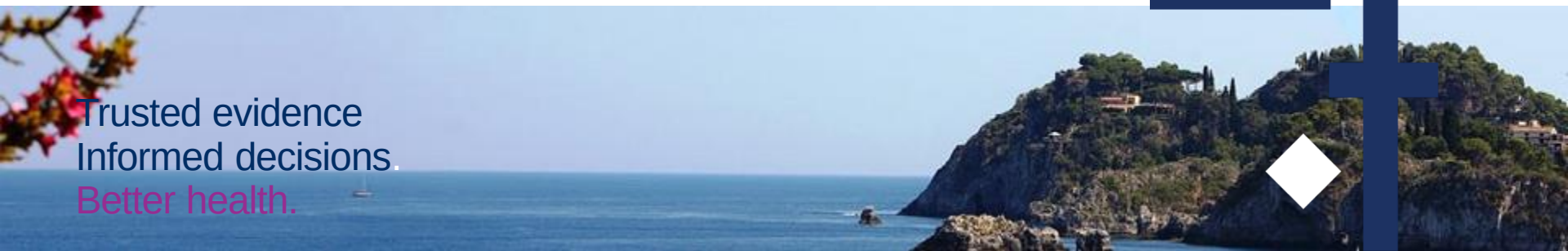
The evolving science of evidence synthesis: lessons learnt from Cochrane reviews

Presentation to:
EBHC Conference 2017,
Taormina, Sicily

David Tovey, Editor in Chief



Declaration of interest

I am a full time employee of Cochrane.

Thanks to James Thomas, Chris Mavergames, Liz Bickerdicke, and Miranda Cumpston for their help in preparing the following slides.

Evidence at a crossroads..

A crisis of ‘realism’

Don’t involve end users enough

Conflict of Interest

Influence of Pharma

Wrong questions

Poor coverage of harms

Scientific misconduct

RCTs too limited

A crisis of ‘realism’

Selection Bias

Don’t involve end users enough

Conflict of Interest

Influence of Pharma

Wrong questions

Attrition Bias

Waste

Publication Bias

Optimism Bias

Selective Outcome Reporting Bias

Scientific misconduct

RCTs too limited

Spin

Poor coverage of harms

Performance bias

EBM Manifesto

1) Expand the role of patients, health professionals and policy makers in research
2) Increase the systematic use of existing evidence
3) Make research evidence relevant, replicable and accessible to end users.
4) Reduce questionable research practices, bias, and conflicts of interests
5) Ensure drug and device regulation is robust, transparent and independent
6) Produce better usable clinical guidelines.
7) Support innovation, quality improvement, and safety through the better use of real world data.
8) Educate professionals, policy makers and the public in evidence-based healthcare to make informed choices.
9) Encourage the next generation of leaders in evidence-based medicine.

Evidence based medicine manifesto for better healthcare
A response to systematic bias, wastage, error, and fraud in research underpinning patient care
BMJ 2017; 357 doi: https://doi.org/10.1136/bmj.j2973

And meanwhile, the world moves on..

- Need answers much more quickly
- Growing interest in ‘real world data’
- More complex / versatile evidence
- Moves towards individualised health care: ‘personalised’ or ‘precision’ medicine

How is Cochrane responding?

The (Cochrane) Ecosystem of Evidence: connecting generation, synthesis & translation

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Cochrane Strategy to 2020

1. Producing high quality systematic reviews that address the priorities of decision makers
   - generation and synthesis

