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## Qualitative Health Research

### 'Codeine is my Helper': Misuse of and dependence on codeine containing medicines in South Africa.

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'Codeine is my Helper': Misuse of and dependence on codeine containing medicines in South Africa

### Title

'Codeine is my Helper': Misuse of and dependence on codeine containing medicines in South Africa.

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*'Codeine is my Helper'*: Misuse of and dependence on codeine containing medicines in South Africa

### **Abstract**

Misuse of codeine containing medicines is an emerging global public health concern. The majority of research has been conducted in developed countries (European Members States, Australia, United States). This study aimed to gain an understanding of unique individual and collective experiences of trajectories of codeine misuse and dependence in South Africa. In-depth interviews were conducted with a purposive sample of adult codeine misusers and dependents (n=25). Narratives were analyzed using the Empirical Phenomenological Psychological five step method. Nine themes with 63 categories emerged, with two additional high levels of abstraction. Findings are illustrated participant profile and product preferences; motives for use; transitioning to misuse and dependence; pharmacy purchasing and alternative sourcing routes; effects and withdrawal experiences; help-seeking and treatment experiences; and strategies for prevention. The study underscores the need for continued support for enhanced patient awareness of risk of habit forming use and related health consequences and professional pharmacovigilance.

### **Key Words**

Codeine, dependence, misuse, opiate, over-the-counter, qualitative

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*'Codeine is my Helper'*: Misuse of and dependence on codeine containing medicines in South Africa

Misuse of and dependence on codeine containing medicines is an emerging global public health concern, given widespread availability of this weak opiate for the symptomatic relief of mild to moderate pain or cough (Lessenger & Feinberg, 2008; UNODC, 2011; Van Hout et al., 2014). Prescribed and non-prescribed opiate misuse trends appear driven by enhanced regulatory encouragement of patient self-care, prescribing trends and pharmacy retail availability (Collins & McAllister, 2006; Cooper, 2013a). Misuse is broadly defined as 'the use of a medicine, with or without a doctor's prescription, clearly outside of accepted medical practice or guidelines, for recreational purposes or in the framework of self-medication, in greater dosages or for longer periods than were prescribed, in which the risks and problems associated with use outweigh the benefits' (Casati, Sedefov & Pfeiffer-Gerschel, 2012:229-230).

Codeine or 3-methylmorphine is a methylated morphine derivative which occurs naturally in the poppy seed. Recommended adult daily oral doses ranges between 30-60mg every four hours and to a maximum of 240mg (Derry, Karlin, & Moore, 2013). Patient responses to codeine vary due to genetic variability in metabolism (Ingelman-Sundberg, 2007). Given codeine's sedating and euphoric effect and development of tolerance within a relatively short timeframe on repeated use, products containing codeine carry identified abuse potential as reported in drug administration trials (Babalonis, Lofwall, Nuzzo, Siegel, & Walsh, 2013) and the case reporting of patient dependence (Sproule, Busto, Somer, Romach, & Sellers, 1999; Frei, Nielsen, Dobbin & Tobin, 2010; Nielsen, Cameron & Pahoki, 2010). Increased consumption of codeine containing medicines whether for therapeutic or non-therapeutic reasons results in neuro-adaptation and development of dependence symptomatology (Nielsen et al., 2010; McAvoy, Dobbin & Tobin, 2011; Reed et al., 2011). Two-way and reciprocal displacement between prescribed and over the counter codeine misuse is reported in the literature (Cooper, 2013b). Withdrawal symptoms include cravings, preoccupation with seeking and taking codeine containing medicines, and lack of control of consumption patterns despite negative side effects (Romach, Sproule, Sellers, Somer, & Busto, 1999).

Harms relating to misuse of and dependence on codeine containing medicines are well documented in clinical case reporting (Robinson, Robinson, McCarthy, & Cameron, 2010) and center on adverse health consequences relating to additives (such as ibuprofen, paracetamol or acetaminophen) contained in combination analgesic products. These include hypokalaemia, nephro-toxicity, gastrointestinal hemorrhage, acute hemorrhagic necrotizing pancreatitis and inflammatory bowel conditions (for an extensive review see Van Hout et al., 2014). Codeine misuse is also recognized as an iatrogenic cause of psychiatric co-morbidity (Manchia, Alda, & Calkin, 2013). Depression and dysphoric mood states are associated with long term use of

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codeine containing medicines (Romach et al., 1999; Frei et al., 2010; Nielsen et al., 2010; McAvoy, Dobbin & Tobin, 2011).

