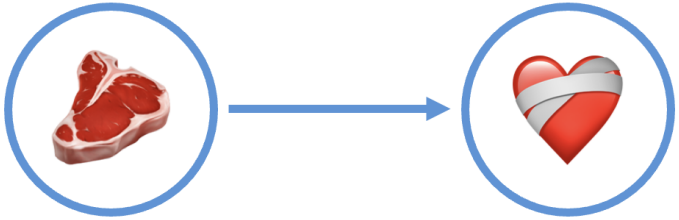
From Correlation to Causality

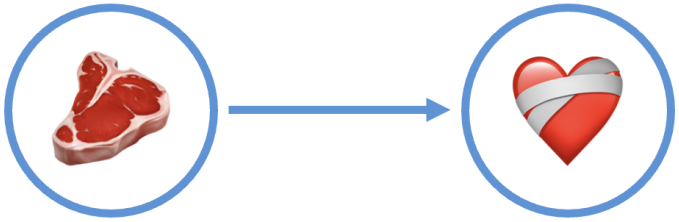


How to Assess the Validity of Epidemiological Studies

Dr. Alexander Bauer

Plant-Based Health Professionals UK

www.statswithalex.com



Research question

Does unprocessed red meat affect the risk for heart disease?

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Meat Increases Heart Risks, Latest Study Concludes

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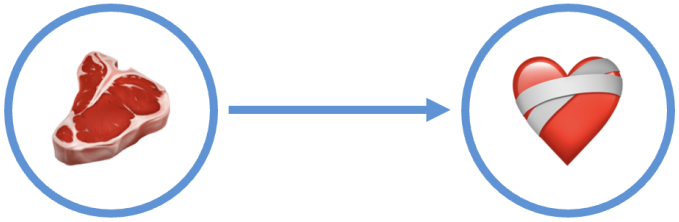

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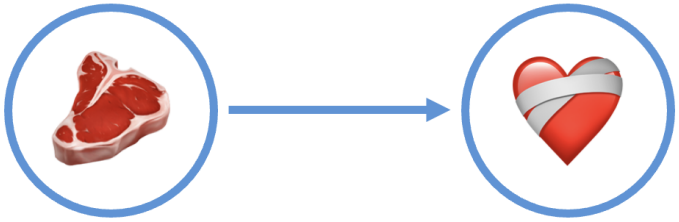
Eat Less Red Meat, Scientists Said. Now Some Believe That Was Bad Advice.

nytimes.com (30 September 2019), based on Johnston et al. (2019)



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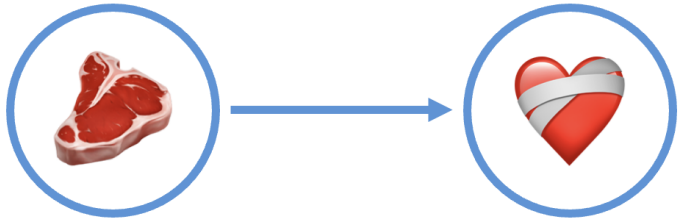


Research question

Does unprocessed red meat affect the risk for heart disease?

Survey time!

Question 1

What is your level of expertise regarding statistical analysis?

1 – *Let's not talk about it...*

2 – *I can interpret basic statistics like medians and standard deviations*

3 – *I can interpret more advanced analyses like regression models*

4 – *I can plan and design some statistical aspects of studies*

5 – *I can defend all statistical aspects of (my) studies*

Question 2

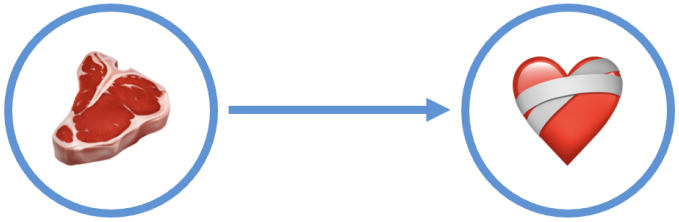
Would you feel confident in explaining the difference between substantial relevance (= effect sizes) and statistical significance (= p-values)?

