research

Current use of some common NSAIDs associated with increased risk of acute myocardial infarction
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Processed and unprocessed red meat linked to increased risk of mortality
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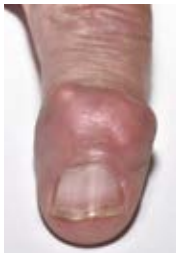

The DASH diet as preventive strategy for men at risk of gout
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ORIGINAL RESEARCH Bayesian meta-analysis of individual patient data

Risk of acute myocardial infarction with NSAIDs in real world use

Bally M, Dendukuri N, Rich B, et al

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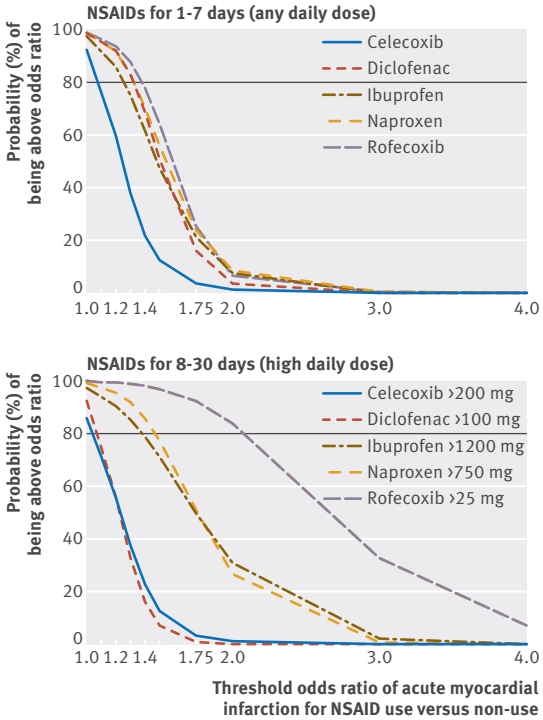
Find this at: http://dx.doi.org/10.1136/bmj.j1909

Study question What are the risks of acute myocardial infarction associated with use of common non-steroidal anti-inflammatory drugs (NSAIDs) under real life practice circumstances?



Plot of probability of exceeding odds ratios of acute myocardial infarction with current non-steroidal anti-inflammatory drug (NSAID) use at any dose for 1-7 days and at high dose for 8-30 days versus non-use

Methods Patient level data from studies sourced from healthcare databases were pooled in a bayesian meta-analysis, which estimated the risk of acute myocardial infarction corresponding to various clinical patterns for use of NSAIDs. The onset of risk and effects of duration of use and daily dose were characterised for celecoxib, diclofenac, ibuprofen, naproxen, and rofecoxib.

Study answer and limitations A cohort of 446 763 individuals including 61 460 with acute myocardial infarction was acquired. All NSAIDs were associated with an increased risk of acute myocardial infarction. Onset of risk occurred within the first week of use. With use for one to seven days the probability of increased myocardial infarction risk (posterior probability of odds ratio >1.0) was 92% for celecoxib, 97% for ibuprofen, and 99% for diclofenac, naproxen, and rofecoxib. The corresponding odds ratios (95% credible intervals) were 1.24 (0.91 to 1.82) for celecoxib, 1.48 (1.00 to 2.26) for ibuprofen, 1.50 (1.06 to 2.04) for diclofenac, 1.53 (1.07 to 2.33) for naproxen, and 1.58 (1.07 to 2.17) for rofecoxib. Risk was greatest with higher doses and during the first month of NSAID use without obvious further increase with continued use. As with all studies from healthcare databases, the inherent limitations are potential non-adherence to prescriptions and residual confounding.

What this study adds Naproxen was associated with the same risk of myocardial infarction as that documented for other NSAIDs. The risk associated with celecoxib was comparable to that of traditional NSAIDs and was lower than for rofecoxib.

Funding, competing interests, data sharing This study was part of a doctoral research thesis in epidemiology. Author JMB reports serving on the Data Monitoring Committee for the PRECISION trial, which was sponsored by Pfizer, during the conduct of the study. No additional data are available.

Meat consumption and risk of mortality

ORIGINAL RESEARCH Population based cohort study

Mortality from different causes associated with meat, haem iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study

Etemadi A, Sinha R, Ward MH, et al
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Study question Does an association exist between intake of different types of meat and meat associated compounds and overall and cause specific mortality in the general population?

