

Principles of problem formulation and approaches to considering mechanistic data

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- What is 'problem formulation' for a review?
 - Approaches to evidence review
 - Formulating problems around effects of interventions
 - mechanisms of action
 - Formulating problems around effects of exposures
 - mechanisms of action
 - Closing remarks
-
- Disclaimer: mechanistic evidence is not my area

What is problem formulation?

1. Define the **underlying question driving the review** (the review's purpose, or scope)
2. Decide the **methodological approach** to be taken for the review
3. Define the **review question(s)** to be answered
4. Define **criteria for including studies** in the review

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Approaches to evidence review

Systematicness

High (protocol; explain)
vs Low

Comprehensiveness

High (thorough search)
vs Low

Depth

Deep (synthesis)
vs Shallow (description)

Rigour

High (duplicate tasks, RoB)
vs Low

Breadth

Broad
vs Narrow

Review Article

A typology of reviews: an analysis of 14 review types and associated methodologies

Maria J. Grant* & Andrew Booth†. *Salford Centre for Nursing, Midwifery and Collaborative Research

(Salford
Univ)

CORRESPONDENCE

Open Access



What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences

Zachary

COMMENTARY

Open Access

Clarifying differences between review designs and methods

David Gough*, James Thomas and Sandy Oliver

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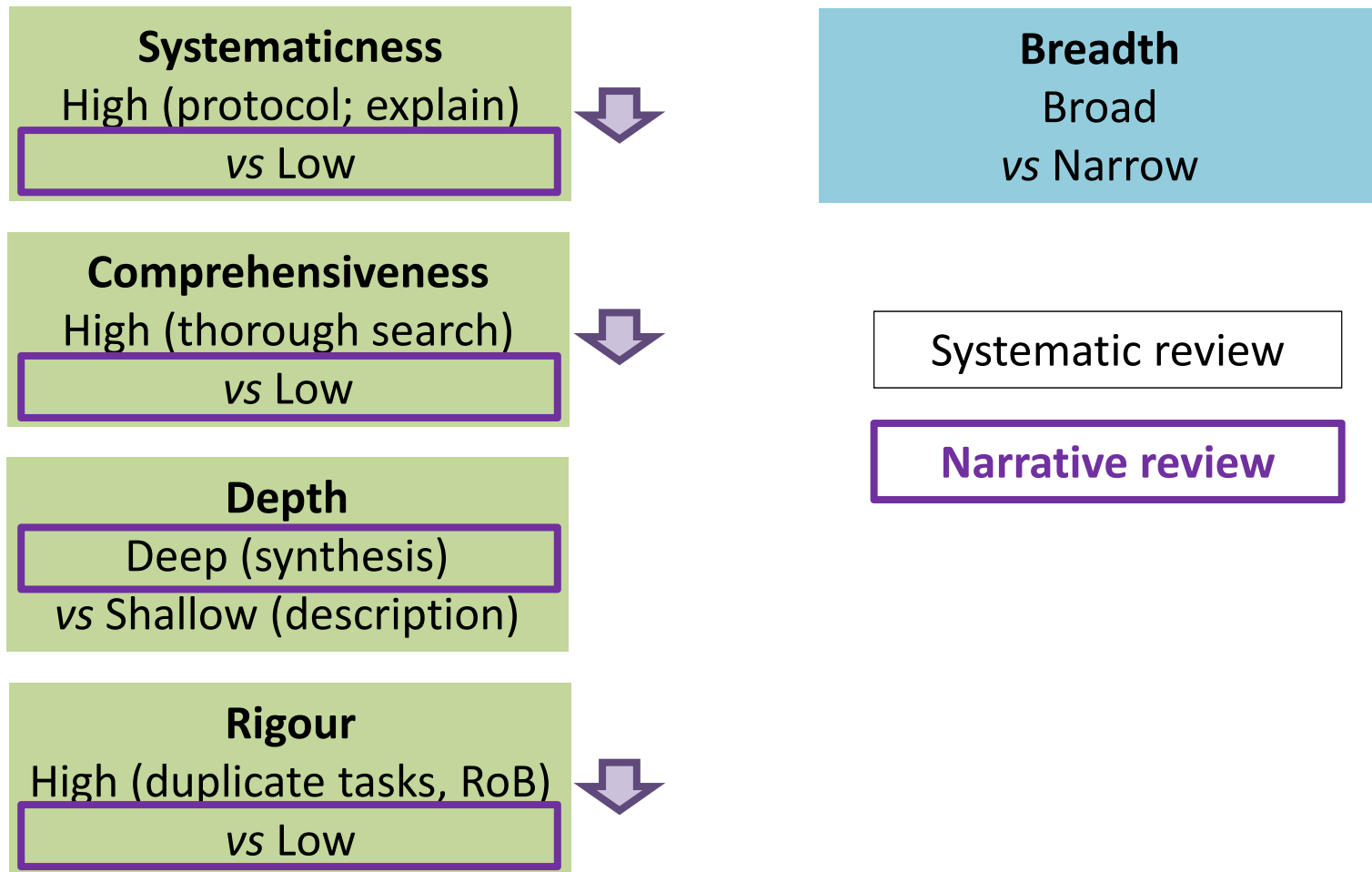
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Systematic review

