



Original Article

Meat intake and cancer risk: prospective analyses in UK Biobank

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Abstract

Background: Red and processed meat have been consistently associated with colorectal cancer risk, but evidence for other cancer sites and for poultry intake is limited. We therefore examined associations between total, red and processed meat and poultry intake and incidence for 20 common cancers.

Methods: We analyzed data from 474 996 participants (54% women) in UK Biobank. Participants were aged 37–73 years and cancer-free at baseline (2006–10). Multivariable-adjusted Cox proportional hazards models were used to determine associations between baseline meat intake and cancer incidence. Trends in risk across the baseline categories were calculated, assigning re-measured intakes from a subsample.

Results: During a mean follow-up of 6.9 years, 28 955 participants were diagnosed with malignant cancer. After correction for multiple testing, red and processed meat combined, and processed meat, were each positively associated with colorectal cancer risk [hazard ratio (HR) per 70 g/day higher intake of red and processed meat 1.32, 95% confidence interval 1.14–1.53; HR per 20 g/day higher intake of processed meat 1.18, 1.03–1.31] and red meat was associated with colon cancer risk (HR per 50 g/day higher intake of red meat 1.36, 1.13–1.64). Positive associations of red meat intake with colorectal and prostate cancer, processed meat intake with rectal cancer and poultry intake with cancers of the lymphatic and haematopoietic tissues did not survive multiple testing.

Conclusions: Higher intake of red and processed meat was specifically associated with a higher risk of colorectal cancer; there was little evidence that meat intake was associated with risk of other cancers.

Key words: Cancer risk, meat, red meat, processed meat, poultry, prospective cohort study

Key Messages

- In this large British prospective study, we took an outcome-wide analytic approach to systematically investigate the association between meat intake and 20 common cancer sites.
- The only robust finding was a positive association between red and processed meat and colorectal cancer, which was in line with previous evidence.
- Some other positive associations were found, but these were not robust to correction for multiple testing.

Introduction

The International Agency for Research on Cancer (IARC) Monograph's expert group has classified processed meat as Group 1, carcinogenic to humans, and red meat as Group 2A, probably carcinogenic to humans, based on their associations with colorectal cancer, with equivalent classifications from the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR).^{1,2} To date, evidence for associations between red and processed meat intake and risk for cancers at sites other than the colorectum remains uncertain, and no conclusions on poultry intake and cancer risk were reached.²

Although meta-analyses by the WCRF suggested links between processed and/or red meat intake and other cancer sites such as oesophageal, stomach, pancreatic, lung and breast cancer, the pooled estimates were highly influenced by findings from single studies, and some showed evidence for high heterogeneity (breast, lung cancer).^{3–7} Furthermore, most studies on meat and cancer showed differences in exposure definitions (such as what constitutes processed meat), in dietary measurement, and in the handling of confounders and cohort specifics such as length of follow-up or sample size.² Hence, there is a gap in knowledge regarding whether there is an association of meat intake with risk for other cancer sites, or whether the association with colorectal cancer is specific. A specific effect on colorectal cancer is plausible because most proposed carcinogenic mechanisms (haem iron, polycyclic aromatic hydrocarbons, heterocyclic amines and N-nitroso-compounds) primarily apply to local effects in the digestive tract, and where pathways have been suggested to explain associations with other cancer sites the evidence for these is often restricted to animal models.⁸ For instance, in rodents the heterocyclic amine 2-amino-3-methylimidazo[4,5-*b*]pyridine (PhIP) has been shown to have oestrogenic activity that could explain an increase of breast cancer risk,⁹ but previous epidemiological research in humans did not support this hypothesis.^{10–12}

By investigating the association between meat intake and multiple cancer sites in a comprehensive analysis in the same cohort using an outcome-wide analytic approach,

definitions and analyses can be standardized, bias in outcome selection based on the results can be eliminated and the specificity of the association with colorectal cancer can be investigated.^{13–16} Thus, the aim of this study was to investigate the associations between intakes of total, red and processed meat (both separately and combined) and poultry and cancer across the 20 common cancer sites.

Methods

Study population, exposure and outcome assessment

Between 2006 and 2010, 9.2 million individuals registered with the National Health Service (NHS) in England, Wales and Scotland were invited to participate in the UK Biobank study.^{17,18} In total, 503 317 men and women aged 37–73 years consented to participate and attended the baseline assessment.¹⁹ By 5 February 2020, 502 506 participants remained in the study. For our analyses, 27 174 were excluded due to a cancer diagnosis at baseline (excluding non-melanoma skin cancer, C44), 334 participants were excluded in whom genetic sex differed from reported gender, and 2 due to zero person-years of follow-up, resulting in a maximal study sample of 474 996 participants. The study was approved by The National Information Governance Board for Health and Social Care and the NHS North West Multicentre Research Ethics Committee (06/MRE08/65), and participants provided informed consent at baseline and to be followed up using data-linkage.

Dietary intake data were collected at recruitment using a self-report touchscreen questionnaire (<http://biobank.ctsu.ox.ac.uk/showcase/showcase/docs/TouchscreenQuestionsMainFinal.pdf>). Meat intake was based on five questions concerning processed meat (including both red and white meat) and unprocessed meat (poultry, beef, lamb/mutton and pork). Intakes of unprocessed beef, lamb/mutton and pork were combined and classified as red meat intake. To investigate additive effects, red and processed meat intakes were combined and all types were combined as total meat intake. Meat intakes were categorized into intake groups depending on distribution as

follows: total meat <3, 3 to <5, 5 to <7 and ≥ 7 times/week; red and processed meat 0 to 1, >1 to <3, 3 to <5 and ≥ 5 times/week; red meat 0 to <1, 1 to <2, 2 to <4 and ≥ 4 times/week; processed meat 0 to <1, 1 to <2 and ≥ 2 times/week; poultry 0 to <1, 1 to <2 and ≥ 2 times/week.