Methods This cohort study used the baseline dietary data of 536 969 members of the American Association of Retired Persons aged 50-71 participating in the US NIH-AARP Diet and Health Study and 16 year follow-up data for mortality until 31 December 2011. Intake of total, processed, and unprocessed red (beef, lamb, and pork) and white (poultry and fish) meat, haem iron, and nitrate/nitrite from processed meat was estimated on the basis of the dietary questionnaire. Adjusted Cox proportional hazards regression models were used, with the lowest fifth of calorie adjusted intakes as reference categories.

Study answer and limitations Red meat intake was associated with an increased risk of all cause mortality (hazard ratio for highest versus lowest fifth 1.26, 95% confidence interval 1.23 to 1.29) and death due to nine different causes. The increased mortality associated with processed red meat was influenced by nitrate intake (37.0-72.0%) and to a lesser degree by haem iron (20.9-24.1%). When the total meat intake was constant, the highest fifth of white meat intake was associated with a 25% lower risk of all cause mortality. However, a single dietary assessment at the beginning of follow-up was used, and changes in diet could not be evaluated.

What this study adds These results show increased risks of all cause mortality and death due to nine different causes associated with both processed and unprocessed red meat, accounted for, in part, by haem iron and nitrate/nitrite from processed meat.

Funding, competing interests, data sharing This study was supported by the Intramural Research Program in the Division of Cancer Epidemiology and Genetics, the US National Institutes of Health, National Cancer Institute.

COMMENTARY Contemporary meat consumption harms human health and is equally bad for the planet

Analyses from the NIH-AARP study have previously shown that mortality was higher among participants with a high meat intake. With a total of more than 7.5 million person years of observation, further analyses by Etemadi and colleagues now show an association between high intakes of red and processed meat and elevated total mortality and mortality from most major causes: cardiovascular disease, diabetes, cancer, and hepatic, renal, and respiratory diseases.[1] They explored the possible role of meat constituents and established that haem iron (from red meat) and nitrate/nitrite (from processed meats) provide explanatory power and, perhaps, information on causation. That poultry and fish intake are inversely related to risk and contain little of these agents adds plausibility to their causal interpretation.

The problem is, however, that red and processed meats are likely to be harmful to humans in many different ways, often linked to more than one outcome. Simply choosing one or two from a list of probably highly correlated constituents does not further inform prevention strategies. For instance, evidence shows harm from protein degradation,[2] saturated fat,[3] N-nitroso compounds,[4] cooking related carcinogens,[5] feed related contaminants,[7] and reduced plant food intake.[3] Importantly, the current patterns of consumption of red and processed meat are not good for humans.

Although our closest primate relatives are vegetarian (gorilla) or only occasional consumers of meat (chimpanzee, and bonobo), and although good evidence shows that some of our hominin cousins were largely plant eaters,[8-10] humans have a long history of meat consumption.[11] By the end of the last ice age, 10-12 000 years ago, humans had both highly honed hunting skills and a taste for meat,[12] devastating populations of megafauna and even birds on many islands and across all continents except Africa.

Changing diets

With the transition to a pastoral lifestyle, we began to raise animals for meat and milk in settlements or as nomads. Meat was rare and largely celebratory in ancient Greece,[13] and in traditional European agricultural societies it was eaten once a week or less often, with intake rarely more than 5-10 kg per person per year.[12] Current consumption in rich countries is unprecedented. In the US, Australia, and New Zealand, people now consume about 110-120 kg/person/year (at least an order of magnitude increase).[14] Livestock have colonised more than 30% of the earth's land surface, mostly on permanent pasture, but this total also includes 33% of global arable land that is used to produce feed.[15] Meat and dairy animals account for about 20% of the total terrestrial animal biomass—about four times the biomass of humans.[15]

This shift from animal protein as a modest supplement to a plant based diet to providing up to 15-20% of total energy has consequences for human health, as Etemadi and colleagues describe.[1] Other outcomes include accelerated human sexual development, either as a result of meat and fat consumption itself or arising from naturally occurring or exogenous growth promoting hormones in meat[16 17]; extensive antibiotic resistance following antibiotic use to promote the growth of livestock[18]; a reduction in available human food and consequent hunger, as high value grains and legumes are fed to cattle (more than 97% of global soymeal production is fed to livestock[15]); and higher risks of infected food from animals raised using inappropriate feeding practices or in concentrated animal feeding operations using inappropriate feeding practices.[19 20] Such operations for pigs can act as a point source and "mixing vessel" for recombination of epidemic influenza strains, and use of multiple animal vaccines in a factory farm has been shown to result in the emergence of a virulent strain after recombination of two attenuated strains.[21]

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Association of meat and meat associated compounds with all cause death

