Editor—The use of opioids for non-cancer pain indeed remains a controversial subject. Simpson has given an excellent overview. One particular area of concern is that there are few available data regarding the efficacy and safety of high dose opioids given over years rather than months. Whereas it was previously thought that unlimited dose escalation was at least safe, this dogma has recently been questioned. Long-term use of opioids may be associated with the development of abnormal sensitivity to pain, immunosuppression, and hormonal changes. I have found measurement of testosterone levels and replacement therapy to be an important consideration in male patients presenting with loss of libido in such circumstances.

Patients with chronic pain may have symptoms that last 24 h a day, but short-acting opioids offer relief for only 3–4 h. For these patients, I generally recommend the use of long-acting opioids. Use of long-acting opioids may result in more predictable serum levels, less abuse, less reinforcement of drug-taking behaviours, and improved sleep, compared with short-acting opioids. The toxicity of acetaminophen is also avoided.

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Editor—Thank you for the opportunity to respond to the letter from Dr Gajraj about my Editorial. The point is well made that there are few available data regarding the efficacy of opioids for persistent pain, even in the short term. The reference from Ballantyne and Mao is required reading for all opioid prescribers. A recent systematic review only identified 16 assessable randomized controlled trials on this important topic. There was insufficient evidence to prove that different long-acting opioids were associated with different efficacy or safety profiles. There was also insufficient evidence to determine whether long-acting opioids were more effective or safer than short-acting opioids. Not a single study could be rated as good using standard evidence-based grading systems. Many studies only observe patients for a very few weeks; this is not particularly helpful in those with long-term pain, in whom it is important to gather information about opioid use over many months and years. A recent study concerning cognitive function and opioids, monitoring patients over 12 months, illustrates some of the difficulties inherent in such research, for example the inevitably high drop out rate. In this trial, only 18 of the initial cohort of 28 were still taking morphine at the end of the study period. It is important that investigators, funding bodies, and those in industry are encouraged to support well-designed, long-term trials. Regulatory bodies will increasingly require long-term studies; many are already specifying 12 weeks of data for chronic pain. Prolonged use of opioids can cause hyperalgesia, neuroendocrine and immune effects; this is well recognized. The clinical significance of these effects is uncertain, but we need to monitor them closely in both males and females. Most national guidelines favour the use of modified release or transdermal opioids for long-term use and suggest avoiding the use of short-acting preparations. There are good theoretical reasons for this, but again little hard evidence. At present we just do not have adequate information on which to base treatment of persistent non-cancer pain with opioids, so it is important to work within common recommendations and monitor patients closely.

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