

# Codeine addiction and abuse

## Introduction

Young adults in South Africa are using codeine-based cough syrup and sugary drinks (with or without alcohol) to give them a 'high' prior to going out to parties/social events. Referred to as 'lean' or 'purple', these drinks are becoming a regular feature of many of today's teenagers' social lives.

Less easy for the clinician to identify is misuse of codeine; in other words, its use outside of normal, acceptable medical practice. This may take the form of self-medicating at higher doses than needed and for longer periods than advisable. Addicted adults may even recognise their addiction and refer to codeine as 'my companion, my secret solace' to others. Others regard codeine as a 'relatively safe' over-the-counter medication and do not recognise their increasing reliance on this medication.

A lot has been written about codeine abuse in South Africa, including a current review of the issue of over-the-counter availability of cough syrups with codeine by the South African Health Products Regulatory Authority (SAHPRA). Medical professionals in South Africa are generally cautious when prescribing codeine, particularly in children under the age of 12 years, but still have clinical concerns around recognising, screening and detecting codeine abuse.<sup>1</sup> The recent South African Medical Research Council survey among medical practitioners provides useful insights on their perspectives and questions about codeine use and abuse in South Africa.

*"We are seeing a dramatic increase in the number of people under the age of 18 years coming in for treatment for problems related to the abuse of codeine."*

Professor Charles Parry,  
South African Medical  
Research Council



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## LEARNING OBJECTIVES

You will learn:

- The principles of pain management and how to avoid prescribing potentially addictive medicine to patients at high risk
- How to identify codeine misuse and abuse
- The latest evidence of the actual pain relief obtained from low-dose over-the-counter codeine
- The clinical evidence for pain relief and the numbers needed to treat (NNTs) for prescription-level codeine and non-opioid pain-relieving medicines
- Which non-opioid pain relievers have the best evidence for which common clinical conditions
- How to manage codeine misuse and abuse.

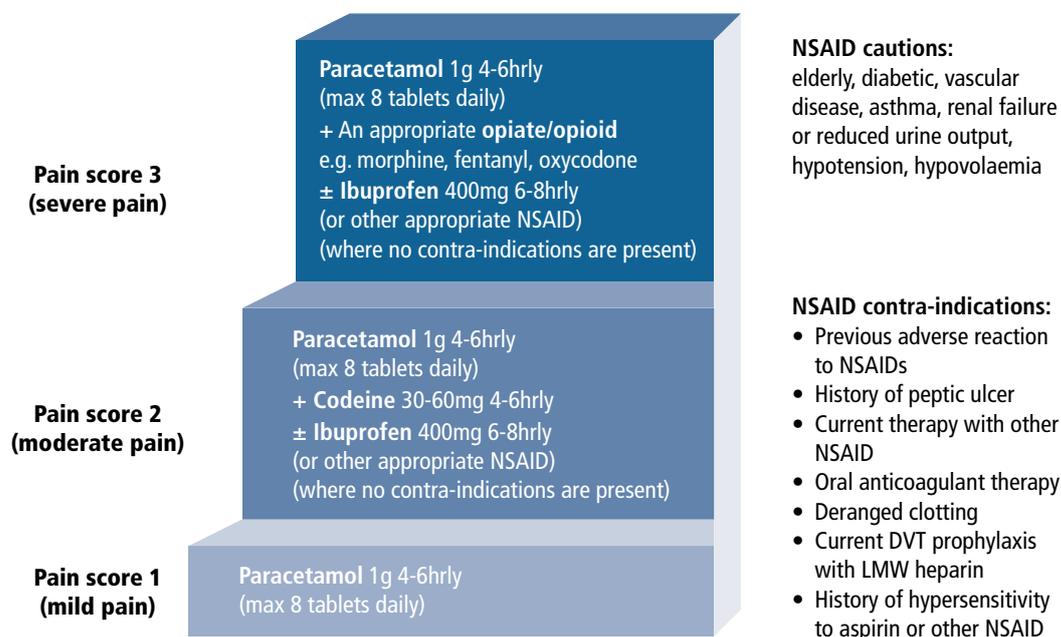
## South African medical professionals' perspectives on codeine prescribing, misuse and abuse

Codeine (3-methylmorphine) is a weak opioid; it undergoes O-demethylation by CYP2D6 to morphine and morphine-6-glucuronide. Only 5-10% of codeine is metabolised in this pathway, the remainder is converted to inactive metabolites and excreted.