Mean meat intakes (g/day) in each category were derived from a subsample of 69 076 participants who had participated repeatedly (≥ 3 times, participant-specific means were averaged over repeated measurements) in the Oxford WebQ, an additional web-based 24 h-dietary-recall questionnaire, and were without a cancer diagnosis at data collection.^{20–22} These average intakes in the categories for the subsample were then assigned to the intake categories in all participants to calculate trends in risk. Further details on the method and subsample are given in [Supplementary Methods](#) and [Supplementary Table S1](#), available as [Supplementary Data](#) at *IJE* online.

Cancer sites were chosen based on the most commonly diagnosed sites in the UK.²³ Data on cancer diagnoses were provided by the Medical Research Information Service of the NHS (participants resident in England or Wales) and the Information Services Division of NHS Scotland (participants resident in Scotland).²⁴ The end-points were first incident cancer diagnosis or cancer first recorded in death certificates [all coded using the 10th revision of the World Health Organization's International Statistical Classification of Diseases (ICD-10), cases diagnosed/cases first recorded in death certificates]: oral (C00–C14, cases = 560/0), oesophagus (C15, cases = 534/3), stomach (C16, cases = 35/2), colorectum (C18–C20, cases = 3235/4) including colon (C18, cases = 2139/2) and rectum (including rectosigmoid junction; C19–C20, cases = 1118/2), liver (C22, cases = 300/5), pancreas (C25, cases = 606/3), lung in never smokers (C34, cases = 271/0), malignant melanoma (C43, cases = 1608/0), breast in women (C50, 5677/11), endometrium (C54, cases = 871/0), ovary (C56, cases = 578/3), prostate (C61, cases = 5958/6), kidney (C64–C65, cases = 728/2), bladder (C67, cases = 63/3), brain and other central nervous system (CNS) and intracranial tumors (C70–C72, C75.1–C75.3, D32–D33, D35.2–D35.4, D42–D43, D44.3–D44.5, cases = 588/16), thyroid (C73, cases = 241/0), lymphatic and haematopoietic tissues (C81–C96, cases = 2485/24) and the subgroups non-Hodgkin lymphoma (NHL) (C82–C85, cases = 1187/6), multiple myeloma (C90, cases = 435/2) and leukaemia (C91–C95, cases = 710/15).

Statistical analysis

Each cancer site of interest was treated as a different end-point for Cox proportional hazards regressions, with age

as the underlying time variable. The person-years of follow-up were calculated from baseline assessment until the first registration of malignant cancer, date of death due to cancer if not diagnosed previously, date of death, loss or end of follow-up (31 March 2016 for England and Wales, 31 October 2015 for Scotland), whichever came first. Meat intakes were included in the regression models categorically and continuously as a trend in risk expressing the hazard ratios (HR) in increments (for details see [Supplementary Methods](#), available as [Supplementary Data](#) at *IJE* online). Participants who reported 'prefer not to answer' or 'do not know' for meat intake were excluded from respective analyses (total meat 1.5%, red and processed meat 1.4%, red meat 1.3%, processed meat 0.4%, and poultry 0.3%). Covariates were chosen based on the literature and availability at baseline. Participants with missing data on covariates were included in analyses but assigned to a 'missing' category for each respective variable.

Minimally adjusted models (Model 0) were stratified by geographical region of baseline assessment centre (10 regions: London, North-West, North-East, Yorkshire and Humber, West Midlands, East Midlands, South-East, South-West, Wales, Scotland), sex, and age-group at recruitment (<45, 45 to <50, 50 to <55, 55 to <60, 60 to <65 and ≥ 65 years). Subsequently, multivariable models (Model 1) were adjusted for ethnicity (four groups where possible: White, Asian or Asian British, Black or Black British, and mixed race or other; and two groups: White, Non-White for oral, oesophagus, stomach cancer and malignant melanoma due to low numbers of cases for Non-White ethnicity), Townsend deprivation score (quintiles), educational qualifications (college or university degree/vocational qualification; national examination at ages 17–18 years; national examination at age 16 years; other qualifications were treated as missing), employment status (in paid employment, pension, not in paid employment), living with a spouse/partner (yes, no), height (sex-specific quintiles), smoking (never, former, current <15, current ≥ 5 cigarettes/day, current amount unknown), physical activity (low, moderate, high), alcohol intake (non-drinker, <1, 1 to <10, 10 to <20, ≥ 20 g/day), total fruit and vegetable intake (<3, 3 to <4, 4 to <6, ≥ 6 servings/day), estimated cereal fibre intake (sex-specific quintiles),²¹ cheese intake (<1, 1, 2–4, >4 times/week), milk added to tea, coffee and cereal as a proxy for milk consumption (none, <150, 150 to <300, ≥ 300 ml/day),²⁵ oily fish intake (none, <1, 1, ≥ 2 times/week) and non-oily fish intake (<1, 1, ≥ 2 times/week). In women, Model 1 was additionally adjusted for menopausal status (pre-, post-menopausal), parity (nulliparous, 1–2, ≥ 3), hormone-replacement therapy (never, past, current) and oral contraceptive pill use (never, past, current). Model 2 was additionally adjusted for measured

body mass index (BMI, sex-specific quintiles). Analyses for meat intake and melanoma skin cancer were additionally adjusted for skin colour (very fair, fair, light olive, dark olive, brown/black), hair colour (blonde, red, light brown, dark brown, black), skin reaction to sun exposure (get very tanned, moderately tanning, mildly/occasionally tanning, never tanning only burning), sun or UV protection use (never/rarely, sometimes, most of the time, always, do not go out in the sunshine), sunburns before age 15 (never, ever) and solarium use (never, 1–2 times/year, ≥ 3 times/year). Information on data-collection of covariates is given in the [Supplementary Methods](#), available as [Supplementary Data](#) at *IJE* online.

We conducted three sensitivity analyses: (i) to investigate reverse causality, we excluded the first 2 years of follow-up; (ii) to investigate residual confounding by smoking, we excluded current and former smokers; (iii) to investigate potential sex differences, we compared models with and without an interaction term by sex using likelihood-ratio tests, based on earlier findings of sex differences in associations between meat intake and colorectal cancer risk in this cohort.²⁵

All analyses were performed using Stata release 15.1 and Bonferroni correction was used to account for multiple testing in the main analyses (for 22 tests, $P < 0.0023$).^{26,27}

Results

During a mean follow-up of 6.9 (standard deviation 1.3) years, a total of 28 955 participants (6.1%) were newly diagnosed with any type of malignant cancer (excluding non-melanoma skin cancer, C44).

