



# WHY EVIDENCE-BASED MEDICINE IS SO IMPORTANT FOR DESIGNING CLINICAL RESEARCH AND CLINICAL PRACTICE

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Editor in Chief, *The Cochrane Library*

# Evidence and research



# Why are systematic reviews important in research?



- Can identify uncertainties and guide research
- Can improve the conduct and reporting of primary research

# Why are systematic reviews important in research?

“investment in additional research should always be preceded by systematic assessment of existing evidence.”



How to increase value and reduce waste when research priorities are set  
Iain Chalmers DSc, Prof Michael B Bracken PhD, Prof Ben Djulbegovic PhD, Silvio Garattini MD, Jonathan Grant PhD, A Metin Gülmezoglu PhD, David W Howells PhD, Prof John P A Ioannidis MD, Sandy Oliver PhD  
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DOI: 10.1016/S0140-6736(13)62229-1

# Putting clinical studies into context

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### Putting research into context—revisited

[Stephanie Clark](#) <sup>a</sup>, [Richard Horton](#) <sup>a</sup>

“Authors should either report their own, up-to-date systematic review or cite a recent systematic review of other trials, putting their trial into context... A systematic review is the key component of putting research into context. We believe that this guideline should apply to all research, not only to randomised trials. “

# Case example

## Corticosteroids for acute traumatic brain injury (Review)

Alderson P, Roberts I



### Authors' conclusions

Neither moderate benefits nor moderate harmful effects of steroids can be excluded. The widely practicable nature of the drugs and the importance of the health problem suggest that **large simple trials are feasible**, and worthwhile, to establish whether there are any benefits from corticosteroids in this situation.

Title:	Corticosteroids for acute traumatic brain injury
Byline:	Alderson P, Roberts I
Publ. status:	Published in Issue 4, 2002 - Issue 4, 2004

# Case example

## Corticosteroids for acute traumatic brain injury (Review)

Alderson P, Roberts I



### Authors' conclusions

A new large study with about 80% of the total participants was completed by the time of the 2006 update of this review. This study, called CRASH, showed a significant increase in number of deaths in patients given steroids compared with patients who received no treatment. **The significant increase in deaths with steroids suggests that steroids should no longer be routinely used in people with traumatic head injury.**

Title:	Corticosteroids for acute traumatic brain injury
Byline:	Alderson P, Roberts I
Publ. status:	Published in Issue 2, 2007

# Why are systematic reviews important in research?

Systematic reviews can improve the quality of primary research...



How to increase value and reduce waste when research priorities are set  
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# Systematic review methods can improve the quality of clinical studies



Enhancing the QUALity and  
Transparency Of health Research



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## Toolkits

This section of our website will help you to use guidance listed in our Library to promote, teach and practice accurate, complete and ethical publication of health research.

In addition we also provide practical resources for groups developing reporting guidelines to ensure the highest standards and usefulness of these guidelines.



### Authors

Information and resources for authors



## Key reporting guidelines

<a href="#">CONSORT</a>	<a href="#">Full Record</a>   <a href="#">Checklist</a>   <a href="#">Flow Diagram</a>
<a href="#">STROBE</a>	<a href="#">Full Record</a>   <a href="#">Checklist</a>
<a href="#">PRISMA</a>	<a href="#">Full Record</a>   <a href="#">Checklist</a>   <a href="#">Flow Diagram</a>
<a href="#">STARD</a>	<a href="#">Full Record</a>   <a href="#">Checklist</a>   <a href="#">Flow Diagram</a>
<a href="#">COREQ</a>	<a href="#">Full Record</a>
<a href="#">ENTREQ</a>	<a href="#">Full Record</a>
<a href="#">SQUIRE</a>	<a href="#">Full Record</a>   <a href="#">Checklist</a>
<a href="#">CHEERS</a>	<a href="#">Full Record</a>   <a href="#">Checklist</a>
<a href="#">CARE</a>	<a href="#">Full Record</a>   <a href="#">Checklist</a>
<a href="#">SAMPL</a>	<a href="#">Full Record</a>



Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ang 2008	?	?	-	+	+	+	+
Assmus 2006	+	?	-	+	+	+	+
Assmus 2012	?	?	?	?	?	+	+
Chen 2006	?	?	-	?	+	+	+
Erbs 2005	?	?	+	+	+	+	+
Hendriks 2006	+	+	+	+	+	+	+
Honold 2012	?	?	?	?	+	+	+
Hu 2011	+	?	+	+	+	+	+
Kang 2006	+	?	-	?	+	+	+
Losordo 2007	+	?	+	+	+	+	+
Losordo 2011	+	+	+	+	+	+	+