2. Ensuring that our evidence is accessible and used
   - translation

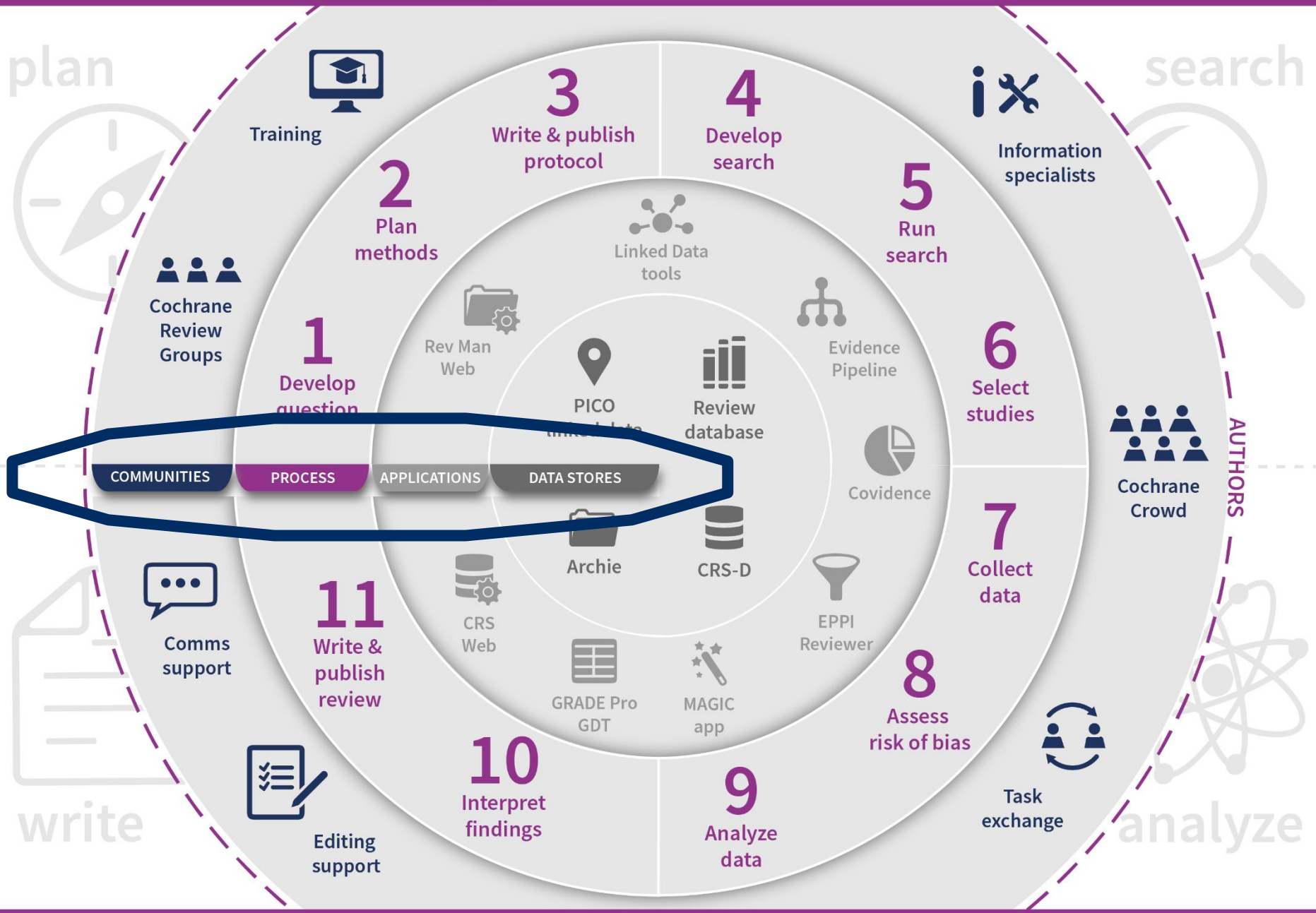
3. Advocating for Evidence
   - generation, synthesis and translation

4. Building an effective and sustainable organisation
   - generation, synthesis and translation

Cochrane

Trusted evidence.
Informed decisions.
Better health.

New Cochrane Review Ecosystem



The (Cochrane) Ecosystem of Evidence: generation and synthesis

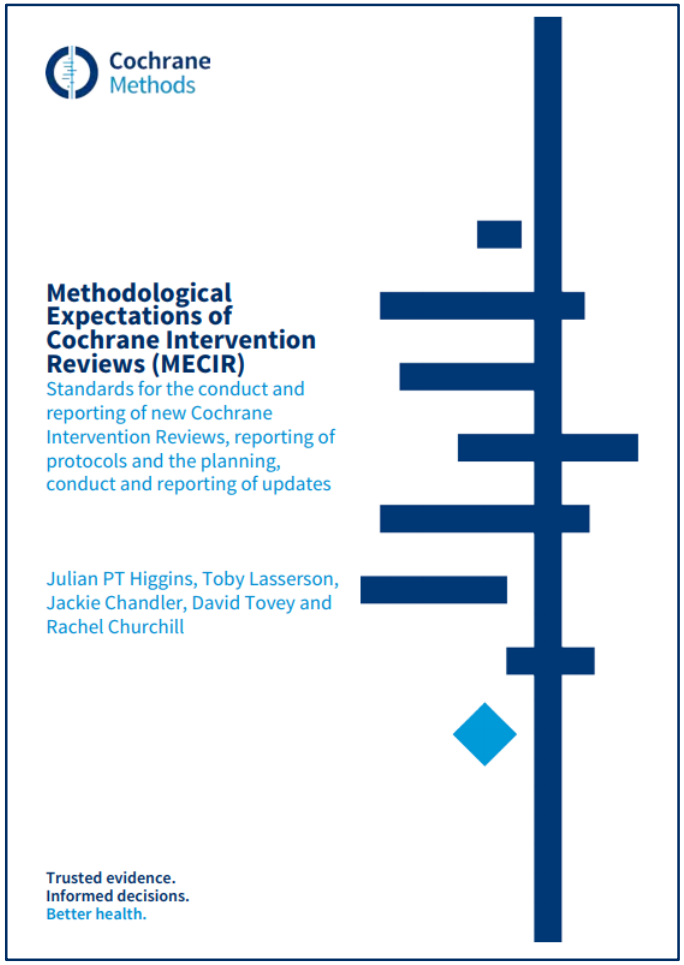
Improved engagement with key stakeholders

Knowledge Translation strategy

GRADE: at the heart of every review

- Outcomes not study based
- Intuitive and flexible
- Aids understanding & communication
  - Harms
  - Relative and absolute effects
  - Certainty of effect estimates
  - Improvements to the narrative
  - Provides an alternative to reliance on ‘statistical significance’

Adherence to quality standards



http://methods.cochrane.org/mecir

Cochrane Editorial Unit (CEU) Screening

- CEU has been screening new reviews against **key MECIR standards** since September 2013.

