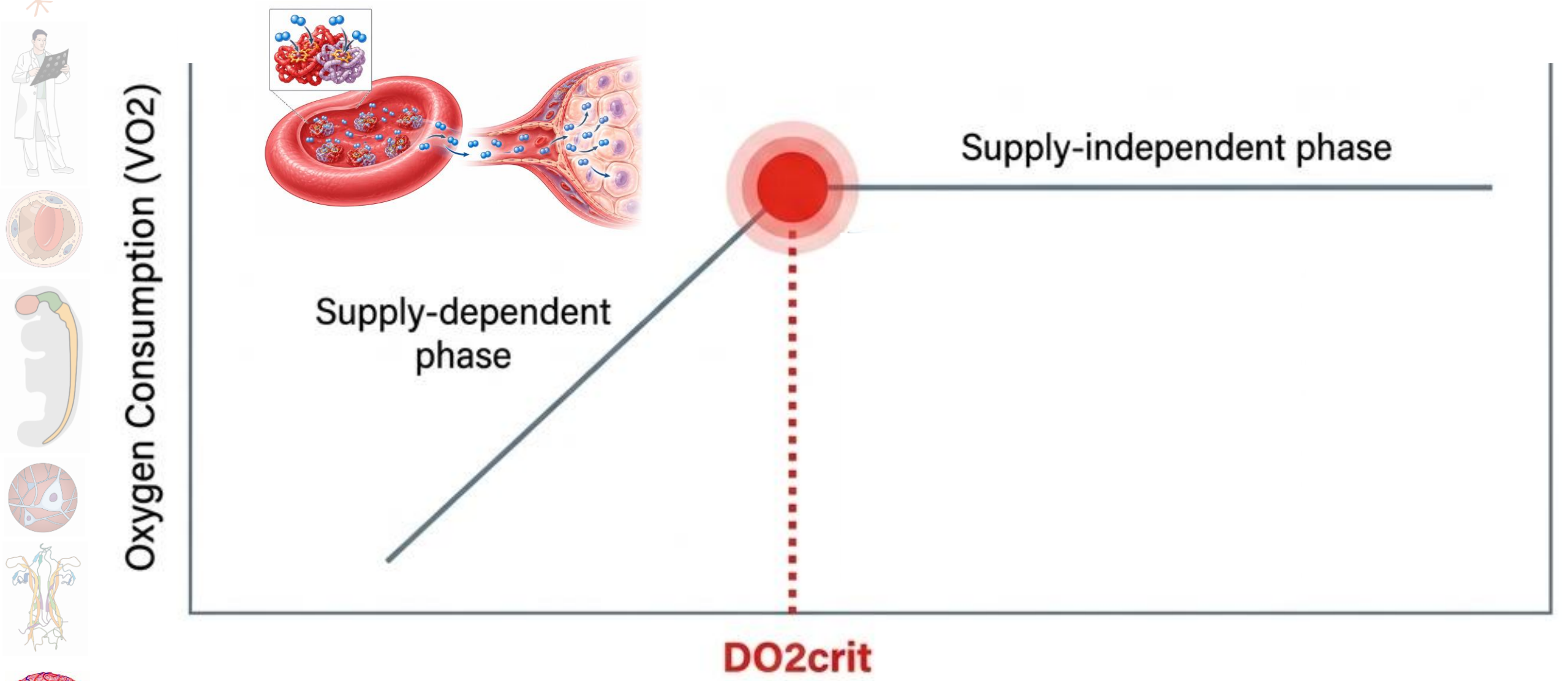
Data from large databases have indicated that liberal blood transfusion strategies in critically ill patients may be associated with improved outcomes.

The RCT gurus will say that even the best propensity analysis cannot take all factors into account, but I will counter that RCTs based on Hb concentrations cannot take into account all the factors that can and should influence the medical decision to transfuse"


MATH OR MEDICINE ?
7.2... that's below 7.5... so we should transfuse, right ?
Hb = 7.2 g/dL
YES
< 7 ?
TRANSFUSE
NO
7-9 ?
MAYBE ?
NO
> 9 ?
NO TRANSFUSION
THRESHOLDS
ALGORITHMS
TRIALS
STATISTICS
TRUST THE NUMBER?
Let's look at the patient, not only the number !
78
115/68
(MAP 81)
98
DOE'S HE NEED A TRANSFUSION ?
Signs of inadequate tissue oxygenation ?
Ongoing bleeding ?
Increasing oxygen requirement ?
Acute brain or cardiac ischemia ?
Severe hemodynamic instability ?
Individual factors ? (comorbidities, tolerance, trend, symptoms)


CaO_2
Arterial oxygen content
(Hb, SaO_2, PaO_2)
O_2
Q_{max}
Maximal oxygen delivery
(cardiac output)
Physiological Reserve
DO_2
Oxygen delivery
(CaO_2 × cardiac output)

CAN WE INDIVIDUALIZE RBCT ?



