Systematic Reviews and Meta-analysis

PPIE Meets Statistics – Webinar
Tuesday 3rd December 2024
10:00 – 11:30am

Pradeep S. Virdee
Senior Statistician
Cancer Theme, Nuffield Dept. of Primary Care Health Sciences
University of Oxford

BETTA | UNIVERSITY OF OXFORD | NIHR | Statistics Group | NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES Medical Sciences Division | NIHR | School for Primary Care Research

Introductions

By

Sue Duncombe

PPI contributor

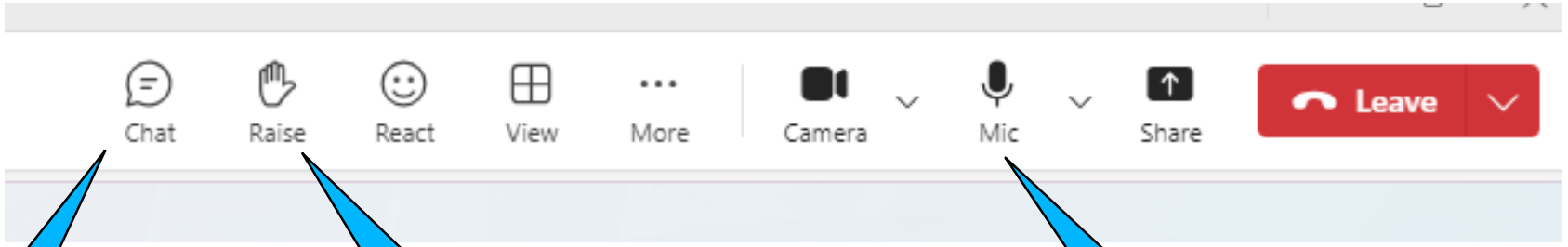
Working practices

- It’s okay to leave the meeting if you need to
- Respect each other
- Don’t interrupt others
- Everyone is equal
- It’s okay to ask questions – there are no silly questions!
- Let us know if we’ve lost you

Working practices

Wait until end of section to ask:

- Verbal chat – put your hand up on teams
- Teams chat – type your question at any point



Put any comments in the chat

Use this function to ask a question

Have on mute during presentations

Part 1:

Systematic reviews

By
Pradeep Virdee

By the end of the session…

1. What is a systematic review?
2. Why are they important?
3. How can they influence practice?
4. How do you conduct them?
5. What is a meta-analysis?

Types of reviews

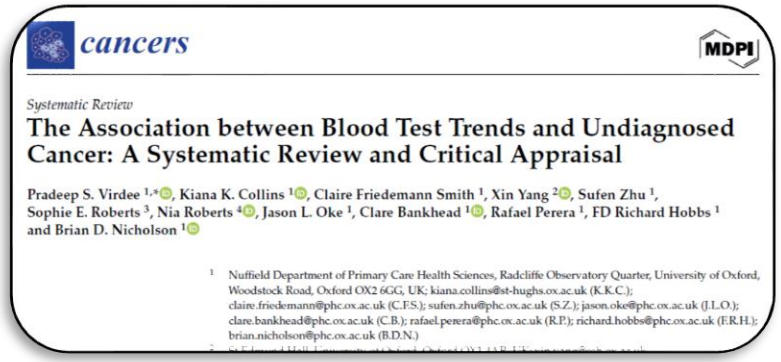
[1]

Critical review
Literature review
Mapping review/systematic map
Mixed studies review/mixed methods review
Overview
Qualitative systematic review/qualitative evidence synthesis
Rapid review
Scoping review
State-of-the-art review
Systematic review
Systematic search and review
Systematised review
Umbrella review

What is a systematic review?

A structured approach to collate and summarise research evidence in a reproducible, transparent, and unbiased way

Examples of a systematic review



cancers

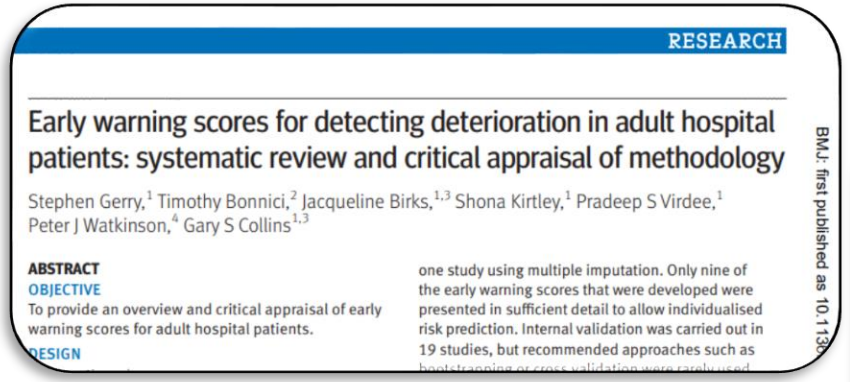
MDPI

Systematic Review

The Association between Blood Test Trends and Undiagnosed Cancer: A Systematic Review and Critical Appraisal

Pradeep S. Virdee [1,*], Kiana K. Collins [1], Claire Friedemann Smith [1], Xin Yang [2], Sufen Zhu [1], Sophie E. Roberts [3], Nia Roberts [4], Jason L. Oke [1], Clare Bankhead [1], Rafael Perera [1], FD Richard Hobbs [1] and Brian D. Nicholson [1]

[1] Nuffield Department of Primary Care Health Sciences, Radcliffe Observatory Quarter, University of Oxford, Woodstock Road, Oxford OX2 6GG, UK; kiana.collins@st-hughs.ox.ac.uk (K.K.C.); claire.friedemann@phc.ox.ac.uk (C.F.S.); sufen.zhu@phc.ox.ac.uk (S.Z.); jason.oke@phc.ox.ac.uk (J.L.O.); clare.bankhead@phc.ox.ac.uk (C.B.); rafael.perera@phc.ox.ac.uk (R.P.); richard.hobbs@phc.ox.ac.uk (F.R.H.); brian.nicholson@phc.ox.ac.uk (B.D.N.)



RESEARCH

Early warning scores for detecting deterioration in adult hospital patients: systematic review and critical appraisal of methodology

Stephen Gerry,[1] Timothy Bonnici,[2] Jacqueline Birks,[1,3] Shona Kirtley,[1] Pradeep S Virdee,[1] Peter J Watkinson,[4] Gary S Collins[1,3]

BMJ: first published as 10.1136

ABSTRACT

OBJECTIVE

To provide an overview and critical appraisal of early warning scores for adult hospital patients.

DESIGN

one study using multiple imputation. Only nine of the early warning scores that were developed were presented in sufficient detail to allow individualised risk prediction. Internal validation was carried out in 19 studies, but recommended approaches such as

JOURNAL OF MENTAL HEALTH RESEARCH IN INTELLECTUAL DISABILITIES
https://doi.org/10.1080/19315864.2024.2397403

Routledge
Taylor & Francis Group

OPEN ACCESS Check for updates

Suicidality and Intellectual Disability: A Systematic Review

Wai Man Raymond Chan and Ritesh Bhandarkar

Department of Psychiatry, Monash Health, Melbourne, Australia

ABSTRACT

Background: Suicidality in individuals with intellectual disability is a critical but under-researched area. This systematic review aims to synthesize existing literature on the prevalence, risk factors, and interventions for suicidality among individuals with intellectual disability.

Methods: Adhering to the PRISMA guidelines, a comprehensive review of databases was conducted for empirical studies on suicidality in intellectual disability. Data were extracted on sample characteristics, methodologies, and key findings.

KEYWORDS

Intellectual disability; mental retardation; developmental disability; suicide; suicide attempt

Journal of Affective Disorders 367 (2024) 701–712

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

ELSEVIER

Social media use, mental health and sleep: A systematic review with meta-analyses

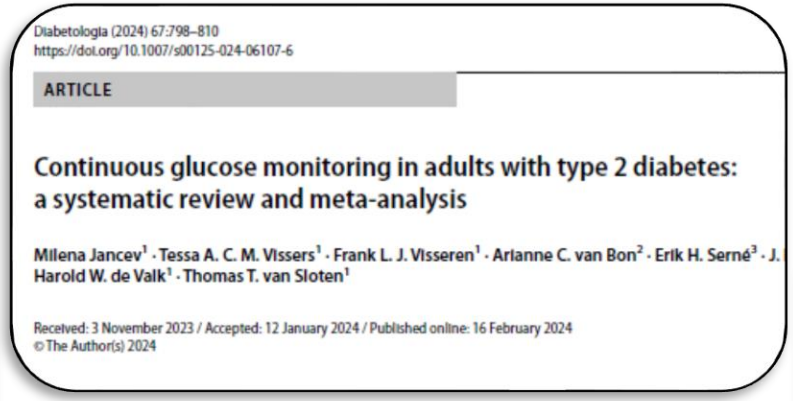
Oli Ahmed [a,*], Erin I. Walsh [a], Amy Dawel [b], Khawlah Alateeq [a,c], Daniela Andrea Espinoza Oyarce [a], Nicolas Cherbuin [a]

[a] National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australia
[b] School of Medicine and Psychology, Australian National University, Canberra, Australia
[c] Radiological Science, College of Applied Medical Science, King Saud University, Riyadh, Saudi Arabia

ARTICLE INFO

ABSTRACT

Background: The literature investigating the relationship between social media use, produced inconsistent findings. Younger people spend more time on social media more likely to be impacted by social media use. This systematic review



Diabetologia (2024) 67:798–810
https://doi.org/10.1007/s00125-024-06107-6

ARTICLE

Continuous glucose monitoring in adults with type 2 diabetes: a systematic review and meta-analysis

Milena Jancev[1] · Tessa A. C. M. Vissers[1] · Frank L. J. Visseren[1] · Arianne C. van Bon[2] · Erik H. Serné[3] · J. Harold W. de Valk[1] · Thomas T. van Sloten[1]

Received: 3 November 2023 / Accepted: 12 January 2024 / Published online: 16 February 2024
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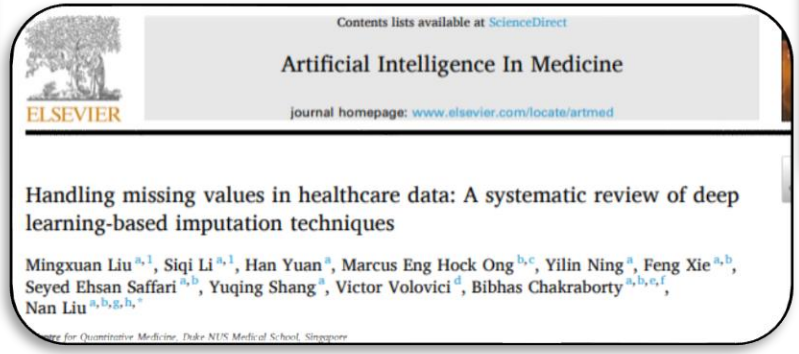


Contents lists available at ScienceDirect

Artificial Intelligence In Medicine

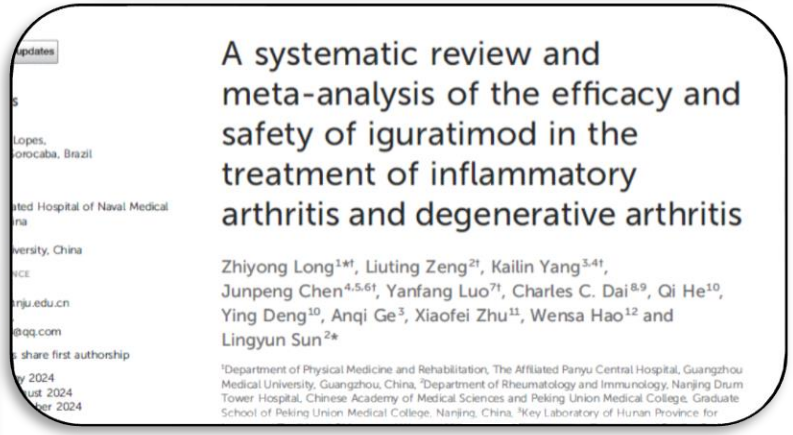
journal homepage: www.elsevier.com/locate/artmed

ELSEVIER

Handling missing values in healthcare data: A systematic review of deep learning-based imputation techniques

Mingxuan Liu [a,1], Siqi Li [a,1], Han Yuan [a], Marcus Eng Hock Ong [b,c], Yilin Ning [a], Feng Xie [a,b], Seyed Ehsan Saffari [a,b], Yuqing Shang [a], Victor Volovici [d], Bibhas Chakraborty [a,b,e,f], Nan Liu [a,b,g,h,*]

[*] Centre for Quantitative Medicine, Duke-NUS Medical School, Singapore



updates

Lopes, Sorocaba, Brazil

ated Hospital of Naval Medical

versity, China

share first authorship

2024
ust 2024
ber 2024

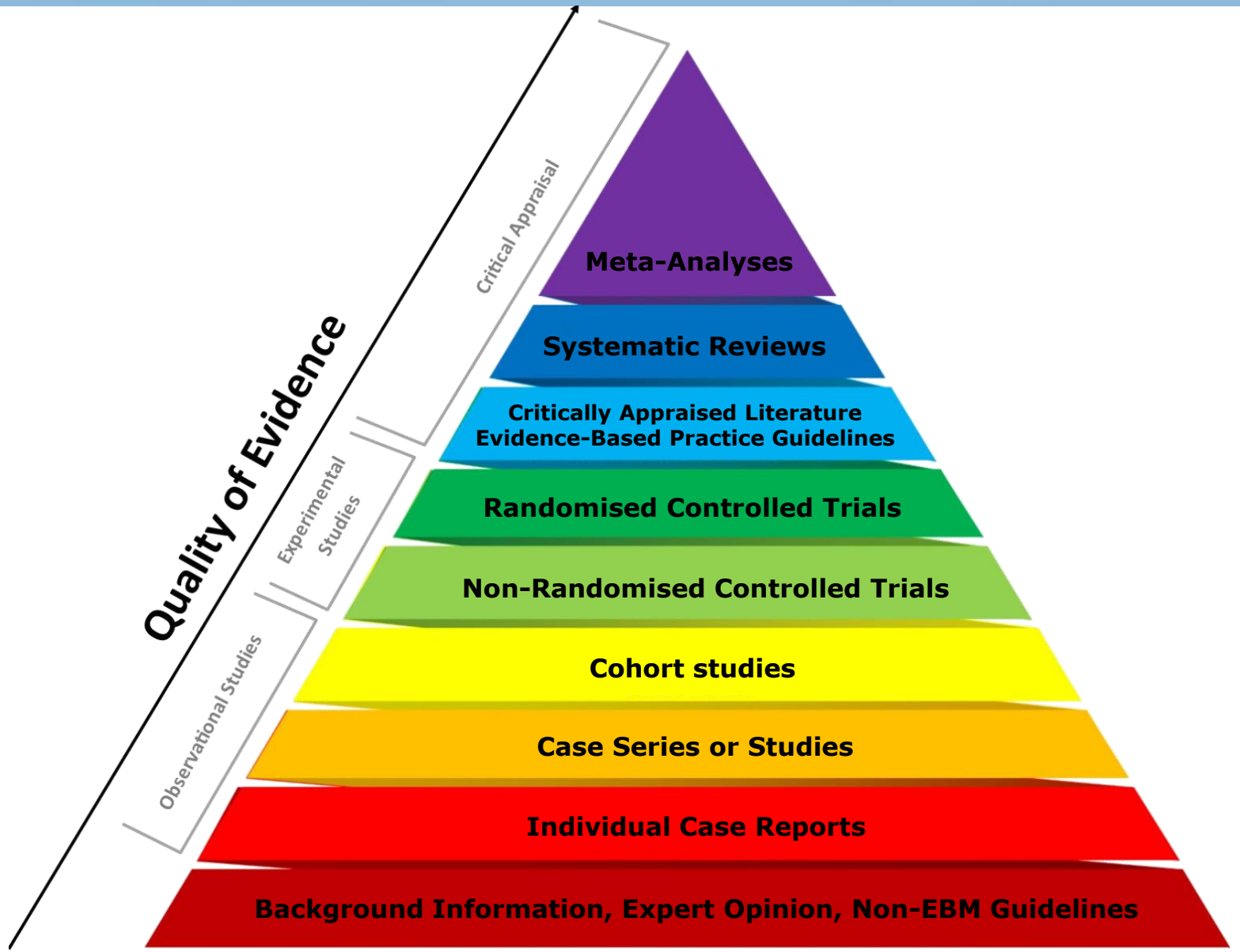
A systematic review and meta-analysis of the efficacy and safety of iguratimod in the treatment of inflammatory arthritis and degenerative arthritis

Zhiyong Long[1*†], Liuting Zeng[2†], Kailin Yang[3,4†], Junpeng Chen[4,5,6†], Yanfang Luo[7†], Charles C. Dai[8,9], Qi He[10], Ying Deng[10], Anqi Ge[3], Xiaofei Zhu[11], Wensa Hao[12] and Lingyun Sun[2*]

[1]Department of Physical Medicine and Rehabilitation, The Affiliated Panyu Central Hospital, Guangzhou Medical University, Guangzhou, China, [2]Department of Rheumatology and Immunology, Nanjing Drum Tower Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Graduate School of Peking Union Medical College, Nanjing, China, [3]Key Laboratory of Hunan Province for

Importance of systematic reviews

[2]



Why do a systematic reviews?

