Impact of Modifiable Risk Factors, Including Diabetes, and Diabetes-Related Complications, on Dementia Risk in Older USA Adults: Mutually Adjusted Estimates from a Population-Based Cohort

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Conflicts of interest: The author's research stay at the University of Michigan was supported by grants from the William Demant Foundation, the Danish Diabetes Association, the Hede Nielsen Family Foundation, and the Dagmar Marshall Foundation; and the author has received support for attending meetings/travel from Novo Nordisk and Viatris.

Acknowledgements: The author thanks the All of Us Research Program for the permission to use data for this study.

Keywords: Dementia, diabetes, diabetes complications, population attributable fraction (PAF), risk factors.

Citation: EMJ Diabet. 2026;14[1]:39-40. https://doi.org/10.33590/emj/MG320X07

SUMMARY OF KEY RESEARCH FINDINGS

The 2024 Lancet Commission on Dementia estimated that 45% of dementia cases could potentially be prevented by eliminating 14 modifiable dementia risk factors.[1] This estimate is based on population-attributable fractions (PAF), which quantify the proportion of disease cases theoretically attributable to a given risk factor in a population. However, many of these risk factors coexist, making it challenging to estimate their individual contributions to the overall dementia burden and highlighting the importance of validating these estimates in real-world populations.

Using data from 83,370 adults aged over 50 years in the National Institutes of Health (NIH) All of Us Research Program, associations between 12 established modifiable risk factors, diabetes-related complications, and incident dementia were examined.[2] Over a median follow-up of 8.1 years, 2,327 participants developed dementia.[2]

After mutual adjustment, several established risk factors, including traumatic brain injury (hazard ratio [HR]: 2.66), depression (HR: 2.22), lower education (HR: 1.48), diabetes (HR: 1.42), and hypertension (HR: 1.40), were associated with increased dementia risk.[2] The total PAF was 11.1%, substantially lower than the Lancet Commission estimate. Diabetes-related complications, including stroke (HR: 2.22), amputation (HR: 2.05), neuropathy (HR: 1.81), peripheral vascular disease (HR: 1.25), and chronic kidney disease (HR: 1.21), were independently associated with dementia. However, incorporating these complications did not materially change the total PAF (10.7%).[2]

WHAT CHALLENGE DOES THIS ADDRESS?

Accurately estimating the proportion of dementia cases attributable to modifiable risk factors is important for informing prevention strategies and public health priorities. Although the Lancet Commission estimated a prevention potential of approximately 45%, several population-based studies have reported considerably lower estimates, generally between 15% and 25%.[3-5] The author's findings add to this evidence, with an estimated PAF of 11.1%.[2] However, differences in risk factor definitions, exposure timing, population characteristics, and statistical approaches complicate direct comparisons and highlight the uncertainty surrounding estimates of dementia prevention potential. This study also addresses whether diabetes-related complications contribute additional dementia risk

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beyond diabetes itself, distinguishing their potential relevance for identifying high-risk individuals from their contribution to population-level prevention.

RELEVANCE TO EUROPEAN PRACTICE

With ageing populations and increasing diabetes prevalence across Europe, identifying individuals at elevated dementia risk is becoming increasingly important. These findings reinforce the relevance of diabetes and cardiometabolic health to dementia prevention. They also suggest that diabetes-related complications may provide clinically useful information for identifying patients at particularly high risk. Neuropathy, for example, was associated with an approximately 80% higher dementia risk, even after adjustment for diabetes and other established risk factors. For European healthcare professionals, these findings support greater awareness of cognitive health in patients with diabetes, particularly those with established complications. Such patients may benefit from closer attention to cognitive symptoms and assessment when clinically indicated. However, these observational findings do not establish that preventing or treating diabetes-related complications will directly reduce dementia incidence.

WHAT ARE THE NEXT STEPS FOR THE RESEARCH?

Further studies should validate these findings in European populations, where healthcare systems, risk factor prevalence, and population characteristics may differ from those in the USA. Future research should also address limitations of electronic health record-based studies, including potential underdiagnosis of dementia and diabetes-related complications. Longer follow-up, repeated risk factor assessments, and more comprehensive cognitive evaluations could improve our understanding of how dementia risk evolves over time.

Importantly, future studies should investigate whether diabetes-related complications improve dementia risk prediction beyond established risk factors, particularly among individuals with diabetes. Ultimately, intervention studies are needed to determine whether targeting modifiable risk factors in high-risk individuals can reduce cognitive decline and dementia risk.

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