# Evidence and clinical practice



# Trust in medicine

- ❑ Compassion
- ❑ Competence
- ❑ Shared power
- ❑ Personal care
- ❑ Realism

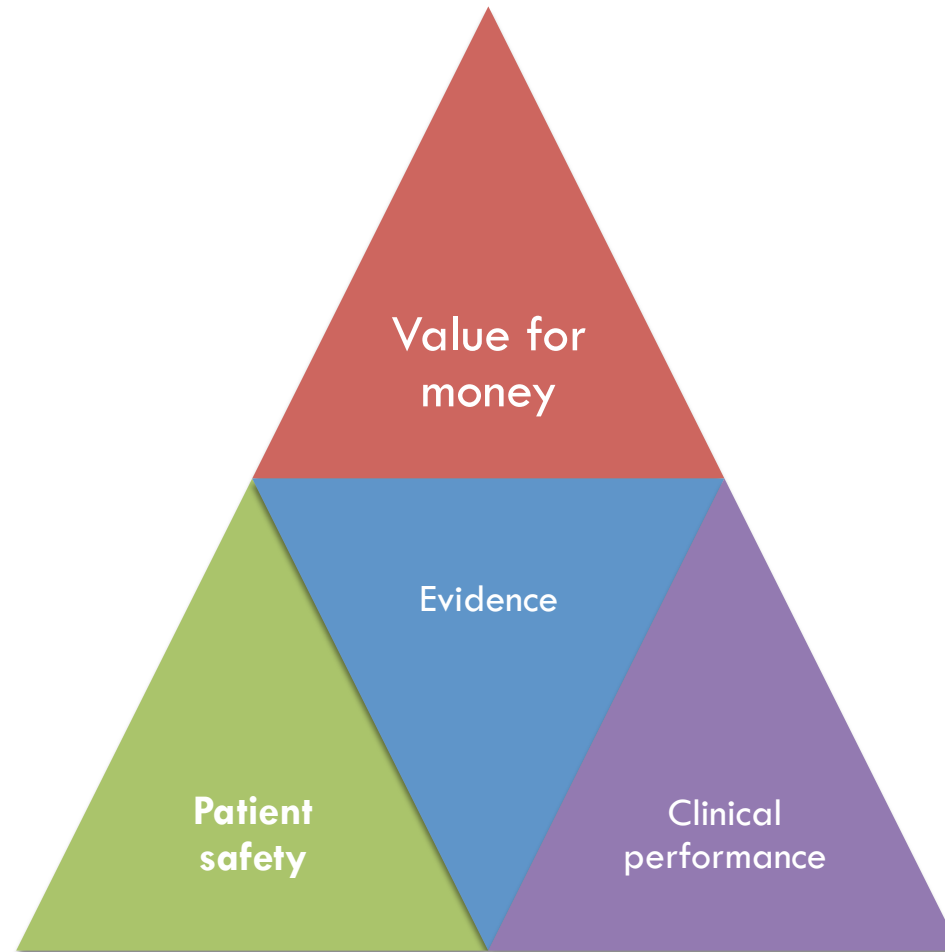


# Trust in medicine

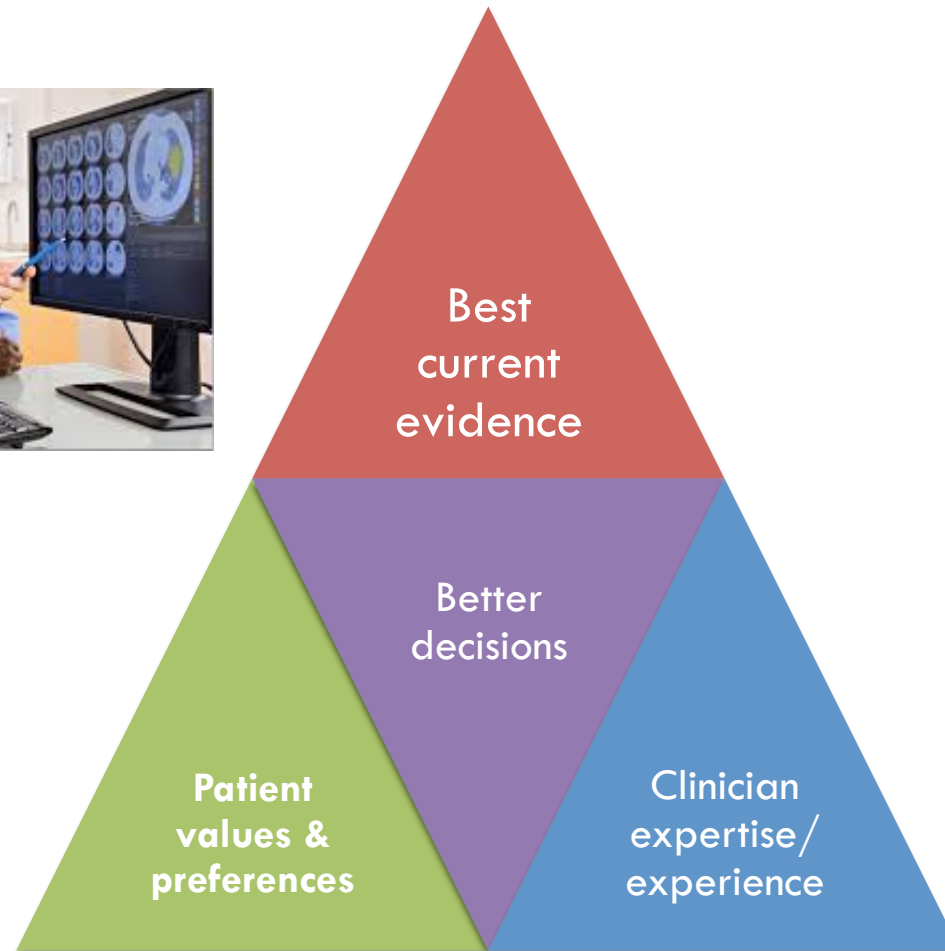
- ☐ Compassion
- ☐ Competence
- ☐ Shared power
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- ☐ Realism



