



INTERNATIONAL
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ICC-PBM

FRANKFURT
2018

PROCESS OF DEVELOPING RECOMMENDATIONS: THE USE OF A FORMAL CONSENSUS FORMAT AND EVIDENCE-BASED METHODOLOGY

HANS VAN REMOORTEL
COORDINATING RESEARCHER
CENTRE FOR EVIDENCE-BASED PRACTICE (CEBAP)
BELGIAN RED CROSS
WWW.CEBAP.ORG





Conflicts of interests

- Employee of Belgian Red Cross-Flanders, providing safe blood products to hospitals in Flanders and Brussels which did not influence his contribution to ICC-PBM 2018 Frankfurt
- No conflicts of interest to declare



Outline

1. Patient Blood Management: 3 topics of interest and 17 PICO questions
2. Using a formal consensus methodology: the Consensus Development Conference
3. Using an evidence-based methodology: the GRADE approach



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Patient Blood Management

	Optimize erythropoiesis	Minimize blood loss	Manage anemia
PREOPERATIVE	<ul style="list-style-type: none">• Identify, evaluate, and treat underlying anemia• Preoperative autologous blood donation• Consider erythropoiesis stimulating agents (ESA) if nutritional anemias ruled out/treated• Refer for further evaluation if necessary	<ul style="list-style-type: none">• Identify and manage bleeding risk (past/family history)• Review medications (antiplatelet, anticoagulation therapy)• Minimize iatrogenic blood loss• Procedure planning and rehearsal	<ul style="list-style-type: none">• Compare estimated blood loss with patient-specific tolerable blood loss• Assess/optimize patient's physiologic reserve (e.g., pulmonary and cardiac function)• Formulate patient-specific management plan using appropriate blood conservation modalities to manage anemia
INTRAOPERATIVE	<ul style="list-style-type: none">• Time surgery with optimization of erythrocyte mass (note: unmanaged anemia is a contraindication for elective surgery)	<ul style="list-style-type: none">• Meticulous hemostasis and surgical techniques• Blood-sparing surgical techniques• Anesthetic blood conserving strategies• Acute normovolemic hemodilution• Cell salvage/reinfusion• Pharmacologic/hemostatic agents	<ul style="list-style-type: none">• Optimize cardiac output• Optimize ventilation and oxygenation• Evidence-based transfusion strategies
POSTOPERATIVE	<ul style="list-style-type: none">• Manage nutritional/correctable anemia (e.g., avoid folate deficiency, iron-restricted erythropoiesis)• ESA therapy if appropriate• Be aware of drug interactions that can cause anemia (e.g., ACE inhibitor)	<ul style="list-style-type: none">• Monitor and manage bleeding• Maintain normothermia (unless hypothermia indicated)• Autologous blood salvage• Minimize iatrogenic blood loss• Hemostasis/anticoagulation management• Be aware of adverse effects of medications (e.g., acquired vitamin K deficiency)	<ul style="list-style-type: none">• Maximize oxygen delivery• Minimize oxygen consumption• Avoid/treat infections promptly• Evidence-based transfusion strategies



Patient Blood Management: 3 topics of interest & 17 PICO questions

Scientific Committee



Pierre Albaladejo (Grenoble University Hospital, France/ISTH)

Shubha Allard (NHS Blood & Transplant/ISBT)

Cécile Aubron (Academic Hospital of Brest, France/SFTS)

Kari Aranko (European Blood Alliance/EBA)

Dana Devine (Canadian Blood Services/CBS)

Craig French (Western Health, Melbourne Australia)

Kathrine P. Frey (Fairview Health Services and Patient Readiness Institute, Minneapolis MN/AABB)

Christian Gabriel (Ludwig Boltzmann Institute for clinical and experimental traumatology, Austria/DGTI)

Richard Gammon (One Blood, Orlando/AABB)

Andreas Greinacher (Institut für Immunologie und Transfusionsmedizin Greifswald/ICTMG)

