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**Conflict of interest:** Mayo Clinic has licensed AI technology that Dr. Friedman co-invented to Eko, Anumana, and AliveCor, and medical device technology to MediCool and Murani Health. Mayo Clinic and Dr. Friedman may receive financial benefit from the commercialization of these technologies. Dr. Friedman serves as investigator and/or advisory board member for Medtronic, Boston Scientific, and Abbott, with funds directed to Mayo Clinic.

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## Weekly Journal Scan

# Worsening of risk factor control in US diabetic patients: a call to action

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Comment on 'Trends in Diabetes Treatment and Control in U.S. Adults, 1999–2018' which was published in the *N Engl J Med*, doi:10.1056/NEJMsa2032271, and on 'Trends in Prevalence of Diabetes and Control of Risk Factors in Diabetes Among US Adults, 1999–2018' which was published in the *JAMA*, doi:10.1001/jama.2021.9883

### Key points

- Two cross-sectional analyses were performed on the US population observed over 10 cycles by the National Health and Nutrition Examination Survey (NHANES) (from 1999 through 2018). The aims of these studies were to assess trends in glycaemic, lipid, and blood pressure (BP) control in diabetic patients<sup>1</sup> and to estimate the age-standardized prevalence of diabetes and control of cardiovascular (CV) risk factors in the overall population,<sup>2</sup> respectively.
- In the population of 6653 diabetic patients, trends for glycaemic, BP, and lipid control were non-linear. Glycaemic control (glycated haemoglobin level <7.0%) was achieved in a higher percentage of patients in the 2007–10 period [57%; 95% confidence interval (CI), 53–62] compared with 1999–2002 (44%; 95% CI, 39–49), but then declined to 50% (95% CI, 46–55) in 2015–18. The percentage of participants who obtained BP control (mean BP <140/90 mmHg) rose from 64% (95% CI, 59–68) in 1999–2002 to 74% (95% CI, 71–77) in 2011–2014 but then declined to 70% (95% CI, 67–74) in 2015–18, with consistent trends when a more stringent BP target of <130/80 mmHg was considered. The percentage of participants in whom lipid control [non-high-density lipoprotein (HDL) cholesterol level <130 mg/dL, and low-density lipoprotein (LDL) cholesterol level <100 mg/dL in sensitivity analyses] was achieved, increased from 25% (95% CI, 21–30) in 1999–2002 to 52% (95% CI, 49–55) in 2007–10 and subsequently levelled off (56% in 2015–18; 95% CI, 51–60).<sup>1</sup>
- Glycaemic, BP, and lipid control in the diabetic population were obtained in 9% (95% CI, 7–12) of participants in 1999–2002, rising up to 25% (95% CI, 21–29) in 2007–10, but then remaining stable at 22% in 2015–18 (95% CI, 18–27).<sup>1</sup>
- In the second analysis performed in the overall population including 28 143 participants, the estimated age-standardized prevalence of diabetes increased significantly from 10% (95% CI, 9–11) in 1999–2000 to 14% (95% CI, 13–16) in 2017–18 (*P* for trend <0.001). In 2015–18, 67% (95% CI, 63–70), 48% (95% CI, 45–52), and 60% (95% CI, 54–65) of adults with diabetes achieved HbA1c, BP (<130/80 mmHg) and LDL cholesterol (<100 mg/dL) targets, respectively. The achievement of the goals for all three risk factors was obtained in only 21% of the population (95% CI, 15–27), being even lower in young adults aged 18–44 years (7%) and in non-Hispanic black adults (12%).<sup>2</sup>

## Comment

These cross-sectional studies<sup>1,2</sup> show negative trends in the rate of successful control of diabetes and CV risk factors in the most recent cycle of NHANES. The growing prevalence of diabetes as well as the decline in the achievement of the recommended glycaemic, lipid, and BP therapeutic goals in diabetic patients represent a source of concern, especially in consideration of the heavy CV burden related to diabetes. Although age, racial, and ethnic characteristics of participants remained stable, while education grade, income, and health insurance improved, the prevalence of diabetes significantly increased from 1999–2000 to 2017–18, and adequate glycaemic control was obtained in only 50%<sup>1</sup> and 67%<sup>2</sup> in the diabetic population in the two analyses. In the diabetic population, BP control declined and lipid control levelled off,<sup>1,2</sup> in spite of more stringent recommended targets.<sup>3–6</sup>

The unsatisfactory results observed in the US population are paralleled in Europe by the reports of the EUROASPIRE (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) V survey, performed to identify risk factors in high-risk patients with and without diabetes.<sup>7</sup> Among the 8261 subjects at very-high CV risk involved in the EUROASPIRE V, only 42% achieved BP level <140/90 mmHg, 54% had glycated haemoglobin level <7.0% and about 70% had LDL cholesterol <70 mg/dL.<sup>7</sup>

This finding is indeed surprising in consideration of the numerous public campaigns, increased awareness, and much larger availability of effective and safe treatment strategies.<sup>3</sup>

A possible explanation may be represented by unhealthy lifestyle behaviours together with inadequate drug therapy due to inappropriately low doses of antihypertensive, lipid-lowering, and anti-diabetic medications and underuse of combination therapies. In the NHANES registry, a stabilization in the use of BP-lowering drugs was registered after a 16% increase from 1999–2002 to 2007–10. Statin use increased by 28% from 1999–2002 to 2011–14 before levelling off.<sup>1</sup> The percentage of patients who received combination glucose-lowering and antihypertensive therapies declined after 2010, also among subjects with uncontrolled risk factors. Indeed, only 61% of participants with a glycated haemoglobin level  $\geq$ 7% and 53% of those with a BP  $\geq$ 140/90 mmHg were treated with more than one medication.

This clinical inertia is in contrast with the recommendations of the most recent guidelines, which suggest starting and maintaining treatment with more aggressive therapeutic approaches.<sup>3–6</sup> In high-risk diabetic patients, an intensified multifactorial intervention with tight glucose control and use of appropriate doses of renin-angiotensin system blockers, aspirin, and lipid-lowering agents has shown sustained beneficial effects with respect to vascular complications and rates of death from any cause and from CV causes.<sup>8</sup>

Accordingly, several recent studies and meta-analyses have supported the ‘the lower, the better’ concept in the treatment of hypertension, diabetes, and dyslipidaemia, showing that a tighter control of these risk factors significantly improves CV protection, and prompting progressive reductions in the recommended therapeutic goals.<sup>3–6,9,10</sup>

Although treatment intensification requires a careful consideration of the risk-benefit ratio, the results of the NHANES surveys<sup>1,2</sup> underline the need for more intensive and integrated therapeutic strategies, especially in high-risk patients such as those with diabetes, prompting an urgent ‘call to action’ to promote more effective prevention

programmes both at population and individual levels. Public campaigns, education, and physicians should synergistically work to raise awareness of the importance of prevention of diabetes and control of risk factors, as well as to encourage healthy lifestyles, early start of pharmacological treatment, and improvement in the adherence to medical prescriptions.

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