The majority of research on the misuse of and dependence on codeine containing medicines has been conducted in developed countries (United Kingdom (UK), Australia, France and the United States). Scoping reviews have underscored the heterogeneous nature of codeine misusers and those in treatment for dependence relating to age, gender, socio-economic status, presence of co-morbidity and substance disorders, and as distinct from other opiate using populations (Nielsen, Cameron & Lee, 2011; Van Hout et al., 2014; Nielsen et al., 2015). Prevalence of such diverse patterns of codeine misuse and dependence remain problematic in terms of surveillance and monitoring systems, with estimates based on treatment cases for codeine dependence (Pates, McBride, Li, & Ramadan, 2002; Skurtviet, Faru, Borchgrevink, Handal, & Fredheim, 2011; Roussin, Bouyssi, Pouche, Pourcel, & Lapeyre-Mestre, 2013). Low uptake for treatment is reportedly due to patient lack of recognition of problematic codeine use, and with individuals dependent on codeine generally perceiving themselves to be different from other drug users (Romach et al., 1999; Pates et al., 2002; Nielsen et al., 2010). Barriers to treatment uptake for codeine dependence centre on stigma and poor consideration of needs (Reed et al., 2011).

In South Africa codeine containing medicines are currently available both over-the-counter (OTC) in pharmacies and as prescribed formulations. At the time of writing, the Medicines Control Council and the South African Department of Health are considering introducing regulations to reduce the amount of codeine in a single tablet to 10 mg and further tighten up on the sale of OTC medications containing codeine. Efforts to intervene and regulate the safe supply of codeine containing medicines have additionally centered on the "Codeine Care Project", which uses a 2D barcode printed on the packs of all codeine containing medicines and a secure central database which monitors the national purchase of these medicines with national restrictions of sale set at 4g. This initiative incorporates additional customer informational and self-screening support in the form of a free phone app.

Until recent times, national surveillance of problematic codeine consumption in South Africa was limited. Myers, Siegfried, and Parry (2003) in their study of 9 063 patients from 23 specialist substance abuse treatment centers in Cape Town, South Africa found that 1.25% of treatment admissions were using analgesics as a secondary substance of abuse, of which 40.4% reported the misuse of codeine-containing medication. The South African Community Epidemiology Network on Drug Use (SACENDU) initiated the measurement of codeine misuse in 2014. According to the latest SACENDU data collected (July to December 2014) at

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specialist drug treatment centers, (Dada et al., 2015) 263 (of 10197) treatment admissions involved codeine misuse or dependence as a primary or secondary substance of abuse (2.6% of all admissions). Out of 263 codeine misuse admissions, only 78 had codeine as their primary substance of abuse. In contrast to earlier studies reporting majority middle aged female representation (Myers et al., 2003), the majority of patients misusing or dependent on codeine in the SACENDU 2014 reporting period (Dada et al., 2015) were male with age ranging from 11 to 70 years. The highest proportion of patients was aged 20 to 29 (30.8%), followed by 30-39 years (22.8%); and just over 18% under the age of 20 years. The majority of patients had a high school education or above and under half (45.2%) reported being currently employed. Nearly a third (34.4%) had received prior treatment.

To date, qualitative investigations around user and patient experiences of codeine misuse and dependency have been conducted in the United Kingdom (Cooper, 2011, 2013b), Australia (Nielsen et al., 2010; Nielsen et al., 2011; Nielsen, Cameron, & Pahoki, 2013), and with drug users interacting in online drug forums (Van Hout, 2015). To date, little qualitative research on the issue of misuse of prescribed and over the counter available codeine medicines has been conducted in the developing world. In this study we aimed to gain an understanding of unique individual and collective experiences of trajectories of codeine misuse and dependence in South Africa.

### Method

#### *Participants*

The study was undertaken as part of a large scale international collaborative research consortium ("CODEMISUSED") on codeine use, misuse and dependence in Ireland, the UK and South Africa. A purposive sampling strategy was used to identify adult individuals in South African treatment centres with experience of codeine misuse and/or dependence. Exclusion criteria centred on the following: participants under 18 years of age; non-S.A residents; individuals reporting codeine use within accepted medical guidelines; individuals suffering from serious mental health problems and individuals with a known history of violence or aggressions.