1 – *No*

2 – *I could try*

3 – *I think so*

4 – *Yes!*



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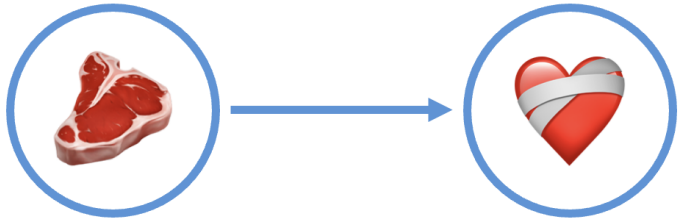

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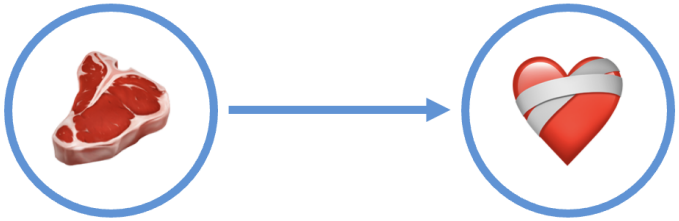
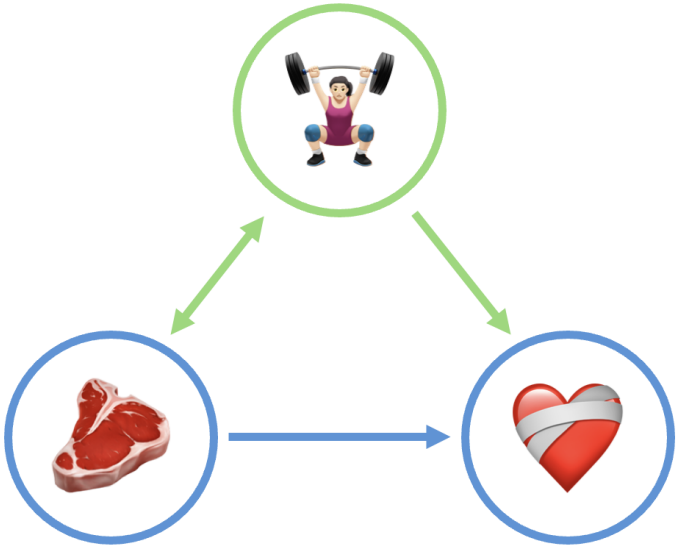
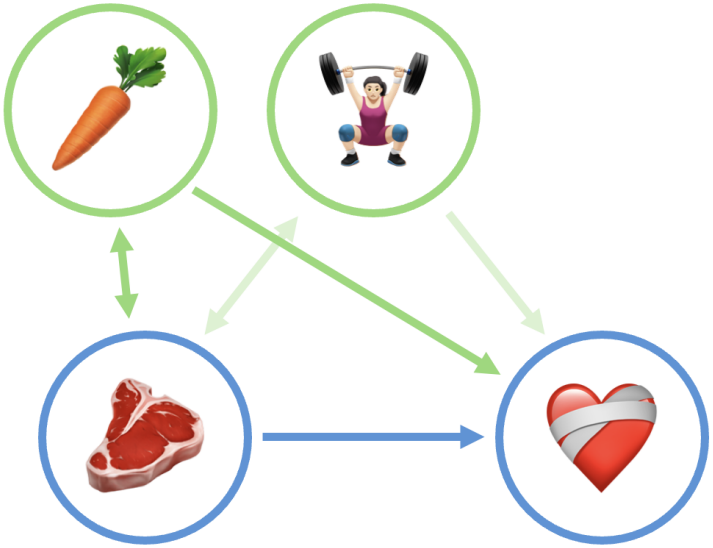
Does unprocessed red meat affect the risk for heart disease?

