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Substitution of unprocessed and processed red meat with poultry or fish and total and cause-specific mortality

Tine Bjerg Nielsen[1]*, Anne Mette Lund Würtz[1], Anne Tjønneland[2,3], Kim Overvad[1,4] and Christina Catherine Dahm[1]

[1]*Department of Public Health, Aarhus University, DK-8000 Aarhus C, Aarhus, Denmark*
[2]*Danish Cancer Society Research Center, DK-2100 Copenhagen Ø, Copenhagen, Denmark*
[3]*Department of Public Health, University of Copenhagen, DK-1014 Copenhagen K, Copenhagen, Denmark*
[4]*Department of Cardiology, Aalborg University Hospital, DK-9000 Aalborg, Aalborg, Denmark*

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Abstract

Recent studies found positive associations between intake of red meat and processed meat and total mortality; however, substitution of red meat with poultry and fish has been poorly investigated. We aimed to investigate associations for substitutions of red meat (unprocessed/processed) and total mortality and deaths due to cancer or CVD. We used data from the Danish Diet, Cancer and Health cohort, including 57 053 participants aged 50–64 years at baseline. Information on diet was collected through a validated 192-item FFQ. Information regarding total mortality, deaths due to cancer and deaths due to CVD was obtained by record linkage. Cox proportional hazards models were used to estimate the hazard ratio (HR) of 150 g/week substitutions of red meat with poultry or fish. During a follow-up (mean 16·1 years), 8840 deaths occurred (4567 were due to cancer; 1816 due to CVD). The adjusted HR for total death when substituting 150 g/week total red meat with poultry was 0·96 (95 % CI 0·95, 1·00) and with fish 0·99 (95 % CI 0·97, 1·01). Corresponding HR for cancer death or CVD death were similar. Substitution of processed red meat with fish or poultry was more consistently associated with a lower mortality than substitution of unprocessed red meat. For example, the adjusted HR for total death when substituting 150 g/week processed red meat with poultry was 0·95 (95 % CI 0·92, 0·98). We found that replacing processed red meat with poultry or fish was associated with a lower risk of total mortality and deaths due to cancer, but not deaths due to CVD.

Key words: Substitution: Red meat: All-cause mortality: CVD death: Cancer death: Cohort study

Non-communicable diseases such as CVD, stroke and cancer caused 71 % of deaths globally in 2018, ranging from 37 % in low-income countries to 88 % in high-income countries[1]. These diseases are partly attributable to diet and lifestyle[2]. Thus, primary prevention through shifting population diets towards more healthy habits is a global priority.

An unhealthy diet including red and processed meat, as well as saturated fat from meat, is among the risk factors associated with the leading causes of death[2], and the International Agency for Research on Cancer has classified consumption of processed meat as carcinogenic to humans[3,4]. The biological mechanisms underlying the association between red and processed meat and mortality are not yet fully established, but may include added nitrite and nitrate salts in processed red meat and the natural content of haem iron in red meat[5–9].

Recent studies have explored associations between intakes of red meat, poultry and fish with all-cause mortality[10], and positive associations between processed meat intake and risk of premature mortality are consistently observed[11]. However, because dietary guidelines recommend that individuals consume more healthy foods while maintaining a stable weight, following such guidelines requires isoenergetic replacement of less healthy energy-containing foods. Few studies have directly modelled the health effects of food substitutions within habitual dietary intakes that entail following dietary recommendations to reduce red and processed meat intake[5,6,9,12]. It is likely that a lower total red meat intake would be accompanied by an increase in other meat products, which may have independent health effects. Consuming poultry in place of total red meat has been suggested to be associated with lower risk of all-cause mortality, but the associations for unprocessed red meat or for substitutions with fish are less clear, particularly in European populations[5,6,9,12]. Better understanding of the health effects of lowering total red meat, unprocessed and processed meat

Abbreviation: HR, hazard ratio.

