ICC-PBM 2018

Recommendations pour les seuils transfusionnels (partie 2)

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Aucun conflit d'intérêt

PICO questions

- ***Intervention :*** **more restrictive RBC transfusion triggers**
- ***Comparison :*** **more liberal RBC transfusion triggers**

- ***Population 1/2 :*** **Stable critically ill intensive care adults & Adults with septic shock**

- ***Population 3 :*** **Adults with orthopaedic surgery**

- ***Population 4 :*** **Adults with coronary heart disease**

- ***Population 5 :*** **Adults with cardiac surgery**

- ***Population 6/7 :*** **Adults with acute gastrointestinal bleeding**

- ***Outcomes :*** **mortality, morbidity-related outcomes that occured during hospitalisation, RBC utilization**

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Acute interventions & intensive care

Critically ill stable patients
Septic shock patients

Studies' characteristics

Author, year, country	Study design	Population	Restrictive RBC transfusion trigger	Liberal RBC transfusion trigger
Bergamin, 2017, Brazil	RCT	**300** cancer adults with septic shock, **1 site**	**Hb <7 g/dL**	**Hb <9 g/dL**
Palmieri, 2017, USA	RCT	**345** burned adults, ≥20% total body surface area burn, **18 sites**	**Hb <7 g/dL** target Hb 7.0-8.0 g/dL	**Hb <10 g/dL** target Hb 10.0-11.0 g/dl
Holst, 2014, Denmark	RCT	**998** patients with septic shock in the ICU, **32 sites**	**Hb ≤7 g/dL**	**Hb ≤9 g/dL**
Walsh, 2013, UK	RCT	**100** ICU patients, ≥55 years, mechanical ventilation for ≥ 96 hours, and expected to require ≥ 24 hours of further MV, **6 sites**	**Hb <7 g/dL** target Hb 7.1-9.0 g/dL	**Hb <9 g/dL** target Hb 9.1-11.0 g/dL
Hébert, 1999, Canada	RCT	**838** euvolaemic critically ill participants, **25 sites**	**Hb <7 g/dL** target Hb 7.0-9.0 g/dL	**Hb <10 g/dL** target Hb 10.0-12.0 g/dL
Hébert, 1995, Canada	RCT	**69** euvolaemic critically ill participants, **5 sites**	**7.0<Hb<7.5 g/dL** target Hb 7.0-9.0 g/dL	**10.0<Hb<10.5 g/dL** target Hb 10.0-12.0 g/dL

OUTCOMES

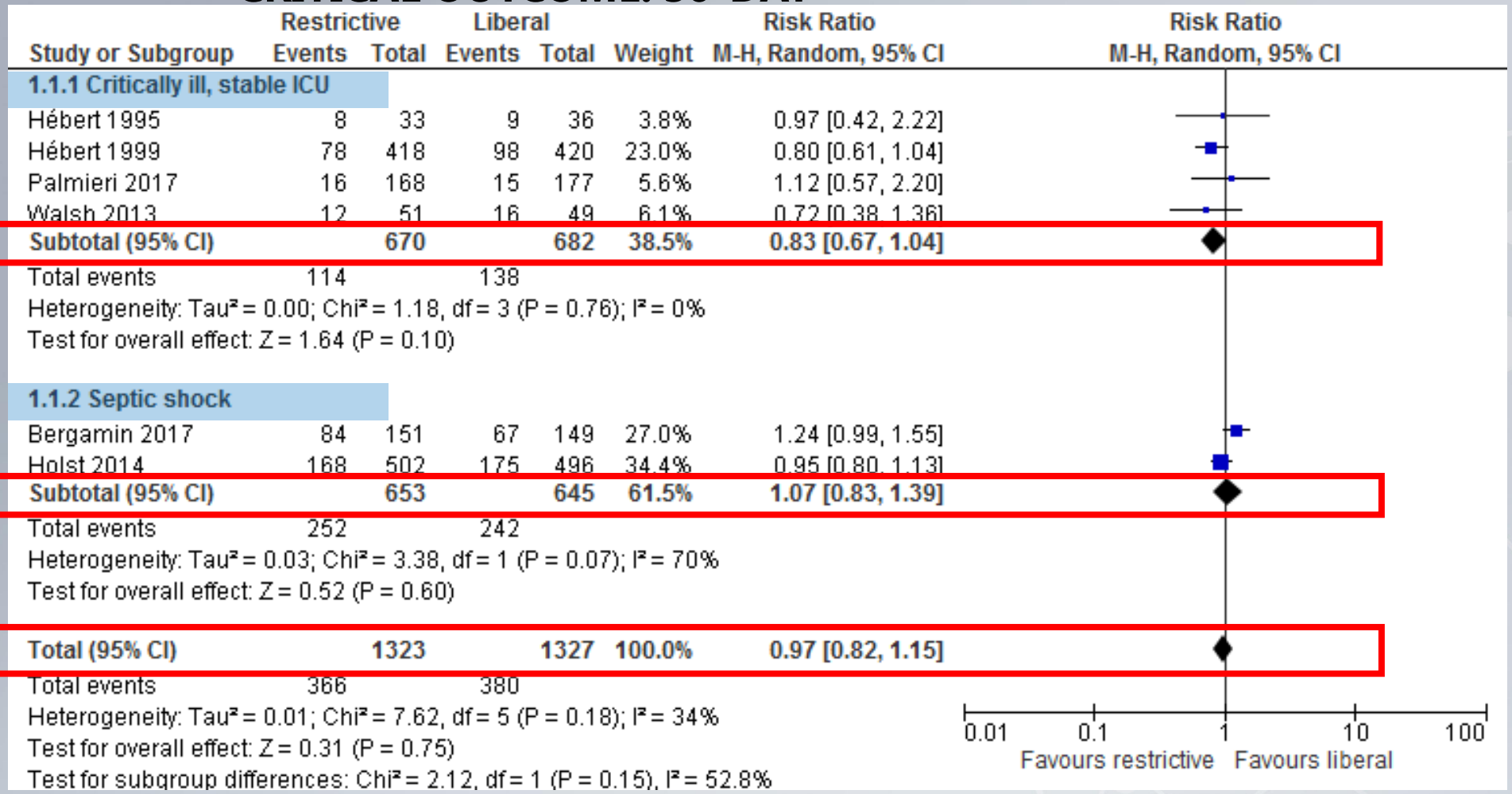
Critical outcomes
Hospital mortality
30-day mortality
60-day mortality
90-day mortality
Cardiac events
Myocardial infarction
CVA stroke
Renal failure

Important outcomes
Exposure to RBC transfusion Volume of RBC transfused Hb concentration
Infections (BSI, UTI, wound infection, pneumonia)
Rebleeding
SF-36: physical component summary score
SF-36: mental component summary score
Congestive heart failure
EQ-5D

Acute intervention & intensive care

Critically ill, stable ICU + septic shock

CRITICAL OUTCOME: 30-DAY



Study or Subgroup	Restrictive Events	Total	Liberal Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Critically ill, stable ICU						
Hébert 1995	8	33	9	36	3.8%	0.97 [0.42, 2.22]
Hébert 1999	78	418	98	420	23.0%	0.80 [0.61, 1.04]
Palmieri 2017	16	168	15	177	5.6%	1.12 [0.57, 2.20]
Walsh 2013	12	51	16	49	6.1%	0.72 [0.38, 1.36]
Subtotal (95% CI)		**670**		**682**	**38.5%**	**0.83 [0.67, 1.04]**
Total events	114		138			
Heterogeneity: Tau² = 0.00; Chi² = 1.18, df = 3 (P = 0.76); I² = 0%						
Test for overall effect: Z = 1.64 (P = 0.10)						
1.1.2 Septic shock						
Bergamin 2017	84	151	67	149	27.0%	1.24 [0.99, 1.55]
Holst 2014	168	502	175	496	34.4%	0.95 [0.80, 1.13]
Subtotal (95% CI)		**653**		**645**	**61.5%**	**1.07 [0.83, 1.39]**
Total events	252		242			
Heterogeneity: Tau² = 0.03; Chi² = 3.38, df = 1 (P = 0.07); I² = 70%						
Test for overall effect: Z = 0.52 (P = 0.60)						
Total (95% CI)		**1323**		**1327**	**100.0%**	**0.97 [0.82, 1.15]**
Total events	366		380			
Heterogeneity: Tau² = 0.01; Chi² = 7.62, df = 5 (P = 0.18); I² = 34%						
Test for overall effect: Z = 0.31 (P = 0.75)						
Test for subgroup differences: Chi² = 2.12, df = 1 (P = 0.15), I² = 52.8%						

Certainty of the evidence (GRADE)

⊕⊕⊕◯ MODERATE[a]

‘Acute intervention & intensive care’

Critically ill, stable ICU + septic shock

CRITICAL OUTCOME: 30-DAY MORTALITY in subgroup

Subgroups	Difference (restrictive (< 7-8 g/dL) versus liberal (<9-10 g/dL) RBC transfusion triggers	Relative effect (95% CI)
Less severe patients (APACHE-II score ≤20) N = 434, 1 study	**74 fewer per 1.000** (110 fewer to 13 fewer)	**RR 0.54** (0.32 to 0.92)
Younger patients (<55 years) N = 334 , 1 study	**73 fewer per 1.000** (102 fewer to 12 fewer)	**RR 0.44** (0.22 to 0.91)
Patients with cardiac disease N= 326, 1 study	**23 fewer per 1.000** (94 fewer to 82 more)	**RR 0.90** (0.59 to 1.36)

Certainty of the evidence (GRADE)
⨁⨁◯◯ LOW[b,c]

Acute intervention & intensive care

Critically ill, stable ICU

IMPORTANT OUTCOMES

Desirable effects of the restrictive transfusion strategy?