Meat/meat associated compound	Odds ratio (95% CI) for highest *v* lowest fifth of consumption*
Total red meat	1.26 (1.23 to 1.29)
Processed	1.15 (1.13 to 1.17)
Unprocessed	1.20 (1.17 to 1.22)
Total white meat	0.75 (0.74 to 0.77)
Processed	0.95 (0.93 to 0.96)
Unprocessed	0.76 (0.74 to 0.78)
Haem iron	1.15 (1.13 to 1.17)
Nitrate	1.15 (1.13 to 1.17)
Nitrite	1.16 (1.14 to 1.18)

*Adjusted for sex, age at entry to study, marital status, ethnicity, education, fifths of composite deprivation index, perceived health at baseline, history of heart disease, stroke, diabetes, and cancer at baseline, smoking history, body mass index, vigorous physical activity, usual activity throughout day, alcohol consumption, fruit and vegetable intakes, total energy intake, and total meat intake

Current consumption in rich countries is unprecedented

Damage to planetary health includes depletion of aquifers[15] (producing 1 kg of meat protein requires >110 000 L of water[22]); production of 37% of anthropogenic methane (with 23 times the global warming potential of CO_2) and 65% of anthropogenic nitrous oxide (almost 300 times the potential of CO_2); groundwater pollution; and 64% of anthropogenic ammonia emissions, which contribute significantly to acid rain and acidification of ecosystems.[15] Rainforest destruction for livestock and the production of greenhouse gases by livestock contribute more to climate change than do fossil fuels used for transport.[15]

The research community collectively understands the problem—overconsumption of meat is bad for our health and for the health of our planet; research even provides clear underpinnings for evidence based policy that could limit harm to both,[23] but these underpinnings are not linked to action. As with many contemporary problems of resource overuse and maldistribution, we need to decide whether to act now to reduce human meat consumption or wait until the decay of sufficient parts of the global system tip us into much poorer planetary, societal, and human health.[24]

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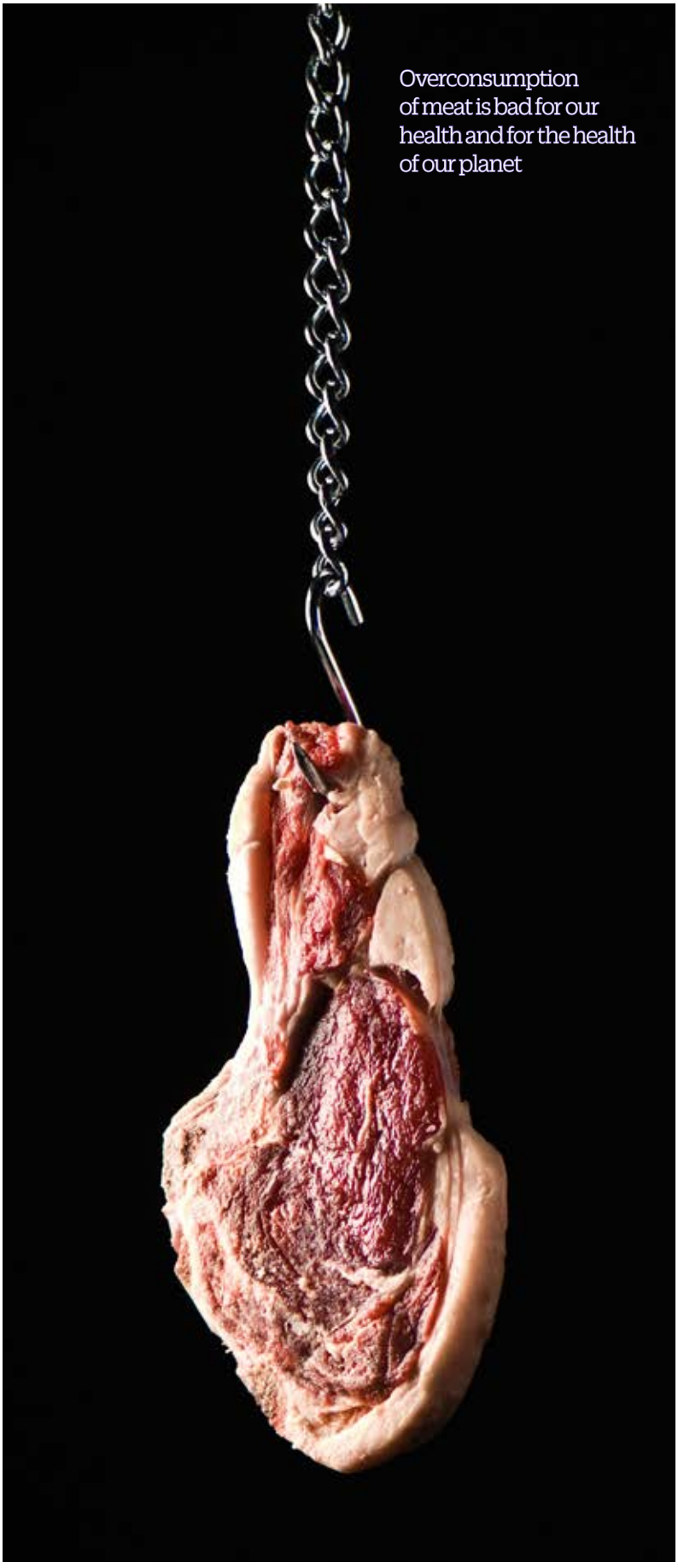