- Evolved to consider 3 core components of reviews as major determinants of overall review quality:
  1. implementation of protocol methods
  2. interpretation of findings
  3. consistency of reporting

- Development of a triage tool

The triage tool encourages…

- Spotting outliers and avoiding possible data errors:
  e.g. transposition, transcription and transformation errors
- Appropriate analysis of non-standard study designs:
  cluster RCTs, within-patient designs (e.g. X-over)
- Clear and consistent downgrading decisions in SoF tables
- Consistent interpretation
- Emphasising effect estimation over statistical significance
- Consistent reporting of data
- Complete reporting of important outcomes in summary versions

Consistent interpretation

Plain language summary: *"The effects of the intervention compared with control are uncertain"*

Main results: *"The intervention was also associated with statistically significantly greater improvements than control; however, the risk of bias in this RCT was high".*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
Outcome X	The mean measure of Outcome X in the control group was 6 points	The mean measure of Outcome X in the intervention groups was **0.47 points lower** (0.86 lower to 0.08 lower)		30 (1 study)	⊕⊖⊖⊖ **very low**[1]	

Footnotes

1 Imprecision due to sparse data; risk of bias due to lack of blinding, high rate of attrition, reporting and other bias

Emphasising effect estimation over statistical significance

Main results: *For the outcome of mortality at the end of the follow-up period, we found no statistical difference between the intervention and control groups (RR 1.46, 95% CI 0.99 to 2.13; I^2 = 10%; P = 0.05; low quality).*

Authors' conclusions: *The current evidence does not show a difference in the risk of mortality.*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
Mortality	**91 per 1000**	**131 per 1000** (90 to 193)	**RR 1.46** (0.99 to 2.13)	816 (6 RCTs)	⊕⊕⊖⊖ **low**	

Intervention Y may increase mortality by about 4% (low quality evidence).

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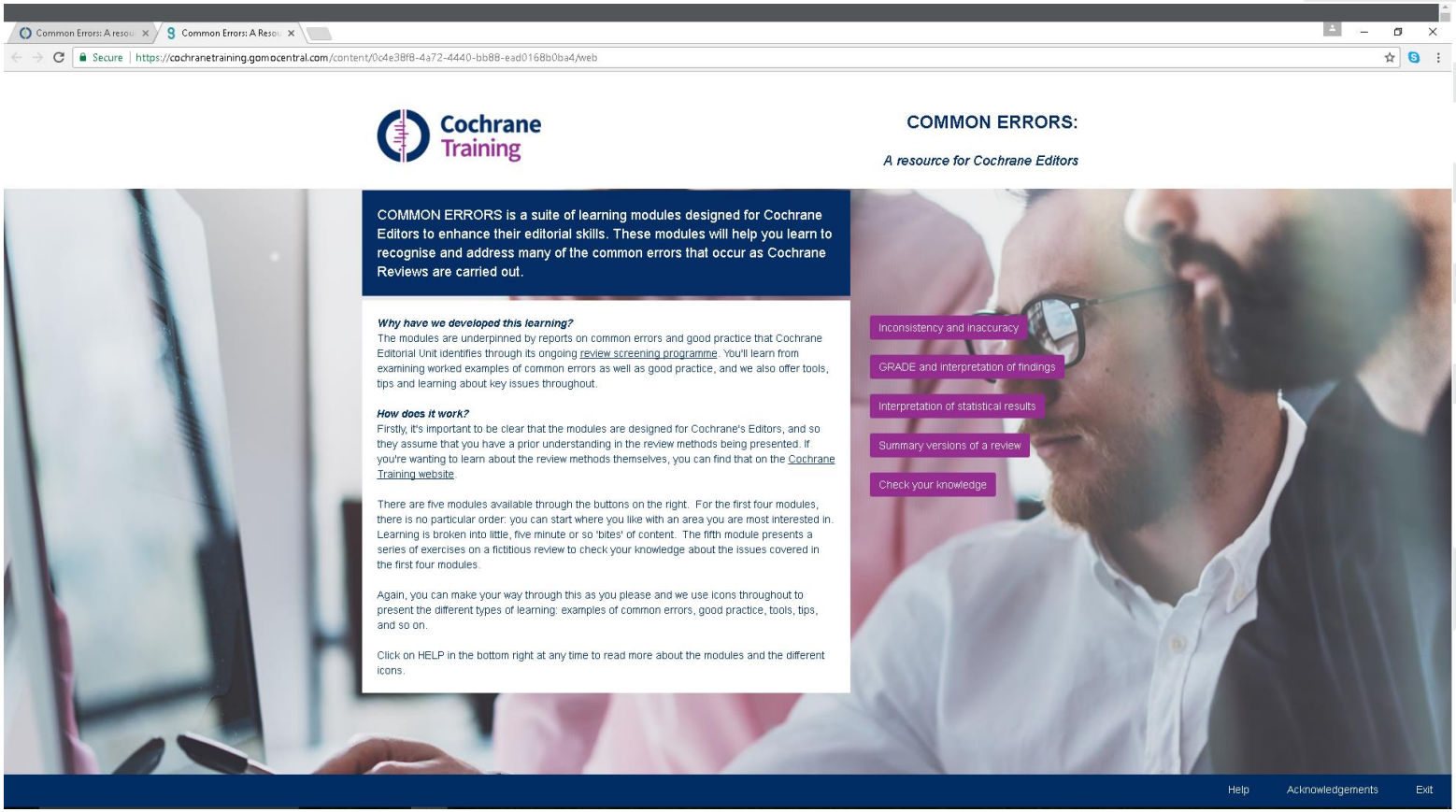
http://training.cochrane.org/common-errors



