

## Diabetes

### Afternoon exercise more beneficial for blood glucose than morning exercise in type 2 diabetes

A small but well designed pilot study from Scandinavia has suggested that afternoon exercise improves blood glucose in type 2 diabetes more effectively than exercise in the morning.

Eleven men with type 2 diabetes controlled by diet alone or with metformin were selected for the study. Inclusion criteria were age 45-68 years and BMI 23-33 kg/m<sup>2</sup>. Exclusion criteria included treatment with insulin, a history of smoking in the past 6 months or the presence of another systemic illness i.e. cardiovascular, rheumatoid, blood borne or neoplastic disease. The study design was a randomised crossover trial. The research team were not blinded to the group assignment.

The trial involved two weeks of either morning or afternoon high intensity interval training for three sessions per week on a bicycle ergometer supervised in the gym. This was followed by a two-week washout period and then two weeks of the opposite regimen. Patients were fitted with continuous glucose monitors and data were collected for two weeks before training commenced, to give baseline measurements, and throughout the trial period.

Morning high intensity interval training was associated with higher glucose levels (6.9 ± 0.4 mmol/L) on the exercise days during week 1, compared

with both the pretraining period (6.4 ± 0.3 mmol/L) and afternoon exercise (6.2 ± 0.3 mmol/L and 6.1 ± 0.4 mmol/L for weeks 1 and 2, respectively).

Conversely, high intensity interval training in the afternoon reduced the continuously monitored glucose levels during weeks 1 and 2 compared with both the pre-training period and the morning exercise regimen.

Of the other biochemical parameters measured, high intensity interval training was associated with a rise in TSH generally, and reduced T4 levels with afternoon exercise, and unchanged levels with morning exercise. This is interpreted by the authors as evidence of afternoon exercise potentiating TSH and T4 responses.

Because many of the systems affected by exercise are subject to circadian rhythm, the researchers were interested in establishing whether time of day affected the response to high intensity interval training. Previous research has shown that both skeletal muscular strength and mitochondrial function peak in late afternoon.

The study authors state: 'Our results are clinically relevant, showing that timing of exercise affects the glycaemic response to high intensity interval training in men with type 2 diabetes.'

'Our data highlight the importance of optimising the timing of exercise sessions to improve glycaemic control in people with type 2 diabetes,' they add.

This was a pilot study, and a study involving larger numbers of participants with longer duration of each of the interventions is planned.

'Future studies are warranted to characterise the underlying hormonal and metabolic changes to exercise training at different times of day in healthy and diseased populations,' the study authors say.

Many patients find sustained lifestyle change challenging, and GPs should always support any increase in activity as a positive outcome. Giving the optimum advice to this group is important.

#### DR MATTHEW LOCKYER

Savikj M, Gabriel BM, Alm P et al. Afternoon exercise is more efficacious than morning exercise at improving blood glucose levels in individuals with type 2 diabetes: a randomised crossover trial. *Diabetologia* 2019;62(2):233-37

## Addiction

### Deaths associated with opioid overdose increase

A study from Ontario, Canada, has found that prescribed, diverted and illicit opioids all play an important role in the recent increase in opioid-related deaths.

The investigators conducted a population-based cohort study, examining data on 2,833 residents of Ontario who died of opioid-related causes between January 2013 and December 2016. Active opioid prescribing was defined as having at least one day's supply of a drug overlapping the date of death, and recent opioid prescriptions as those dispensed 30 days, 180 days, one year, two years, and three years before the date of death. The study also reviewed benzodiazepine and specific aspects of fentanyl prescribing. Post mortem toxicology results were obtained for all deaths.

The mean age at death was 43 years, and 67% of those who died were male. Nearly 9% had been admitted for non-fatal opioid overdose in the year before death, 26% had a diagnosis of alcohol misuse disorder and 42% had visited an emergency department for the management of a mental health problem in the preceding three years.

In 2013, 38% of those dying of opioid-related causes had an active opioid prescription on their date of death. Although the absolute number of deaths involving an active prescription increased by 15% between 2013 and 2016 (from 241 to 278 deaths), the proportion of all deaths with an active opioid prescription fell to 32.5% in 2016. However, in 2016, 80% of those attending an emergency department for an 'opioid toxicity event' had received a prescription opioid in the

past three years. Among people with active opioid prescribing at the time of death, 38% also had evidence of non-prescribed opioid use on post mortem toxicology.

