Centre for Evidence Based Health Care

Systematic reviews

…..taking stock of existing knowledge

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Review?

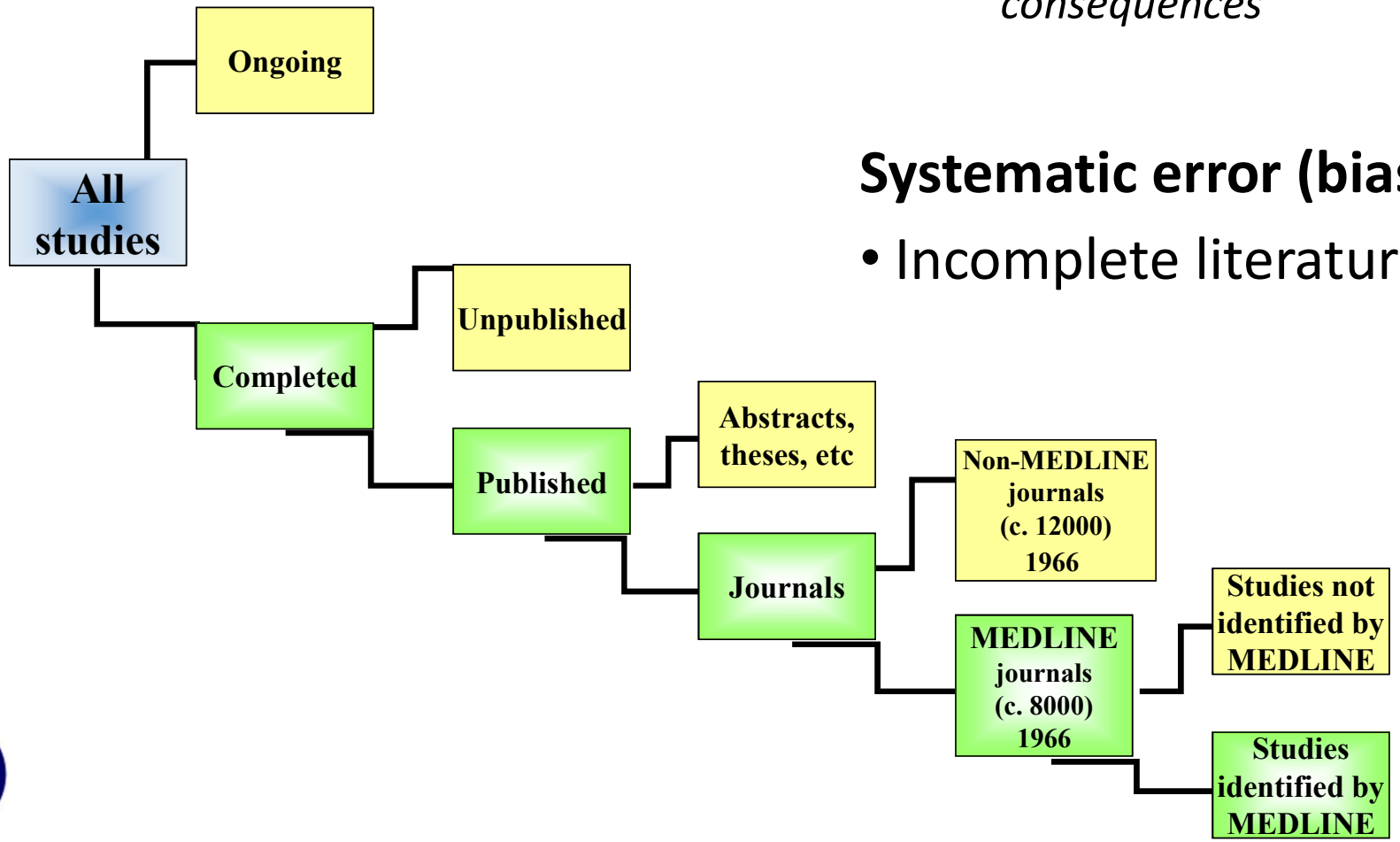
Re'-view or **'further look'** at what has previously been written on a particular subject

Not merely a summary of previous findings but a critical examination and synthesis of existing reports

Caution: Access to research is haphazard and often biased

Shortcomings of traditional reviews

"…may be biased, leading to false conclusions and potentially serious consequences"



Systematic error (bias) from

- Incomplete literature searches

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Shortcomings of traditional reviews

"….may be biased, leading to false conclusions and potentially serious consequences"

Systematic error (bias) from

- Selective inclusion of studies

Studies cited in reviews often reflect mainly the authors' perspectives, field, language and country

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Shortcomings of traditional reviews

"….may be biased, leading to false conclusions and potentially serious consequences"

Systematic error (bias) from

- Insufficient attention given to study quality

Design and quality of research vary widely

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Shortcomings of traditional reviews

Many studies by themselves are too small to give conclusive results

Random error (play of chance)

- Insufficient attention given to sample size

" … we still have no clear evidence that beta-blockers improve long-term survival after infarction despite almost 20 years of clinical trials ."