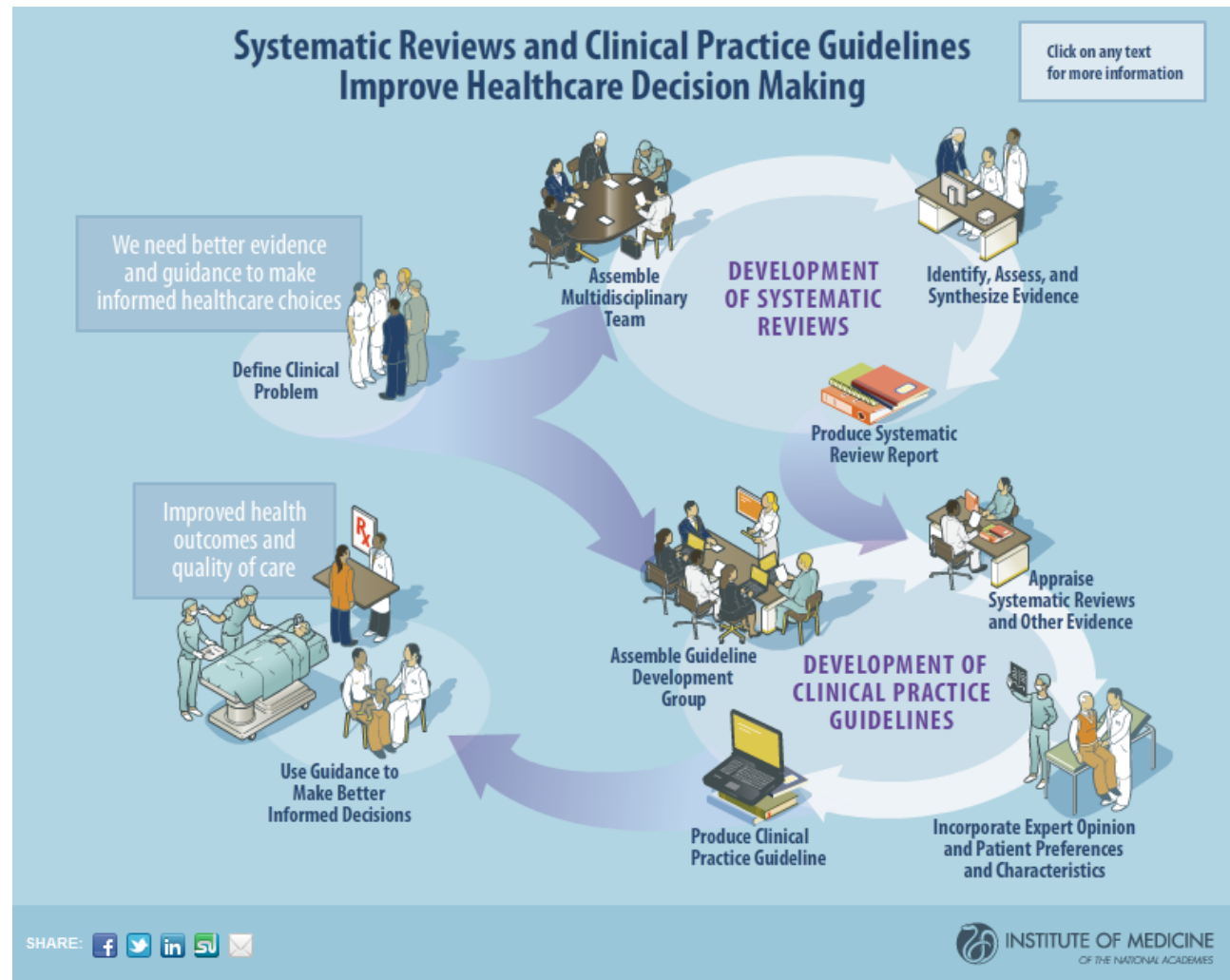
# Why is evidence important?



# Why is evidence important?



# Why are systematic reviews important in guiding practice and policy?





# Why are systematic reviews important in guiding practice and policy?

- Aim to capture all the relevant high quality evidence (comprehensive search)
- Analyse the risk of bias of included studies and the quality of the evidence
- May provide a pooled estimate of effect from all studies (increase power and precision)
- May represent the highest quality evidence to guide practice and policy decision making

