

Lifestyle change for microvascular gain

In this retrospective study of the UK Biobank cohort, Geng and colleagues followed more than 15 000 people with type 2 diabetes free of microvascular and macrovascular complications at baseline, and explored the association of multiple healthy lifestyle behaviours with risks of individual and all microvascular complications, and the extent to which metabolic biomarkers mediated this association. After adjusting for sociodemographic characteristics, hypertension, glycaemic control and medication, participants who adhered to 4-5 healthy lifestyle factors compared with one or no factors had a 46% lower risk of developing any microvascular complication, a 35% lower risk of diabetic retinopathy, a 57% decreased risk of diabetic kidney disease and a 54% lower risk of diabetic neuropathy. The combination of the biomarkers albumin, HDL-cholesterol, triglycerides, apolipoprotein A, C-reactive protein and HbA_{1c} explained just over 23% of the associations between lifestyle and microvascular complications. These findings support actively encouraging people with type 2 diabetes to adopt a variety of healthy lifestyle behaviours as early as possible.



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icrovascular complications (retinopathy, nephropathy and neuropathy) can reduce quality of life for people with type 2 diabetes and are present in up to 50% of people at diabetes diagnosis. They are also responsible for significant healthcare costs. Retinopathy is the commonest diabetes complication, occurring in around 30% of people with type 2 diabetes, and is often cited as the complication that people fear most, due to the risk of sight loss. Glucose-lowering drugs can improve glycaemia, and tight blood pressure control and optimising lipids can reduce microvascular complications. ACE inhibitors, ARBs, SGLT2 inhibitors and GLP-1 receptor agonists have been demonstrated to reduce the risk and progression of nephropathy. However, the impact of combined healthy lifestyle behaviours on microvascular complications has varied between studies.

In this retrospective cohort study of participants in the UK Biobank, more than 15 000 people with type 2 diabetes who were free of complications at baseline were followed for an average of 8.1 years to identify any association between healthy lifestyle behaviours and risk of new microvascular complications. The authors also sought to identify how well biomarkers of glycaemic control, inflammation, liver function and lipids would explain the relationship.

The five healthy lifestyle factors included in the study were:

- Not currently smoking.
- Healthy waist circumference (<80 cm in women and <94 cm for men).
- Moderate alcohol intake (<14 g/day for women and <28 g/day for men; around 1.5 and 3 units/day, respectively).
- Physical activity (those in the top third of activity levels).
- A low-risk diet containing five or more ideal diet components (e.g. fruit and vegetables, whole grains, fish, dairy).

These low-risk lifestyle behaviours were assessed at Biobank recruitment, and a limitation of the study is that these could change over time but were not revisited during the follow-up.

During the study, 10.9% of participants died and 8.6% developed one or more of the microvascular complications, with 3.7% developing retinopathy, 4.1% diabetic kidney disease and 2.1% diabetic neuropathy. After

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adjustment for hypertension, glycaemic control, medication histories and socioeconomic factors, compared with those who adhered to one or no healthy lifestyle behaviours, participants who adhered to 4-5 healthy behaviours had a significant 46% lower risk of the composite of microvascular complications, a 35% lower risk of retinopathy, a 57% lower risk of diabetic kidney disease and a 54% lower risk of diabetic neuropathy. For each incremental low-risk lifestyle behaviour adhered to, there was an 18%, 13%, 22% and 27% lower risk of all microvascular complications, diabetic retinopathy, diabetic nephropathy and diabetic neuropathy, respectively.

Six biomarkers (albumin, HDL-cholesterol, triglycerides, apolipoprotein A, C-reactive protein and HbA,) collectively explained just over 23% of the association between lifestyle behaviours and microvascular complications.

Strengths of the study include the large sample size, long follow-up period and the use of biomarker data, allowing exploration of potential mechanisms. The key limitation was potential under-reporting of microvascular complications, since complications were identified using hospital inpatient admission records and death registries rather than GP records. Other limitations were the lack of ethnic diversity; the fact that Biobank participants are not representative of the overall UK population; and the observational study design, which means a risk of residual confounders persists despite attempts to adjust for possible confounders.

An emerging pattern

In an associated perspective piece, Yogini Chudasama and Kamlesh Khunti, from the Leicester Real World Evidence Unit, share similar findings from a cohort of more than 26000 people with diabetes in the China Kadoorie Biobank study, in whom combined low-risk lifestyle behaviours were also associated with a lower risk of microvascular complications, particularly retinopathy (Chudasama and Khunti, 2023). They highlight the very low adherence rates to healthy lifestyle factors in both studies: only 10.3% of the UK cohort and 14.4% of the Chinese cohort adhered to 4-5 healthy lifestyle factors. This emphasises the importance of promoting population- and policy-level interventions. Chudasama and Khunti also note that longitudinal studies, inclusion of participants from socioeconomically deprived backgrounds and exploration in more ethnically diverse groups would be useful in extending the real-world evidence base.

A recently published prospective cohort study of more than 7000 people with type 2 diabetes from the Nurses' Health Study and Health Professionals Follow-Up Study considered BMI 18.5-<25 kg/m² instead of waist circumference, alongside the other four low-risk lifestyle behaviours outlined here (Liu et al, 2023). The authors looked at healthy lifestyle factors before and after diabetes diagnosis and found a 27% lower risk of all microvascular complications associated with \geq 4 versus zero low-risk behaviours before diagnosis, and a very similar 32% lower risk in those with ≥4 versus zero behaviours adopted after diagnosis. This study suggests that adopting healthy lifestyle behaviours even after type 2 diabetes diagnosis is worthwhile and may be associated with a substantial reduction in microvascular complications.

Concluding remarks

We encourage people with type 2 diabetes to make lifestyle changes, but many do not choose to heed the advice or find change too difficult. It is hoped that, armed with the results from these studies, we will help more people realise the benefits of self-care and behaviour change to reduce their risk of retinopathy, nephropathy and neuropathy.

Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study

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Chudasama YV, Khunti K (2023) Healthy lifestyle choices and microvascular complications: New insights into diabetes management. PLoS Med 20: e1004152

Liu G, Li Y, Pan A et al (2023) Adherence to a healthy lifestyle in association with microvascular complications among adults with type 2 diabetes. JAMA Netw Open 6: e2252239