Reducing dementia risk while delivering diabetes care

Up to 45% of the population attributable fraction of dementia is potentially preventable, according to this report from the 2024 *Lancet* Commission on dementia. This includes 17% of risk attributable to factors which are discussed and influenced in diabetes consultations, with an additional 17% attributable to vision or hearing loss, depression and social isolation, which we may also be aware of in primary care. Much of this risk is now recognised to occur during midlife, defined as age 18–65 years, rather than in later life, as was proposed in the previous version of the report in 2020. Other potential risk factors where the evidence base for a direct contribution to dementia risk remains uncertain include sleep, diet, infection, bipolar disorder and other psychoses, anxiety, post-traumatic stress disorder, early menopause and hormone replacement therapy. The authors outline the evidence for 14 potentially modifiable risk factors, including diabetes, high LDL cholesterol and hypertension, and conclude that it is never too early or too late to reduce dementia risk.

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People are living longer and this is increasing the number of people living with dementia globally, even though the age-specific incidence is decreasing in some high-income countries, partly due to reducing vascular damage. The 2024 *Lancet* Commission on dementia report presents a hopeful picture, highlighting that the evidence is increasing, and is stronger than in its previous 2020 report, that tackling 14 potentially modifiable risk factors can significantly reduce the risk of dementia (Livingston et al, 2024). The report focuses on prioritising systematic reviews and meta-analyses demonstrating how the Commission's existing 12 risk factors and two new factors – vision loss and high LDL cholesterol – influence dementia risk.

The Commission has calculated the population attributable fractions (PAFs) from worldwide estimated relative risks and prevalence of risk factors, using these to generate a new, comprehensive life-course perspective on dementia prevention, including highlighting the importance of remaining cognitively, physically and socially active in midlife (age 18–65 years). Full details of how these PAFs were calculated can be found in the report.

The potentially modifiable risk factors are listed in *Box 1*. Many of the risk factors are comorbidities or areas of lifestyle that we will discuss and manage in our diabetes consultations, making this report important reading for those involved in delivering diabetes care, as well as

Box 1. Population attributable fractions of 14 potentially modifiable risk factors for dementia.

The percentage reduction in dementia cases if each risk factor is eliminated is presented in brackets.

Early life

- Less education (5%) – modifiable with midlife cognitive activity

Midlife

- Hearing loss (7%) – hearing aids make an impact
- High LDL cholesterol (7%) – new risk factor 2024
- Depression (3%)
- Traumatic brain injury (3%)
- Physical inactivity (2%)
- Diabetes (2%)
- Smoking (2%)
- Hypertension (2%)
- Obesity (1%)
- Excessive alcohol (1%)

Late life

- Social isolation (5%)
- Air pollution (3%)
- Visual loss (2%) – new risk factor 2024

Total: 45% potentially modifiable

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How to manage diabetes in later life

Clinical considerations when caring for older or frail people with diabetes. A quick reference guide.

Diabetes & Primary Care **22**: 5–6

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everyone interested in taking action to reduce their own risk and that of family members.

The full report discusses not just prevention, which I explore here, but also dementia intervention and care, and clinicians are encouraged to read the whole report for more details of the latest evidence on these additional two areas of dementia care.

Diabetes, cognitive impairment and dementia

The population attributable risk associated with diabetes alone is surprisingly low, at 2%, and is designated to have its impact mainly in midlife. However, elevated levels of LDL cholesterol, hypertension and obesity confer additional risk and are likely to occur in people with diabetes, and they are comorbidities that we will discuss and manage along with diabetes. We also have the opportunity to discuss lifestyle factors such as smoking, low physical activity and alcohol intake, meaning that overall we can explore and potentially help influence 17% of population attributable risk in our diabetes clinics.

One study which influenced the Commission to reclassify diabetes as a midlife rather than late-life risk factor demonstrated that the risk of dementia increases for every 5-year decrease in age of type 2 diabetes onset (hazard ratio 1.24) up to the age of 70 years (Barbiellini Amidei et al, 2021). Diabetes in late life, long diabetes duration and suboptimal glycaemic control also increase risk of dementia. However, effective management of diabetes may not translate into reduced dementia risk, and intensive therapy – with its possible associated risk of hypoglycaemia – has not been demonstrated to be better for dementia risk than standard control. Potential mechanisms for diabetes increasing dementia risk are still incompletely understood but are likely to include vascular impacts (including stroke), insulin resistance peripherally impacting brain metabolism and signalling, increased oxidative stress and neuroinflammation.

Obesity in midlife, which is shown to be increasing in many studies, is associated with increased risk of both dementia and type 2 diabetes, and higher waist circumference in people aged >65 years is associated with increased dementia risk. Some of the impact on dementia risk may occur indirectly through increased diabetes risk, and some may be related to decreased physical activity. Even 2 kg of weight loss achieved through lifestyle changes such as healthier diet and physical activity has been shown to improve cognition.

SGLT2 inhibitors, GLP-1 receptor agonists and DPP-4 inhibitors are associated with lower dementia risk, and some metformin studies show an association with lower risk, whereas sulfonylurea treatment is associated with increased dementia risk. The Look AHEAD study demonstrated an inverse relationship between HbA_{1c} and cognition, but low blood glucose and weight loss alone were not associated with a lower dementia risk.

Other risk factors reviewed in diabetes consultations and actions to decrease dementia risk include the following:

- Midlife hypertension increases the risk of all-cause dementia, Alzheimer's disease and vascular dementia.
  - ➤ Prevent or reduce hypertension, aiming to keep systolic blood pressure (SBP) <130 mmHg in those over 40 years who are free of dementia. However, SBP appears to decrease by around 10 mmHg in the 2–5 years prior to developing dementia (Peters et al, 2020).
  - ➤ Antihypertensive medication appears to be protective against cognitive impairment and dementia.
- Each 1 mmol/L increase in LDL cholesterol is associated with an 8% increase in incidence of all-cause dementia (Wee et al, 2023), while an LDL cholesterol of >3 mmol/L was associated with a hazard ratio for dementia of 1.33 (Mukadam et al, 2023).
  - ➤ Detect and treat raised LDL cholesterol.
- Identify and help people manage obesity as early as possible; this should also help reduce diabetes.
- Midlife smoking appears to be a stronger risk factor for dementia than smoking in later life, as was suggested in the 2020 report. The evidence is strong that smoking cessation reduces dementia risk.
  - ➤ Signpost to cessation services at all ages.

Implications for practice

This new report highlights that almost half of dementia risk could be reduced if the 14 risk factors were avoided altogether or, in some

cases, managed successfully. When delivering diabetes care, we have a huge opportunity to help people understand and manage their risk of dementia from diabetes, high LDL cholesterol, hypertension, obesity, low levels of physical activity, smoking and excess alcohol intake, which together account for 17% of the population attributable risk of dementia.

In addition, as clinicians we will likely be aware of significant hearing loss, visual loss, depression and possibly social isolation. This new report highlights particularly the benefits of prompt referral and provision of hearing aids for those with hearing loss, which should change our practice. Through referral into social prescribing schemes and depression management, we might also have a small influence further reducing the impact of dementia risk.

Understanding the strong evidence base behind the association of these 14 risk factors with 45% of dementia risk, and that these risks can be reduced in most people – even those with the high-risk *APoE4* genotype – should motivate us to help not just those we see in our clinical work but also ourselves and family and friends to reduce dementia risk. With the clear message from the *Lancet* Commission report that *"it is never too early or too late to reduce dementia risk,"* let's do our very best to make every contact count. ■

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Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission

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