

# Systematic Review & Meta Analysis

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# Systematic Review

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In a systematic review, all relevant studies would be gathered and analysed using a reproducible approach **to answer a particular research question**.

This method estimates whether research results are **consistently and universally applicable across demographics, settings, and intervention variations or whether there are significant differences between subgroups.**

- Literature Review
- Inclusion/exclusion criteria should be pre-defined
- Objective (Review Protocol)
- Critical Appraisal--> PICOS

# Why Systematic Reviews are Needed

- Health care decisions for individual patients and for public policy should be informed by **the best available research evidence.**
- Practitioners and decision-makers are encouraged to make use of the latest research and information about best practice, and to ensure that **decisions are demonstrably rooted in this knowledge.**
- However, **this can be difficult given the large amounts of information generated by individual studies** which may be biased, methodologically flawed, time and context dependent, and can be misinterpreted and misrepresented.

## Traditional pyramid



## Current model



ce: Adapted from the article: Proposed new evidence-based medicine pyramid<sup>5</sup>.

This should be  
exhaustive,  
systematic and  
use  
several database  
s of publications

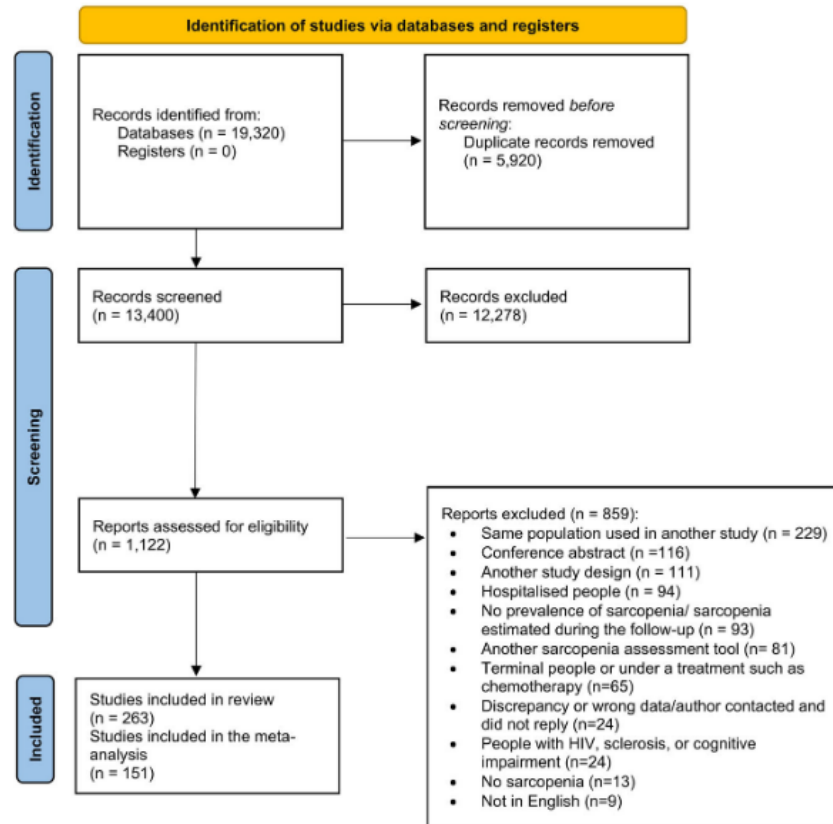


Figure 1 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram.

# PICOS

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Was the review question clearly defined in terms of **population, interventions, comparators, outcomes and study designs** (PICOS)?

## Box 1.2: Example review objective and PICOS elements for a review protocol

### Review objective

The objective of this review is to assess the clinical effectiveness of treatments for childhood retinoblastoma.<sup>14</sup>

### Participants

Studies of participants diagnosed with retinoblastoma at the age of 18 years or under.

Studies of adults where childhood retinoblastoma was followed up into adulthood.

Studies of mixed diagnoses if outcomes were reported separately for children with retinoblastoma.