Approaches to evidence review



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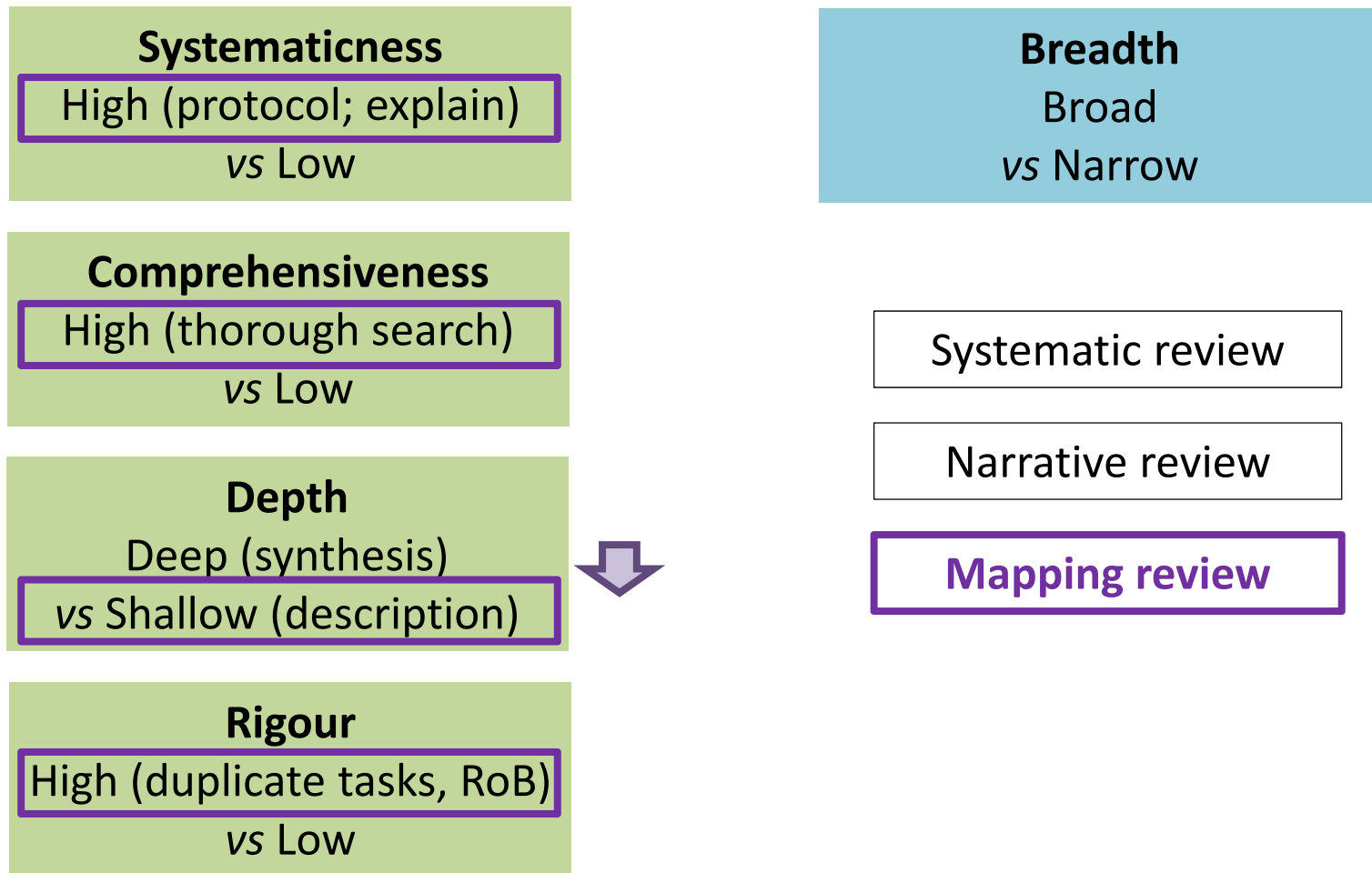
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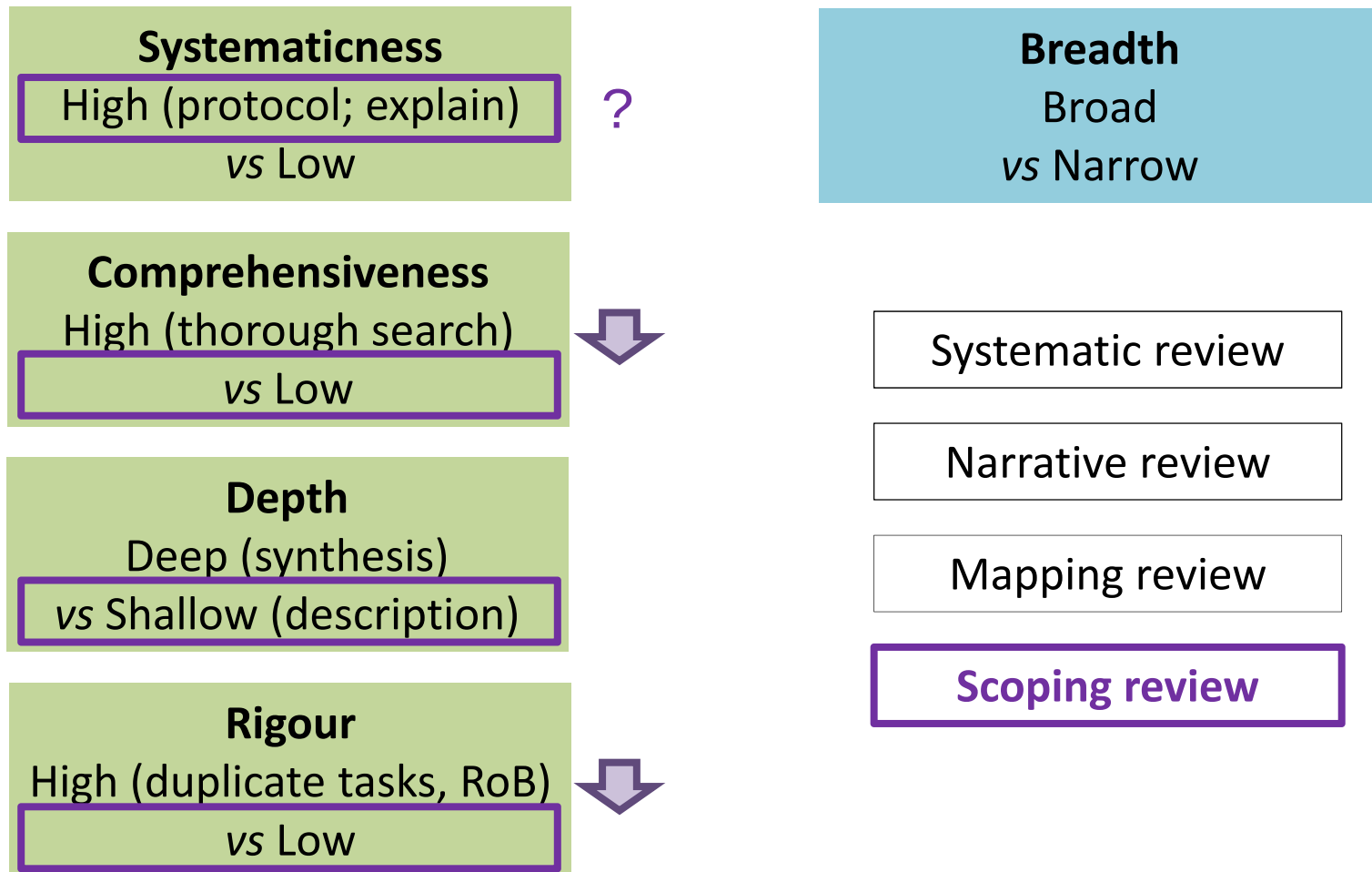
Systematic review