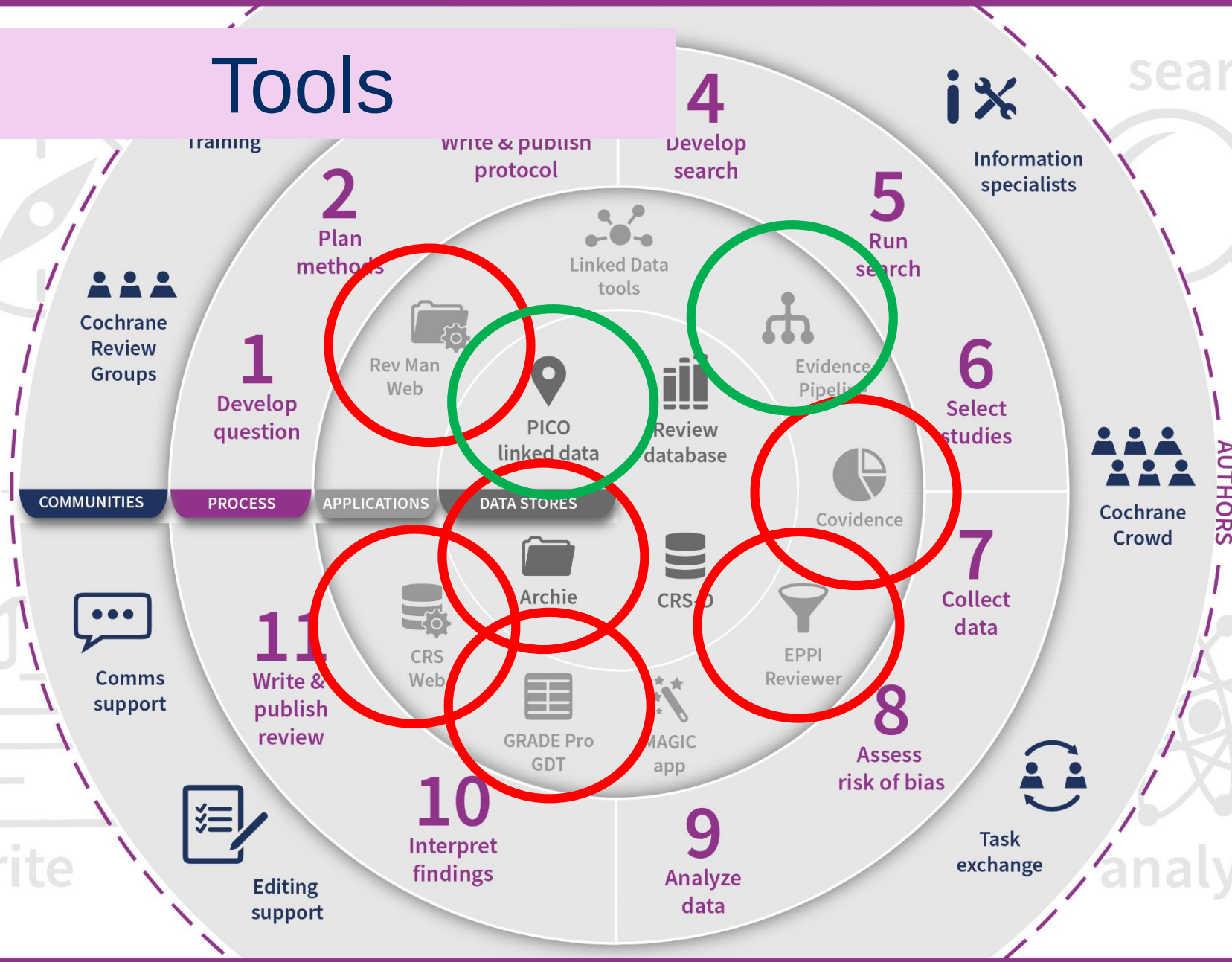
Improving the efficiency of production

- Removing roadblocks
- Increased use of professional teams
- Technology and ‘the crowd’

Cochrane
Trusted evidence.
Informed decisions.
Better health.

