

## Processed and unprocessed red meat intake and bladder cancer risk: A pooled analysis of 30 cohorts

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**Background :** Processed meat is a Group 1 carcinogen, while unprocessed red meat is considered probably carcinogenic to humans. Previous analyses of meat consumption and bladder cancer risk conducted using individual cohort studies have generated inconsistent results. We assessed associations between processed meat and unprocessed red meat intakes and bladder cancer risk using data from the Pooling Project of Prospective Studies of Diet and Cancer.

**Methods :** Associations with bladder cancer risk were assessed using individual-level data from 30 cohort studies from North America, Europe, Australia and Asia that assessed usual diet at enrolment using validated food frequency questionnaires or diet histories. Multivariable Cox regression, adjusting for smoking habits (status and duration) and other confounders, was used to estimate hazard ratios (HR) and 95% confidence intervals (CIs). Random effects meta-analysis was used to combine study- and sex-specific results.

**Results :** Over median follow-up of 8-29 years of across cohorts in 2,429,536 participants, 21,789 were diagnosed with bladder cancer. Processed meat intake was associated with increased bladder cancer risk (HR comparing  $\geq 40$  with  $< 5$  g/day = 1.08; 95% CI: 1.01-1.15; HR per 20g/day increment = 1.02; 95% CI: 1.00-1.03). Weaker evidence of an association with increased risk was observed for unprocessed red meat (HR comparing  $\geq 100$  with  $< 20$  g/day = 1.06; 95% CI: 0.99-1.13; HR per 50g/day increment = 1.01; 95% CI: 0.99-1.03). Results were generally consistent by study, sex, smoking status, and geographical region.

**Conclusions :** Consumption of processed meat was associated with a small increase in bladder cancer risk. Weaker evidence of an association was observed for unprocessed red meat intake. These findings support cancer prevention guidelines that recommend limiting consumption of processed meat.

## Association between sarcopenia and protein intake calibrated using biomarkers

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**Background :** Proposing desirable dietary habits as modifiable factors for sarcopenia, which indicates a decrease in muscle mass and strength, is an urgent task.

**Aim:** We conducted a cross-sectional study of 1251 community-dwelling older Japanese to examine the association between protein intake calibrated using urinary biomarkers and the prevalence of sarcopenia in a general Japanese population.

**Methods :** The mean age of the participants was 69 years, and the percentage of women was 57%. Sarcopenia was defined according to the AWGS 2019 by low muscle mass (LMM), low muscle strength (LMS), and low physical performance (LPP). Protein intake was assessed using a food frequency questionnaire and calibrated using a regression calibration equation derived from 24-hour urinary total nitrogen (gold standard for evaluating protein intake). The calibrated protein intake was divided into tertiles by sex, and the odds ratios and 95% confidence intervals (CI) for sarcopenia and its components were calculated using a logistic regression model, adjusted for age, body mass index, smoking habits, drinking habits, daily physical activity, and energy intake.

**Results :** The proportions of sarcopenia and its components were 8% for sarcopenia, 26% for LMM, 8% for LMS, and 18% for LPP. The calibrated mean protein intake was 87 g/day for men and 70 g/day for women. Compared to the lowest protein intake group (T1), the multivariable-adjusted odds ratios (95% CI) for sarcopenia prevalence in the intermediate intake group (T2) and highest intake group (T3) were 0.53 (0.33-0.87) and 0.37 (0.22-0.64), respectively (trend  $p<0.001$ ). We also observed significant inverse associations between calibrated protein intake and the sarcopenia components of LMM, LMS, and LPP.

**Conclusion :** Significant inverse associations were found between the prevalence of sarcopenia and protein intake calibrated using a regression equation derived from objective measures in community-dwelling older Japanese individuals.

## Eating until full and longitudinal mean levels in glycemic markers: the Toon Health study

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**Background :** Eating until full has shown to be positively associated with body weight, a major risk factor for diabetes, in both cross-sectional and longitudinal studies. However, no longitudinal study has examined the association between eating until full and glycemic markers. Thus, we aim to examine the longitudinal relationship between eating until full and glycemic markers, and to examine whether body mass index (BMI) explains these associations.

**Methods :** Study design was longitudinal with baseline (2009-2012) and 5-year follow-up (2014-2018) surveys from Toon Health Study, an ongoing epidemiological cohort study. The data from 1,007 participants aged 30 to 65 years at baseline was used for the analysis. "Eating until full" was assessed using self-administered questionnaire. Fasting glucose, 2-hour post-load glucose (after a 75g oral glucose tolerance test), and fasting insulin concentrations were measured, and homeostasis model assessment for insulin resistance (HOMA-IR) was calculated. Multivariable-adjusted means of glycemic indicators were calculated at both baseline and follow-up using linear mixed models. Models were adjusted successively for major confounding factors, and finally BMI in final model. This study was approved by the institutional review board of Ehime University Hospital (#170511; Approved 2017/5/22).