Codeine is commonly prescribed in primary care for pain-related conditions in adults as well as for the treatment of cough and, to a lesser extent, diarrhoea. In South Africa, codeine combination products containing paracetamol, ibuprofen or aspirin are sold without a medical prescription (<20mg codeine). Codeine linctus syrups commonly contain up to 10mg of codeine phosphate per 5ml. In 2017, the Food and Drug Administration (FDA) announced restrictions on the use of codeine in children younger than

12 years of age and warned that codeine products should not be used to treat pain or cough in children. A number of organisations, including the WHO and the European Medicines Agency, have issued warnings against the use of codeine in children. Typically, South African products containing codeine carry a warning that they should not be used in children under 12 years of age.

The South African survey among general practitioners of attitudes to codeine prescribing was unfortunately biased towards older doctors with an average period in practice of more than 20 years.<sup>1</sup> Nonetheless, these practitioners displayed uncertainty about the effectiveness of <20mg codeine in pain relief, even when used according to the WHO analgesia ladder (Figure 1).



**Figure 1. Recommended analgesia for adult patients**  
(Based on the WHO analgesia ladder and provided by [www.pain-talk.co.uk](http://www.pain-talk.co.uk))

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These family practitioners also noted that pharmacists are well placed to address the issue of patient understanding

of potential codeine overuse, particularly when providing over-the-counter codeine-containing medicines.

## ISSUE

### How to avoid prescribing potentially addictive medicine to patients at higher risk of dependency or abuse?

Prescribers should assess and monitor risk by asking about over-the-counter use, also observing patient behaviour. Patient

behaviour can alert the clinician to potential misuse (Table 1).

**Table 1. Patient behaviours that should trigger suspicion of codeine misuse**

• Requesting treatment with codeine-containing medication or other opioid medication
• History of addiction
• Unresolved pain/cough
• Physical/psychological symptoms (doctor- or pharmacy-hopping, pain out of proportion to identified cause, losing script or medication)
• Aberrant behaviour (missed appointments, history of no therapeutic response to any treatment except opioids, signs of over-sedation).

*South African family practitioners routinely ask about the use of over-the-counter medicine and feel that patients do not understand the risk of dependence when using codeine-containing medication*

