Comparing food substitution models in nutritional epidemiology: An application for processed red meat and hypertension

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Outline of presentation

1) Review models in nutritional epi and how they **extend to specified substitutions models**

2) Obtain estimates from common methods using **substituting processed meat for fatty fish or vegetables** on hypertension as example

3) Discuss the **assumptions**, and **applicability** of each method

Relevant public health questions

Nutritional epidemiology exists to help people make better choices regarding diet

Does high processed meat consumption cause hypertension?
Eat what instead ?

Can ask this question using **food substitution models**

Ibsen DB, et al. Food substitution models for nutritional epidemiology. Am J Clin Nutr. 2021

Model choice in nutritional epidemiology

Common situation (**standard model**) - adjust on total energy intake, typically as a proxy for confounding & to reduce measurement error

Alternatively (**energy partition model**) - mutually adjust on all energy providing components, confounding adjustment due to the compositional nature of the data

Q : models estimands are different, does that affect substitution ?

Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. Am J Clin Nutr. 1997
Georgia D Tomova *et al*, Adjustment for energy intake in nutritional research: a causal inference perspective, Am J Clin Nutr, 2022

	Standard model	Energy partition model
Equation form of model	**f(y) = a1A + a2B + a3(A + B + C)** * C represents other foods in the diet, not explicitly adjusted on	**f(y) = c1A + c2B + c3C** * All energy components mutually adjusted
Interpretation of exposure coefficient	For some increase of PM there is some % change in HTA risk Total energy, and foods B constant. Energy substitution of food C **Non-energy components of food**	For some increase in carbohydrates, some % change in disease risk Energy from other foods B & C constant” **Absolute intake**

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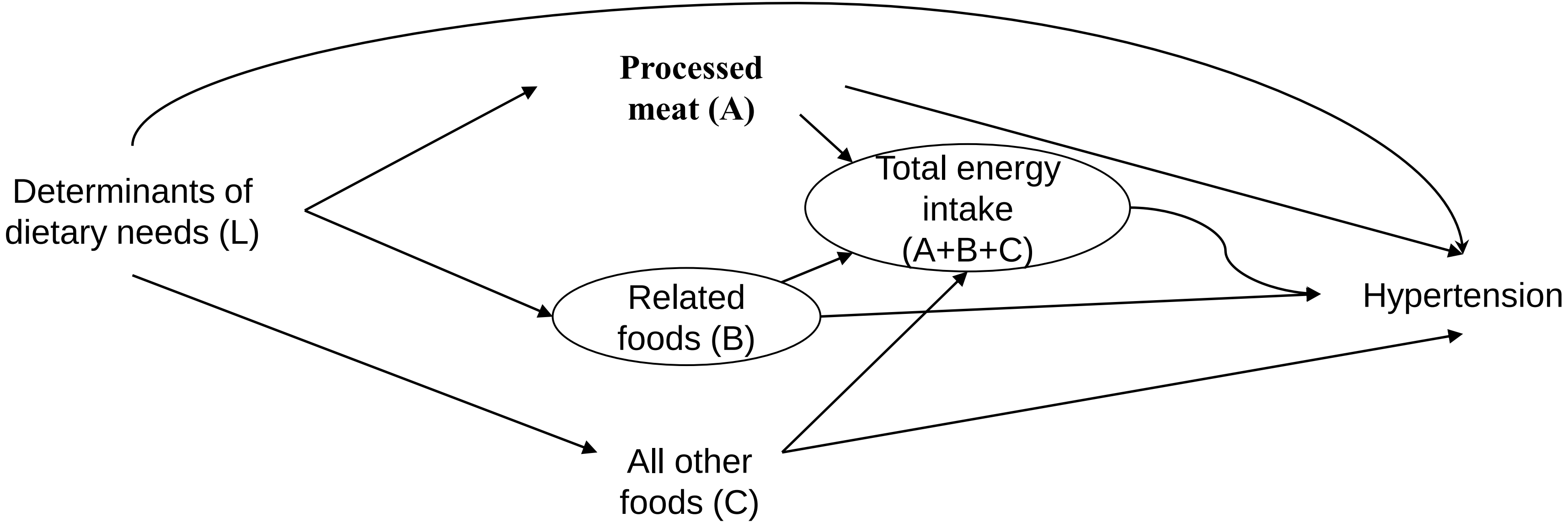
Simple DAG 1 – Standard model

Standard model

Log(f(y)) = a1A + a2B + a3(A + B + C) + a4L

Interpretation of a1: For some increase in PM energy there is some change in HTA risk, total energy, and foods B constant. Energy substitution of food C

