

consistent across all three cohorts.

For patients with unhealthy lifestyle scores and low birthweight, the risk of developing new type 2 diabetes was increased by more than the simple sum of the two individual risk factors.

Across the cohorts studied, the new cases of type 2 diabetes could be attributed as follows:

- Low birthweight alone 22% (95% CI: 18.3-26.4%)
- Poor lifestyle alone 59% (95% CI: 57.1-61.5%)
- Additive interaction between low birthweight and unhealthy lifestyle 18% (95% CI: 13.9-21.3%)

Low birthweight is a surrogate for intrauterine stress, which is known to produce hyperglycaemia and increase the risk of diabetes. Poor lifestyle, especially obesity, an unhealthy diet and lack of exercise, is already strongly linked to the current high incidence of type 2 diabetes. This study shows that a combination of the two increases the risk by more than the addition of the risks associated with each individual factor.

The authors conclude: 'The finding suggests that most cases of type 2 diabetes could be prevented by the adoption of a healthier lifestyle, but simultaneous improvement of both prenatal and postnatal factors could further prevent additional cases.'

This is another brick in the wall of evidence that change at population level is needed to stem the current flood of new diabetes cases that underlie the statistics.

DR MATTHEW LOCKYER

● Li Y, Ley SH, Tobias DK et al. Birth weight and later life adherence to unhealthy lifestyles in predicting type 2 diabetes: prospective cohort study. *BMJ* 2015;351:h3673

Addiction

Arrhythmia risk higher with methadone than buprenorphine

Buprenorphine appears to be a safer option to methadone in terms of reduced risk of ventricular arrhythmia and sudden death from cardiac arrest, a study from the United States has shown.

The authors used pharmacovigilance data routinely submitted to the US Food and Drug Administration between 1969 and 2011 to analyse methadone- and buprenorphine-related adverse events.

The primary outcome was the composite of ventricular arrhythmia and cardiac arrest, and the secondary outcome the composite of QTc prolongation and torsade de pointes. The proportional reporting ratio (PRR) was used to identify disproportionate reporting.

A total of 4,418,215 cases were evaluated, of which 7,283 involved buprenorphine and 14,915 methadone. There were 132 (1.8%) cases of ventricular arrhythmia/cardiac arrest and 19 (0.3%) cases of QTc prolongation/torsade de pointes associated with buprenorphine prescribing compared with 1,729 (11.6%) cases of ventricular arrhythmia/cardiac arrest and 390 (2.6%) cases of QTc prolongation/torsade de pointes involving methadone prescribing.

PRR for buprenorphine was not significant for ventricular arrhythmia/cardiac arrest, 1.10 (95% CI: 0.93-1.31) or QTc prolongation/torsade de pointes, 1.03 (95% CI: 0.66-1.62) but was for methadone 7.20 (95% CI: 6.88-7.52) and 10.7 (95% CI: 9.66-11.8) respectively.

When choosing between the two drugs, the prescribing physician will balance the benefits associated with each (methadone has a cost advantage and is associated with better engagement in treatment for example) against potential problems, including the risk of adverse effects.

In the UK, as in the United States, there are only two opioid medications licensed for the management of opioid dependence – methadone and buprenorphine. Both are known to have the potential to delay cardiac repolarisation causing prolongation of the QTc interval, and predisposing to the potentially fatal arrhythmia torsade de pointes.

However, in vitro data suggest that the impact of buprenorphine in this area is relatively small, and there is some epidemiological evidence to suggest that buprenorphine prescribing is associated with a lower risk of sudden death than methadone.

As a result buprenorphine has been recommended as a safer alternative to methadone in patients at risk of QTc prolongation. Despite this, one recent study has suggested that some patients treated with high-dose transdermal buprenorphine may develop significant QTc prolongation.

Acknowledging the limitations necessarily associated with data from voluntary reporting, and the differing timelines for marketing approval for the two drugs and relative prescribing volumes, the authors of this study conclude that, pending direct safety-related research, buprenorphine appears to be a safer option to methadone in terms of reduced risk of ventricular arrhythmia and sudden death from cardiac arrest.

DR JEZ THOMPSON

● Kao DP, Haigney MCP, Mehler PS et al. Arrhythmia associated with buprenorphine and methadone reported to the food and drug administration. *Addiction* 2015;110:1468-75

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