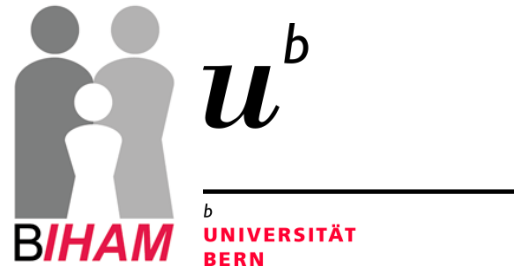# Causal effects of micronutrients: identifying mechanistic estimands applying the target trial framework

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SER mid-year meeting

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#Pop Health Lab

BIHAM

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UNIVERSITÄT BERN

UNI FR

What do we really want to know about ultra-processed foods?

Unbiased Science
15,117 followers
1d

Are processed foods as bad for us as people say?
No. There isn't a direct relationship between whether
a food is processed and its nutritional cc ...see more

Are "processed foods" as bad as people say they are? No.

There is not a direct relationship between whether a food is processed and its nutritional content.

We need to do away with the notion that foods are inherently good or bad. Foods...

THEUNBIASEDSCIPOD.SUBSTACK.COM

This paper by @S_Schlesinger_ provides a very good overview of what we currently know about ultra-processed foods. #UPF
And the main question remains unanswered: is it just a marker of poor diet?

Great to see that @DrCaliff_FDA recognizes the importance of understanding the mechanisms relating ultra-processed foods to chronic, diet-related diseases. Stay tuned!

2 feb.

"We've got to understand ultra-processed foods. It's one of the most complex things I've ever dealt with." - @DrCaliff_FDA

It was the first time the commissioner commented on UPFs, a hot-button issue that has food industry leaders quietly melting down....
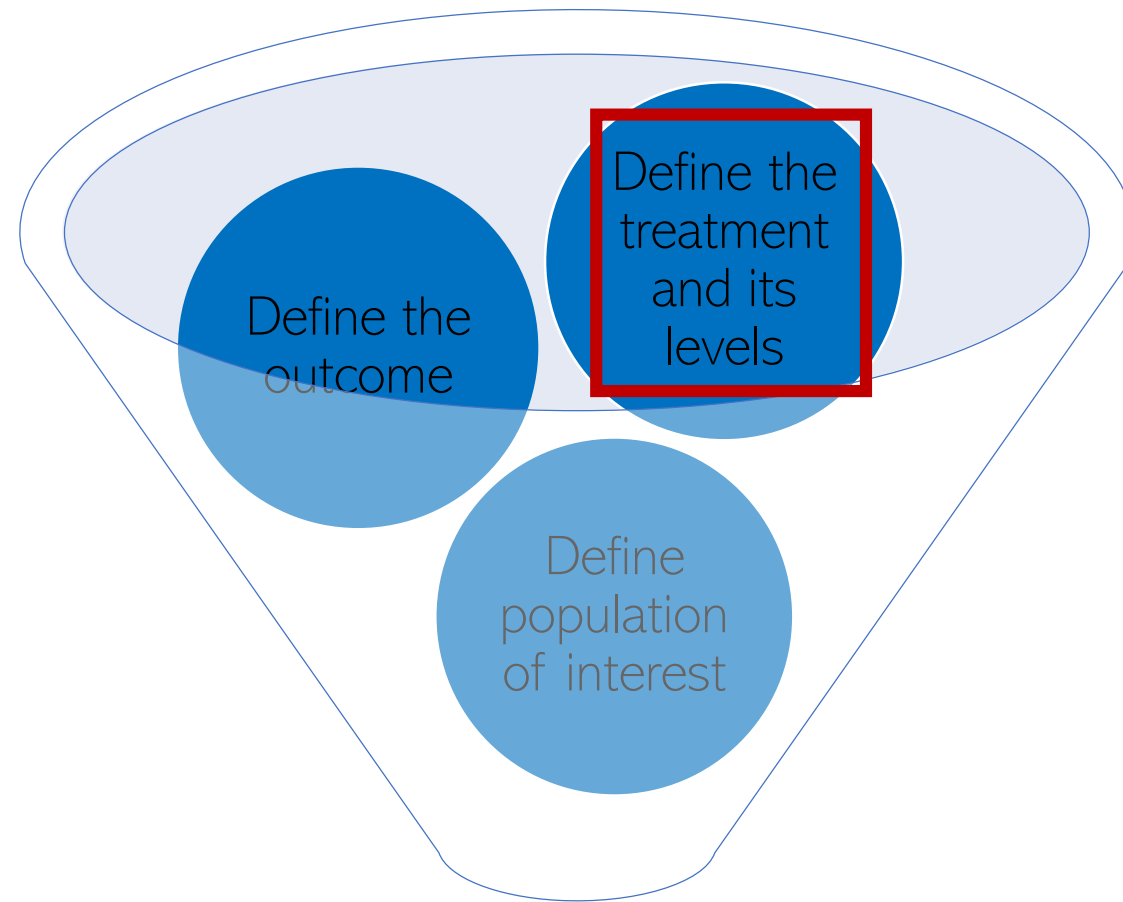Mostrar más

+ Sodium, E-s, sugar =

Causal question

Formalize the potential outcomes, one for each level of the treatment that the study population could have possibly experienced.