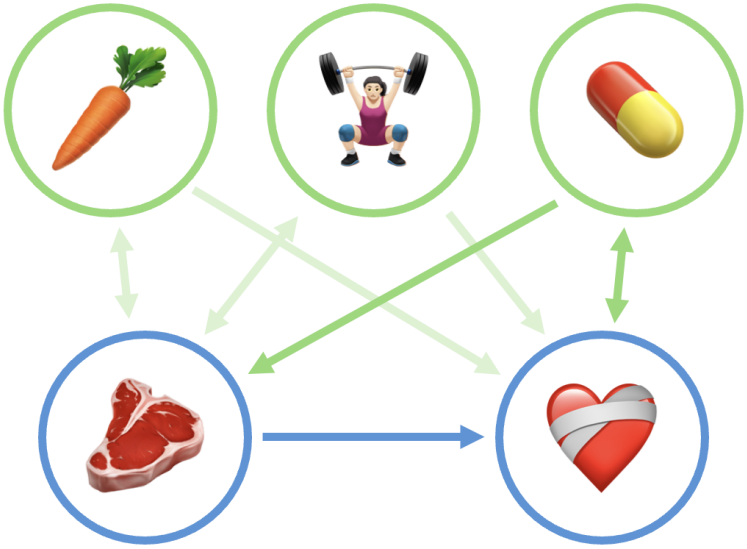
Challenge

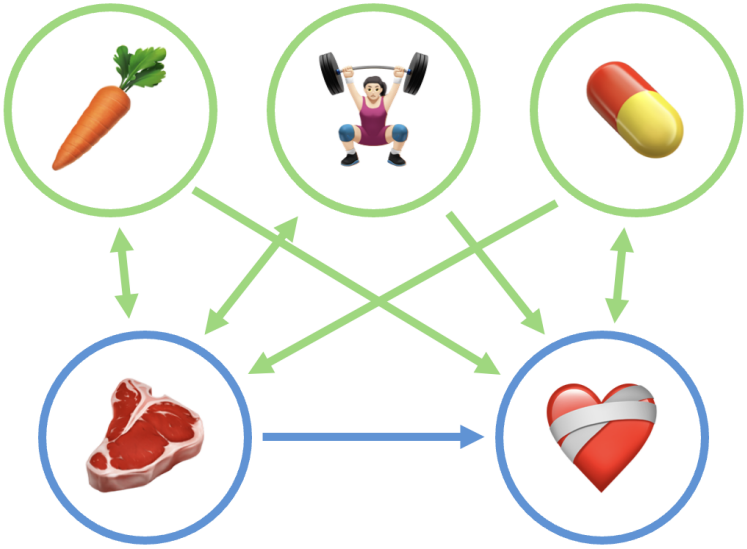
Nutrition is complicated...



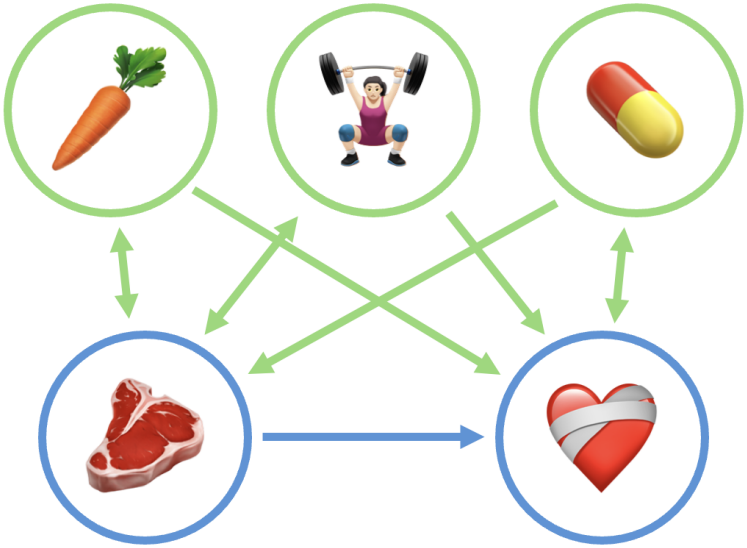








Overview



1. Study design

Are some studies better than others?

2. Correlation vs. causality

Are we estimating the pure effect of red meat?

3. Nutrition remains complex

Are we overinterpreting things?

Exemplary overview studies

Zhong et al. (2020)

"unprocessed red meat [...] was significantly associated with a small increased risk of incident CVD"

Sanders et al. (2024)

"no meaningful effect of daily unprocessed beef intake [...], except for a small effect [on] LDL-cholesterol'

Study design

Study designs for individual studies

Cross-sectional study

Case-control study

Prospective cohort study

Randomised Controlled Trial (RCT)

Study designs for individual studies

Cross-sectional study

One snapshot in time. No temporality "First X, then Y"...