## ISSUE

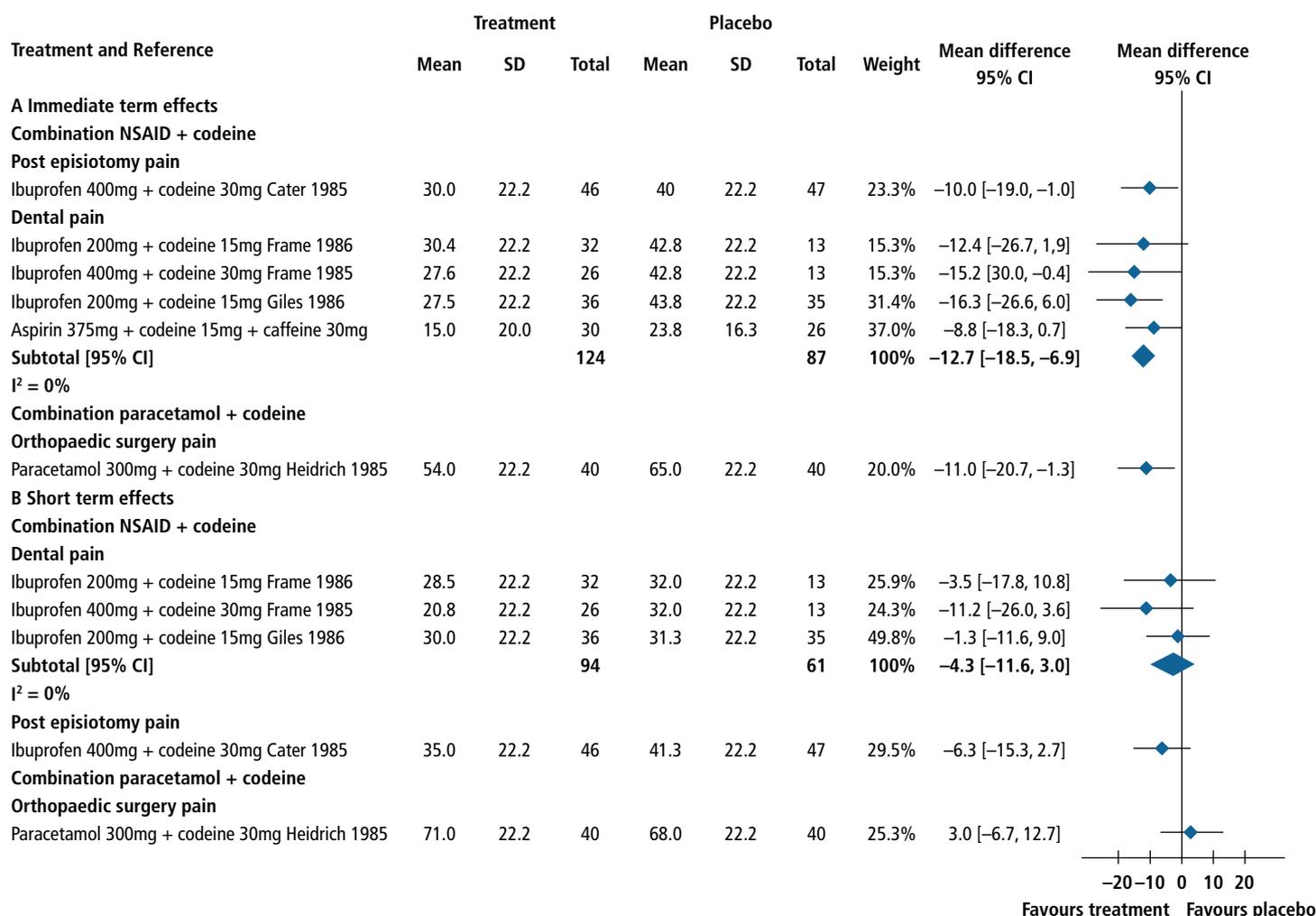
### How effective are low-dose codeine-containing combination analgesics for pain? (i.e. over-the-counter codeine-containing analgesics)

The South African family practitioners' survey expressed doubt as to the efficacy of low-dose codeine combinations typically available in relatively low doses (<30mg/dose). They are frequently formulated as combination medications with either paracetamol or a nonsteroidal anti-inflammatory drug (NSAID) and/or an antihistamine.

The first thorough evaluation of the efficacy of low-dose codeine was published late last year (2019) based on 10 selected randomised clinical (double-blind) trials that met the criteria of evaluating combination analgesics containing codeine (up to 30mg/dose) in combination with (a); ibuprofen/aspirin, or (b); paracetamol and an antihistamine, for any pain condition.<sup>2</sup>

The results, summarised in Figure 2, show the following key clinical findings:

- There is low-to-moderate evidence that single doses of these low-dose combinations provide immediate, but slight pain relief (a reduction of 10 points on a 1-100 scale) for acute nociceptive pain such as dental pain (e.g. after wisdom teeth removal) and pain after surgery
- A short course (up to three days) provides slight pain relief following laser eye surgery and *moderate* pain relief for chronic musculoskeletal conditions, e.g. osteoarthritis
- There is no randomised controlled trial evidence to guide the use of these combinations for either headaches or low back pain.



**Figure 2. Pain relief: meta-analysis of low dose codeine-containing combination analgesics**

A, Pooled immediate-term effects from OTC combination codeine medicines at 3 hours.