# What is Cochrane?



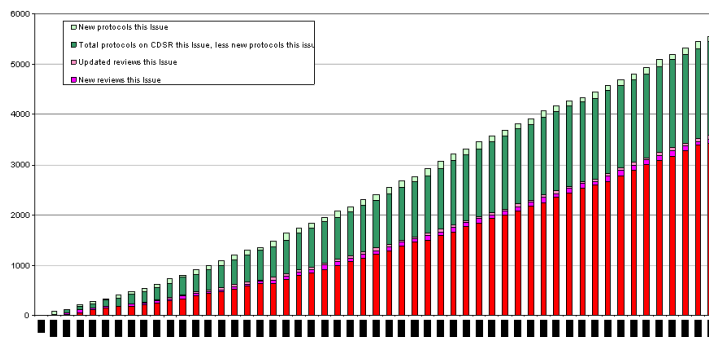
The Cochrane Collaboration is an **international** organisation that aims to help people make **well-informed decisions** about health care by **preparing, maintaining and promoting** the accessibility of **systematic reviews** of the effects of healthcare interventions

>28,000 people

>100 countries



Reviews and protocols for reviews on the  
Cochrane Database of Systematic Reviews

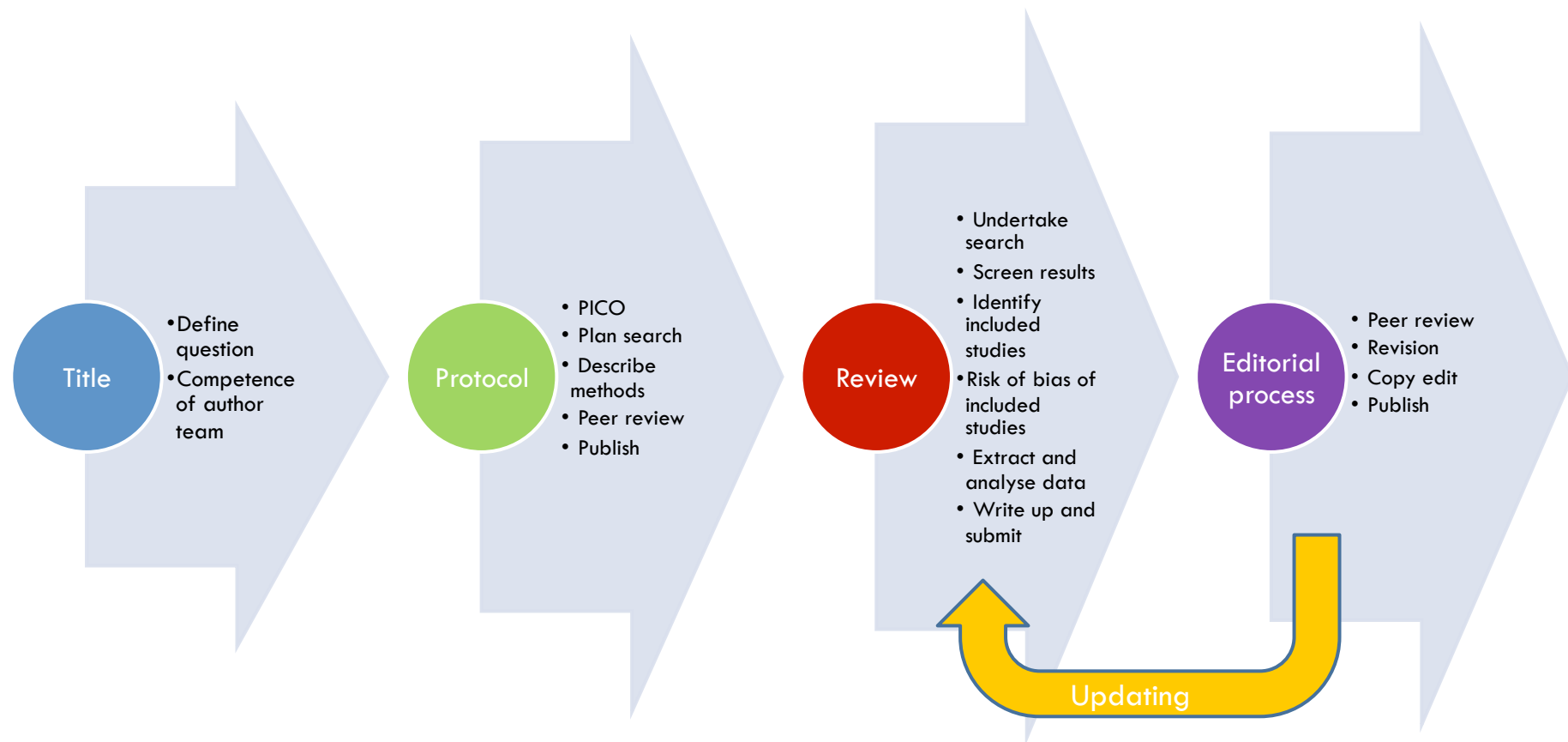


**Advocating** for evidence  
informed decision making

**Cochrane evidence used**  
worldwide by wide range of  
stakeholders in diverse products  
and activities

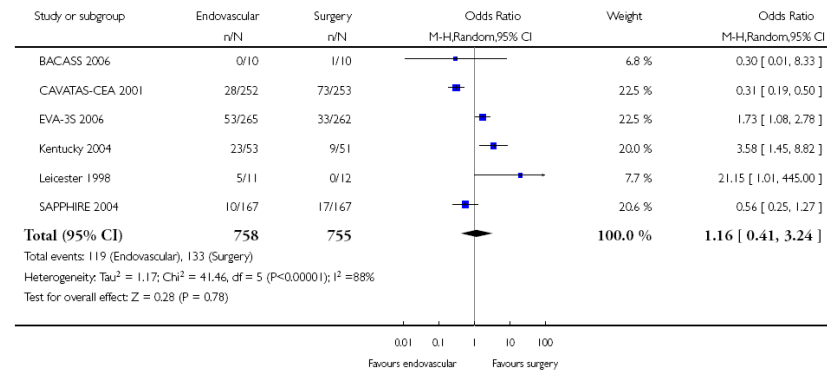
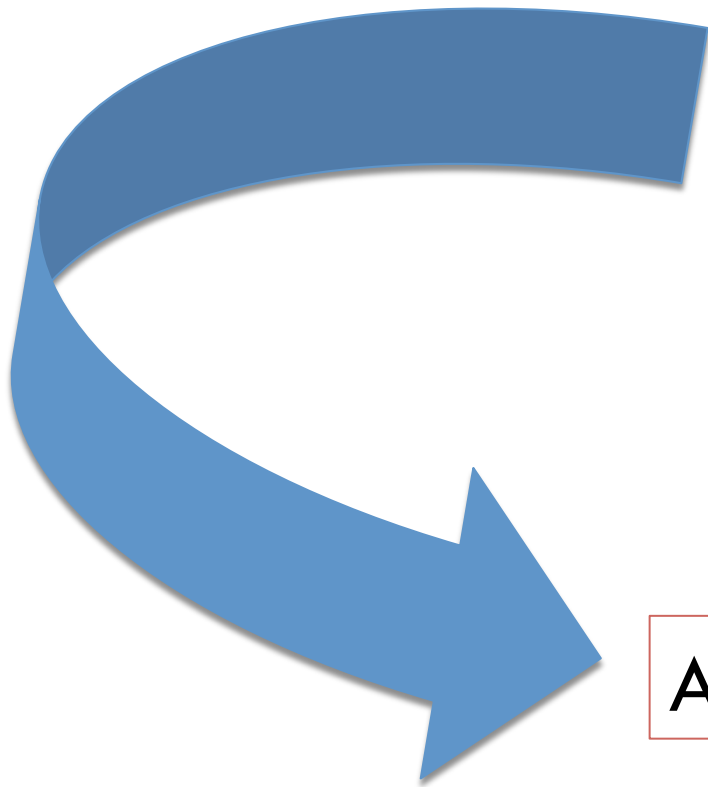
**Advancing** the **science** of  
synthesis

# The Cochrane process



# Cochrane and GRADE..

- What is the problem we are trying to fix?