Recruitment was facilitated by the National Head Office of the South African Council for Alcoholism and Drug Dependence (SANCA) who have over 30 clinics and satellite clinics throughout South Africa. Referrals were requested from addiction treatment providers (gatekeepers) with restrictions to three to six eligible participants

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per centre, and with balance across Gauteng, Western Cape and Kwa Zulu Natal. Additional recruitment of participants was supported by the 64 treatment centres that participate on the SACENDU surveillance system.

#### *Instruments*

An interview guide was developed based on the scoping review conducted by the CODEMISUSED consortium (Van Hout et al., 2014) and on extensive consultation between international partners. The guide centred on patient profile, use, misuse and dependence experiences, sourcing mechanisms, risk perceptions, awareness of harm, and experiences of treatment. In order to assess dependence, participants completed the Severity of Dependence Screener (SDS) (Gossop et al., 1995) prior to interview. SDS is a 5-item questionnaire with scores of over five indicating dependent use of codeine containing medicines in the past 12 months.

#### *Procedure*

All interviews (n=25) with the exception of one were conducted face to face with the participants in a private area at the various treatment centres. Interviews were conducted by one researcher, with a note taker. All interviews were conducted in English, audio-taped with permission and lasted between 30 - 90 minutes. Participants were given a R100.00 shopping voucher in acknowledgment of their time.

#### *Ethical Considerations*

Ethical approval was granted by the Ethics Committee of the South African Medical Research Council (Protocol number EC021-11/2014). All researchers signed a Code of conduct, Data use and Confidentiality Agreement. All participants received an information and consent form, which was explained verbally by the investigator prior to interview. Face to face participants provided written consent prior to interview. In the case of the telephone interview, the interviewer and a witness signed the consent form. Assurances of confidentiality and anonymity were provided to all participants, along with permission to withdraw from the study if desired.

Audio recordings were stored on a password protected encrypted hard drive, and destroyed following transcription. Transcribes were coded for anonymity and stored on a password protected encrypted hard drive, following removal of any personal identifiers (Wilkinson & Thelwall, 2011).



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### *Data Analysis*

Transcribes were transferred in totality into a Word document with the final data set of 122,395 words. The Empirical Phenomenological Psychological (EPP) five step method (Karlsson, 1993) was utilized to analyse the data. This approach facilitates the interpretation of meaning and incremental understanding of lived phenomena (Husserl, 1970) such as the *'life world'* experience of codeine use, misuse and dependence.

Nine themes with 63 categories emerged from the analysis (Table 1). During the final step in the EPP analysis process, two additional higher levels of abstraction above the theme-level emerged and which centred firstly on the concept of misuse of codeine as coping mechanism to manage and pre-empt the occurrence of physical and psychological pain, in many cases relating to severe trauma and distress (for example, 'Eventually there was not any pain, but I was scared of the pain in my mind' (Male Participant) and 'that would be my helper and I would run to my helper [codeine containing medicines]', (Female Participant), and secondly the concept of the reinforcing nature of social circumstances in underpinning addiction (for example 'I actually abused the codeine to suppress my depression and to give that euphoric effect. I felt a lot of isolation, guilt and grief' (Male Participant). All raw data were re-read with these two abstract concepts described by participants in distinct ways.

*Insert Table 1 here*

## **Results**

### *Participant Profile and Product Preferences*

Sixty percent (n=16) of the sample were male and 40% (n=10) were female. Participants ranged from 21 to 74 years (mean age 43) with 67% (n=15) aged between 30-49 years. Sixty four percent (n=16) were unemployed although two of these were studying, one was disabled and a further two were retired. Twenty participants admitted to mis-using codeine within the last 12 months and the majority scored 10 or above (52% n= 13) on the SDS. Thirty-two percent reported codeine tablets as their primary drug of use, 20% reported codeine syrup as their primary drug of use and 12% reported consuming both.

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***Insert Table 2 about here***

In terms of tablet formulations containing codeine, Stilpane®, Syndol®, Myprodol® and Adcodol® were amongst the most common codeine containing medicines misused (Table 2) while a number of participants also had a history of using illicit drugs such as heroin, cannabis, cocaine and ecstasy. Some used codeine in combination with alcohol with a small number of female participants combining with diet pills.