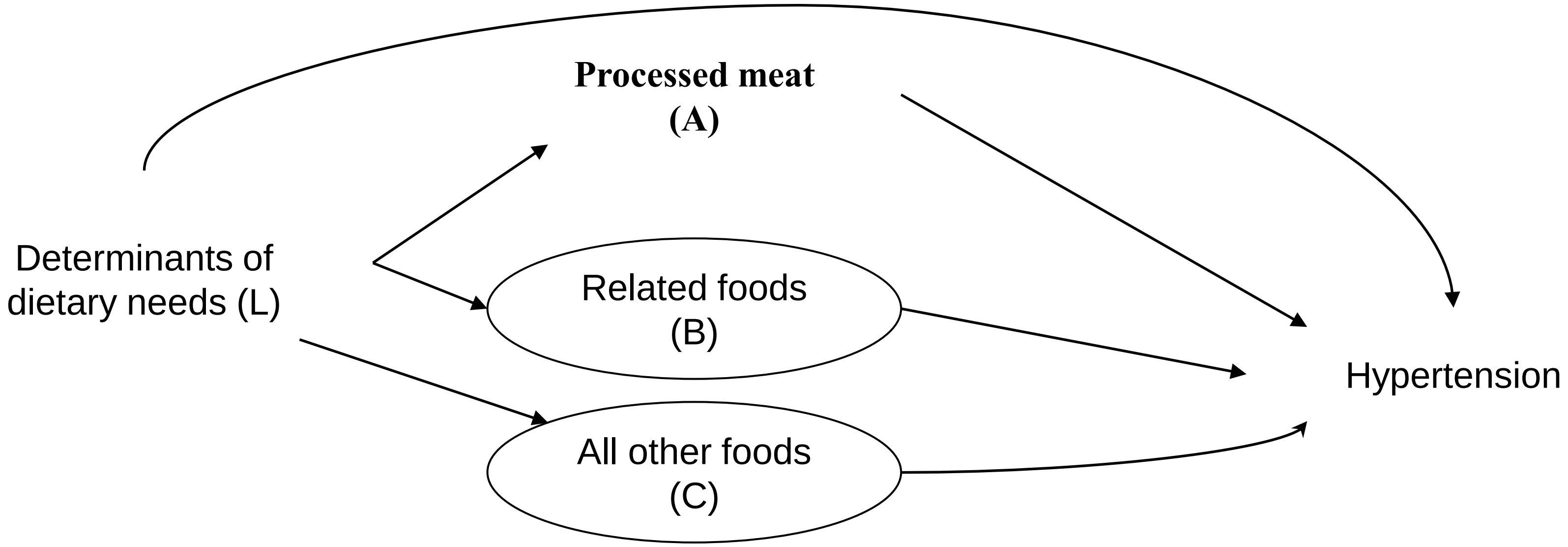


Simple DAG 2 - Energy partition model

Energy partition model

f(y) = c1A + c2B + c3C + c4L

Interpretation of c1 : For some increase of processed meat, some change in risk of hypertension keeping energy from other foods B & C constant



Substitutions

	Standard model	Energy partition model
Equation form of model	**f(y) = a1A + a2B + a3(A + B + C)** * C represents other foods in the diet, not explicitly adjusted on	**f(y) = c1A + c2B + c3C** * All energy components mutually adjusted
Interpretation of exposure coefficient	**Non-energy** components of food	**Absolute** intake
Substitution of A for B	**exp(a2 - a1)**	**exp(c2 - c1)**

Are the estimates the same in real data and is the interpretation the same?

Song, M., Giovannucci, E. Substitution analysis in nutritional epidemiology: proceed with caution. *Eur J Epidemiol* **33,** 137–140 (2018).

Methods – Estimating food substitutions in the E3N cohort

Estimate relative association between processed meat & fish/veg on hypertension

Data from the E3N cohort study - longitudinal cohort study with self reported dietary data, drug validated hypertension diagnosis, 20 years of followup, 100k participants

Included women who responded to 208 item diet history questionnaire in 1993, no prevalent CVD or HTA, and report meat or fish consumption (n = 45,771)

Food substitutions modelled using standard & energy partition models, standard model mutually adjusted on fish & vegetable intake & TE, energy partition on 26 groups of energy providing foods

Cox models adjusted on age, BMI, physical activity, alcohol, smoking, education, and menopause & confidence interval estimated via bootstrapping

Results - Table 1

Characteristics at baseline * Mean (sd) ’ median (IQR)	Lowest 20 % of processed meat intake	Highest 20 % of processed meat intake
Age, years*	53.0 (6.6)	51.1 (5.9)
BMI, kg / m2*	22.0 (2.7)	23.0 (3.1)
Physical activity, MET-h / week*	62.1 (37.6)	53.9 (29.8)
Smoker (%)	13.4	16.7
Total calories, kcal/day’	1,825 (1,529 : 2,154)	2,395 (2,040 : 2,792)
Intake of fatty fish, g/day’	6 (2 : 11)	6 (3 : 10)
Intake of vegetables, g/day’	181 (114 : 260)	171 (114 : 235)
Alcohol intake units/day’	2.7 (0.3 : 7.9)	7.0 (2.1 : 15.0)

Results - Substitutions

- 12,327 cases of hypertension identified during followup
- Standard and energy partition models provided same estimate

	Standard model	Energy partition model
Processed meat for fatty fish (100 kcal)	0.95 [0.93: 0.97]	0.94 [0.91: 0.98]
Processed meat for vegetables (100 kcal)	0.98 [0.97: 0.99]	0.98 [0.97: 0.99]

Are the substitutions the same ?

	Standard model	Energy partition model
Estimate of substituting PM with fatty fish	0.95 [0.93: 0.97]	0.94 [0.91: 0.98]
Individual coefficient interpretation	**Non-energy compoent** of food, compared to average background diet	**Absolute increase**
Substitution of A for B interpretation	Difference in **non-energy** components	Difference in **energy** and **non-energy** components
Assumption for isocaloric substitution	**Residual substitutions** for both foods should be the same	Effect of **calories** should be the same

Discussion - Practical issues

Both models require **specified substitutions**

Food advice in servings may be more useful for patients, **units of energy may be hard to interpret**

Approaches are based on a **comparison of regression coefficients** for the whole population, **no actual substitutions** take place

Grouping of total energy intake is more complicated for foods when using energy partition model

Limitations of this work

DAGs used are **simplistic**, but were reversed engineered from published work

Other approaches are possible, not considered in this work (e.g. nutrient density or residual model)

Assume **no unmeasured confounding**, confounding factors for different food pairs **may not overlap**

Did not consider **measurement error**, a major reason to adjust on total energy

Conclusion

No major differences when comparing relative effects of food pairs from two common approaches

Model coefficients explicitly estimate different things, but **substitutions are the same under certain assumptions**

Measurement error & **confounding** are still important considerations

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