Outcomes	Absolute effect Difference (restrictive *versus* liberal (<9-10 g/dL) RBC transfusion strategies)	Relative effect (95% CI)
Participants exposed to blood transfusion	**302 fewer per 1.000** (349 fewer to 264 fewer)	**RR 0.68** (0.63 to 0.72)
Units of blood transfused	Mean difference **3 units lower** (3.64 lower to 2.36 lower)	-
Haemoglobin concentration	Mean difference **1.66 g/dL lower** (2.15 lower to 1.16 lower)	-
Number of RBC transfusions	**Median 8 RBC transfusions lower** (0 to 0)	-
Congestive heart failure	**55 fewer per 1.000** (75 fewer to 21 fewer)	**RR 0.49** (0.30 to 0.80)
Sepsis-bacteraemia	**24 fewer per 1.000** (50 fewer to 18 more)	**RR 0.75** (0.48 to 1.19)
Pneumonia or wound infection	**19 fewer per 1.000** (51 fewer to 29 more)	**RR 0.84** (0.57 to 1.24)

Acute intervention & intensive care

Critically ill, stable ICU

IMPORTANT OUTCOMES

Undesirable effects of the restrictive transfusion strategy?

Outcomes	Absolute effect Difference (restrictive *versus* liberal RBC transfusion strategies)	Relative effect (95% CI)
Pneumonia	**7 more per 1.000** (36 fewer to 61 more)	**RR 1.03** (0.84 to 1.27)
Blood stream infections	**0 fewer per 1.000** (74 fewer to 109 more)	**RR 1.00** (0.69 to 1.46)
Wound infections	**0 fewer per 1.000** (52 fewer to 93 more)	**RR 1.00** (0.56 to 1.78)
Urinary tract infection	**7 more per 1.000** (52 fewer to 106 more)	**RR 1.05** (0.62 to 1.78)

Acute intervention & intensive care

Septic shock

IMPORTANT OUTCOMES

Desirable effects?

Outcomes	Absolute effect Difference restrictive (<7 g/dL) versus liberal (<9 g/dL) RBC transfusion triggers	Relative effect (95% CI)
Patients exposed to RBC transfusion	**306 fewer per 1.000** (342 fewer to 270 fewer)	**RR 0.66** (0.62 to 0.70)
Haemoglobin concentration	MD **1.7 lower** (1.82 lower to 1.58 lower)	-
1-year mortality	**11 fewer per 1.000** (71 fewer to 55 more)	**RR 0.98** (0.87 to 1.10)
Mortality at the time of longest follow-up	**43 fewer per 1.000** (98 fewer to 18 more)	**RR 0.93** (0.84 to 1.03)
Danish short form health survey questionnaire (SF-36): physical component summary score	MD **0.4 points higher** (4.05 lower to 4.85 higher)	-
Danish short form health survey questionnaire (SF-36): mental component summary score	MD **0.5 points higher** (5.26 lower to 6.26 higher)	-

Undesirable effects? NONE

Critically ill and Septic Shock

Strong recommendation (Y/N)

- The ICC-PBM guideline panel recommends a transfusion trigger of 7 g/dL for treatment of anaemia in critically ill patients who are not actively bleeding. *(strong recommendation, moderate certainty)*
- This recommendation may not apply to patients with acute coronary syndromes and CNS injury/cerebral perfusion disorders.
- The ICC-PBM guideline panel suggests further research in these areas.

Justification: No evidence of increased mortality or other undesirable effects, and substantial reduction in red cell exposure and utilisation.

Notes:

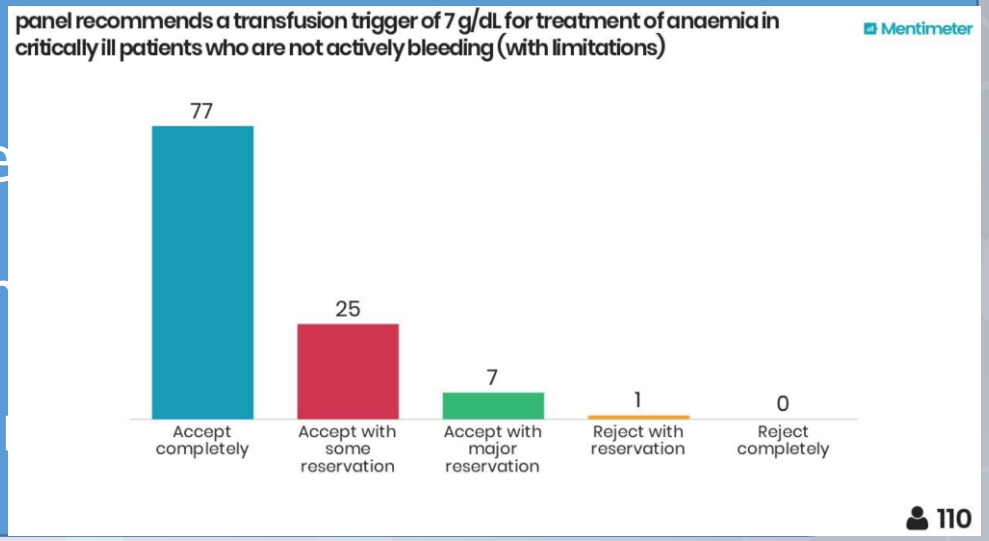
- Critical care population highly heterogeneous (reason for qualification)
- Includes septic shock (originally separate PICO question 8)
- Hb 7g/dL trigger represents the value used in the included trials
- Panel had extensive discussion on whether the “may not apply” should include patients with a history of coronary artery disease/other cardiovascular disease

Critically ill and Septic Shock

L'ICC-PBM recommande un seuil transfusionnel restrictif 7g/dL (recommandation forte, niveau de preuve modéré)

Mais :

- Population hétérogène
- Ce seuil ne s'applique peut-être pas à ce patients dont SCA, pathologies CV chron
- Besoin de recherche pour ces populatio



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Cardiac surgery

Should more restrictive RBC transfusion triggers ***(Intervention)*** versus more liberal RBC transfusion triggers ***(Comparison)*** be used in adult patients undergoing cardiac surgery? ***(Population 5)***

Study characteristics

Cardiac surgery : 8 studies

Author, year, country	Study design	Population	Restrictive RBC transfusion trigger	Liberal RBC transfusion trigger
Koch, 2017, USA	RCT	**717** adults undergoing CABG surgery or valve procedures	Haematocrit <24% (Hb <8 g/dL)	Haematocrit <28% (Hb <9.3 g/dL)
Laine, 2017, Finland	RCT	**80** patients non-emergency CABG simple, one valve (aortic or mitral) replacement or both, requiring cardiopulmonary bypass	Hb <8.0 g/dL	Hb <10.0 g/dL
Mazer, 2017, Canada	RCT	**5243** adults (from 19 countries across the world) non-emergency cardiac surgery with cardiopulmonary bypass	Hb <7.5 g/dL intraoperatively or postoperatively	Hb <9.5 g/dL intraoperatively or postoperatively in ICU or if Hb <8.5 g/dL in non-ICU ward
Murphy, 2015, UK	RCT	**2007** participants older than 16 years of age who were undergoing non-emergency cardiac surgery	post-surgery Hb <7.5 g/dL	post-surgery Hb <9.0 g/dL
Shehata, 2012, Canada	RCT	**50** adults undergoing cardiac surgery	Hb ≤7.0 g/dL during cardiopulmonary bypass and ≤7.5 g/dL postoperatively	Hb ≤ 9.5 g/dL during cardiopulmonary bypass and ≤10 g/dL postoperatively
Hajjar, 2010, Brazil	RCT	**502** adults undergoing cardiac surgery with cardiopulmonary bypass	Haematocrit <24% (~Hb <8 g/dL)	Haematocrit <30% (~Hb <10 g/dL)
Bracey, 1999, USA	RCT	428 participants undergoing elective primary coronary artery bypass graft surgery	postoperative Hb <8.0 g/dL	individual physician who considered **clinical assessment** of the patient and the institutional guidelines, which proposed a Hb <9.0 g/dL

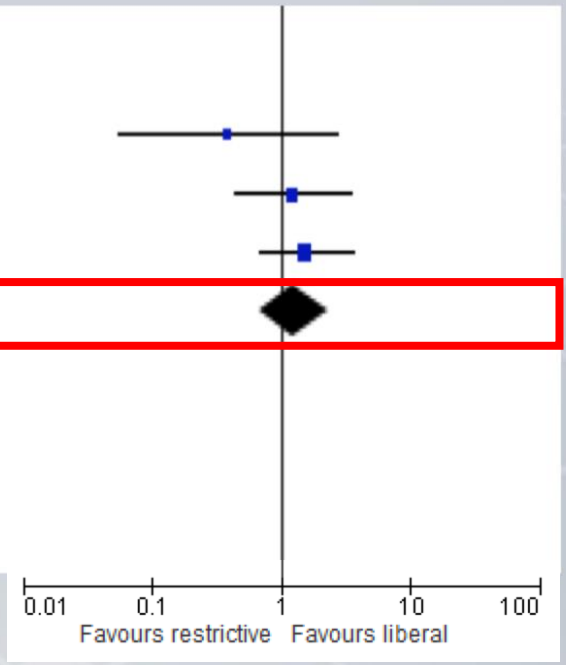
Cardiac Surgery

- **CRITICAL OUTCOME : 30-day mortality**

1.1.3 Cardiac surgery						
Bracey 1999	3	215	6	222	4.5%	0.52 [0.13, 2.04]
Hajjar 2010	15	249	13	253	13.9%	1.17 [0.57, 2.41]
Murphy 2015	26	1000	19	1003	19.2%	1.37 [0.76, 2.46]
Subtotal (95% CI)		**1464**		**1478**	**37.6%**	**1.18 [0.77, 1.81]**
Total events	44		38			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.65$, $df = 2$ ($P = 0.44$); $I^2 = 0\%$