RESEARCH Open Access



Using arterial-venous oxygen difference to guide red blood cell transfusion strategy

Alberto Fogagnolo[1†], Fabio Silvio Taccone[2†], Jean Louis Vincent[2], Giulia Benetto[1], Elaine Cavalcante[2], Elisabetta Marangoni[1], Riccardo Ragazzi[1], Jacques Creteur[2], Carlo Alberto Volta[1] and Savino Spadaro[1*]

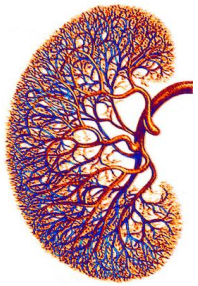


n=177

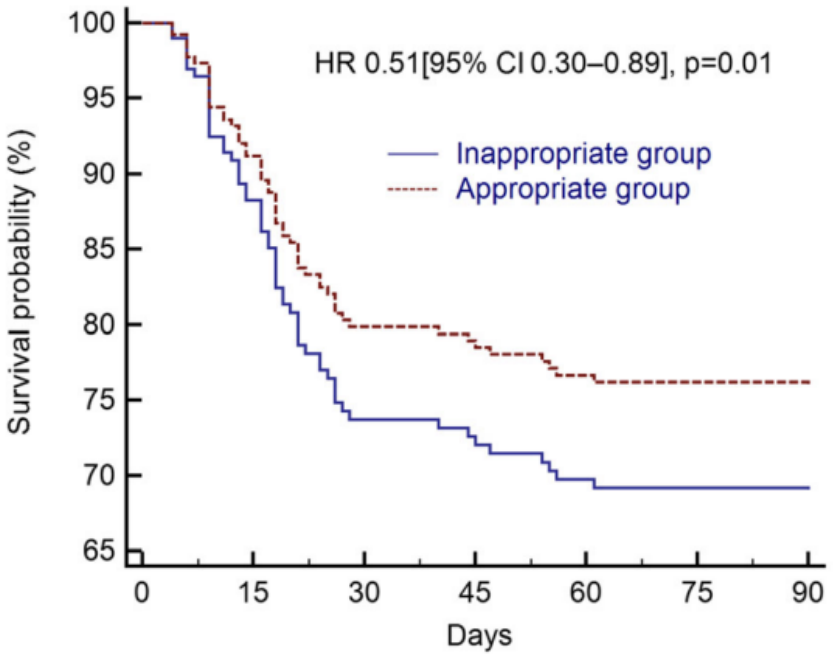
$$CaO_2 = SaO_2 \times Hb \times 1.39 + (PaO_2 \times 0.0031)$$

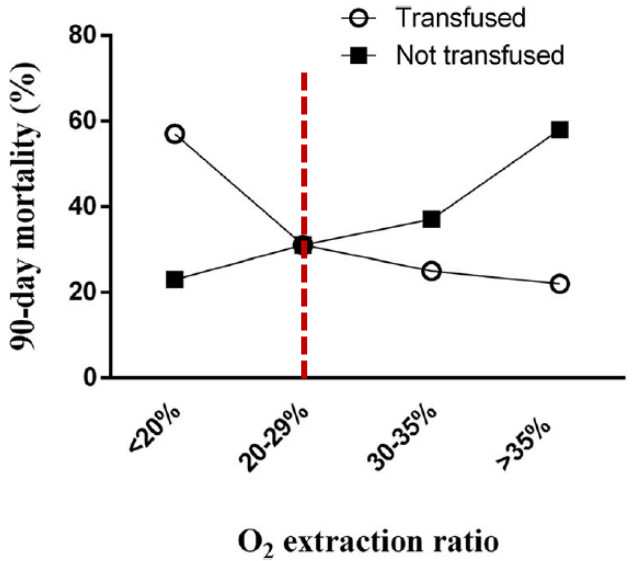
and

$$CcvO_2 = ScvO_2 \times Hb \times 1.39 + (PcvO_2 \times 0.0031).$$



AKI
26% vs. 13%





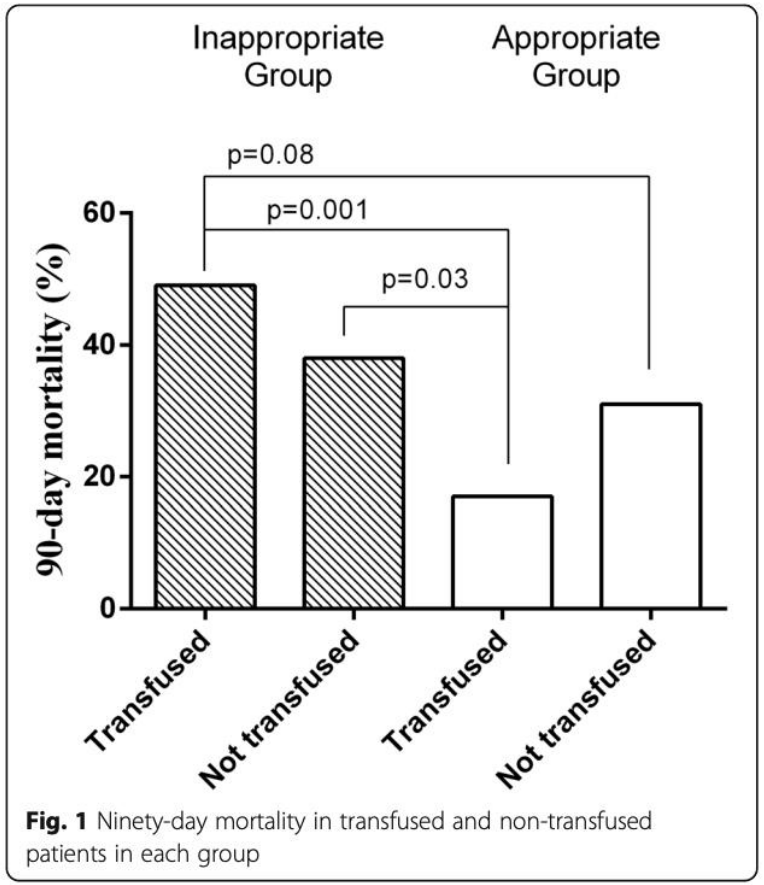


Fig. 1 Ninety-day mortality in transfused and non-transfused patients in each group