Marian van Kraaij (Sanquin, the Netherlands/EBA)

Jerrold Levy (Duke University School of Medicine, North Carolina/ISTH)

Giancarlo Liumbruno (Italian National Institute of Health/EBA)

Patrick Meybohm (University Clinics of the Johann Wolfgang Goethe University Frankfurt/Main)

Markus Müller (Institute for Transfusion Medicine and Immunohaematology Frankfurt/EBA)

Mike Murphy (NHS Blood & Transplant and AABB/EBA)

Hans Van Remoortel (Centre for Evidence-Based Practice, Belgian Red Cross)

Ben Saxon (Australian Red Cross Blood Service/ARCBS)

Erhard Seifried (German Red Cross Blood Transfusion Services/EBA) **(chair)**

Nadine Shehata (Mount Sinai Hospital Toronto/ICTMG)

Pierre Tiberghien (French National Blood Service/EBA)

Claudio Velati (Società Italiana di Medicina Trasfusionale e Immunoematologia)

Erica Wood (Epidemiology and Preventive Medicine at Monash University/ISBT)

Face-to-face meeting SciCom February 2017



Patient Blood Management: 3 topics of interest & 17 PICO questions

P	I	C	O
Population Patient Problem	Intervention Or Exposure	Comparison	Outcome
Who are the patients? What is the problem?	What do we do to them? What are they exposed to?	What do we compare the intervention with?	What happens? What is the outcome?



Patient Blood Management: 3 topics of interest

Scientific Committee



Topic 1: Preoperative anaemia

- ✓ Definition and diagnosis (PICO 1 and PICO 2)
- ✓ Treatment (PICO 3)

Topic 2: RBC transfusion triggers

- ✓ Intensive care and acute interventions (PICO 4-9 & PICO 14)
- ✓ Haematology and oncology (PICO 10 & PICO 11)
- ✓ Neurology (PICO 12 & PICO 13)