Test for overall effect: $Z = 0.74$ ($P = 0.46$)



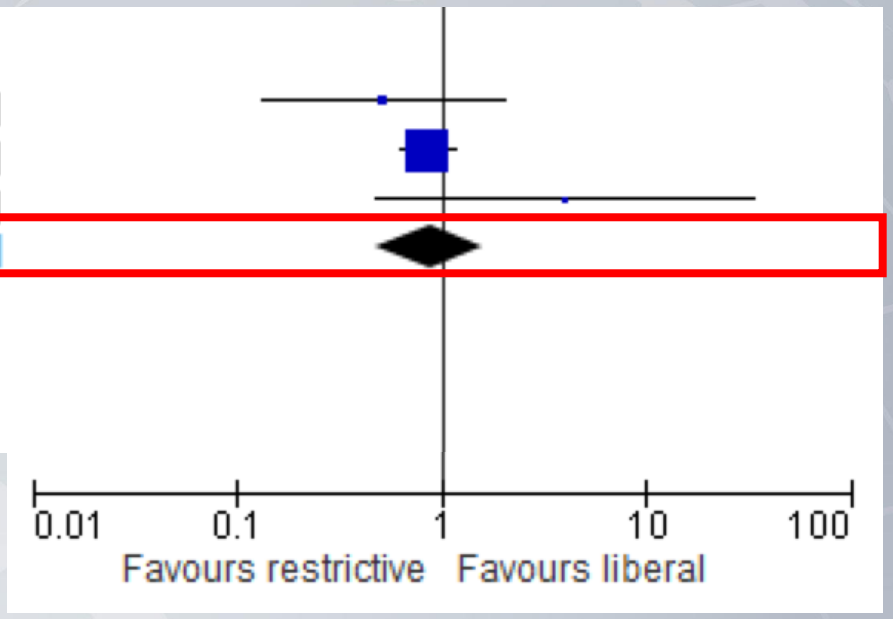
Cardiac Surgery

- **CRITICAL OUTCOME : hospital mortality**

1.2.3 Cardiac surgery						
Bracey 1999	3	215	6	222	3.9%	0.52 [0.13, 2.04]
Mazer 2017	74	2427	87	2429	75.4%	0.85 [0.63, 1.15]
Shehata 2012	4	25	1	25	1.6%	4.00 [0.48, 33.33]
Subtotal (95% CI)		**2667**		**2676**	**81.0%**	**0.88 [0.48, 1.62]**
Total events	81		94			

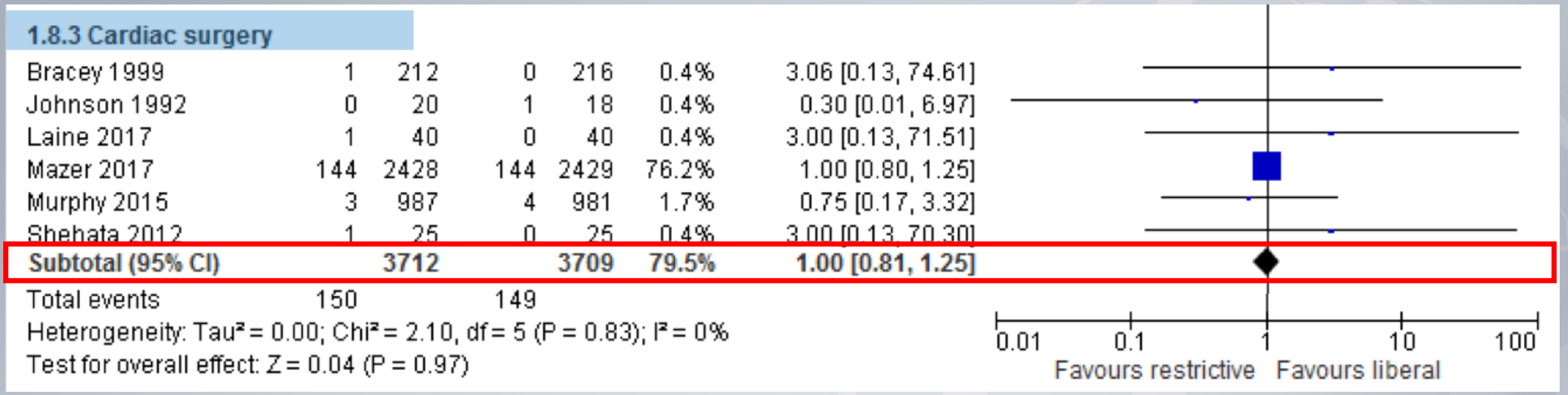
Heterogeneity: Tau² = 0.10; Chi² = 2.56, df = 2 (P = 0.28); I² = 22%

Test for overall effect: Z = 0.40 (P = 0.69)



Cardiac Surgery

- **Myocardial Infarction**



1.8.3 Cardiac surgery						
Bracey 1999	1	212	0	216	0.4%	3.06 [0.13, 74.61]
Johnson 1992	0	20	1	18	0.4%	0.30 [0.01, 6.97]
Laine 2017	1	40	0	40	0.4%	3.00 [0.13, 71.51]
Mazer 2017	144	2428	144	2429	76.2%	1.00 [0.80, 1.25]
Murphy 2015	3	987	4	981	1.7%	0.75 [0.17, 3.32]
Shehata 2012	1	25	0	25	0.4%	3.00 [0.13, 70.30]
Subtotal (95% CI)		**3712**		**3709**	**79.5%**	**1.00 [0.81, 1.25]**
Total events	150		149			

Heterogeneity: Tau² = 0.00; Chi² = 2.10, df = 5 (P = 0.83); I² = 0%

Test for overall effect: Z = 0.04 (P = 0.97)

Cardiac Surgery

CRITICAL OUTCOME: 30-day mortality (subgroup analyses)

Outcomes	Difference (restrictive (< 7.5/8 g/dL) versus liberal (<9-10 g/dL) RBC transfusion triggers	Relative effect (95% CI)
30-day mortality (subgroup: patients <60 years)	**2 fewer per 1.000** (31 fewer to 93 more)	**RR 0.95** (0.28 to 3.20)
30-day mortality (subgroup: patients ≥60 years)	**28 more per 1.000** (20 fewer to 152 more)	**RR 1.54** (0.61 to 3.93)
Renal failure (subgroup: patients <60 years)	**7 more per 1.000** (18 fewer to 116 more)	**RR 1.27** (0.29 to 5.55)
Renal failure (subgroup: patients ≥60 years)	**26 fewer per 1.000** (56 fewer to 54 more)	**RR 0.77** (0.24 to 1.73)

Cardiac Surgery

IMPORTANT OUTCOMES

Desirable effects?

Outcomes	Difference (restrictive (<7,5/8 g/dL) versus liberal (<9-10 g/dL) RBC transfusion triggers)	Relative effect (95% CI)
Patients exposed to RBC transfusion	**240 fewer per 1.000** (263 fewer to 209 fewer)	**RR 0.69** (0.66 to 0.73)
RBC units transfused (mean)	MD **0.87 units lower** (1.29 lower to 0.45 lower)	-
Haemoglobin concentration	MD **1.4 lower** (3.1 lower to 0.3 higher)	-
Rebleeding	**3 fewer per 1.000** (11 fewer to 11 more)	**RR 0.87** (0.51 to 1.48)
Health-related quality of life EQ-5D at 6 weeks	MD **0.01 points higher** (0.02 lower to 0.03 higher)	-
Vascular morbidity (aortic or femoral artery dissection or acute limb ischaemia)	**7 fewer per 1.000** (8 fewer to 14 more)	**RR 0.14** (0.01 to 2.69)
Reoperative morbidity (for bleeding/tamponade, graft occlusion, valve dysfunction)	**3 fewer per 1.000** (18 fewer to 32 more)	**RR 0.88** (0.36 to 2.13)

Undesirable effects?

Outcomes	Difference (restrictive (<7,5/8 g/dL) versus liberal (<9-10 g/dL) RBC transfusion triggers)	Relative effect (95% CI)
Pneumonia or wound infection	**7 more per 1.000** (6 fewer to 21 more)	**RR 1.07** (0.94 to 1.22)
Health-related quality of life EQ-5D at 3 months	MD **0 points** (0.03 lower to 0.02 higher)	-
Pulmonary morbidity (pneumonia, pulmonary embolus or prolonged postoperative ventilation >24 hours)	**10 more per 1.000** (19 fewer to 61 more)	**RR 1.18** (0.65 to 2.13)
Gastrointestinal morbidity	**8 more per 1.000** (3 fewer to 65 more)	**RR 2.44** (0.48 to 12.48)

Cardiac surgery

Strong recommendation:
The ICC-PBM guideline panel recommends using a transfusion trigger of Hb <7.5 g/dL in cardiac surgery patients, based on moderate certainty in the evidence of effects. (Y/N)

(Strong recommendation, moderate level of evidence)