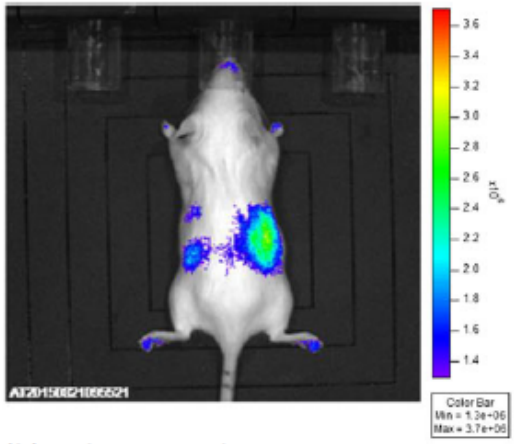
Anemia-Induced Renal Hypoxia as a Potential Mechanism for Acute Kidney Injury (AKI)

Hare, 2020

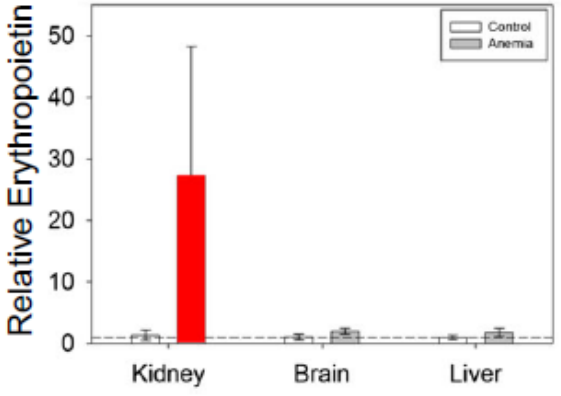
Moderate Anemia (Hb ~90g/L) is Associated with Renal Hypoxia in Mice

(a) *HIF-Luciferase Radiance in Model of Moderate Anemia*

A



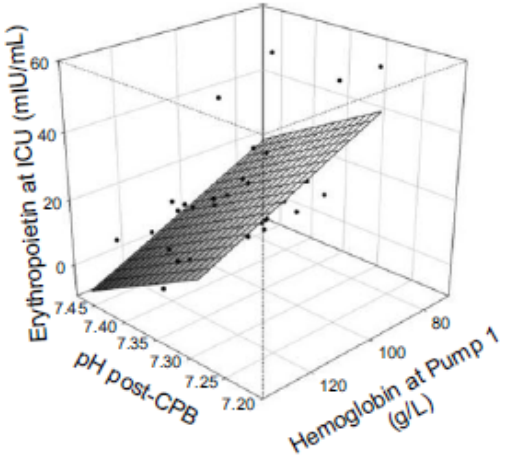
(b) *Relative Erythropoietin mRNA Measured by RT-PCR in Different Organs in a Model of Moderate Anemia*



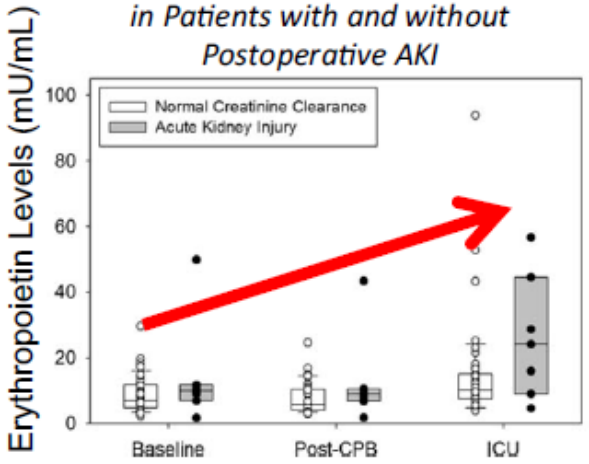
Evidence of Renal Hypoxia and AKI in Anemic Patients on Cardiopulmonary Bypass

(c) *Relationship Between Erythropoietin in the ICU, Arterial pH Post-CPB and Hemoglobin 15 min After Start of CPB*

B

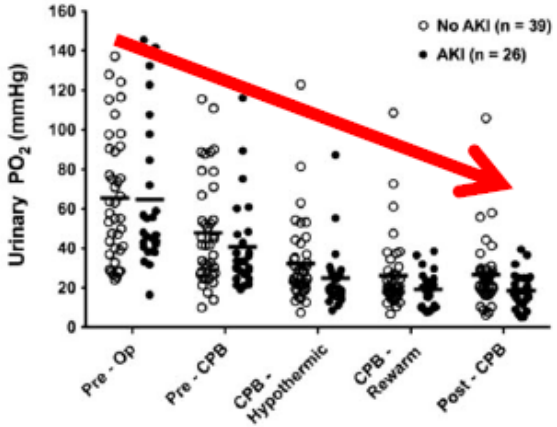


(d) *Comparison of Erythropoietin Levels in Patients with and without Postoperative AKI*