New Cochrane Review Ecosystem

Tools



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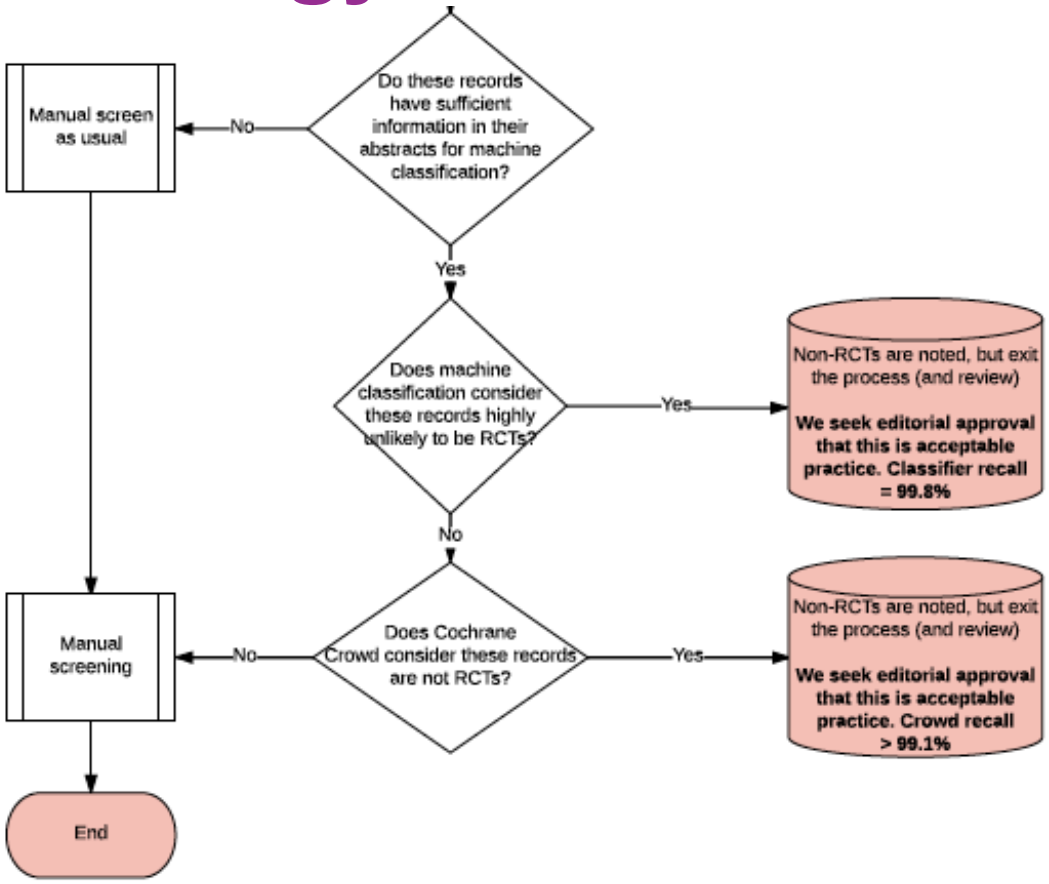
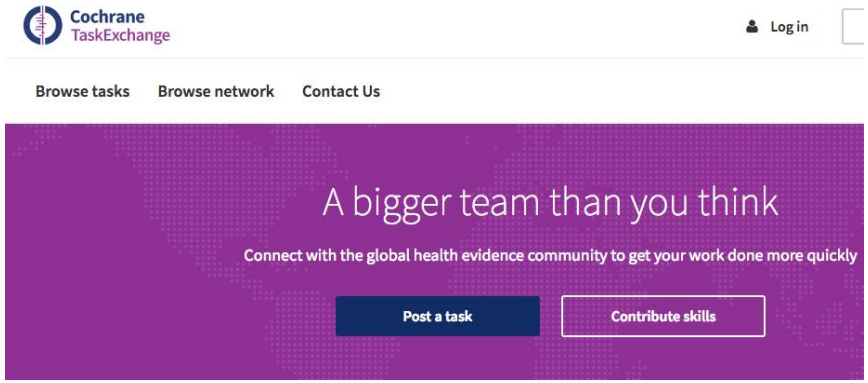
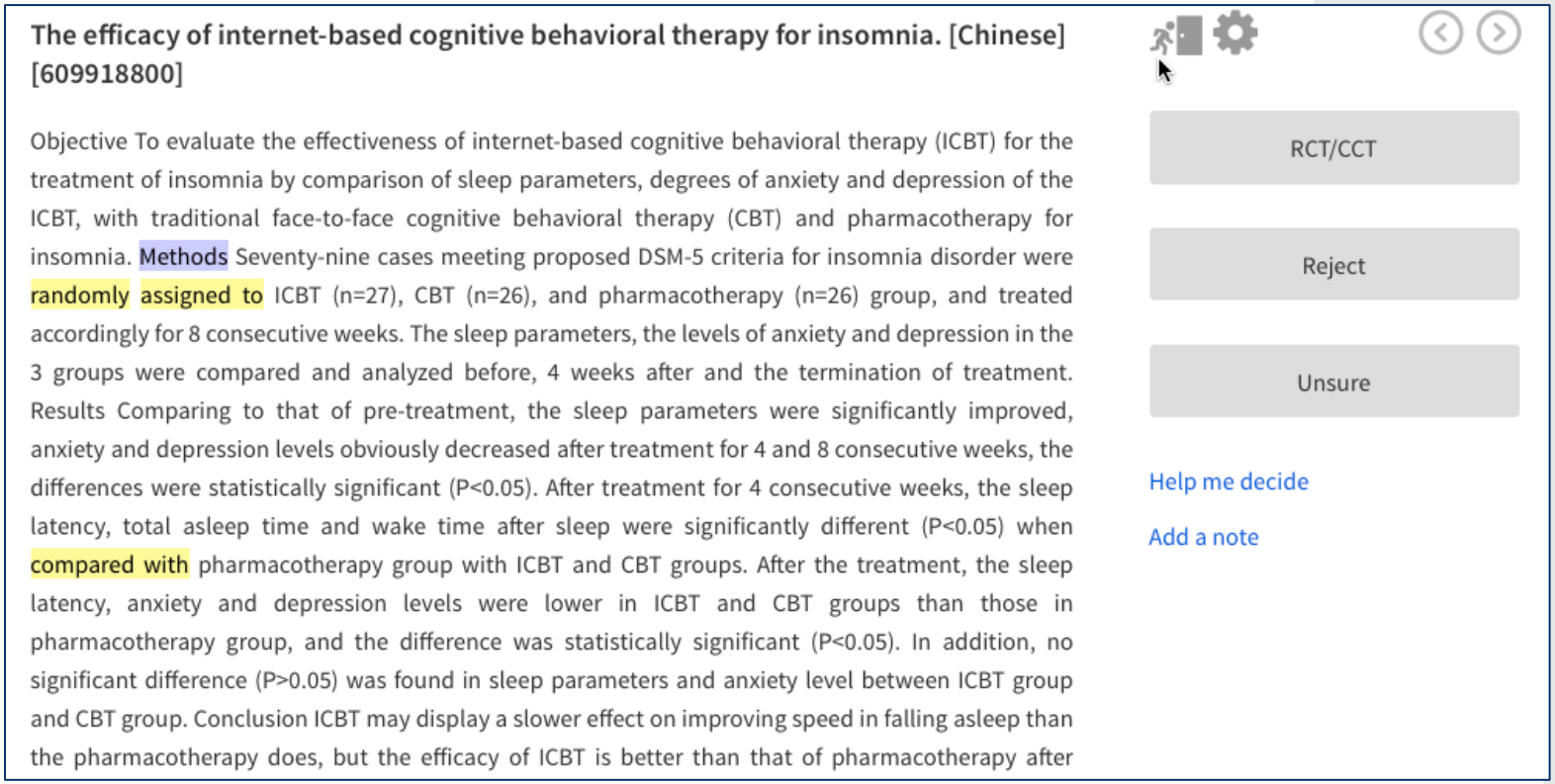
Technology and ‘the crowd’