[Table 1](#) shows characteristics of all participants and those who developed a cancer during follow-up. Participants who developed cancer were older, less physically active and had a higher BMI, were more likely to be retired and have adverse health behaviours compared with participants as a whole. Participants reporting higher meat intakes were among other things more likely to be men, from more affluent areas (measured by Townsend score), to drink more alcohol, to report lower fruit, vegetable, cereal fibre, cheese and fish intake, and had a higher BMI. Intakes of different meat types were positively correlated, with a high proportion of those reporting high intakes of one type of meat also reporting high intakes of other types (see [Supplementary Table S2](#), available as [Supplementary Data](#) at *IJE* online).

[Figures 1–5](#) depict estimated HRs and 95% confidence intervals (CIs) of each individual cancer site associated with an incremental increase in meat intake for the fully adjusted models (Model 2). [Supplementary Tables S3–S7](#), available as [Supplementary Data](#) at *IJE* online, show

estimated HRs by meat intake categories and per incremental increase in intake at three or four levels of adjustment.

Total meat intake was positively associated with the risk of colorectal (HR per 100 g/day higher intake 1.29, 95%-CI 1.10–1.51) and colon (1.30, 1.07–1.58) cancer ([Figure 1](#)). Red and processed meat intake was associated with a higher risk of colorectal (HR per 70 g/day higher intake 1.32, 95%-CI 1.14–1.53) and colon (1.40, 1.17–1.68) cancer, but not rectal cancer (1.15, 0.90–1.48) ([Figure 2](#)). Red meat intake was associated with a higher risk of colorectal cancer (HR per 50 g/day higher intake 1.22, 95%-CI 1.05–1.42), colon (1.36, 1.13–1.64), but not rectal (0.99, 0.77–1.27) cancer, and also with risk of prostate cancer (1.13, 1.01–1.27) ([Figure 3](#)). Processed meat intake was positively associated with the risk of colorectal (HR per 20 g/day higher intake 1.18, 95%-CI 1.06–1.31), rectal (1.26, 1.05–1.51), but not colon (1.14, 1.00–1.29) cancer ([Figure 4](#)). There was a positive association between total, red and processed meat intake and lung cancer risk, but not after exclusion of former and current smokers ([Supplementary Tables S3–7](#), available as [Supplementary Data](#) at *IJE* online, [Figures 1–4](#)). Poultry intake was associated with a higher risk of cancers of lymphatic and haematopoietic tissues (HR per 30 g/day higher intake 1.17, 95%-CI 1.03–1.33; [Figure 5](#)). Only the associations between intake of total, red and processed meat, processed meat and colorectal cancer risk, and between intake of red and processed meat, red meat and colon cancer risk were robust when accounting for multiple testing ([Figures 1–4](#)).

Associations were largely unchanged when excluding the first 2 years of follow-up ([Supplementary Figures S1–S5](#), available as [Supplementary Data](#) at *IJE* online). In analyses restricted to never smokers, total and red meat intake were additionally positively associated with rectal cancer risk (HR per 100 g/day higher intake of total meat 1.86, 95%-CI 1.21–2.86; per 50 g/day higher intake of red meat 1.52, 1.03–2.25), red meat intake was no longer associated with prostate cancer risk (HR per 50 g/day higher red meat intake 1.13, 95%-CI 0.96–1.33), and poultry was additionally associated with ovarian cancer risk (HR per 30 g/day higher intake 1.50, 95%-CI 1.05–2.14) and no longer associated with risk of cancers of lymphatic and haematopoietic tissues (1.12, 0.94–1.35, [Supplementary Figures S1–S5](#), available as [Supplementary Data](#) at *IJE* online).

There was evidence for heterogeneity by sex for associations with colorectal, colon and rectal cancer, only ([Supplementary Table S8](#), available as [Supplementary Data](#) at *IJE* online). Whereas in men red and processed meat intake was associated with a higher risk of colorectal cancer (HR per 70 g higher intake 1.52, 95%-CI

Table 1 Baseline characteristics of included UK Biobank participants

Characteristics ^a	All participants (<i>n</i> = 474 996)	Participants who developed any malignant cancer (<i>n</i> = 28 955)
Sociodemographic		
Sex, <i>n</i> (%)		
Women	255 957 (53.9)	13 832 (47.8)
Men	219 039 (46.1)	15 123 (52.2)
Age (years)	56.3 (8.1)	60.2 (6.8)
Ethnicity, <i>n</i> (%)		
White	446 166 (93.9)	27 788 (96.0)
Asian or Asian British	11 156 (2.3)	394 (1.4)
Black or Black British	7776 (1.6)	303 (1.0)
Mixed race or other	7242 (1.5)	303 (1.0)
Unknown	2656 (0.6)	167 (0.6)
Townsend deprivation, <i>n</i> (%)		
Most affluent (mean −4.7)	95 020 (20.0)	5875 (20.3)
2 (mean −3.3)	94 817 (20.0)	5920 (20.4)
3 (mean −2.1)	94 810 (20.0)	5782 (20.0)
4 (mean −0.9)	94 876 (20.0)	5624 (19.4)
Most deprived (mean 3.8)	94 879 (20.0)	5730 (19.8)
Unknown	594 (0.1)	24 (0.1)
Qualification, <i>n</i> (%)		
College or university degree/vocational qualification	281 491 (59.3)	15 840 (54.7)
National examination at ages 17–18 years	25 814 (5.4)	1430 (4.9)
National examination at age 16 years	78 723 (16.6)	4448 (15.4)
Other/unknown	88 968 (18.7)	7237 (25.0)
Employment, <i>n</i> (%)		
In paid employment	276 119 (58.1)	12 902 (44.6)
Pension	140 137 (29.5)	12 535 (43.3)
Not in paid employment	53 268 (11.2)	3236 (11.2)
Unknown	5472 (1.2)	282 (1.0)
Living with a spouse/partner, <i>n</i> (%)		
Living with partner	343 740 (72.4)	20 955 (72.4)
Not living with partner	129 236 (27.2)	7891 (27.3)
Unknown	2020 (0.4)	109 (0.4)
Anthropometric		
Standing height (cm) in women	162.4 (6.3)	162.5 (6.3)
Standing height (cm) in men	175.6 (6.9)	175.2 (6.8)
Body mass index (kg/m ²)	27.1 (5.2)	27.8 (4.2)
Lifestyle		
Smoking, <i>n</i> (%)		
Never	259 515 (54.6)	13 508 (46.7)
Former	162 266 (34.2)	11 482 (39.7)
Current <15 cigarettes/day	14 475 (3.0)	974 (3.4)
Current ≥15 cigarettes/day	19 942 (4.2)	1737 (6.0)
Current, amount unknown	16 034 (3.4)	1061 (3.7)
Unknown	2764 (0.6)	193 (0.7)
Physical activity level, <i>n</i> (%)		
High ≥50 excess metabolic equivalents	75 477 (15.9)	4419 (15.3)
Moderate 10 to <50 excess metabolic equivalents	230 655 (48.6)	13 731 (47.4)
Low <10 excess metabolic equivalents	149 653 (31.5)	9576 (33.1)
Unknown	19 211 (4.0)	1229 (4.2)