* **Corresponding author:** Tine Bjerg Nielsen, email tine.bjerg@hotmail.com

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consumption while concomitantly increasing consumption of other meat products is necessary when updating national dietary guidelines. Therefore, we aimed to estimate the association of substitution of 150 g/week red meat with 150 g/week of poultry or fish on the outcomes total mortality and deaths due to cancer or CVD. We also investigated substitution of unprocessed and processed red meat separately, since intake of processed red meat has more consistently been associated with a higher risk of premature mortality than unprocessed red meat in studies that did not specify substitutions.

Methods

Study design and population

We used data from the Diet, Cancer and Health study. This cohort was initiated between December 1993 and May 1997, when 79 729 women and 80 996 men were invited to participate, of whom 57 053 consented (Supplementary Fig. 1). Participants were recruited from the greater Copenhagen and Aarhus areas. Inclusion criteria for participation were age between 50 and 64 years, born in Denmark and not previously registered in the Danish Cancer Registry. Informed consent was obtained from all participants included in the study. The Diet, Cancer and Health study was approved by the Danish Data Protection Agency and the regional ethical committees on human studies in Aarhus and Copenhagen. A detailed description of the Diet, Cancer and Health study has been published elsewhere[13].

Exposure assessment

All participants filled in a validated 192-item semi-quantitative FFQ before visiting one of the two study centres in Copenhagen and Aarhus. Development and description of the FFQ have been published elsewhere[14–16]. Participants were asked to report their average dietary consumption over the past 12 months, in twelve response categories ranging from 'never' to 'eight times or more per day'. The daily intake of foods was calculated for each participant by using a software programme developed for the Diet Cancer and Health study, FoodCalc, using sex-specific portion sizes[15,16]. In total, sixty-three questions covered the intake of meat, poultry and fish and dishes with meat as an ingredient. For the present study, meat was subdivided into total red meat, consisting of both unprocessed and processed red meat. Unprocessed red meat consisted of cooked and uncooked red meat, including beef, veal, pork, lamb and offal. Processed red meat consisted of all red meat that had undergone processing such as smoking, salting or curing, including sausages, salami, smoked or cooked ham, bacon and liver pate. Poultry included chicken (meat and skin) and turkey. Fish included all types of fish and shellfish, such as raw fish, cold cuts, roe, shellfish and prepared/cooked fish. The FFQ was checked for reading errors and missing information at the visit to the clinic; no missing data were accepted.

Covariates

After handing in the FFQ, all participants visited a study centre where they filled in a lifestyle questionnaire containing questions on health status, social factors and lifestyle habits. The potential confounders of the present study were chosen *a priori*, based on directed acyclic graphs created after a literature review (Supplementary Fig. 2–4). Information about educational level; time spent weekly in leisure time physical activities such as walking, jogging and gardening during summer and winter seasons; smoking habits; hypertension, diabetes and hypercholesterolaemia was retrieved from the lifestyle questionnaire. Answers to questions on whether a doctor had ever diagnosed hypertension, diabetes or high cholesterol were combined with answers to questions on medication and was used to determine the participants' history of hypertension, diabetes or hypercholesterolaemia. At the visit to the study centre, height and weight were recorded by trained health professionals. Height was measured without shoes, and weight was recorded to the nearest 100 g using a digital scale. Information on alcohol consumption, fruit and vegetable intake and total energy intake was obtained from the FFQ.

Case ascertainment

The outcome of the present study was all-cause and cause-specific mortality. Cause-specific mortality (cancer and CVD) was defined from the International Classification of Diseases 10th revision, codes C00-C97 for cancer mortality and codes I00-I99 for CVD mortality. Total mortality and deaths due to cancer or CVD were obtained by record linkage to the Danish National Patient Register and the Cause of Death Register. Study end dates were 13 July 2015 for total mortality and 30 December 2013 for cause-specific mortality.

Exclusions

Participants diagnosed with cancer but not registered in the Danish Cancer Registry before baseline (due to processing delay) were subsequently excluded, as were those with a previous CVD diagnosis (myocardial infarction or stroke). Furthermore, participants with missing information on covariates were excluded.