Plans for change: Technology and the changing patterns of contribution



The microtask: is it an RCT?



Is it an RCT?

The (Cochrane) Ecosystem of Evidence: translation

More diversity in production and delivery of content

Knowledge Translation strategy

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Presentation and delivery

- More diverse and bespoke summaries that meet the needs of end users e.g. policy briefs, evidence to decision summaries
- Multi-lingual presentation and search
- Exploitation of PICO annotation and Linked Data to communicate with other systems / products
  - MAGIC app
  - Decision support tools

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‘Living’ Systematic Reviews

‘a *systematic review which is continually updated, incorporating relevant new evidence as it becomes available*.’

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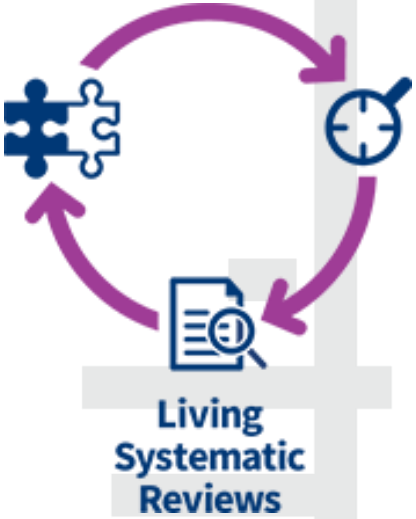
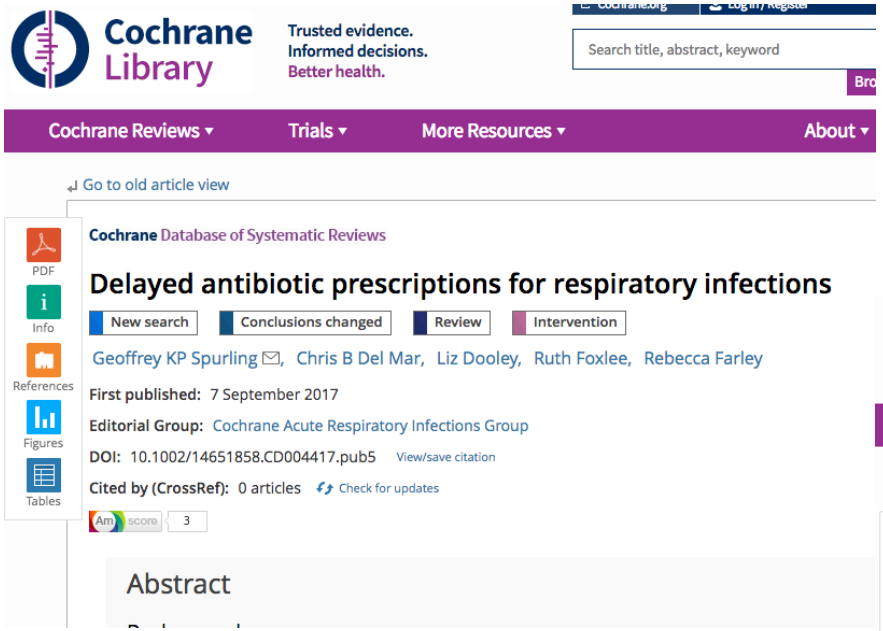
First two Living SRs published