Narrative review

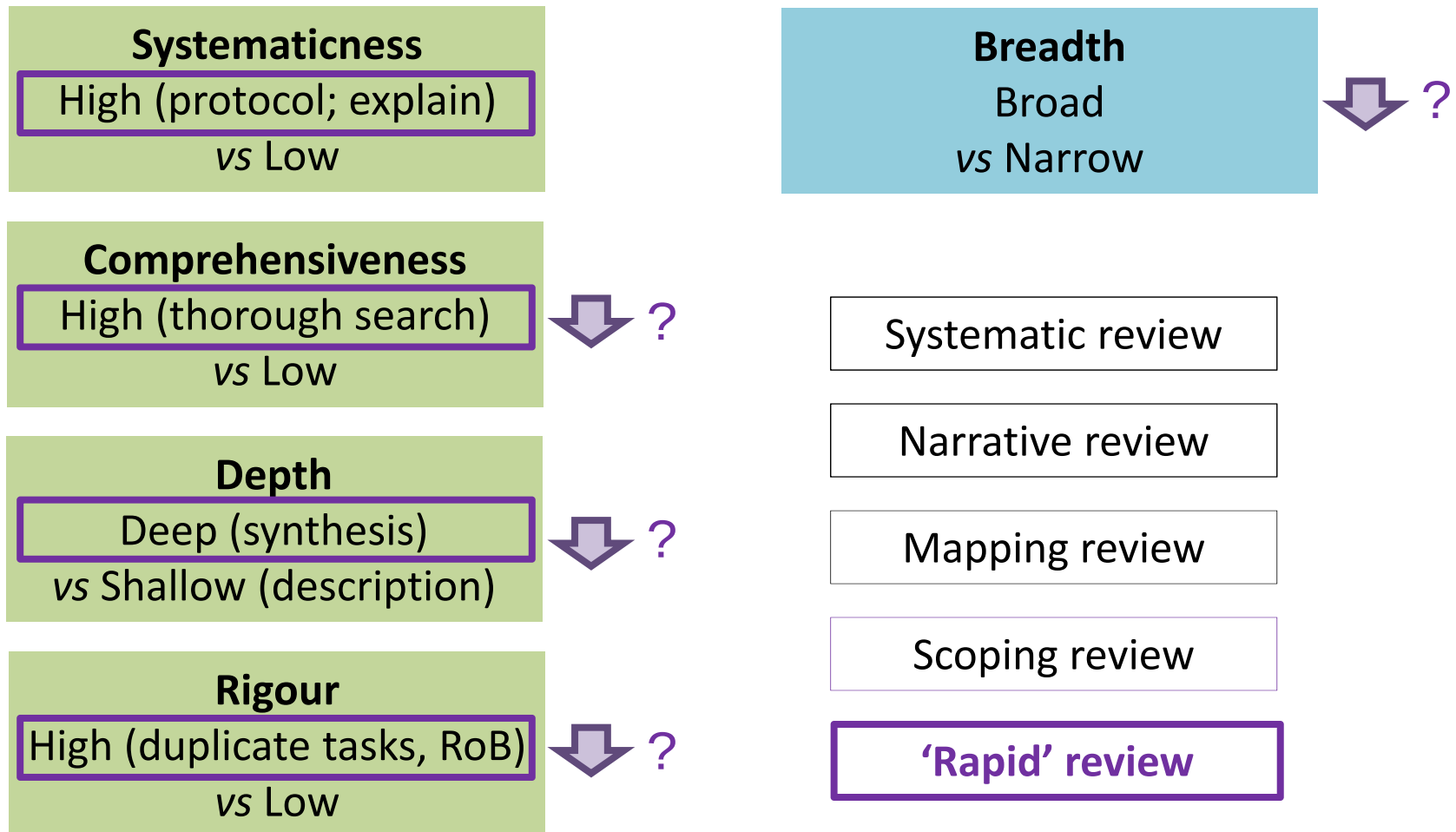
Approaches to evidence review



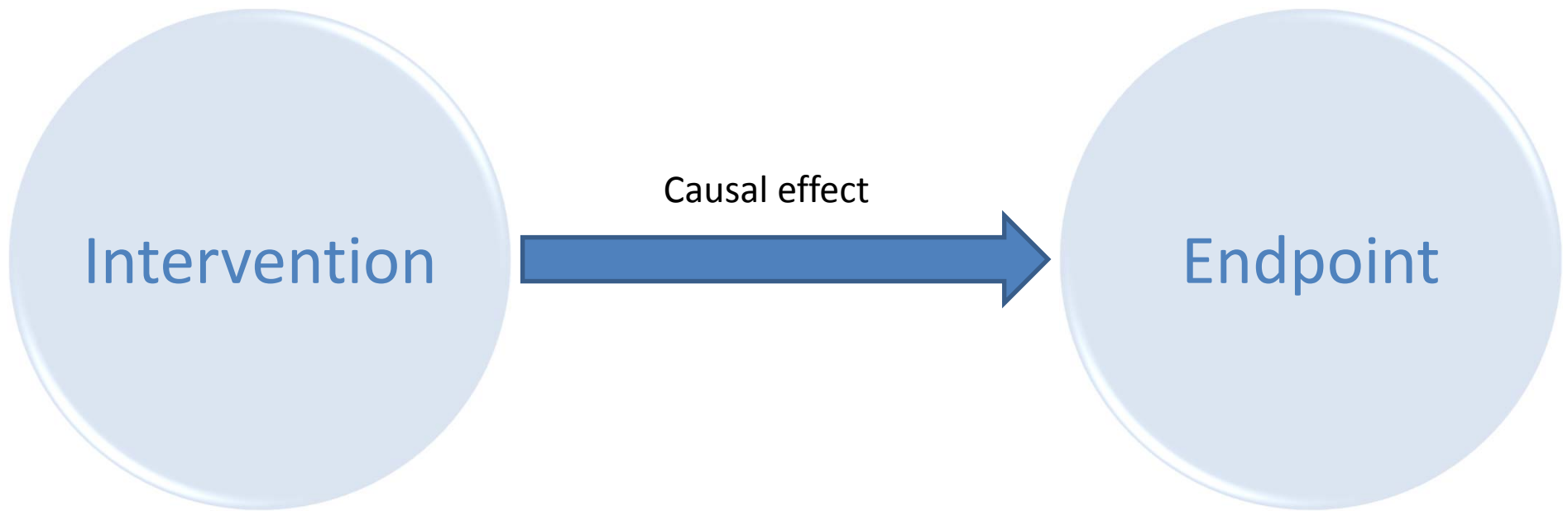
Approaches to evidence review



Approaches to evidence review



The beauty of randomized trials



- Question driving the review
- Methodological approach
- Review question(s)
- Criteria for including studies in the review

Review PICO

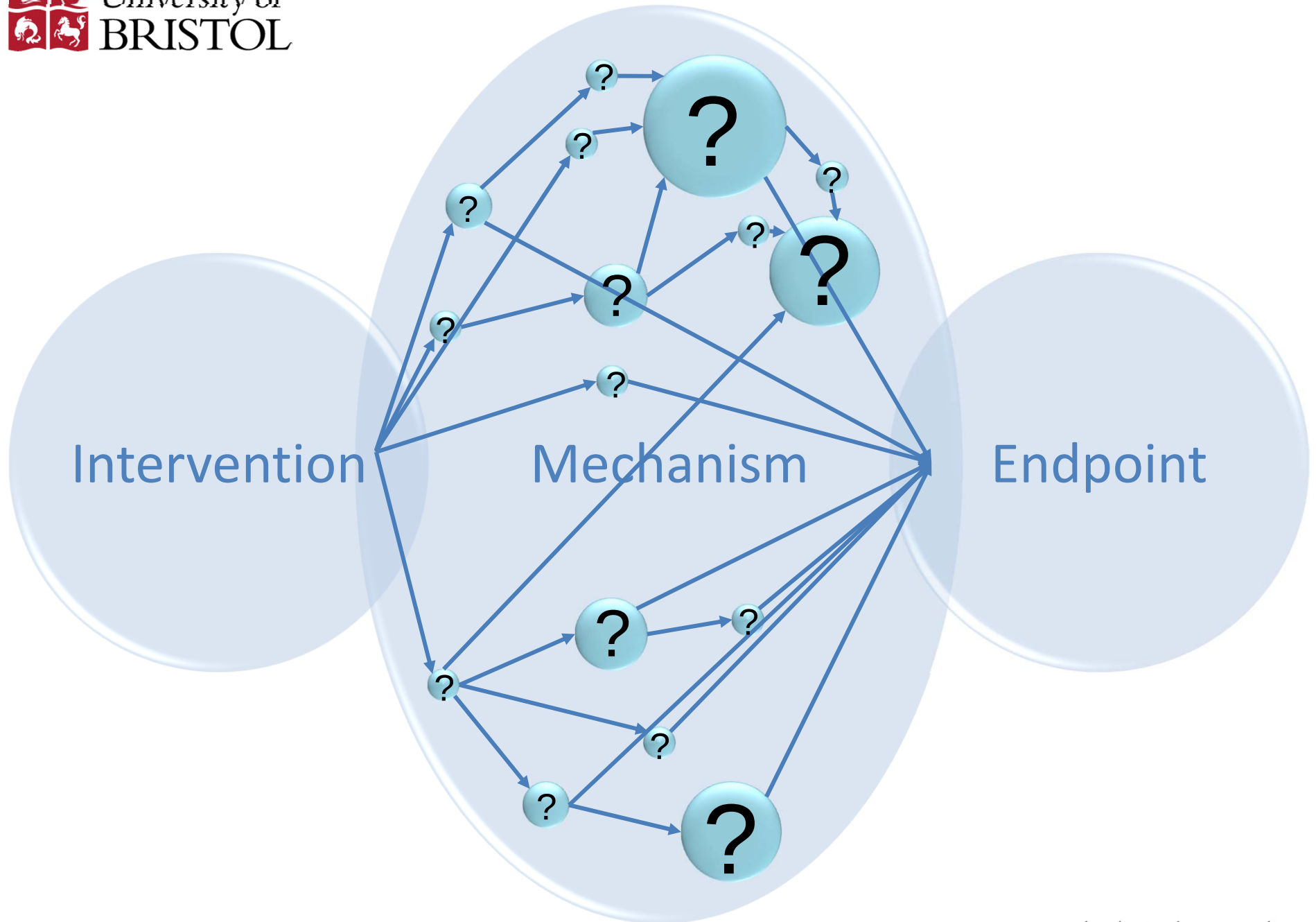
- criteria for eligibility of studies for the review