(Continued)

Table 1 Continued

Characteristics ^a	All participants (<i>n</i> = 474 996)	Participants who developed any malignant cancer (<i>n</i> = 28 955)
Alcohol intake, <i>n</i> (%)		
Non-drinkers	53 263 (11.2)	3260 (11.3)
<1 g/day	148 397 (31.2)	8394 (29.0)
1 to <10 g/day	102 294 (21.5)	6052 (20.9)
10 to <20 g/day	129 461 (27.3)	8733 (30.2)
≥20 g/day	38 106 (8.0)	2309 (8.0)
Unknown	3475 (0.7)	207 (0.7)
Diet		
Fruit and vegetable intake (servings/day)	4.69 (2.61)	4.64 (2.49)
Estimated cereal fibre intake (g/day)	4.50 (2.94)	4.54 (2.93)
Milk added to tea/coffee/cereal, <i>n</i> (%)		
None	17 040 (3.6)	985 (3.4)
<150 ml/day	80 738 (17.0)	4475 (15.5)
150 to <300 ml/day	270 361 (56.9)	16 611 (57.4)
≥300 ml/day	102 525 (21.6)	6644 (22.9)
Unknown	4332 (0.9)	240 (0.8)
Cheese intake, <i>n</i> (%)		
<1 time/week	92 781 (19.5)	5603 (19.4)
1 time/week	99 145 (20.9)	6274 (21.7)
2–4 times/week	208 693 (43.9)	12 664 (43.7)
>4 times/week	60 962 (12.8)	3556 (12.3)
Unknown	13 415 (2.8)	858 (3.0)
Non-oily fish, <i>n</i> (%)		
<1 time/week	159 806 (33.6)	9125 (31.5)
1 time/week	234 307 (49.3)	14 854 (51.3)
≥2 times/week	77 341 (16.3)	4784 (16.5)
Unknown	3542 (0.7)	192 (0.7)
Oily fish, <i>n</i> (%)		
None	52 235 (11.0)	2815 (9.7)
<1 time/week	156 563 (33.0)	9161 (31.6)
1 time/week	177 663 (37.4)	11 227 (38.8)
≥2 times/week	84 636 (17.8)	5520 (19.1)
Unknown	3899 (0.8)	232 (0.8)
Women's health		
Menopausal status, <i>n</i> (%)		
Premenopausal	60 789 (23.7)	2005 (14.5)
Postmenopausal	180 492 (70.5)	11 259 (81.4)
Unknown	14 687 (5.7)	568 (4.1)
Parity, <i>n</i> (%)		
0 births	47 641 (18.6)	2565 (18.5)
1–2 births	145 715 (56.9)	7759 (56.1)
≥3 births	61 840 (24.2)	3470 (25.1)
Unknown	761 (0.3)	38 (0.3)
Hormone replacement therapy use, <i>n</i> (%)		
Never	158 212 (61.8)	7446 (53.8)
Past	80 647 (31.5)	5291 (38.3)
Current	15 612 (6.1)	1017 (7.4)
Unknown	1486 (0.6)	78 (0.6)
Oral contraceptive pill use, <i>n</i> (%)		
Never	47 529 (18.6)	3035 (21.9)
Past	202 245 (79.0)	10 532 (76.1)
Current	4855 (1.9)	203 (1.5)
Unknown	1328 (0.5)	62 (0.4)

^aMean (standard deviation) unless otherwise specified.