Statistical methods

Baseline characteristics of the participants were summarised using medians and 25th and 75th percentiles for continuous variables and proportions for categorical variables.

The participants were followed up from the date of entry into the Diet, Cancer and Health study until the date of death, emigration, loss to follow-up or the relevant outcome end date, whichever occurred first. The association between substitution of red meat with poultry or fish and death was investigated by Cox proportional hazards models, in which hazard ratios (HR) and corresponding 95 % CI were calculated. The participant's age was included as the underlying timescale. The observation time was calculated as the time between study entry and end of follow-up for each participant. The analysis was carried out for total mortality, deaths due to cancer and deaths due to CVD.

Intakes of 150 g/week, reflecting a usual serving size of meat or fish in Denmark, were investigated for each meat item. To construct substitution models, a sum-variable including each participant's total intake in servings of processed and unprocessed red meat, poultry and fish was entered into the Cox regression model in addition to each of these food groups separately, except for the food group to be replaced. For example, to investigate substitution of total red meat with poultry or fish, we held the total intake of unprocessed and processed red meat, poultry and fish constant using the sum-variable and added the specific variables for poultry and fish into the Cox regression model leaving out the specific variable for total red meat. The calculated HR may be interpreted as the HR for substitution of the omitted variable. The calculated HR in this example reflect substitution of 150 g/week total red meat with 150 g/week of poultry or fish. This method has been described previously[17,18].

All analyses were stratified by date of enrolment (quartiles) to allow for differences in the baseline hazards and adjusted for total energy (continuous, kJ/week) and age (model 1). In model 1a, the following risk factors were additionally included: sex and tertiary educational level (categorical: none, short, medium or long) as a measure of socio-economic status, BMI (categorical: <18·5 kg/m^2, 18·5–25 kg/m^2, <25–30 kg/m^2, >30 kg/m^2), alcohol consumption (abstainer, ≤0·5 units, >0·5–1 units, >1–2 units, >2–4 units, ≥5 units), physical activity (<30 min/d, ≥30 min/d) and smoking (never, former, current < 15 g tobacco/d, current 15–25 g tobacco/d, current > 25 g tobacco/d). In model 2, potential intermediary lifestyle diseases were additionally included: hypertension (yes, no, do not know), hypercholesterolaemia (yes, no, do not know) and diabetes (yes, no, do not know). Model 3 included, besides the risk factors in model 1a, fruit intake (continuous, g/week) and vegetable intake (continuous, g/week).

To investigate possible effect modification, we stratified models of substitution analyses by sex or BMI (categorised, <18·5 kg/m^2, 18·5–25 kg/m^2, <25–30 kg/m^2, >30 kg/m^2).

The proportional hazards assumption was investigated using Schoenfelds Residuals Test and diagnostic plots. No deviation from proportionality was detected. All analyses were performed using Stata 15.0 (StataCorp LLC).

Results

After excluding participants with cancer (*n* 569) or CVD (*n* 1443) before baseline, missing lifestyle questionnaires (*n* 42) and missing data for covariates (*n* 770), 54 229 participants were available for the analyses. During a mean follow-up time of 16·1 years, 8840 deaths occurred. Among cause-specific deaths, 4567 were due to cancer and 1816 due to CVD.

Table 1 presents baseline characteristics of the entire cohort and the participants who died during follow-up. Those who died during follow-up had a higher intake of red meat (unprocessed and processed) and a lower intake of poultry and fish than the cohort as a whole. Furthermore, they were more likely to be men, older, overweight or obese, more physically active, and current smokers and have a higher alcohol consumption, and lower consumption of fruit and vegetables than the cohort as a whole. They were also more likely to have a history of hypertension, hypercholesterolaemia and diabetes.

