Clinical reviews

Our panel of GPs review recent research papers in their specialist areas that may influence the way you practise

Reviewers

Addiction
Dr Jez Thompson
MB ChB MSc MRCGP
GPwSI substance misuse, Leeds, UK

Cardiovascular disease
Dr Peter Savill
BSc (Hons) MBBS PGDipCard
Former GP, Community Cardiology Specialist, Southampton and Mid Hampshire, UK

Diabetes
Dr Matthew Lockyer
MB BS DCH DRCOG DFFP MRCGP
Former GP with an interest in diabetes, Suffolk, UK

Mental health
Dr Phillip Bland
BA BM BCh MRCGP DRCOG
Former GP with an interest in mental health, Dalton-in-Furness, UK

Obstetrics and gynaecology
Dr Chris Barclay
MB ChB FRCOG
GP with an interest in O&G, Suffolk, UK

Paediatrics and allergy
Dr Peter Saul
MB ChB DCH DRCOG FRCGP
GP with an interest in paediatrics and allergy, Wrexham, Associate GP Dean N. Wales, Visiting Professor Glyndwr University, UK

Respiratory disease
Dr Peter Saul
MB ChB DCH DRCOG FRCGP
GP with an interest in respiratory disease, Wrexham, Associate GP Dean N. Wales, Visiting Professor Glyndwr University, UK

Sexual health
Dr Richard Ma
MRCGP DFSRH DCH DRCOG DipGUM DrPH
GP with an interest in sexual health and NIHR Research Fellow, Imperial College, London, UK

Smoking cessation
Dr Jez Thompson
MB ChB MSc MRCGP
GPwSI substance misuse, Leeds, UK

Paediatrics

Do inhaled corticosteroids in the early years affect growth?

Use of inhaled corticosteroids (ICS) in young children was associated with a slightly reduced height at the age of six but only in those who continued treatment into their sixth year, in a prospective study from Denmark.

ICS usage was documented in two cohorts of children from the Copenhagen Prospective Studies on Asthma in Childhood up to the age of six years. There were 411 children in the first study which commenced in 2000 and 700 children in the latter study which began in 2010.

Height was measured regularly until age six and dual energy X-ray absorptiometry (DXA) scans were carried out at ages six to seven years to calculate bone mineral composition.

The cumulative dose of ICS was calculated. ICS usage was categorised into four groups. The reference group included those children with no use or a cumulative ICS dose ≤ 10 weeks of treatment with standard ICS dosage (400 mcg budesonide daily or equivalent). The remaining children were divided into tertiles of increasing ICS exposure.

The primary outcomes were height and bone mineral content at age six.

Overall, 930 children (84%) from the two cohorts had had a height measurement at six years and 792 (71%) had had a DXA scan.

Of the 930 children with height measured at age six, 291 (31%) had received a cumulative ICS dose equivalent to > 10 weeks of standard treatment before the age of six.

Those in the group with highest exposure had received a cumulative ICS dose corresponding to a median of 2.9 years of standard treatment.

A total of 111 children were identified as being on treatment between the ages of five and six.

- After adjusting for confounders, such as gestational age and length and weight at birth, the cumulative ICS dose as a continuous measure from 0 to six years was inversely associated with height at age six: -0.26 cm (95% CI: −0.45 to -0.07; P = 0.006) height difference per year of standard treatment
- However, this was mainly driven by children still treated after age five: −0.31 cm (95% CI: −0.52 to −0.10; P = 0.004) height difference per year of standard treatment
- There was no significant association for those not treated after age five: −0.09 cm (95% CI: −0.46 to 0.28; P = 0.64) height difference per year of standard treatment
- In the subgroup of children having received the largest cumulative dose of ICS, and still receiving ICS in the sixth year, there was a height difference of -1.16 cm (95% CI: −1.94 to −0.38; P = 0.004)

There was no association between ICS use and bone mineralisation at age six.

The study authors conclude: 'We found evidence that ICS use was associated with reduced height at age six years but only in children with continued treatment in the sixth year of life. We found no effect on bone mineral content.'

'A subgroup of children with continued use of ICS and the largest cumulative doses showed evidence of a minor height difference. The height development of this group of children into adulthood should be explored,' they add.

For young children the use of ICS seems to have no adverse effects on growth at age six providing it has been stopped by age five.

DR PETER SAUL

Kunøe A, Sevelsted A, Chawes BLK et al. Height and bone mineral content after inhaled corticosteroid use in the first 6 years of life. *Thorax* Published Online First 19 January 2022

Smoking cessation

E-cigarettes fail to help smokers quit

Using e-cigarettes for smoking cessation neither improved the chance of quitting successfully nor helped to improve relapse rates, in a large nationally representative cohort study from the USA.

Data were analysed from respondents in the PATH Study who were established cigarette smokers in 2016 and who reported a recent quit attempt. In 2017, the study included data on 3,578 previous year smokers with a recent quit attempt and 1,323 recent former smokers. Respondents reported using e-cigarettes or other products to quit smoking cigarettes.

Study outcomes included at least 12 months of cigarette abstinence in 2019.

Smokers who reported using e-cigarettes to help them in their most recent cigarette quit attempt were less likely rather than more likely than other quit attempters to achieve successful cigarette cessation.