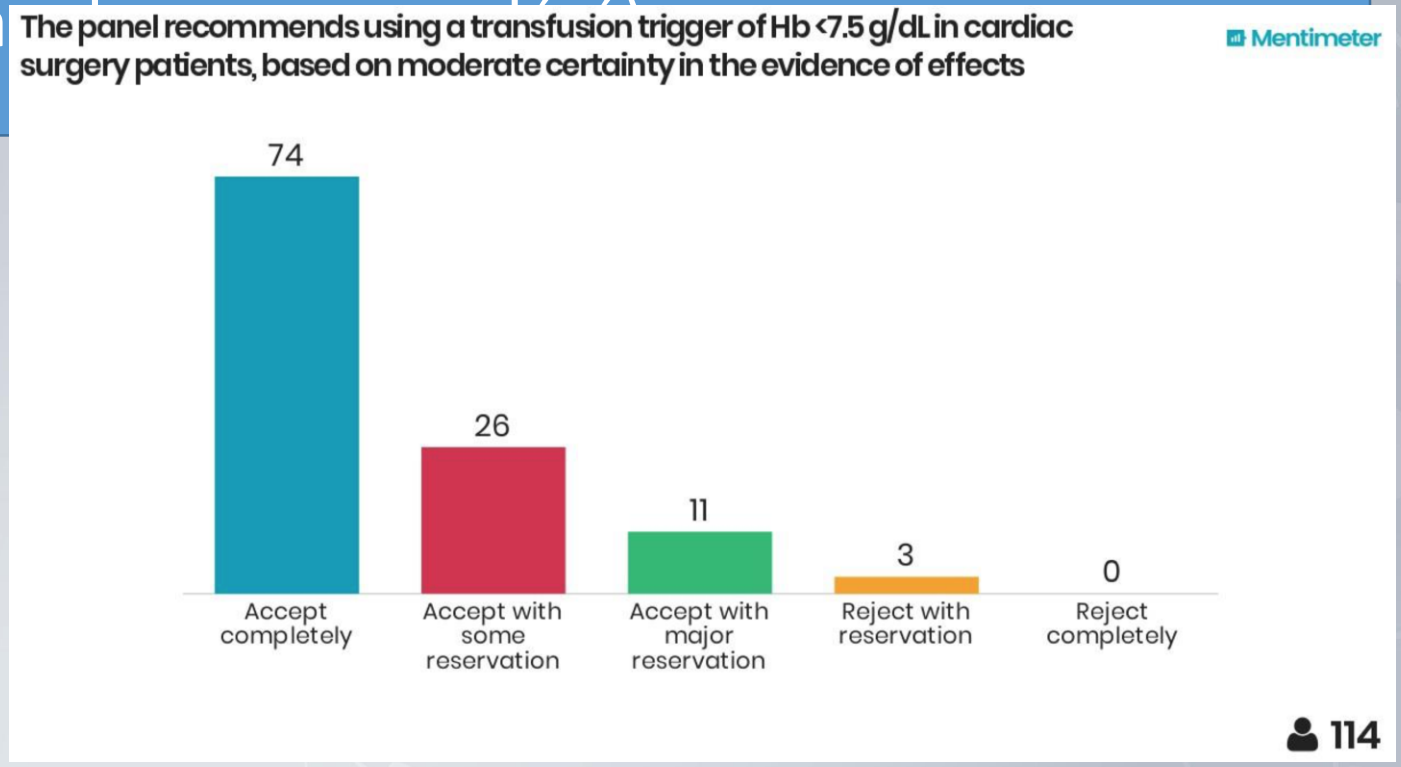
Justification: No evidence of increased mortality or other undesirable effects, and substantial reduction in red cell exposure and utilisation.

Note: 7.5g/dL trigger represents the value used in the included trials

Cardiac surgery

L'ICC-PBM recommande un seuil transfusionnel restrictif 7.5g/dL

(recommandation forte, nivea



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Orthopaedic surgery

Should more restrictive RBC transfusion triggers (**Intervention**) versus more liberal RBC transfusion triggers (**Comparison**) be used in adult patients undergoing orthopaedic surgery? ***(Population 3)***

Study characteristics

Orthopaedic surgery 10 : studies

Author, year, country	Study design	Population	Restrictive RBC transfusion trigger	Liberal RBC transfusion trigger
Gregersen, 2015, Denmark	RCT	284 participants (≥65 years), hip fracture surgery with postoperative 9.7 g/dL<Hb 11.3 g/dL	**Hb<9.7 g/dL** until target achieved with **max 2 units per day**	**Hb<11.3 g/dL** until target achieved with **max 2 units per day**
Fan, 2014, China	RCT	186 participants (>65 years), elective unilateral total hip replacement	If **symptoms of anemia or Hb<8g/dL**	Transfuse enough blood to maintain **Hb>10 g/dL**
Nielsen, 2014, Denmark	RCT	66 participants (>18 years), elective hip revision surgery	**Hb<7.3 g/dL** ; target Hb 7.3-8.9 g/dL	**Hb<8.9 g/dL** with target >8.9 g/dL
Parker, 2013, UK	RCT	200 participants (>60 years), with hip fracture, 8.0 g/dL<Hb<9.5 g/dL	O**nly if definite symptoms of anemia**	Transfusion of at least 1 unit of blood and then maintained **>10.0 g/dL**
So-Osman, 2013, The Netherlands	RCT	603 participants in 3 hospitals undergoing elective orthopaedic surgery	According to new protocol hospital 1 and 2 and to the standard protocol in hospital 3 Hb threshold values were based on age and comorbidities, details are provided in Appendix paper So-Osman et al. (2013)	According to standard protocol in hospital 1 and 2 and to new protocol in hospital 3 Hb threshold values were based on age and comorbidities, details are provided in Appendix paper So-Osman et al. (2013)
Carson, 2011, USA	RCT	2016 participants (>50 years), after hip fracture surgery with Hb<10.0 g/dL with cardiovascular disease or cardiovascular risk factors	If **symptoms of anaemia or Hb<8g/dL**; 1 unit at a time until symptoms disappeared or Hb increased >8 g/dL	Immediately transfuse 1 unit after randomisation (Hb<10 g/dL) and transfuse enough blood to maintain **Hb>10 g/dL**
Foss, 2009, Denmark	RCT	120 participants (>65 years) hip fracture	**Hb <8.0** g/dL (7.2 g/dL<Hb<8 g/dL: 1 unit of RBC; 5.6 g/dL<Hb≤7.2 g/dL: 2 units of RBC; Hb<5.6 g/dL: 3 units of RBC; all transfusions followed by control of Hb)	Hb **<10.0 g/dL** (8.8 g/dL<Hb<10 g/dL: 1 unit of RBC; 7.2 g/dL<Hb≤8.8 g/dL: 2 units of RBC; Hb<7.2 g/dL: 3 units of RBC, all transfusions followed by control of Hb)
Grover, 2006, UK	RCT	260 participants (>55 years) undergoing elective lower limb joint replacement surgery	**Hb<8.0** g/dL; target Hb 8.0-9.5 g/dL	**Hb<10.0 g/dL**, Target Hb : 10.0-12.0 g/dL
Lotke, 1999, USA	RCT	152 participants undergoing primary total knee arthroplasty (TKA)	Transfusion of the 2 units of autologous blood if Hb <9.0 g/dL	Transfusion of the 2 units of autologous blood immediately after surgery in the recovery room
Carson, 1998		84 hip fracture participants (in USA and Scotland) undergoing	If symptoms of anemia or **Hb<8g/dL**; 1 unit at a time	Immediately transfuse 1 unit after randomisation

Orthopaedic surgery

CRITICAL OUTCOME: 30-day mortality

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Orthopaedic surgery						
Carson 1998	1	42	1	42	1.2%	1.00 [0.06, 15.47]
Carson 2011	43	1009	52	1007	31.7%	0.83 [0.56, 1.22]
Foss 2009	5	60	0	60	1.1%	11.00 [0.62, 194.63]
Gregersen 2015	21	144	12	140	15.6%	1.70 [0.87, 3.32]
Lotke 1999	0	62	0	65		Not estimable
Parker 2013	5	100	3	100	4.3%	1.67 [0.41, 6.79]
Subtotal (95% CI)		**1417**		**1414**	**53.9%**	**1.27 [0.72, 2.25]**
Total events	75		68			

Heterogeneity: Tau² = 0.14; Chi² = 6.46, df = 4 (P = 0.17); I² = 38%

Test for overall effect: Z = 0.82 (P = 0.41)

Risk Ratio M-H, Random, 95% CI

CRITICAL OUTCOME: myocardial infarction

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 Orthopaedic surgery						
Carson 2011	38	1009	23	1007	14.7%	1.65 [0.99, 2.75]
Fan 2014	0	94	1	92	0.4%	0.33 [0.01, 7.91]
Foss 2009	1	60	0	60	0.4%	3.00 [0.12, 72.20]
Grover 2006	0	109	1	109	0.4%	0.33 [0.01, 8.09]
Lotke 1999	1	62	0	65	0.4%	3.14 [0.13, 75.72]
Subtotal (95% CI)		**1334**		**1333**	**16.2%**	**1.58 [0.97, 2.56]**
Total events	40		25			

Heterogeneity: Tau² = 0.00; Chi² = 2.22, df = 4 (P = 0.70); I² = 0%

Test for overall effect: Z = 1.83 (P = 0.07)

Risk Ratio M-H, Random, 95% CI

Orthopaedic surgery

IMPORTANT OUTCOMES

Desirable effects?

Outcomes	Difference restrictive (<8-9 g/dL) versus liberal (<10 g/dL) RBC transfusion triggers	Relative effect (95% CI)
Patients exposed to RBC transfusion	**408 fewer per 1.000** (506 fewer to 269 fewer)	**RR 0.50** (0.38 to 0.67)
RBC units transfused	MD **0.23 units lower** (0.85 lower to 0.39 higher)	-
Haemoglobin concentration	MD **0.99 lower** (1.53 lower to 0.45 lower)	-
Sepsis-bacteraemia	**0 fewer per 1.000** (4 fewer to 27 more)	**RR 0.96** (0.14 to 6.55)
Pneumonia	**10 fewer per 1.000** (22 fewer to 5 more)	**RR 0.83** (0.63 to 1.09)
Pneumonia or wound infection	**33 fewer per 1.000** (69 fewer to 22 more)	**RR 0.76** (0.50 to 1.16)
Mental confusion	**8 fewer per 1.000** (34 fewer to 29 more)	**RR 0.92** (0.65 to 1.30)

Undesirable effects?

