

Hidden adverse effects: what are the long-term harms of taking opioids?

Bottom line (21st June 2016):

Long term harms identified were important and far reaching. Evidence for increased risk of overdose (of opioids and non-opioids), opioid use disorder, death and motor vehicle crashes was convincing. For these outcomes, adverse events were more likely with increasing morphine equivalent doses (e.g. >50mg day) as well as patient factors such as comorbid mental health conditions and substance misuse disorders and co-prescription with medications such as benzodiazepines. Evidence also suggested increased risk of fractures, cardiovascular events, opioid induced hyperalgesia, endocrinological harms (e.g. increased need for testosterone replacement) and respiratory problems. Having been convinced about the wide ranging and significant harms the EBP group felt that their bottom line was to first “stop starting” opioids on long term prescriptions (>3 months), closely review opioids when they are started for beneficial outcomes before further prescriptions are issued, and to try and “start stopping” opioids, however the group expressed that this is a significant challenge for long-term users of opioids.

Context:

This question was raised from the observation of an EBP group member that “It is not uncommon for older adults to be taking regular (i.e. daily) opioids and still some are taking regular benzodiazepines. In general practice it feels hard to get people off these medications when there is clinical suspicion that they are no longer required. To counsel patients effectively it would be helpful to have a good understanding of the risks of taking this medication. It was felt that short term adverse effects such as constipation, nausea and dizziness may (and in clinical experience do), in themselves, serve as a deterrent to ongoing use of opioids. Therefore, the group wished to focus on the more hidden long term harms, which may only appear in future.

PICO:

Population – (Older) adults

[‘older’ was not defined in the evening – however, over the course of the meeting evidence concerning adults of all ages was considered]

Intervention – Long-term use of opioid

[defined as 2 prescriptions in the last 90 days (based on definition used in UK cohort study) for any non-cancer, non-palliative and non-end of life indication (from CDC guidelines)]

Control – Equivalent older people not taking opioid

Outcome – Mortality, falls/fracture, memory problems, menstrual disturbance, early menopause, hypogonadism, overdose

[not to include immediate side effects which are likely to preclude ongoing use of opioids]

Evidence sources:

Primary research evidence was presented to the group by Professor Kate Dunn, key take home messages were:

- [Trends in opioid prescribing have shown increases over the last 10 years](#)
- There is evidence that opioids work in the short term for acute pain (e.g. post-operative pain) but no evidence that they work (that is there is limited evidence of poor quality which suggests that they do not work) in the long-term for non-cancer pain
- Long-term opioids are associated with fractures and [overdose](#)
- Try not to give long term opioids, but if you feel this is clinically necessary, try to use the lowest possible dose
- Cohort studies consistently suggest that those on opioids do consistently worse (including on pain scores), than those who are not, at 1 year
- Consider the CDC Guidelines for Prescribing Opioids for Chronic Pain as these have been produced on the background of a concerted effort to reduce opioid prescribing in the USA and keep watch from emerging USA data as drug companies are now required to undertake high quality surveillance to acquire licences for opioids
- Be aware that the negative outcomes from opioids are enhanced when co-prescribed with hypnotics and in the presence of multimorbidities

Evidence cited within the following guidelines was also examined:

- CDC Guideline Prescribing Opioids for Chronic Pain (March 2016) (<http://www.cdc.gov/drugoverdose/prescribing/guideline.html>)
- Faculty of Pain Medicine opioids aware (<http://www.fpm.ac.uk/faculty-of-pain-medicine/opioids-aware>)
- Canadian Long-acting opioids for chronic non-cancer pain: a review of the clinical efficacy and safety (August 2015) (http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0086009/pdf/PubMedHealth_PMH0086009.pdf)
- SIGN Management of Chronic Pain (December 2013) (<http://www.sign.ac.uk/guidelines/fulltext/136/>)

Evidence update: since we examined the literature in EBP group, further research evidence has been published by [Bedson J et al \(2019\)](#) highlighting the far reaching and significant adverse events associated with opioid use

Impact:

Two GPs undertook audits of current prescribing practice – how many patients aged 65yr or older have had 2 or more opioid prescriptions in the last 90 days (opioids at dose equivalent to codeine 30mg or above – thus excluding pholcodine linctus, co-codamol 8/500, co-codamol 15/500, codeine 15mg). In two different practices, roughly 2% of the practice list size were identified as taking opioids as per this definition.

*I have “stopped starting” opioids on repeat compared to what I used to do
(GP Partner)*

*If opioids are not having a beneficial effect, I am very cautious about
escalating the dose and am now much more likely to just stop them
instead (GP Partner)*

I am much clearer about the rules about driving when taking opioids and am better at advising patients about this when prescribing opioids (GP Partner)

I use these findings to talk to medical students I teach in the practice about prescribing for chronic pain. I had not heard of opioid induced hyperalgesia before and often nor have they. (GP Partner)

Due to the shared difficulty identified within this topic by primary care health professionals, a subsequent Chronic Pain Masterclass (www.keele.ac.uk/agp) was hosted by the Keele Academic General Practice to support local clinicians to manage patients with chronic pain while reducing use of opioids.