- Collate and summarise all studies in a relevant field using exhaustive eligibility criteria
- Minimise bias by including all relevant studies
- Keep us up to date in the field
- Help identify research gaps
- Risk of bias assessments
- Reproducible and transparent

Influencing practice

Systematic reviews provide evidence-based information to help inform decision making

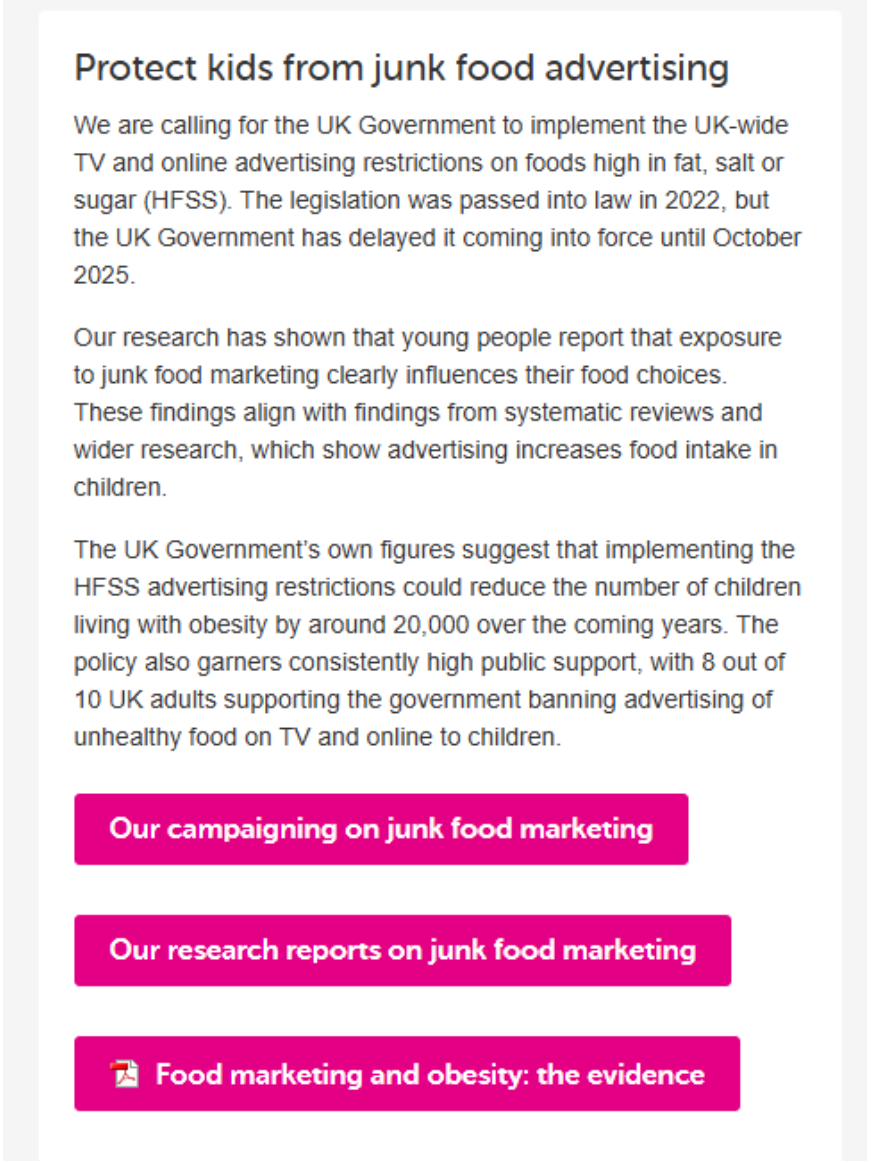
For example:

- Healthcare providers can to apply current evidence to patient care
- Can inform national policy making
- Contribute to the development of clinical guidelines to support clinicians in decision making

Influencing practice – example

[3]

Cancer Research UK (CRUK) uses systematic reviews and other research to inform their policy on obesity and diet. For example, CRUK's research shows that exposure to junk food marketing influences young people's food choices. This aligns with findings from systematic reviews and other research that show advertising increases food intake in children. CRUK is calling for the UK Government to implement restrictions on TV and online advertising of unhealthy food to children



Protect kids from junk food advertising

We are calling for the UK Government to implement the UK-wide TV and online advertising restrictions on foods high in fat, salt or sugar (HFSS). The legislation was passed into law in 2022, but the UK Government has delayed it coming into force until October 2025.

Our research has shown that young people report that exposure to junk food marketing clearly influences their food choices. These findings align with findings from systematic reviews and wider research, which show advertising increases food intake in children.

The UK Government's own figures suggest that implementing the HFSS advertising restrictions could reduce the number of children living with obesity by around 20,000 over the coming years. The policy also garners consistently high public support, with 8 out of 10 UK adults supporting the government banning advertising of unhealthy food on TV and online to children.

Our campaigning on junk food marketing

Our research reports on junk food marketing

Food marketing and obesity: the evidence

Main steps to undertaking a systematic review

[4]

Protocol development

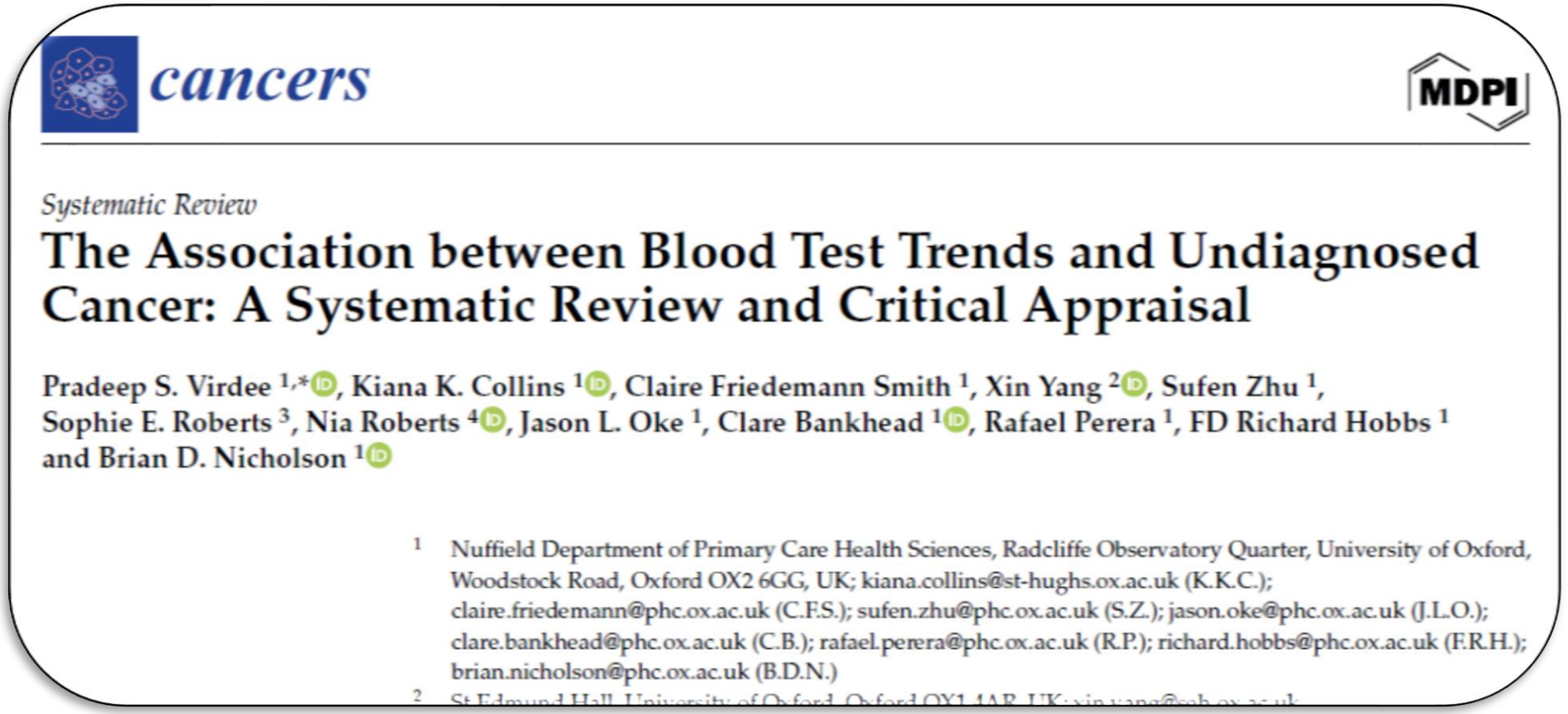
Study search

Screening

Data extraction

Data analysis

Example we'll be following today



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[2] St Edmund Hall, University of Oxford, Oxford OX1 4AR, UK; xin.yang@seh.ox.ac.uk

Main steps to undertaking a systematic review

[4]

Protocol development

Study search

Screening

Data extraction

Data analysis

Published evidence

Relevant evidence

Pre-specify our goals and methods

Protocol development

Background:

- What is/isn't known
- Rationale and aims for this review

Methods (pre-specified):

- Patient eligibility criteria
- Search strategy
- Study selection
- Data extraction
- Analysis methods
- Register of reviews: PROSPERO

Discussion

- Potential impact

Protocol development

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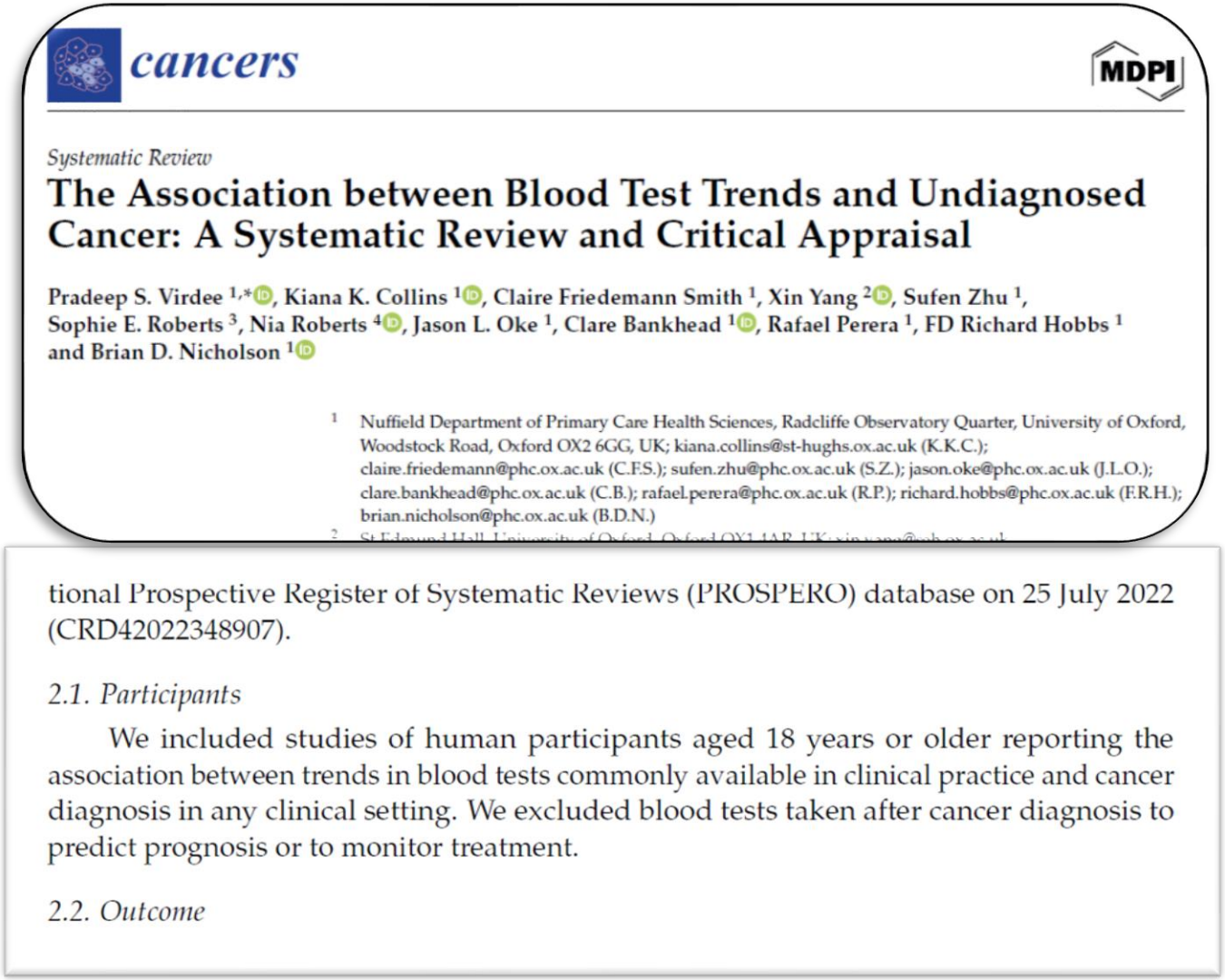

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[2] St Edmund Hall, University of Oxford, Oxford OX1 4AR, UK; xin.yang@phc.ox.ac.uk

tional Prospective Register of Systematic Reviews (PROSPERO) database on 25 July 2022 (CRD42022348907).

2.1. Participants

We included studies of human participants aged 18 years or older reporting the association between trends in blood tests commonly available in clinical practice and cancer diagnosis in any clinical setting. We excluded blood tests taken after cancer diagnosis to predict prognosis or to monitor treatment.

2.2. Outcome

Protocol development

Background:

- What is/isn't known
- Rationale and aims for this review

Methods (pre-specified):

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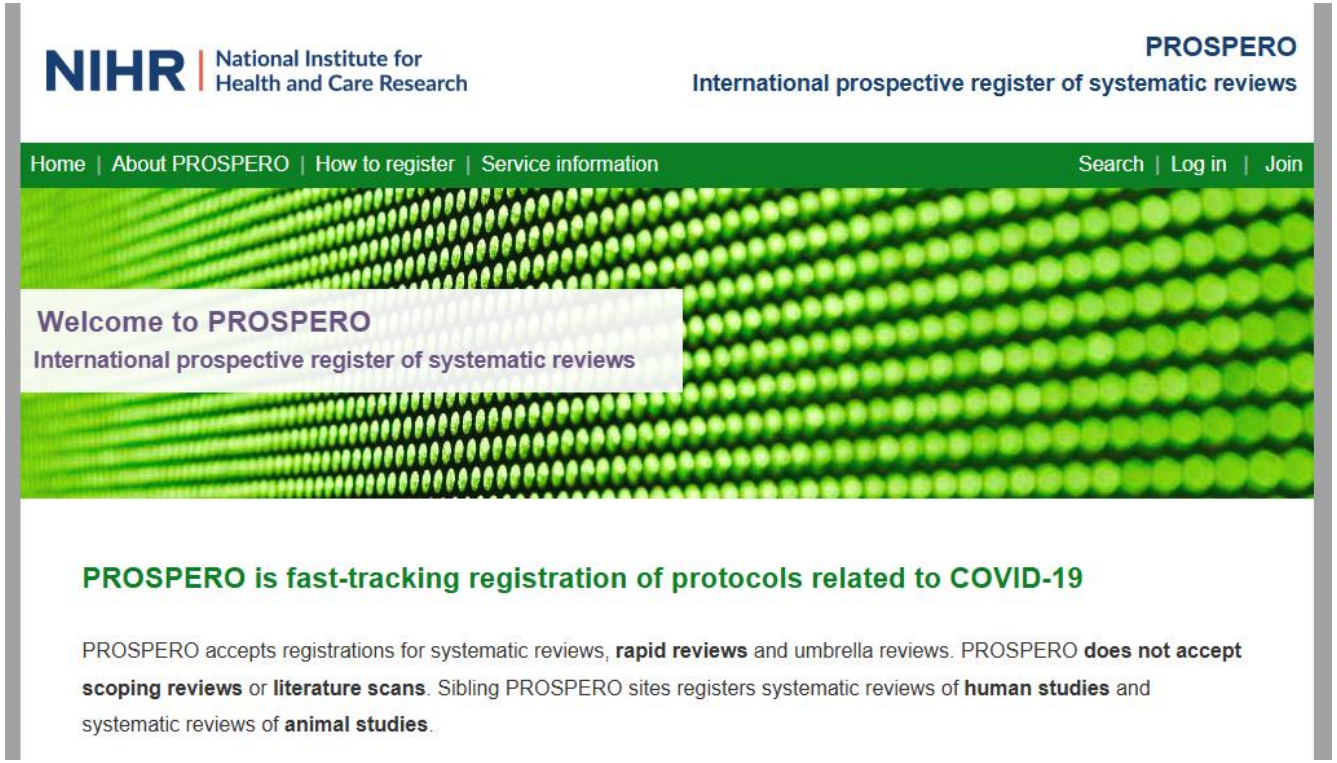
- Potential impact

https://www.crd.york.ac.uk/prospero/



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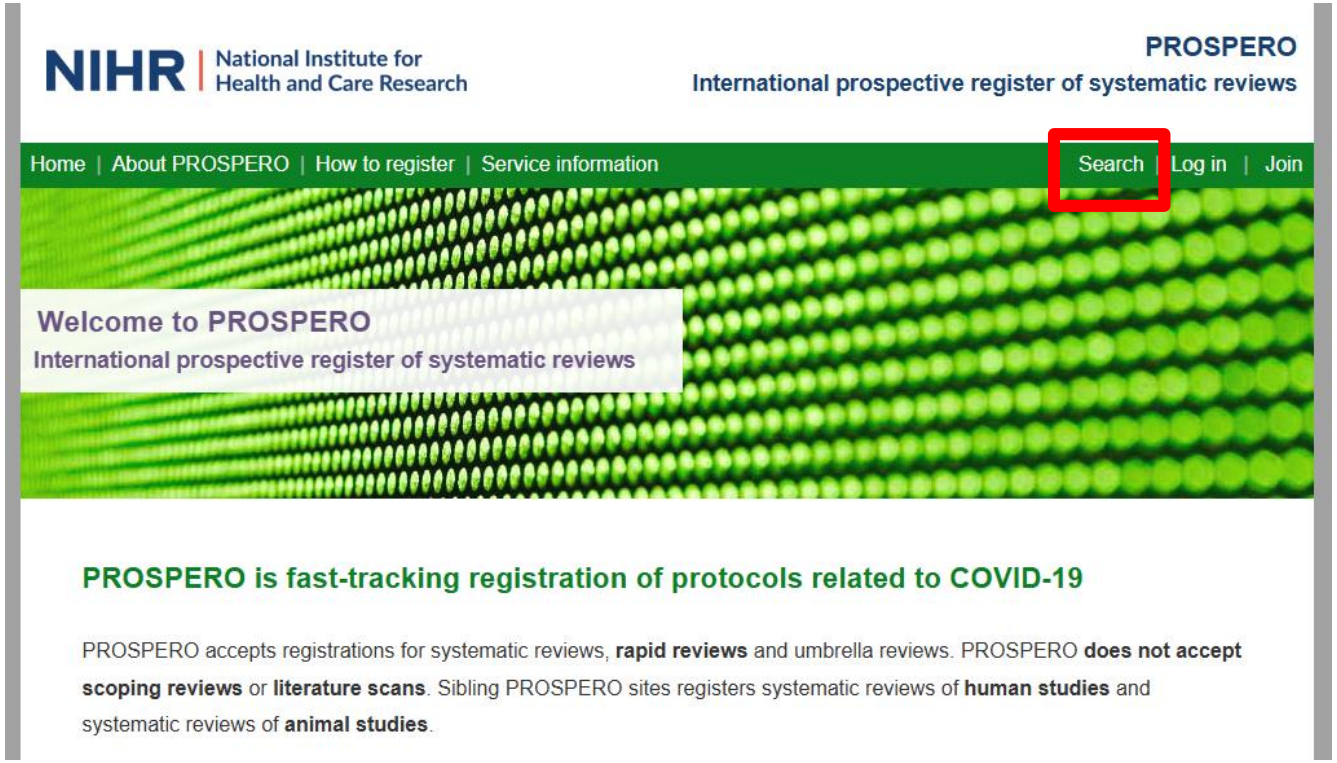