Table 2 shows the associations for substitution of total red meat, unprocessed red meat or processed red meat with poultry or fish. In the adjusted model (model 1a), substitution of 150 g/week total red meat with 150 g/week poultry or fish was associated with a lower total mortality (HR 0·97 (95 % CI 0·94, 1·00), HR 0·98 (95 % CI 0·96, 1·00). After additional adjustment for fruit and vegetables intakes, the associations were slightly weaker (model 3). The association with total mortality was only statistically significant for substitution of processed red meat with poultry (HR 0·95 (95 % CI 0·92, 0·98)) or fish (HR 0·96 (95 % CI 0·94, 0·98)). The association with death due to cancer when substituting red meat with poultry or fish showed a lower risk, but was only statistically significant for substitution of processed red meat with poultry (HR 0·93 (95 % CI 0·90, 0·97)) or fish (HR 0·93 (95 % CI 0·90, 0·96)). For deaths due to CVD, we found no associations for the investigated substitutions. For example, when substituting 150 g/week total red meat with poultry, it showed a HR 1·03 (95 % CI 0·98, 1·09) and with fish, it showed a HR 1·00 (95 % CI 0·96, 1·04). The pattern of associations was similar after additional adjustment for hypertension, hypercholesterolaemia and diabetes (model 2).

Results of analyses stratified by sex, and by BMI group, were similar to the main results (data not shown).

Discussion

In this follow-up study, we found an inverse association with total mortality when replacing total red meat and processed red meat with poultry or fish. Statistically significant inverse associations for processed red meat were only found for replacement with poultry or fish for total mortality and death due to cancer. However, inverse associations were found when replacing total red meat with poultry or fish for both total mortality and death due to cancer. The patterns of associations did not differ by sex or BMI.

Our study has some limitations and some strengths. Due to the very low proportion of participants lost to follow-up, it is unlikely that selection bias has influenced our results. Information about habitual diet was obtained from a self-administered FFQ, the data from which are likely to be affected by random as well as systematic measurement error. Random error is likely to bias our estimates towards the null. Systematic errors, such as underreporting of red meat intake according to sex, could also bias our results towards the null. However, at the time of dietary intake assessment, the major focus for healthy diets was lowering saturated fat intake and meat as such was considered neither particularly healthy nor unhealthy in the Danish population. The Danish dietary guidelines from 1994 recommend choosing low-fat meat products and eating fish often. Thus, in our study, while differential misreporting of foods containing saturated fat is possible due to social desirability bias, it is unlikely that this would influence self-report of total meat intake. We modelled substitutions of red meat, fish and poultry with and without adjustment for fruit and vegetables. When adjusting for other dietary components in model 3, we emulate the pure association between choosing fish or poultry instead of red meat. However, it is possible that dishes including fish or poultry differ in vegetable content compared with red meat dishes, and thus it may be that a greater overall health benefit could be achieved by

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Table 1. Baseline characteristics for the entire diet, cancer and health cohort, and those participants who died during follow-up
(Numbers and percentages; mean values and standard deviations; median and 25th and 75th percentiles)

