# Obesity

## Sweet dreams: Sleep and diabetes

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We spend a significant part of our lives sleeping, yet the full functions of sleep remain to be elucidated. In the last decade, there has been great interest in the role of sleep in the regulation of metabolism (Spiegel et al, 1999; Taheri et al, 2004; Taheri, 2007). Increasing evidence from studies, which have included examining multiple age groups from different countries, points towards a negative linear association between sleep duration and obesity. This relationship appears to be more robust in children and adolescents. In adults, a U-shaped relationship has been observed, with both short and long sleep duration found to be associated with obesity, metabolic syndrome and diabetes (Arora et al, 2011; Jackson et al, 2013; Ju and Choi, 2013). Major problems with epidemiological studies have included cross-sectional designs and a lack of objective measures of sleep duration and quality (Arora et al, 2013). Also, a common complication of obesity, obstructive sleep apnoea (OSA), has not been fully characterised in the studied populations. Longitudinal studies are, however, reporting similar associations with cross-sectional studies (Ayas et al, 2003; Chaput et al, 2009). Experimental sleep restriction in healthy volunteers confirms there are metabolic derangements that are commonly associated with diabetes or predispose to obesity (Tasali et al, 2009; Spiegel et al, 2011). Several mechanisms for the association between sleep and metabolism have been proposed, but these remain to be confirmed (Taheri, 2007). A common link between sleep (a brain phenomenon) and peripheral metabolism is the activation of the sympathetic nervous system (Spiegel et al, 2004).

In a study summarised alongside, Liu and colleagues selected healthy overweight and obese individuals to examine the relationship between sleep duration and insulin resistance. They excluded those with OSA. They used a modified insulin suppression test to determine insulin-mediated glucose uptake. Using this technique, they subdivided the participants into insulin-resistant and insulin-sensitive groups. The participants were asked the number of hours they slept every night, and less than 7 hours was the cut-off point used for short sleep duration. Apart from insulin resistance and higher triglyceride levels, the insulin-resistant group did not differ in results from the insulin-sensitive group. The insulin-resistant group had a shorter sleep duration and were more likely to report shorter sleep.

While this study supports the potential relationship between sleep duration and insulin resistance and uses a robust method to determine metabolic regulation, it has several limitations including a cross-sectional design, an inability to assess reverse causality, and the use of a single question to determine sleep patterns.

The importance of sleep duration and quality is increasingly being recognised for individuals with diabetes, who are also at increased risk of sleep disorders, such as OSA. The study by Liu and colleagues is yet another piece of supporting evidence for the role of sleep in metabolism. There is a lot to learn from the individuals we see with diabetes if only we were to ask them about their sleep as part of comprehensive patient-centred assessments. Apart from the potential impact on metabolism, sleep may be the link between diabetes and depression.

Sleep appears to be an important pillar of lifestyle that also includes diet and physical activity. There is a major need for studies using validated measures of sleep duration and quality in well-characterised populations. These studies can be combined with randomised controlled trials to determine whether improving or extending sleep could reverse insulin resistance, with potential downstream effects on glycaemic control in patients with diabetes. Conducting randomised controlled studies in sleep is likely to be challenging, but the time is right to gain more definitive knowledge that will impact on public health and clinical practice (Taheri and Thomas, 2008).


Arora T, Jiang CQ, Thomas GN et al (2011) *Diabetes Care* **34**: 2317–9

Arora T, Broglia E, Pushpakumar D et al (2013) *PLoS One* **8**: e72406

Ayas NT, White DP, Al-Delaimy WK et al (2003) *Diabetes Care* **26**: 380–4

Chaput JP, Després JP, Bouchard C et al (2009) *Sleep Med* **10**: 919–24

Jackson CL, Redline S, Kawachi I, Hu FB (2013) *Diabetes Care* **36**: 3557–65

Ju SY, Choi WS (2013) *Nutr Diabetes* **13**: e65

Spiegel K, Leproult R, Van Cauter E (1999) *Lancet* **23**: 1435–9

Spiegel K, Leproult R, L'hermite-Balériaux M et al (2004) *J Clin Endocrinol Metab* **89**: 5762–71

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Taheri S (2007) *Sleep Med Rev* **11**: 159–62

Taheri S, Thomas GN (2008) *Sleep Med Rev* **12**: 299–302

Tasali E, Leproult R, Spiegel K (2009) *Prog Cardiovasc Dis* **51**:381–91


METABOLISM

## Link between short sleep duration and insulin resistance

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓ |
| WOW! factor | ✓✓ |

**1** The aim of this study was to assess whether habitual short sleep duration (defined as <7 hours sleep) was independently related to insulin resistance in non-diabetic obese and overweight people.

**2** Participants were split into two cohorts: those that had a steady-state plasma glucose (SSPG) concentration of ≥180 mg/dL (≥10.0 mmol/L; termed the insulin-resistant cohort) and those with a SSPG of ≤120 mg/dL (≤6.7 mmol/L; termed the insulin-sensitive cohort).

**3** In total, 35 insulin-resistant and 21 insulin-sensitive participants were asked in a questionnaire, "On average, how many hours sleep do you get per night?"

**4** The insulin-resistant cohort reported fewer hours of sleep than the insulin-sensitive cohort, after adjustment for BMI (6.53 ± 1.1 versus 7.24 ± 0.9 hours respectively; $P<0.05$). A shortened sleep duration was also more common in the insulin-resistant group (60% compared to 40% in the insulin-sensitive cohort [$P<0.05$]).