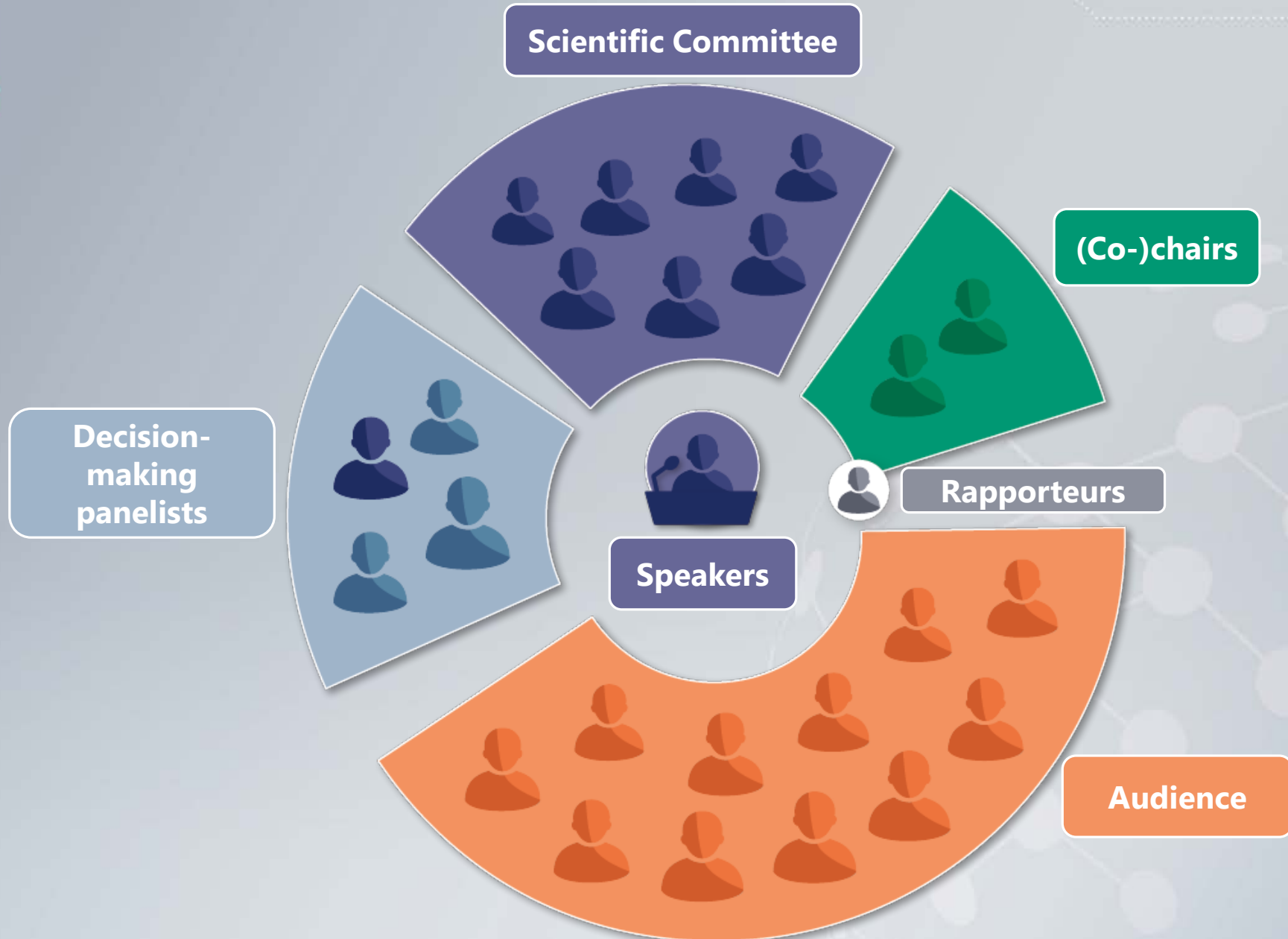
Topic 3: PBM implementation

- ✓ Effectiveness implementation of 'comprehensive' PBM programs (PICO 15)
- ✓ Effectiveness behavioural interventions (PICO 16)
- ✓ Effectiveness decision support systems (PICO 17)



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Consensus Development Conference (CDC)





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Consensus Development Conference (CDC)

Major steps?



Tuesday 24 April 2018

3 Parallel sessions



Rapporteurs



Audience



(Co-)chairs



Panelists



Speakers

Session 1: Preoperative anaemia



+



- ✓ Definition and diagnosis (PICO 1 and PICO 2)
- ✓ Treatment (PICO 3)

Session 2: RBC transfusion triggers



+



- ✓ Intensive care and acute interventions (PICO 4-9 & PICO 14)
- ✓ Haematology and oncology (PICO 10 & PICO 11)
- ✓ Neurology (PICO 12 & PICO 13)

Session 3: PBM implementation



+



- ✓ Effectiveness implementation of 'comprehensive' PBM programs (PICO 15)
- ✓ Effectiveness behavioural interventions (PICO 16)
- ✓ Effectiveness decision support systems (PICO 17)



Part 1: Plenary

- Evidence presented by
- Based on Evidence-to-Decision (EtD) framework
 - Discussion with
 - moderated by
 - Notes recorded by



Part 2: Closed (private/executive session)

- Based on EtD framework
 - Draft recommendations by
 - Moderated by
 - Notes recorded by



Draft conclusions at the end of day 1



Closed session with chairs/decision-making panels/rapporteurs

TYPE OF RECOMMENDATION	Strong recommendation against the intervention <input type="checkbox"/>	Conditional recommendation against the intervention <input type="checkbox"/>	Conditional recommendation for either the intervention or the comparison <input type="checkbox"/>	Conditional recommendation for the intervention <input type="checkbox"/>	Strong recommendation for the intervention <input type="checkbox"/>
RECOMMENDATION	<p>Option 1: Formulation of a strong or conditional recommendation Terminology strong recommendation: “we recommend...” – “clinicians should...” – “clinicians should not...” – “Do...” – “Don’t.....” Terminology weak/conditional recommendation: “we suggest...” – “clinicians might...” – “we conditionally recommend...”</p> <p>Option 2: No recommendation</p> <p>Option 3: Research recommendation</p>				
JUSTIFICATION	...				
SUBGROUP CONSIDERATIONS	...				
IMPLEMENTATION CONSIDERATIONS	...				
MONITORING AND EVALUATION	...				
RESEARCH PRIORITIES	...				