### Interventions

Any intervention or combination of interventions given for the treatment of retinoblastoma, including (but not restricted to) enucleation, external beam radiotherapy, chemotherapy, brachytherapy, cryotherapy, thermotherapy and photocoagulation.





















### Outcomes

Any clinical outcome, including (but not restricted to) survival, progression-free survival, tumour response, preservation of the eye, visual acuity, disease remission and adverse effects.

### Study design

Randomised controlled trials (RCTs) and controlled trials. However, it is not anticipated that many studies of these designs will be available. Therefore, if information from controlled trials is not available, cohort studies are eligible for inclusion provided that data from a comparison group are reported.

Case series and case reports are excluded from the review owing to the high potential for bias in these study designs. Case-control studies (except where nested as part of a cohort study) and economic evaluations are also excluded.

<a href="#">Search ID#</a> ▾	Search Terms	Search Options	Actions
<input type="checkbox"/> S15	 S11 AND S14	<b>Expanders</b> - Apply equivalent subjects  <b>Search modes</b> - Boolean/Phrase	 <a href="#">View Results</a> (1,177)    <a href="#">View Details</a>    <a href="#">Edit</a>
<input type="checkbox"/> S14	 S12 OR S13	<b>Expanders</b> - Apply equivalent subjects  <b>Search modes</b> - Boolean/Phrase	 <a href="#">View Results</a> (3,385)    <a href="#">View Details</a>    <a href="#">Edit</a>
<input type="checkbox"/> S13	 TI ( (Pediatr* Qualit* of Life Inventor* or PedsQL) ) OR AB ( (Pediatr* Qualit* of Life Inventor* or PedsQL) )	<b>Expanders</b> - Apply equivalent subjects  <b>Search modes</b> - Boolean/Phrase	 <a href="#">View Results</a> (1,504)    <a href="#">View Details</a>    <a href="#">Edit</a>
<input type="checkbox"/> S12	 TI ( ("Strength* and Difficult* Questionnaire** or SDQ*") ) OR AB ( ("Strength* and Difficult* Questionnaire** or SDQ*") )	<b>Expanders</b> - Apply equivalent subjects  <b>Search modes</b> - Boolean/Phrase	 <a href="#">View Results</a> (1,928)    <a href="#">View Details</a>    <a href="#">Edit</a>
<input type="checkbox"/> S11	 S5 OR S10	<b>Expanders</b> - Apply equivalent subjects	 <a href="#">View Results</a> (480,565)    <a href="#">View Details</a>    <a href="#">Edit</a>

Limit/Sort

Resource Subject ▾

Healthcare and Biomedical Sciences

All Formats ▾

System Sorted ▾

Sort

Search

Save marked records

Save all on page

Num	Mark	Resource Subjects (1-3 of 3)	Entries 37 Found
1	<input type="checkbox"/>	Healthcare and Biomedical Sciences Additional Databases	14
2	<input type="checkbox"/>	Healthcare and Biomedical Sciences Key Databases	6
3	<input type="checkbox"/>	Healthcare and Biomedical Sciences Reference Resources	17

Save marked records

Save all on page

# Example search strategy (Queries)

1 exp Child Abuse

2 Adverse Childhood Experiences

3 (child\* adj5 (abus\* or maltreat\* or neglect\* or trauma\*)).ti,ab.

4 (Adverse Childhood Experience\* or ACE).ti,ab.

5 1 or 2 or 3 or 4

6 child, preschool/ or exp infant/

7 ((preschool or pre-school) adj5 child\*).ti,ab.

8 infant\*.ti,ab.

9 6 or 7 or 8

10 5 or 9

11 ("Strength\* and Difficult\* Questionnaire\*" or SDQ\*).ti,ab.

12 (Pediatr\* Qualit\* of Life Inventor\* or PedsQL).ti,ab.

