Evidence supports prediabetes treatment

In his News Feature on prediabetes (“Dubious diagnosis,” 8 March, p. 1026), C. Piller asserts that prediabetes diagnoses and treatment may be ineffective and sullied by conflicts of interest. As current and former chairs of the American Diabetes Association’s (ADA’s) Professional Practice Committee [the group that reviews and updates the Standards of Medical Care in Diabetes (Standards) each year], we disagree. Prediabetes is a useful term to convey future risk of diabetes, and recommendations for diabetes prevention are based on best current evidence.

The ADA classifies prediabetes as a risk factor for diabetes that can be mitigated by lifestyle changes or, in limited circumstances, with the addition of metformin. Piller reports that prediabetes does little or no harm on its own and that fewer than 2% of people with prediabetes progress to diabetes each year. The risk of progressing from prediabetes to diabetes varies according to the diagnostic criteria used (1), but even a 2% progression rate per year would translate to nearly 1 of 5 people with prediabetes developing diabetes within 10 years. Also, many individuals with prediabetes have a multiplicity of risk, due to ethnicity, body weight, and other factors, and these may render their annual risk much higher.

In the online “Key takeaways” box (<https://scim.ag/prediabetes>), Piller states that “Many studies suggest that for most people the usual treatments for prediabetes, diet and exercise, do little to further reduce the risk of diabetes.” However, healthy eating and regular physical activity (2) have been shown (along with the medication

metformin for select patients) to delay or prevent progression to diabetes (3–5). Accordingly, the Standards place a heavy emphasis on these lifestyle interventions.

Piller writes that the ADA lists costly medications for diabetes prevention, sold by pharmaceutical companies from which Professional Practice Committee members have collected “large sums.” We disagree that this funding affected the committee’s positions. No pharmaceutical agents have been FDA-approved for diabetes prevention, and the only recommended medication is metformin, which has been shown to be effective and safe (3, 6) and is available for as little as \$4 per month [e.g., (7)], rendering the conflicts of interest described in the article irrelevant to the current ADA recommendations for diabetes prevention. In fact, metformin may save costs over a 10-year period when used for diabetes prevention (6). The Standards of Care mentions pharmacologic agents other than metformin, including glucose-lowering and weight loss therapies that have been studied for diabetes prevention (3), but these agents are not recommended by the ADA for diabetes prevention. Additionally, the ADA states that metformin should be considered for those who have prediabetes, especially those who have a body mass index (BMI) of at least 35 kg/m², are under the age of 60 years, or have a history of gestational diabetes mellitus (2). These recommendations highlight the importance of risk stratification and individualization of therapy.

We acknowledge that unanswered questions surrounding prediabetes and its management remain important issues that warrant open discussion. Indeed, the ADA has not shied away from such debate (8, 9). It is important to engage in these discussions with full consideration of the available evidence.

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COMPETING INTERESTS

W.H.H. serves as chair for a Data Safety Monitoring Board for Merck Sharp & Dohme. C.H.W. receives institutional research support from Mylan and Novo Nordisk; she has received honoraria from Abbott, AstraZeneca, Boehringer Ingelheim, Dexcom, Janssen, Novo Nordisk, and Sanofi. S.E.I. has served as a consultant to Boehringer Ingelheim, AstraZeneca, Novo Nordisk, Sanofi/Lexicon, and Eisai (TIMI) and has lectured for Boehringer Ingelheim. I.B.H. receives institutional research support from Medtronic Diabetes and serves as a consultant for Abbott Diabetes Care, Roche, Bigfoot, and Becton Dickinson. V.A.F. declares a duality of interest: research support (to Tulane) (grants from Bayer and Boehringer Ingelheim), honoraria for consulting and lectures (Takeda, Novo Nordisk, Sanofi-Aventis, Eli-Lilly, Abbott, Astra-Zeneca, Intarcia, and Asahi), stock options (Microbiome Technologies, Insulin Algorithms, and BRAVO4Health), and stock (Amgen). J.B.B.’s contracted consulting fees are paid to the University of North Carolina by Adocia, AstraZeneca, Dance Biopharm, Dexcom, Elcelyx Therapeutics, Eli Lilly, Fractyl, GI Dynamics, Intarcia Therapeutics, Lexicon, MannKind, Metavention, NovaTarg, Novo Nordisk, Orexigen, PhaseBio, Sanofi, Senseonics, Shenzhen HighTide, Takeda, vTv Therapeutics, and Zafgen; he reports grant support from AstraZeneca, Eli Lilly, GI Dynamics, GlaxoSmithKline, Intarcia Therapeutics, Johnson & Johnson, Lexicon, Medtronic, Novo Nordisk, Orexigen, Sanofi, Scion NeuroStim, Takeda, Theracos, and vTv Therapeutics; he is a consultant to Cirus Therapeutics Inc., CSL Behring, and Neurimmune AG; he holds stock or options in Mellitus Health, PhaseBio, and Stability Health.

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