Wednesday 25 April 2018



Rapporteurs









Audience



(Co-)chairs



Panelists

- Plenary session with the general audience (all 3 topics)
 - Presentation draft recommendations/justifications by 
 - Discussion with , moderated by the 
 - Notes recorded by 
- Closed sessions with the decision-making panelists and (co-)chairs
 - Formulation of final recommendations by , moderated by the 



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Patient blood management (PBM) is a patient-focused, **evidence-based and systematic approach** to optimize the management of patient and transfusion of blood products for quality and effective patient care.

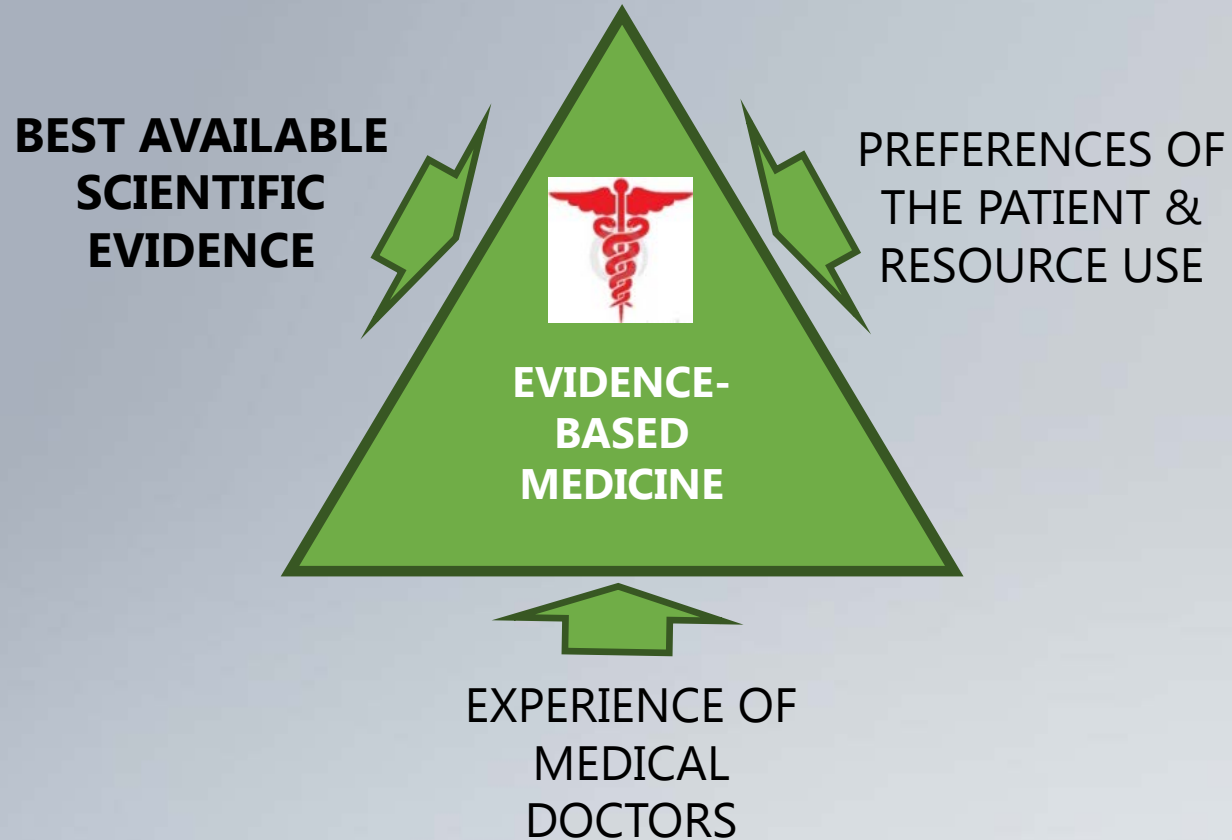


World Health
Organization



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Evidence-based methodology



GRADE

<http://www.gradeworkinggroup.org/>

- **G**radings of **R**ecommendations **A**ssessment, **D**evelopment and **E**valuation
- Common, sensible and transparent approach to grading:
 - Quality (or certainty) of evidence
 - Strength of recommendations



GRADE approach

From evidence to recommendations – transparent and sensible

March 2017 – February 2018

Screening ~18.000 references in
4 databases from date of
inception until January 2018
with **142 studies** finally included

Formulate question
Select outcomes
Rate importance

P I C O	Outcome	Critical	
	Outcome	Critical	
	Outcome	Important	
	Outcome	Not important	