13 11 or 12

14 10 and 13



# Example search strategy (Queries)

S1 (MH "Child Abuse+")

S2 (MH "Adverse Childhood Experiences")

S3 TI ( (child\* N5 (abus\* or maltreat\* or neglect\* or trauma\*)) ) OR AB ( (child\* N5 (abus\* or maltreat\* or neglect\* or trauma\*)) )

S4 TI ( (Adverse Childhood Experience\* or ACE) ) OR AB ( (Adverse Childhood Experience\* or ACE) )

S5 S1 OR S2 OR S3 OR S4

S6 (MH "Child, Preschool")

S7 (MH "Infant+")

S8 TI ( ((preschool or pre-school) N5 child\*) ) OR AB ( ((preschool or pre-school) N5 child\*) )

S9 TI infant\* OR AB infant\*

S10 S6 OR S7 OR S8 OR S9

S11 S5 OR S10

S12 TI ("Strength\* and Difficult\* Questionnaire\*" or SDQ\*) OR AB ("Strength\* and Difficult\* Questionnaire\*" or SDQ\*) )

S13 TI ( (Pediatr\* Qualit\* of Life Inventor\* or PedsQL) ) OR AB ( (Pediatr\* Qualit\* of Life Inventor\* or PedsQL) )

S14 S12 OR S13

S15 S11 AND S14

# Meta Analysis

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A statistical technique for combining data from independent studies to produce a single estimate of effect and associated uncertainty around this estimate.

Meta-analysis combines quantitative information from independent studies addressing the same question .





# Why Meta Analysis are Needed

- Increases statistical power to test hypothesis (bigger n; smaller SE; tighter confidence intervals) .
- To confirm **generalisability of results** (e.g., in different demographic groups) or to identify heterogeneity between studies.
- Resolve controversy between directly contradictory results.

## **Term of generalisability**

*How closely a study reflects routine practice or the usual setting where the intervention would be implemented.*

## HIV testing and engagement with the HIV treatment cascade among men who have sex with men in Africa: a systematic review and meta-analysis

[James Stannah MPH](#)<sup>a \*</sup>, [Elizabeth Dale MBBS](#)<sup>a \*</sup>, [Jocelyn Elmes PhD](#)<sup>c</sup>, [Roisin Staunton MSc](#)<sup>a</sup>, [Prof Chris Beyrer MD](#)<sup>d</sup>, [Kate M Mitchell PhD](#)<sup>a b †</sup>, [Prof Marie-Claude Boily PhD](#)<sup>a b †</sup>  

Ambient and household air pollution on early-life determinants of stunting—a systematic review and meta-analysis

[Vivian C. Pun](#) , [Russell Dowling](#) & [Sumi Mehta](#)

*Environmental Science and Pollution Research* **28**, 26404–26412 (2021) | [Cite this article](#)

**3973** Accesses | **21** Citations | **19** Altmetric | [Metrics](#)

### Abstract

Stunting is an important risk factor for early growth and health implications throughout the life course, yet until recently, studies have rarely focused on populations exposed to high levels of particulate matter pollution or on developing countries most vulnerable to stunting and its associated health and developmental impacts. We systematically searched for epidemiologic studies published up to 15 August 2020 that examined the association between ambient and household particulate exposure and postnatal stunting (height-for-age z-score) and prenatal determinants (small for gestational age or SGA, or equivalent) of stunting. We conducted the literature search in PUBMED, MEDLINE, EMBASE, and Web of Science databases in August

Research article | [Open Access](#) | Published: 10 April 2007

## Boys are more stunted than girls in Sub-Saharan Africa: a meta-analysis of 16 demographic and health surveys

[Henry Wamani](#) , [Anne Nordrehaug Åstrøm](#), [Stefan Peterson](#), [James K Tumwine](#) & [Thorkild Tylleskär](#)


*BMC Pediatrics* **7**, Article number: 17 (2007) | [Cite this article](#)

### Abstract

#### Background

Many studies in sub-Saharan Africa have occasionally reported a higher prevalence of stunting in male children compared to female children. This study examined whether there are systematic sex differences in stunting rates in children under-five years of age, and how the sex differences in stunting rates vary with household socio-economic status.

