Clinical*DIGEST 2*

Management & prevention of type 2 diabetes



Sleeping, strength and risk of type 2 diabetes

Jason Gill

Reader in Exercise and Metabolism, Institute of Cardiovascular and Medical Sciences, University of Glasgow

besity and lack of physical activity are well established as risk factors for type 2 diabetes (Jeon et al, 2007; Abdullah et al, 2010), which are commonly incorporated into screening instruments, such as FINDRISC, to estimate diabetes risk (Lindström and Tuomilehto, 2003). There is clear and convincing evidence from a number of large, long-term randomised controlled trials that lifestyle intervention incorporating weight loss and increased physical activity are effective at reducing incidence of diabetes in those with impaired glucose regulation (IGR; Gill and Cooper, 2008). However, a substantial proportion of individuals do still progress to diabetes despite the undergoing current gold-standard lifestyle interventions, and there is scope for cost-effective refinement of screening instruments to better identify those at increased diabetes risk. Thus, identification of other easily measurable and potentially modifiable diabetes risk factors could potentially help inform future risk screening and diabetes prevention strategies. Evidence from recent prospective studies, suggests that two such factors may be strength and sleep.

In a report from Li and colleagues (summarised alongside), 133 353 women without diabetes from the Nurses' Health Study and the Nurses' Health Study II were asked how much difficultly they had in falling asleep and staying asleep over the previous 4 weeks, their sleep duration and how frequently they snored. There were 6407 cases of incident diabetes over 10 years of follow-up. Women with sleep difficulty had a 45% increased risk of diabetes. Almost half of this excess risk was mediated by obesity, hypertension and depression, but even after adjustment for these factors (and a comprehensive range of other confounders) difficulty in sleeping was associated with a 22% increase in type 2 diabetes risk. Other studies have highlighted the association between short sleep duration and diabetes risk (Cappuccio et al, 2010); this study makes an important further contribution to the evidence base that sleep-related variables may make a more important contribution to diabetes risk than is often recognised.

In another report, coincidentally by Li and colleagues (I assume no relation; summarised on the following page), 1682 men in the MAILES (Men Androgen Inflammation Lifestyle Environment and Stress) study had body composition measured by dual-energy X-ray absorptiometry (DXA) and grip strength measured using a hand grip dynamometer. They were followed up for 5 years, during which time 146 men developed type 2 diabetes. Muscle mass was not associated with incident diabetes, but every 5-kg increase in grip strength was associated with 13% lower incidence of type 2 diabetes. While this association likely reflects a relationship between overall muscle function – rather than grip strength per se – and risk of diabetes, grip strength is quick and easy to measure and could potentially be incorporated into routine clinical consultations.

Thus, while the available data are relatively limited, and further study is needed, there is now emerging evidence that sleep variables and grip strength may contribute to an individual's risk of type 2 diabetes. Intervention studies are needed to determine whether altering sleep behaviours and improving strength could, alongside weight loss and increasing physical activity, potentially help reduce risk of developing type 2 diabetes in individuals at high risk.

References on following page

Diabetologia

Sleeping difficulty and T2D in women

Readability	5555
Applicability to practice	<i>」</i>
WOW! Factor	<i>」</i>

In this prospective study, the authors examined the association between sleeping difficulty and the risk of developing T2D, the joint effect between sleeping difficulty and other sleep-related factors, and the extent to which the effects of sleeping difficulty on T2D are mediated through BMI, hypertension and depression.

2 Data from 133 353 women without diabetes, cardiovascular disease or cancer at baseline in the Nurses' Health Study (NHS) and Nurses' Health Study II (NHSII) was analysed during up to 10 years of follow-up.

3 Sleeping difficulty was defined as having difficulty initiating or maintaining sleep most or all of the time. At baseline, 5.9% of women in the NHS and 4.8% in the NHSII reported such difficulty.

4 During follow-up, 6407 cases of T2D were documented. There was an increased risk of women with sleeping difficulty developing T2D compared to those without sleeping difficulty. After adjustment for lifestyle factors, the hazard ratio (HR) for T2D was 1.45 (95% confidence interval [CI], 1.33–1.58).

5 After further adjustment for status of hypertension, depression and BMI, the HR between sleeping difficulty and T2D fell to 1.22 (95%Cl, 1.12–1.34).

6 Women who reported four sleep conditions had a greatly increased likelihood of developing T2D (HR, 4.17; 95% Cl, 2.93–5.91).

7 The investigators conclude that sleeping difficulty is associated with T2D and is partially explained by associations with hypertension, BMI and depression.

Li Y, Gao X, Winkelman JW et al (2016) Association between sleeping difficulty and type 2 diabetes in women. *Diabetologia* **59**: 719–27

Type 2 diabetes

Grip strength is quick and easy to measure and could potentially be incorporated into routine clinical consultations."