Comparison PICO

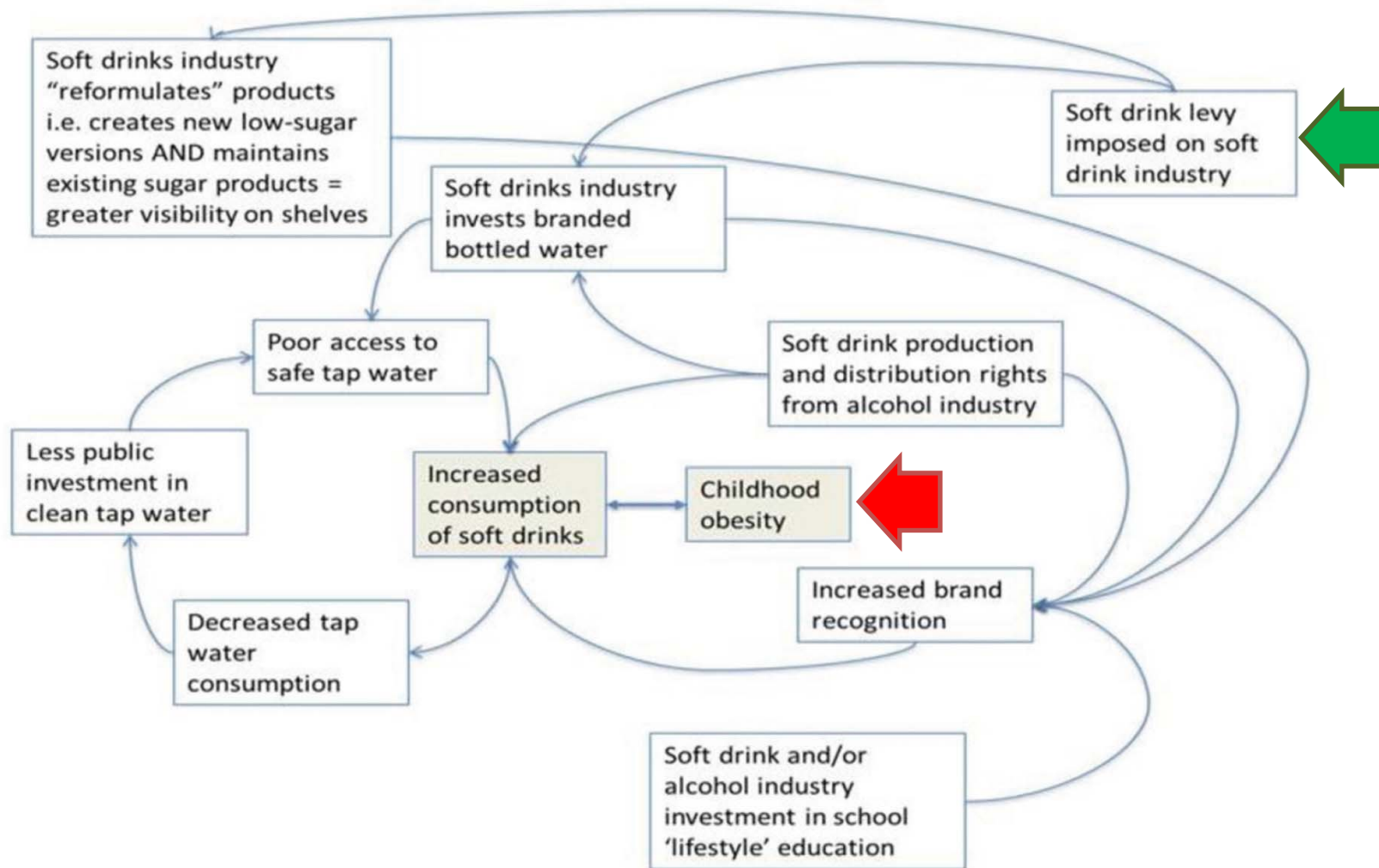
- specific questions within a review, for different population subgroups, specific interventions, endpoints, timepoints etc

Included study PICO

- question(s) addressed by each included study
- *New Cochrane Handbook* (version 6, 2019) will encourage specification of **comparison PICO**s in the protocol
 - increased focus to the review
 - potential value of scoping out what is available



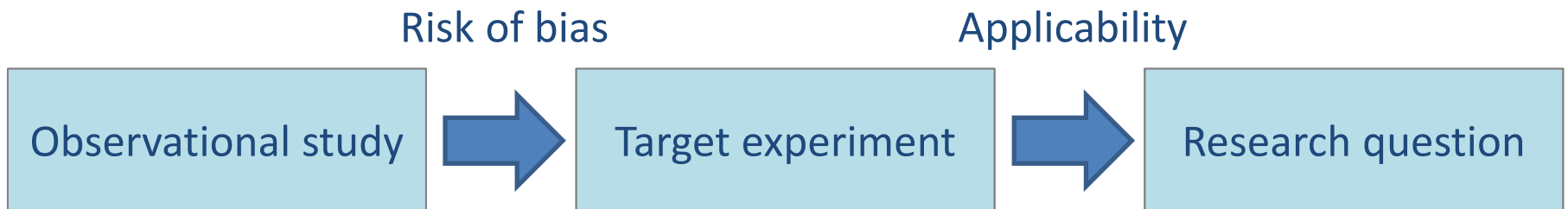
Logic models: the review's starting point



- The difference is that interventions are (often) developed and/or applied because of a **theory about the mechanism**

