changes in multiple diet and lifestyle factors, and the previous analysis[5] suggested a modest correlation among changes in different dietary and behavioral factors. However, residual and unmeasured confounding from other lifestyle behaviors is still possible.

In conclusion, in these 3 cohorts of US adults, increases in red meat intake within a 4-year period were associated with a higher risk of T2DM in the subsequent 4-year interval. In addition, a reduction in red meat intake was associated with a lower incidence of T2DM during a subsequent long-term follow-up. Our results confirm the robustness of the association between red meat and T2DM and add further evidence that limiting red meat consumption over time confers benefits for T2DM prevention.

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Invited Commentary

Oxygen-Carrying Proteins in Meat and Risk of Diabetes Mellitus

William J. Evans, PhD

The article by Pan et al[1] confirms previous observations that the consumption of so-called red meat is associated with an increased risk of type 2 diabetes mellitus (T2DM). While previous studies have been cross-sectional in nature, the present study demonstrated that a relatively short-term (4-year) increase in red meat consumption is associated with subsequent risk, even in individuals who initially consumed low amounts of red meat. The authors demonstrated that consuming more red meat is also associated with weight gain, and a statistical adjustment for change in body weight attenuates but does not eliminate the risk, indicating that increased weight is not the only cause of a greater risk of T2DM associated with red meat consumption. The data in this article are valuable for those considering strategies to decrease the risk of developing T2DM.

The designation of meat according to its "redness" does not provide an adequate description of the category of meat exam-

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ined, however. The color (or lack thereof) of meat is determined by its myoglobin and, to a lesser extent, hemoglobin content. The authors have not described why, in the designation of red meat, they asked study participants to classify red meat as pork, beef, or lamb. Many cuts of chicken have more myoglobin than does pork, and cuts of tuna have almost twice the myoglobin content of beef. The description of red meat as a category of food, therefore, has little value and may be misleading. There is no evidence that the amount or type of protein in meat has an effect on insulin resistance or the risk of T2DM. Perhaps a better description of the characteristics of the meat consumed with the greatest effect on risk is the saturated fatty acid (SFA) content rather than the amount of oxygen-carrying proteins. Indeed, previous studies have demonstrated that despite many coldwater fish having a rich myoglobin content, the presence of ω-3 fatty acids may decrease the risk of heart disease.[2] Although the influence of dietary ω-3 fatty acids on the risk of T2DM is equivocal, they have been associated with reduced inflammation and a favorable lipid profile. However, increased consumption of SFAs has a powerful short- and long-term effect on insulin action. Processed meat is rich in total fatty acids and SFAs. A recent report[3] demonstrated that only processed meat consumption was associated with increased mortality. A recent meta-analysis[4] reported that the consumption of processed meat, not other types of meat, was associated with a greater risk of incident coronary heart disease, stroke, and T2DM.

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Meat and dairy products are the main sources of SFAs in the US diet. One potential way for the investigators to examine this issue might be to determine the influence of nonmeat saturated fat, primarily from higher-fat dairy products, on the risk of T2DM. If the primary cause of increased body mass among those who consume more meat is due to an increase in saturated fat intake, then palmitate and stearate would likely accumulate in adipocytes, the liver, and skeletal muscle. Adipocytes filled with SFAs activate macrophages to a far greater extent than do adipocytes filled with unsaturated fatty acids.[5] This increased inflammation in adipose tissue, along with more intake of SFAs, has been demonstrated to raise insulin resistance through increased oxidative stress and the generation of reactive oxygen species and ceramide production. Saturated fat also has been shown to have a direct effect on skeletal muscle insulin resistance. Accumulation of palmitate increases the amount of diacylglycerol in the muscles, which has been demonstrated to have a potent effect on muscle insulin resistance.[6] These effects of the type of dietary fatty acids are extremely difficult to control for in an observational study such as this one.

The interaction of the many genetic and lifestyle factors that contribute to the cause of T2DM is remarkably complex and still not well understood. The major factors associated with risk are levels of physical activity, body fatness, distribution of body fat, and diet. Previous cross-sectional analysis of red and processed meat consumption by Pan et al[7] shows a similar association with risk of T2DM. However, that study also demonstrated that substitution of nuts or fish for red meat reduced the risk of T2DM, strongly suggesting that the composition and amount of fatty acid consumption play a powerful role in the development of insulin resistance and T2DM. Meat rich in myoglobin and hemoglobin contains many important nutrients, not the least of which is heme iron, the most bioavailable form of iron in food. A recommendation to consume less red meat may help to reduce the epidemic of T2DM. However, the overwhelming preponderance of molecular, cellular, clinical, and epidemiologic evidence suggests that public health messages should be directed toward the consumption of high-quality protein that is low in total and saturated fat. This is particularly true for elderly people, who may have a greater need for dietary protein and a reduced need for energy than do younger people.[8] These public health recommendations should include cuts of red meat that are also low in fat, along with fish, poultry, and low-fat dairy products. It is not the type of protein (or meat) that is the problem; it is the type of fat.

ARTICLE INFORMATION

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