A quantitative approach to aetiological triangulation: case study of beta-carotene and cardiovascular disease

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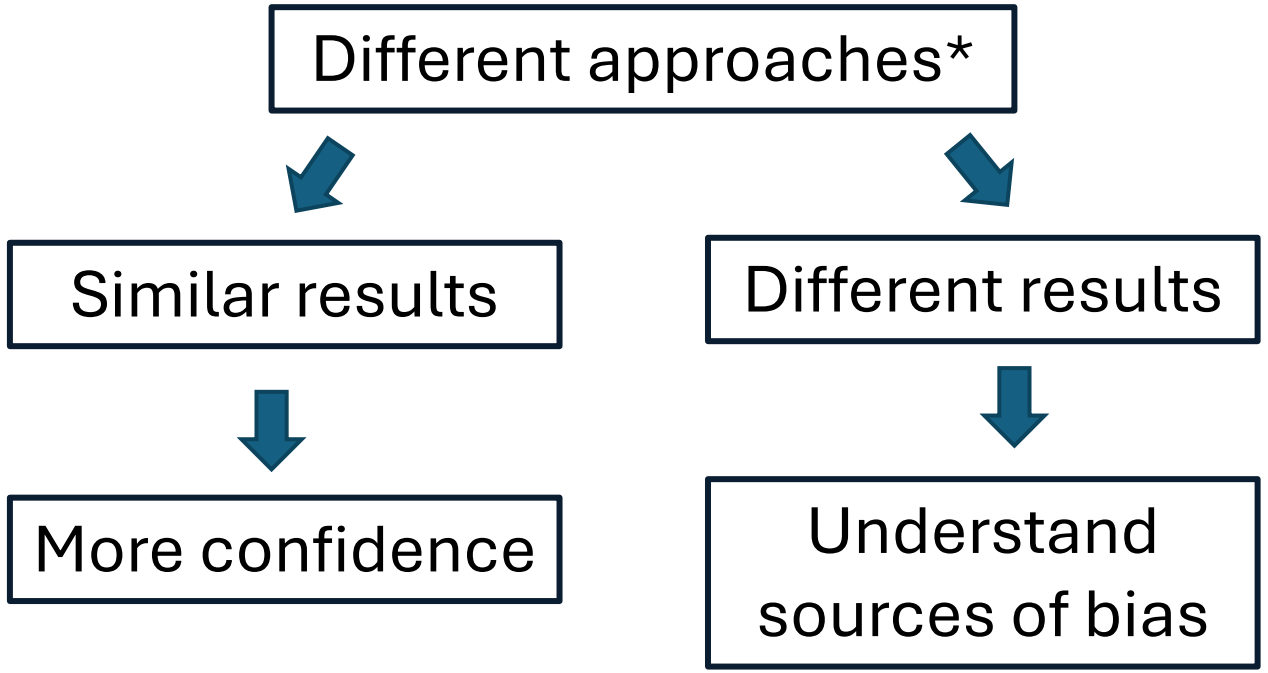
25th of September

WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024

Triangulation in epidemiology



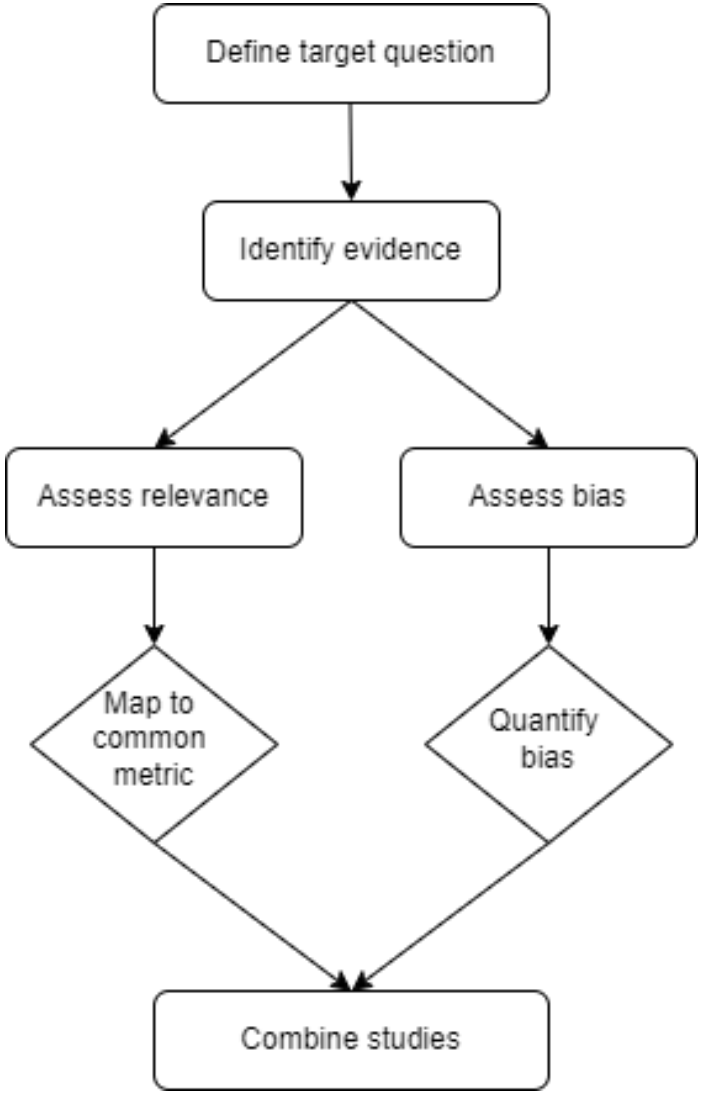
* With different and unrelated potential biases (preferably that point in opposite directions).