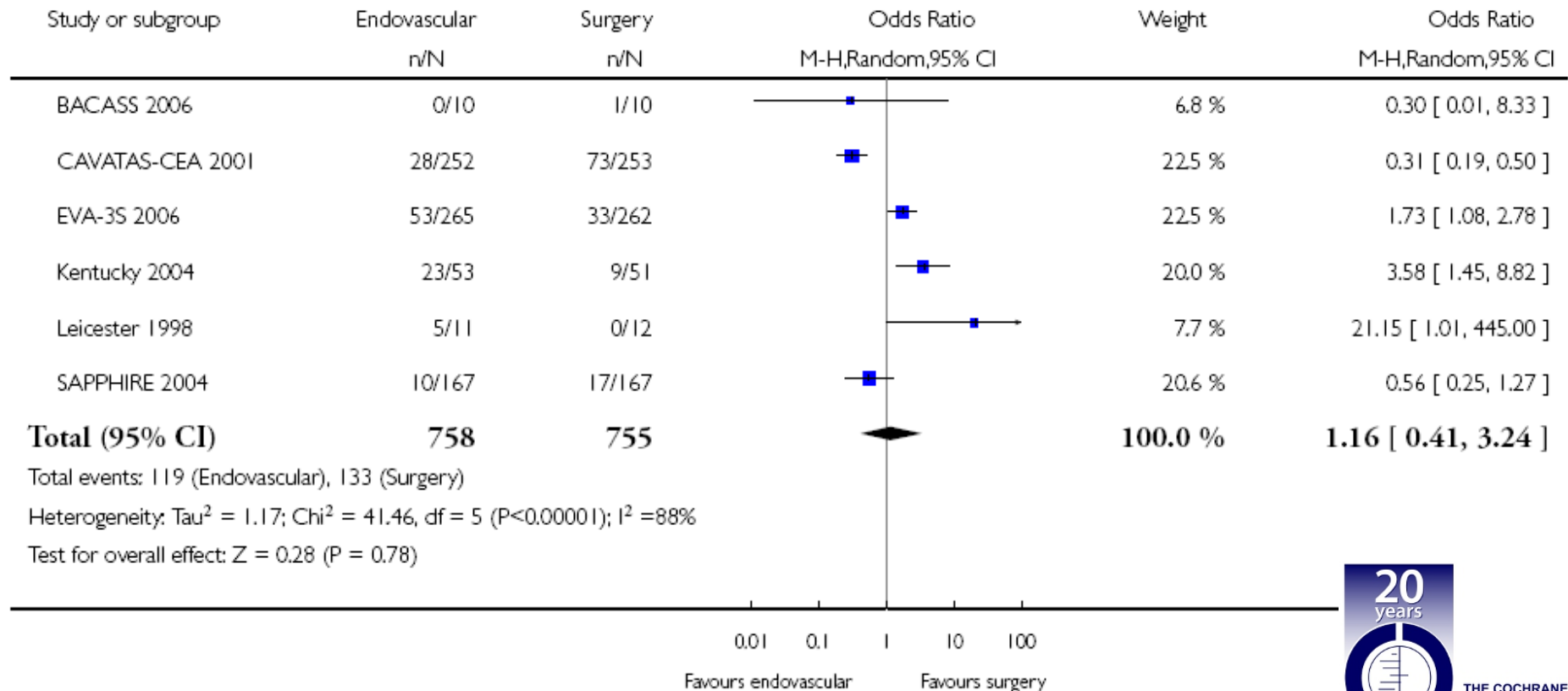
Authors' conclusions

# Cochrane and GRADE



- For a given **outcome and comparison** is there any effect/difference?
- If so, which **drug/treatment** came out better?
- By how much?
- How certain are we?

# Cochrane and GRADE



# Judging quality: summary

Quality of evidence	Study design	Lower if...	Higher if...
High	Randomized trial	Study limitations	Large effect (e.g., RR 0.5) Very large effect (e.g., RR 0.2)
Moderate		Inconsistency	Evidence of dose-response gradient
Low	Observational study	Indirectness	All plausible confounding would reduce a demonstrated effect
Very low		Imprecision	
		Publication bias	

# Conceptualizing quality

High	We are <b>very confident</b> that the true effect lies close to that of the estimate of the effect.
Moderate	We are <b>moderately confident</b> in the estimate of effect: The true effect is likely to be close to the estimate of effect , but possibility to be substantially different.
Low	Our <b>confidence</b> in the effect <b>is limited</b> : The true effect may be substantially different from the estimate of the effect.
Very low	We have <b>very little confidence</b> in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.



# Cochrane and GRADE


## Parenteral anticoagulation for patients with cancer

**Patient or population:** patients with advanced cancer

**Settings:** Outpatient

**Intervention:** Parenteral anticoagulation

Outcomes	Absolute risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of evidence (GRADE)	Comments
	Control	Parenteral anticoagulation				
<b>Mortality at 12 months</b> Follow-up: 1-7 years	<b>Study population</b>		<b>RR 0.87</b> (0.8 to 0.95)	1174 (5 studies)	⊕⊕⊕⊕ <b>high</b>	
	<b>663 per 1000</b>	<b>577 per 1000</b> (530 to 630)				
	<b>Low risk population</b>					
	<b>500 per 1000</b>	<b>435 per 1000</b> (400 to 475)				
	<b>High risk population</b>					
	<b>900 per 1000</b>	<b>783 per 1000</b> (720 to 855)				
<b>Major bleeding</b> Follow-up: 1-7 years	<b>15 per 1000</b>	<b>22 per 1000</b> (4 to 132)	<b>RR 1.5</b> (0.26 to 8.8)	814 (3 studies)	⊕⊕⊕⊖ <b>moderate</b> <sup>1</sup>	
<b>Minor bleeding</b> Follow-up: 1-7 years	<b>13 per 1000</b>	<b>27 per 1000</b> (10 to 72)	<b>RR 2.07</b> (0.78 to 5.51)	760 (3 studies)	⊕⊕⊕⊖ <b>moderate</b> <sup>1</sup>	
<b>DVT</b> Follow-up: 1-7 years	<b>9 per 1000</b>	<b>5 per 1000</b> (1 to 44)	<b>RR 0.61</b> (0.08 to 4.91)	458 (2 studies)	⊕⊖⊖⊖ <b>very low</b> <sup>2,3</sup>	