References from commentary

Abdullah A, Peeters A, de Court, Stoelwinder J (2010) The magnitude of association between overweight and obesity and the risk of diabetes: a metaanalysis of prospective cohort studies. *Diabetes Res Clin Pract* **89**: 309–19

Cappuccio FP, D'Elia L, Strazzullo P, Miller MA (2010) Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care 33: 414–20

Gill JM, Cooper AR (2008) Physical activity and prevention of type 2 diabetes mellitus. *Sports Med* **38**: 807–24

Jeon CY, Lokken RP, Hu FB, van Dam RM (2007) Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care* **30**:744–52

Lindström J, Tuomilehto J (2003) The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care* **26**: 725–31

Metabolism

Grip strength as a predictor of T2D

Readability	<i>」</i>
Applicability to practice	<i>」</i>
WOW! Factor	<i>」</i>

1 These investigators examined the association between measures of skeletal muscle mass and strength with incident T2D, and whether testosterone or inflammation mediate that association.

2 Participants in MAILES (Men Androgens Inflammation Lifestyle Environment and Stress), a longitudinal study of a cohort of community-dwelling men, underwent assessment for hand grip strength (using a dynamometer), testosterone and inflammatory markers. Body composition was measured in a subset by dual-energy X-ray absorptiometry (DXA).

3 Of 1632 men, incident diabetes not present at baseline occurred in 146 (8.9%) over a median follow-up of 4.95 years. Findings from the DXA analysis were that muscle mass was not associated with incident T2D.

Grip strength was inversely associated with T2D, as was arm muscle quality (grip strength divided by arm lean mass).

5 In mediation analysis, neither circulating testosterone nor inflammation significantly mediated the inverse associations between grip strength or arm muscle guality and T2D.

6 These associations were strong in non-obese men, but were not significant in obese men. The authors suggest that grip strength could be used to help identify non-obese men at risk of T2D.

7 Low muscle mass may be an effect of T2D, rather than a predictor

of its development. The association between muscle strength and incident T2D requires further studies to establish which factors may contribute to it.

Li JJ, Wittert GA, Vincent A et al (2016) Muscle grip strength predicts incident type 2 diabetes: Populationbased cohort study. *Metabolism* **65**: 883–92

Diabetes Care

Effects of interrupting sitting

Readability	<i>」</i>
Applicability to practice	<i></i>
WOW! Factor	<i>」</i>

This study compared the effects on postprandial cardiometabolic risk of uninterrupted sitting (SIT) with sitting plus brief bouts of light-intensity walking (LW) and sitting plus simple resistance activities (SRA), in adults with T2D.

2 Overweight or obese (BMI, $\geq 25 \text{ kg/m}^2 \text{ but } <40 \text{ kg/m}^2 \text{ men}$ (n=14) and women (n=10) with T2D, who did not follow current physical activity guidelines, were recruited to this crossover trial.

3 After randomisation, participants underwent the following three conditions for 7 hours on three separate days, with 6–14 days of washout: SIT (control); sitting plus 3-minute bouts of LW every 30 minutes; and sitting plus 3-minute bouts of SRA (half-squats, calf raises, gluteal contraction and knee raises) every 30 minutes. Standardised meals were consumed.

A Net incremental area under the curve (iAUC) during both LW and SRA was significantly attenuated compared with SIT for glucose, insulin and C-peptide (all *P*<0.001). The iAUC for triglycerides was attenuated significantly for SRA compared with SIT (*P*<0.001), but not for LW compared with SIT.

5 The magnitude of the glucose attenuation for LW compared with SIT was greater in women (-58%) than in men (-26%). For SRA compared with SIT, the trend was not significant.

6 Both activity conditions were easily tolerated and well accepted. The results suggest that beneficial metabolic effects can be achieved with different modes of light-intensity activity.

Dempsey PC, Larsen RN, Sethi P (2016) Benefits for type 2 diabetes of interrupting prolonged sitting with brief bouts of light walking or simple resistance activities. *Diabetes Care* **39**: 964–72

Diabetes Care

Weight loss in T2D and brain structure

Readability	<i>」</i>
Applicability to practice	<i>」</i>
WOW! Factor	<i>」</i>

Adults with T2D are at increased risk for brain atrophy and cerebrovascular disease. This study set out to assess whether intentional weight loss can mitigate these adverse effects.

2 The study group enrolled a subset of the Look AHEAD trial participants. During that study, overweight or obese adults with T2D were randomly assigned to receive 10 years of behavioural intervention to promote and maintain weight loss, or to a control group that received support through group sessions and education.

3 Subsequently, 319 participants entered the Look AHEAD Brain study. They underwent standardised structural brain magnetic resonance imaging (MRI) and tests of cognitive function.

The MRI results showed that total brain and hippocampus volumes were similar between the two groups. The mean white matter hyperintensity volume was 28% smaller in the lifestyle group compared to the control group. Mean ventricle volume was 9% lower in the intervention group.

5 The lifestyle intervention was not associated with consistent differences in cognitive function compared to the control.

6 Long-term intensive weight-loss intervention may delay the adverse impact of diabetes on brain structure. This finding further supports the importance of implementing behavioural interventions in adults with T2D.

7 More research is needed to determine whether the beneficial effects of intensive intervention can ultimately lead to better cognitive functioning and lower risk of impairment.

Espeland MA, Erickson K, Neilberg RH et al (2016) Brain and white matter hyperintensity volumes after 10 years of random assignment to lifestyle intervention. *Diabetes Care* **39**: 764–71