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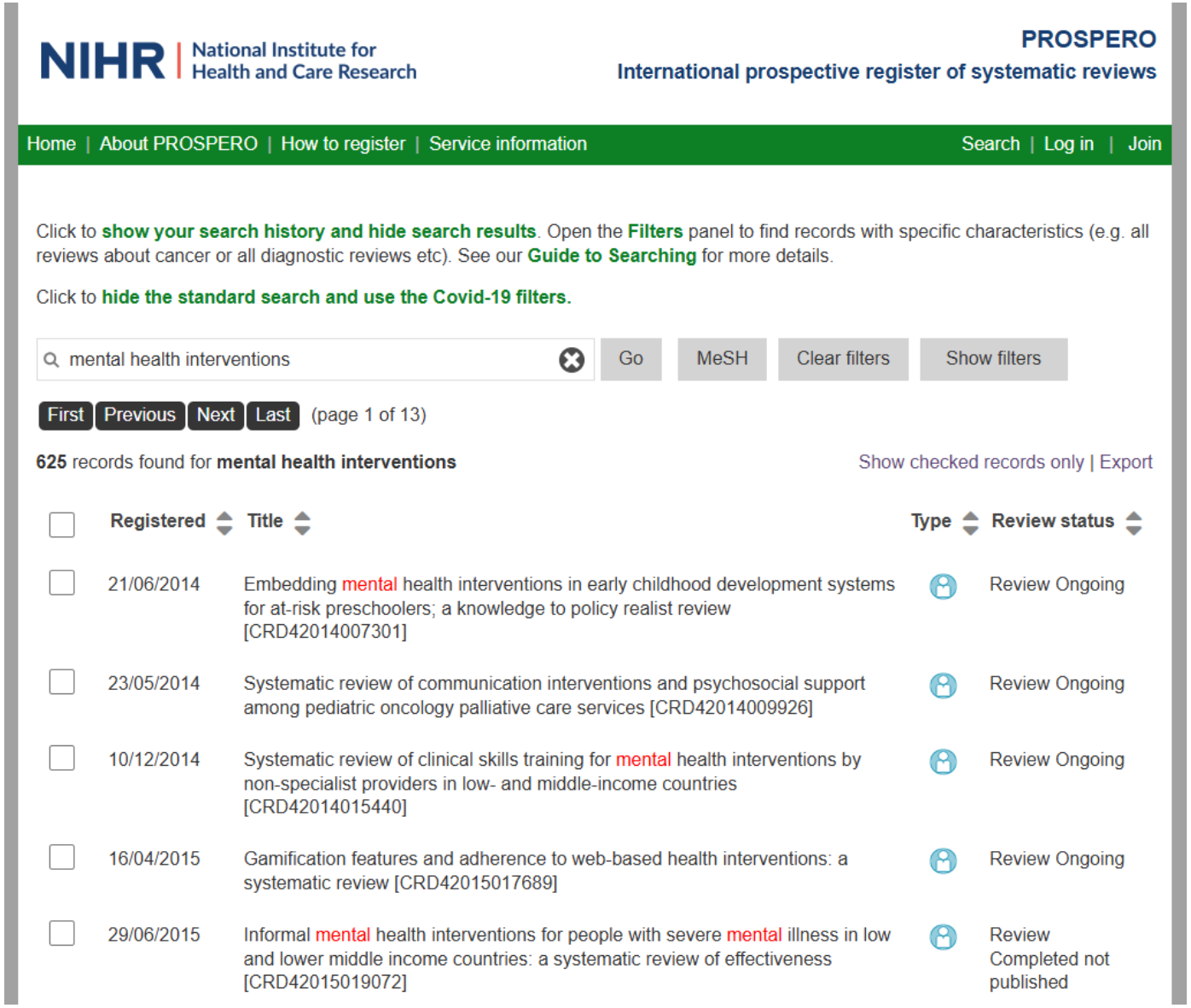

NIHR | National Institute for Health and Care Research

PROSPERO
International prospective register of systematic reviews

Home | About PROSPERO | How to register | Service information — Search | Log in | Join

Click to **show your search history and hide search results**. Open the **Filters** panel to find records with specific characteristics (e.g. all reviews about cancer or all diagnostic reviews etc). See our **Guide to Searching** for more details.

Click to **hide the standard search and use the Covid-19 filters.**

mental health interventions | Go | MeSH | Clear filters | Show filters

First | Previous | Next | Last (page 1 of 13)

625 records found for **mental health interventions** — Show checked records only | Export

Registered	Title	Type	Review status
21/06/2014	Embedding mental health interventions in early childhood development systems for at-risk preschoolers; a knowledge to policy realist review [CRD42014007301]		Review Ongoing
23/05/2014	Systematic review of communication interventions and psychosocial support among pediatric oncology palliative care services [CRD42014009926]		Review Ongoing
10/12/2014	Systematic review of clinical skills training for mental health interventions by non-specialist providers in low- and middle-income countries [CRD42014015440]		Review Ongoing
16/04/2015	Gamification features and adherence to web-based health interventions: a systematic review [CRD42015017689]		Review Ongoing
29/06/2015	Informal mental health interventions for people with severe mental illness in low and lower middle income countries: a systematic review of effectiveness [CRD42015019072]		Review Completed not published

Main steps to undertaking a systematic review

[4]

Protocol development

Study search

Screening

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Data analysis

How do we find studies?

Things to understand

We will first cover these two things:

- Indexing
- Grey literature

Understanding indexing

- A process done by journals
- When an article gets published, it gets “indexed”
- This means it gets filed in an online register/database

Understanding indexing

Google Scholar

MEDLINE

CINAHL Database

Scopus 20

IEEE
Advancing Technology for Humanity

PubMed®

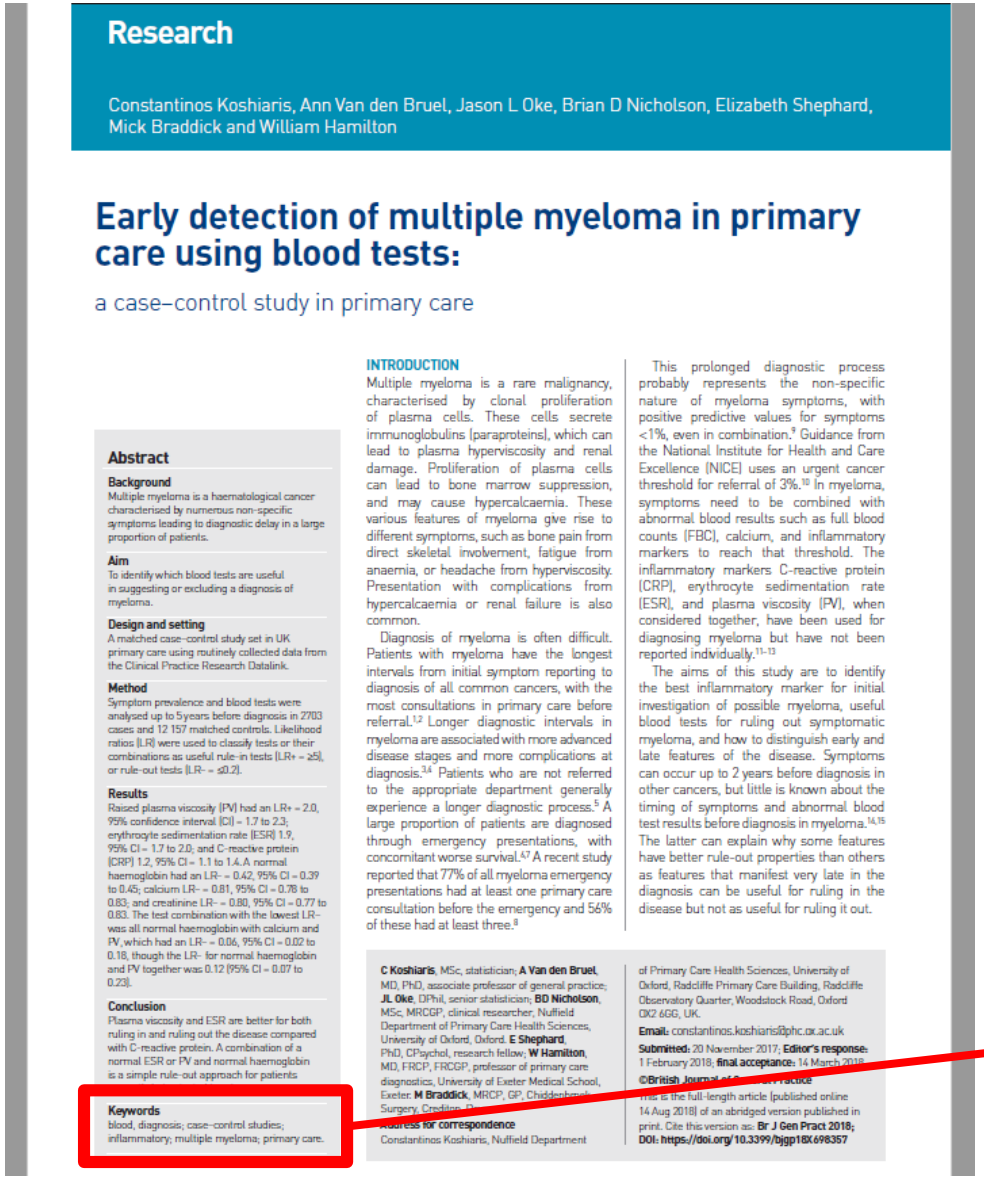
ProQuest
Part of Clarivate

Web of Science™

JSTOR

Embase

Understanding indexing



Research

Constantinos Koshiaris, Ann Van den Bruel, Jason L Oke, Brian D Nicholson, Elizabeth Shephard, Mick Braddick and William Hamilton

Early detection of multiple myeloma in primary care using blood tests:

a case–control study in primary care

Abstract

Background
Multiple myeloma is a haematological cancer characterised by numerous non-specific symptoms leading to diagnostic delay in a large proportion of patients.

Aim
To identify which blood tests are useful in suggesting or excluding a diagnosis of myeloma.

Design and setting
A matched case–control study set in UK primary care using routinely collected data from the Clinical Practice Research Datalink.

Method
Symptom prevalence and blood tests were analysed up to 5 years before diagnosis in 2703 cases and 12 157 matched controls. Likelihood ratios (LR) were used to classify tests or their combinations as useful rule-in tests (LR+ ≥5), or rule-out tests (LR− ≤0.2).

Results
Raised plasma viscosity (PV) had an LR+ = 2.0, 95% confidence interval (CI) = 1.7 to 2.3; erythrocyte sedimentation rate (ESR) 1.9, 95% CI = 1.7 to 2.0; and C-reactive protein (CRP) 1.2, 95% CI = 1.1 to 1.4. A normal haemoglobin had an LR− = 0.42, 95% CI = 0.39 to 0.45; calcium LR− = 0.81, 95% CI = 0.78 to 0.83; and creatinine LR− = 0.80, 95% CI = 0.77 to 0.83. The test combination with the lowest LR− was all normal haemoglobin with calcium and PV, which had an LR− = 0.06, 95% CI = 0.02 to 0.18, though the LR− for normal haemoglobin and PV together was 0.12 (95% CI = 0.07 to 0.23).

Conclusion
Plasma viscosity and ESR are better for both ruling in and ruling out the disease compared with C-reactive protein. A combination of a normal ESR or PV and normal haemoglobin is a simple rule-out approach for patients

Keywords
blood, diagnosis; case–control studies; inflammatory; multiple myeloma; primary care.

INTRODUCTION

Multiple myeloma is a rare malignancy, characterised by clonal proliferation of plasma cells. These cells secrete immunoglobulins (paraproteins), which can lead to plasma hyperviscosity and renal damage. Proliferation of plasma cells can lead to bone marrow suppression, and may cause hypercalcaemia. These various features of myeloma give rise to different symptoms, such as bone pain from direct skeletal involvement, fatigue from anaemia, or headache from hyperviscosity. Presentation with complications from hypercalcaemia or renal failure is also common.

Diagnosis of myeloma is often difficult. Patients with myeloma have the longest intervals from initial symptom reporting to diagnosis of all common cancers, with the most consultations in primary care before referral.[1,2] Longer diagnostic intervals in myeloma are associated with more advanced disease stages and more complications at diagnosis.[3,4] Patients who are not referred to the appropriate department generally experience a longer diagnostic process.[5] A large proportion of patients are diagnosed through emergency presentations, with concomitant worse survival.[4,7] A recent study reported that 77% of all myeloma emergency presentations had at least one primary care consultation before the emergency and 56% of these had at least three.[8]

This prolonged diagnostic process probably represents the non-specific nature of myeloma symptoms, with positive predictive values for symptoms <1%, even in combination.[9] Guidance from the National Institute for Health and Care Excellence (NICE) uses an urgent cancer threshold for referral of 3%.[10] In myeloma, symptoms need to be combined with abnormal blood results such as full blood counts (FBC), calcium, and inflammatory markers to reach that threshold. The inflammatory markers C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and plasma viscosity (PV), when considered together, have been used for diagnosing myeloma but have not been reported individually.[11–13]

The aims of this study are to identify the best inflammatory marker for initial investigation of possible myeloma, useful blood tests for ruling out symptomatic myeloma, and how to distinguish early and late features of the disease. Symptoms can occur up to 2 years before diagnosis in other cancers, but little is known about the timing of symptoms and abnormal blood test results before diagnosis in myeloma.[14,15] The latter can explain why some features have better rule-out properties than others as features that manifest very late in the diagnosis can be useful for ruling in the disease but not as useful for ruling it out.

C Koshiaris, MSc, statistician; **A Van den Bruel**, MD, PhD, associate professor of general practice; **JL Oke**, DPhil, senior statistician; **BD Nicholson**, MSc, MRCGP, clinical researcher; Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford. **E Shephard**, PhD, CPsychol, research fellow; **W Hamilton**, MD, FRCP, FRCGP, professor of primary care diagnostics, University of Exeter Medical School, Exeter. **M Braddick**, MRCP, GP, Chiddenbrook Surgery, Crediton. **Address for correspondence** Constantinos Koshiaris, Nuffield Department of Primary Care Health Sciences, University of Oxford, Radcliffe Primary Care Building, Radcliffe Observatory Quarter, Woodstock Road, Oxford OX2 6GG, UK.
Email: constantinos.koshiaris@phc.ox.ac.uk

Submitted: 20 November 2017; **Editor's response:** 1 February 2018; **final acceptance:** 14 March 2018.
©British Journal of General Practice
This is the full-length article (published online 14 Aug 2018) of an abridged version published in print. Cite this version as: **Br J Gen Pract 2018; DOI: https://doi.org/10.3399/bjgp18X698357**

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Keywords
blood, diagnosis; case–control studies; inflammatory; multiple myeloma; primary care.

Understanding grey literature

Study results are conventionally reported as a paper in a journal
Journals ask for an “Article Processing Charge” – a payment
A ‘commercial” approach

Grey literature: papers published outside of ‘commercial publishing’
Examples are:

- PhD thesis
- Conference abstract
- Ongoing research
- Pre-print

Open Access
Theses and Dissertations

ClinicalTrials.gov

overton

Understanding grey literature

[5]

Systematic reviews can include grey literature

Advantages include:

- Capture research not available in journal articles
- Capture research which is ongoing (not yet formally published)
- Reduces positive results publication bias (negative results are less likely to be published in a journal)

Disadvantages include:

- Peer review process is unclear – may contain inaccuracies
- Additional papers to screen – can add substantially to timelines
- Don’t always have complete results

Back to our systematic review…

Planned list of databases:

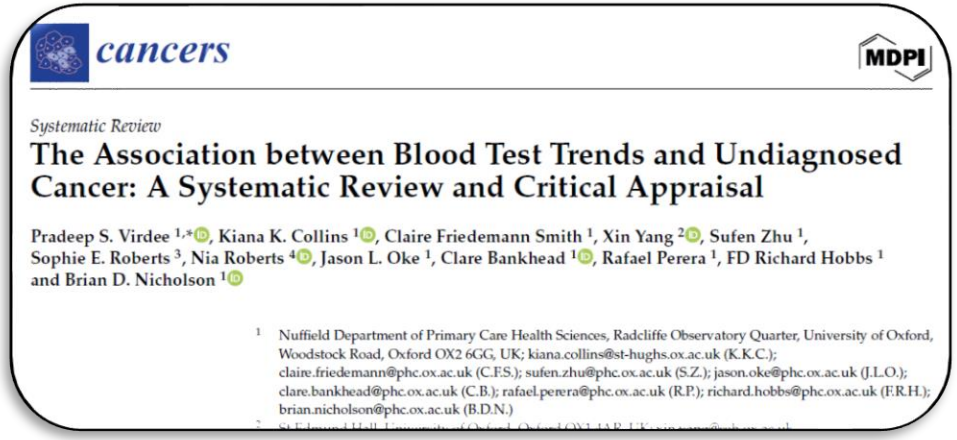
MEDLINE

EMBASE

PubMed

CINAHL

Web of Science



cancers

MDPI

Systematic Review

The Association between Blood Test Trends and Undiagnosed Cancer: A Systematic Review and Critical Appraisal

Pradeep S. Virdee [1,*], Kiana K. Collins [1], Claire Friedemann Smith [1], Xin Yang [2], Sufen Zhu [1], Sophie E. Roberts [3], Nia Roberts [4], Jason L. Oke [1], Clare Bankhead [1], Rafael Perera [1], FD Richard Hobbs [1] and Brian D. Nicholson [1]

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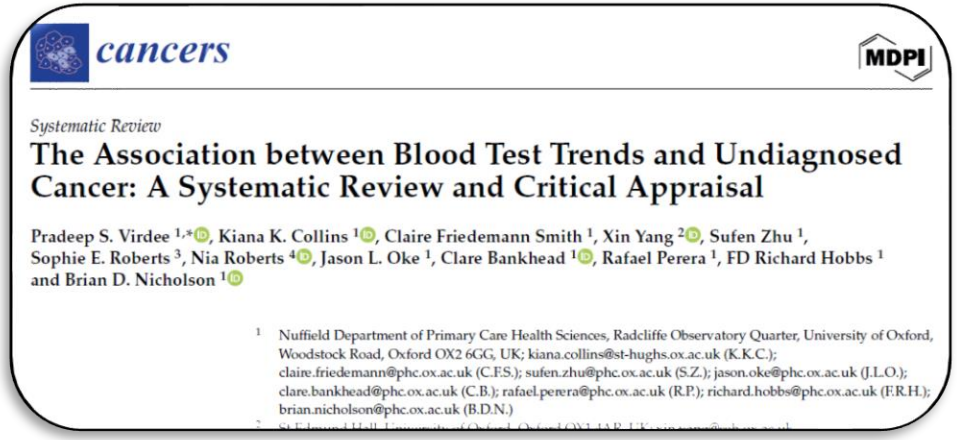
Consult an experienced librarian

Search strategy

Find articles
We need a list of relevant key words:

“blood test”
“haematological test”
“haemoglobin”

“cancer”
“tumour”
…



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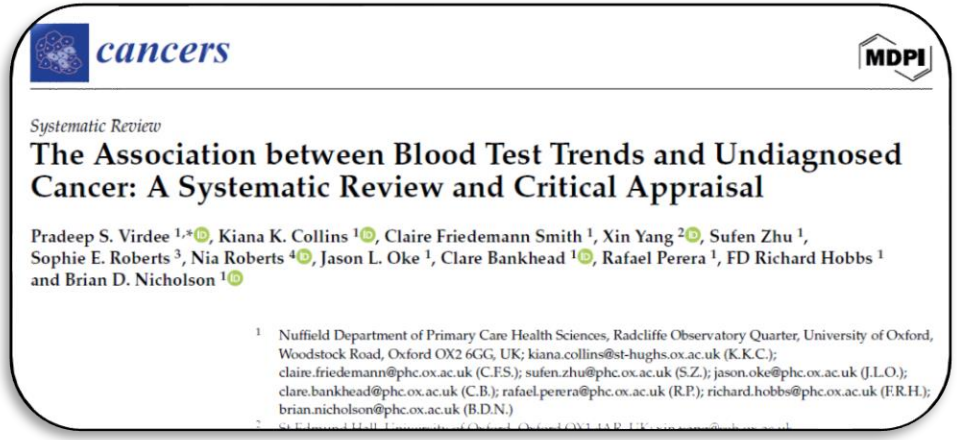
…



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Can you think of other potential keywords?