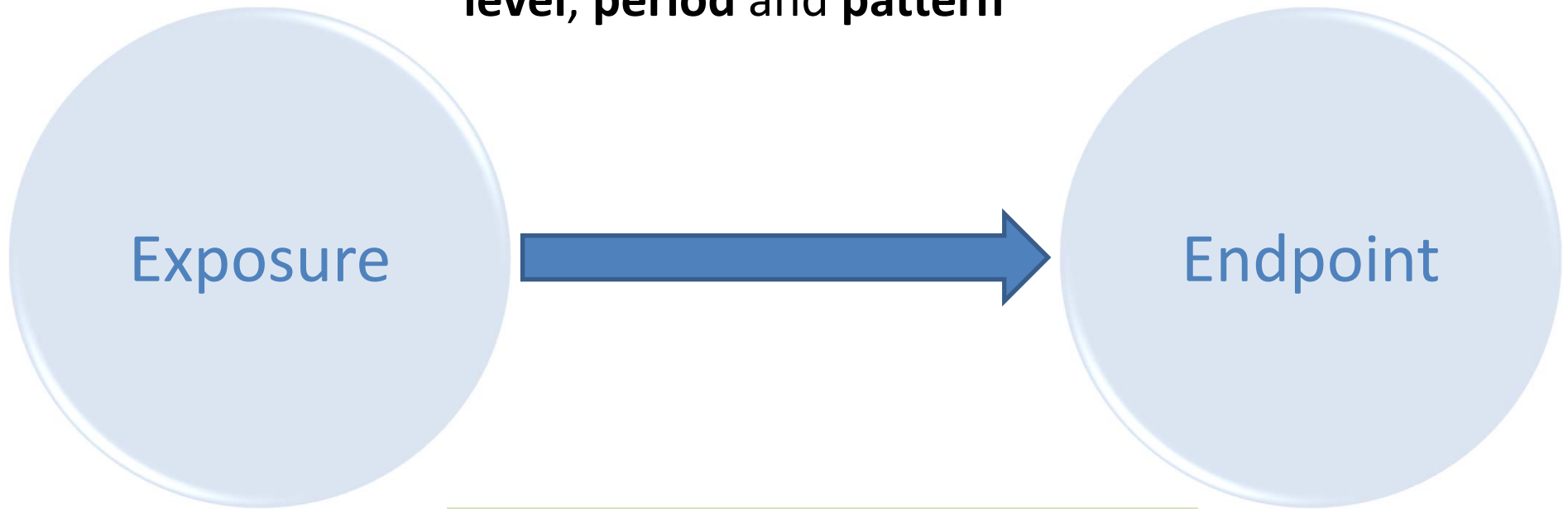
What about exposures?

- Systematic reviews of observational studies face much greater challenges
 - which studies are sufficiently relevant? (PECO)
 - which studies are sufficiently 'good'? (risk of bias)
- To inform consideration of biases in each study, ROBINS-E considers a **hypothetical experiment** examining the same exposure in the same population (transported from ROBINS-I)



Target experiment:

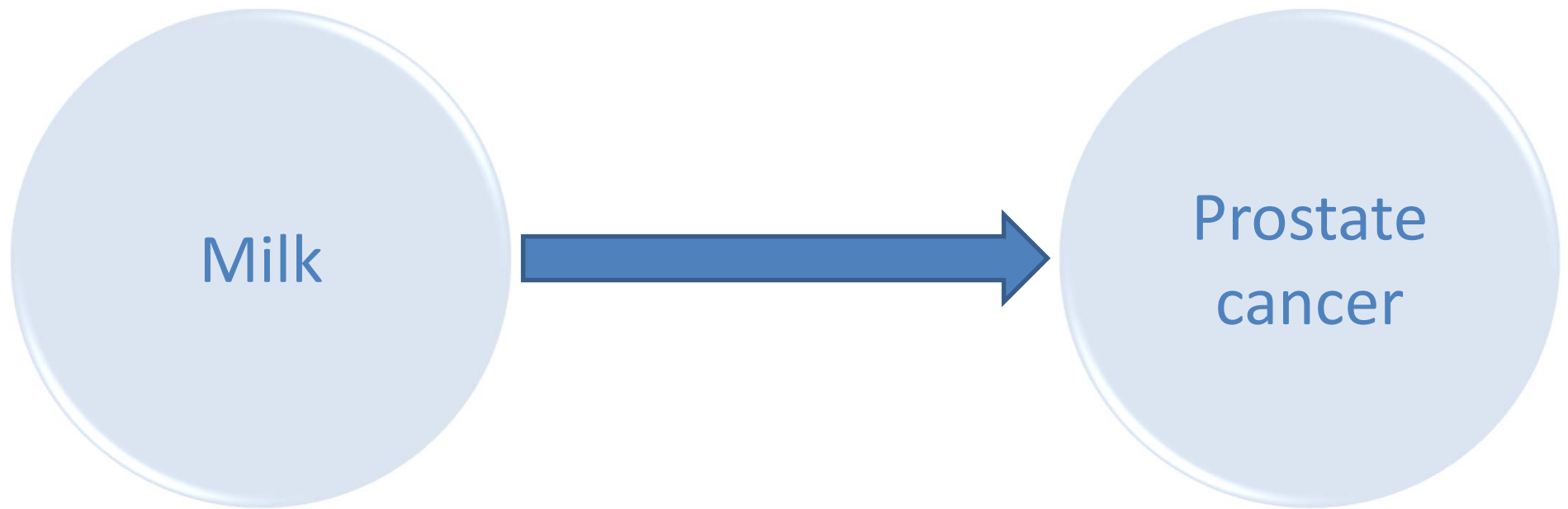
Define the factor whose causal effect is of interest, including **time of onset**, **level**, **period** and **pattern**