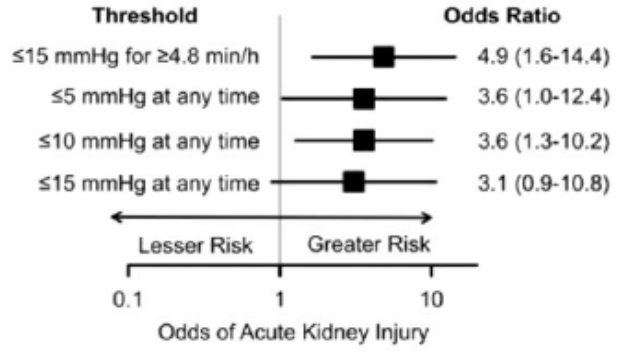


(e) Comparison of *Urinary Oxygen Tension During CPB in Patient Presenting with and without Postoperative AKI*

C

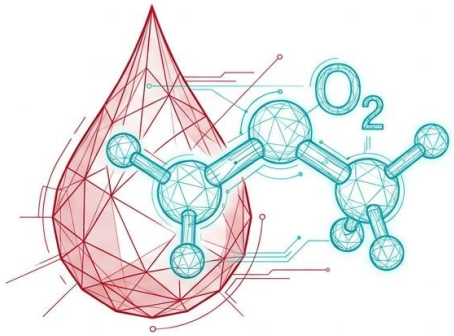


(f) *Association Between Urinary Hypoxia and Risk of AKI (95% Confidence Interval)*



BMJ Open

Oxygen extraction–guided transfusion strategy in critically ill patients: study protocol for a randomised, open-labelled, controlled trial



OXYTRIP

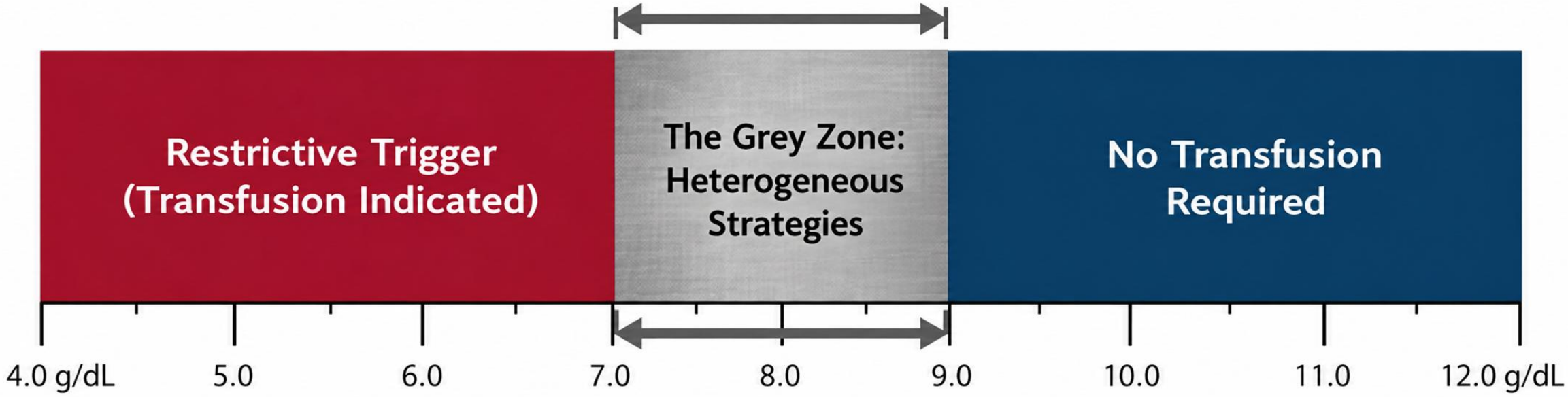
Alberto Fogagnolo ,[1] Danila Azzolina,[2] Fabio Silvio Taccone,[3] Emma Pedarzani,[2,4] Gianluca Pasa,[5] Daniele Marianello,[5] Giorgia Valpiani,[2] Chiara Marchesini,[6] Filippo Annoni,[3] Anthony Moureau,[3] Carlo Alberto Volta,[1] Federico Franchi,[5] Savino Spadaro [6,7]