JRA Mitchell. BMJ 1981;282:1565-70

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Which steps can be taken to make reviews (syntheses) more reliable?

Features of a systematic review

- Clear set of objectives
- Explicit, reproducible methodology
  - Predefined study eligibility criteria
  - Comprehensive search strategy
  - Assessment of validity of study findings
  - Appropriate quantitative and qualitative synthesis of findings
- Systematic, complete presentation of the findings

Current state of knowledge with strengths and limitations of underlying research

Systematic review

- A review in which bias has been reduced by the systematic identification, appraisal, synthesis, and, if relevant, statistical aggregation of all relevant studies on a specific topic according to a predetermined and explicit method

(Moher et al. Lancet 1999; 354: 1896-900)

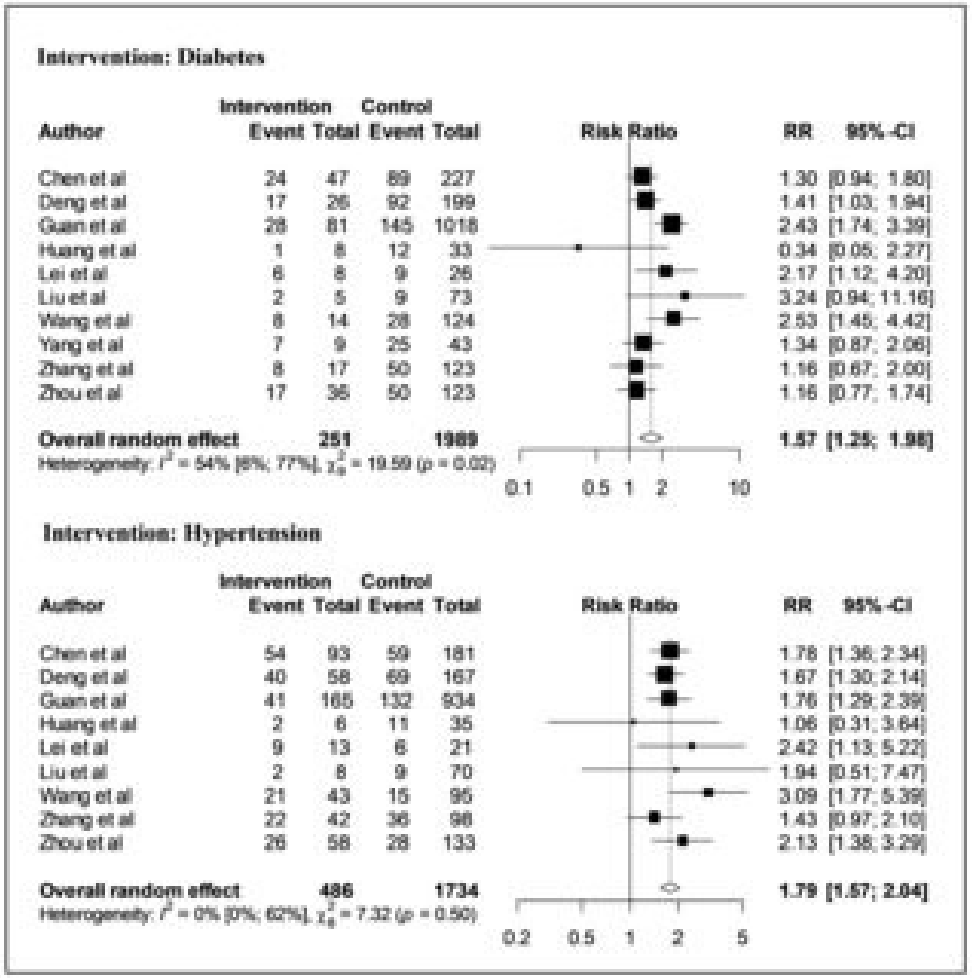
SR vs. meta-analysis

- A **meta-analysis** is *"a statistical procedure that integrates the results of several independent studies considered to be combinable."*