## Association of meat, vegetarian, pescatarian and fish-poultry diets with risk of 19 cancer sites and all cancer: findings from the UK Biobank prospective cohort study and meta-analysis

[Solange Parra-Soto](#), [Danay Ahumada](#), [Fanny Petermann-Rocha](#), [Jirapitcha Boonpoor](#), [Jose Lara Gallegos](#), [Jana Anderson](#), [Linda Sharp](#), [Fiona C. Malcomson](#), [Katherine M. Livingstone](#), [John C. Mathers](#), [Jill P. Pell](#), [Frederick K. Ho](#) & [Carlos Celis-Morales](#) 


*BMC Medicine* **20**, Article number: 79 (2022) | [Cite this article](#)

**3970** Accesses | **3** Citations | **12** Altmetric | [Metrics](#)

## Association Between Initial Use of e-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults

### A Systematic Review and Meta-analysis

[Samir Soneji](#), PhD<sup>1,2</sup>; [Jessica L. Barrington-Trimis](#), PhD<sup>3</sup>; [Thomas A. Wills](#), PhD<sup>4</sup>; [et al](#)

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- A thick yellow horizontal bar spans the width of the slide, with a vertical yellow bar extending downwards from its right end.
- It should be emphasized that NOT ALL SYSTEMATIC REVIEWS will contain a META-ANALYSIS. This will depend on whether the systematic review has located studies that are sufficiently similar to make it reasonable to consider combining their results.

# Two types of models that we can use to obtain an average (or pooled) effect size

## **FIXED EFFECT MODEL**

- There is only one true underlying effect size and that the effect sizes observed across different studies only vary due to sampling variation (between study variation).

## **RANDOM EFFECT MODEL**

- Each study effect size comes from an underlying distribution of effect sizes so that there are two sources of variation. (i) variation between studies and (ii) variation within studies

*Choosing a preferred model is not always easy*

# Forest Plot

A thick yellow horizontal bar spans the width of the slide, with a vertical yellow bar extending downwards from its right end.

- Meta analyses are often presented along with forest plots so that we can better visualise the heterogeneity amongst studies.

# Forrest Plot

- The **horizontal line** correspond to the 95% confidence intervals for each study, with corresponding **box area** drawn proportional to weight for that individual study.
- The wider is the confidence interval the smaller is the **box area**.
- The **diamond** and the **broken vertical line** represents the summary estimate, and the confidence interval for the summary estimate corresponds to the width of the diamond.
- The **unbroken vertical line** is at the null value 1 of the odds ratio, and is equivalent to no treatment effect.