Diet information biased since only retrospective...

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Costly and lengthy, but captures long-term effects (e.g., cancer risk).

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Useful for analysing rare diseases.
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Prospective cohort study

Can suggest causality as of full observed temporality.
Costly and lengthy, but captures long-term effects (e.g., cancer risk).

Randomised Controlled Trial (RCT)

Strongest causal evidence as of randomisation
Often costly, mostly short-term effects only.

Study design

Study designs for overview studies

Goal: Analysis of all (high quality) studies on a topic

Study design

Study designs for overview studies

Goal: Analysis of all (high quality) studies on a topic

"What is the consensus among multiple studies?"

"Do studies agree on a research topic?"

"What is the average effect observed over all studies?"

Study designs for overview studies

Pure systematic review

Comprehensive summary of all evidence on a question.

Systematic review with meta analysis

Statistical pooling of data for more precise effect estimates.

Rating our exemplary studies

Zhong et al. (2020)

6 prospective cohort studies

Sanders et al. (2024)

20 randomised controlled trials

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⇒ **Zhong is worse than Sanders**
since RCTs are better than cohort studies!

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6 prospective cohort studies
(on long-term cardiovascular health)

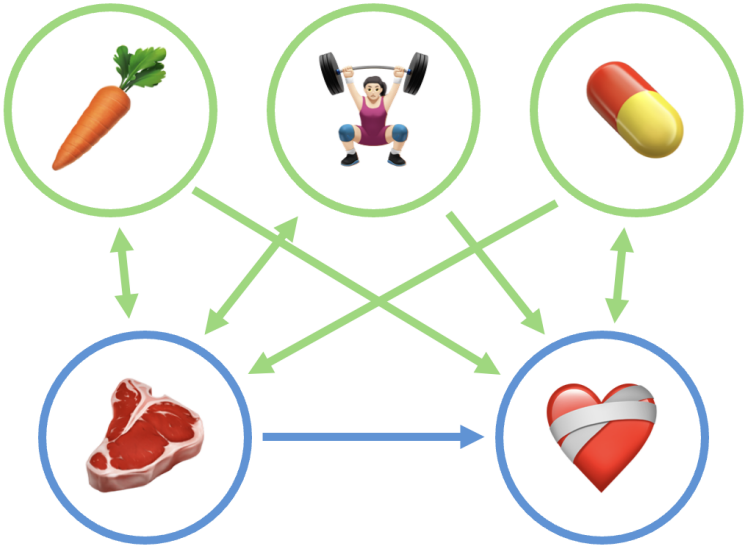
Sanders et al. (2024)

20 randomised controlled trials
(on short-term blood marker change)

⇒ **Zhong is worse than Sanders**
since RCTs are better than cohort studies!

⇒ **Zhong is (slightly) better than Sanders**
since focus is on diseases rather than short-term blood indicator changes

Causality



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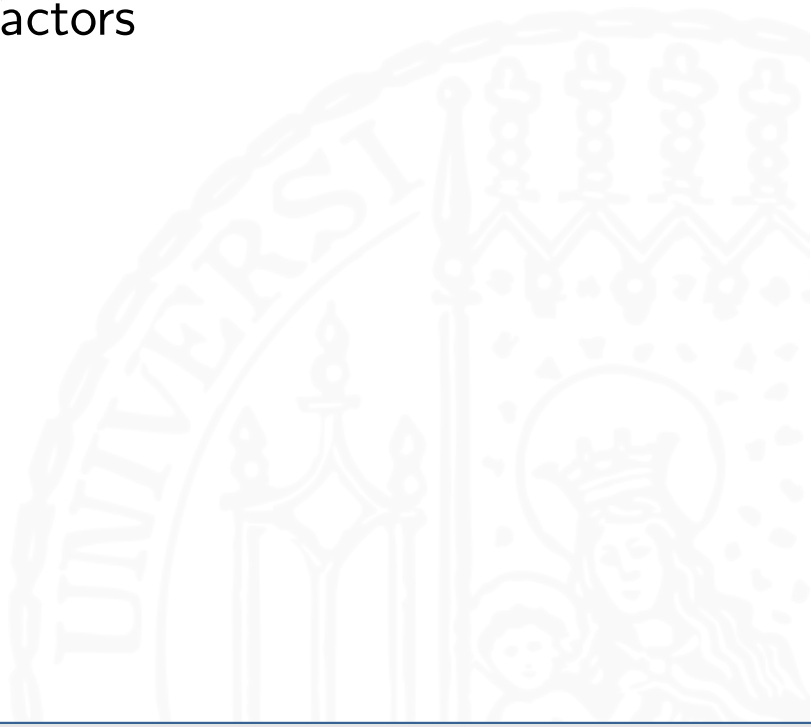
Causality

An effect can only be causal if ...