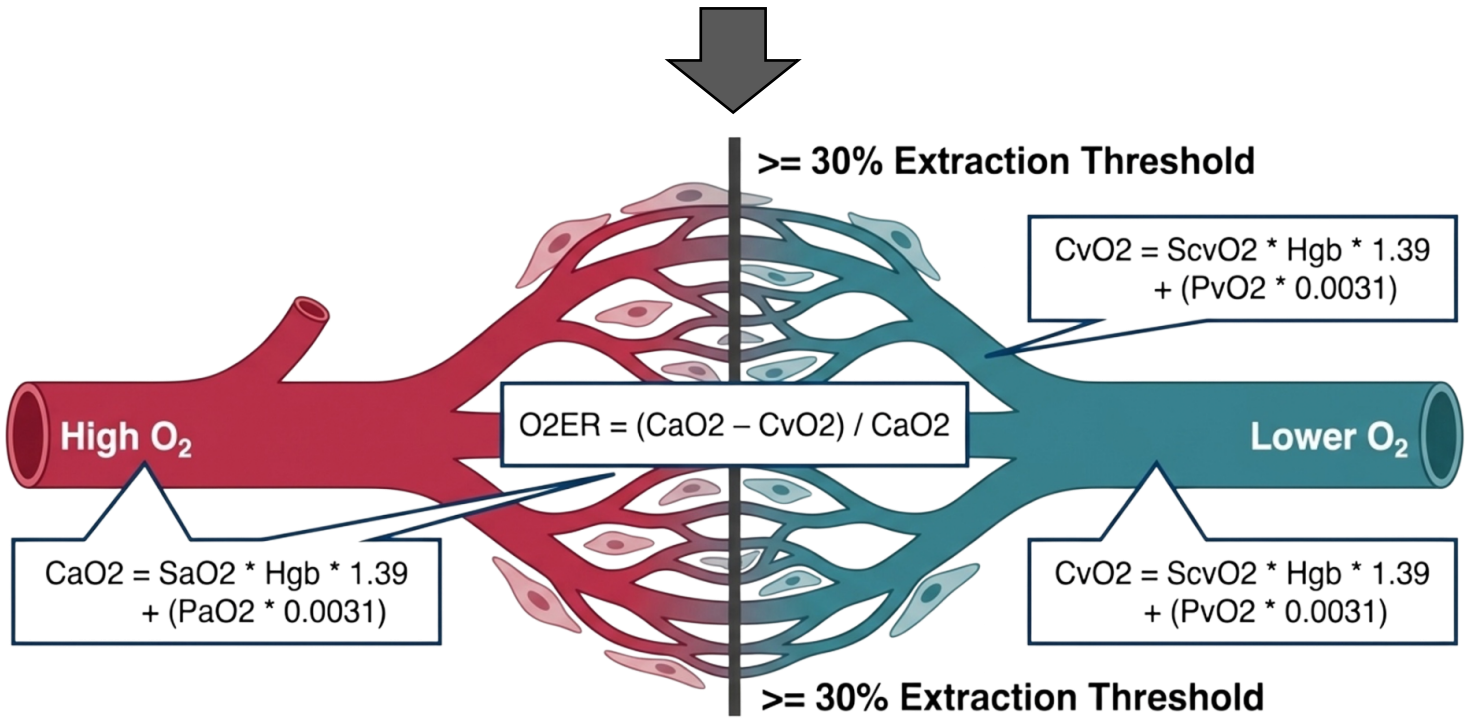
Alberto FOGAGNOLO



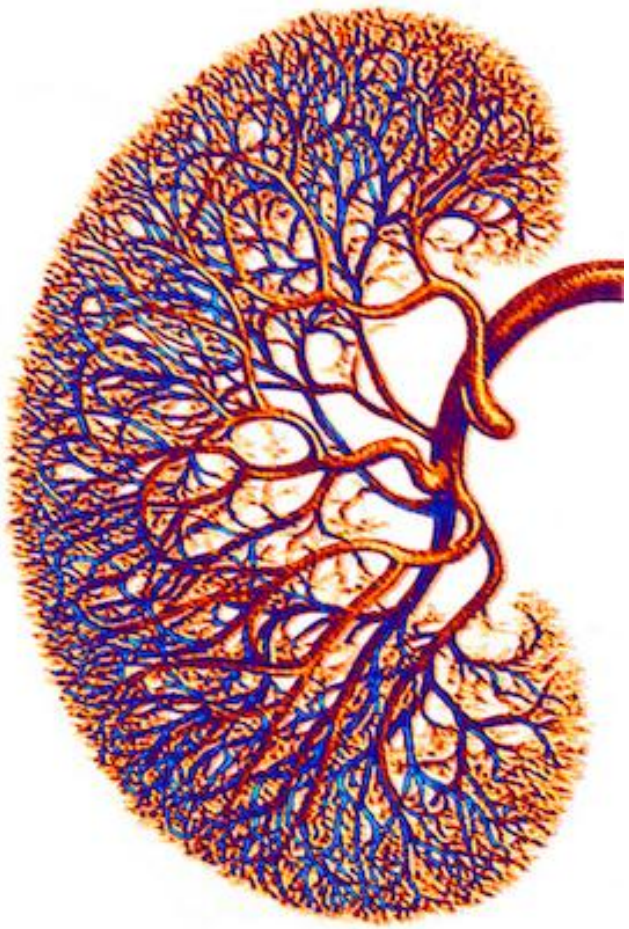


Savino SPADARO


Restrictive Trigger
(Transfusion Indicated)
The Grey Zone:
Heterogeneous
Strategies
No Transfusion
Required
4.0 g/dL
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0 g/dL


>= 30% Extraction Threshold
CvO2 = ScvO2 * Hgb * 1.39
+ (PvO2 * 0.0031)
High O_2
O2ER = (CaO2 – CvO2) / CaO2
Lower O_2
CaO2 = SaO2 * Hgb * 1.39
+ (PaO2 * 0.0031)
CvO2 = ScvO2 * Hgb * 1.39
+ (PvO2 * 0.0031)
>= 30% Extraction Threshold

STUDY HYPOTHESES



1. Primary Hypothesis

O2ER-guided Red Blood Cell Transfusion (RBCT) reduces the occurrence of **Acute Kidney Injury (AKI)** in non-bleeding ICU patients.

2. Secondary Hypothesis

This individualized strategy will favorably impact overall 90-day mortality.