**5** These findings may suggest that shorter sleep duration has a negative effect on glucose metabolism, which is independently associated with insulin resistance in obese, disglycaemic individuals without diabetes.

**6** The association between short sleep and risk of T2D highlights the importance of sleep behaviour modifications to reduce the risk of cardio-metabolic disease.


Liu A, Kushida CA, Reaven GM (2013) Habitual shortened sleep and insulin resistance: An independent relationship in obese individuals. *Metabolism* **62**: 1553–6

*"Glycaemic response to gastric bypass is predicted by higher baseline BMI, shorter disease duration and higher fasting C-peptide."*

DIABETES CARE

## Liraglutide for weight loss in those with prediabetes

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓ |
| WOW! factor | ✓✓ |

1 The authors carried out a double-blind, ramdomised, placebo-controlled study of liraglutide's ability to augment weight loss and improve insulin resistance and cardiovascular disease (CVD) risk factors in an overweight and obese population with prediabetes.

2 Liraglutide is a glucagon-like peptide-1 (GLP-1) agonist. GLP-1 agonist action has been associated with weight loss in those with T2D.

3 In total, 68 participants were enrolled to receive either liraglutide (1.8 mg) or placebo for 14 weeks, and all were encouraged to decrease their calorie intake by 500 kcal/day.

4 Eleven of the 35 participants in the liraglutide cohort discontinued the study; 8 of which because of adverse events, such as gastrointestinal side effects and injection site reactions.

5 In total, 88% of the liraglutide cohort and 22% of the placebo cohort lost 5% of their baseline weight, and the liraglutide cohort lost twice as much weight as those in the placebo group (6.7 kg versus 3.3 kg; $P<0.001$).

6 The liraglutide cohort also had a significant improvement in insulin resistance (measured by steady-state plasma glucose concentrations), and a significantly greater lowering of systolic blood pressure, and fasting glucose and triglyceride concentrations.

7 The authors suggest that liraglutide could significantly augment weight loss compared to placebo when a calorie-restricted diet is in place in overweight or obese individuals at risk from T2D and CVD.

Kim SH, Abbasi F, Lamendola C et al (2013) Benefits of liraglutide treatment in overweight and obese older individuals with prediabetes. *Diabetes Care* **36**: 3276–82

DIABETIC MEDICINE

## Gastric bypass: Pre-operative predictors of glycaemic control

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓ |
| WOW! factor | ✓✓ |

1 Based in South Korea and Taiwan, this study's aim was to find the pre-operative predictors that influence glycaemic control after gastric bypass surgery in patients with T2D and BMI <30 kg/m$^2$.

2 This prospective study of 103 patients defined post-operative "excellent glycaemic control" as $HbA_{1c}$ <42 mmol/mol (<6%) and inadequate response as $HbA_{1c}$ >53 mmol/mol (>7%).

3 At year 1, 30% of participants achieved "excellent glycaemic control" and 33% of participants had an inadequate response.

4 The independent pre-operative predictors of "excellent glycaemic control" were a short diabetes duration of <7 years and BMI >27 kg/m$^2$. The independent predictors of poor glycaemic control were BMI <27 kg/m$^2$ and a baseline fasting C-peptide of ≤20 ng/mL.

5 The likelihood for "excellent glycaemic control" can be estimated using $\log_e$(Odds) = −6.7 + (0.26 x BMI) + (−1.2 x diabetes duration).

6 There was a strong correlation between percentage weight loss after surgery and final $HbA_{1c}$ (C&S $R^2$=0.54, $P<0.001$). Therefore, percentage weight loss after surgery was the key determinant of glycaemic outcome at 1 year.

7 Post-operative glycaemic response to gastric bypass surgery is predicted by higher baseline BMI, shorter disease duration and higher fasting C-peptide.

Dixon JB, Hur KY, Lee WJ et al (2013) Gastric bypass in type 2 diabetes with BMI < 30: weight and weight loss have a major influence on outcomes. *Diabet Med* **30**: e127–34

DIABETES CARE

## Enhancing insulin sensitivity with one low-intensity exercise session

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓ |
| WOW! factor | ✓✓ |

1 The effect of modest exercise on insulin sensitivity and fatty acid uptake the day after exercise was investigated in 11 sedentary obese adults.

2 The participants were aged 18–45 years and completed three experimental trials performed in a random order and separated by ≥7 days: one "no-exercise" control and two exercise-based trials where subjects exercised until they had expended 350 kcal at 50% $VO_2$ peak ([EX50]; ~55 minutes) and 65% $VO_2$ peak ([EX65]; ~70 minutes).

3 The next day, insulin sensitivity and whole-body fatty acid uptake were measured.

4 The authors found that exercise increased insulin sensitivity; there was a 35% significant improvement after EX50 compared to the control, and there was a 20% improvement after EX60, but this was not significant.

5 Systemic fatty acid uptake was reduced after EX50 compared to EX65, but not significantly reduced compared to the control.

6 The authors concluded that a relatively mild session of exercise in obese adults could improve insulin sensitivity the next day and reduce systemic fatty acid uptake in the several hours after exercise.

7 However, the exercise protocols were very vigorous (e.g. 65% $VO_2$ peak for ~70 minutes) and so may not reflect realistic exercise expectations for most sedentary obese adults.

Newsom SA, Everett AC, Hinko A, Horowitz JF (2013) A single session of low-intensity exercise is sufficient to enhance insulin sensitivity into the next day in obese adults. *Diabetes Care* **36**: 2516–22