  Egger et al, BMJ 1997

- If appropriate, meta-analysis can be part of a systematic review

Risk Factors of the Severity of COVID-19: a Meta-Analysis



Meta-analysis

KEEP CALM ITS JUST A FOREST PLOT

Cochrane Library

Cochrane Database of Systematic Reviews

Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff (Review)

Verbeek JH, Rajamaki B, Ijaz S, Sauni R, Toomey E, Blackwood B, Tikka C, Ruotsalainen JH, Kilinc Balci FS

To evaluate which type of full-body PPE and which method of donning or doffing PPE have the least risk of contamination or infection for HCW, and which training methods increase compliance with PPE protocols.

VerbeekJH, RajamakiB, IjazS, SauniR, ToomeyE, BlackwoodB, TikkaC, RuotsalainenJH, Kilinc BalciFS. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare sta.. *Cochrane Database of Systematic Reviews* 2020, Issue 5. Art. No.: CD011621. DOI: 10.1002/14651858.CD011621.pub5.

Search methods

We searched CENTRAL, MEDLINE, Embase and CINAHL to 20 March 2020.

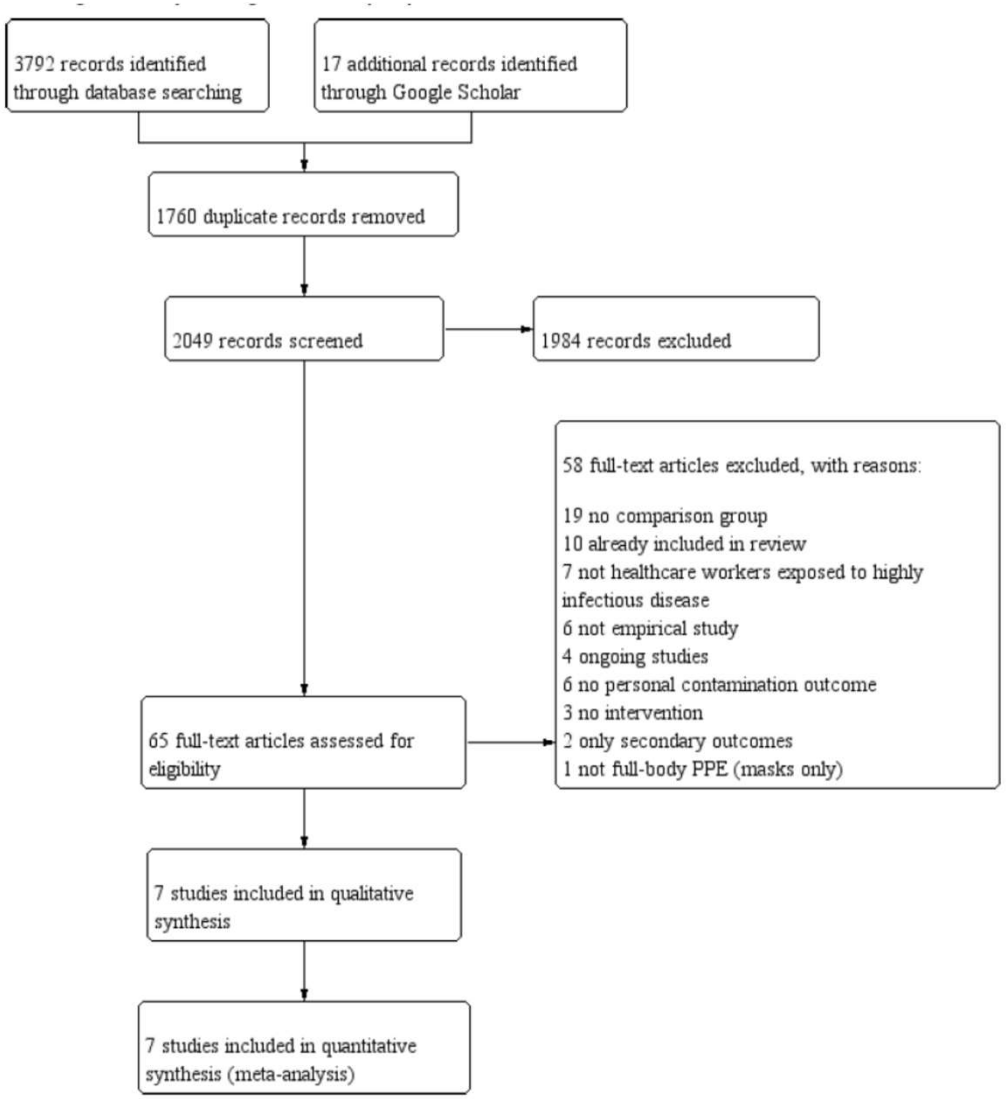
Selection criteria

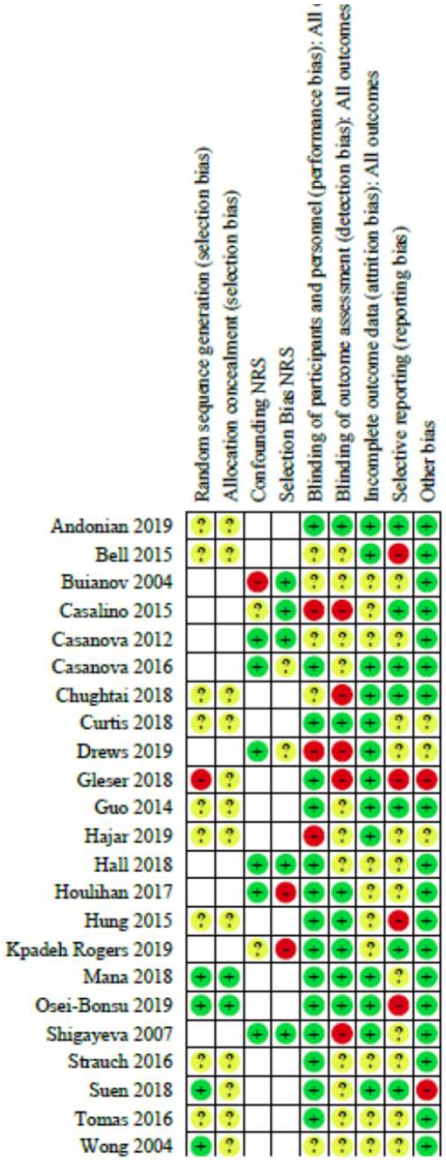
We included all controlled studies that evaluated the effect of full-body PPE used by HCW exposed to highly infectious diseases, on the risk of infection, contamination, or noncompliance with protocols. We also included studies that compared the effect of various ways of donning or doffing PPE, and the effects of training on the same outcomes.