B, Pooled short-term effects of combination OTC medicines containing codeine at time points from 4 to 6 hours. CI indicates confidence interval; NSAID, nonsteroidal anti-inflammatory; OTC, over-the-counter

Longer duration of use must be carefully balanced against the risk of adverse

effects and the possibility of provoking continued opioid use in the long term.

## ISSUE

### How effective is prescription codeine (60mg), alone or in combination, in achieving pain relief?

The latest Cochrane review of single-dose oral analgesics for acute post-operative pain in adults provides reliable data on which to base short- and longer-term therapy using these pain-relieving agents.<sup>3</sup>

The review provides NNTs to achieve effective pain relief, according to reliable

published data not regarded as subject to potential publication bias (Figure 3).

Adverse effects and potential for abuse must be considered when assessing a patient for longer-term prescribing, i.e. more than a few days per week.

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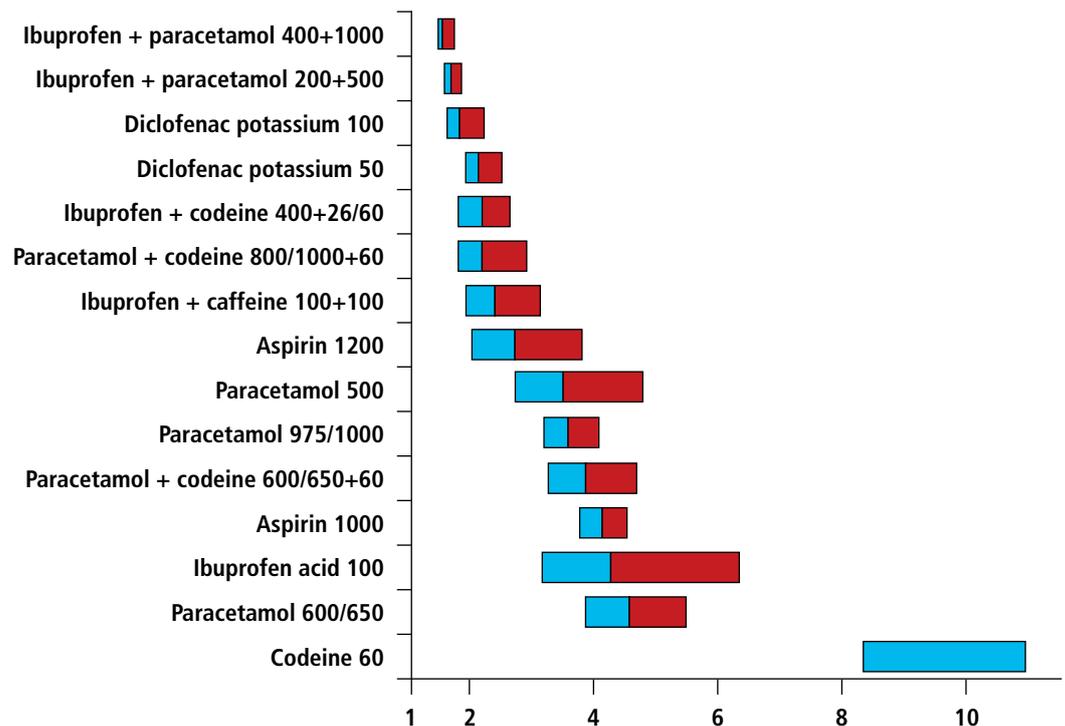


Figure 3. Single-dose oral analgesics in moderate or severe pain: NNTs to achieve at least 50% maximum pain relief over 4-6 hours

NNT for at least 50% pain relief (95% CI) compared to placebo

*The reviewers conclude that it is appropriate to consider the use of low doses of combination medicines containing codeine (<30mg) as an initial opioid treatment (step 2 on the WHO analgesia ladder) for the treatment of moderate-to-severe acute pain conditions*

## ISSUE

### Which non-opioid alternatives can be used for effective pain relief in adults?

The WHO analgesia ladder suggests the use of non-opioid medications first and, if this does not achieve the desired results, particularly when treating chronic pain, the clinician can consider the use of codeine-containing analgesics.