Outcomes	Difference restrictive (<8-9 g/dL) versus liberal (<10 g/dL) RBC transfusion triggers	Relative effect (95% CI)
Congestive heart failure	**7 more per 1.000** (5 fewer to 25 more)	**RR 1.28** (0.80 to 2.05)

Orthopaedic surgery

Quality of the body of evidence (critical outcomes)?

Outcomes	Certainty of the evidence (GRADE)
30-day mortality	⊕⊕⊕◯ MODERATE[a]
Hospital mortality	⊕⊕◯◯ LOW[a,d]
90-day mortality	⊕⊕◯◯ LOW[a,g]
Cardiac events	⊕⊕⊕⊕ HIGH
Myocardial infarction	⊕⊕⊕◯ MODERATE[a]
CVA-stroke	⊕⊕◯◯ LOW[a,d]
Thromboembolism	⊕⊕⊕◯ MODERATE[a]
Renal failure	⊕⊕◯◯ LOW[a,h]
Inability to walk or death at 30/60 days	⊕⊕⊕◯ MODERATE[c]

a. Imprecision: large variability in results
b. Risk of bias: selection bias (randomization + allocation concealment unclear), performance bias (lack of blinding unclear), reporting bias (no pre-registration study protocol).
c. Indirectness: lack of generalizibility: Single centre study conducted in the USA
d. Risk of bias: detection bias and reporting bias
e. Indirectness: lack of generalizibility: Single centre study conducted in Greece
f. Imprecision: low number of events, limited sample size and/or large variability in results
g. Indirectness: lack of generaliziblity: 2 small single centre studies form UK and Denmark
h. Risk of bias: detection bias and selection bias

Orthopaedic surgery

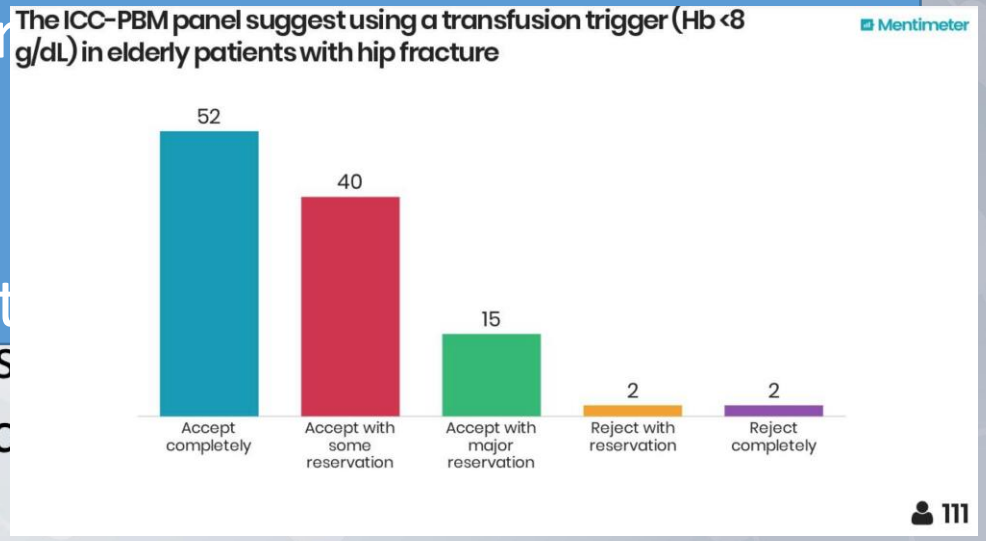
Conditional recommendation (Y/N)

The ICC-PBM guideline panel suggest using a transfusion trigger (Hb <8 g/dL) in elderly patients with hip fracture

- L'ICC-PBM suggère un seuil transfusionnel restrictif (Hb <8 g/dL) (recommandation conditionnelle, niveau de preuve modéré)
- Pas d'effet sur la mortalité ou l'état fonctionnel
- Extrapolation des études à toute la chirur
- Doute sur les EI de la stratégie restrictive
- Recommandation de conduire d'autres ét

surgery? And other non-ortho, non-cardiac s

- Major evidence gaps in these areas - researc



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Coronary heart disease

Should more restrictive RBC transfusion triggers (**Intervention**) versus more liberal RBC transfusion triggers (**Comparison**) be used in adult patients with coronary heart disease? ***(Population 4)***

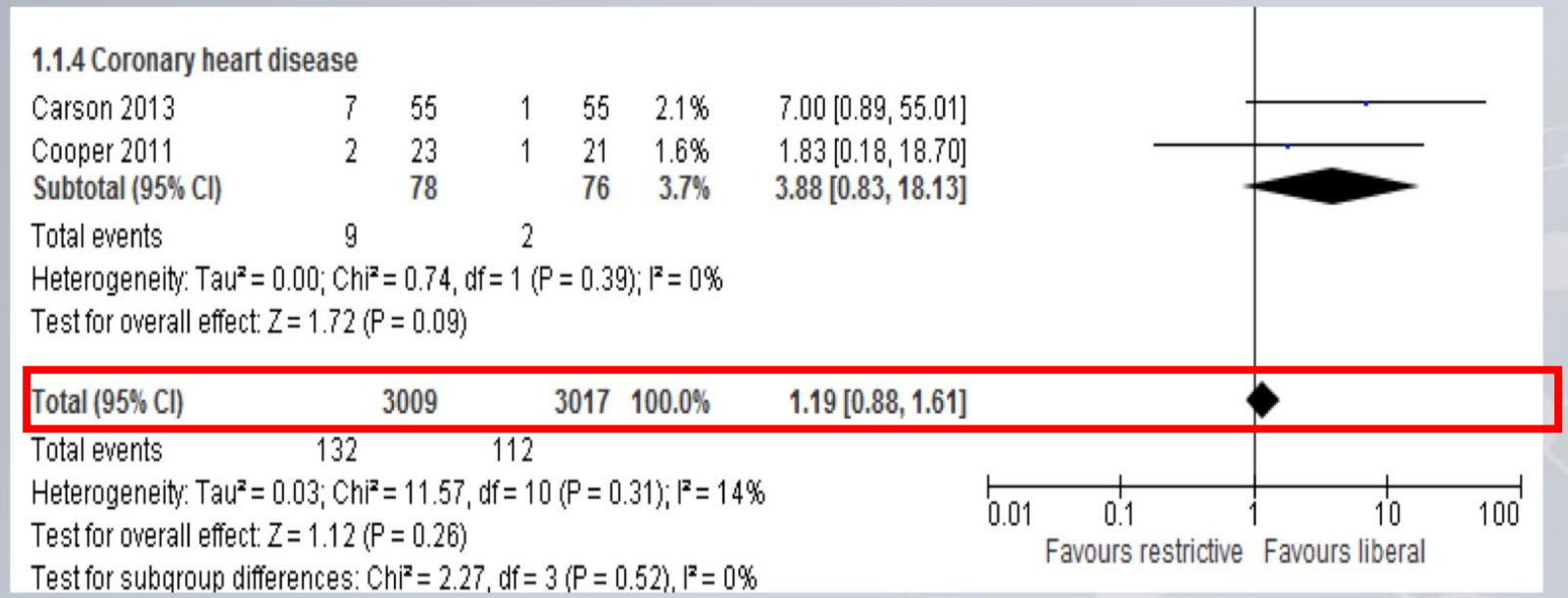
Study characteristics

Coronary heart disease

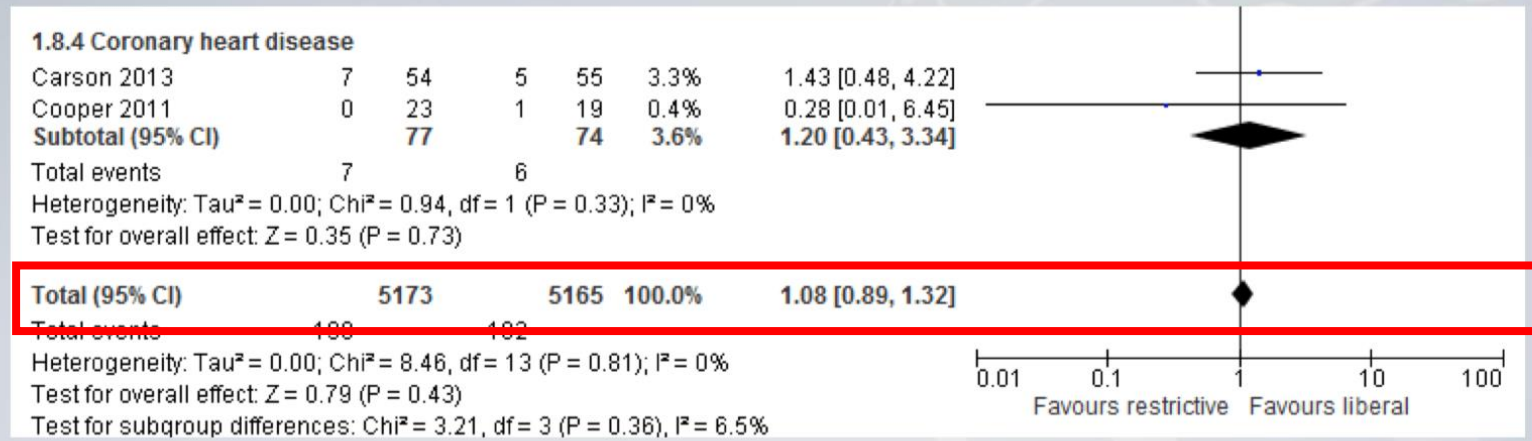
Author, year, country	Study design	Population	Restrictive RBC transfusion trigger	Liberal RBC transfusion trigger
Carson, 2013, USA	RCT	110 participants with AMI or undergoing cardiac catheterization	If **symptoms of anemia or Hb<8 g/dL**; 1 unit at a time until symptoms disappeared or Hb increased >8 g/dL	1 unit after randomisation (**Hb<10 g/dL**) and transfuse enough blood to maintain Hb>10 g/dL
Cooper, 2011, USA	RCT	45 participants with AMI	Haematocrit <24%; target Ht 24-27% (Hb: 8-9 g/dL)	Haematocrit <30%; target Ht: 30-33% (Hb: 10-11 g/dL)