Lawlor et al. IJE 2017

Our framework for combining multiple studies

Two types of variability between studies occurs during triangulation:

- *Relevance*: What causal effect the studies are estimating and how is it relevant to your causal question; and
- *Bias*: risk of bias in each study when estimating its causal effect.



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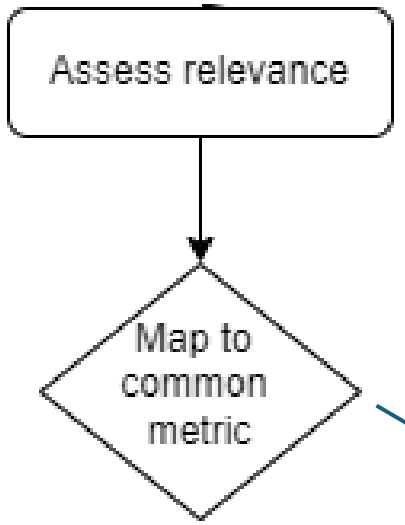
Defining the target causal question

- The population
- Exposure measure
- Exposure window
- How exposure is to be summarized over time
- Outcome measure
- The statistical parameter to be estimated

Defining the target causal question

- The population: *Adults (above age 40) initially free from diagnosed CVD.*
- Exposure measure: *Dietary β-carotene*
- Exposure window: Over 20-year period in mid-life
- How exposure is to be summarized over time: Average daily exposure
- Outcome measure: *Cardiovascular disease (CVD) and secondary is coronary heart disease (CHD)*
- The statistical parameter to be estimated: Risk ratio

Relevance in identified evidence



From published manuscript
The population, exposure and outcome are generally derived easily from the eligibility criteria and outcome measurements used in the study.

The tricky part
Exposure window and how exposure is to be summarized over time.

May not have the exact causal question asked (i.e. different exposure or different population), but maybe can be mathematically converted? (for example, BMI vs percentage of fat mass).

Relevance

Relevance was assessed in terms of the six criteria. Transformations include;

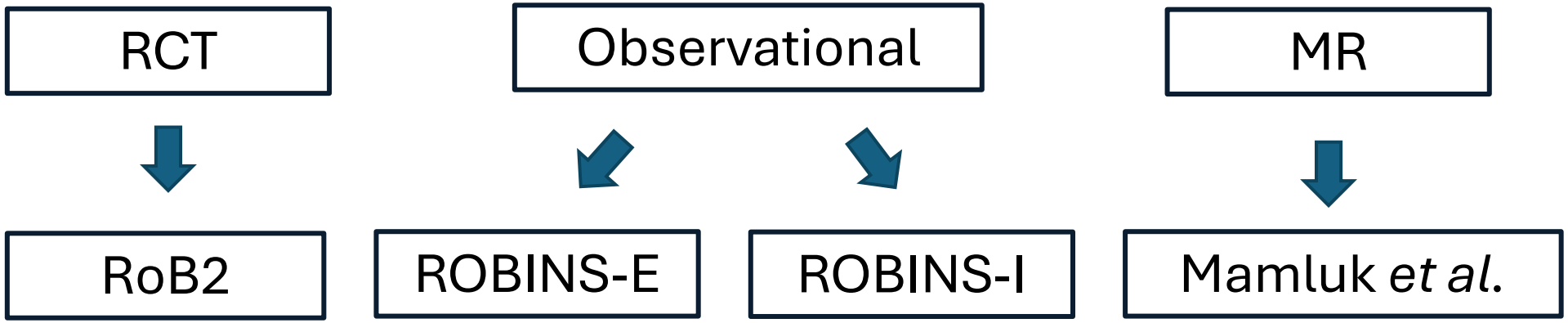
Mendelian randomisation study
Convert log-transformed circulating β-carotene to per 5,000 µg/d dietary β-carotene.

Randomised controlled trials
Convert different dosages to per 5,000 µg/d dietary β-carotene.