Causal parameter - contrast between the potential outcome distributions.

Define the treatment and its levels

- Diets

- Foods and macronutrients

- Micronutrients

– Biologically active chemical compounds found in foods

– Exist within a mixture of other **active components** forming the food matrix.

↓

they co-influence the health outcomes or functions of interest

Goals

1) To conceptualize mechanistic and recommendation research questions related to micronutrients

2) To propose three estimands

3) To assess under which data structure and assumptions it is possible to identify the proposed estimands

Causal questions for micronutrients

1) Biological mechanism of action on a health outcome, in which case we want to get rid of the effect of the food matrixes in which the micronutrient is contained.

What is the effect of salt on hypertension in population A?

2) Recommendations about optimal intake requirements that involve increasing or decreasing the consumption of foods containing the micronutrient

What is the effect on hypertension of obtaining salt from broccoli compared to processed meat in population A?

Foods and macronutrients

Causal questions for micronutrients

1) Biological mechanism of action on a health outcome, in which case we want to get rid of the effect of the food matrixes in which the micronutrient is contained.

What is the effect of salt on hypertension in population A?

Treatment Outcome Population   Potential
✓   ✓   ✓   Outcomes

Causal estimands for mechanistic micronutrient effect

We can use natural experiments happening in foods

Target trial emulation

Target trial emulation

Point treatment – per protocol effect (full adherence and no-loss to follow-up), isocaloric intervention

a_0 Baseline unprocessed meat consumption (no salt content)

a_1 Baseline processed meat consumption (added salt)

Y Hypertension

No unmeasured confounding assumption   Unprocessed meat + salt ≠ processed meat

$$E(Y^{a_1} = 1 | L, C = 0) - E(Y^{a_0} = 1 | L, C = 0)$$

Causal estimands for mechanistic micronutrient effect

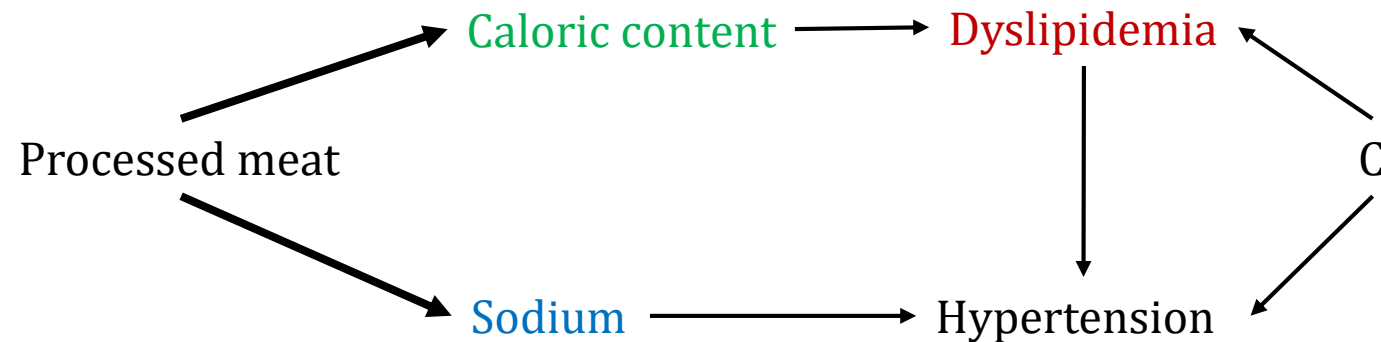We can use natural things happening in foods

Target trial emulation

Separable effects

Conditional separable effects

We can identify **conditional separable direct effect** if...