List of databases to search

Planned list of databases:

MEDLINE

EMBASE

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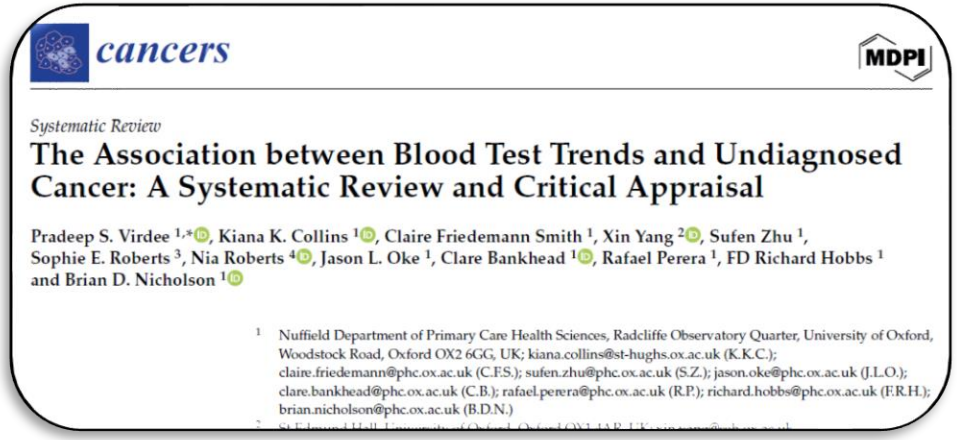

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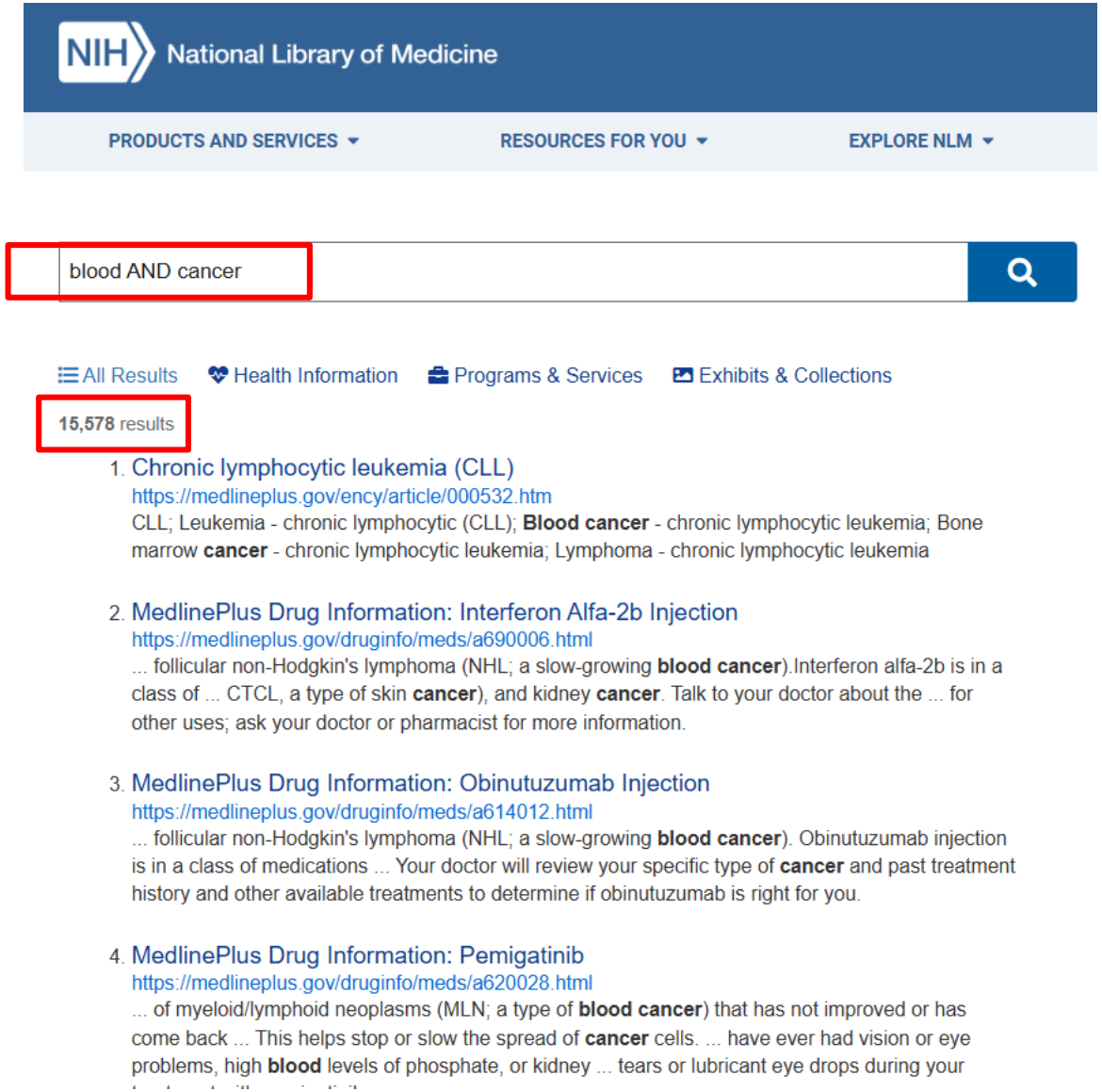
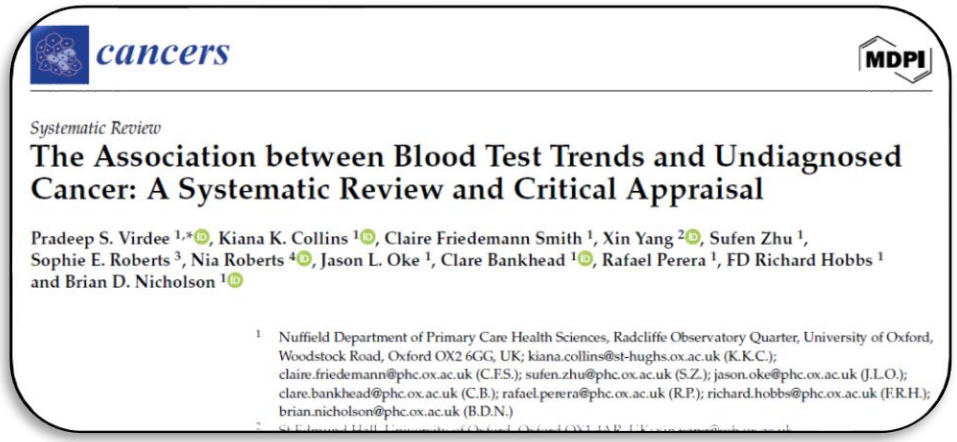
Search strategy – MEDLINE example

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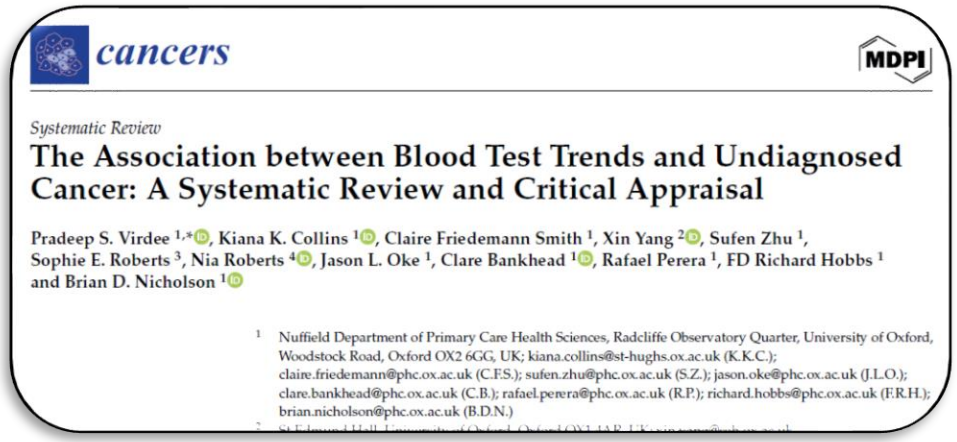
Consult an experienced librarian

Search strategy - MEDLINE

1 exp Neoplasms/bl [Blood]
2 exp Neoplasms/
3 (neoplas* or tumor* or tumour* or cancer* or malignan* or carcino* or sarcom* or leukaem* or leukem* or lymphom* or melano* or metasta* or mesothelio* or mesotelio* or carcinomatos* or gliom* or glioblastom* or osteosarcom* or blastom* or neuroblastom* or oncolog* or myelodysplas* or adenocarcinoma* or choriocarcinoma*).ti.
4 2 or 3
5 Hematologic Tests/
6 exp Blood Cell Count/
7 exp Blood Cells/an
8 Blood Sedimentation/
9 Blood Viscosity/
10 exp Hemoglobins/an, bl
11 Hematocrit/
12 Erythrocyte Indices/ or Erythrocytes/an, bl
13 platelet function tests/ or mean platelet volume/
14 Liver Function Tests/
15 alanine transaminase/an, bl or exp aspartate aminotransferases/an, bl
16 Albumins/an or Albuminuria/bl, ur
17 serum albumin/ or serum albumin, human/
18 exp Bilirubin/an, bl
19 alpha-Fetoproteins/an, bl
20 Alkaline Phosphatase/an, bl [Analysis, Blood]
21 exp Kidney Function Tests/
22 Sodium/an, bl, ur
23 Potassium/an, bl, ur
24 Creatinine/an, bl, ur
25 Urea/an, bl, ur
26 Amylases/an, bl
27 Calcium/an, bl, ur
28 Glycated Hemoglobin A/an, bl or Blood Glucose/an, bl
29 Blood Proteins/an, bl
30 C-Reactive Protein/an, bl
31 exp Thyrotropin/an, bl
32 ((hemoglobin? or haemoglobin? or hb) adj3 (variation? or level? or concentration? or declin* or mean cell)).ti,ab,kf. or (hemoglobin? or haemoglobin?).ti.
33 ((complete blood or whole blood or blood cell or white cell or erythrocyte? or leukocyte? or platelet? or lymphocyte? or eosinophil? or neutrophil? or basophil? or monocyte?) adj2 (count? or variation?)).ti,ab,kf.
34 ((lymphocyte? or eosinophil? or neutrophil? or basophil? or monocyte?) adj2 (percent* or "%")).ti,ab,kf.
35 (erythrocyte sedimentation or blood sedimentation or blood viscosity or mean platelet or mean cell volume or hematocrit? or haematocrit? or ((blood cell or erythrocyte?) adj2 (index or indices or distribution))).ti,ab,kf.
36 ((c-reactive protein or crp) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (c-reactive protein or crp).ti.
37 ((total or serum or blood or plasma) adj2 protein?).ti,ab,kf. or protein.ti.
38 ((albumin? adj3 (plasma or serum or blood or variation? or level? or concentration? or declin*)) or albumin creatinine ratio?).ti,ab,kf. or albumin*.ti.
39 ((alkaline phosphatase or alp) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (alkaline phosphatase or alp).ti.
40 ((aminotransferase or ast or sgot or alt or sgpt) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (aminotransferase or ast or sgot or alt or sgpt).ti.
41 (bilirubin adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or bilirubin.ti.
42 (liver enzyme? adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (liver enzyme? or liver function).ti. or liver function test*.ti,ab,kf.
43 (renal funtion test* or kidney function test*).ti,ab,kf. or (renal function or kidney function).ti.
44 (sodium adj3 (plasma or serum or blood or variation? or level? or concentration? or declin*)).ti,ab,kf. or sodium.ti.
45 (potassium adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or potassium.ti.
46 (creatinine adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or creatinine.ti.
47 ((urea adj3 (plasma or serum or blood or variation? or level? or concentration? or decline?)) or urea cycle?).ti,ab,kf. or urea.ti.
48 (amylase adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or amylase.ti.
49 (((glucose or hba1c) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)) or fasting glucose).ti,ab,kf. or (glucose or hba1c).ti.
50 (calcium adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or calcium.ti. or calcium adjusted.ti,ab,kf.
51 (((thyrotropin? or thyroid stimulating hormone?) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)) or fasting glucose).ti,ab,kf. or (thyrotropon? or thyroid stimulating hormone?).ti.
52 anemia/ or anemia, hypochromic/ or anemia, iron-deficiency/ or exp anemia, macrocytic/
53 (an?emia? or an?emic or microcytosis or microcytic).ti,ab,kf.
54 or/5-53
55 4 and 54
56 1 or 55
57 exp Neoplasms/di
58 early diagnosis/ or "early detection of cancer"/
59 (detect* or diagnos* or screen*).ti.
60 ((neoplas* or tumor* or tumour* or cancer* or malignan* or carcino* or sarcom* or leukaem* or leukem* or lymphom* or melano* or metasta* or mesothelio* or mesotelio* or carcinomatos* or gliom* or glioblastom* or osteosarcom* or blastom* or neuroblastom* or oncolog* or myelodysplas* or adenocarcinoma* or choriocarcinoma*) adj3 (diagnos* or detect* or screen*)).ti,ab,kf.
61 57 or 58 or 59 or 60
62 56 and 61
63 (trend? or pattern? or lead time* or timeline* or time line* or time frame? or time frame? or interval?).ti,ab,kf.
64 ((longterm or long-term) adj2 (variation? or chang* or difference* or declin* or decreas* or increas* or elevat* or level? or concentration)).ti,ab,kf.
65 (prediagnos* or pre-diagnos* or ((before or prior) adj2 diagnos*)).ti,ab,kf.
66 ((risk? or predict*) adj5 (model* or logarithm* or algorithm* or maching learning)).ti,ab,kf.
67 (model* or logarithm* or algorithm* or maching learning).ti.
68 (risk? adj2 (scor* or model* or index or indices or tool* or assessment? or measurement?)).ti,ab,kf.
69 (Models, Biological/ or Models, Statistical/) and exp Risk/
70 63 or 64 or 65 or 66 or 67 or 68 or 69
71 62 and 70
72 exp animals/ not humans/
73 71 not 72



cancers

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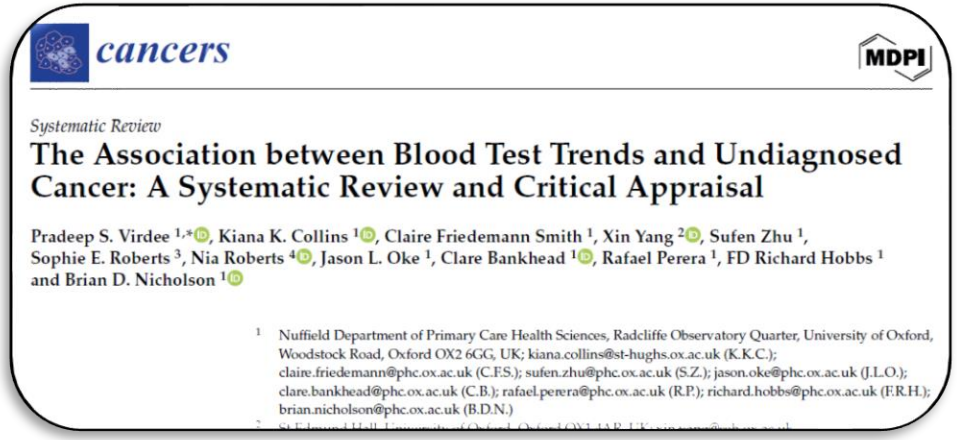
Search strategy - MEDLINE



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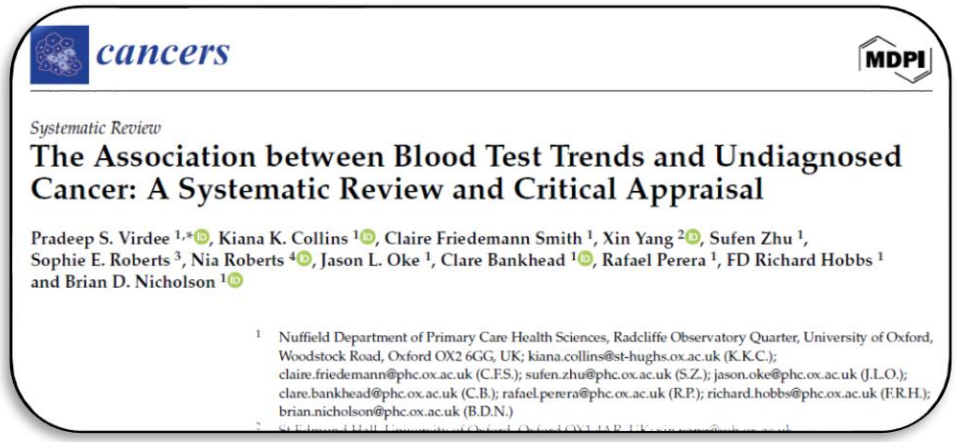
60 ((neoplas* or tumor* or tumour* or cancer* or malignan* or carcino* or sarcom* or leukaem* or leukem* or lymphom* or melano* or metasta* or mesothelio* or mesotelio* or carcinomatos* or gliom* or glioblastom* or osteosarcom* or blastom* or neuroblastom* or oncolog* or myelodysplas* or adenocarcinoma* or choriocarcinoma*) adj3 (diagnos* or detect* or screen*)).ti,ab,kf.