The National Institute for Health and Care Excellence (NICE) has produced useful primary care guidance for

mild-to-moderate pain based on current evidence;<sup>4</sup> it points out firstly that the underlying cause of the pain should be treated wherever possible and a full therapeutic dose should be used before switching to another stepped-up analgesic (Table 2). Ideally, single agents should be used and titrated upwards before using combination analgesia.

Table 2. Common acute pain conditions and the recommended evidence-based analgesia

Lower back pain	NSAIDs, e.g. diclofenac 100mg twice/three times per day. Use at the lowest possible dose for the shortest period possible. Do not give paracetamol only
Tension-type headache	Aspirin (300mg 3 x daily), or paracetamol or a NSAID – taking patient preference and comorbidities into account
Sprains and strains	Paracetamol (500mg–1g 4 x daily) or topical NSAID. Consider oral NSAID if after 24 hours post-injury
Period pain	NSAID unless contra-indicated due to, for example, gastrointestinal bleeding/ulcer, severe liver/ kidney impairment

**ISSUE****How to detect and manage codeine dependency?**

The extent of codeine misuse and dependence in South Africa is not well documented. The best data are available from the South African Community Epidemiology Network on Drug Use, some 66 treatment centres across South Africa that voluntarily provide data on their patient profiles. In 2014, 17 260 drug-dependent admissions were recorded and 2.5% of these involved codeine as

a primary or secondary substance of abuse/misuse.<sup>5</sup> It should be noted that these are high-dose or recreational-use dependencies requiring specialist centre intervention.

The severity of codeine dependency encountered in clinical practice varies from therapeutic dependence, arising from long-term use, to high-dose dependency (Table 3).<sup>6</sup>

**Table 3. Types of codeine dependency**

**Therapeutic dependence – long term over-the-counter use**

- Taking daily recommended dose for prolonged periods (years)
- Dose escalation – intended to manage pain, commonly headaches
- Lifting mood, reducing anxiety or numbing emotions

**Non-medical dependence/recreational use**

- Using purely for euphoric effect, often with good knowledge of ingredients and harms
- Use of addictive agent only by extraction (e.g. cold water extraction)
- Possibly originating with pain control needs and transitioning

**High-dose dependence**

- Very high daily doses (over 100 tablets in some cases)
- Opioid withdrawal; continued use despite harm; multiple pharmacy visits each day

**ISSUE****How to treat therapeutic dependency at a low level of use (<12 tablets/day)**

The approach to treating these patients is based on:

- Slow, gradual withdrawal of the codeine-containing medication
- Providing alternative non-opioid analgesia
- Reassuring the patient
- Providing information on and treatment of any withdrawal symptoms such as runny eyes and nose, sneezing,

sweating, hot flushes, loss of appetite, goose-bumps (Figure 4).

At a moderate or high level of use (>12 tablets/day) referral to specialist services should be considered, as opiate withdrawal at this level presents specific challenges requiring hospitalisation or in-facility care.