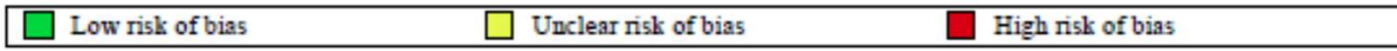
Data collection and analysis

Two review authors independently selected studies, extracted data and assessed the risk of bias in included trials. We conducted random-effects meta-analyses were appropriate.

Flow diagram







Risk of bias graph

Selection bias

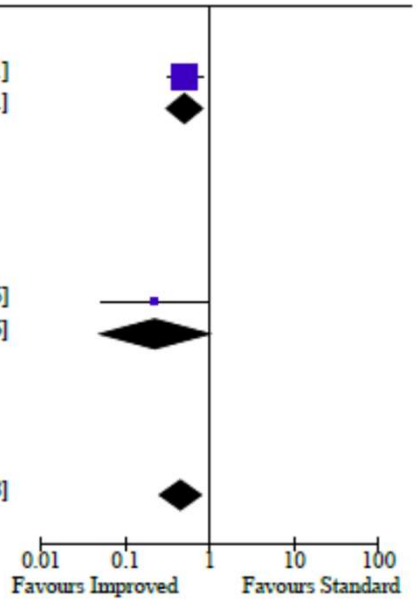
Performance bias

Detection bias

Attrition bias

Analysis 8.1. Comparison 8: Gown with gown-glove improvement vs standard gown-gloves, Outcome 1: People with contamination

Study or Subgroup	Improved interface Events	Total	Standard Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
8.1.1 Improved vs standard						
Hajar 2019	16	60	32	60	86.4%	0.50 [0.31 , 0.81]
Subtotal (95% CI)		60		60	86.4%	**0.50 [0.31 , 0.81]**
Total events:	16		32			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.82 (P = 0.005)						
8.1.2 Improved plus education vs standard plus education						
Hajar 2019	2	40	9	40	13.6%	0.22 [0.05 , 0.96]
Subtotal (95% CI)		40		40	13.6%	**0.22 [0.05 , 0.96]**
Total events:	2		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.01 (P = 0.04)						
Total (95% CI)		100		100	100.0%	**0.45 [0.26 , 0.78]**
Total events:	18		41			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 1.11$, df = 1 (P = 0.29); $I^2 = 10\%$						
Test for overall effect: Z = 2.83 (P = 0.005)						
Test for subgroup differences: $Chi^2 = 1.06$, df = 1 (P = 0.30), $I^2 = 5.5\%$						