Coronary heart disease

CRITICAL OUTCOME: 30-day mortality



CRITICAL OUTCOME: myocardial infarction



Acute coronary disease

Recommendation: The ICC-PBM guideline panel decided to formulate a recommendation for further research on the use of restrictive transfusion trigger in patients with acute coronary syndromes (Y/N)

Justification: There is an overall low level of evidence, and concern regarding undesirable effects with a restrictive strategy

Note: A conditional recommendation for either strategy cannot be made because of the concern over the possibility for undesirable effects in the restrictive group

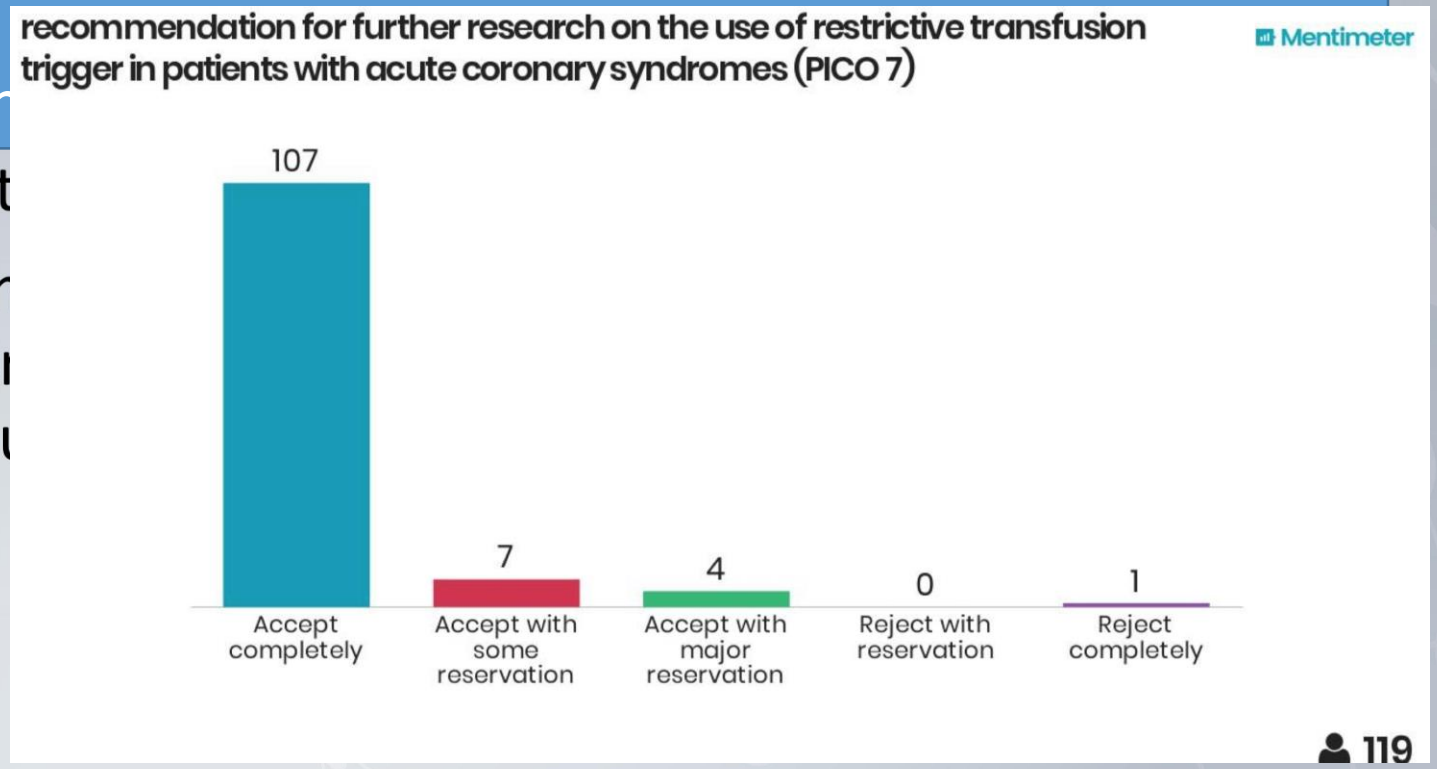
Acute coronary disease

L'ICC-PBM recommande plus de recherche pour définir la stratégie transfusionnelle chez les patients avec SCA

Pas de preuve suffisante quan

regarding undesirable effect

Note: A conditional recomm
made because of the concer
effects in the restrictive grou



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Acute interventions & intensive care

Acute gastrointestinal bleeding

Acute bleeding

Study characteristics

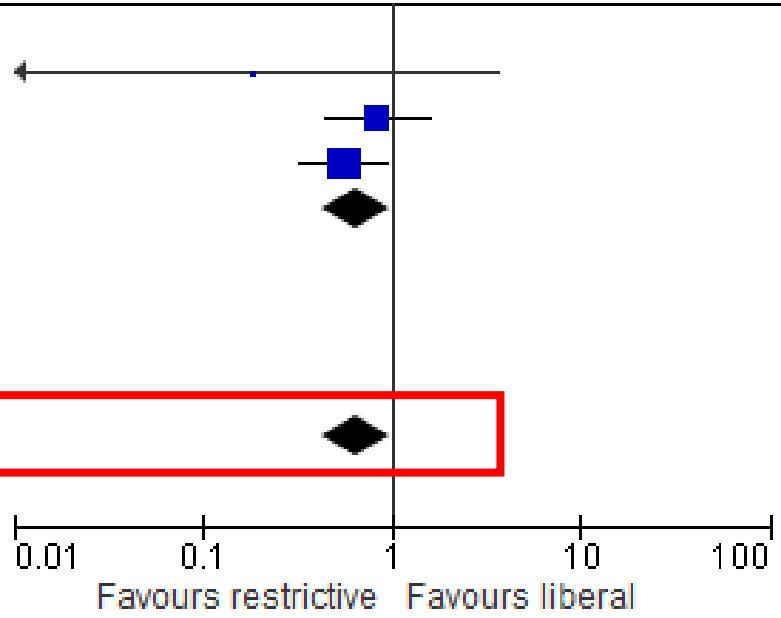
Author, year, country	Study design	Population	Restrictive RBC transfusion strategy	Liberal RBC transfusion strategy
Jairath, 2015, UK	RCT	**936** participants with upper GI bleeding, **6 sites**	**Hb<8 g/dL** target Hb of 8.1–10.0 g/dL	**Hb<10 g/dL**, target Hb of 10.1–12.0 g/dL
Villanueva, 2013, Spain	RCT	**889** participants with upper GI bleeding, **1 site**	**Hb<7 g/dL** target Hb of 7-9 g/dL	**Hb<9 g/dL** target Hb of 9-11 g/dL
Blair, 1986, UK	RCT	**50** consecutive participants with severe upper GI bleeding (without OV)	**Hb <8.0 g/dL or shock persisted** after initial resuscitation	At least 2 units of RBC during their **first 24 hours in hospital**
Fisher, 1956, UK	RCT	**22** trauma participants	Attempt to leave the RBC volume at the end of resuscitation at 70% to 80% of normal.	To achieve 100% or more of the RBC volume at the **end of resuscitation**.

Acute intervention & intensive care

Acute (gastrointestinal) bleeding

CRITICAL OUTCOME: 30-DAY MORTALITY

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Acute gastrointestinal bleeding						
Blair 1986	0	26	2	24	1.9%	0.19 [0.01, 3.67]
Jairath 2015	14	257	25	382	41.6%	0.83 [0.44, 1.57]
Villanueva 2013	19	416	34	417	56.5%	0.56 [0.32, 0.97]
Subtotal (95% CI)		**699**		**823**	**100.0%**	**0.65 [0.43, 0.97]**
Total events	33		61			
Heterogeneity: Tau² = 0.00; Chi² = 1.55, df = 2 (P = 0.46); I² = 0%						
Test for overall effect: Z = 2.08 (P = 0.04)						
Total (95% CI)		**699**		**823**	**100.0%**	**0.65 [0.43, 0.97]**
Total events	33		61			
Heterogeneity: Tau² = 0.00; Chi² = 1.55, df = 2 (P = 0.46); I² = 0%						
Test for overall effect: Z = 2.08 (P = 0.04)						
Test for subgroup differences: Not applicable						



Certainty of the evidence (GRADE)
⊕⊕◯◯ LOW[a,b]