- Modified treatment
- Isolation
- Need to measure all common causes of Y and W

$$E\left(Y^{a_Y,a_W} \middle| W^{a_Y,a_W}, C = 0\right)$$

Causal estimands for mechanistic micronutrient effect

We can use natural things happening in foods

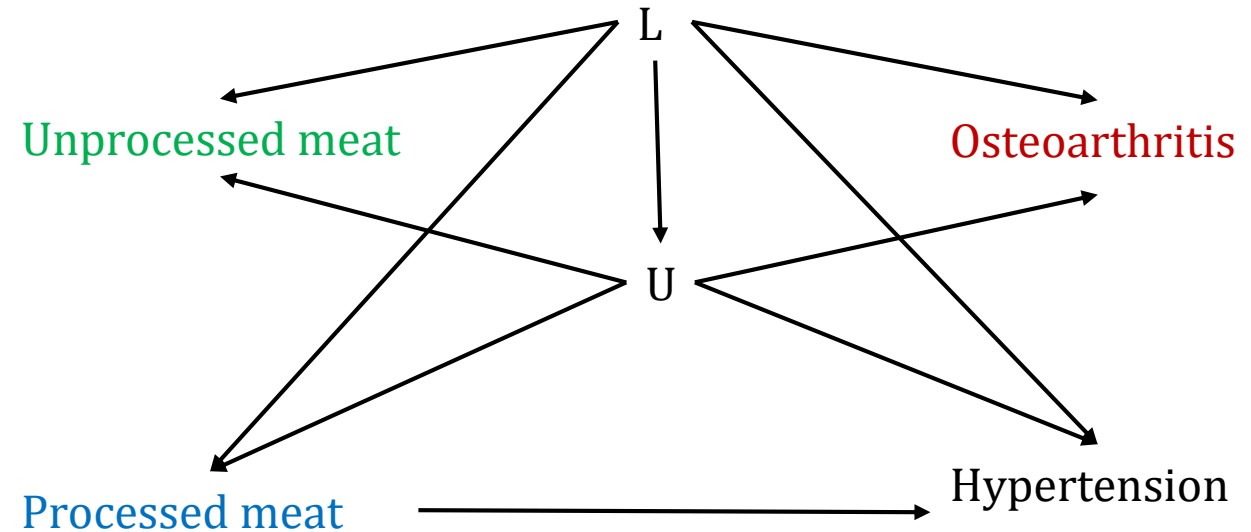Target trial emulation

Separable effects

Double negative controls

Double negative controls

Method to identify debiadsed Average Causal Effect under

- i.i.d

- Unprocessed meat must not be directly related to hypertension given C and U

$$\beta_a = \log\left(\frac{\Pr(Y^{a=1} = 1|W,U) \,/\, \Pr(Y^{a=1} = 0|W,U)}{\Pr(Y^{a=0} = 1|W,U) \,/\, \Pr(Y^{a=0} = 0|W,U)}\right)$$

Estimation: Y ~ A+logit(Pr(W=1|A,Z,Y=1))+W

Zivich et al. 2023 10.1093/aje/kwad077
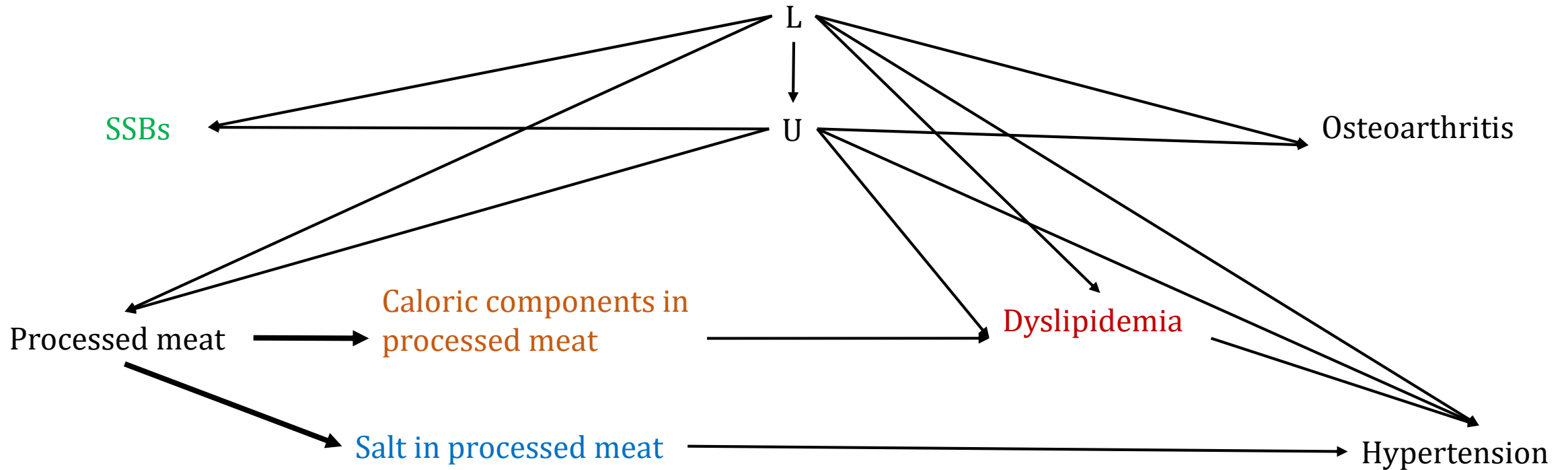Liu et al. 2024 10.48550/arXiv.2402.00335

Causal estimands for mechanistic micronutrient effect

We can use natural things happening in foods

Target trial emulation

Separable effects

Double negative controls

Proximal conditional separable effects

$$\tau^*_{CSE}(a_D) = \varphi^*(1, a_D) - \varphi^*(0, a_D), \ \varphi^*(a_Y, a_D) = E\{Y^{(a_Y, a_D)} | D^{(a_Y, a_D)} = 0\}$$

Next steps - Results

Allow for U (Yes: use DNC)	Estimand	
	Estimate - Typicial OLS estimator (95% CI)	Estimate - Conditional separable direct effect (95% CI)
Yes		
No		

Conlcusion

- Identification of micronutrient mechanistic effects from observational data is possible.

- Point interventions

- We do still make assumptions.

- «Choose your adventure» depending on the micronutrient and health outcome of interest.

Thanks!

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