- Although sales of high nicotine e-cigarettes increased in the USA in 2017 this did not translate to more smokers using these e-cigarettes to quit smoking. In 2017, 12.6% (95% CI: 11.3-13.9%) of recent quit attempters used e-cigarettes to help with their quit attempt. This was a reduction compared with previous years
- Cigarette abstinence for e-cigarette users was lower than for those who used no product to help them quit; 9.9% (95% CI: 6.6-13.2%) vs 18.6% (95% CI: 16.0-21.2%)
- The adjusted risk difference (aRD) for e-cigarettes compared with pharmaceutical aids was −7.3% (95% CI: −14.4 to -0.4%); and for e-cigarettes vs no product use −7.7% (95% CI: −12.2 to -3.2%)
- A very small proportion, only 2.2% (95% CI: 0.0-4.4%) of recent former smokers switched to high nicotine e-cigarettes
- Those respondents who switched to e-cigarettes appeared to have a higher relapse rate to cigarette smoking than those who did not switch to e-cigarettes. However, this difference was not statistically significant; aRD 9.4% (95% CI:-5.0 to 22.8%)

The study authors state: 'In this analysis of the most recent PATH Study data, smokers who reported using e-cigarettes to help them in their most recent cigarette quit attempt were less rather than more likely than other quit attempters to achieve either successful cigarette cessation or to become tobacco and e-cigarette free.

'Rather than e-cigarettes adding four additional successful cigarette quitters per 100 quit attempters compared with pharmaceutical aid users as concluded by a systematic review of RCT data,[1] in this study e-cigarette use was associated with seven fewer successful quitters per 100 quit attempters.'

'Furthermore, switching to e-cigarettes did not reduce the risk of relapse to cigarette smoking compared with other recent former smokers. Instead, nearly 60% of recent former smokers who were daily e-cigarette users had relapsed to cigarette smoking by 2019,' they add.

DR JEZ THOMPSON

Chen R, Pierce JP, Leas EC et al. Effectiveness of e-cigarettes as aids for smoking cessation: evidence from the PATH Study cohort, 2017–2019. *Tob Control* Published Online First 7 February 2022

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1 Hartmann-Boyce J, McRobbie H, Lindson N et al. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev* 2020;10:CD010216

Addiction

Chronic use of prescription opioids and initiation of injecting drug use

The risk of initiating injecting drug use is eight times higher for patients who receive long-term prescription opioid medication for non-cancer pain compared with that of opioid naïve patients, a large retrospective cohort study from Canada has found. However, the five-year cumulative probability of injecting drug use initiation in this group was only 4%.

The authors used data from a large administrative data source, the Integrated Data and Evaluative Analytics (IDEAs) cohort, covering approximately 1.7 million people in British Columbia to investigate any association between prescription opioid treatment for non-cancer pain and initiation of injecting drug use among individuals without a history of substance misuse at baseline.

Prescription of opioid medication for non-cancer pain was identified from PharmaNet, a province-wide database, for drugs dispensed between 2000 and 2015.

Prescribing episodes were classified by length and intensity of opioid use into acute, episodic, and chronic.

Injecting drug use initiation was identified by means of a high specificity algorithm.

A total of 59,804 participants (14,951 from each opioid use category) were included in the matched cohort. Around half, 30,140, of the participants were male and the median age was 44. Median follow-up was 5.8 years. Overall, 1,149 participants commenced

injecting drug use during the study period.

Half of the chronic opioid episodes were longer than two years.

The cumulative probability of injecting drug use initiation at five years was highest for participants with chronic prescription opioid use and lowest in those who were opioid naïve:

- Chronic prescription opioid use (4.0%)
- Episodic use (1.3%)
- Acute use (0.7%)
- Opioid naïve (0.4%)

Initiation of injecting use was eight times higher, hazard ratio (HR) 8.4 (95% CI: 6.4-10.9), for those with chronic prescription opioid use compared with those who were opioid naïve.

Initiation of injecting drug use was more frequent at higher opioid doses and younger ages.

In a sensitivity analysis limited to individuals with a history of chronic pain, cumulative risk for those with chronic use (3.4% within five years) was lower than the primary results. However, the hazard ratio was higher; HR 9.7 (95% CI: 6.5-14.5).

The risk of developing substance misuse problems while on long-term prescribed opioid medication is well documented, and a systematic review of prescription opioid treatment for chronic pain estimated average rates of opioid misuse and addiction to be 21-29% and 8-12%, respectively.[1] However, little is known about the risk of initiation of injecting drug use.

The study authors conclude: 'The rate of injection drug use initiation among individuals who received chronic prescription opioid treatment for non-cancer pain was infrequent overall (3-4% within five years), but 8-10 times higher than opioid naïve individuals. Rate of initiation was more frequent with greater doses and at younger ages.'

However, they caution that their findings 'should not be used as a reason to inappropriately taper or discontinue long term prescription opioid treatment.'

Though initiation of injecting use was relatively uncommon in those prescribed opioid medication for the management of chronic non-cancer pain, GPs should be aware of this potential harm when considering prescribing opioids.

DR JEZ THOMPSON

Wilton J, Abdia Y, Chong M et al. Prescription opioid treatment for non-cancer pain and initiation of injection drug use: large retrospective cohort study *BMJ* 2021;375:e066965

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1 Vowles KE, McEntee ML, Julnes PS et al. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *Pain* 2015;156:569-76

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If you would like to comment on any of the clinical reviews write to: **editor@thepractitioner.co.uk**