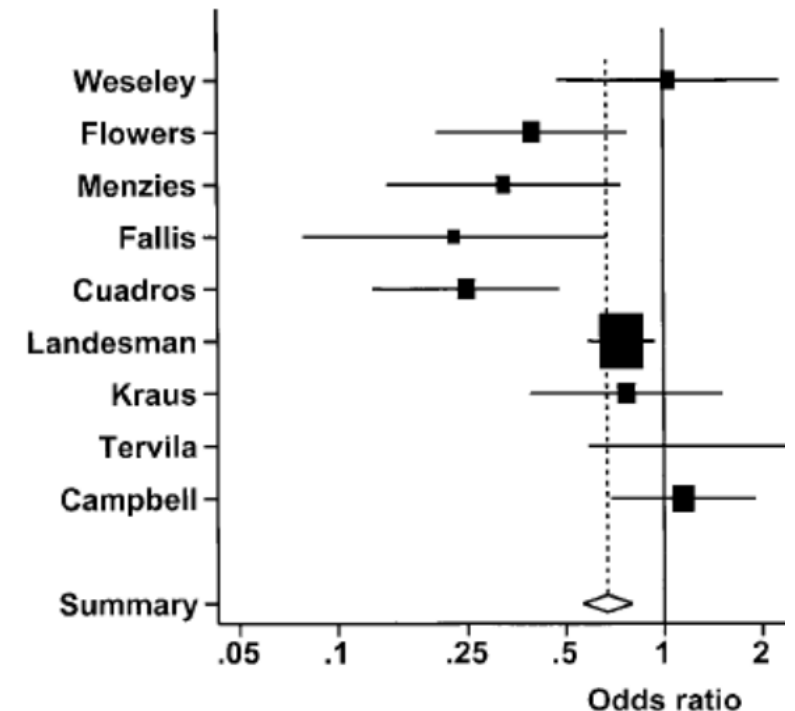
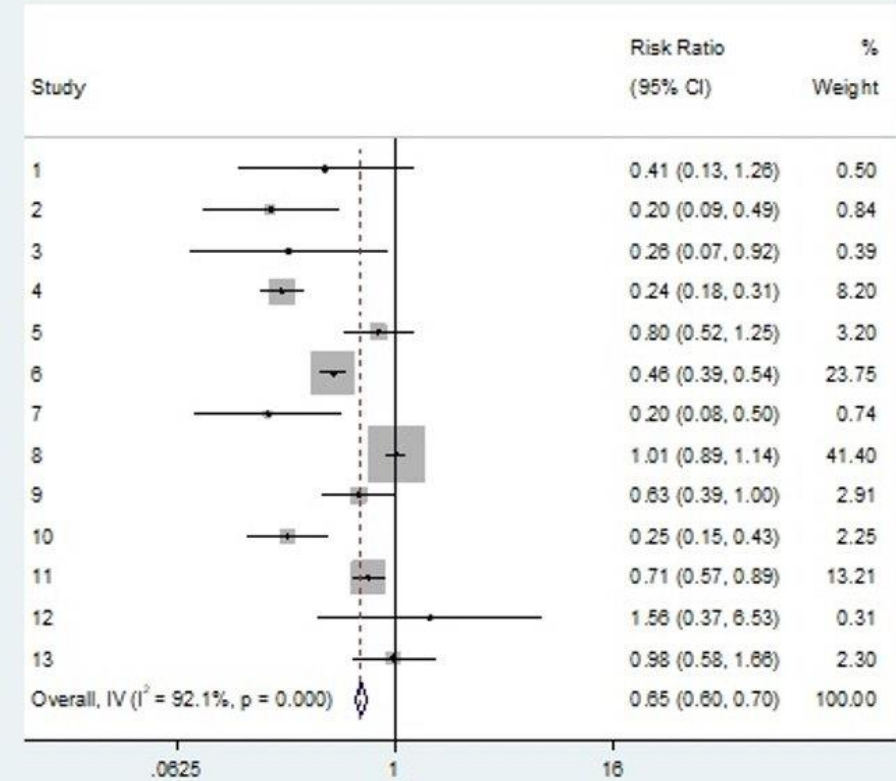


Fig. 32.1 Forest plot of the results of a fixed-effect meta-analysis of nine stu pregnancy.



- Overall effect size is 0.65 (0.60,0.70) and this is significantly different from 1.
- The BCG vaccine reduces the risk of TB by 35%
- Significant heterogeneity among the studies ( $P < 0.001$ )