	Cohort		Total mortality		Deaths due to cancer		Deaths due to CVD	
	%	*n*	%	*n*	%	*n*	%	*n*
Total *n*	54 229		8840		4567		1816	
Women	53	28 684	41	3716	37	1772	31	593
Age baseline								
Mean	56		58		58		59	
SD	4		4		4		4	
Meat consumption								
Total red meat (g/week)								
Median	742		819		843		858	
25p; 75p	531; 1020		585; 1114		604; 1144		622; 1151	
Unprocessed red meat (g/week)								
Median	548		586		597		605	
25p; 75p	395; 749		419; 804		427; 820		438; 834	
Processed red meat (g/week)								
Median	172		204		212		216	
25p; 75p	99; 279		119; 326		123; 344		129; 343	
Poultry (g/week)								
Median	125		117		117		122	
25p; 75p	72; 193		64; 185		63; 185		67; 189	
Fish (g/week)								
Median	267		273		276		280	
25p; 75p	178; 386		179; 407		178; 416		183; 427	
Energy (kJ/d)								
Median	8895		9030		9123		9275	
25p; 75p	7343; 10 678		7366; 10 925		7400; 11 088		7572; 110 190	
Smoke								
Never	35	19 346	20	1780	19	850	18	335
Former	29	15 460	24	2134	25	1125	25	447
Current < 15 g/d	13	7050	15	1320	16	730	16	287
Current 15–25 g/d	16	8691	27	2377	27	1225	17	495
Current > 25 g/d	7	3682	14	1229	14	637	14	252
Alcohol (units/d)								
Abstainer	2	1237	4	382	5	231	4	79
≤0·5	23	12 441	22	1988	22	1011	22	395
>0·5–1	21	11 610	17	1477	16	730	16	289
>1–2	24	12 908	20	1801	20	895	22	407
>2–4	20	10 766	19	1716	19	856	21	374
≥5	10	5267	17	1476	18	844	15	272
BMI (kg/m^2)								
>18·5	1	421	2	145	2	87	1	20
18·5–25	43	23 509	39	3471	37	1671	31	566
<25–30	4214	22 529	41	3603	41	1876	44	804
<30		7770	18	1621	20	933	24	426
Physical activity (min/d)								
<30	60	32 733	67	5888	68	3097	68	1241
≥30	40	21 496	33	2952	32	1470	32	575
Tertiary educational level								
None	15	7985	20	1738	20	916	20	358
Short	23	12 480	23	2077	22	1036	20	369
Medium	40	21 726	36	3196	37	1675	39	698
Long	22	12 038	21	1829	21	940	21	391
Hypertension								
Yes	16	8467	21	1814	25	1238	31	556
No	71	38 639	65	5788	60	2771	54	986
Do not know	13	7123	14	1238	14	654	15	274
Diabetes								
Yes	2	1057	4	394	7	299	6	104
No	93	50 702	90	7933	87	3995	88	1602
Do not know	5	2470	6	513	6	273	6	110
Hypercholesterolaemia								
Yes	7	3655	8	722	9	432	12	213
No	51	27 451	49	4328	48	2204	46	840
Do not know	43	23 123	43	3790	42	1931	42	763
Fruit (g/week)								
Median	1006		885		879		898	
25p; 75p	521; 1680		385; 1509		372; 1521		389; 1537	

Table 1. (*Continued*)

	Cohort		Total mortality		Deaths due to cancer		Deaths due to CVD	
	%	*n*	%	*n*	%	*n*	%	*n*
Vegetables (g/week) median (25p 75p)								
Median	2146		2077		2097		2076	
25p; 75p	1611; 2780		1501; 2753		1492; 2753		1511; 2742	

Table 2. Substitution of total red meat, unprocessed red meat and processed red meat with poultry or fish and risk of death, per 150 g/week (Hazard ratios (HR) and 95 % confidence intervals)