Looking forward: a new content strategy

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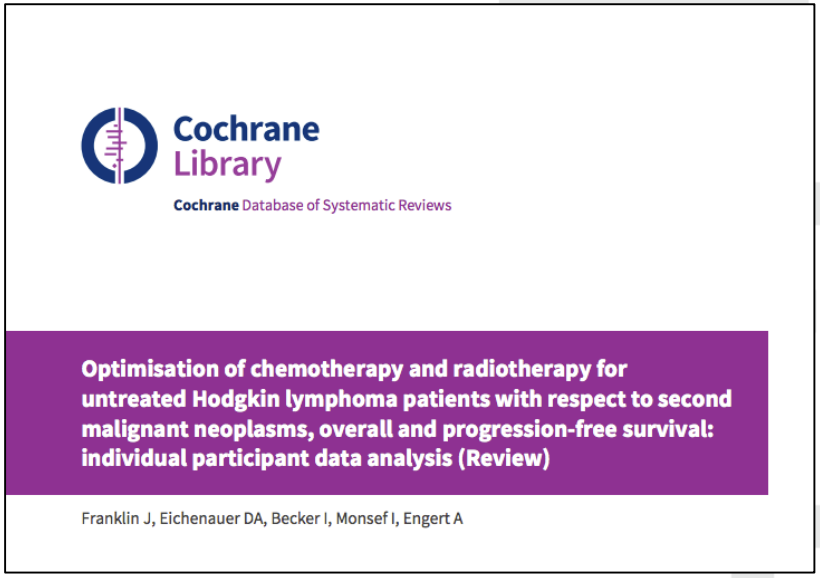
Different ways to address conventional questions: evidence sources



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Different ways to address conventional questions: evidence methods

Cochrane Library

Cochrane Database of Systematic Reviews

Interventions for the management of malignant pleural effusions: a network meta-analysis (Review)

Clive AO, Jones HE, Bhatnagar R, Preston NJ, M

Cochrane Methods

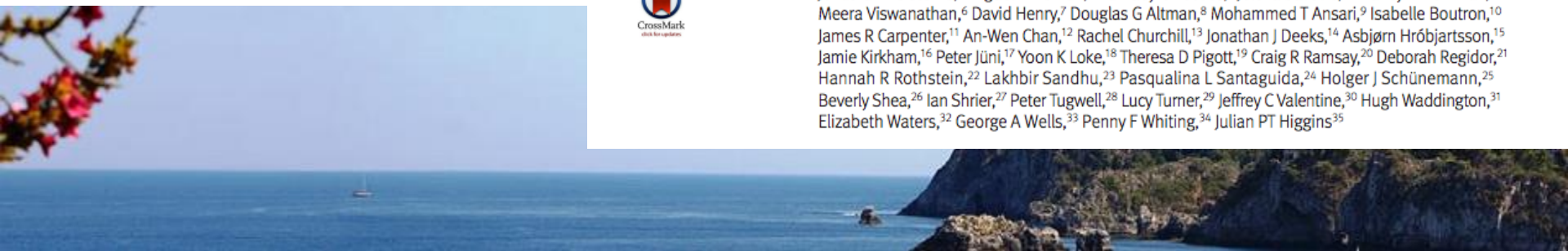
Guidance for using the iCAT_SR: Intervention Complexity

RESEARCH METHODS AND REPORTING

OPEN ACCESS

ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions

Jonathan AC Sterne,[1] Miguel A Hernán,[2] Barnaby C Reeves,[3] Jelena Savović,[1,4] Nancy D Berkman,[5] Meera Viswanathan,[6] David Henry,[7] Douglas G Altman,[8] Mohammed T Ansari,[9] Isabelle Boutron,[10] James R Carpenter,[11] An-Wen Chan,[12] Rachel Churchill,[13] Jonathan J Deeks,[14] Asbjørn Hróbjartsson,[15] Jamie Kirkham,[16] Peter Jüni,[17] Yoon K Loke,[18] Theresa D Pigott,[19] Craig R Ramsay,[20] Deborah Regidor,[21] Hannah R Rothstein,[22] Lakhbir Sandhu,[23] Pasqualina L Santaguida,[24] Holger J Schünemann,[25] Beverly Shea,[26] Ian Shrier,[27] Peter Tugwell,[28] Lucy Turner,[29] Jeffrey C Valentine,[30] Hugh Waddington,[31] Elizabeth Waters,[32] George A Wells,[33] Penny F Whiting,[34] Julian PT Higgins[35]