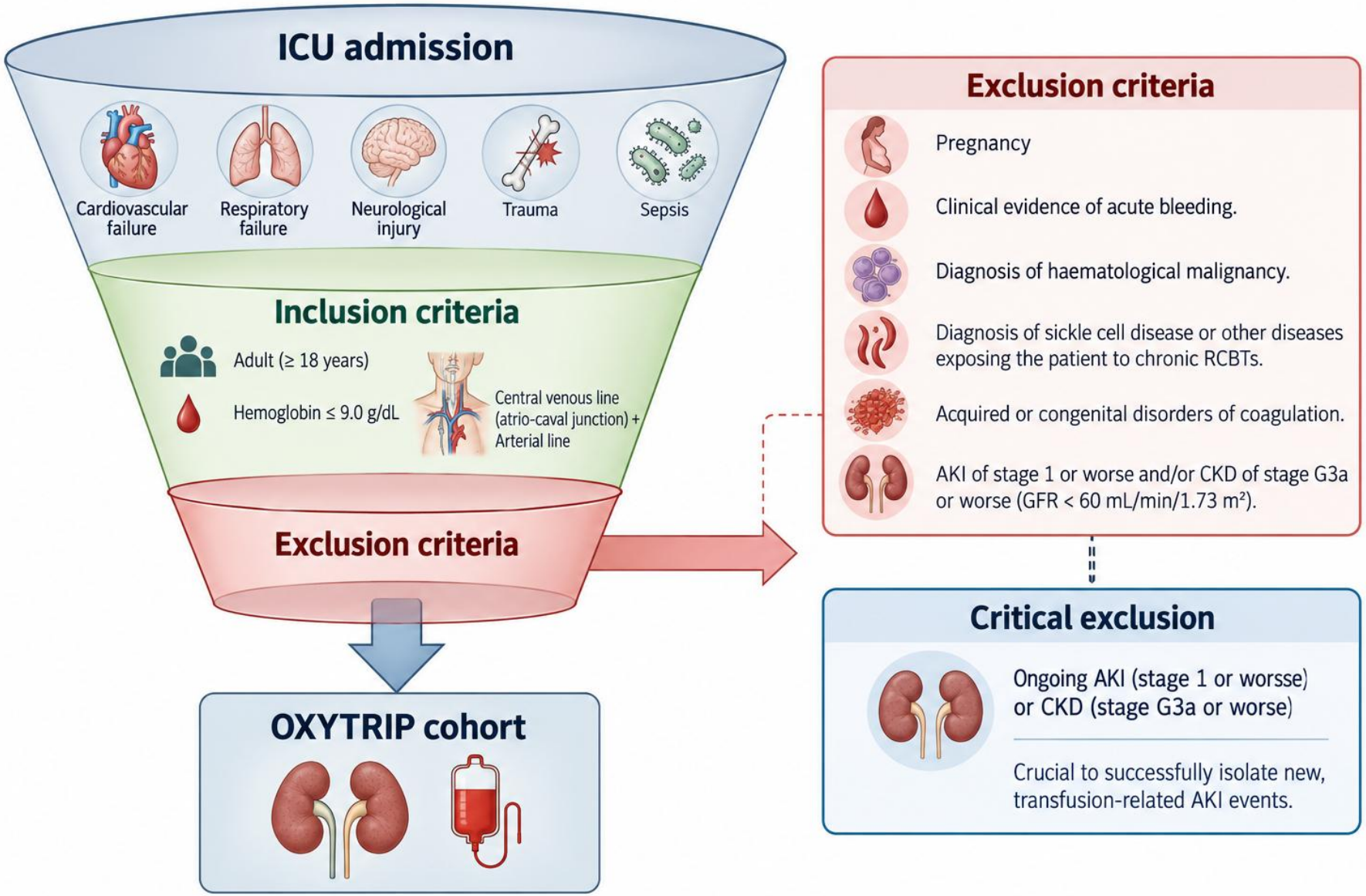
STUDY DESIGN



Design

Randomised, open-labelled, controlled superiority trial (1:1 allocation).

PATIENTS SELECTION



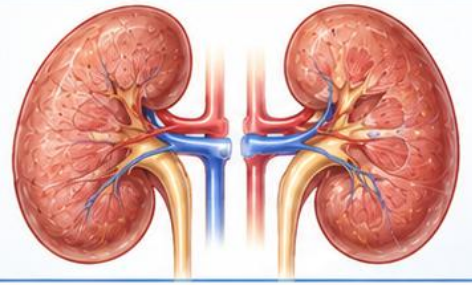
STUDY INTERVENTIONS

	Control Group (Standard ESICM)
The Trigger Rule	Transfusion restricted to Hb < 7.0 g/d (regardless of O2ER). Exceptions allowed for ACS/Surgery
The Safety Net	Standard clinical judgment.
Monitoring	Daily assessment of Hb and O2ER.

STUDY OUTCOMES

Primary outcome

Incidence of AKI
at **7 days**



Statistical Design & Power Validation

13%

Absolute Risk Reduction

Powered to detect a drop in AKI from 26% (control) to 13% (intervention).

80%

Power (alpha = 0.05)

Two-sided superiority Z test without continuity correction.

324

Total Patients

162 patients allocated per arm.

Interim Analysis

Planned at exactly 50% enrollment (162 patients) utilizing an O'Brien-Fleming boundary for early efficacy stopping.

Rigorous multi-tiered analysis plan

Oversight & Modeling

Logistic regression for binary endpoints. Linear mixed-effects models for longitudinal data.
Continuous review by an independent Data Safety Monitoring Board (DSMB).



Intent-To-Treat (ITT)

Assesses real-world treatment efficacy including protocol deviations.