	Model 1*		Model 1A†		Model 2‡		Model 3§	
Substitutions of 150 g/week meat	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI
Total mortality (*n* 9482)								
Poultry for total red meat	0·88	0·86, 0·90	0·97	0·94, 1·00	0·96	0·93, 0·98	0·96	0·95, 1·00
Fish for total red meat	0·91	0·90, 0·93	0·98	0·96, 1·00	0·98	0·96, 1·00	0·99	0·97, 1·01
Poultry for unprocessed red meat	0·91	0·89, 0·94	0·99	0·96, 1·01	0·98	0·95, 1·00	0·99	0·96, 1·02
Fish for unprocessed red meat	0·95	0·93, 0·97	1·00	0·98, 1·02	1·00	0·97, 1·02	1·00	0·98, 1·02
Poultry for processed red meat	0·84	0·81, 0·86	0·94	0·91, 0·97	0·93	0·90, 0·96	0·95	0·92, 0·98
Fish for processed red meat	0·87	0·85, 0·89	0·95	0·93, 0·98	0·95	0·93, 0·97	0·96	0·94, 0·98
Deaths due to cancer (*n* 5062)								
Poultry for total red meat	0·88	0·85, 0·91	0·97	0·94, 1·00	0·95	0·92, 0·98	0·98	0·94, 1·01
Fish for total red meat	0·90	0·87, 0·92	0·97	0·95, 1·00	0·96	0·94, 0·99	0·97	0·95, 1·00
Poultry for unprocessed red meat	0·92	0·89, 0·96	1·00	0·96, 1·04	0·97	0·94, 1·01	1·00	0·97, 1·04
Fish for unprocessed red meat	0·94	0·91, 0·97	1·00	0·97, 1·03	0·99	0·96, 1·02	1·00	0·97, 1·02
Poultry for processed red meat	0·83	0·80, 0·86	0·93	0·90, 0·97	0·91	0·88, 0·95	0·94	0·90, 0·98
Fish for processed red meat	0·85	0·82, 0·87	0·93	0·90, 0·96	0·92	0·90, 0·95	0·94	0·91, 0·97
Deaths due to CVD (*n* 2145)								
Poultry for total red meat	0·93	0·88, 0·98	1·03	0·98, 1·09	1·01	0·95, 1·06	1·04	0·99, 1·10
Fish for total red meat	0·90	0·87, 0·94	1·00	0·96, 1·04	0·99	0·95, 1·03	1·01	0·96, 1·05
Poultry for unprocessed red meat	0·97	0·92, 1·03	1·06	1·00, 1·12	1·03	0·98, 1·09	1·06	1·01, 1·13
Fish for unprocessed red meat	0·95	0·90, 0·99	1·03	0·98, 1·08	1·02	0·97, 1·07	1·03	1·00, 1·08
Poultry for processed red meat	0·87	0·83, 0·93	0·99	0·93, 1·05	0·96	0·90, 1·02	1·00	0·94, 1·06
Fish for processed red meat	0·85	0·81, 0·89	0·96	0·91, 1·00	0·95	0·90, 1·00	0·97	0·92, 1·02

* Adjusted for age, total energy and date of enrolment.
† Further adjusted for sex, educational level, BMI, alcohol consumption, physical activity and smoking.
‡ Further adjusted for hypertension, hypercholesteraemia and diabetes.
§ Adjusted for sex, educational level, BMI, alcohol consumption, physical activity, smoking (model 1a) and for fruit consumption and vegetable consumption.

shifting dietary patterns from red meat dishes to fish- or poultry-based dishes. We therefore also presented the results in model 1a. We used directed acyclic graphs to illustrate our assumptions about the relationships between potential confounders and to guide our choice for adjustment (Supplementary Fig. 2–4). However, residual confounding cannot be ruled out. Our models assessing all-cause mortality are not affected by competing risks. However, the analyses of cause-specific death should be interpreted as the instantaneous risk of the particular cause of death, given survival from all other causes of death.

We compared participants who had an identical total energy intake and an identical total intake of red meat, poultry and fish, but for whom the intake of each of the three meat types differed. Controlling for the total amount of red meat, poultry and fish and at the same time including two of the three meat types in the statistical models allowed us to specify the substitutions between these three meat types. The substitution method is a relatively new investigation method in studies of meat intake and health outcomes, and Pan *et al.*'s[5] study is the earliest paper that we identified to use this method in relation to mortality. When using this method, it is possible to investigate the effect of modelled substitutions of intake of specific foods, mimicking changes in dietary composition. This is likely to be more useful for public health strategies to improve health than targeting changes in total energy intake, unless physical activity or body weight is similarly changed[19]. For this reason, we chose to model substitutions of 150 g/week, corresponding to one serving size, thus facilitating the translation of our results into dietary recommendations that would be feasible in this population. The magnitudes of the associations we determined were modest, but would be consistent with a meaningful impact on preventing premature mortality in the population, upon shifting dietary habits as recommended by dietary guidelines were the effect causal.

A limitation of our study was that we investigated all deaths due to cancer and all deaths due to CVD. It is likely that diet affects risk of cancer and CVD mortality differently depending on the site of the cancer or the specific vascular disease. However, by investigating all deaths due to these causes, we reduced potential misclassification in the outcome that may arise due to errors in death certificate completion. Further, the associations for total mortality and total cancer and total CVD are of major importance from a public health point of view.