- **temporality**

  ... the exposure precedes the outcome
- **no confounding**

  ... the exposure is not mixed up with other factors



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- **temporality**

  ... the exposure precedes the outcome
- **no confounding**

  ... the exposure is not mixed up with other factors

$\Rightarrow$ RCTs and prospective cohort studies both ensure temporality

$\Rightarrow$ Only RCTs can isolate the exposure.

Cohort studies are susceptible to confounding!

Main limitations listed by our exemplary studies

Zhong et al. (2020)

6 prospective cohort studies
(on long-term cardiovascular health)

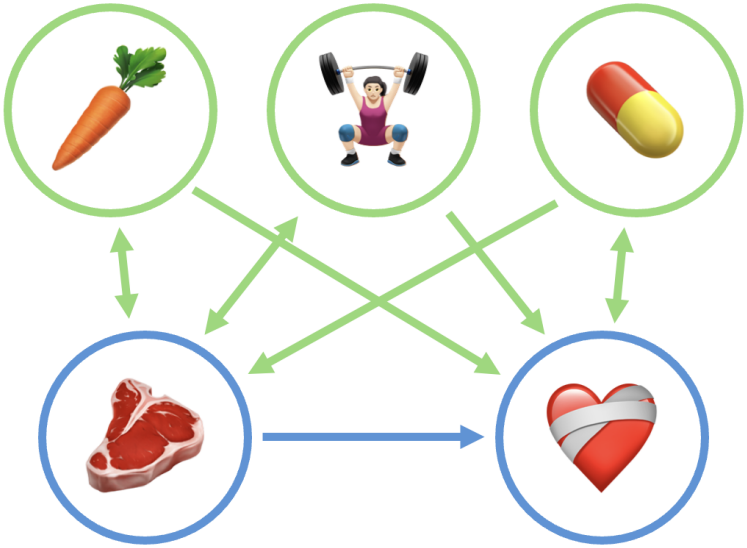
"this study should not establish causality"

Sanders et al. (2024)

20 randomized controlled trials
(on short-term blood marker change)

Evaluation only of beef

Interpretation



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Substantial relevance vs. statistical significance

Substantial relevance vs. statistical significance

Zhong et al. (2020)

"Each additional 2 servings of unprocessed red meat consumed per week was significantly associated with incident CVD (Hazard Ratio 1.03 [...])"

$\Rightarrow$ a 3% risk increase might be irrelevant for individuals,
but relevant on a societal level

Substantial relevance vs. statistical significance

Zhong et al. (2020)

"Each additional 2 servings of unprocessed red meat consumed per week was significantly associated with incident CVD (Hazard Ratio 1.03 [...])"

⇒ a 3% risk increase might be irrelevant for individuals,
but relevant on a societal level

⇒ Interpret both, effect sizes (i.e., relevance) and uncertainty (i.e., significance)

⇒ Potentially differentiate between the individual level and the societal level

Exemplary systematic review

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Is Red Meat Bad for Your Heart? It May Depend on Who Funded the Study.