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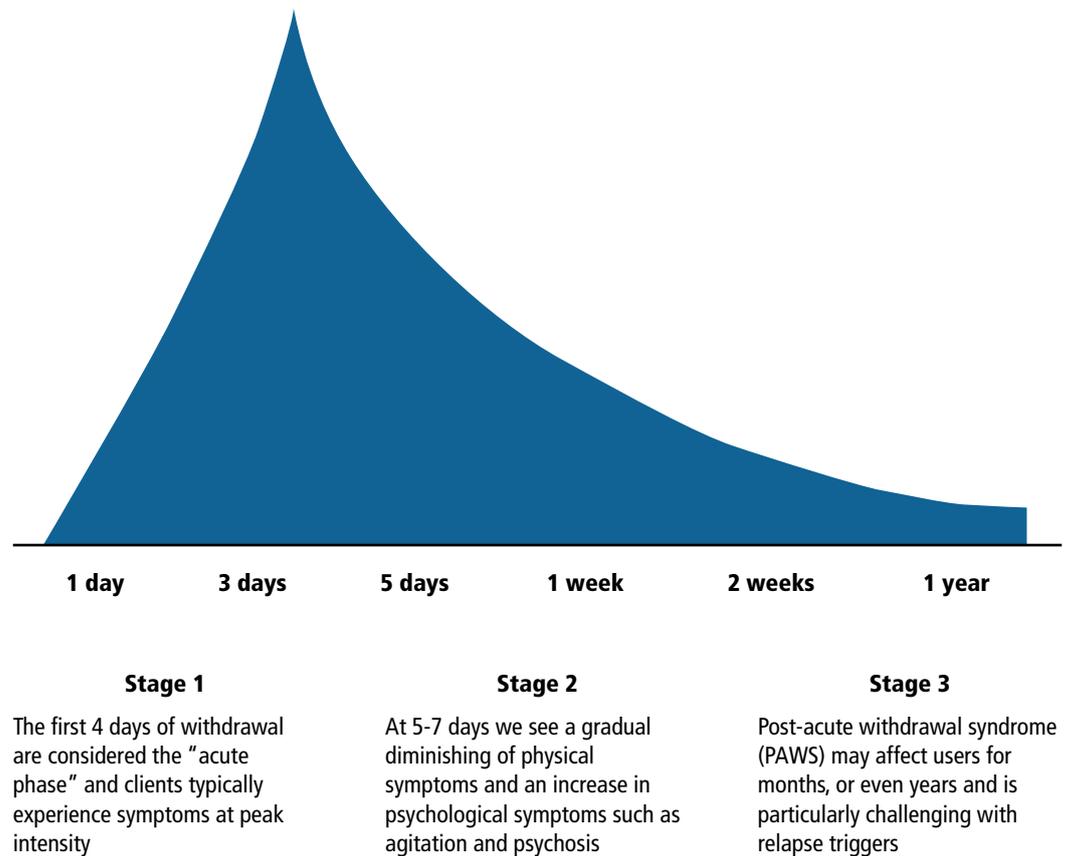


Figure 4. Codeine withdrawal timeline

## ISSUE

### How to maintain abstinence after withdrawal

Sustained abstinence is dependent on successfully addressing:

- Pain issues – discuss and develop a personalised pain management plan with the patient
- Mental health issues – patients frequently experience or are already being treated for anxiety, depression and/or stress
- The need for psychological support to deal with relationship issues, family discord and possibly the social network that the patient may belong to whose members are also users of medication, alcohol or other opioid drugs
- Regular monitoring of the patient's progress.

## Conclusion

Appropriate use of non-opioid painkillers can help to reduce a patient's exposure to and risk of developing codeine-dependency. Greater awareness among the general population of the risk of misuse of

over-the-counter codeine would be helpful. Clinicians should warn patients that over-the-counter products offer benefits, but should not be used chronically without medical support.

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## KEY LEARNINGS

- Codeine abuse and misuse, outside normal medical prescribing, is on the increase in South Africa
- Cochrane reviews show moderate pain relief with low-dose codeine treatment in musculoskeletal conditions, and minor relief of acute pain, such as dental and post-surgery pain
- Prescription of codeine, which is an opioid, albeit only a weak opioid, should follow the WHO principles of analgesic medicine: use non-opioids at the first step in pain management, followed by opioids as needed
- Red flags with regard to potential codeine misuse/abuse are evident in patient behaviour (lost prescriptions, requests for opioids) and symptoms
- Useful alternatives to codeine are NSAIDs, aspirin and paracetamol, which should be matched to clinical circumstance and need, e.g. back pain, headache and dysmenorrhoea
- Primary care management of low-level codeine abuse (<12 tablets/day) involves slow withdrawal, replacement of codeine with other pain relievers, treatment of withdrawal symptoms, patient support and education.

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