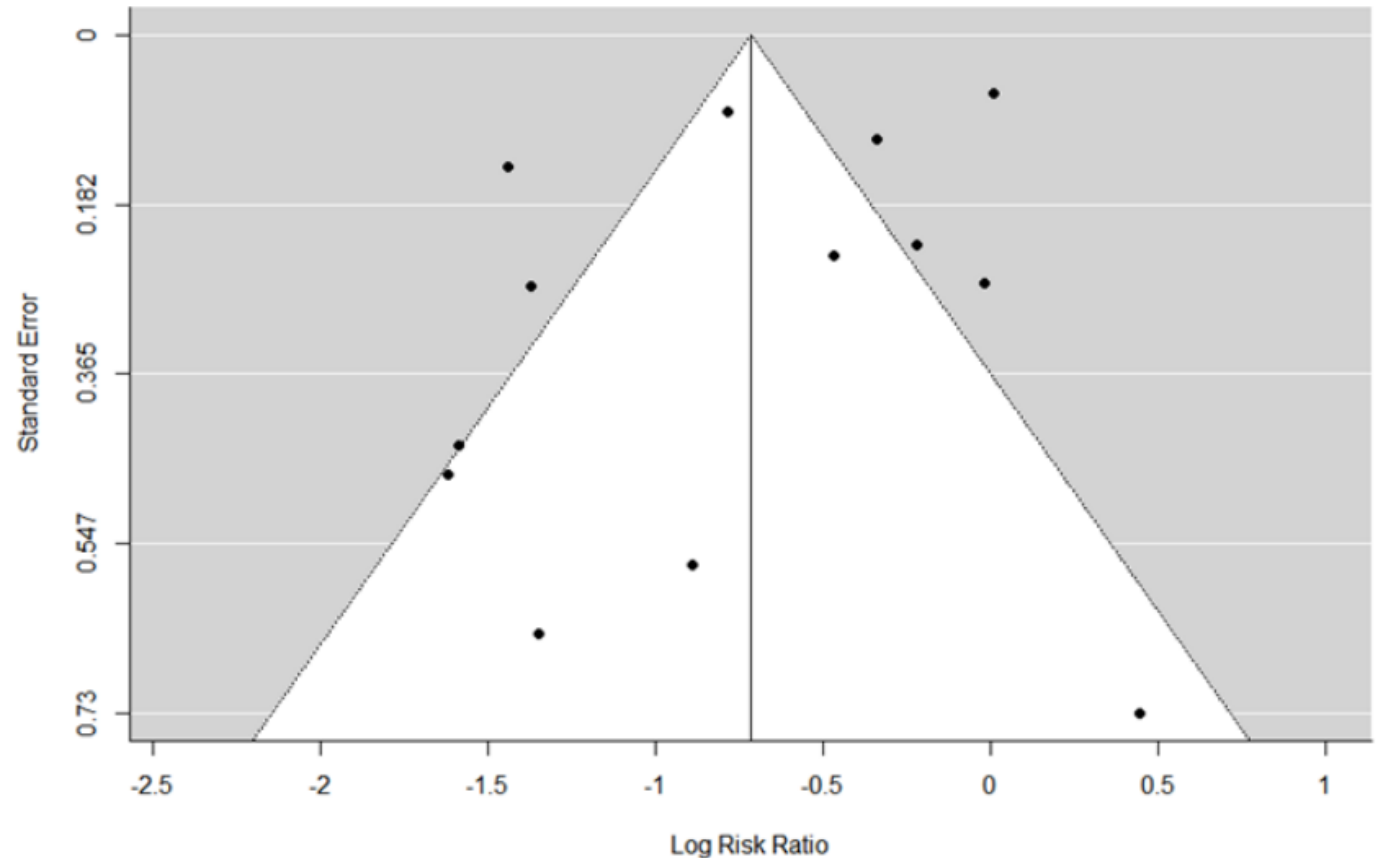


# Funnel Plot

- The existence of publication bias may be examined graphically using funnel plots. The name funnel plot is based on the fact that the precision in the estimation of the underlying treatment effect will increase as the sample size of component studies increases.
- Effect estimates from small studies will therefore scatter more widely at the bottom of the graph, with the spread narrowing among larger studies.
- In the absence of bias the plot will resemble a symmetrical inverted funnel.

# Funnel Plot

- The resulting plot shows little visual evidence of asymmetry because the effect estimates from the different studies appear randomly scattered throughout the plot. Whilst the above is a visual check for small study/publication bias, formal statistical tests based on a regression model also exist and are called tests for bias.



# Meta Analysis in R

- Harrer M, Cuijpers P, Furukawa TA, Ebert DD. Doing Meta-Analysis with R A HandsOn Guide Chapman and Hall/CRC; 2021 [Available from: [https://bookdown.org/MathiasHarrer/Doing\\_Meta\\_Analysis\\_in\\_R/](https://bookdown.org/MathiasHarrer/Doing_Meta_Analysis_in_R/)].