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New question types

Cochrane Library

Cochrane Database of Systematic Reviews

Lay health workers in primary and community health care for maternal and child health and the management of infectious diseases (Review)

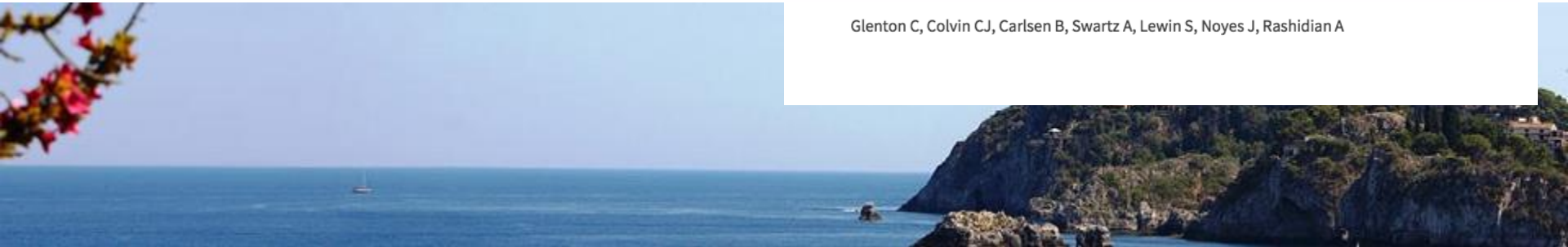
Lewin S, Munabi-Babigumira S, Glenton C, Daniels K, Bosch-Capblanch X, van Wyk BE, Odgaard-Jensen J, Johansen M, Aja GN, Zwarenstein M, Scheel IB

Cochrane Library

Cochrane Database of Systematic Reviews

Barriers and facilitators to the implementation of lay health worker programmes to improve access to maternal and child health: qualitative evidence synthesis (Review)

Glenton C, Colvin CJ, Carlsen B, Swartz A, Lewin S, Noyes J, Rashidian A



Teaching and learning developments

Cornerstone of our approach to Goal 4 of Strategy to 2020

Cochrane Interactive Learning

- 9 modules of self-directed, interactive & engaging learning
- Written by world-leading experts in systematic review methods
- Learn at your own pace on laptop, tablet and mobile
- Assessment & certification

Module 1: Introduction to conducting systematic reviews

30 min

What systematic reviews are, why they are useful, framing a review question, process for reviews. Read more

Free module, login required

Log in and start module

Module 2: Writing the review protocol

30 min

Why protocols are a crucial step, components of a protocol, framing eligibility criteria. Read more

Restricted

Log in and start module

Module 4: Selecting studies and collecting data

60 min

How to select studies for inclusion, systematically collecting different data types that meet criteria. Read more

Restricted

Log in and start module

Module 5: Introduction to study quality and risk of bias

90 min

What bias is, how to assess the risk of bias in randomized trials in different sources. Read more

Restricted

Log in and start module

W: interactivelearning.cochrane.org

E: interactivelearning@cochrane.org

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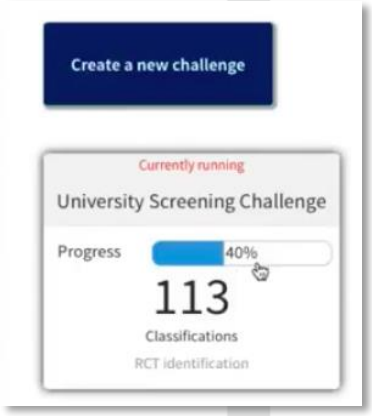
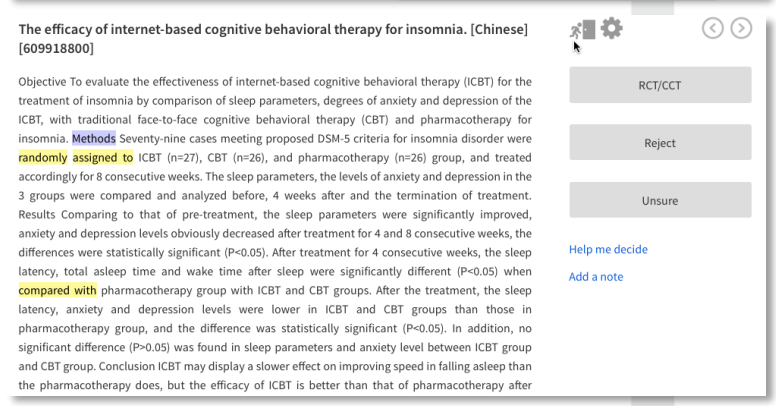
Cochrane Crowd

Cochrane Classmate

- Innovative online teaching tool – demonstrate, challenge and compete!
- Identify study designs & screen abstracts
- Contribute to live Cochrane Crowd citizen science microtasks
- For teachers of research methods & evidence synthesis





crowd.cochrane.org/classmate

Conclusion

Interesting, challenging times!

- There is still a need for high quality, relevant evidence, efficiently produced, but..
- The Eco-system model provides a useful framework, built on..
  - People and communities
  - Technology
  - Process
  - Networks that build on inclusiveness and diverse skills