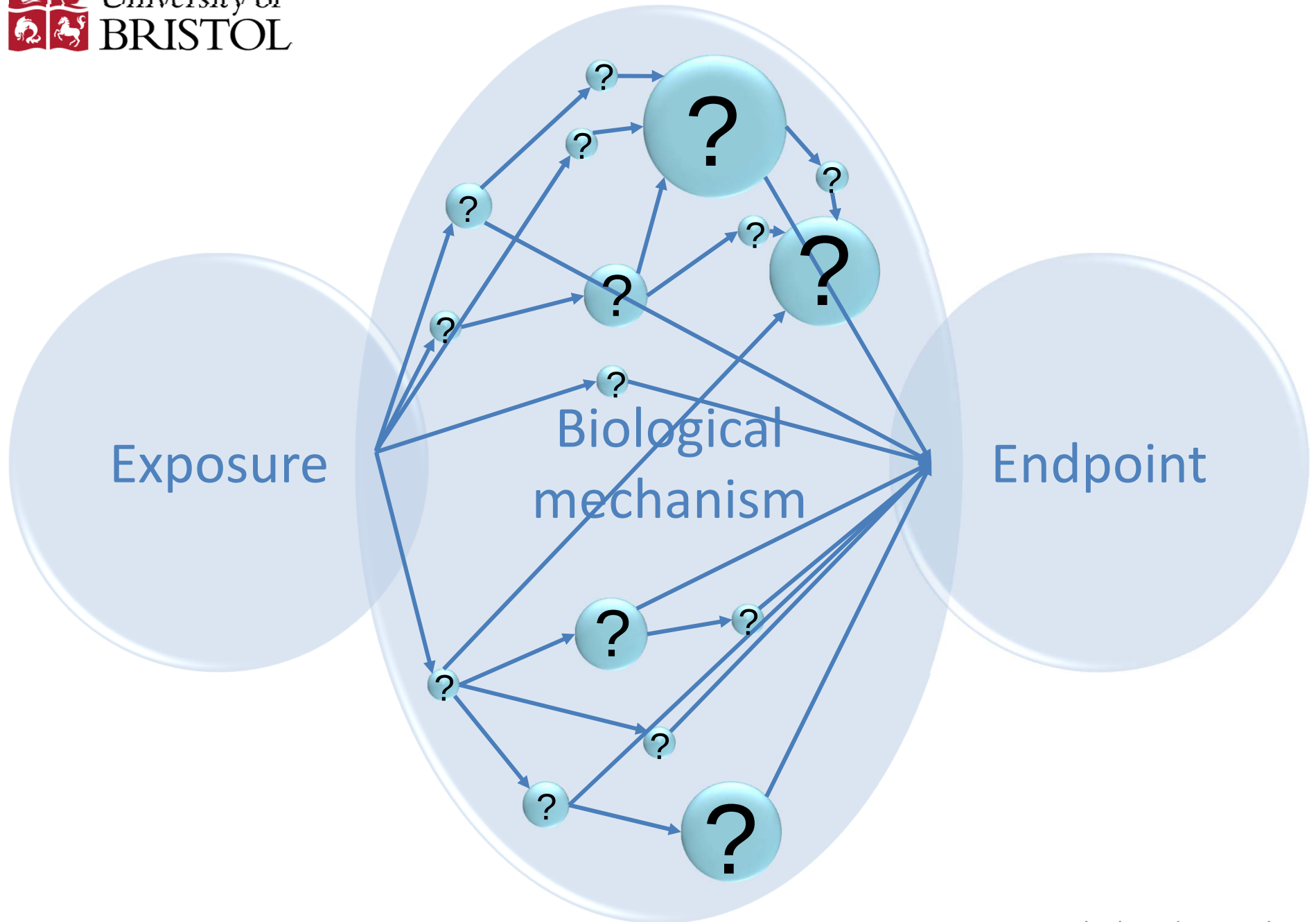


Review PECO

Comparison PECO

Included studies PECO





Applicability and Feasibility of Systematic Review for Performing Evidence-Based Risk Assessment in Food and Feed Safety

E. AIASSA,¹ J.P.T. HIGGINS,² G.K. FRAMPTON,³ M. GREINER,⁴ A. AFONSO,⁵ B. AMZAL,⁶
J. DEEKS,⁷ J.-L. DORNE,⁸ J. GLANVILLE,⁹ G. L. LÖVEL,¹⁰ K. NIENSTEDT,¹¹
A.M. O'CONNOR,¹² A.S. PULLIN,¹³ A. RAJIĆ,¹⁴ and D. VERLOO¹

¹European Food Safety Authority, Assessment and Methodological Support Unit, Parma, Italy

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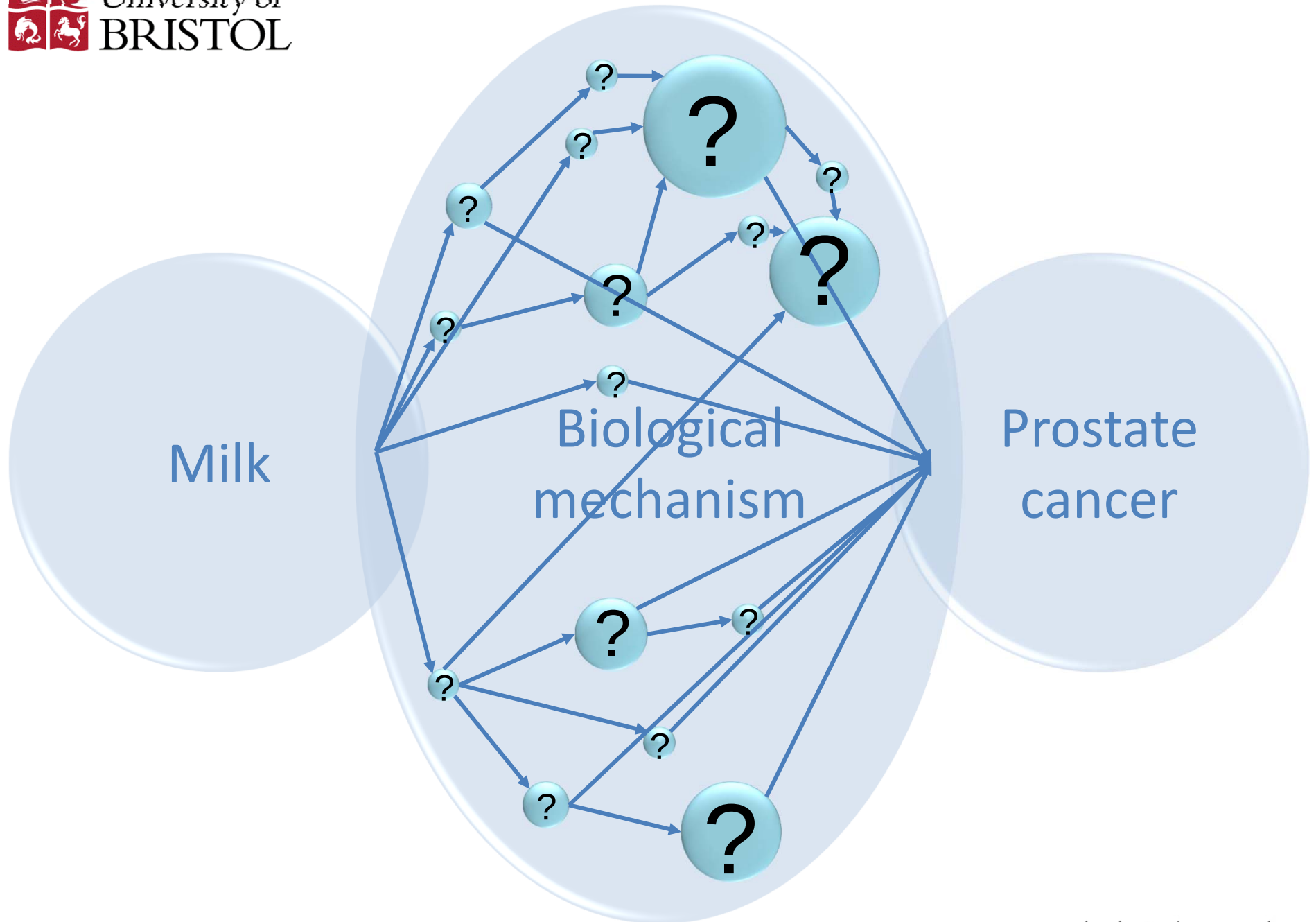
³Southampton Health Technology Assessments Centre (SHTAC), Faculty of Medicine, University of Southampton,
Southampton, UK

Closed-framed vs Open-framed questions, e.g.