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Four previous studies have investigated the association of substitution of red meat with poultry and fish with the risk of death. Pan *et al.* found that substitution with one serving per day (85 g/day) total red meat with one serving poultry per day was associated with statistically significant lower risk for total mortality (HR 0·86 (95 % CI 0·82, 0·91)) and a statistically significant lower risk when substituting with fish (HR 0·93 (95 % CI 0·90, 0·97))[5]. These findings from a US cohort are in agreement with the findings in our study. In another US cohort, Etemadi *et al.* found that for each 20 g/1000 kcal increase in daily intake of white meat (including both unprocessed and processed white meat and fish) and same decrease in processed red meat and unprocessed red meat, the HR for all-cause mortality was 0·92 (95 % CI 0·91, 0·93), the HR for deaths due to cancer was 0·93 (95 % CI 0·92, 0·94) and 0·92 (95 % CI 0·91, 0·94) for deaths due to CVD[9]. Although the substituted amounts were different, the association for total mortality and deaths due to cancer points in the same direction as the findings in our study. Van den Brandt found that substitution of 50 g/d processed meat with 50 g/d poultry was associated with a lower risk of total mortality (HR 0·81 (95 % CI 0·63, 1·05)), a lower risk of deaths due to cancer (HR 0·81 (95 % CI 0·61, 1·07)) and a lower risk of deaths due to CVD (HR 0·76 (95 % CI 0·56, 1·05)) in a Dutch cohort, albeit with statistical uncertainty[6]. In contrast, our results indicate that substitution of processed meat for poultry is primarily associated with total mortality and death due to cancer. Finally, in a Middle Eastern cohort, Farvid *et al.* found that substituting one serving/d of fish for one serving/d of total red meat was associated with a lower risk of all-cause mortality (HR 0·63 (95 % CI 0·47, 0·84))[12], but the mean consumption of total red meat in the Iranian study population was only 0·19 serving/d. The finding in Farvid *et al.* is in agreement with our findings, taken the cultural context and substitution amount in consideration.

Multiple mechanisms might explain the observed findings. Red meat is a source of saturated fat and haem Fe, and processed red meat additionally typically contains nitrate, nitrite and Na salts. In the gastrointestinal tract, nitrite reacts with amines to form nitrosamines, which are carcinogenic to humans[3]. The formation of these redox active compounds is promoted by haem Fe[3]. Haem iron and nitrite are also pro-oxidants that can promote oxidative damage and inflammation in vital organs and can lead to arteriosclerosis[8,20]. Furthermore, replacement of saturated fat with PUFA has showed significant advantages in CVD development, and sodium consumption contributes to hypertension, which is a major risk factor for CVD and CVD death[21–24]. Poultry and fish are generally not preserved using nitrite-based salts and are often lower-fat alternatives to red meat. Fatty fish contains *n*-3 PUFA, which are beneficial to cardiometabolic health and might have a beneficial effect in cancer prevention and treatment[23,25,26]. Substitution of red and processed meat with these alternatives may thus have a protective effect on incidence of diseases and thus premature death due to cancer or CVD.

In conclusion, replacing total red meat or processed red meat with poultry or fish was associated with a lower risk of total mortality and deaths due to cancer. The strength of the associations was modest, but our findings may have an important impact in the prevention of premature mortality, if entire populations shifted their dietary habits.

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The authors' contributions are as follows: T. B. N., C. C. D., A. M. L. W., A. T. and K. O. contributed to the study design; A. T. and K. O. collected the data; T. B. N. performed the statistical analyses under guidance of C. C. D. and A. M. L. W.; T. B. N. wrote the first manuscript draft. All authors were involved in the interpretation of the data and critical revision of the manuscript; T. B. N. had primary responsibility for the final content. All the authors read and approved the final version of the manuscript.

The authors declares that there is no conflict of interest.

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114521001252

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