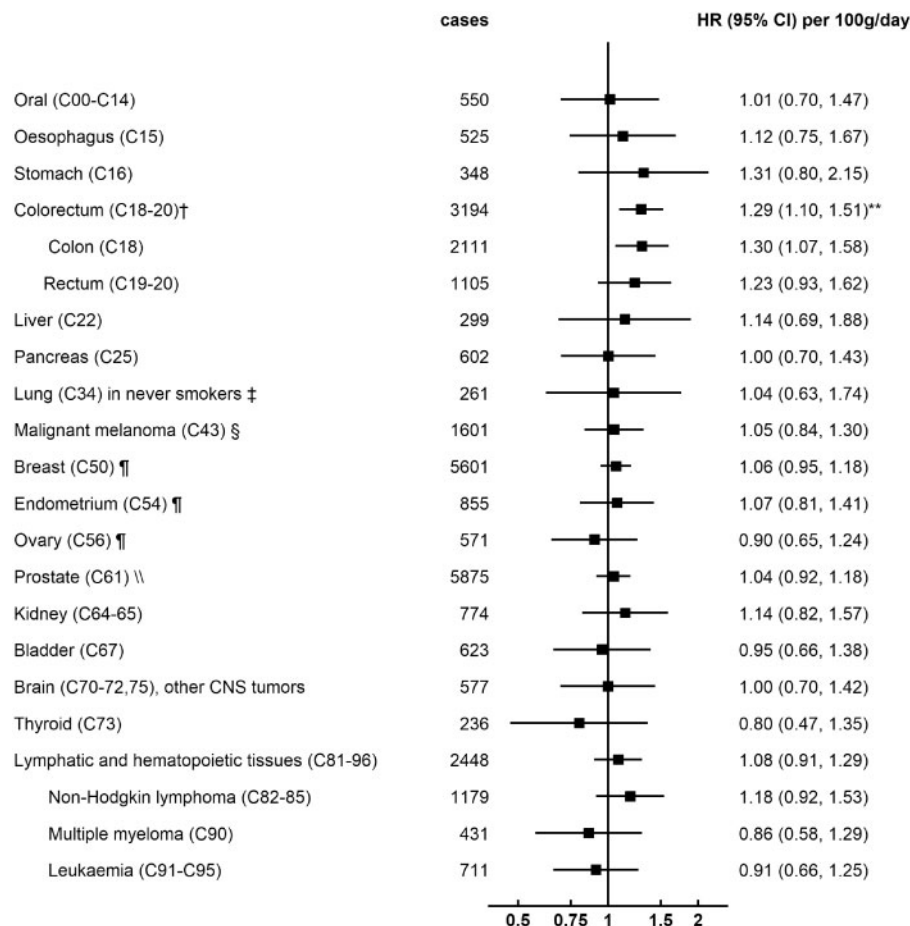


Figure 1 Associations of total meat intake and cancer risk ($n = 467\,395$). **Stratified for sex, age group, region and adjusted for age (underlying time variable), ethnicity, deprivation, qualification, employment, living with a spouse or partner, height, smoking, physical activity, alcohol intake, total fruit and vegetable intake, estimated cereal fibre intake, cheese intake, milk added to tea/coffee/cereal, oily fish intake, non-oily fish intake, BMI, and in women: menopausal status, parity, hormone replacement therapy and oral contraceptive pill use. †In 22 colorectal cancer cases colon and rectal cancer diagnoses coincided. ‡Restricted to never smokers ($n = 256\,996$). §Additionally adjusted for skin colour, hair colour, skin reaction, UV protection use, sunburns before age 15 years, solarium use. ¶Restricted to women ($n = 252\,252$). ¶Restricted to men ($n = 215\,143$). **Findings $P < 0.0023$, Bonferroni corrected.

1.23–1.88), there was no association in women (1.16, 0.95–1.43; $P_{\text{heterogeneity}} = 0.0067$). Similarly, there was no association of red and processed meat with rectal cancer in women, (in women: 0.91, 0.62–1.31; in men: 1.37, 0.98–1.91; $P_{\text{heterogeneity}} = 0.027$). The heterogeneity was less marked for associations of red and processed meat with colon cancer (in women: 1.27, 1.00–1.61; in men: 1.64, 1.24–2.16; $P_{\text{heterogeneity}} = 0.040$). There was a weak inverse association between poultry intake and rectal cancer in women and a positive association in men (HR per 30 g higher intake in women: 0.72, 95%-CI 0.52–0.98; in men: 1.27, 1.00–1.62; $P_{\text{heterogeneity}} = 0.0045$).

Discussion

In this British prospective study of 474 996 participants investigating the association between meat intake and risk for common cancer sites, red and processed meat intake

was positively and robustly associated with risk of colorectal cancer. Additional positive associations were not robust to correction for multiple testing and therefore likely due to chance.

We found that a 70 g/day higher red and processed meat intake was associated with a 32% greater risk of colorectal cancer and a 40% greater risk of colon cancer. This association was in the same direction but of somewhat greater magnitude than results from the WCRF/AICR meta-analysis (risk ratio for colorectal cancer 1.12, 95%-CI 1.04–1.21 per 100 g/day), and most more recent research, including a previous study in UK Biobank investigating associations between diet and colorectal cancer with a shorter follow-up and fewer cases.^{25,28–33} The difference in magnitude might be partly explained by the use of repeated measurements of meat intake, which likely reduces measurement error. Measurement error tends to bias associations towards the null, therefore the reduction of error