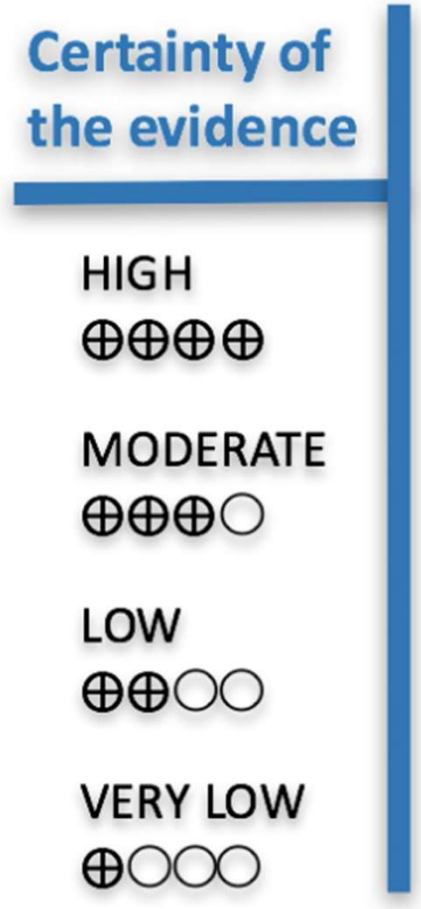
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
	Risk with standard gown and gloves	Risk with gown with gown-glove improvement			
People with contamination	410 per 1000	185 per 1000 (107 to 320)	RR 0.45 (0.26 to 0.78)	50 (2 RCTs)	⊕⊕## **Low** [1,2]

GRADE

Quality = a measure of ‘confidence’ in the effect estimates

5 factors to consider

- Risk of bias — Were the studies well conducted?
- Inconsistency — Do the trials find different results?
- Indirectness — Where, who and how were the trials done?
- Imprecision — Is the result statistically and clinically important?
- Other — Is there any suggestion of publication Bias?



Different types of questions answered by reviews

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Systematic Reviews

Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review (Review)

Piechotta V, Chai KL, Valk SJ, Doree C, Monsef I, Wood EM, Lamikanra A, Kimber C, McQuilten Z, So-Osman C, Estcourt LJ, Skoetz N

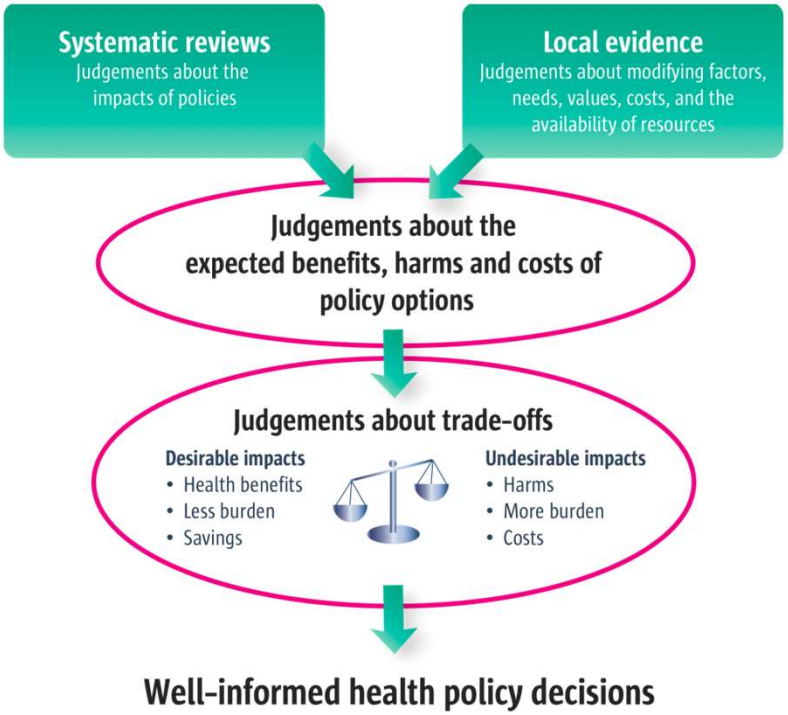
combination with other public health OVID-19: a rapid review (Review)

obrescu AI, Chapman A, Persad E, Klerings I, Wagner G, Siebert U, ner G

When is it appropriate to use systematic reviews?