Observational studies
Convert circulating β-carotene to per 5,000 µg/d dietary β-carotene.

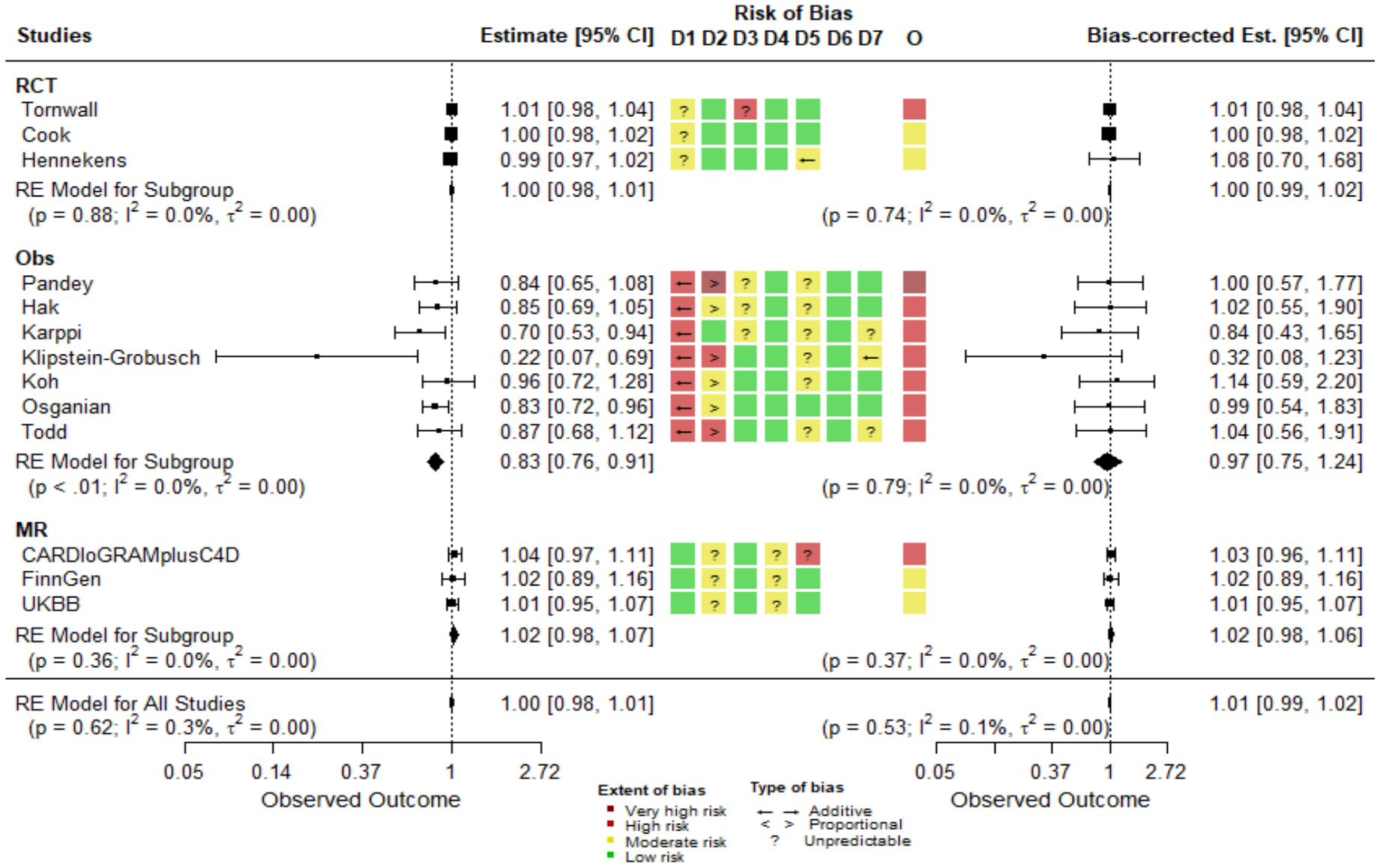
Bias in identified evidence

Depending on study design different risk of bias tools are available:



Each tool cover different bias domains and help the assessors to determine the extent of bias. We used *triangulate* R package for bias visualisation and adjustments.

Risk of bias - β-carotene and CHD



Conclusions

- Bias adjustment is prone to errors but not acknowledge bias and assume all effect estimates are unbiased are even more problematic.
- The future of triangulation is dependent on better and more consistent reporting.

Future work

- RoB for Mendelian randomisation
- Expert elicitation for priors
- Different estimands
- Guidance for relevance

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Acknowledgements

Joshua A. Bell
Maria-Carolina Borges
Ana Goncalves Soares
George Davey Smith
Tom R. Gaunt
Deborah A. Lawlor
Luke A. McGuinness
Kate Tilling
Julian P.T. Higgins

Link to preprint

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