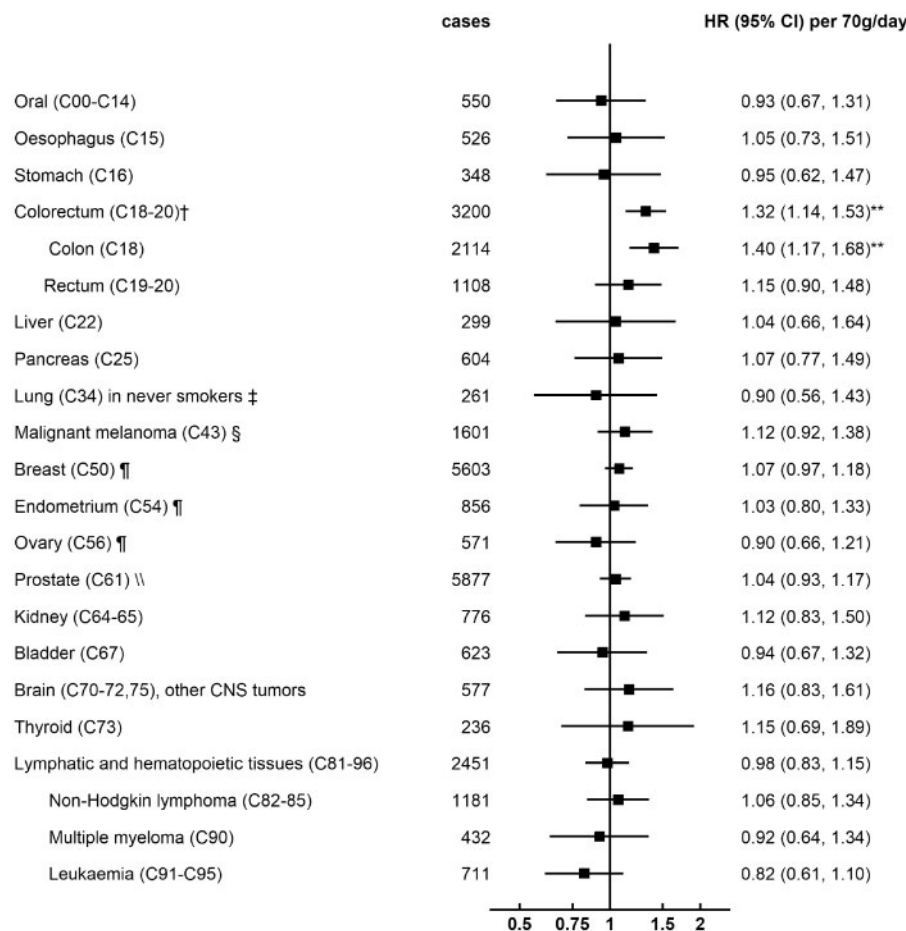


Figure 2 Associations of red and processed meat intake and cancer risk ($n = 467\,752$). **Stratified for sex, age group, region and adjusted for age (underlying time variable), ethnicity, deprivation, qualification, employment, living with a spouse or partner, height, smoking, physical activity, alcohol intake, total fruit and vegetable intake, estimated cereal fibre intake, cheese intake, milk added to tea/coffee/cereal, oily fish intake, non-oily fish intake, BMI, and in women: menopausal status, parity, hormone replacement therapy and oral contraceptive pill use. †In 22 colorectal cancer cases colon and rectal cancer diagnoses coincided. ‡Restricted to never smokers ($n = 256\,169$). §Additionally adjusted for skin colour, hair colour, skin reaction, UV protection use, sunburns before age 15 years, solarium use. ¶Restricted to women ($n = 252\,406$). ¶Restricted to men ($n = 215\,346$). **Findings $P < 0.0023$, Bonferroni corrected.

could strengthen estimates.³⁴ Otherwise, the causes of this difference in magnitude of the association are unknown.

Comparisons of the associations with colorectal cancer risk for different meat types suggested that the association between total meat intake and colorectal cancer was driven by red and processed meat. The associations with red meat intake were robust to restricting the sample to never smokers, but the association between processed meat intake and colon cancer was attenuated to the null, which might suggest residual confounding by smoking or an overall unhealthy lifestyle; one previous study of this sub-group found an association between processed red meat and distal colon cancer after exclusion of smokers at baseline, but had differences in processed meat definition and colon cancer subsite.²⁸ In the current study, associations with red and processed meat were only observed in men, although there was a suggestive similar direction for colon cancer

risk in women; there was also an inverse association between poultry intake and rectal cancer risk in women but a positive association in men. Women in UK Biobank were less likely to consume meat frequently and had a lower incidence of colorectal cancer compared with men, which might have made it more difficult to detect an association. Nevertheless, further investigation of the sex difference is warranted since the difference in risk, especially for rectal cancer, was substantial.

In our study the associations with colon cancer were slightly stronger for red meat than for processed meat, which was not observed by the WCRF/AICR.³³ This might be explained by differences in the definition and composition of processed meat between published studies, which could affect the range of carcinogenic compounds present.^{33,35} Furthermore, red meat and processed meat consumption was strongly correlated, with those reporting

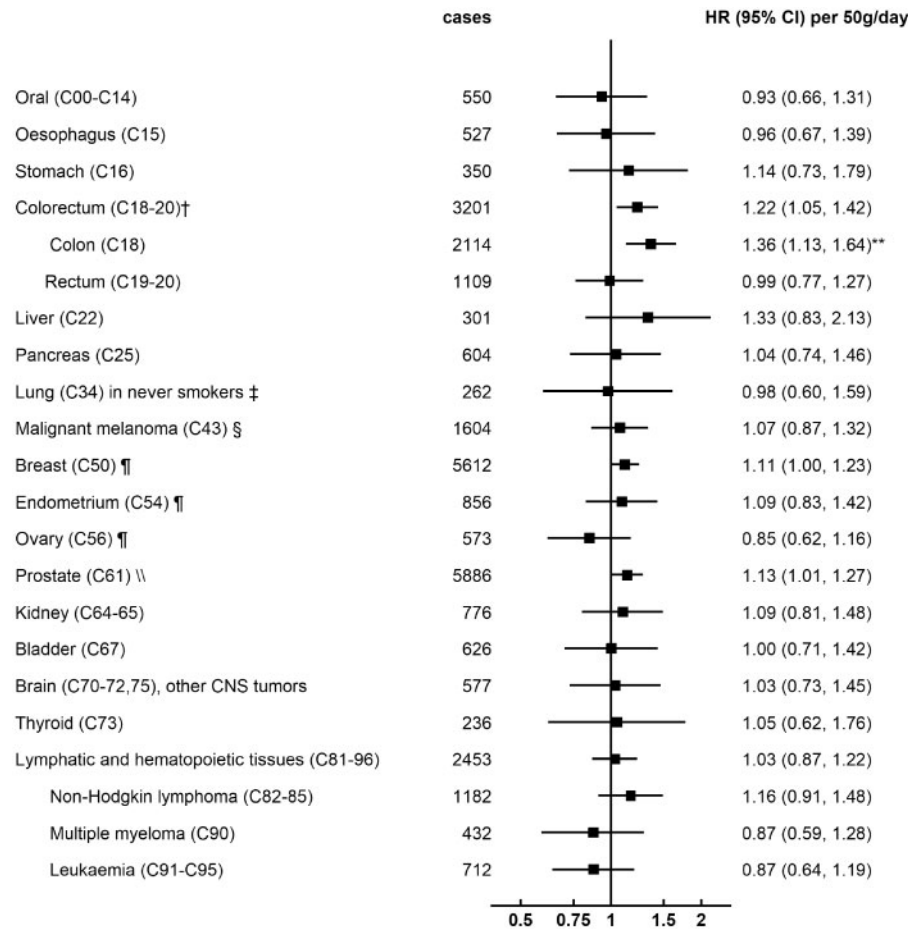


Figure 3 Associations of red meat intake and cancer risk ($n=468\,339$). **Stratified for sex, age group, region and adjusted for age (underlying time variable), ethnicity, deprivation, qualification, employment, living with a spouse or partner, height, smoking, physical activity, alcohol intake, total fruit and vegetable intake, estimated cereal fibre intake, cheese intake, milk added to tea/coffee/cereal, oily fish intake, non-oily fish intake, BMI, and in women: menopausal status, parity, hormone replacement therapy and oral contraceptive pill use. †In 22 colorectal cancer cases colon and rectal cancer diagnoses coincided. ‡Restricted to never smokers ($n=256\,532$). §Additionally adjusted for skin colour, hair colour, skin reaction, UV protection use, sunburns before age 15 years, solarium use. ¶Restricted to women ($n=252\,729$). ¶Restricted to men ($n=215\,610$). **Findings $P<0.0023$, Bonferroni corrected.