Acute intervention & intensive care

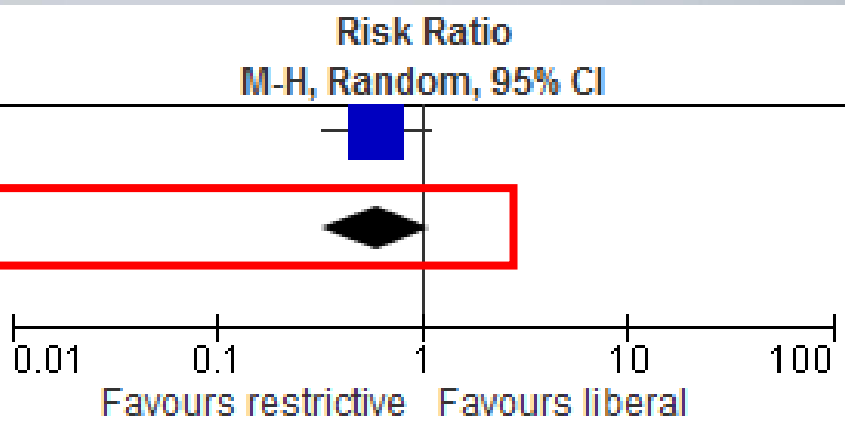
Acute gastrointestinal bleeding

CRITICAL OUTCOME: 30-DAY MORTALITY (subgroup analyses: patients with cirrhosis)

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
Villanueva 2013	15	139	25	138	100.0%	0.60 [0.33, 1.08]
Total (95% CI)		**139**		**138**	**100.0%**	**0.60 [0.33, 1.08]**
Total events	15		25			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.71 (P = 0.09)



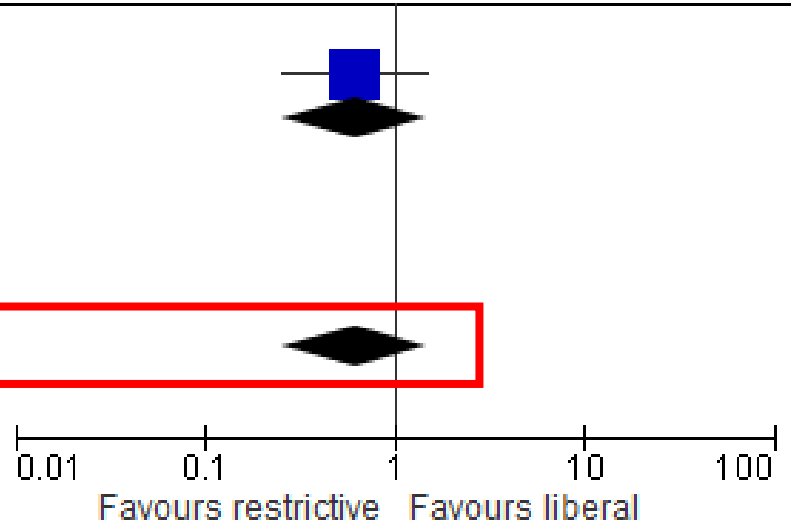
Certainty of the evidence (GRADE)
⨁⨁◯◯ LOW[b]

Acute intervention & intensive care

Acute (gastrointestinal) bleeding

CRITICAL OUTCOME: MYOCARDIAL INFARCTION

Study or Subgroup	Restrictive Events	Total	Liberal Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 Acute gastrointestinal bleeding						
Villanueva 2013	8	444	13	445	100.0%	0.62 [0.26, 1.47]
Subtotal (95% CI)		**444**		**445**	**100.0%**	**0.62 [0.26, 1.47]**
Total events	8		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.28)						
Total (95% CI)		**444**		**445**	**100.0%**	**0.62 [0.26, 1.47]**
Total events	8		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.09 (P = 0.28)						
Test for subgroup differences: Not applicable						



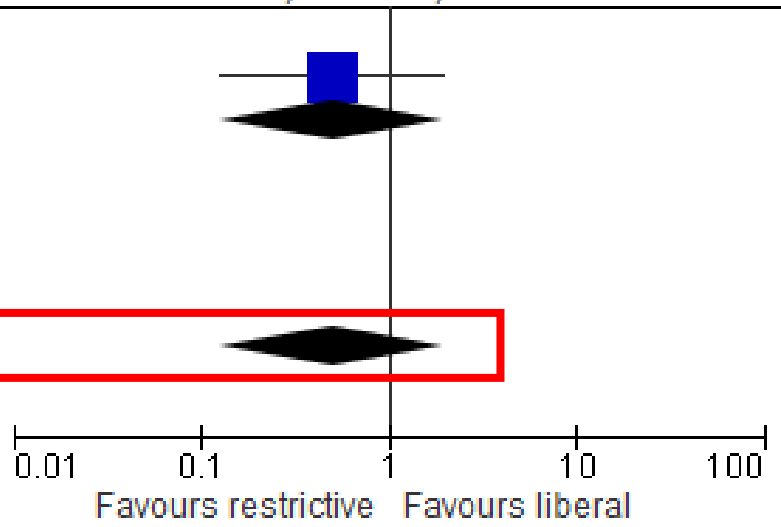
Certainty of the evidence (GRADE)
⊕⊕◯◯ LOW[b,d]

Acute intervention & intensive care

Acute (gastrointestinal) bleeding

CRITICAL OUTCOME: CVA-STROKE

Study or Subgroup	Restrictive Events	Total	Liberal Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 Acute gastrointestinal bleeding						
Villanueva 2013	3	444	6	445	100.0%	0.50 [0.13, 1.99]
Subtotal (95% CI)		**444**		**445**	**100.0%**	**0.50 [0.13, 1.99]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						
Total (95% CI)		**444**		**445**	**100.0%**	**0.50 [0.13, 1.99]**
Total events	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						
Test for subgroup differences: Not applicable						



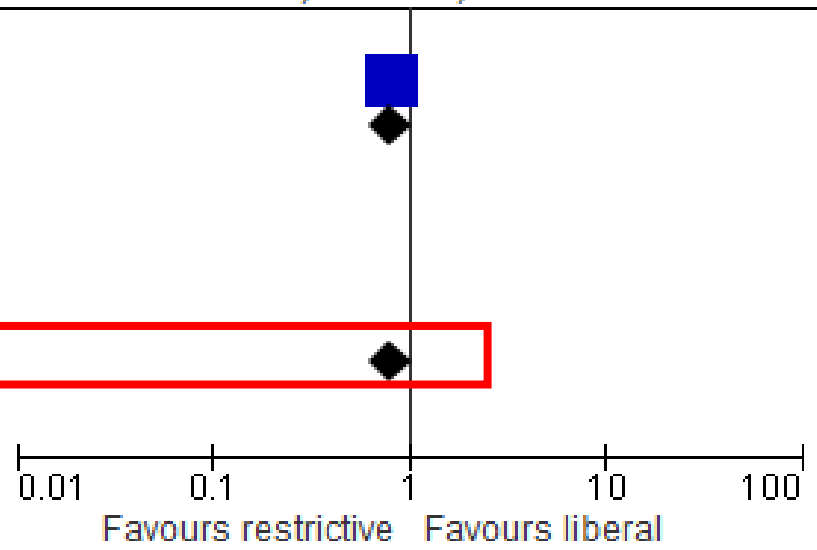
Certainty of the evidence (GRADE)
⊕⊕◯◯ LOW[b,d]

Acute intervention & intensive care

Acute (gastrointestinal) bleeding

CRITICAL OUTCOME: RENAL FAILURE

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
1.12.1 Acute gastrointestinal bleeding						
Villanueva 2013	78	444	97	445	100.0%	0.81 [0.62, 1.05]
Subtotal (95% CI)		**444**		**445**	**100.0%**	**0.81 [0.62, 1.05]**
Total events	78		97			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.58 (P = 0.11)						
Total (95% CI)		**444**		**445**	**100.0%**	**0.81 [0.62, 1.05]**
Total events	78		97			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.58 (P = 0.11)						
Test for subgroup differences: Not applicable						



Certainty of the evidence (GRADE)
⊕⊕◯◯ LOW[b,d]

Acute intervention & intensive care

Acute gastrointestinal bleeding

IMPORTANT OUTCOMES

Desirable effects?

Outcomes	Difference (restrictive (<7-8 g/dL) versus liberal (<9-10 g/dL) RBC transfusion triggers)	Relative effect (95% CI)
Patients exposed to RBC transfusion	**296 fewer per 1.000** (388 fewer to 164 fewer)	**RR 0.55** (0.41 to 0.75)
RBC units transfused	MD **1.79 units lower** (3 lower to 0.58 lower)	-
Haemoglobin concentration	MD **0.89 lower** (1.01 lower to 0.77 lower)	-
Congestive heart failure	**20 fewer per 1.000** (34 fewer to 7 more)	**RR 0.57** (0.29 to 1.15)
Rebleeding	**56 fewer per 1.000** (84 fewer to 121 more)	**RR 0.54** (0.31 to 1.99)
Pneumonia	**11 fewer per 1.000** (42 fewer to 36 more)	**RR 0.90** (0.61 to 1.33)
Pneumonia or wound infection	**11 fewer per 1.000** (58 fewer to 47 more)	**RR 0.96** (0.79 to 1.17)
Function and fatigue (EQ-5D)	MD **0.07 points higher** (0 to 0.14 higher)	-

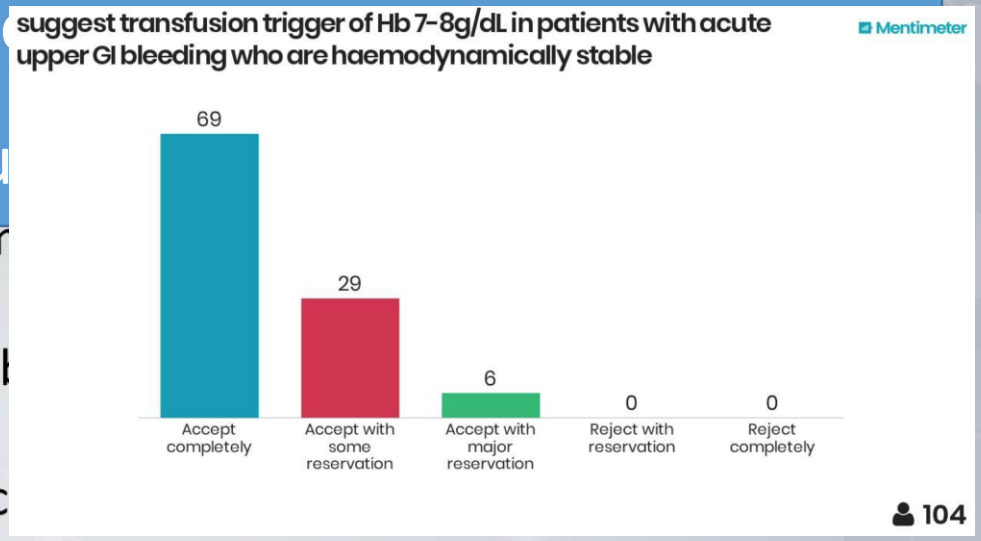
Undesirable effects? NONE

Acute upper gastro intestinal bleeding

Conditional recommendation (Y/N): The ICC-PBM guideline panel suggest transfusion trigger of Hb 7-8g/dL in patients with acute upper GI bleeding who are haemodynamically stable (or "who are not exsanguinating"?)