Search strategy - MEDLINE

1 exp Neoplasms/bl [Blood]
2 exp Neoplasms/
3 (neoplas* or tumor* or tumour* or cancer* or malignan* or carcino* or sarcom* or leukaem* or leukem* or lymphom* or melano* or metasta* or mesothelio* or mesotelio* or carcinomatos* or gliom* or glioblastom* or osteosarcom* or blastom* or neuroblastom* or oncolog* or myelodysplas* or adenocarcinoma* or choriocarcinoma*).ti.
4 2 or 3
5 Hematologic Tests/
6 exp Blood Cell Count/
7 exp Blood Cells/an
8 Blood Sedimentation/
9 Blood Viscosity/
10 exp Hemoglobins/an, bl
11 Hematocrit/
12 Erythrocyte Indices/ or Erythrocytes/an, bl
13 platelet function tests/ or mean platelet volume/
14 Liver Function Tests/
15 alanine transaminase/an, bl or exp aspartate aminotransferases/an, bl
16 Albumins/an or Albuminuria/bl, ur
17 serum albumin/ or serum albumin, human/
18 exp Bilirubin/an, bl
19 alpha-Fetoproteins/an, bl
20 Alkaline Phosphatase/an, bl [Analysis, Blood]
21 exp Kidney Function Tests/
22 Sodium/an, bl, ur
23 Potassium/an, bl, ur
24 Creatinine/an, bl, ur
25 Urea/an, bl, ur
26 Amylases/an, bl
27 Calcium/an, bl, ur
28 Glycated Hemoglobin A/an, bl or Blood Glucose/an, bl
29 Blood Proteins/an, bl
30 C-Reactive Protein/an, bl
31 exp Thyrotropin/an, bl
32 ((hemoglobin? or haemoglobin? or hb) adj3 (variation? or level? or concentration? or declin* or mean cell)).ti,ab,kf. or (hemoglobin? or haemoglobin?).ti.
33 ((complete blood or whole blood or blood cell or white cell or erythrocyte? or leukocyte? or platelet? or lymphocyte? or eosinophil? or neutrophil? or basophil? or monocyte?) adj2 (count? or variation?)).ti,ab,kf.
34 ((lymphocyte? or eosinophil? or neutrophil? or basophil? or monocyte?) adj2 (percent* or "%")).ti,ab,kf.
35 (erythrocyte sedimentation or blood sedimentation or blood viscosity or mean platelet or mean cell volume or hematocrit? or haematocrit? or ((blood cell or erythrocyte?) adj2 (index or indices or distribution))).ti,ab,kf.
36 ((c-reactive protein or crp) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (c-reactive protein or crp).ti.
37 ((total or serum or blood or plasma) adj2 protein?).ti,ab,kf. or protein.ti.
38 ((albumin? adj3 (plasma or serum or blood or variation? or level? or concentration? or declin*)) or albumin creatinine ratio?).ti,ab,kf. or albumin*.ti.
39 ((alkaline phosphatase or alp) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (alkaline phosphatase or alp).ti.
40 ((aminotransferase or ast or sgot or alt or sgpt) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (aminotransferase or ast or sgot or alt or sgpt).ti.
41 (bilirubin adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or bilirubin.ti.
42 (liver enzyme? adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or (liver enzyme? or liver function).ti. or liver function test*.ti,ab,kf.
43 (renal funtion test* or kidney function test*).ti,ab,kf. or (renal function or kidney function).ti.
44 (sodium adj3 (plasma or serum or blood or variation? or level? or concentration? or declin*)).ti,ab,kf. or sodium.ti.
45 (potassium adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or potassium.ti.
46 (creatinine adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or creatinine.ti.
47 ((urea adj3 (plasma or serum or blood or variation? or level? or concentration? or decline?)) or urea cycle?).ti,ab,kf. or urea.ti.
48 (amylase adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or amylase.ti.
49 (((glucose or hba1c) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)) or fasting glucose).ti,ab,kf. or (glucose or hba1c).ti.
50 (calcium adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)).ti,ab,kf. or calcium.ti. or calcium adjusted.ti,ab,kf.
51 (((thyrotropin? or thyroid stimulating hormone?) adj3 (plasma or serum or blood or variation? or level? or concentration? or elevat? or increas* or high*)) or fasting glucose).ti,ab,kf. or (thyrotropon? or thyroid stimulating hormone?).ti.
52 anemia/ or anemia, hypochromic/ or anemia, iron-deficiency/ or exp anemia, macrocytic/
53 (an?emia? or an?emic or microcytosis or microcytic).ti,ab,kf.
54 or/5-53
55 4 and 54
56 1 or 55
57 exp Neoplasms/di
58 early diagnosis/ or "early detection of cancer"/
59 (detect* or diagnos* or screen*).ti.
60 ((neoplas* or tumor* or tumour* or cancer* or malignan* or carcino* or sarcom* or leukaem* or leukem* or lymphom* or melano* or metasta* or mesothelio* or mesotelio* or carcinomatos* or gliom* or glioblastom* or osteosarcom* or blastom* or neuroblastom* or oncolog* or myelodysplas* or adenocarcinoma* or choriocarcinoma*) adj3 (diagnos* or detect* or screen*)).ti,ab,kf.
61 57 or 58 or 59 or 60
62 56 and 61
63 (trend? or pattern? or lead time* or timeline* or time line* or time frame? or time frame? or interval?).ti,ab,kf.
64 ((longterm or long-term) adj2 (variation? or chang* or difference* or declin* or decreas* or increas* or elevat* or level? or concentration)).ti,ab,kf.
65 (prediagnos* or pre-diagnos* or ((before or prior) adj2 diagnos*)).ti,ab,kf.
66 ((risk? or predict*) adj5 (model* or logarithm* or algorithm* or maching learning)).ti,ab,kf.
67 (model* or logarithm* or algorithm* or maching learning).ti.
68 (risk? adj2 (scor* or model* or index or indices or tool* or assessment? or measurement?)).ti,ab,kf.
69 (Models, Biological/ or Models, Statistical/) and exp Risk/
70 63 or 64 or 65 or 66 or 67 or 68 or 69
71 62 and 70
72 exp animals/ not humans/
73 71 not 72



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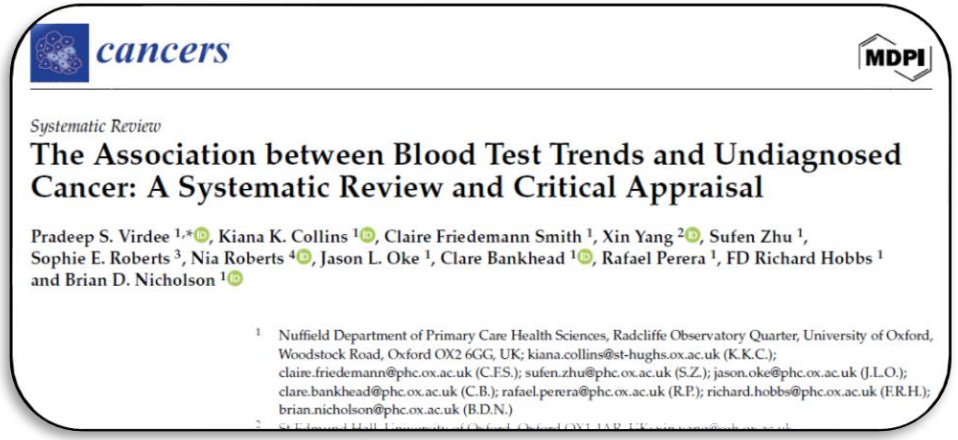
Search strategy – results so far



cancers

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Systematic Review

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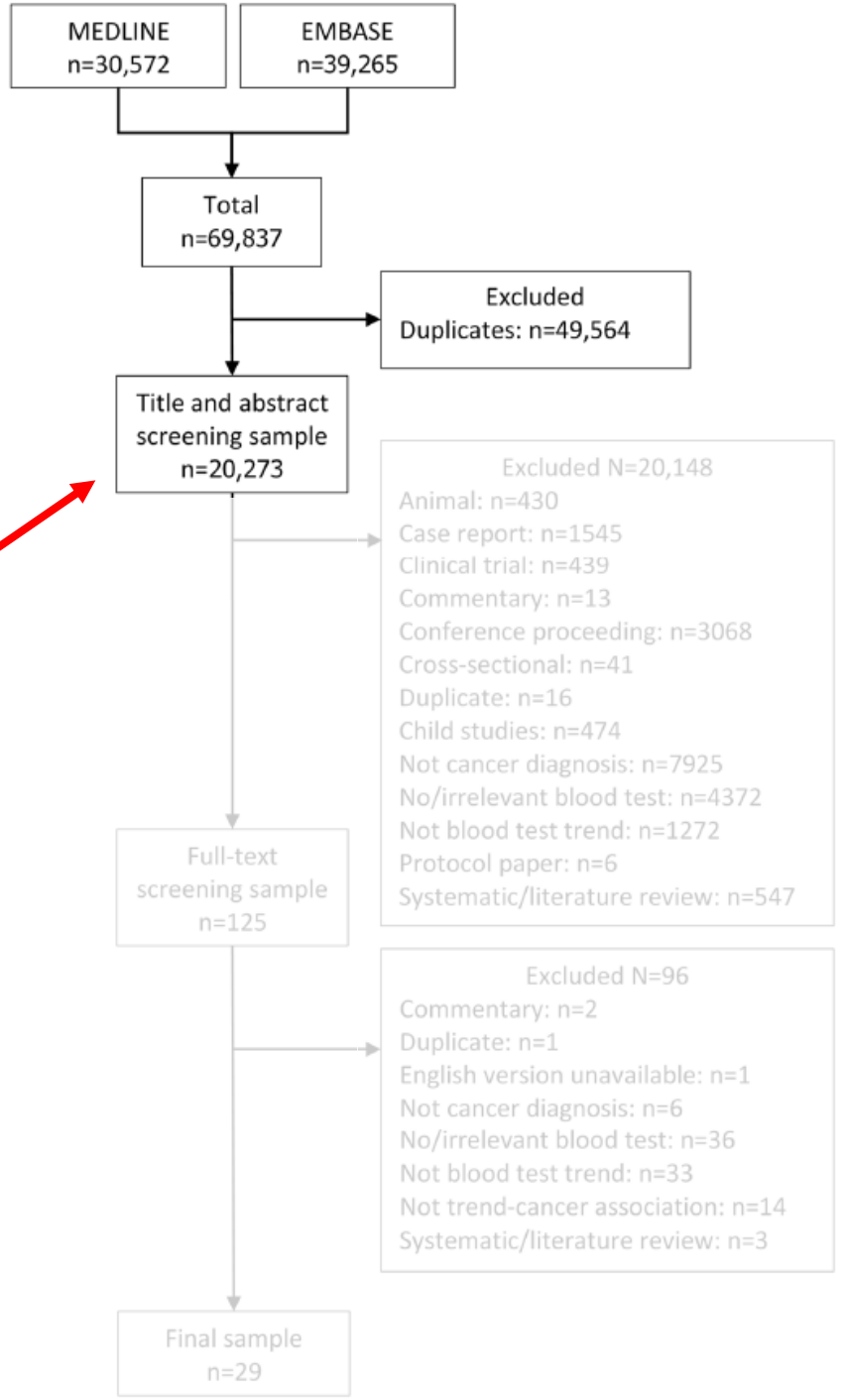
This is a lot of references to screen

Need to balance with practicality



Main steps to undertaking a systematic review

[4]

Protocol development

Study search

Screening

Data extraction

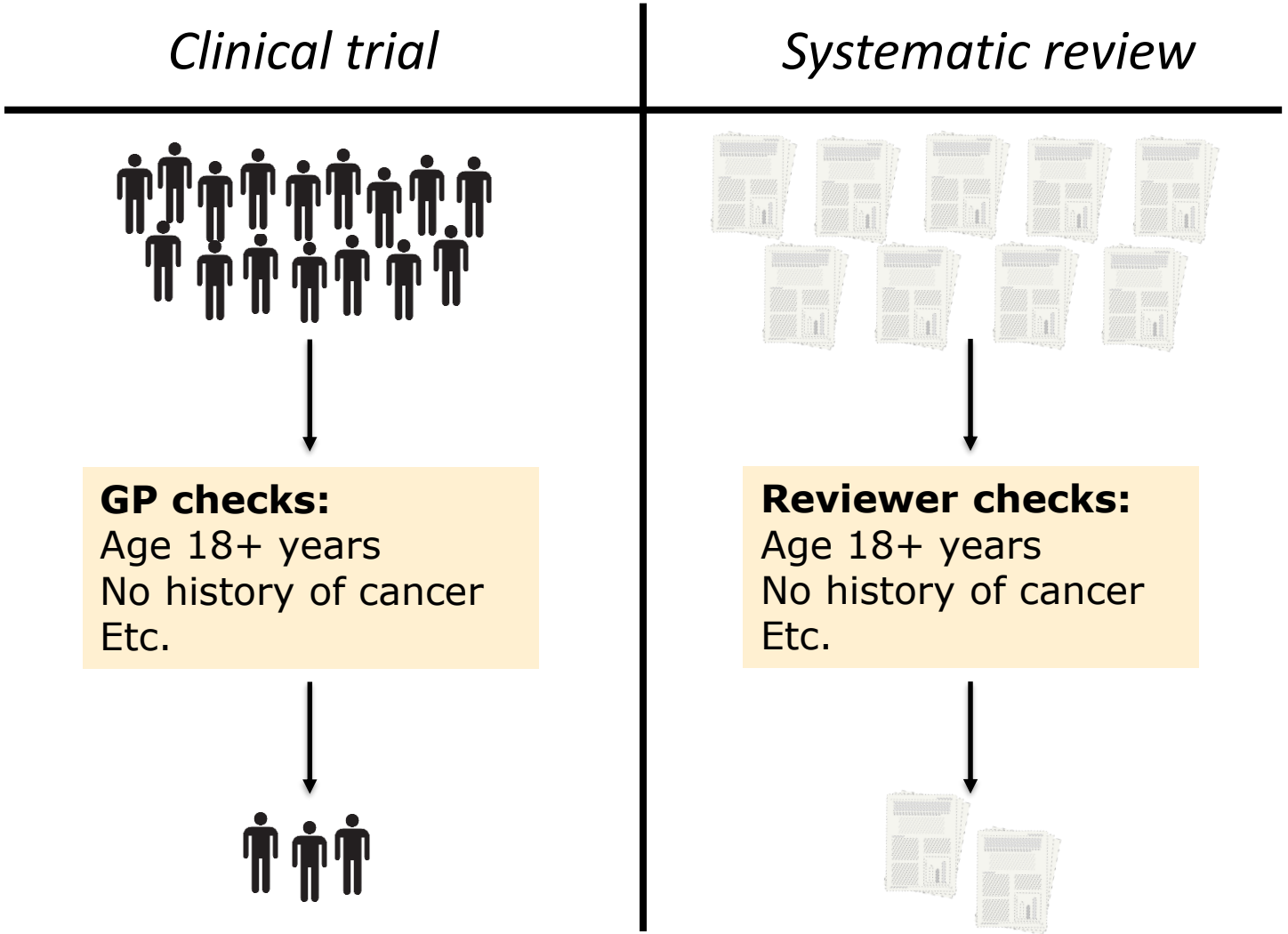
Data analysis

How do we choose studies to include?

Screening

A process of matching each study to your eligibility criteria to identify relevant studies (regardless of their results)

Screening


Clinical trial
Systematic review
GP checks:
Age 18+ years
No history of cancer
Etc.
Reviewer checks:
Age 18+ years
No history of cancer
Etc.

Screening

Usually done in two steps:

Step 1: title and abstract screening
Step 2: full text screening

Two people screen each study independently and compare results

Title and abstract screening – example

Eligibility criteria:

- Humans
- Age 18+ years
- Studying blood tests
- Diagnosis of cancer

Are these studies eligible?

☐ 3 Cite Share

Blood-based **tests** for multicancer early detection (PATHFINDER): a prospective cohort study.

Schrag D, Beer TM, McDonnell CH 3rd, Nadauld L, Dilaveri CA, Reid R, Marinac CR, Chung KC, Lopatin M, Fung ET, Klein EA.

Lancet. 2023 Oct 7;402(10409):1251-1260. doi: 10.1016/S0140-6736(23)01700-2.

PMID: 37805216 **Free PMC article.**

BACKGROUND: Multicancer early detection (MCED) **blood tests** can detect a **cancer** signal from circulating cell-free DNA (cfDNA). PATHFINDER was a prospective cohort study investigating the feasibility of MCED testing for **cancer** screening. ...INTERPRETATIO ...

☐ 8 Cite Share

The prognosis of breast **cancer** patients with bone metastasis could be potentially estimated based on **blood** routine **test** and biochemical examination at admission.

Huang B, Wu FC, Wang WD, Shao BQ, Wang XM, Lin YM, Zheng GX, Dong MM, Liu CT, Xu YW, Wang XJ.

Ann Med. 2023 Dec;55(1):2231342. doi: 10.1080/07853890.2023.2231342.

PMID: 37395196 **Free PMC article.** Clinical Trial.

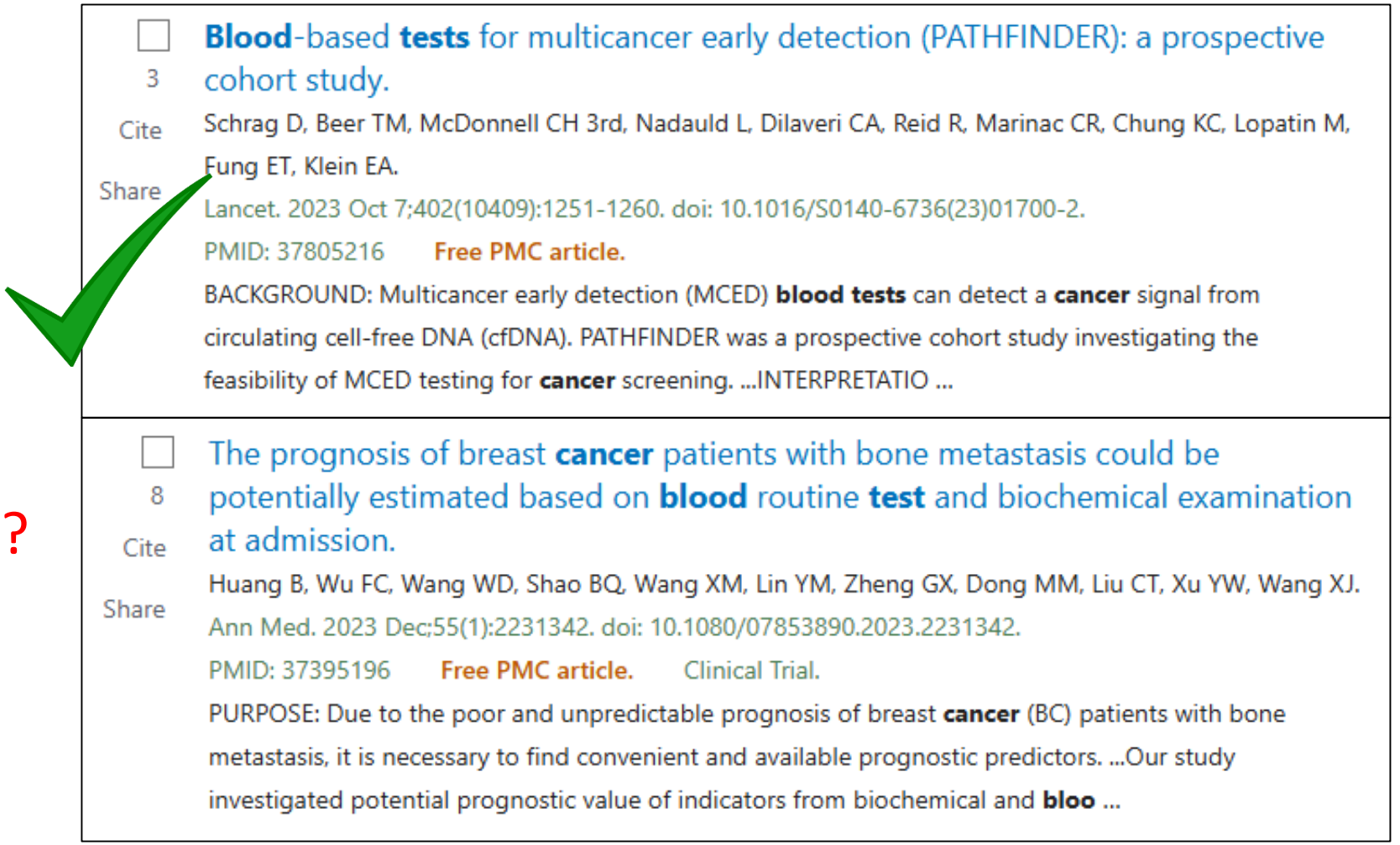
PURPOSE: Due to the poor and unpredictable prognosis of breast **cancer** (BC) patients with bone metastasis, it is necessary to find convenient and available prognostic predictors. ...Our study investigated potential prognostic value of indicators from biochemical and **bloo** ...