high intakes of red meat also reporting high intakes of processed meat. Therefore, it might not be possible to differentiate the relative strength of risk associations between red and processed meat. In our study processed meat was more strongly associated with rectal cancer than with colon cancer. This was not observed in most earlier studies,³³ except one recent cohort study in The Netherlands.²⁹

Several pathways have been suggested by which both red meat and processed meat could increase the risk of colorectal cancer. Haem iron in red meat can catalyze the endogenous *N*-nitrosation of amines and amides to *N*-nitroso compounds, and meat feeding studies in human volunteers and rodents suggest that these compounds generate mutations in the gastro-intestinal mucosa.^{36–40} Haem iron has furthermore been shown to lead to lipid peroxidation in intestinal epithelial cells in rodents and humans, which might induce genetic mutations.^{36,39,41} Meat processing and

cooking can additionally result in the formation of polycyclic aromatic hydrocarbons and heterocyclic amines, which may increase the risk of colorectal cancer.^{42,43} Finally, processed red meat can contain *N*-nitroso compounds as a result of the addition of sodium nitrite or nitrates for preservation.^{43–45}

We also found that red meat intake was positively associated with prostate cancer risk, and poultry intake with the risk for cancers of the lymphatic and haematopoietic tissues; however, these associations were not robust to correction for multiple testing, supporting the specificity of the association with colorectal and colon cancer. The association with prostate cancer risk is consistent with some but not all previous research; the WCRF/AICR meta-analysis and more recent studies found no association between red meat intake and prostate cancer risk, whereas the IARC review noted a possible positive

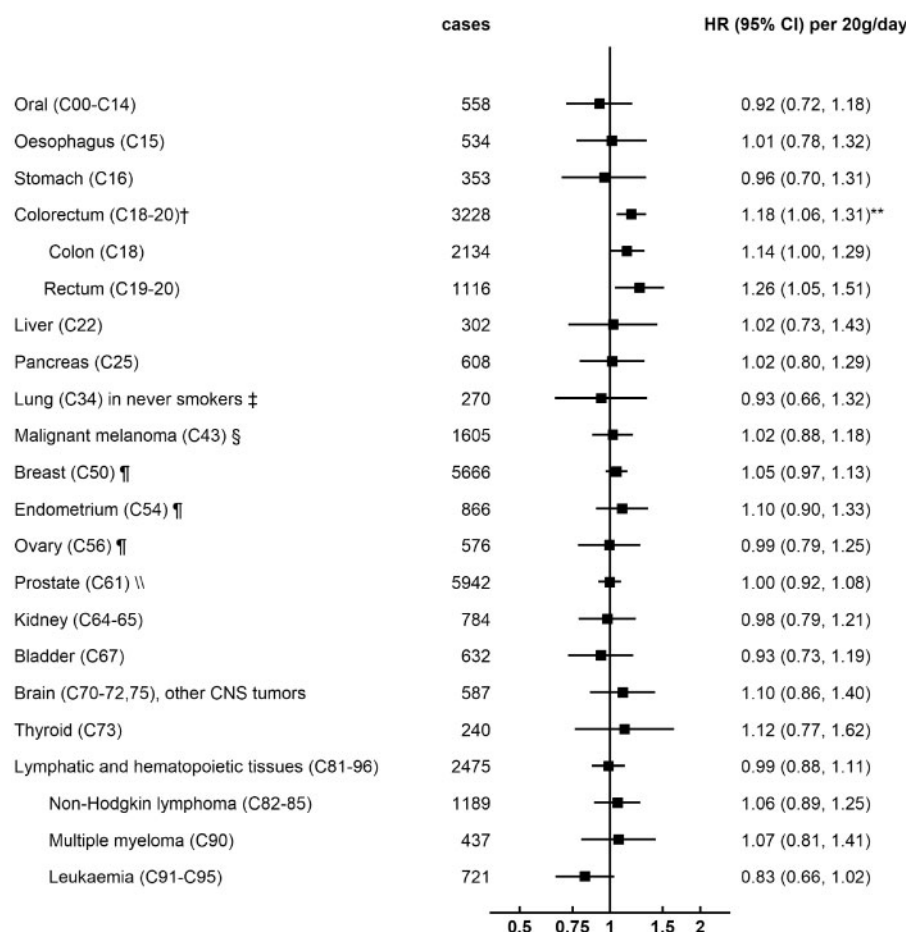


Figure 4 Associations of processed meat intake and cancer risk ($n = 472\,855$). **Stratified for sex, age group, region and adjusted for age (underlying time variable), ethnicity, deprivation, qualification, employment, living with a spouse or partner, height, smoking, physical activity, alcohol intake, total fruit and vegetable intake, estimated cereal fibre intake, cheese intake, milk added to tea/coffee/cereal, oily fish intake, non-oily fish intake, BMI, and in women: menopausal status, parity, hormone replacement therapy and oral contraceptive pill use. †In 22 colorectal cancer cases colon and rectal cancer diagnoses coincided. ‡Restricted to never smokers ($n = 258\,814$). §Additionally adjusted for skin colour, hair colour, skin reaction, UV protection use, sunburns before age 15 years, solarium use. ¶Restricted to women ($n = 254\,893$). \\\Restricted to men ($n = 217\,962$). **Findings $P < 0.0023$, Bonferroni corrected.

association.^{1,46–48} Finally, the association between poultry intake and cancers of the lymphatic and haematopoietic tissues, which seemed to be driven by NHL, was consistent with results from a European study in which higher poultry intake was associated with an increased risk of NHL.⁴⁹ However, two other studies in the USA found no association between poultry intake and NHL.^{50,51}

Major strengths of this study are the prospective design and large sample size. Data linkage to cancer registries reduced the risk of outcome misclassification and selective drop-out. Random error in dietary intakes was reduced by calibrating intakes using repeat measurements to estimate usual dietary intakes in each intake category.^{22,25} Associations were robust after adjustment for a wide range of potential confounders. Finally, the risk of reverse causation was reduced in sensitivity analyses excluding the first 2 years of follow-up, and residual confounding by smoking

was addressed in sensitivity analyses restricted to never smokers.