**Results :** Multivariable-adjusted means of HOMA-IR were significantly higher among those who eat until full (baseline:1.15, follow-up:1.23) than those who did not eat until full (baseline:1.01, follow-up:1.15) ( $p$  for difference  $<0.01$ ). These differences were no longer significant after adjusting for BMI. Multivariable-adjusted mean of 2-hour post-load glucose among those who eat until full was 122.5 mg/dL at baseline and 126.2 mg/dL at follow-up, whereas those who did not eat until full had mean of 122.6 mg/dL at baseline, and 122.0 mg/dL at follow-up. Eat until full was not significantly associated with 2-hour post-load glucose, but increased it compared with not eat until full ( $p$  for interaction 0.054). However, this interaction disappeared after BMI adjustment in the final model. No significant associations of eat until full with HbA1c, and fasting glucose were found ( $p$  value $>0.05$ ).

**Conclusion :** Eating until full was positively associated with higher HOMA-IR for 5 years, and the association attenuated after adjustment for BMI. However, there are no significant association of eating until full with the other glycemic indicators.

## Dairy intake and mortality in Japanese: a pooled analysis of 10 population-based cohort studies

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**Background :** The association between dairy intake and mortality remains unclear, particularly in populations with low dairy consumption, such as the Japanese population. Thus, we investigated the associations between dairy intake and mortality in a pooled analysis of 10 Japanese cohorts.

**Methods :** We analyzed data from 180,267 males and 218,423 females aged  $\geq 35$  years at baseline (1983–2014) without a history of cardiovascular disease (CVD) or cancer. Milk, yogurt, and cheese intakes were assessed using self-administered food frequency questionnaires and categorized by frequency. Daily intake of each dairy item was estimated by multiplying intake frequency by portion size. Total dairy intake was calculated as the sum of individual dairy daily intakes and categorized into quartiles. Multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated for each study, and pooled using random-effects models to examine associations with all-cause and cause-specific mortality.

**Results :** Over 11.5–24.4 years of follow-up, 41,218 males and 28,659 females died. In males, compared to consuming milk <once/week, almost daily was associated with reduced all-cause mortality (HR: 0.94, 95%CI: 0.92–0.97; p-trend<0.0001), CVD mortality (HR: 0.89, 95%CI: 0.82–0.97; p-trend=0.005), and cerebrovascular disease mortality (HR: 0.81, 95%CI: 0.75–0.87; p-trend<0.0001). In females, almost daily milk consumption was associated with reduced cerebrovascular disease mortality (HR: 0.90, 95%CI: 0.82–0.98; p-trend=0.009). The second and third quartiles of total dairy intake were associated with reduced all-cause mortality in both sexes, and cancer mortality in males, although no dose-response association was found. No associations were observed for yogurt or cheese intake in either sex.

**Conclusion :** Dairy intake, particularly daily milk intake, may reduce mortality risk, especially cerebrovascular disease mortality risk, in Japanese males and females.

## CRP may interact with the link between 25-OHVitD and lung function in IBD patients from UK Biobank

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**Rationale :** Previous studies remain unclear whether interaction effects also contribute to this association between serum 25-hydroxyvitamin D (25-OHVitD) levels and pulmonary function in participants with inflammatory bowel disease (IBD). This study aimed to examine the presence of mediation and interaction effects in the association between serum 25-OHVitD and pulmonary function through inflammatory biomarkers using four-way decomposition analysis.

**Methods :** In this study, data were obtained from the UK Biobank, and 4,088 participants with IBD were selected. After excluding participants with serum 25(OH)D levels exceeding 100 ng/mL, 4028 of participants were included. A four-way decomposition analysis was conducted to assess how inflammatory biomarkers mediate or interact in the association between serum 25-OHVitD levels and forced expiratory volume in one second (FEV<sub>1</sub>) and forced vital capacity (FVC) in participants with IBD.

**Results :** We found association of serum 25-OHVitD levels with FEV<sub>1</sub> ( $\beta$ : 1.35; 95% CI: 0.31 to 2.36) and FVC ( $\beta$ : 1.58; 95% CI: 0.30 to 2.91). After adjusting for potential confounders, the results differed from previous findings. Neutrophil counts and white blood cells were identified as mediators in the relationship between serum 25-OHVitD and pulmonary function in participants with IBD. However, there are no significant interaction effects. Notably, four-way decomposition analysis revealed a relatively significant interaction effect of C-reactive protein (CRP) on FVC (mL) ( $\beta$ : 0.931; 95% CI: 0.066 to 1.597;  $p$ =0.017).

**Conclusion :** Neutrophil counts and white blood cells were identified as mediators in the relationship between serum 25-OHVitD and pulmonary function in participants with IBD. Furthermore, CRP may serve as a crucial interaction linking serum 25-OHVitD levels to pulmonary function in individuals with IBD.