Title and abstract screening – example

Eligibility criteria:

- Humans
- Age 18+ years
- Studying blood tests
- Diagnosis of cancer

Are these studies eligible?



3

Cite

Share

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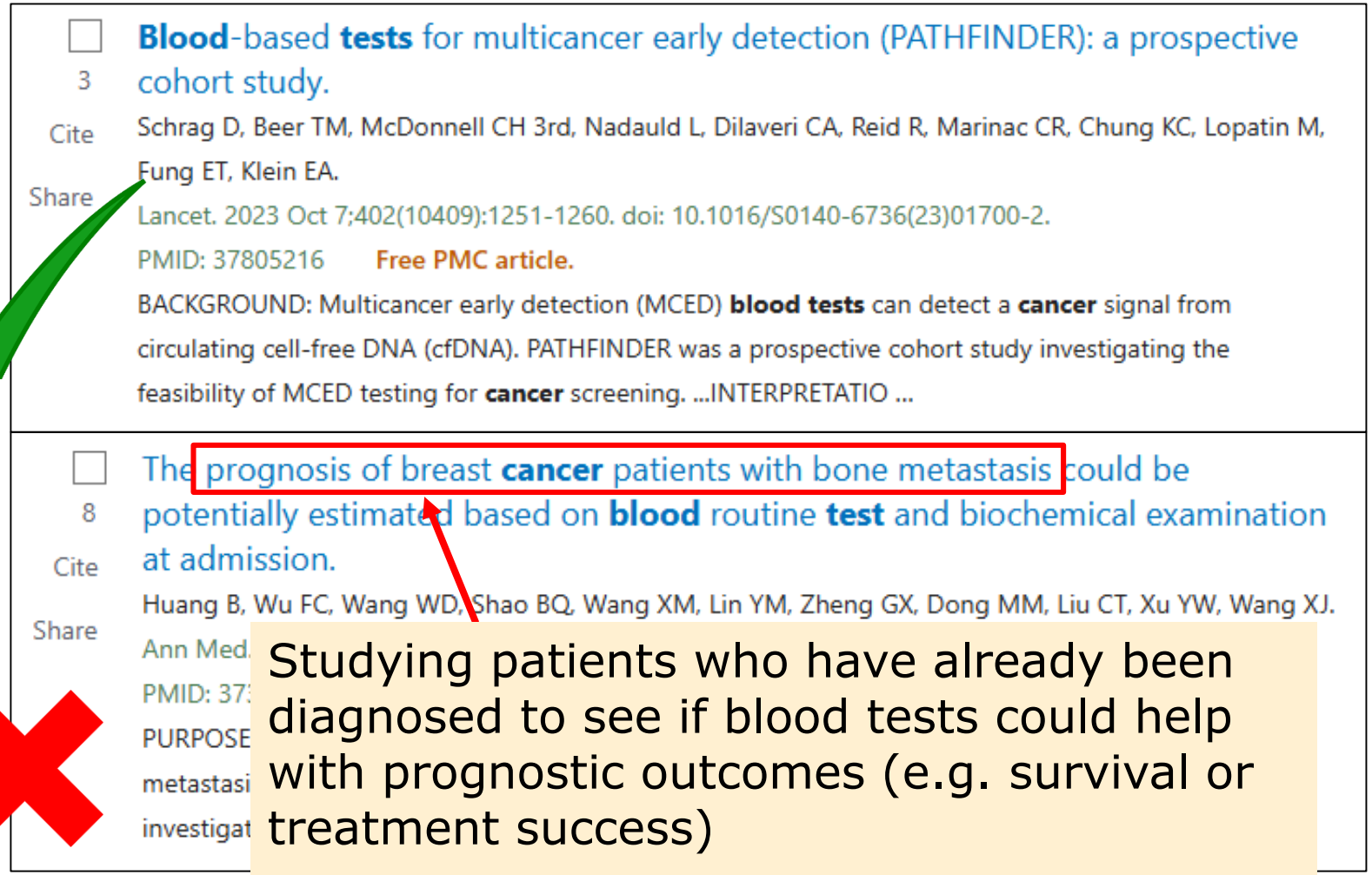
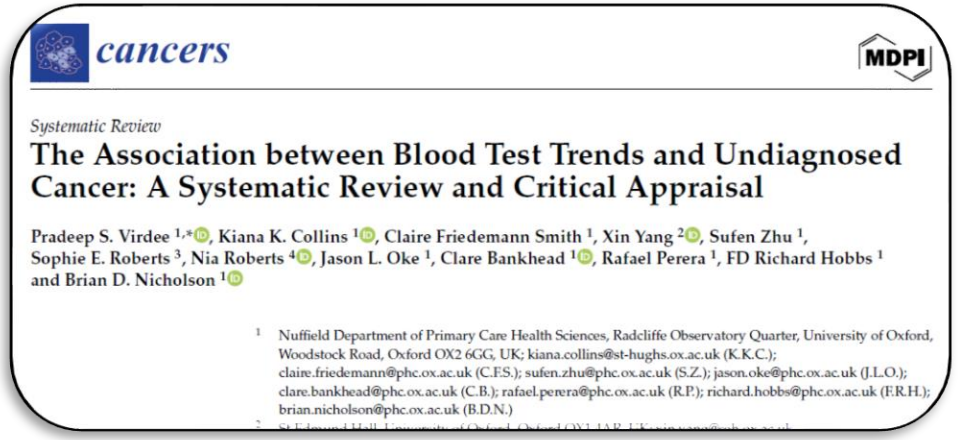


Screening



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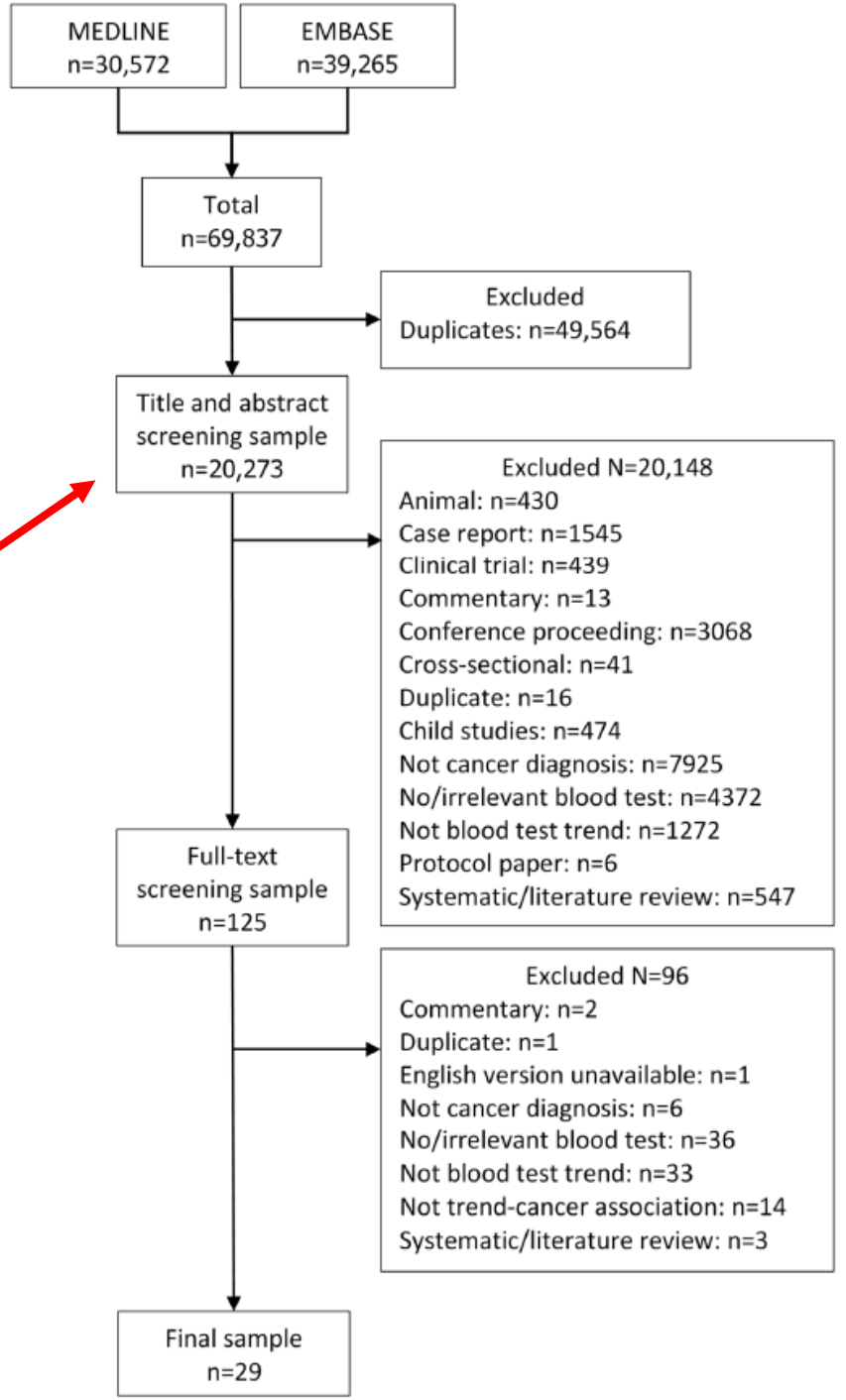
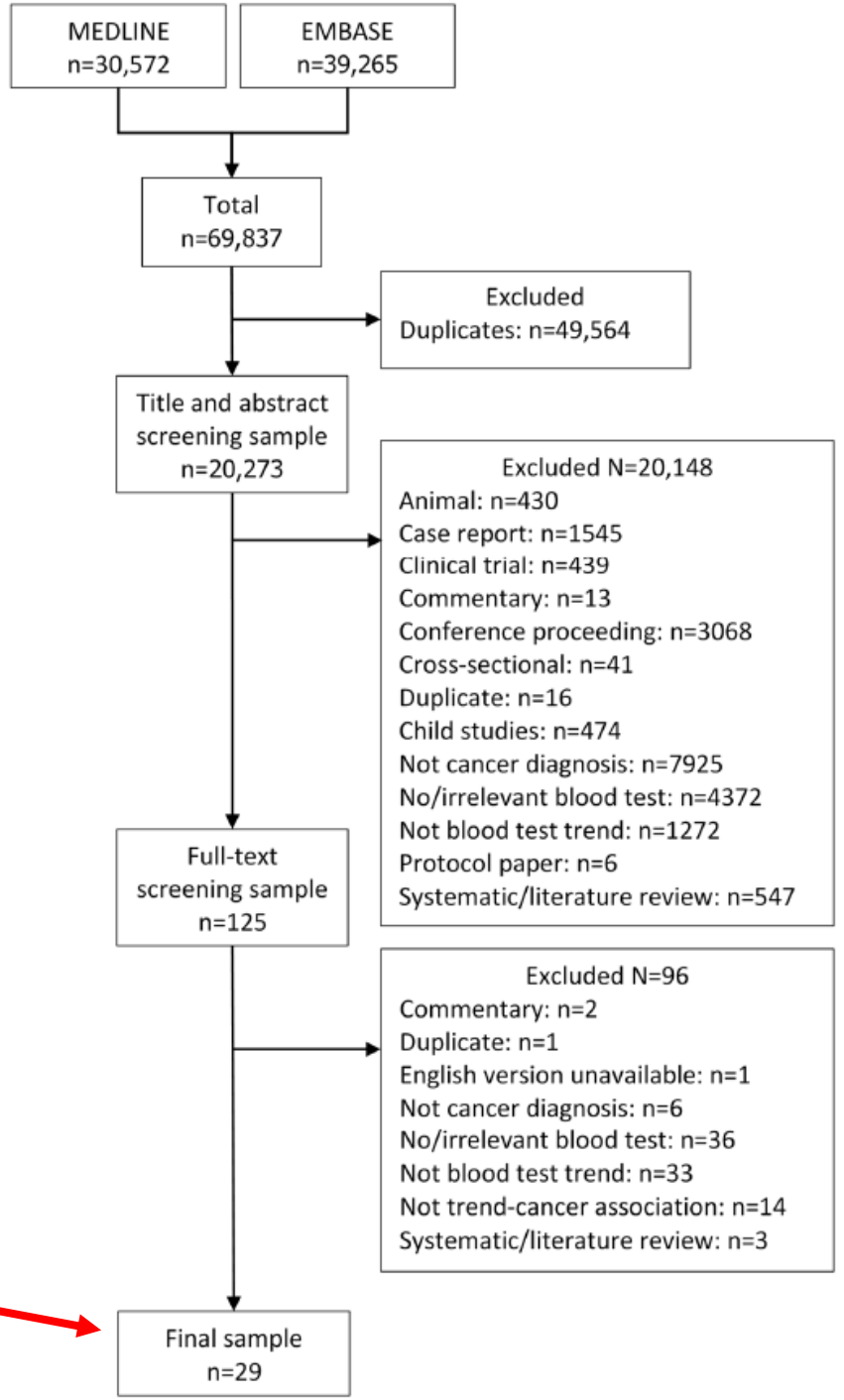


Screening



Final studies included in the review

Main steps to undertaking a systematic review

[4]

Protocol development

Study search

Screening

Data extraction

Data analysis

How do we extract the data needed?

Data extraction

What information is needed from each study?

- Age of patients
- Sex
- Clinical setting
- Number of patients included

And more…

People often record this in Excel

Two people extract from each study independently and compare results

Data extraction

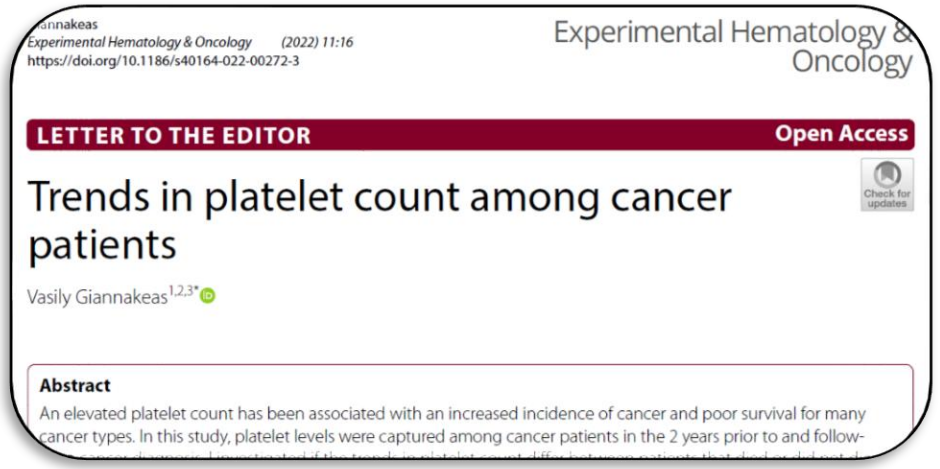
	A	B	C	D	E	F	G	H	I
1	**Publication Details**			**Study Setting**					
2	Who is the first author?	What is the title of the paper?	What is the year of publication?	What is the geographical location of the data (i.e. the country)?	How many patients were recruited?	What is the patient setting?	What is the age at diagnosis/censor date?	What proportion of patients were male?	What proportion of patients were female?
3									
4	**Authors**	**Title**	**YearOfPublicat**	**GeographicalL**	**NumberRecNo**	**Setting**	**AgeAtDiagValu**	**SexMalePropo**	**SexFemalePro**
5	Arrigoni	Pattern analysis c	1988	Italy	164	Secondary care		66%	34%
6	Atkin	Change in blood t	2020	UK	285	Secondary care			
7	Boursi	A Risk Prediction	2016	UK	67988	Primary care	69.72	47%	
8	Chaturvedi	C-Reactive Protei	2010		1262	Other		67%	
9	Choi	Longitudinal Asse	2019	Korea	110	Other		69%	
10	Edgren	Pattern of declini	2010	Sweden and Denr	178370	Other	Cases=52.2; controls=52.1		47%
11	Feng	The association b	2020	China	69742	Unclear		79%	
12	Fuente	Peripheral blood	2019	USA	657	Other		51%	
13	Bird	Alpha-Fetoprotei	2016	UK	49	Secondary care			
14	Furukawa	Clinical significan	1984	Japan	114	Unclear			
15	Giannakeas	Trends in platelet	2022	Canada		Primary care			
16	Lee	Improving Screen	2013		967	Unclear			26%
17	Goldshtein	Variations in hem	2010	Israel	10740	Primary care			
18	Gradel	Longitudinal traje	2020	Denmark	818	Secondary care		54%	
19	Hsieh	Etiologies of Extre	2019	USA	305	Secondary care			
20	Huang	New-Onset Diabe	2020	USA	110699	Unclear			55%
21	Imaeda	A retrospective st	1992	Japan	218	Unclear	Cases=58		
22	Iversen	Rising erythrocyte	1996	Norway	4146	Unclear		55%	

Data extraction – example

We want the number of patients included in the study

What would you say this number is?