What is the effect of A on B? (suitable for systematic review)

VS

What does A affect? (unsuitable for systematic review)



Search	PubMed results
milk and “prostate cancer”	191

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milk and “prostate cancer”	191
milk	131799

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“prostate cancer”	104060

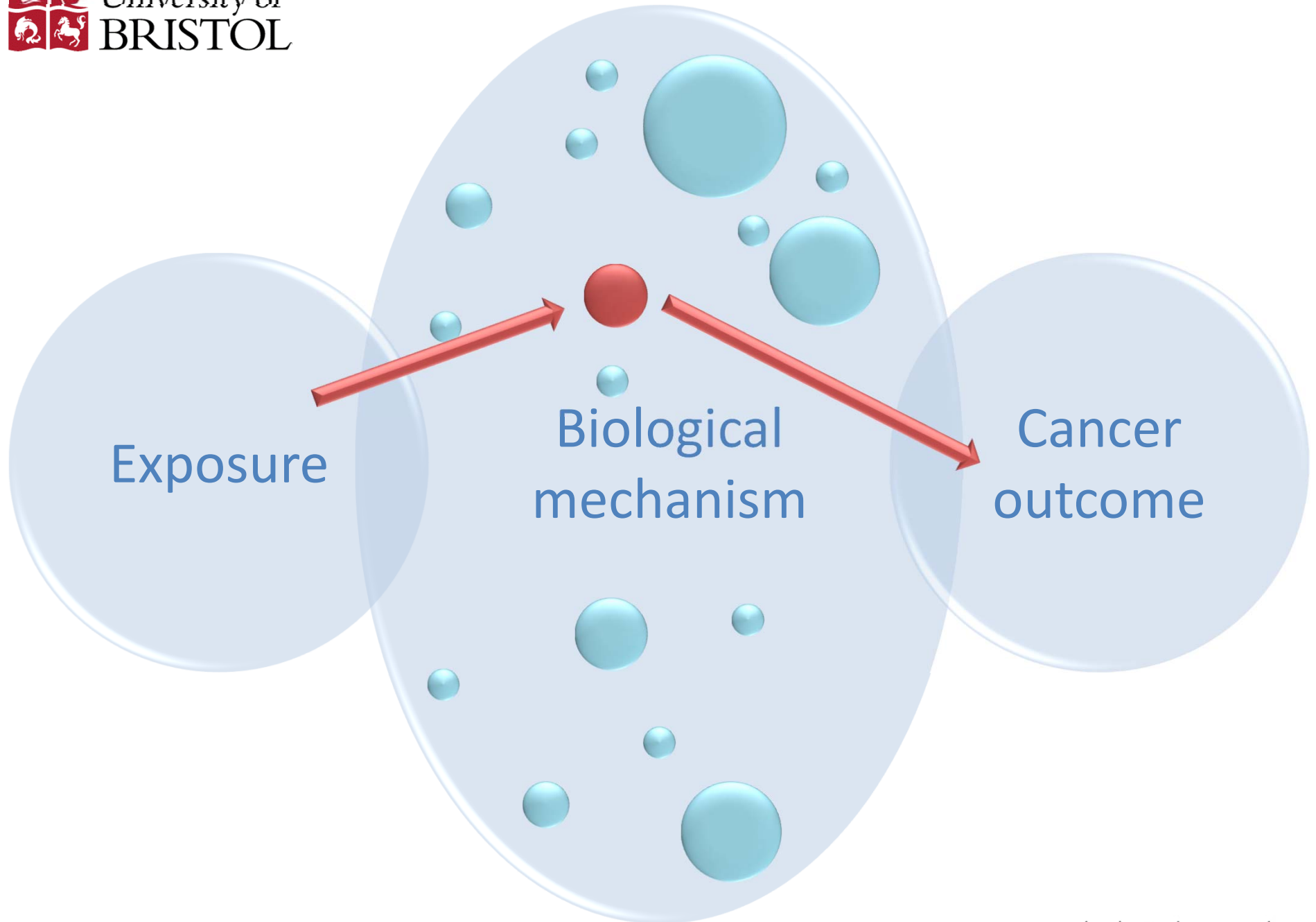
Research Article

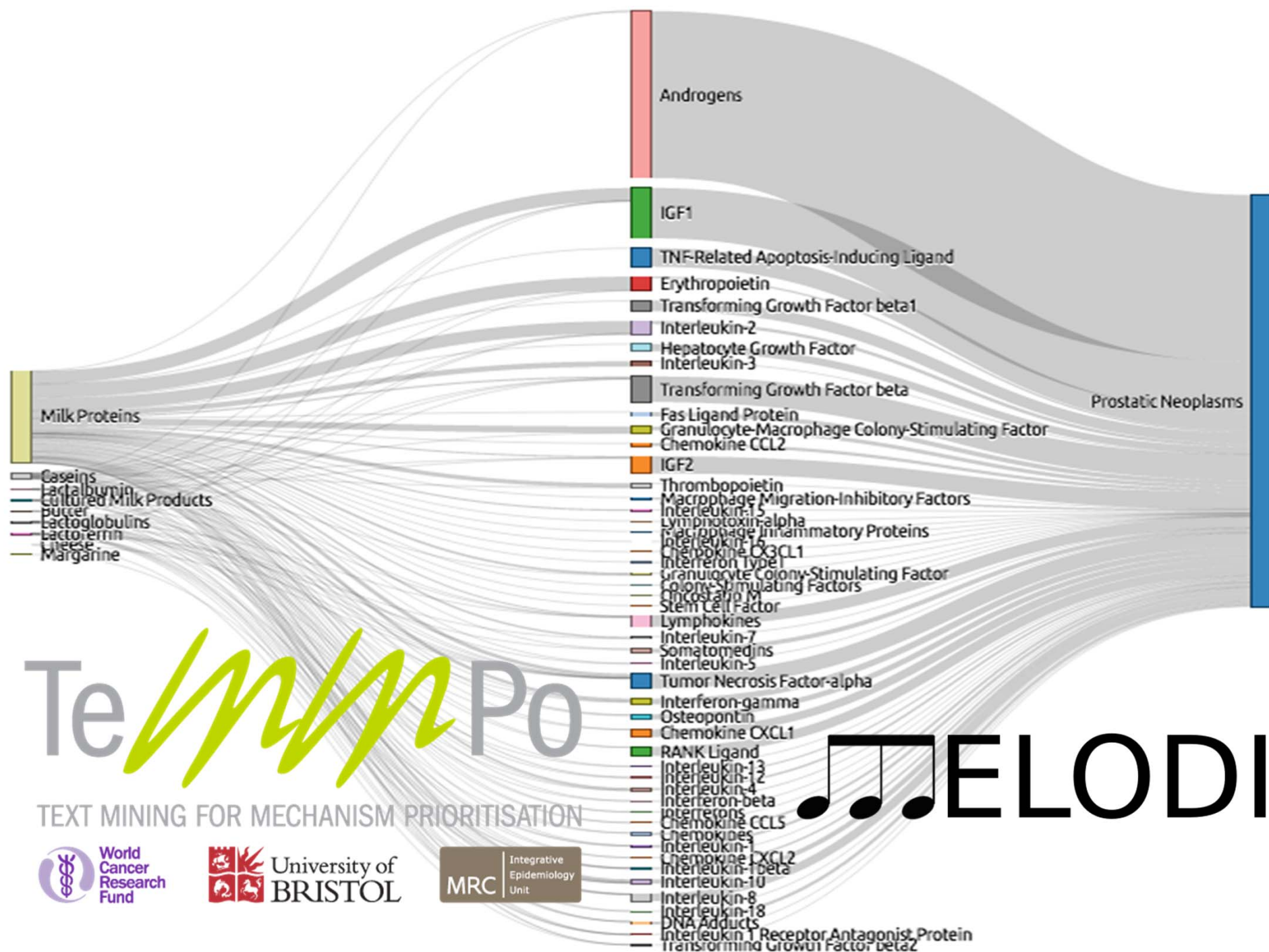
Cancer
Epidemiology,
Biomarkers
& Prevention