It informs…

- New research
- Decision making for action



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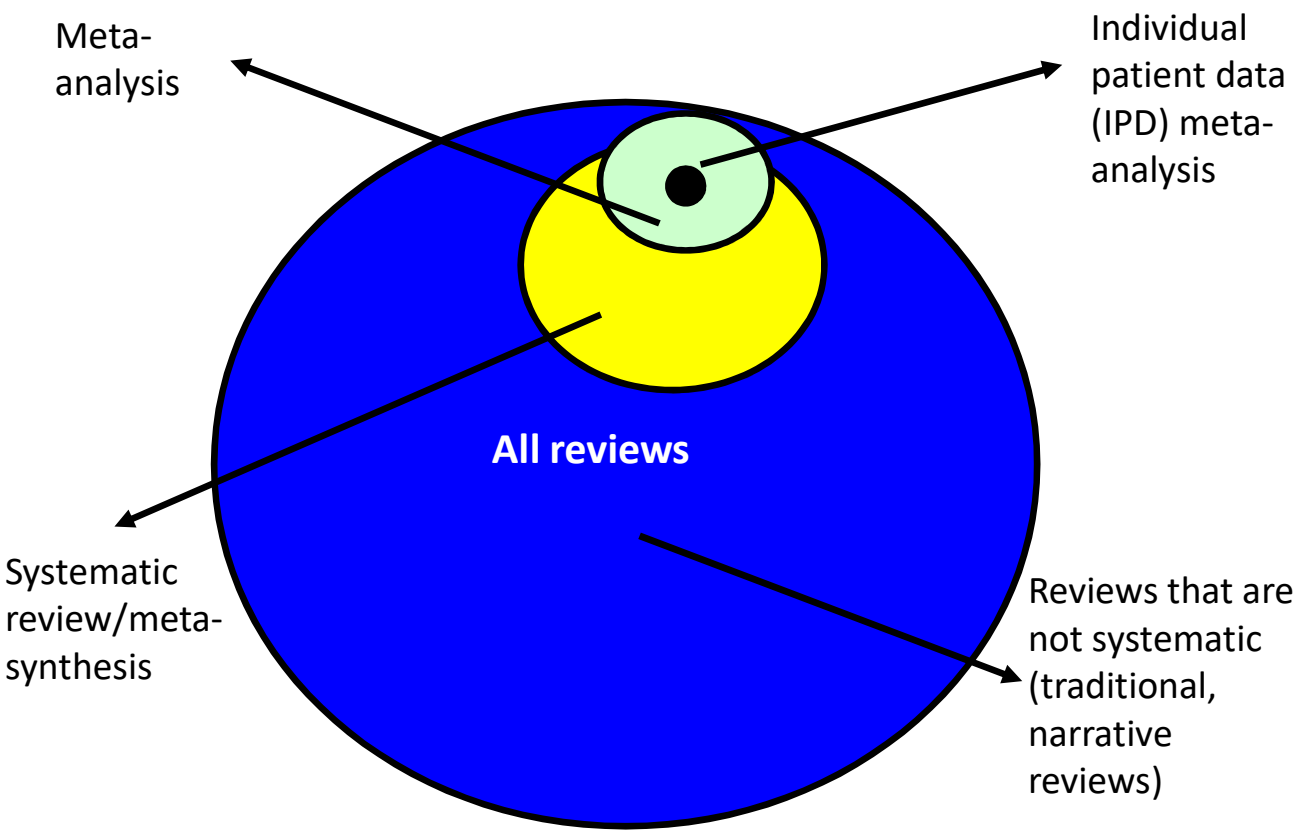
Where can you find systematic reviews?

- https://covid-nma.com/the-project/
- Evidence Aid - Summaries of systematic reviews that may be relevant to COVID-19 in eight broad areas
- L*VE by Epistemonikos (includes existing systematic reviews of effects and the primary studies, including trials, that were included in the reviews)
- LitCovid from PubMed (includes systematic reviews and single studies organized by mechanism, transmission, treatment, case report, and epidemic forecasting)
- TRIP database (includes systematic reviews and single studies organized by document type)

Review articles



We will serve the public more responsibly and ethically when research designed to reduce the likelihood that we will be misled by bias and the play of chance has become an expected element of professional and policy making practice, not an optional add-on.

Iain Chalmers

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