accounted for 20% of this variance in study effects and length of exposure to opioid analgesics accounted for a further 18%. Studies deemed of good quality were associated with a significantly lower incidence (3.1%) than those of fair quality (15.1%).

Strong opioids were associated with a significantly lower incidence (0.7%) than weak opioids (5.5%). Rates of dependence and abuse were found to be lower among those prescribed opioids for a longer period, 3 months or more (2.3%), than in those prescribed opioids for a varied period (10.7%).

Prescribing of opioids in the management of chronic non-cancer pain has been increasing in recent years, and prescribers need to balance their desire to provide relief from pain against the risks of contributing to physical dependence, addiction and diversion of prescribed opioids. This paper provides useful additional information that will assist in getting the balance right.

The study authors caution that differences in aetiology, pain severity or the nature of the pain may account for these counter-intuitive findings.

They conclude: 'There is a need for well designed, rigorously controlled, adequately powered prospective experimental studies examining the incidence – rather than prevalence – of iatrogenic opioid dependence and abuse after analgesic prescribing.'

DR JEZ THOMPSON

Higgins C, Smith BH, Matthews K. Incidence of iatrogenic opioid dependence or abuse in patients with pain who were exposed to opioid analgesic therapy: a systematic review and meta-analysis. *Br J Anaesthesia* 2018;120(6):1335-44

Smoking cessation

Can nicotine preloading help smokers quit?

The use of a nicotine patch before quitting may have a modest effect on abstinence, a large pragmatic randomised trial has found.

Patients listed as smokers on their health records were invited to take part in the trial. Pregnant and breast-feeding women, patients with a skin condition that precluded use of the patches and those with medical conditions potentially aggravated by high nicotine levels were excluded.

A total of 1,792 adults were enrolled from Nottingham, Birmingham, Bristol, and London. All were daily smokers with tobacco dependence.

Around half (889) were randomised to the preloading arm and 893 to the control arm. Patients in the former group used a 21 mg/24 hr nicotine patch daily for approximately four weeks before quit day unless there had been night-time problems during a previous attempt in which case day time only use was advised.

Participants in both arms were referred to the NHS stop smoking service and received standard pharmacotherapy and behavioural support to encourage cessation.

Participants were asked to smoke as normal and not reduce consumption as this would probably lower blood nicotine levels, which could make cigarettes more rewarding and thus undermine the potential benefits of preloading.

At baseline participants' smoking history and basic demographic information were recorded. This included two markers of cigarette dependence: the Fagerstrom test for cigarette dependence, which measures consumption of cigarettes and difficulty in refraining from smoking, and the concentration of exhaled carbon monoxide.

Participants returned one week after the baseline appointment (about three weeks before quit day). Adverse events and adherence to preloading were assessed. They were telephoned one week after quit day and about six weeks after baseline, to collect data on adverse events, adherence to preloading, and use of, and adherence to, other smoking cessation pharmacotherapy.

Data on smoking cessation from the NHS stop smoking service or the participant at + 4 weeks were obtained. At six and 12 months participants were telephoned to obtain data on smoking status and health service use. Abstinence was assessed biochemically by measuring the concentration of expired carbon monoxide.

Biochemically validated abstinence at six months was achieved by 157 of 899 participants (17.5%) in the preloading arm and 129 of 893 (14.4%) in the control arm: difference 3.0% (95% CI: – 0.4 to 6.4%), odds ratio (OR) 1.25 (95% CI: 0.97 to 1.62), P = 0.08 in the primary analysis. When varenicline was used as post-cessation treatment this gave an OR for the effect of preloading of 1.34 (95% CI: 1.03-1.73), P = 0.03: difference 3.8% (95% CI: 0.4 -7.2%).

The investigators conclude: 'Nicotine preloading with a 21 mg/24 hr nicotine patch for four weeks seems to be efficacious, safe, and well tolerated, but probably deters the use of varenicline, the most effective smoking cessation drug. If it were possible to overcome this unintended consequence, preloading could lead to a worthwhile increase in long term smoking abstinence.'

DR PETER SAUL

The Preloading Investigators. Effects on abstinence of nicotine patch treatment before quitting smoking: parallel two arm, pragmatic randomised trial. *BMJ* 2018;361:k2164

»