



COMMENT ON CEFALU ET AL.

The Alarming and Rising Costs of Diabetes and Prediabetes: A Call for Action! Diabetes Care 2014;37:3137–3138

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Cefalu et al. (1) used the findings of a recent study (2) to argue that the category of prediabetes is an important component of the American Diabetes Association's (ADA's) arsenal in diabetes prevention. They disliked our critique of the category (3), suggesting that prediabetes imposes an economic burden in its own right, that the Diabetes Prevention Program (DPP) demonstrates the benefits of intervening in prediabetes, and that by so doing medication use can be reduced.

We believe passionately in tackling the growing burden of diabetes and its complications by preventing obesity and increasing physical activity. Our argument is that a clinical approach by which we medicalize people (i.e., we apply a diagnostic label to them and turn them into patients) and prescribe them glucose-lowering medications may be misguided. We question whether people are better off with such interventions, even though they may prevent the diagnosis of diabetes in people close to the threshold.

We also remain skeptical of the relevance of DPP and the DPP Outcomes Study (DPPOS) findings to patient-important outcomes. The DPP/DPPOS showed an impact on "conversion to diabetes," representing a delay in the glycemic trajectory crossing a cut point (6.5% for A1C, or correspondingly for glucose). A person newly diagnosed with diabetes at an A1C of 7% has a *lifetime* risk of blindness and end-stage renal failure <3% (4). Aged over

65 years, this risk is <0.5%. This is why we consider prediabetes as a risk factor for newly diagnosed mild diabetes, itself a risk factor for end-organ damage. After 15 years of follow-up in the DPPOS, these interventions showed no impact on even surrogate microvascular outcomes (5).

The DPP/DPPOS enrolled high-risk people, selected because they exhibited impaired glucose tolerance, and on placebo, 5–10% per year converted to diabetes. By expanding the category from impaired glucose tolerance to the looser ADA "prediabetes" definition, the at-risk population increases three- to fourfold, but the conversion rate falls to ~2% per year (2) (1.7 million with newly diagnosed type 2 diabetes out of 86 million with prediabetes [<http://www.cdc.gov/media/releases/2014/p0610-diabetes-report.html>]).

There are clear benefits of *lifestyle interventions* in reducing cardiovascular risk factors, and there is indirect evidence in support of reducing the risk of cardiovascular events. But the glucocentric focus of prediabetes predicates glucose-lowering agents when lifestyle interventions fail. Metformin alone has not been shown to reduce the risk of diabetes-related complications, so it is unlikely that its use in the lower-risk prediabetes group will represent anything more than premature diabetes treatment.

In clinical practice, the diagnosis of prediabetes results in a 78% increase in ambulatory endocrine care visits, at an

annual cost per person of \$510 (2). Anything beyond lifestyle advice will increase, not decrease, medication use. Indeed, some experts advocate early off-label use of diabetes drugs (6). Any upside of this health care burden is unproven.

It is our contention that we should change the drivers of the obesity and diabetes epidemic rather than focus on clinical interventions that turn at-risk but healthy people into patients.

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