I'd say unclear



Giannakeas
Experimental Hematology & Oncology (2022) 11:16
https://doi.org/10.1186/s40164-022-00272-3

Experimental Hematology & Oncology

LETTER TO THE EDITOR Open Access

Trends in platelet count among cancer patients

Vasily Giannakeas[1,2,3*]

Abstract

An elevated platelet count has been associated with an increased incidence of cancer and poor survival for many cancer types. In this study, platelet levels were captured among cancer patients in the 2 years prior to and follow-

Table 1 Characteristics of the ovarian cancer patient cohort measured at the diagnosis date

Description	
Number of patients	6451

nosis between January 2007 and December 2015. Study subjects were patients with at least one complete blood count (CBC) record in the two-year period preceding or following a cancer diagnosis of the colon, lung, breast, prostate, stomach, or ovary. The study cohort consisted

Data extraction

	A	B	C	D	E	F	G	H	I
1	**Publication Details**			**Study Setting**					
2	Who is the first author?	What is the title of the paper?	What is the year of publication?	What is the geographical location of the data (i.e. the country)?	How many patients were recruited?	What is the patient setting?	What is the age at diagnosis/censor date?	What proportion of patients were male?	What proportion of patients were female?
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Risk of bias assessment

A systematic error that results in deviations from the true result

Assessed using existing tools, such as:

- QUIPS
- PROBAST
- Cochrane Risk of Bias Tool
- CASP Checklist
- Newcastle-Ottowa Scale

Two people do this independently and compare results

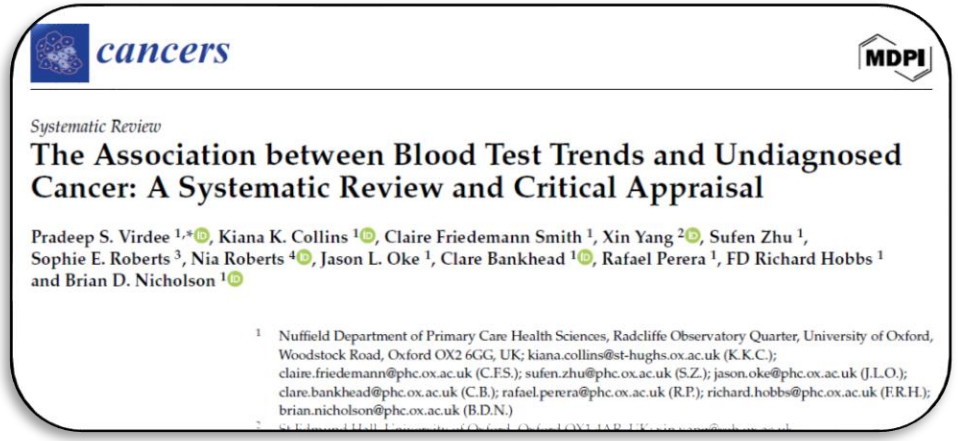
Risk of bias assessment

For example, the Cochrane Risk of Bias Tool asks

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		Y / PY / PN / N / NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns

Risk of bias assessment (QUIPS tool)

Article	Participation	Attrition	Prognostic factor	Outcome	Confounders	Analysis & reporting
Atkin 2020	High	Low	High	High	High	High
Boursi 2016	Low	Low	High	Moderate	Moderate	High
Chaturvedi 2010	High	High	High	Moderate	Moderate	Moderate
Edgren 2010	Moderate	Low	High	Moderate	High	Moderate
Feng 2020	High	High	High	Low	High	Low
Fuente 2019	Moderate	Low	High	Low	High	High
Furukawa 1984	High	High	High	Moderate	High	Moderate
Giannakeas 2022	High	Low	Moderate	Moderate	High	High
Goldshtein 2010	High	Low	Moderate	Moderate	Moderate	High
Gradel 2020	Moderate	Low	High	Moderate	Moderate	High
Hauser 2021	Moderate	Moderate	High	Moderate	High	Moderate
Hsieh 2019	Moderate	Low	Moderate	High	High	High
Huang 2020	Moderate	Low	Low	Low	High	Low
Iversen 1996	Moderate	High	Low	Moderate	High	High
Jacobson 2021	Moderate	High	High	Low	Low	Moderate
Jonsson 2020	Moderate	High	Low	Moderate	Moderate	Moderate
Koshiaris 2018	Low	Low	Low	Low	Low	Low



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Main steps to undertaking a systematic review

[4]

Protocol development

Study search

Screening

Data extraction

Data analysis

Published evidence

Relevant evidence

How do we analyse the data?

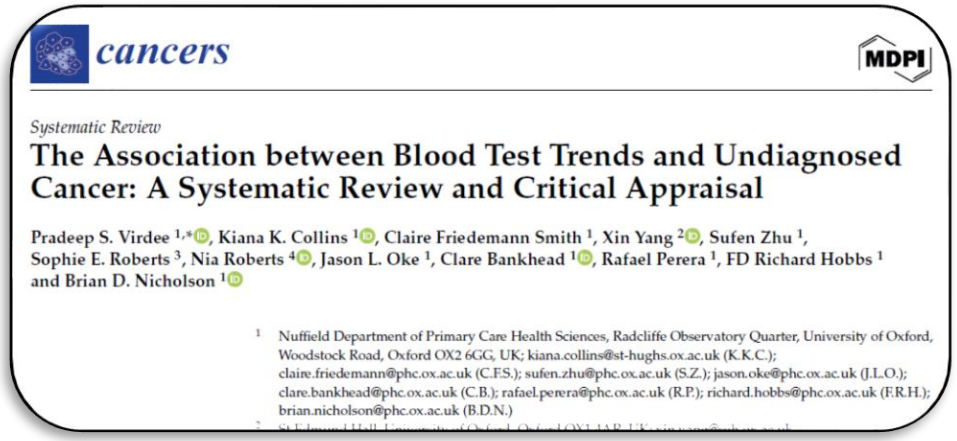
Analysis

Narrative summary/synthesis:

- Descriptively summarise studies
- Usually provide mean value or % of studies

3.1.2. Participants and Setting

The mean number of participants recruited was 1099 among prospective studies and 76,579 among retrospective studies, ranging from 9 to 939,949 participants over all the studies. The 29 articles spanned 12 different countries, with most studies being conducted in the USA (28%, n = 8) and UK (21%, n = 6). The period of recruitment ranged from 1968 to 2022. A total of 41% (n = 12) of studies were conducted in primary care, 14% (n = 4) in secondary care, and 21% (n = 6) in other settings, including: one study each in regards to blood donors, a specific population, postmenopausal women, pregnant women, a printing company, and a screening population. The setting was unclear in 24% (n = 7). Across the 18 studies that reported age, the mean age was 64.6 years (SD = 8.7). Across the 24 studies that described sex, 51.1% (SD = 24.0) of participants included were female.



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Meta-analysis

Workshop

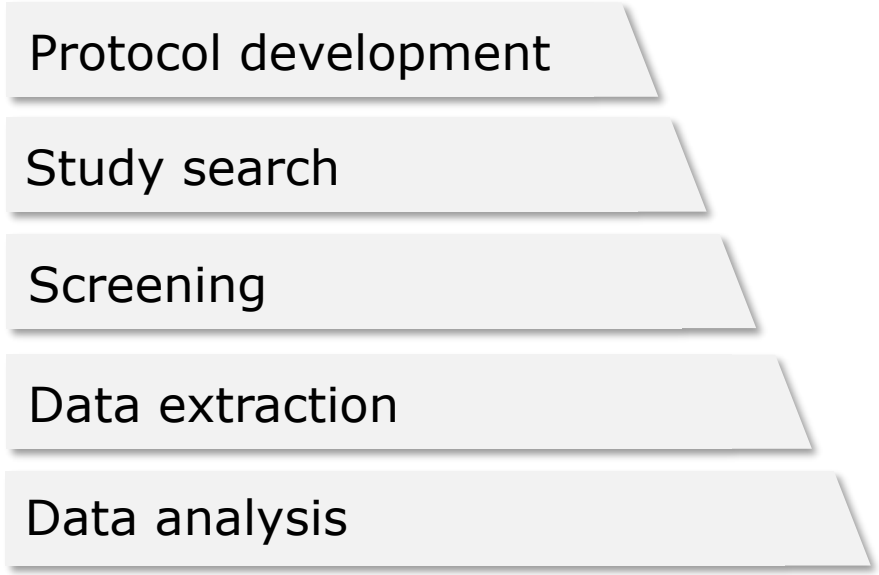
By
Pradeep Virdee

We'd like you to…

Spend <u>5 minutes</u> thinking about:

- Your experience of contributing to systematic reviews
- Where you think PPI could add value

It doesn't matter if you've never contributed to a review before



Please type your thoughts in the chat

Conclusion

Conclusion

1. What is a systematic review?
2. Why are they important?
3. How can they influence practice?
4. How do you conduct them?
5. What is a meta-analysis?

Conclusion

Please put any further questions in the chat before you leave

We will respond by email

What's next?

Part 2 of this session: meta-analysis

More webinars planned

Please let us know if you would like to be kept posted

Please let us know of statistical topics you want to learn of

You can tell us on our feedback form

What's next?

Would you like a session on qualitative research?

Qualitative research captures patient perspectives to inform practice

- Interviews
- Workshops
- Focus groups

Please let us know in the chat

Feedback form

Your feedback is crucial for shaping these talks

Feedback form:
https://forms.office.com/e/fkHJqPcNMP


THANK YOU

Feedback form

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https://forms.office.com/e/fkHJqPcNMP

Part 2:

Meta-analysis

By
Pradeep Virdee

What is a meta-analysis?

Meta-analysis – an analysis of analyses

Results from 2+ studies are pooled together to give one overall result

Better idea of the “true” result

Most commonly seen in randomised controls trials

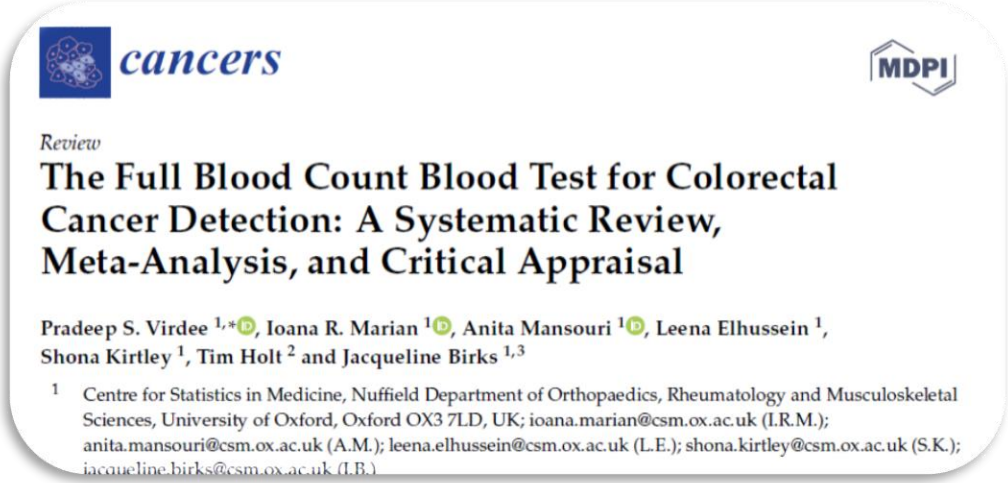
Not every review comes with a meta-analysis
But all meta-analyses come from a review

Example of a meta-analysis

Q: Can blood test results tell us about underlying cancer?

Interested in anaemia (low haemoglobin)

We compared haemoglobin between patients with and without cancer



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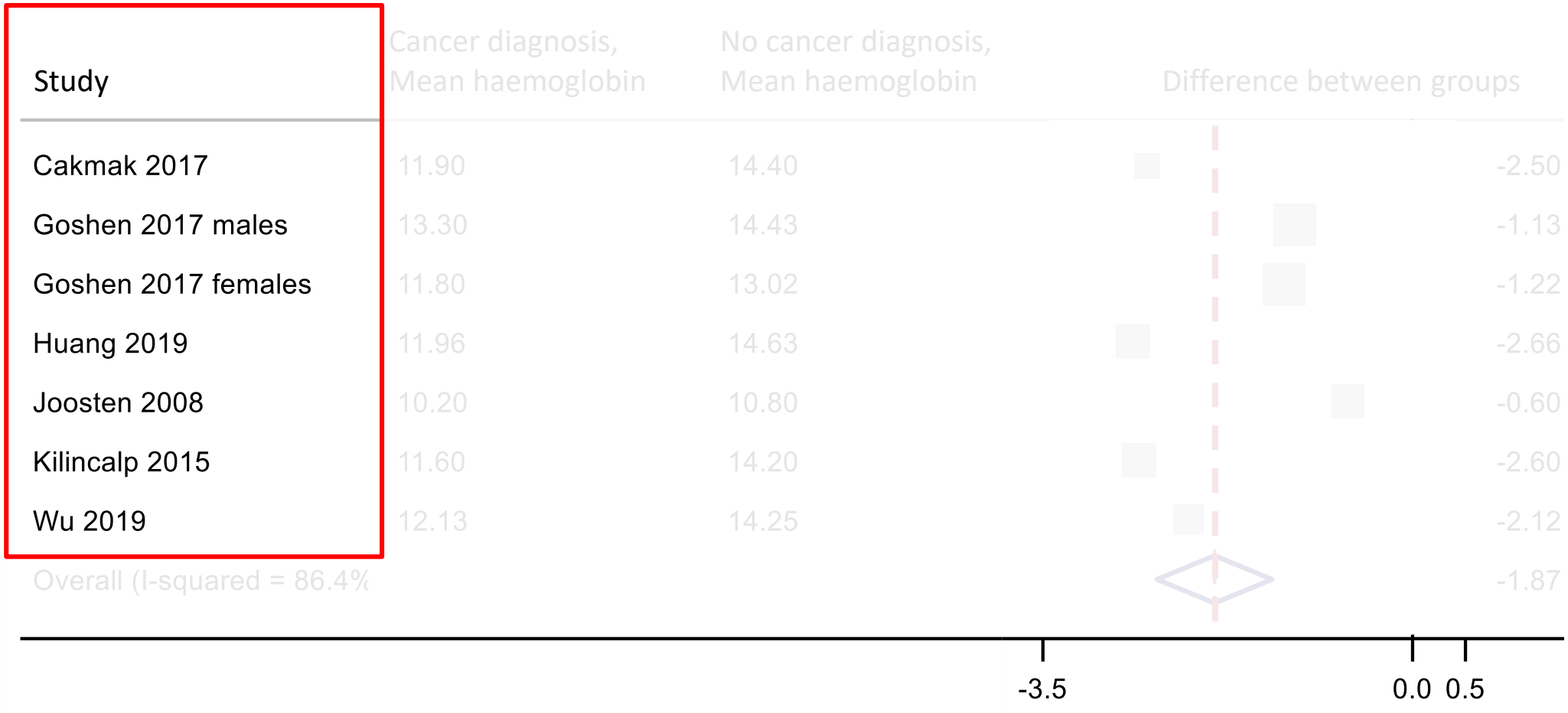
Review

The Full Blood Count Blood Test for Colorectal Cancer Detection: A Systematic Review, Meta-Analysis, and Critical Appraisal

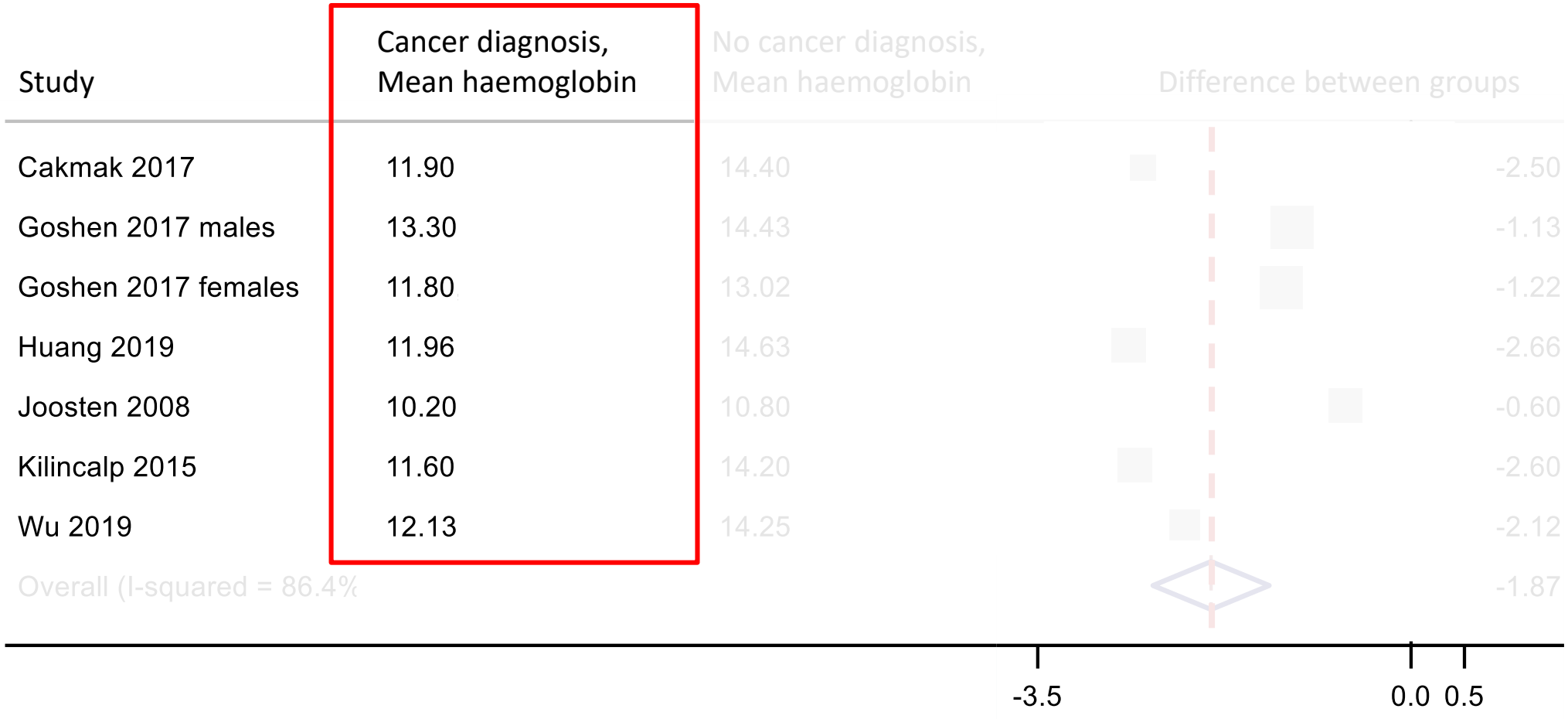
Pradeep S. Virdee [1,*], Ioana R. Marian [1], Anita Mansouri [1], Leena Elhussein [1], Shona Kirtley [1], Tim Holt [2] and Jacqueline Birks [1,3]

[1] Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford OX3 7LD, UK; ioana.marian@csm.ox.ac.uk (I.R.M.); anita.mansouri@csm.ox.ac.uk (A.M.); leena.elhussein@csm.ox.ac.uk (L.E.); shona.kirtley@csm.ox.ac.uk (S.K.); jacqueline.birks@csm.ox.ac.uk (J.B.)

