Manuscript Title: Effect of Unprocessed Red Meat on Obesity and Related Factors. A Systematic Review and Meta-Analysis

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Study Headline: Unprocessed red meat consumption is not an independent risk factor for weight gain, percent body fat, obesity or adverse lipid profile, based on a comprehensive systematic review and meta-analysis of 19 clinical intervention studies.

Background:

Obesity affects 40% of adults in the United States (U.S.) and elevates the risk of numerous chronic diseases, including cardiovascular disease, type 2 diabetes, and hypertension, posing a serious public health concern. Nutrition scientists and health professionals increasingly aim to understand how specific nutrients, foods, and dietary patterns may contribute to obesity risk. Consumers, particularly those with weight concerns, including being overweight or obese, seek guidance on dietary strategies to lose weight for optimal health, but are often met with conflicting information on healthy food choices. *"Beef contains high-quality protein and other essential nutrients, and people enjoy this key source of nourishment – yet they're often discouraged to consume red meat based on recommendations primarily driven by observational evidence,"* noted the lead researcher of the current publication, Nikhil V. Dhurandhar, PhD, chair of the Department of Nutritional Sciences and associate dean for Innovation for the College of Health and Human Sciences at Texas Tech University.

"Protein-rich foods, such as beef, can improve satiety and satisfaction, which can help support lifestyle and dietary behaviors that promote weight loss and healthy weight maintenance," Dhurandhar added. "*Unfortunately, the stigma about beef's role in obesity may prevent many people from reaping the benefits of this nutrient-dense, high-quality protein food."*

Data from observational studies have previously shown associations between the consumption of red meat and higher occurrences of obesity and related metabolic disease (e.g., cardiovascular diseases, cancers, and all-cause mortality); however, it isrecognized that observational evidence establishes associations between variables and cannot establish cause-and-effect relationships. Importantly, this type of research has significant methodological limitations, such as reliance on self-reported dietary and lifestyle recall information, which can often be misreported and/or inaccurate and confound study results and conclusions. The "guilt by association" in linking unprocessed red meat intake and chronic disease risk in observational studies may mistakenly lead to conclusions about the obesogenic properties of unprocessed red meat consumption. The authors note that the correlational nature of observational findings have led to contradictory recommendations for unprocessed red meat in dietary guidance, which do not reflect the totality of the evidence, including gold standard randomized controlled clinical trials (RCTs) and randomized crossover trials (RCOs). Unlike observational research which identify statistical

associations between variables, RCTs and RCOs use controlled interventions and methodological approaches to reduce potential bias and directly assess the effects of specific dietary interventions on health outcomes. Summarizing RCTs and RCOs using a systematic review and meta-analysis is a well-recognized, gold-standard method in nutrition science for providing valuable information for public health leaders and clinicians.

Considering the limitations of observational studies, researchers from Texas Tech University sought to better understand the effect of unprocessed red meat consumption on obesity-related outcomes by using rigorous research methods.

Objective:
To conduct a systematic review and meta-analysis of intervention trials (parallel-arm randomized control trials (RCTs) or randomized crossover trials (RCOs)) to determine the role of unprocessed red meat on obesity-related outcomes (i.e., obesity and/or associated factors, such as body mass index (BMI), weight, percent body fat, and serum levels of total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides).

Study Design:
Systematic reviews and meta-analyses are gold standard evidence, providing valuable information for clinicians, decision makers and consumers by summarizing a substantial body of evidence as it relates to an important research question. The methodology for this current study was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), ensuring a transparent, complete, and accurate account of results and findings.

For this analysis, studies that reported an association between the consumption of unprocessed red meat and obesity-related outcomes were considered for inclusion within the analysis. Unprocessed red meat was defined as meat derived from cow, swine, sheep, goat, and horse, excluding poultry and fish. As processed and unprocessed red meat are compositionally different, the researchers focused their analysis on the effect of unprocessed red meat consumption.

Titles and abstracts were independently screened by two reviewers, and disagreements were resolved by discussion or adjudicated by a third reviewer. Eligible articles were screened through a full text review, followed by detailed assessment of study design, exposure, and outcome. The review included 11 RCTs and 8 RCOs studying an adult population with a control group and a usable measure of variability for meta-analysis. Risks of bias (ROB) of eligible studies were assessed using the Cochrane Collaborations ROB 2.0 tool for parallel and crossover design. Publication bias, defined as the influence of the findings of an article on the likelihood of that article being published, was also examined.

All data were prepared (e.g., combined, pooled) for analysis. RCTs and RCOs were analyzed separately, both unfiltered and filtered. An interactive dashboard was created to publicly share all code, calculations, and data utilized in the analysis.

The systematic review protocol (CRD42020196186) was published in PROSPERO.

Results:

- A comprehensive systematic review and meta-analysis of 19 clinical intervention trials assessing unprocessed red meat consumption and obesity risk factors showed no significant effect of unprocessed red meat on weight gain, obesity, or related metabolic conditions in adults.
    - When considering combined data from both RCTs and RCOs, no significant effect was observed between consumption of unprocessed red meat and weight, BMI, percent body fat, HDL-cholesterol, LDL-cholesterol, or triglycerides.
- Dr. Dhurandhar, lead investigator, noted, *"Our study is the first to fully review the totality of causative evidence, which shows no protective or adverse effect of unprocessed red meat intake on obesity. In fact, while unprocessed red meat consumption has declined in the U.S., the prevalence of obesity, type 2 diabetes, and cardiovascular disease has skyrocketed – which makes a poor case for the role of beef in promoting the obesity epidemic. This study offers a complete view of the research, so clinicians and consumers can make informed decisions about the role of unprocessed beef in healthy lifestyles."*

Study Implications:

- Findings from this gold-standard systematic review and meta-analysis of clinical intervention trials support the consumption of unprocessed red meat without increasing risk of obesity or adverse lipid outcomes.
- Authors noted the added benefits of consuming red meat, including satiety which may be an important consideration for those who are overweight or obese.
    - Nutrient-rich protein foods, such as unprocessed red meats, can help meet nutrient needs as well as improve satiety and satisfaction. Unprocessed red meat may be strategically included in the daily diet to help increase diet compliance to support weight loss or weight maintenance without concern for increasing risk factors for obesity and metabolic disorders.
- As is the case in any systematic analysis, the findings of this study depended on the quality of previously conducted trials. There is a need for additional adequately powered, longer-term clinical trials to assess the effect of unprocessed red meat consumption on obesity and weight loss.

Citation:

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