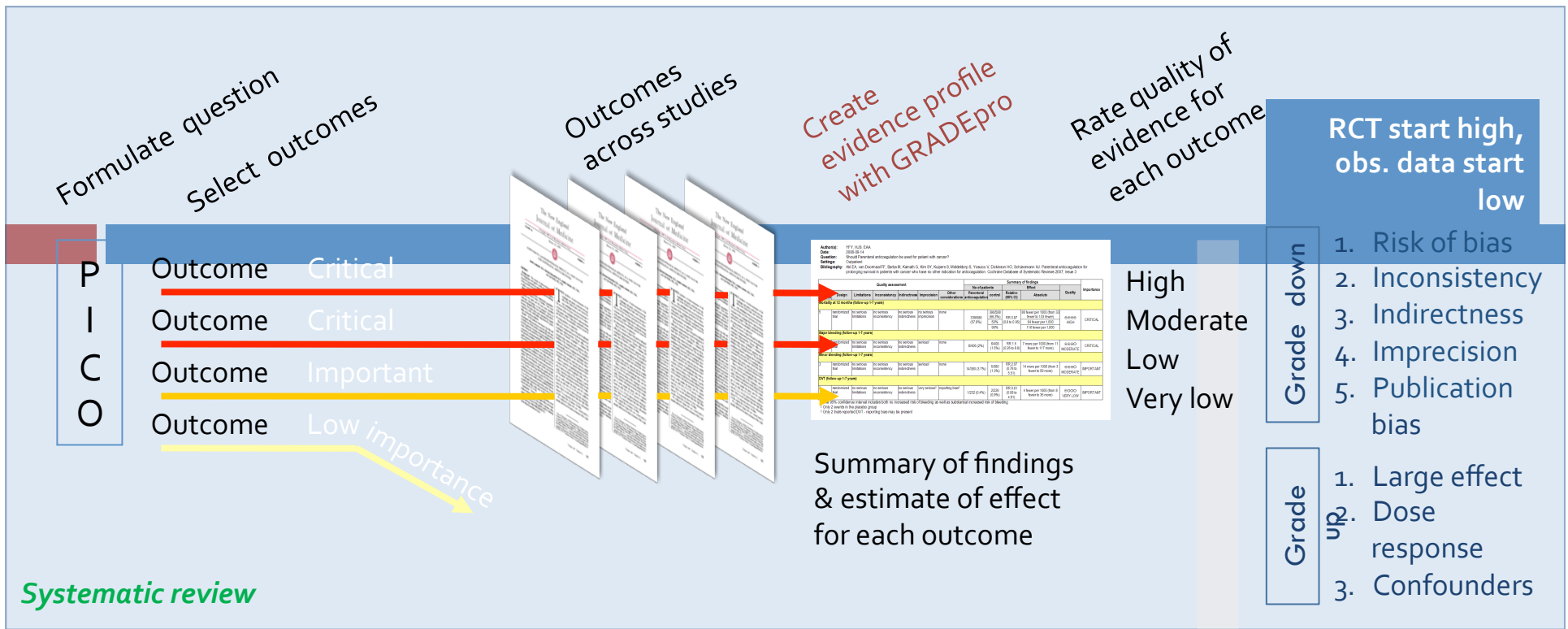
<sup>1</sup> The 95% confidence interval includes both no increased risk of bleeding as well as substantial increased risk of bleeding

<sup>2</sup> Only 2 events in the placebo group

<sup>3</sup> Only 2 trials reported DVT - reporting bias may be present



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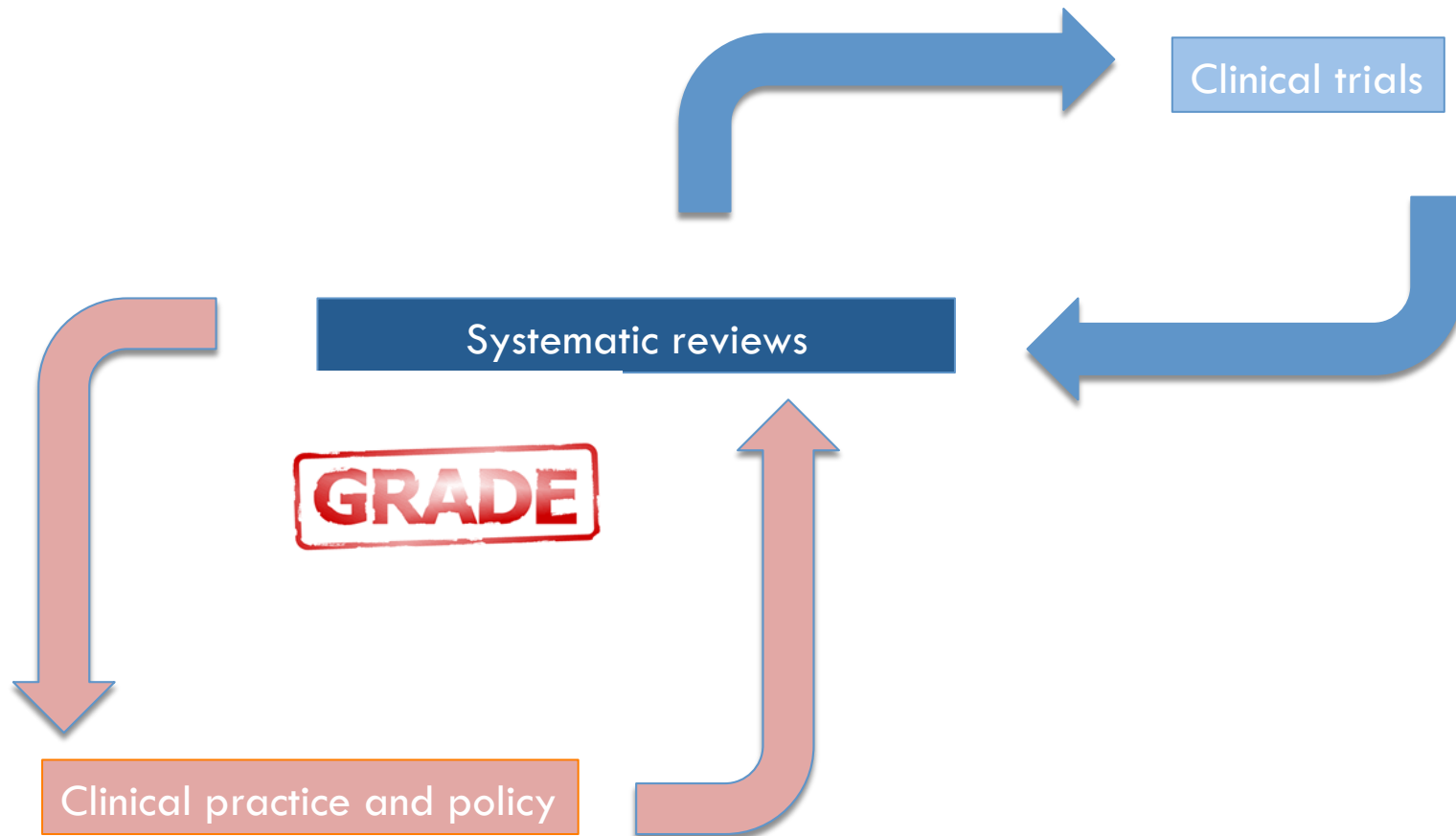