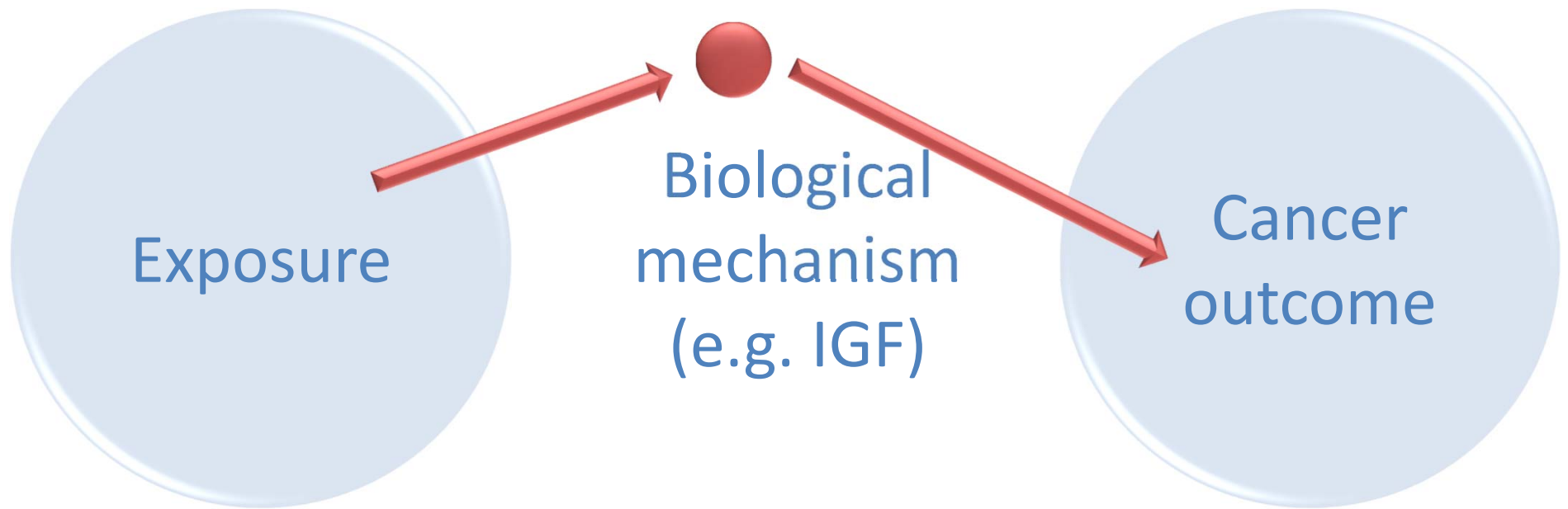
Developing the WCRF International/University of Bristol Methodology for Identifying and Carrying Out Systematic Reviews of Mechanisms of Exposure–Cancer Associations

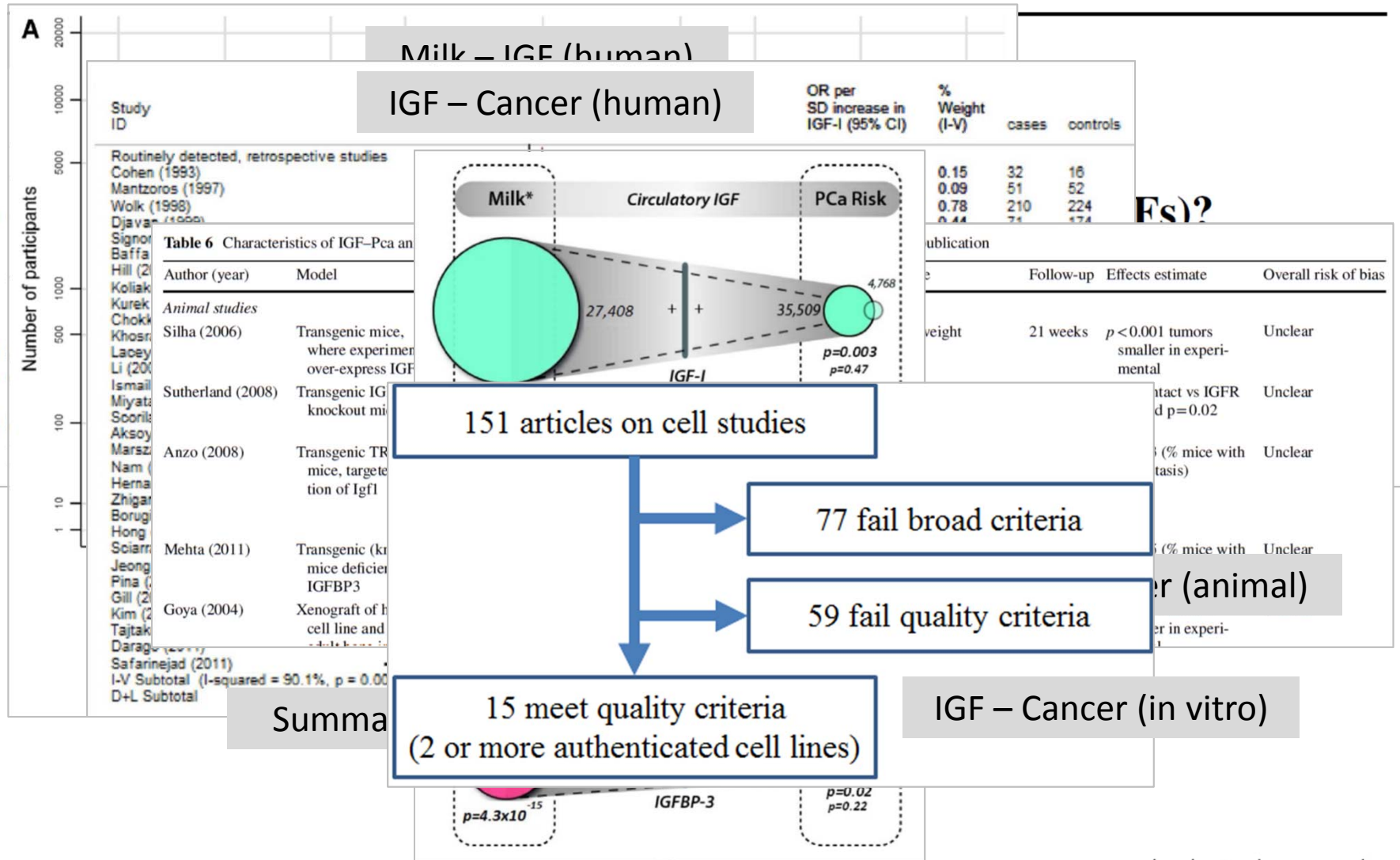


Sarah J. Lewis^{1,2}, Mike Gardner^{1,3}, Julian Higgins¹, Jeff M.P. Holly⁴, Tom R. Gaunt^{1,2}, Claire M. Perks⁴, Suzanne D. Turner⁵, Sabina Rinaldi⁶, Steve Thomas⁷, Sean Harrison^{1,2}, Rosie J. Lennon¹, Vanessa Tan^{1,2}, Cath Borwick^{1,8}, Pauline Emmett¹, Mona Jeffreys¹, Kate Northstone⁹, Giota Mitrou¹⁰, Martin Wiseman¹⁰, Rachel Thompson¹⁰, and Richard M. Martin^{1,2}









Summary remarks

- No easy answers
- Be clear about the purpose of the review to decide the review approach
- Be driven by PECO, recognizing its different roles
- Clearly distinguish bias from relevance
 - the idea of a 'target experiment' is key here
- If taking a fully systematic approach, probably need to specify minimum quality criteria
- Success is largely down to planning
 - scoping what's there
 - but inevitable (unfortunate) circularity of looking at what's there before planning how to review it
 - envisage the tables and figures at the outset, if possible