- L'ICC-PBM suggère de transfuser selon une stratégie restrictive les patients avec HD hautes hémodynamiquement stable (niveau de preuve bas, recommandation conditionnelle)
- Recommandation pour plus de recherch
- Patients instables et HD basses non inclu

- "Massive exsanguinating" patients excluded from lower GI bleeding.
- Guidelines should emphasise that in the acutely b deciding factor for transfusion.
- Trials used Hb triggers (e.g. Hb 7) to achieve spec



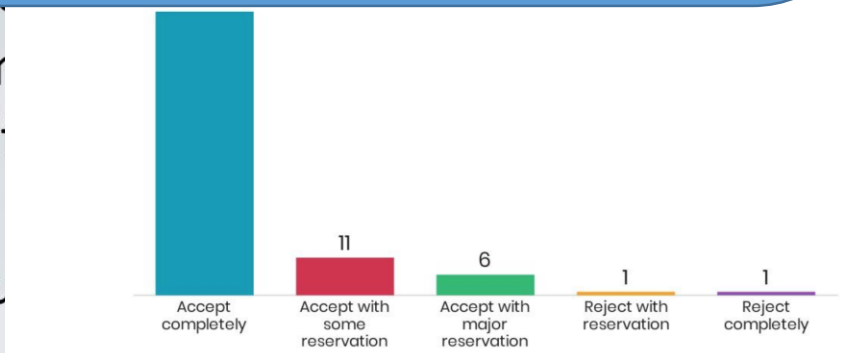
Acute Bleeding

No recommendation for Hb trigger

- L'ICC-PBM ne recommande pas de recherche sur les seuils transfusionnels dans le domaine
- l'Hb n'est pas un déterminant transfusionnel du saignement majeur
- Se référer aux guidelines spécifiques au transfusion massive

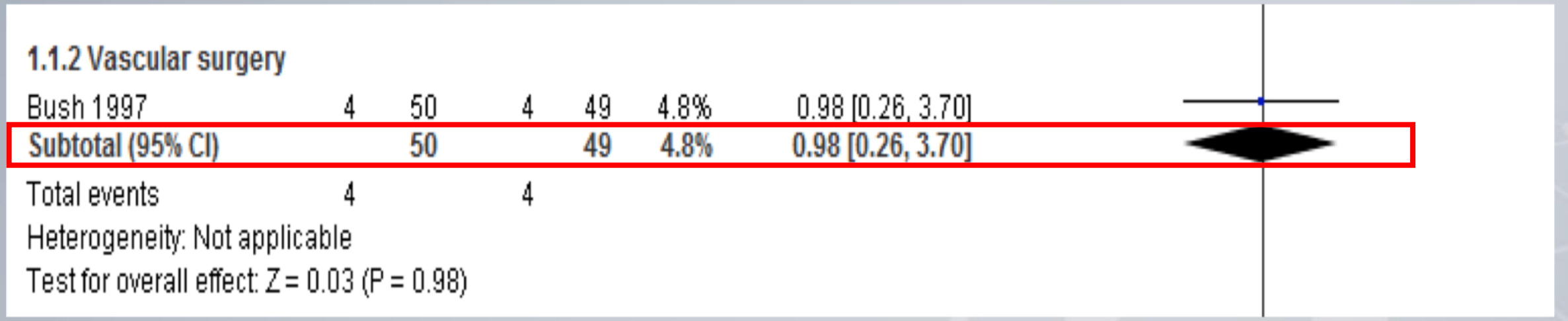
the need for transfusion in an acutely bleeding (i.e. m
scenario. Recommend refer to existing massive trans
haemorrhage protocols/guidelines)

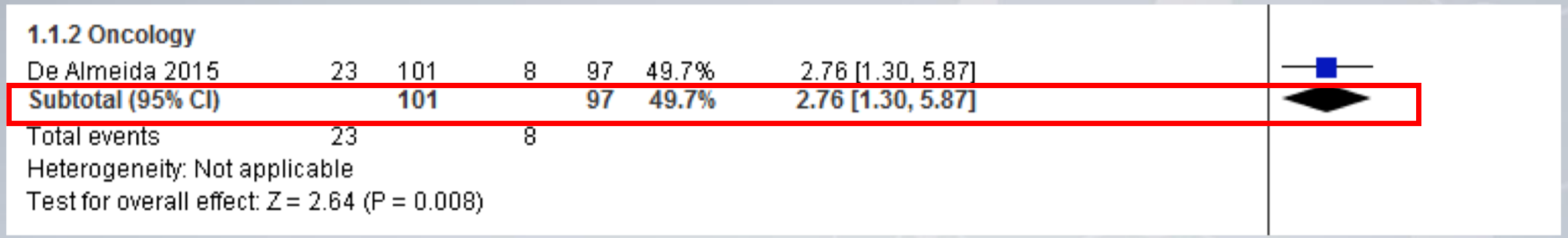
- ICC PBM Guidelines should emphasise that in the acu
is not the deciding factor for transfusion.



Non orthopaedic & non cardiac surgery

CRITICAL OUTCOME: 30-day mortality





Non orthopaedic & non cardiac surgery

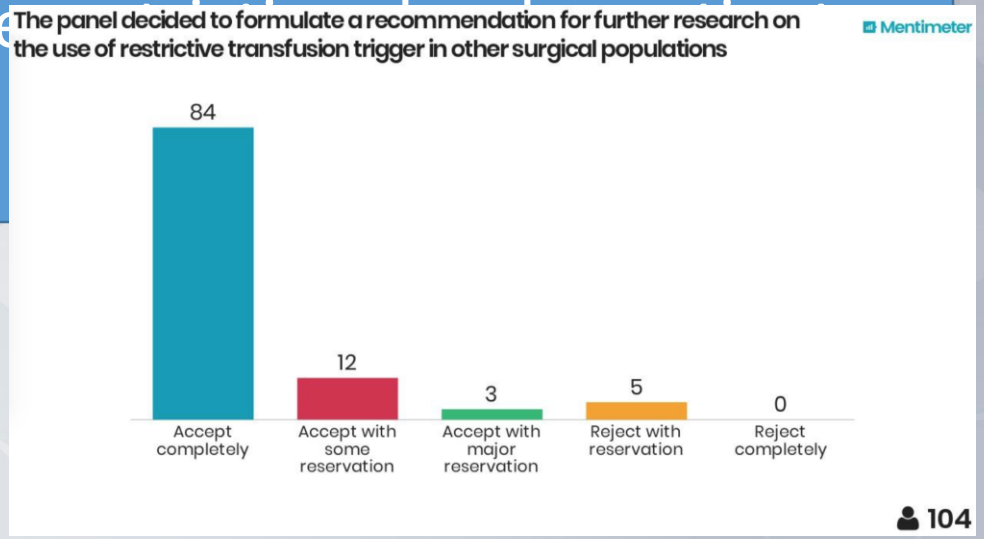
Recommendation: The ICC-PBM guideline panel decided to formulate a recommendation for further research on the use of restrictive transfusion trigger in other surgical populations (Y/N)

Justification: There is an overall low level of evidence, and concern in surgical oncology patient regarding undesirable effects with a restrictive strategy

Note: A conditional recommendation for either strategy cannot be made because of the concern over the possibility for undesirable effects in the restrictive group

Non orthopaedic & non cardiac surgery

- L'ICC-PBM recommande plus de recherche investiguant les bénéfices et risques de la stratégie restrictive en chirurgie
- Pas de preuve suffisante
- Doute sur les potentiels EI de la stratégie [illegible] ayant une chirurgie oncologique



Conclusions :

Recommandations cliniques “seuils transfusionnels” partie 2

- Deux recommandations fortes (*niveau de preuve modéré*)
  - Stratégie transfusionnelle restrictive patients hémodynamiquement stables de réanimation et choc septique (Hb < 7g/dL)
  - Stratégie transfusionnelle restrictive en chirurgie cardiaque (Hb <7.5 g/dL)

- Deux recommandations conditionnelles
  - Stratégie transfusionnelle restrictive hémorragie digestive haute sans défaillance hémodynamique (Hb < 7-8g/dL), *niveau de preuve bas*
  - Stratégie transfusionnelle restrictive (Hb < 8g/dL) après chirurgie de hanche *niveau de preuve modéré*

Conclusions :

Recommandations recherche “seuils transfusionnels” partie 2

- Recommandations pour la réalisation d’études
  - Syndrome coronarien aigu
  - Hémorragie digestive
  - Post chirurgie non orthopédique non cardiaque

- Recommandation pour ne pas réaliser d’étude utilisant l’Hb seule comme seuil transfusionnel (Hb seul) chez les patients avec saignement majeur