Systematic review



Scientific Committee

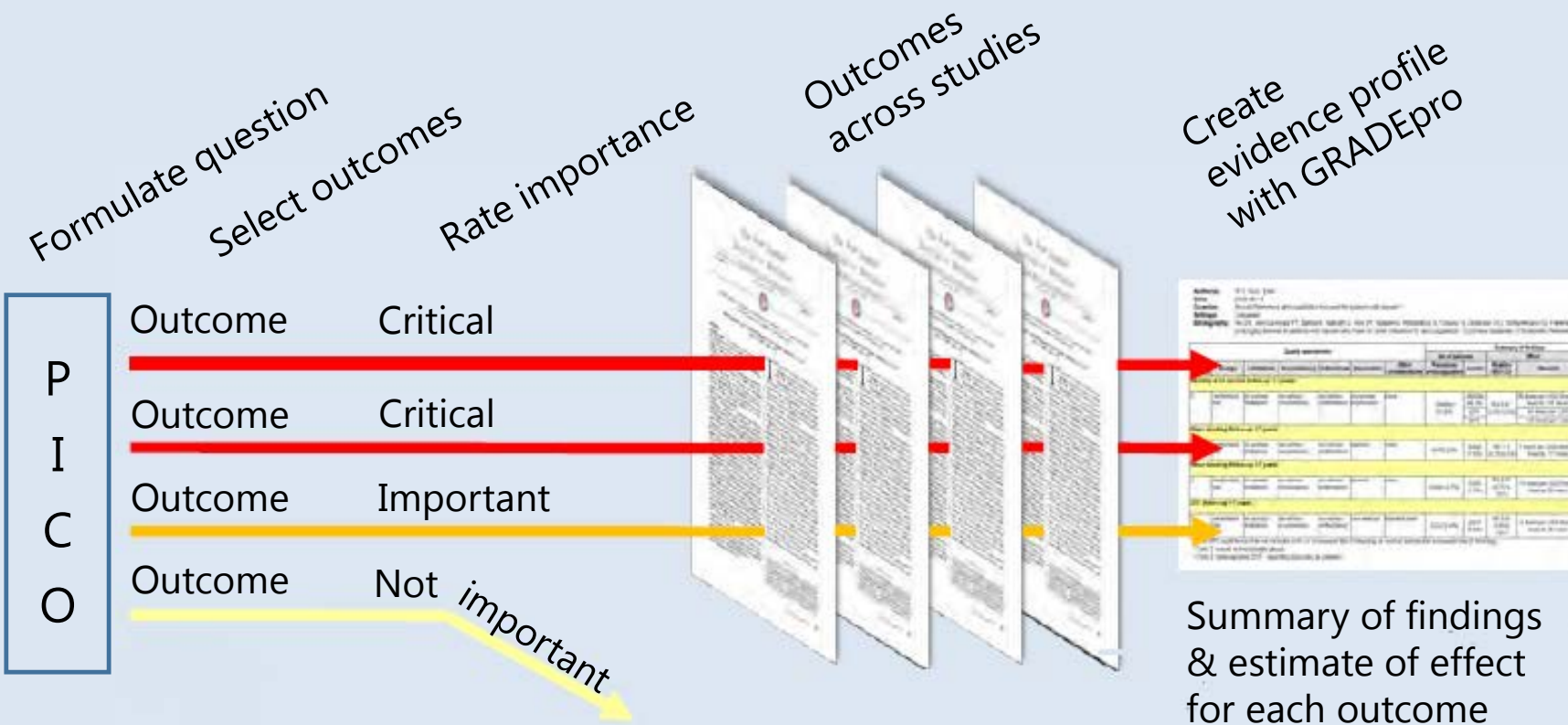




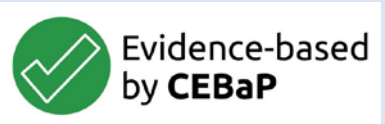
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GRADE approach

From evidence to recommendations – transparent and sensible



Systematic review



Scientific Committee





GRADE approach

From evidence **to recommendations** – transparent and sensible



Guideline development

Decision-making
panelists



Formulation of a recommendation (option 1)

- For or against (direction) ↑↓
- Strong or conditional/weak (strength)



By considering balance of consequences and making judgments on 10 pre-specified criteria



Evidence-to-Decision (EtD) framework



Evidence-to-Decision framework

CRITERIA	JUDGEMENT
1. DESIRABLE EFFECTS	How substantial are the desirable anticipated effects?
2. UNDESIRABLE EFFECTS	How substantial are the undesirable anticipated effects?
3. CERTAINTY OF EVIDENCE	What is the overall quality of the evidence of effects?
4. VALUES	Is there important uncertainty about or variability in how much people value the critical outcomes?
5. BALANCE OF EFFECTS	Does the balance between desirable and undesirable effects favor the intervention or the comparison?
6. RESOURCES REQUIRED	How large are the resource requirements (costs)?
7. COST EFFECTIVENESS	Does the cost-effectiveness of the intervention favor the intervention or the comparison?
8. EQUITY	What would be the impact on health equity?
9. ACCEPTABILITY	Is the intervention acceptable to key stakeholders?
10. FEASIBILITY	Is the intervention feasible to implement?

Example

1. How substantial are the desirable effects?

- Trivial
- Small
- Moderate**
- Large

- Varies
- Don't know

Evidence-to-Decision framework

CRITERIA	JUDGEMENT	RESEARCH EVIDENCE
1. DESIRABLE EFFECTS	How substantial are the desirable anticipated effects?	EVIDENCE
2. UNDESIRABLE EFFECTS	How substantial are the undesirable anticipated effects?	
3. CERTAINTY OF EVIDENCE	What is the overall quality of the evidence of effects?	EVIDENCE
4. VALUES	Is there important uncertainty about or variability in how much people value the critical outcomes?	
5. BALANCE OF EFFECTS	Does the balance between desirable and undesirable effects favor the intervention or the comparison?	EVIDENCE
6. RESOURCES REQUIRED	How large are the resource requirements (costs)?	EVIDENCE
7. COST EFFECTIVENESS	Does the cost-effectiveness of the intervention favor the intervention or the comparison?	
8. EQUITY	What would be the impact on health equity?	
9. ACCEPTABILITY	Is the intervention acceptable to key stakeholders?	
10. FEASIBILITY	Is the intervention feasible to implement?	