MICHELE CONSTANTINI/ALAMY

The Dietary Approaches to Stop Hypertension (DASH) diet, Western diet, and risk of gout in men

Rai SK, Fung TT, Lu N, Keller SF, Curhan GC, Choi HK

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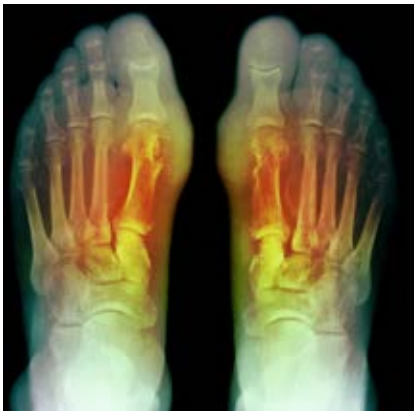
Study question What is the relation between the Dietary Approaches to Stop Hypertension (DASH) and Western diets and the risk of gout in men?

Methods Over a 26 year period, the authors prospectively examined the relation between two dietary patterns and new cases of gout among 44 444 men free of gout at baseline. Validated food frequency questionnaires were used to assign each participant a DASH dietary pattern score (based on intake of fruits, vegetables, nuts and legumes, low fat dairy products, whole grains, sodium, sweetened beverages, and red and processed meats) and a Western dietary pattern score (based on intake of red and processed meats, French fries, refined grains, sweets, and desserts). The authors ascertained the risk of incident gout meeting the American College of Rheumatology criteria, adjusting for potential confounders, including age, body mass index, hypertension, diuretic use, and alcohol intake.



DU CANE MEDICAL IMAGING LTD/SPL

Relative risk of incident gout according to fifths of DASH and Western dietary pattern scores

Variable	Fifths of intake					P value for trend
	First (lowest)	Second	Third	Fourth	Fifth	
DASH diet						
Cases/person years	396/192 891	391/195 970	366/196 511	332/192 697	246/193 455	
Relative risk (95% CI):						
Age adjusted	1.0	0.96 (0.83 to 1.10)	0.88 (0.77 to 1.02)	0.81 (0.70 to 0.94)	0.60 (0.51 to 0.70)	<0.001
Multivariable	1.0	0.90 (0.79 to 1.04)	0.87 (0.76 to 1.01)	0.82 (0.70 to 0.95)	0.68 (0.57 to 0.80)	<0.001
Western diet						
Cases/person years	287/190 572	347/194 533	365/196 671	346/197 114	386/193 182	
Relative risk (95% CI):						
Age adjusted	1.0	1.19 (1.02 to 1.39)	1.25 (1.07 to 1.46)	1.18 (1.01 to 1.38)	1.35 (1.16 to 1.57)	<0.001
Multivariable	1.0	1.09 (0.93 to 1.28)	1.15 (0.98 to 1.36)	1.12 (0.94 to 1.33)	1.42 (1.16 to 1.74)	0.005

Study answer and limitations A higher DASH dietary pattern score was associated with a lower risk of gout (adjusted relative risk for extreme fifths 0.68, 95% confidence interval 0.57 to 0.80, P value for trend <0.001). In contrast, a higher Western dietary pattern score was associated with an increased risk of gout (1.42, 1.16 to 1.74, P=0.005). The study was observational, thus leaving the possibility that unmeasured factors might contribute to the observed associations.

What this study adds The DASH dietary pattern is associated with a lower risk of gout, whereas the Western dietary pattern is associated with a higher risk.

Funding, competing interests, data sharing This research was supported by National Institutes of Health grants R01AR065944 and UM1CA167552. HKC reports grants from AstraZeneca and consulting fees from Takeda and Selecta outside the submitted work. No additional data are available.