The UK Biobank participants are not representative of the UK general population, therefore selection bias might have some impact on risk associations, but exposure–disease relationships are likely to be generalizable because they have been shown to not require representativeness.^{19,52,53} Although the study was based on large case numbers for common cancers, it is possible that we did not have enough power to detect associations in rarer cancer sites. Furthermore, the follow-up time was limited to a maximum of 10 years, which might not be long enough to observe an association. Also, this study did not consider subtypes of cancer sites or tumor characteristics, because this information is not yet available in UK Biobank. Another limitation was the main method of dietary assessment: the touchscreen questionnaire only included a subset

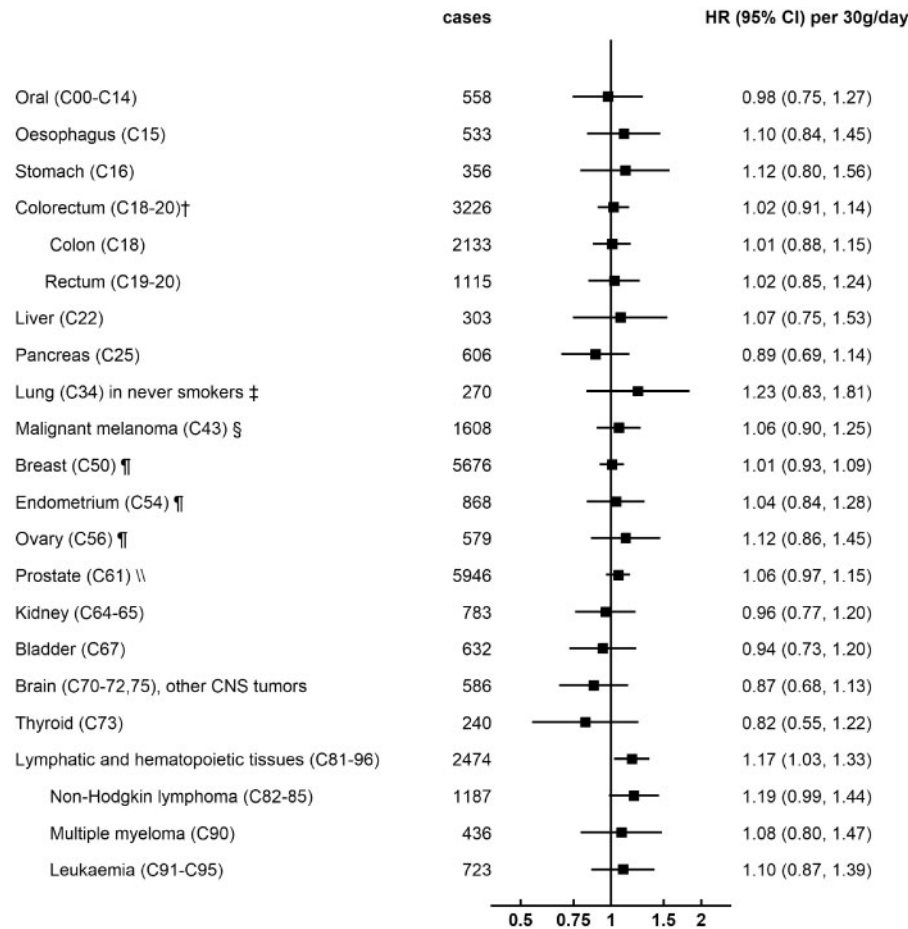


Figure 5. Associations of poultry intake and cancer risk ($n = 473\,022$). **Stratified for sex, age group, region and adjusted for age (underlying time variable), ethnicity, deprivation, qualification, employment, living with a spouse or partner, height, smoking, physical activity, alcohol intake, total fruit and vegetable intake, estimated cereal fibre intake, BMI, and in women: menopausal status, parity, hormone replacement therapy and oral contraceptive pill use. †In 22 colorectal cancer cases colon and rectal cancer diagnoses coincided. ‡Restricted to never smokers ($n = 259\,027$). §Additionally adjusted for skin colour, hair colour, skin reaction, UV protection use, sunburns before age 15 years, solarium use. ¶Restricted to women ($n = 255\,048$). ¶Restricted to men ($n = 217\,974$). **Findings $P < 0.0023$, Bonferroni corrected.

of food items that do not constitute the full scope of dietary intake, for example it was missing questions on intake of staple foods such as pasta and rice and therefore total energy intake could not be calculated. We hence accounted for confounding by energy balance by adjusting for BMI, height and physical activity, and for other dietary factors by adjusting for total fruit, vegetable, cereal fibre, milk, cheese and fish intake; however, there may still be some residual confounding.^{54,55}

In conclusion, the present study supports earlier findings of an association between red and processed meat intake and colorectal cancer, and shows specificity of this association.

Supplementary Data

Supplementary data are available at *IJE* online.

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Author Contributions

A.P.-C. and T.J.K. conceived of the study. A.P.-C. managed the project and was responsible for acquiring the data. T.J.K. was responsible for funding. A.K. performed all analyses and provided statistical figures, supervised by A.P.-C. K.P. and G.K.F. supported data preparation for analyses. All authors offered advice on the study design, analysis and interpretation of the results. A.K. drafted the first manuscript. All authors read, reviewed, revised and approved the final manuscript.

Conflict of Interest

None declared.

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