Speakers



Speakers























Speakers



Speakers

Evidence-to-Decision framework

CRITERIA	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS	
1. DESIRABLE EFFECTS	How substantial are the desirable anticipated effects?	EVIDENCE	 Rapporteurs	 Audience
2. UNDESIRABLE EFFECTS	How substantial are the undesirable anticipated effects?		 Rapporteurs	 Audience
3. CERTAINTY OF EVIDENCE	What is the overall quality of the evidence of effects?	EVIDENCE	 Rapporteurs	 Audience
4. VALUES	Is there important uncertainty about or variability in how much people value the critical outcomes?	OPINION POLL	 Rapporteurs	 Audience
5. BALANCE OF EFFECTS	Does the balance between desirable and undesirable effects favor the intervention or the comparison?	EVIDENCE	 Rapporteurs	 Audience
6. RESOURCES REQUIRED	How large are the resource requirements (costs)?	EVIDENCE	 Rapporteurs	 Audience
7. COST EFFECTIVENESS	Does the cost-effectiveness of the intervention favor the intervention or the comparison?		 Rapporteurs	 Audience
8. EQUITY	What would be the impact on health equity?	OPINION POLL	 Rapporteurs	 Audience
9. ACCEPTABILITY	Is the intervention acceptable to key stakeholders?	OPINION POLL	 Rapporteurs	 Audience
10. FEASIBILITY	Is the intervention feasible to implement?	OPINION POLL	 Rapporteurs	 Audience



How does **GRADE** classify the strength of recommendations?

- Strong recommendation

- Desirable effects of an intervention clearly outweigh the undesirable effects (or clearly do not)
- Moderate/High-quality research with large, precise effect
- Low resource allocation

- Conditional recommendation

- Desirable effects not clearly greater or smaller than undesirable effects
- Low quality evidence with imprecise estimate
- High resource allocation



GRADE approach

From evidence **to recommendations** – transparent and sensible

Guideline development

Decision-making
panelists



Formulation of a recommendation (option 1)

- For or against (direction) ↑↓
- Strong or conditional/weak (strength)

No recommendation (option 2)

- Very low quality evidence
- Trade offs closely balanced

Research recommendation (option 3)

- Insufficient evidence
- Further research has a large potential for reducing the uncertainty about the effect of the intervention

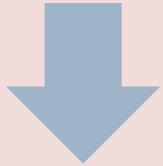


GRADE approach

From evidence **to recommendations** – transparent and sensible

Guideline development

Strong/conditional recommendation
No recommendation
Research recommendation

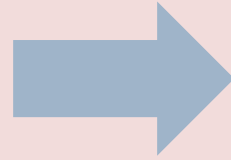


*By considering balance of consequences
(evidence to recommendation)*

- Quality of evidence
- Balance benefits/harms
- Values and preferences
- Resource use (cost(-)effectiveness)
- Equity – Acceptability - Feasibility

EtD framework

Summary of Judgements		Benefits		Harms	
Outcome	Quality	High	Low	High	Low
Outcome 1	High	Yes	No	No	Yes
Outcome 2	Low	No	Yes	Yes	No
Outcome 3	Very Low	No	No	Yes	Yes
Outcome 4	Very Low	Yes	Yes	No	No
Outcome 5	Very Low	No	No	No	No



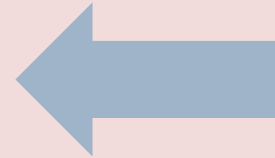
Guideline



Formulate recommendations

- “We recommend using...”
- “We recommend against using...”
- “We suggest using...”
- “We suggest against using...”

Transparency, clear, actionable Research?





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INDICATIVE OPINION POLLS BY AUDIENCE

- GRADE criteria not covered by research evidence (Tuesday)
- Draft recommendations (Wednesday)



 **Mentimeter**

VOTING BY DECISION-MAKING PANELISTS

- Show of hands – consensus = 2/3 majority

MEETING ROOMS

Tuesday | PARALLEL SESSIONS

- Pre-operative Anaemia – BERLIN/KÖLN
- RBC Transfusion Triggers – MARITIM I
- Implementation of PBM – MARITIM II/III

Wednesday | PLENARY SESSION

- Maritim I/II/III