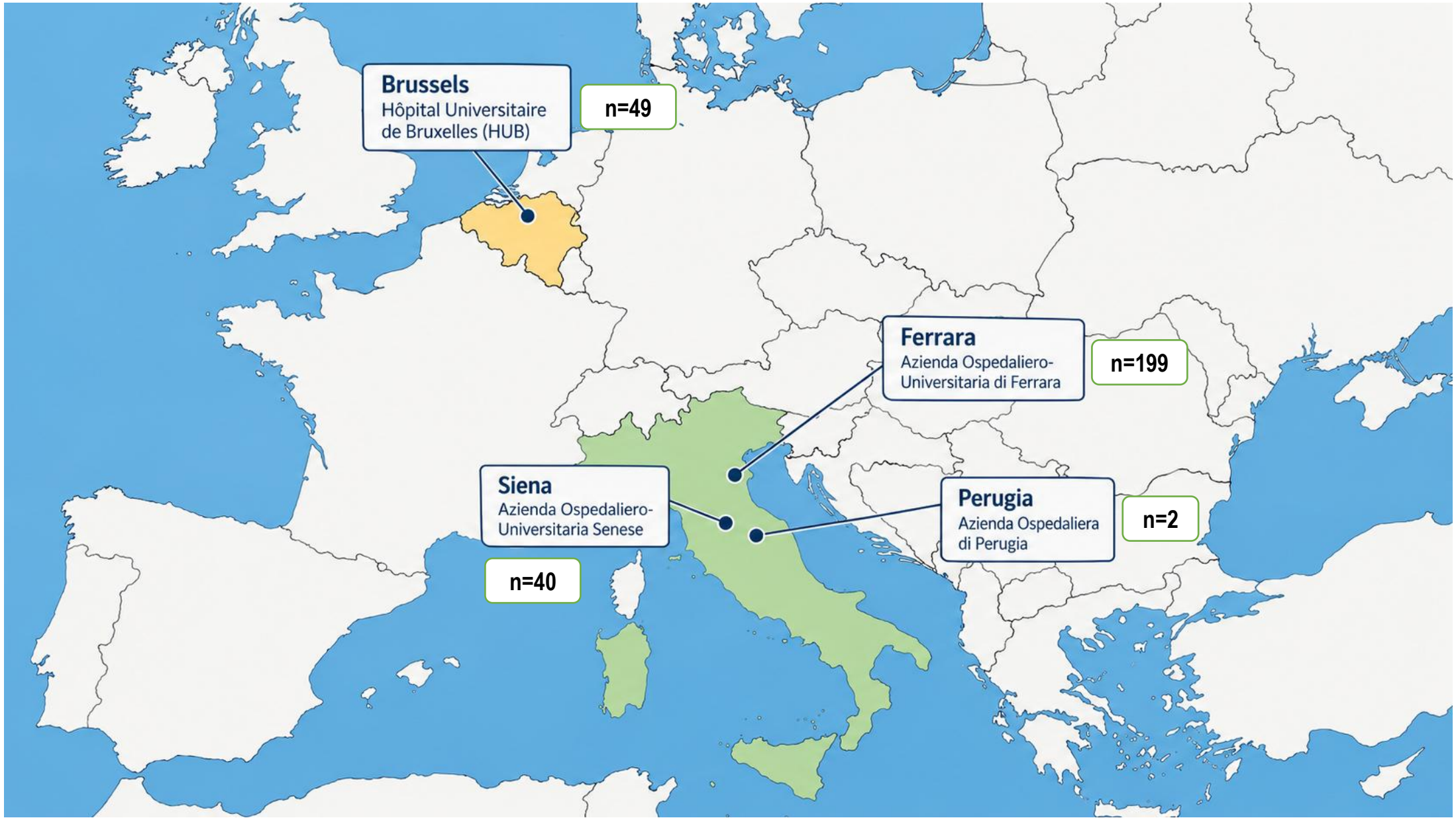
Per-Protocol

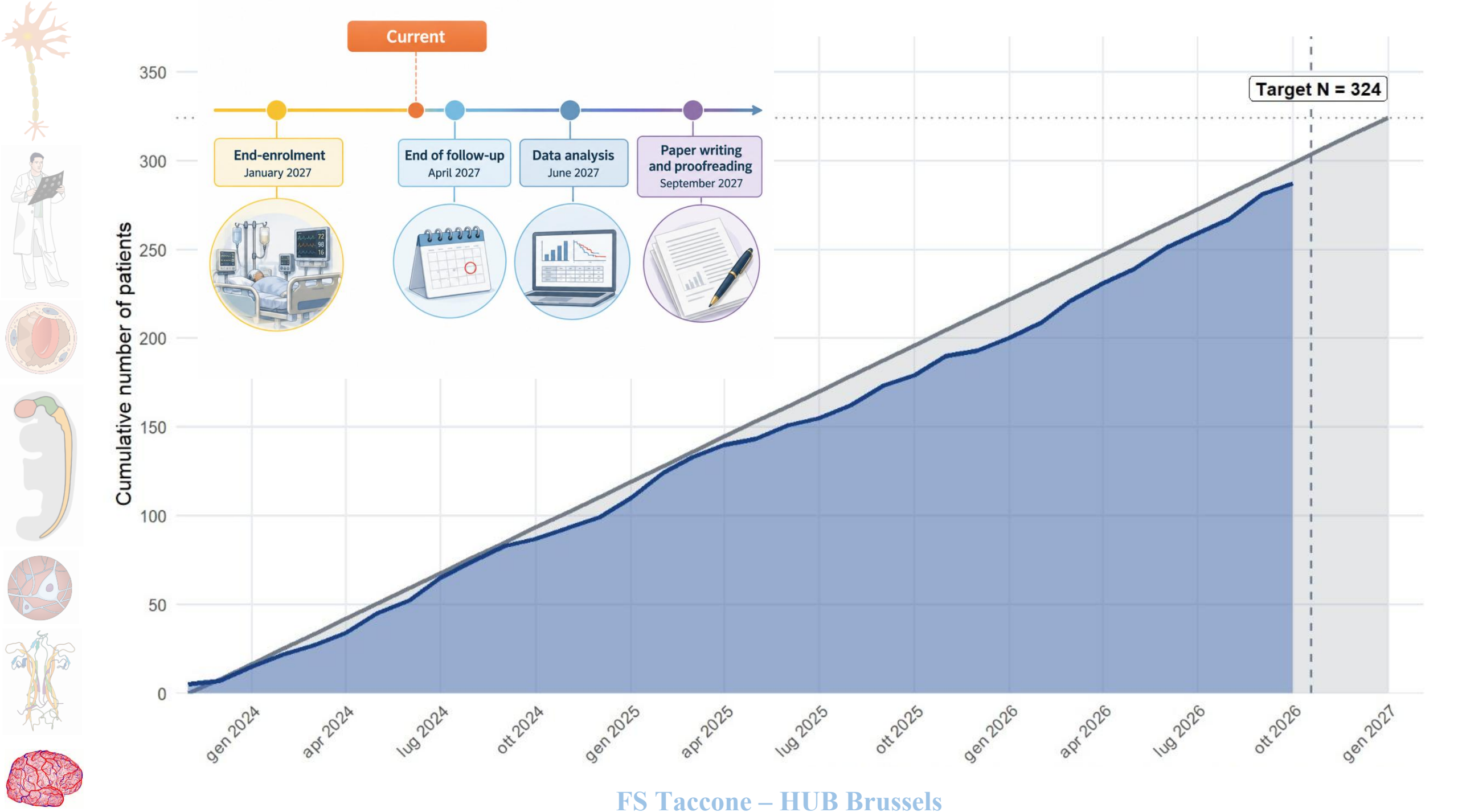
Assesses efficacy under ideal conditions, excluding major deviations.



Safety

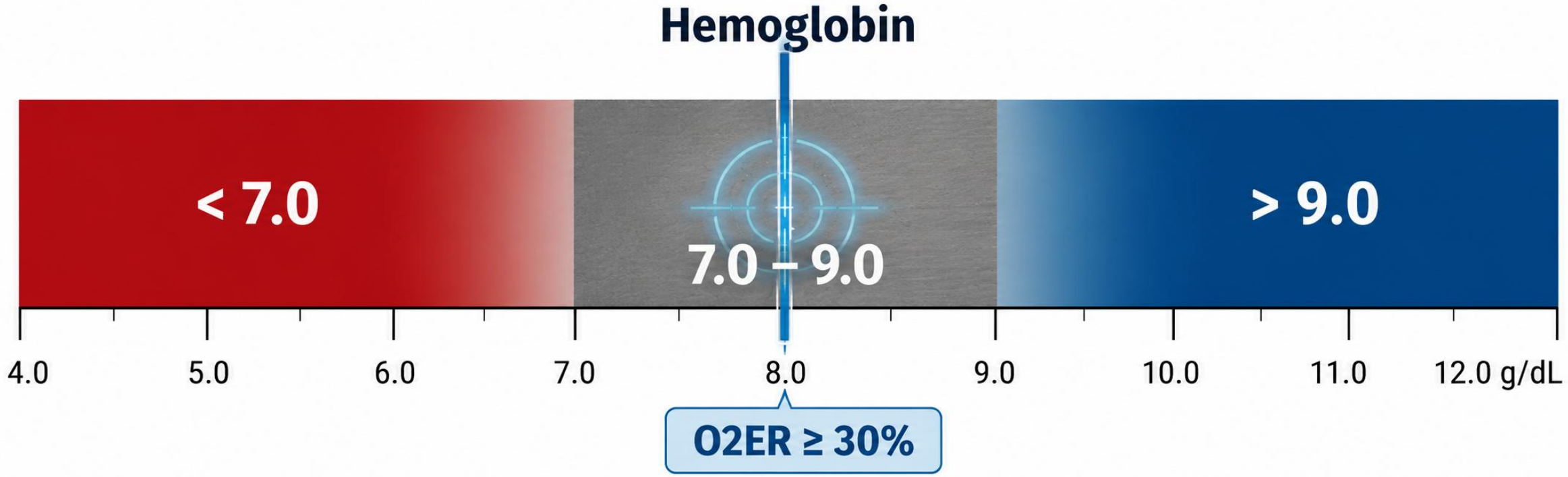
Adverse event monitoring for any patient receiving ≥ 1 day of protocol treatment.


Brussels
Hôpital Universitaire de Bruxelles (HUB)
n=49
Ferrara
Azienda Ospedaliero-Universitaria di Ferrara
n=199
Siena
Azienda Ospedaliero-Universitaria Senese
n=40
Perugia
Azienda Ospedaliera di Perugia
n=2


Current
End-enrolment
January 2027
End of follow-up
April 2027
Data analysis
June 2027
Paper writing
and proofreading
September 2027
Target N = 324
Cumulative number of patients
0
50
100
150
200
250
300
350
gen 2024
apr 2024
lug 2024
ott 2024
gen 2025
apr 2025
lug 2025
ott 2025
gen 2026
apr 2026
lug 2026
ott 2026
gen 2027

CONCLUSIONS

OXYTRIP



Thanks







ISICEM