# What are the key elements

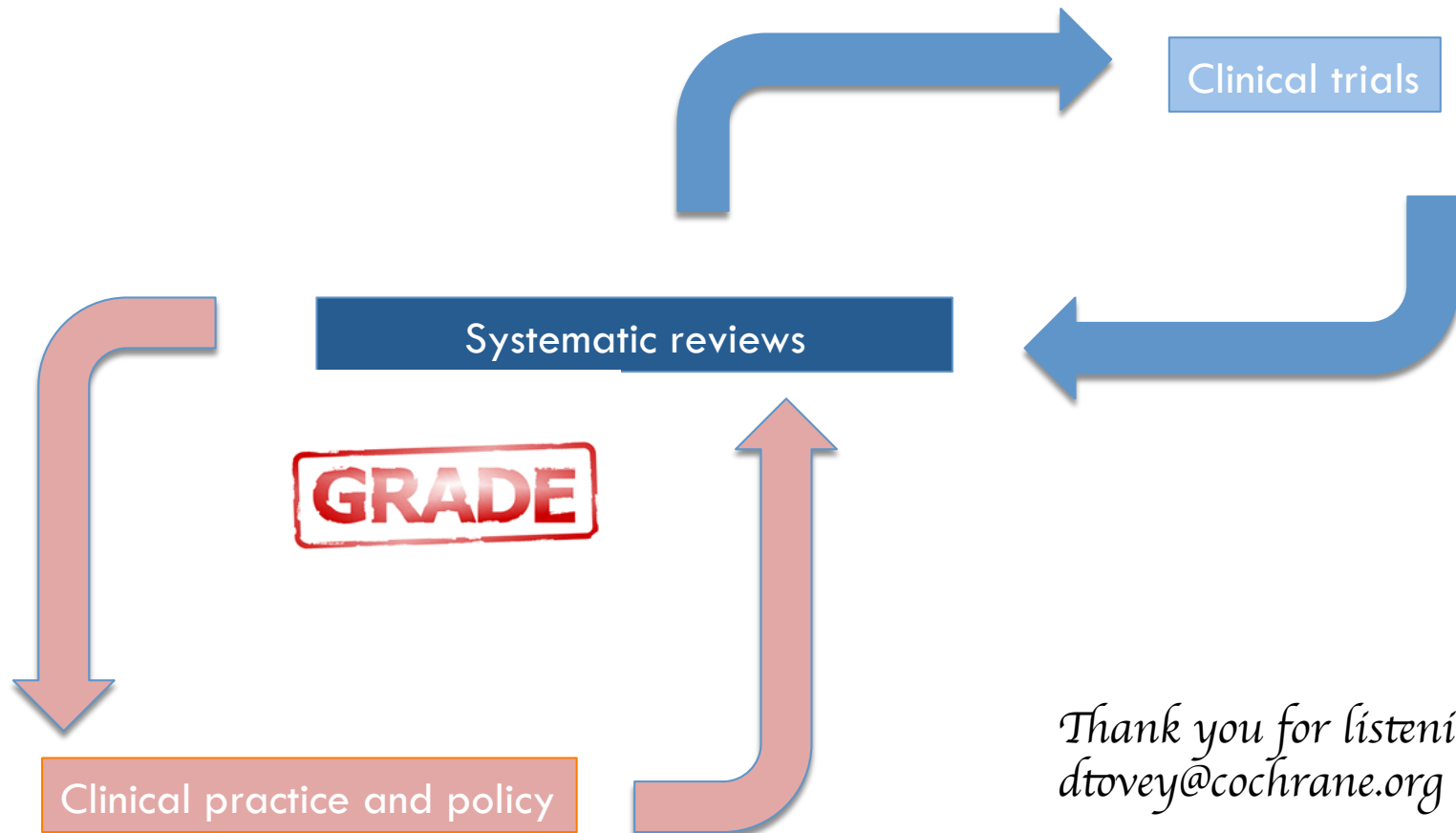


- ❑ Sorted by clinical outcomes that matter (not studies..)
- ❑ Takes into consideration issues that increase/decrease our confidence in the results
- ❑ Flexibility in relation to study type
- ❑ Reports “relative” and “absolute” effects
- ❑ Reduces dependence on arbitrary measure of statistical significance
- ❑ Encourage researchers to consider *a priori* what is the minimum clinically important difference for main outcomes

# Conclusions



# Conclusions



*Thank you for listening  
dtovey@cochrane.org*