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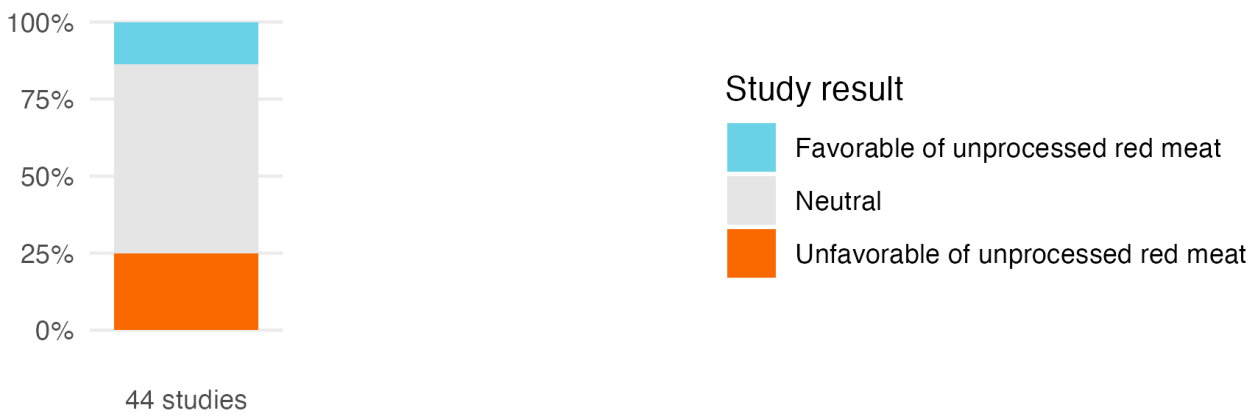

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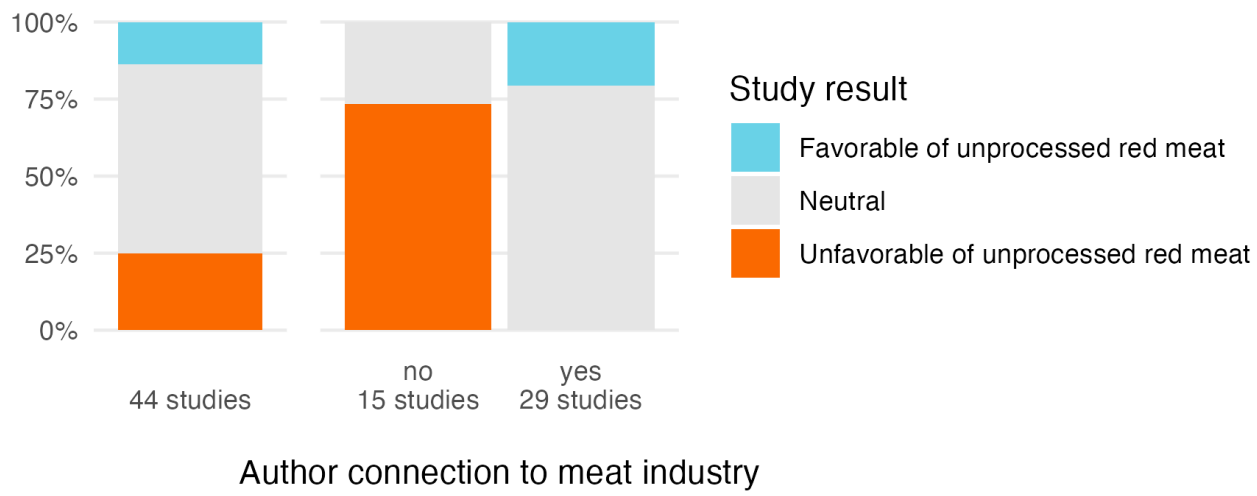

Exemplary systematic review

Asking different questions leads to different answers!

even if the study design is similar...

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even if the study design is similar...

Independent studies

"mainly compared unprocessed red meat with plant protein."

Studies related to the red meat industry

"[typically compared] unprocessed red meat with animal protein or refined carbohydrates."

Take home messages

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Nutrition is complicated, but ...

The simple answer

... systematic reviews generally communicate current (un)certainties well!

Take home messages

Nutrition is complicated, but ...

The simple answer

... systematic reviews generally communicate current (un)certainties well!

The more complex answer

- prioritise systematic reviews
- prioritise randomised controlled trials and prospective cohort studies
- check if results are only significant or also relevant
- check who funded the study

Further Reading

Study design

DiPietro, N. A. (2010). Methods in epidemiology: observational study designs. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 30(10), 973-984.

Substantial relevance vs. statistical significance

Wasserstein, R. L., & Lazar, N. A. (2016). The ASA statement on p-values: context, process, and purpose. *The American Statistician*, 70(2), 129-133.