Although its prevalence declined during the study period, active benzodiazepine prescriptions remained common, and in 2016 28% of people who died of an opioid-related cause had an active benzodiazepine prescription at the time of their death, while 16% had active prescriptions for both benzodiazepines and opioids.

Overall, people over 45 years and women were more likely to have active opioid prescribing at the time of death. Of those people with no active opioid prescribing, 47% of deaths involved fentanyl in 2016, a sharp increase from 20% in 2013.

The rise in opioid-related morbidity and mortality in North America over recent years has been described as an overdose crisis.<sup>1</sup> It has been argued that one contributing factor to this rise has been the rapid increase in opioid prescribing for chronic non-cancer pain. Although opioid prescribing rates may have fallen in Canada in recent years, as many as one in eight residents of Ontario were prescribed opioid analgesia during 2016.<sup>2</sup>

The researchers comment: 'The absolute number of people with an active opioid prescription who died of an overdose increased by 15% over our study period. This reinforces the need for responses to the opioid crisis that address all avenues through which people can access these drugs, including prescriptions, diverted drugs, and illicitly manufactured products.'

#### DR JEZ THOMPSON

Gomes T, Khuu W, Martins D et al. Contributions of prescribed and non-prescribed opioids to opioid related deaths: population based cohort study in Ontario, Canada. *BMJ* 2018;362:k3207

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1 Hadland SE, Kertesz SG. Opioid deaths in Ontario, Canada. *BMJ* 2018;362:k3537

2 Gomes T, Pasricha S, Martins T et al. Behind the Prescriptions: A snapshot of opioid use across all Ontarians. Ontario Drug Policy Research Network, 2017

## Smoking cessation

### Rise in vaping accompanied by fall in youth smoking

An increase in the use of e-cigarettes (vaping) has been associated with a drop in smoking by teenagers and young adults, a time trend analysis from the United States has found.

The investigators carried out a literature search using PubMed for surveys on smoking and vaping up to and including 2017. Data on cigarette use by 15-25 year olds were obtained from five different publicly available surveys.

The first of the surveys began to collect data on vaping in 2011 with all surveys collecting such data by 2014. Information on youth and young adult vaping before 2014 was limited and diverges for the different surveys, but indicates that vaping occurred at relatively low levels from 2011 to 2013, but reached much higher levels by 2014. This year was identified as the tipping point when vaping became popular among young people.

The investigators examined trends within the surveys for both past 30-day use and established smoking among young people. One of the studies indicated that the downward trend in smoking in the past 30 days was more than three times greater in the vaping period, from 2014, (a total annual relative reduction in smoking prevalence of 14.1%) than the long-term trend (an annual relative reduction of 4.6%). With established smoking, trend line analysis of daily cigarette use by 15 to 17 year olds showed about three times the annual relative reduction in the vaping period compared with the long-term trend. This reduction was even more evident

in the 18-21 year age group. Nearly twice the relative reduction in daily smoking was noted in the 22-24 year age group during the vaping period.

The researchers conclude that long-term decline in smoking prevalence among young people in the US accelerated after 2013 when vaping became more widespread. They also found that there was a decline in established smoking, as measured by daily smoking, smoking half a pack a day or having smoked at least 100 cigarettes to date and currently smoking some days or every day, which markedly accelerated when vaping increased.

The authors comment: 'It is possible that trying e-cigarettes is causally related to smoking for some youth, but the aggregate effect of this relationship at the population level may be small enough that its effects are swamped by other factors that influence smoking behaviour.'

In 2018, a report commissioned by Public Health England *Evidence review of e-cigarettes and heated tobacco products* concluded that:

'the evidence does not support the concern that e-cigarettes are a route into smoking among young people.'<sup>1</sup> This was at variance with the US National Academies of Sciences, Engineering and Medicine which published a report that concluded there was substantial evidence that vaping among young people is strongly associated with progression to smoking.<sup>2</sup>

This paper, based on data gathered from young people in the USA, helps shed further light on this dissonance.

#### DR PETER SAUL

Levy DT, Warner KE, Cummings KM et al. Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check. *Tob Control* Epub ahead of print 2018;0:1-7. doi:10.1136/tobaccocontrol-2018-054446

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2 National Academies of Sciences, Engineering and Medicine. Public health consequences of e-cigarettes. The National Academies Press. Washington DC, USA. 2018

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