Example of a meta-analysis – forest plot

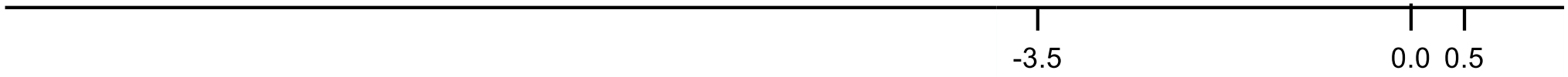


Example of a meta-analysis – forest plot

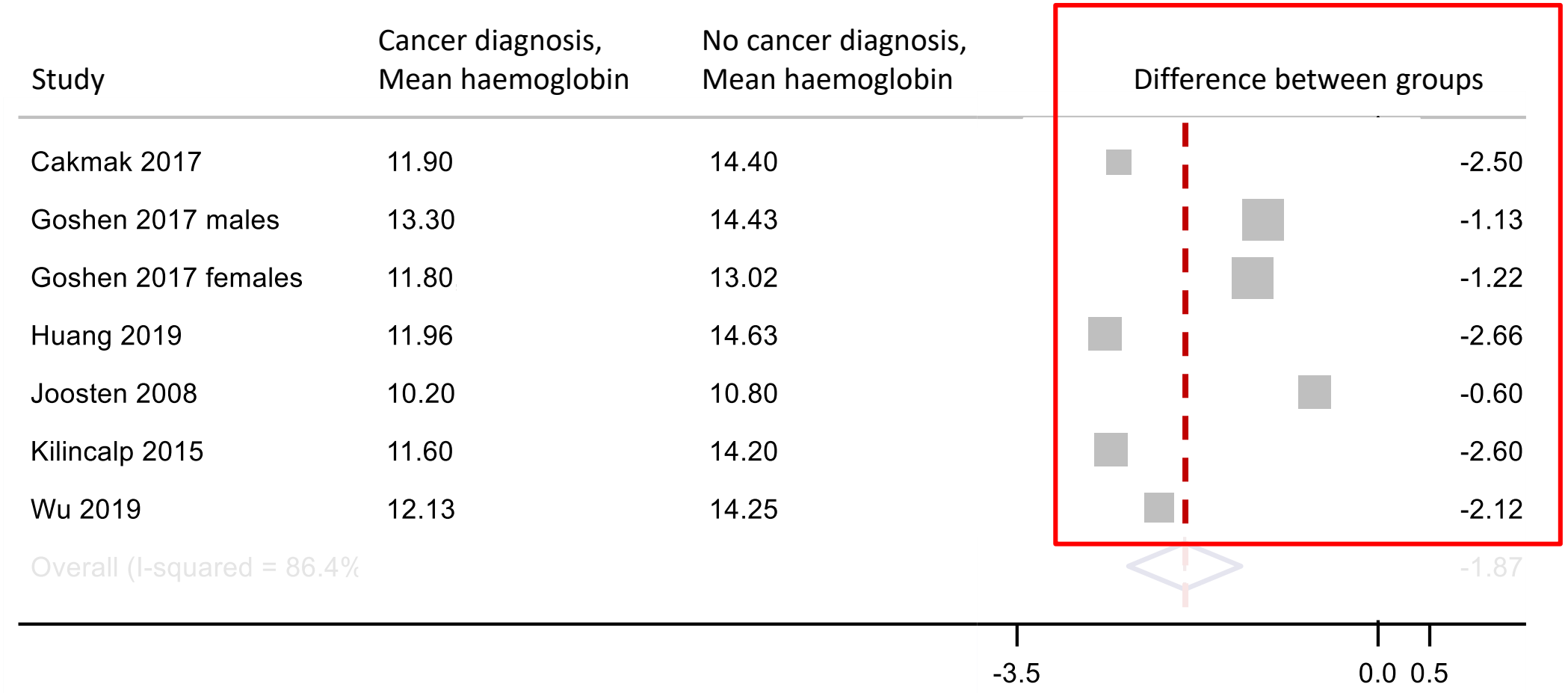


Example of a meta-analysis – forest plot

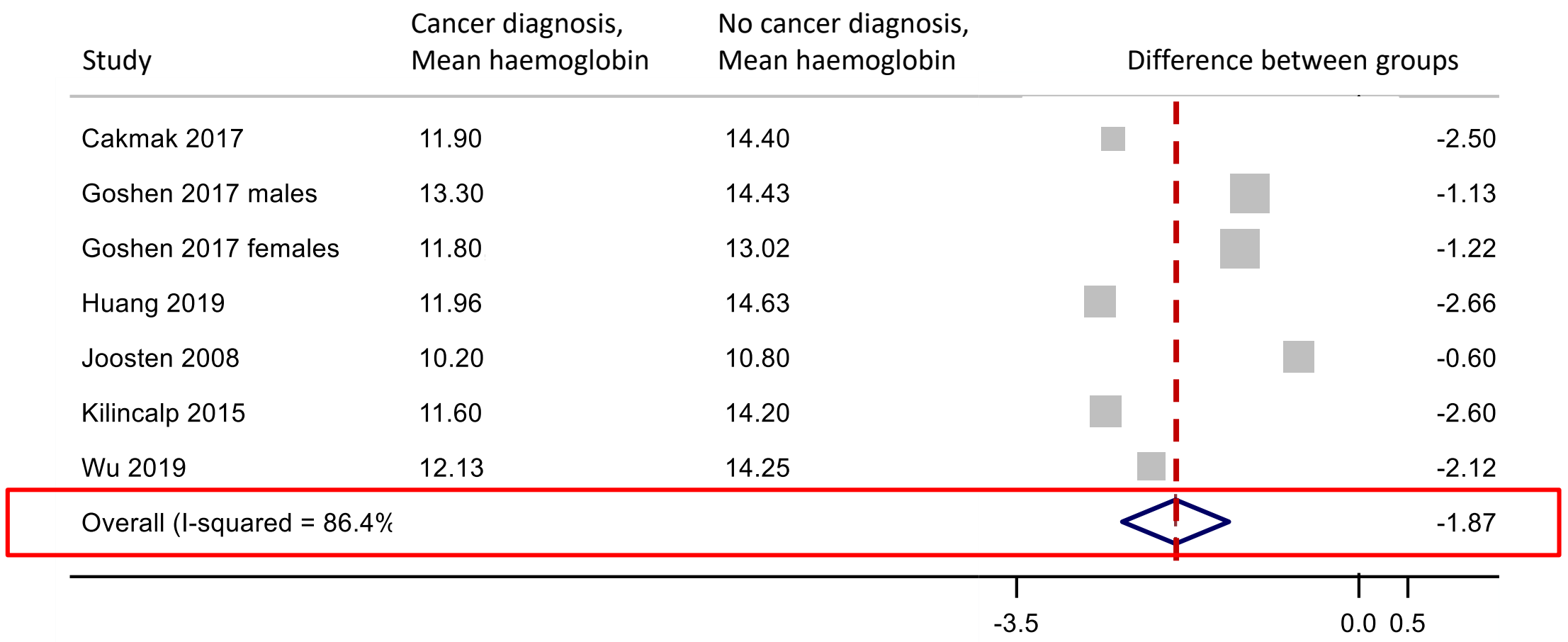
Study	Cancer diagnosis, Mean haemoglobin	No cancer diagnosis, Mean haemoglobin	Difference between groups
Cakmak 2017	11.90	14.40	-2.50
Goshen 2017 males	13.30	14.43	-1.13
Goshen 2017 females	11.80	13.02	-1.22
Huang 2019	11.96	14.63	-2.66
Joosten 2008	10.20	10.80	-0.60
Kilincalp 2015	11.60	14.20	-2.60
Wu 2019	12.13	14.25	-2.12
Overall (I-squared = 86.4%			-1.87



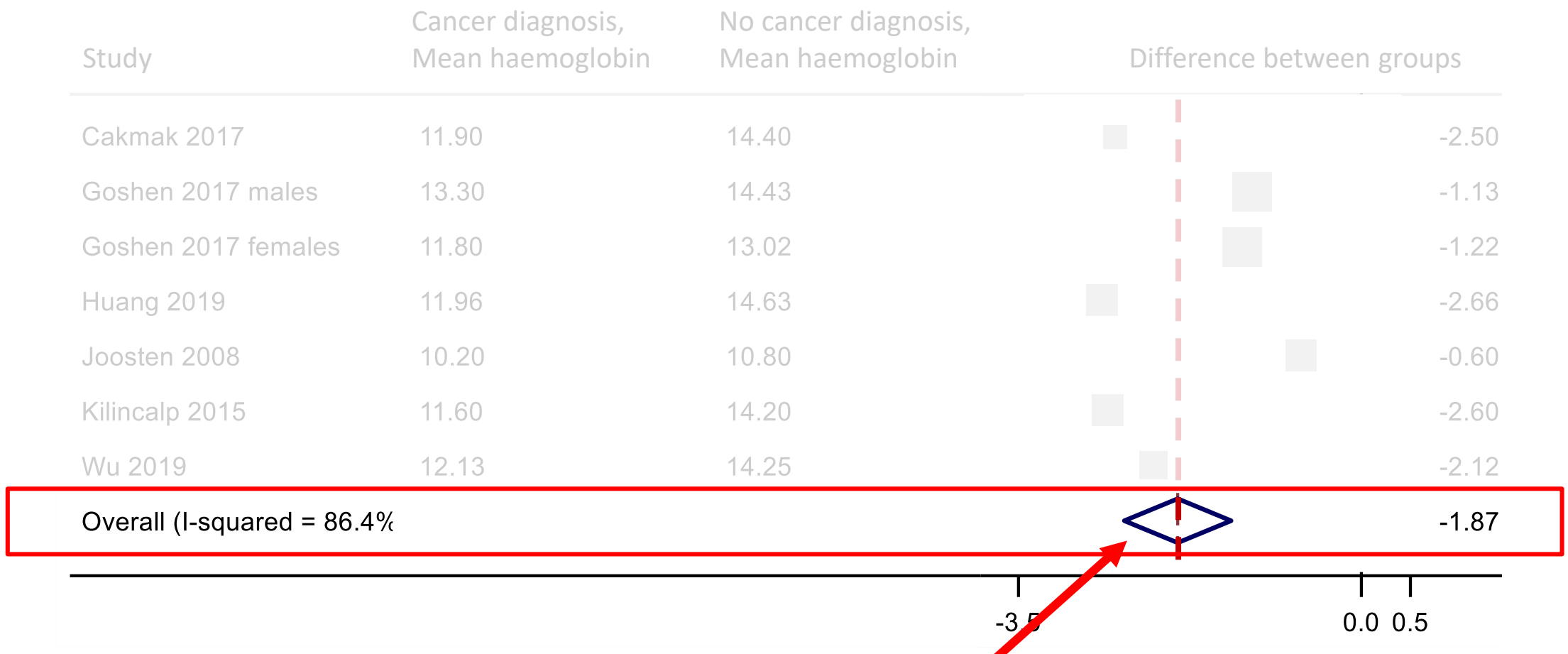
Example of a meta-analysis – forest plot



Example of a meta-analysis – forest plot

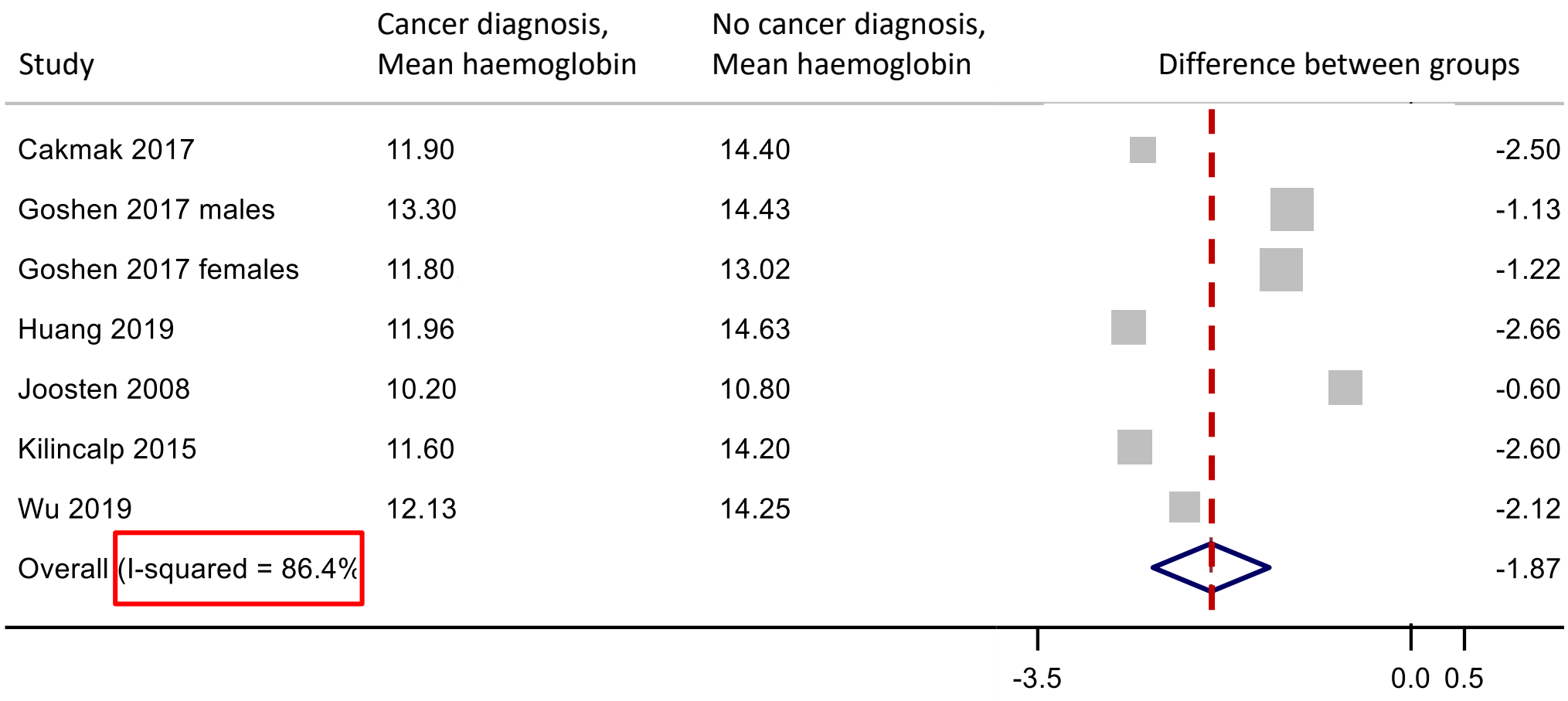


Example of a meta-analysis – forest plot



This is the generally the mean of the individual studies

Example of a meta-analysis – heterogeneity

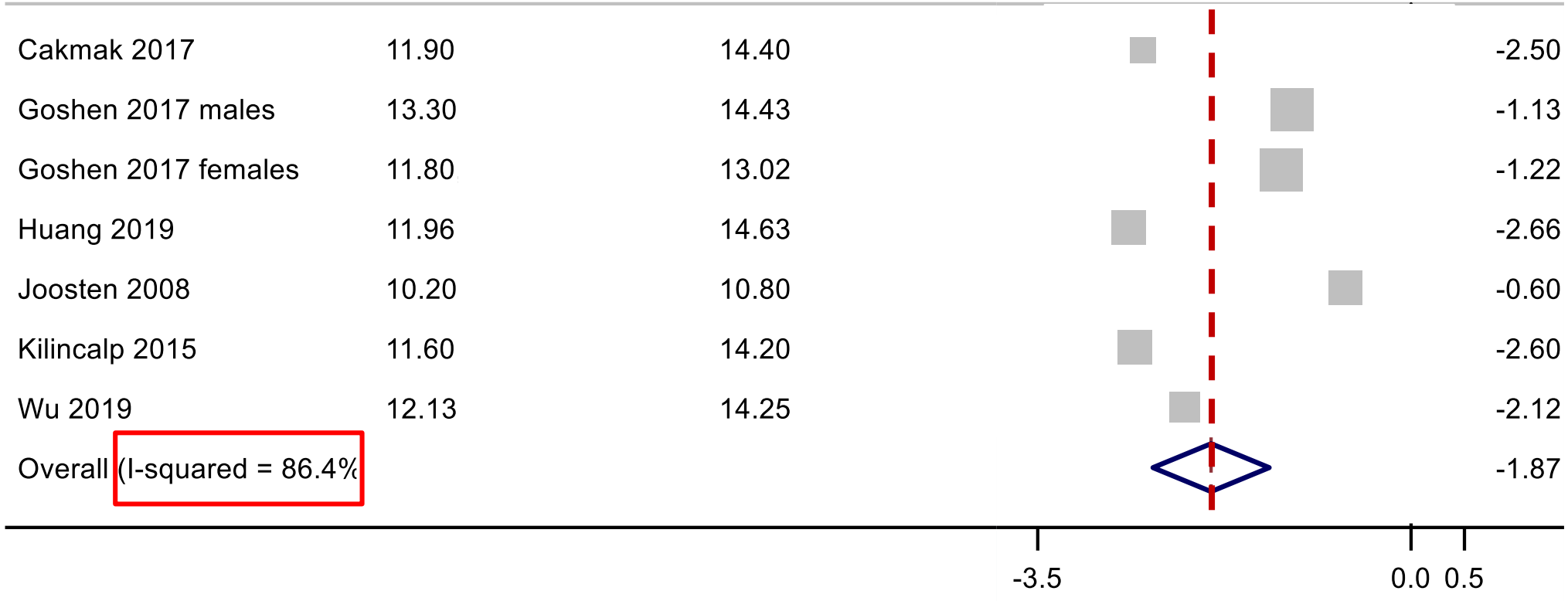


Heterogeneity

I-squared:
The proportion of variability between study results that is explained by study differences

Example of a meta-analysis – heterogeneity

Study	Cancer diagnosis, Mean haemoglobin	No cancer diagnosis, Mean haemoglobin	Difference between groups
Cakmak 2017	11.90	14.40	-2.50
Goshen 2017 males	13.30	14.43	-1.13
Goshen 2017 females	11.80	13.02	-1.22
Huang 2019	11.96	14.63	-2.66
Joosten 2008	10.20	10.80	-0.60
Kilincalp 2015	11.60	14.20	-2.60
Wu 2019	12.13	14.25	-2.12
Overall (I-squared = 86.4%			-1.87



Heterogeneity

I-squared:
The proportion of variability between study results that is explained by study differences

0% to 40%: might not be important
30% to 60%: may represent moderate heterogeneity
50% to 90%: may represent substantial heterogeneity
75% to 100%: considerable heterogeneity

References

[1] https://guides.mclibrary.duke.edu/sysreview/types
[2] https://ucsd.libguides.com/systematic-review
[3] https://www.cancerresearchuk.org/about-us/we-develop-policy/our-policy-on-preventing-cancer/our-policy-on-obesity-and-diet-1#:~:text=Protect%20kids%20from%20junk%20food,TV%20and%20online%20to%20children.
[4] https://slidemodel.com/templates/sales-funnel-diagram-template-powerpoint/
[5] https://libguides.kcl.ac.uk/systematicreview/greylit
[6] https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials