

Prescribing...

May 2018 Hot Topics

- ✚ A large review of opioids for chronic non-cancer pain found that they were associated with far more adverse effects than previously reported in trials.
- ✚ 46% of diabetics diagnosed in the last 6 years achieved remission when given an ultra-low calorie diet plus intensive support from specialist nurses and dieticians in a Scottish Primary Care study.

Opioids for Chronic Non-Cancer Pain

A review, recently published in the *Drugs and Therapeutics Bulletin*, adds further weight to the arguments against using opioids for chronic non-cancer pain (CNCP). It reported very high rates of adverse effects, a result that is important as the harms of opioids for CNCP may have been under-estimated.

The study was a review of *Cochrane* systematic reviews which assessed the occurrence and nature of adverse events associated with opioids. The review assessed any opioid agent (any dose, frequency or route of administration) used on a medium- or long-term basis for the treatment of CNCP in adults. The overview included 16 reviews (61 studies, 18,679 participants), of which 14 presented unique quantitative data on 14 different opioid agents that were administered for periods of 2 weeks or longer. The longest study lasted 13 months, with most in the 6- to 16-week range. The reviews included 61 studies with a total of 18,679 randomised participants.

In the study's main findings, opioids significantly increased the risk of any adverse event compared with placebo (risk ratio [RR] **1.42**, 95% CI 1.22 to 1.66) or with a non-opioid active pharmacological comparator (RR **1.21**, 95% CI 1.10 to 1.33). Opioids also significantly increased the risk of a serious adverse event (RR **2.75**, 95% CI 2.06 to 3.67). Opioids were associated with significantly increased risk ratios for the following adverse events: constipation, dizziness, drowsiness, fatigue, hot flushes, increased sweating, nausea, pruritus and vomiting. The absolute event rate for any adverse event with opioids in trials using a placebo as comparison was **78%**, with an absolute event rate of 7.5% for any serious adverse event.

The *Cochrane* authors note that the studies and reviews reported a limited range of specific adverse events. In particular, the studies did not provide information on some significant harms including addiction, cognitive dysfunction, respiratory depression, sleep apnoea or sleep-disordered breathing.

The lack of data on some important adverse effects is of concern. The review's authors suggest that "reliance on earlier studies with less robust methodology may have contributed to the current opioid use epidemic and opioid overdoses and deaths." A letter published in 1980 has been inappropriately cited as evidence that addiction with long-term opioid therapy is rare. Recently updated guidelines on the management of CNCP have highlighted the risks associated with opioids and encouraged use of non-opioid drugs and non-pharmacologic therapy, rather than a trial of opioids.

As has been highlighted on a number of occasions, the prescribing of opioids by Primary Care in Guernsey and Alderney has fallen steadily since 2014. Costs, a minor concern, are now approximately £40,000 less per annum lower than they were in 2014. The largest fall has been in the prescribing of fentanyl, mainly in the 100microgram strength of the patch. We all want individual patients to have the analgesia they need, but given the world-wide issue of the over-prescribing of opioids, this is really good news. Details are overleaf.

Figure 1 : G & A Primary Care Prescribing of Opioids	Fentanyl	Oxycodone	All opioids
Quarterly prescribing 2014	679	275	4,490
Quarterly prescribing 2015	607	262	4,423
Quarterly prescribing 2016	533	213	3,913
Quarterly prescribing 2017	530	235	3,906
Change since 2014	-22%	+17%	-13%

Intensive weight management for remission of type 2 diabetes

Intensive weight management delivered within a primary care setting as an intervention for achieving remission of type 2 diabetes has been assessed in a randomised trial. The premise of the intervention was that people with type 2 diabetes can be returned to normal glucose control by calorie restriction and the entire study was funded by Diabetes UK.

This open-label, cluster-randomised trial was conducted at 49 primary care practices in Scotland and northern England. Practices were randomly assigned to provide either a weight management programme (intervention) or best-practice care by guidelines (control). The co-primary outcomes were a reduction in weight of ≥ 15 kg and remission of diabetes, defined as HbA_{1c} <6.5% (<48mmol/mol) after at least 2 months off all antidiabetic medications, from baseline to month 12.

A nurse or dietitian in each intervention practice was given a total of 8 hours structured training. Participants in the intervention group were asked to follow a weight management programme with the aim of achieving and maintaining weight loss of at least 15kg. Weight loss was induced with a total diet replacement phase using a low energy formula diet (825-853kcal/day) for 3-5 months followed by structured food reintroduction and support for long-term weight loss maintenance. All oral antidiabetic and antihypertensive drugs were discontinued on day 1 of the weight management programme.

The trial included 306 participants aged 20-65 years with type 2 diabetes diagnosed within the past 6 years, a body-mass index (BMI) of 27-45kg/m², who were not receiving insulin. At baseline, the mean weight and BMI of participants was 100kg and 35kg/m², respectively. **At 12 months, weight loss of ≥ 15 kg was recorded in 36 (24%) participants in the intervention group and no participants in the control group (p<0.0001).** Diabetes remission was achieved in 68 (46%) participants in the intervention group and six (4%) participants in the control group (odds ratio 19.7, 95% CI 7.8 to 49.8). Remission varied with weight loss in the whole study population, with the likelihood of remission directly related to the amount of weight lost. Remission of diabetes occurred in 31 (86%) of 36 participants who lost ≥ 15 kg but not in any of the 76 participants. At 12 months, 109 (74%) of 148 participants in the intervention group were taking no antidiabetic medications (mean HbA_{1c} 6.4% [46.8mmol/mol]) compared with 27 (18%) of 148 participants in the control group (mean HbA_{1c} 7.2% [54.6mmol/mol]; p=0.0032).

Development of type 2 diabetes is strongly associated with weight gain and this study provides impressive evidence of the effect of a weight management programme in achieving remission. Its results mirror some others. While the findings of the study only apply to those with type 2 diabetes diagnosed within 6 years and longer term follow up is required, it is encouraging that remission was achieved in so many patients.

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References : Opioids in Chronic Non-Cancer Pain DTB March 2018, Intensive weight management in primary care improved weight loss and remission of type 2 diabetes Lancet Vol 391, February 2018