Thins? [Diet pills]. And that's actually how I started [codeine], experiencing feeling good.

(Female Participant).

Some had previous experiences of misusing codeine based cough mixtures either on their own or with codeine containing tablets.

***Motives for Codeine Use***

Bio-psycho-social motives were identified as to why participants initially used or continued to misuse codeine containing medicines. Two male participants describe how they were socially exposed to codeine and the psychosocial reasons as to why they continued to take it:

A friend of mine introduced it to me at a party. So I started taking it, to relax my mood. It is all exhausting, all the stress in my life. (Male Participant).

Many participants reported taking codeine based medications to manage physical pain as a result of chronic conditions such as arthritis, migraine and severe headaches or to relieve pain (acute or chronic) following surgical interventions. One woman's description typifies this trajectory of codeine use leading to misuse:

I had a hysterectomy almost two years ago [and] that is when I started to use codeine, and also I got it through my sister. I had a problem with insomnia and then headaches because you are not sleeping. (Female Participant).

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Many experienced various psychological issues in their lives, for example, depression, anxiety and stress related conditions and used codeine to deny or suppress their symptoms.

I actually started using codeine as I was very depressed. I used it to lift up my moods, all the grief. (Male Participant).

Social issues were viewed as both contributing to and a consequence of codeine use and misuse. Some reported that emotional and tangible support from family and friends sustained them through difficult times associated with their codeine use, misuse and dependence. Alternatively, poor social support, for example, lone parenting, marital and relationship disharmony, childhood experiences of a negative divorce process, unemployment and low self-esteem were reported as contributing stressful life factors that led to and sustained their codeine misuse and dependence. Consequences of misuse were loss of social support networks, for example, family, friends and work. A male participant summarises how codeine misuse and dependence led him to become:

More and more isolated from life. I didn't care. I robbed myself through my own actions of human connectivity. I love my wife, I've always loved her, but I loved the drugs more at that point. Codeine was a real gateway, numbing yourself to the [social] world. (Male Participant).

*Transitioning from Codeine Use to Misuse and Dependence*

Initially, for many participants their use of codeine containing medicines was appropriate and used for legitimate reasons, prescribed or over the counter, to manage discrete episodes of pain. They were largely unaware of codeine's addictive potential and the harms related to additives in Adcodol® or Myprodol®. Some were totally unaware of their actual addiction to codeine despite increase in their use; desire to continue to misuse and not being able to stop. Awareness of habit forming use and related tolerance was a gradual and subtle process with often a sudden realisation that they were consuming more than normal, sometimes recreationally, with their *'bodies'* experiencing withdrawal and requiring more codeine containing medicines.

Others commented on how:

You can get very quickly addicted. (Female Participant).

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Furthermore, one female health care worker describes how this pattern of use would *'escalate'* especially as a result of on-going life events negatively impacting upon her to a position where:

Things... go wrong ...and I would run to my 'helper' [codeine containing medicine] and I would abuse whatever I took [beyond] the prescribed dose. (Female Participant).

Daily use progressed within several weeks and many described how various stressors in their lives rapidly escalated their use of codeine containing medicines. Their daily use helped participants cope and tolerance grew quickly due to the medicines relaxing effects and pain management qualities. An increase in daily use,

It creeps up on you particularly if you've got an addictive personality. (Male Participant).

Others observed the pre-empting of physical pain and stated:

It escalated from a prescribed dose that said take two to three times a day or two to eight hourly, I would just take six or eight at one time. It would be nothing to take two packs of Stilpane®. In the beginning it wasn't a problem, but as things started to go wrong, that would be my helper and I would run to my helper [codeine containing medicines] (Female Participant).

Use of codeine containing medicines was characterised by intense craving and the need to consume in order to function throughout the day. One participant observed that if the cravings could:

just disappear, it would make it easier [to manage use]. (Male Participant).

### *Process of Pharmacy Purchasing*

Many participants were of the view that over the counter codeine containing medicines were not drug[s] per se due to their free availability to purchase without any real regulations or protocols guiding their sale. Only a

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minority (two) reported reading the product information leaflet and both were health professionals and aware of the addictive potential and related harms.

Pharmacies were the primary source for purchasing codeine containing medicines. Most participants purchased over the counter with a few using scripts from their doctors. All described accessing multiple pharmacies in different locations and at various times in order to avoid suspicion. One male participant summarised a typical purchasing regime for many codeine misusers:

I used to just walk in every week and ask for a hundred Adcodol® tablets. I used to use certain pharmacies in the area where I knew I could, like with the Stilpane® you obviously needed a script, I knew which pharmacies to go to without a script and I'd get it. (Male Participant).

Participants described how it became a feature of their purchasing regime to identify the pharmacies within an area and to use intentionally each to build up their supply of codeine. Another male participant provides the following account:

[When] I walk into a mall, I immediately pick up on the amount of pharmacies that are in the mall and it became a very engrained thing for me [to do]. If I drive around I can see there's a pharmacy, there's a pharmacy, there's a pharmacy, so I would go around [pharmacy shopping] one day a week. (Male Participant).

The male participant then proceeds to describe how he would purchase with relative ease and little or no questioning by pharmacy staff:

Just drive around inside there picking up cough syrup bottles from large pharmacies, different pharmacies and the thing is they don't really have a system to track it between pharmacies, [and] just give it out very, very, easily. (Male Participant ).

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However, he had to exercise caution as certain pharmacy chains had computer monitoring systems that were linked and this appeared to act as a deterrent. He describes how one major pharmacy chain questioned his recent purchasing history:

XXXX [pharmacy chain] did notice at one time and asked me; 'What happened? You bought from us like a week ago. It's a 200ml bottle, it's supposed to last like 2 months, not a week', and so I just said 'my bottle fell and broke' and she gave me another one but said next time I'm going to need a prescription. (Male Participant).

Being prepared to answer queries in a deceitful manner was a regular occurrence. Participants were manipulative when negotiating a script from their doctor or when purchasing codeine containing medicines. One male participant described this process and his awareness of how best to extract codeine from combination formulations (cold water filtration).

I'd go and find another doctor, lie to them. It just became [part of] myself, a habitual liar, deceiving people, exaggerating. Exaggerating symptoms and manipulating the conversation. I always had an answer. I was pre-prepared before I went in. My response to a good result would be 'thanks very much' and walk out [of] the pharmacy wash it out [cold water extraction] and drink it. Some of the pharmacies are very responsible, [and] they ask you questions but the end result is always the same [you get your codeine]. (Male Participant).

Some suggested that they are so many pharmacists in the cities and some are 'corrupt... and this presents major problems' (Male Participant) for South Africa and their regulation and monitoring of over the counter sales of codeine. It was felt that some 'pharmacies will just give you prescription drugs with no script.' (Female Participant).

*Diverse Alternative Sourcing Routes*

Alternative methods for sourcing codeine containing medicines centred on internet purchasing and diversion via prescriber, street and family routes. Travel to other jurisdictions with less stringent regulations around pharmacy

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supply was reported, for example, to the Netherlands, UK and Ireland. Online access was an option for some and was favoured due to its accessibility with little or no questioning with regards to purchase transactions.

I looked on the internet. I found that there are different kinds of opioids and that codeine was easily accessible. No one questioned me when I went to buy it. (Male Participant).

Two participants described how their overseas travels created ideal opportunities for them to purchase over the counter codeine containing medicines. Others described purchasing on the 'black market' (Male Participant). Consulting several doctors was favoured by some especially when they were away from their home territory. They would report exaggerated 'pain symptoms' (Female Participant) to the doctors so as to yield scripts. Additionally, one health care worker described how her professional role and workplace facilitated her access to:

All prescribed painkillers and I used to be able to get hold of them quite easily. I was working in places where I could get it. (Female Participant).

### *The Codeine Effect*

Initial use of codeine containing medicines centred on physical pain. This use for the management of pain was accompanied by recognition of codeine's pleasurable effects and it giving a 'buzz' (Male Participant), as well as its relief of some negative emotional symptoms related to stress, anxiety or depression. There is an 'ultimate feeling of euphoria, relaxation and fulfil[ment] otherwise known as [the] 'honeymoon phase... a sense of feeling good' (Female Participant).

You're taking it to stop pain and then you start realising it's taking the pain away but it's also making me feel good. (Female Participant).

Consumption of codeine containing medicines was a coping mechanism for many. One male participant described how he initially used cocaine but when he started misusing codeine his pain (physical and psychological) was subjectively better managed:

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Eventually there was not any pain, but I was scared of the pain in my mind. The cocaine was an uplift. It makes you feel stronger, awake, alert. But the moment I found the codeine, it would bring me down, calm me down, [I] don't have to be present. All the things in the world that is horrible are just gone, all the physical pain would go away. (Male Participant).

Another male participant stated how he used to feel depressed and that 'the world is against you' and how 'codeine would make you feel better and [he would] go, go back [to how he normally felt]' (Male Participant). Others reported taking codeine with alcohol and marijuana. The 'high' (Male Participant) associated with codeine was sustained longer when taken with marijuana, whilst combined with alcohol produced a 'more relaxed [feeling] and... took... the edge off [you emotionally]' (Male Participant). Furthermore, some who drank copious amounts of codeine based cough syrup as well as misusing codeine tablets experienced gross disturbances of perception leading to various types of visual and auditory 'hallucinations' (Male Participant) coupled with suspicious or paranoid thought processes.

Common side effects reported were gastrointestinal related, for example, dry mouth, loss of appetite and weight, vomiting, nausea, stomach cramps and constipation. Other common adverse side effects included headaches, dizziness, excessive perspiration, 'goosebumps', tachycardia and palpitations. Some participants were aware of the long term effects that codeine misuse could lead to, for example, liver and kidney damage caused by additives in combination products containing paracetamol (acetaminophen), and depression and anxiety relating to codeine itself.

#### *Withdrawal Experiences*

Experiences of unpleasant withdrawal symptoms such as pain (physical and psychological), fear, crying, self-pity, irritability, anxiety, aggression, disturbed sleep patterns, perspiration, 'the turkey skin and shivering' (Male Participant) and 'shocks down my body' (Male Participant) were described. Such experiences often contributed to their continued use of codeine products. One woman describes her initial reason for use and her trajectory for sustained misuse as a consequence of withdrawal experiences:



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It starts off with real pain. And then it [codeine] helps that pain because now you're feeling good. You start noticing that every time taking it, I'm feeling good. Then you start taking it to feel good. But then another headache comes and you're taking more. It's a vicious cycle. Before you know it you're withdrawing and you will walk into a chemist and buy it. (Female Participant).

Two women describe their experiences in trying to stop taking codeine:

It's horrific; it's terrible its wrong but you can't stop yourself. It's like you say today is the last day and maybe you skip one day but the next day as soon as that chemists opens you're there.

You can't stop; it's a non-stop train and I'm so scared. (Female Participant).

Some report resorting to other illicit drugs or engaging a hobby as a means for managing the cravings for codeine. As one young man states:

I only smoked weed [cannabis] every now and then. It helps to calm me and helps with the relief of craving for codeine. That's not going to help me going from one drug to the next. I just try and do a hobby. I'm still battling. (Male Participant).

While most participants described strong cravings and withdrawal effects, another young male reported how he successfully managed to reduce his misuse of codeine:

Every time I tried to stop on my own I'd just taper down and just use fewer and fewer and fewer. There were still a little bit of withdrawal symptoms but it wasn't as bad as what it could have been if I just like stopped immediately. (Male Participant).

### *Help-seeking and Treatment Experiences*

Help-seeking and treatment for dependency involved detoxification, rehabilitation and counselling interventions. Many described their experiences of attending 'rehab centres' and the importance of dealing with underlying issues that impacted upon their addictions. Acceptance of being an addict and the impact this had

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both psychologically and socially (family and work) motivated many to seek help. As one male participant describes:

I just drowned in drugs [codeine and other drugs] and all this stuff is coming up again. I have relapsed so many times because I have never dealt with it. (Male Participant)

Some had preference for psychological interventions, for instance seeing a psychologist to help them cope with their depression, anxiety or stressful situations. One young man felt that his 'on-going use of [codeine] cough syrup to numb [his] depression' was exhausting and negatively impacting upon his life; whilst others reported Suboxone® as being a very effective substitute in helping them 'not to crave for the codeine' (Male Participant). Some participants commented that an integrated pharmacy led detoxification treatment approach could complement existing treatment services or perhaps offer an alternative to mainstream drug treatment clinics.

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*Strategies for Prevention*

While over the counter codeine containing medicines are regarded by many as effective medicines, a number of strategies were highlighted to promote more responsible use and minimise the risk of misuse and dependence. Areas highlighted were legislative changes and the up scheduling of codeine products; greater awareness and education of consumers by professionals that prescribe and dispense the medicines; enhanced implementation of strategies already in place, for example, the 'Codeine Care' project; greater enforcement of regulations governing the sales of codeine products and marketing strategies by manufacturers that clearly highlight to consumers that 'codeine is highly addictive' (Female Participant). The provision of information leaflets alone was regarded as ineffective as most people tend not to read them. A female participant makes an analogy that:

[unlike] the cigarette companies...We don't have any warnings. Just that small little paper [leaflet]. Who reads that; doctors tell us [but we] don't really read it. Put the warning [on the box] that it's addictive. (Female Participant).

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**Discussion**

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In this study we illustrated unique qualitative and contextual insights into codeine misuse and dependence in South Africa, and is the first study of its kind investigating this form of opioid pharmaceutical misuse and dependence within a developing country. The study builds on growing interest into codeine misuse and dependence pathways and trajectories as distinct from other forms of opiate dependence in the UK (Cooper, 2011), and Australia (Nielsen et al., 2010). We recognise limitations of the study given the relatively small sample size, presence of history of prior drug taking histories and the effects of poly substance use behaviours. However 'trustworthiness' of the data gathered (Lincoln & Guba, 1985) in illustrating the codeine misuse and dependence phenomenon is enhanced by the verification of extensive similarities across the lived experiences and social contexts of these South African participants relating to codeine misuse as coping aid for physical pain and psychological pain, and dependence trajectories affected by social circumstance and isolation. Horizontal and vertical consistency was visible in the interpretation of the data, and supported by partial phenomenological psychological reduction (Karlsson, 1993).

Estimation and surveillance of misuse of codeine containing products is hampered by widespread and easy availability and the heterogeneous and hidden nature of misuse (Van Hout et al., 2014). Accessing of multiple pharmacies in a variety of locations and at different times, and to lesser extent, prescribers appeared common (Hamer, Spark, Wood, & Roberts, 2013). Efforts to secure multiple purchases appeared grounded in accessing many pharmacies, with little or no intervention from staff, existence of so called corrupt pharmacies, and free availability exempt from protocols or regulations guiding safe supply of non-prescription codeine-containing medicines. Integrated pharmacy chain monitoring systems represented a deterrent. Diversion, '*drug tourism*' and web sourcing offered alternative mechanisms to avoid detection. Similar to SACENDU data (Dada et al., 2015), Stilpane®, Syndol®, Myprodol® and Adcodol® were commonly misused. Of interest is that in South Africa, misuse and dependence on codeine cough syrup (CCS) (Benylin®) was reported, in contrast with user preferences for codeine containing tablets elsewhere (Cooper, 2013b; Van Hout, 2015). Misuse and dependence on CCS is reported in the US southern states (Elwood, 1999; Peters et al., 2003; Peters et al., 2007; Agnich, Stogner, Miller, & Marcum, 2013) Poly pharming to potentiate the effect with illicit drugs, alcohol, and diet pills was reported.

Similar to studies in Australia, France and the UK (Nielsen et al., 2010; Nielsen et al., 2011; Nielsen et al., 2013; Roussin et al., 2013; Cooper, 2013b) and SACENDU data in 2014 (Dada et al., 2015), daily use of codeine containing medicines for more than six months was common, and progressed within weeks of commencing use. Side effects of use were typically opioid related (constipating, stomach cramps, nausea,

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emesis, headache). Awareness of both the medicines abuse and addiction potential, and harms related to additive (paracetamol or acetaminophen, ibuprofen) content in combination products was generally low. Also of note was whilst the recognition of the pleasurable effect was central, individuals' lack of awareness of therapeutic and non-therapeutic forms of tolerance, escalation in frequency and dosage used, cravings and withdrawal symptoms mediated pathways toward dependence. Patient difficulties in self-identification of problems associated with their codeine use were common (Pates et al., 2002; Nielsen et al., 2010), and appeared grounded in the context of self-regulation vulnerabilities (Khantzian, 1997; Markou, Kosten & Koob, 1998; Nielsen et al., 2010) such as the pre-empting of the occurrence of physical pain related to chronic conditions such as arthritis, migraine and severe headaches or to relieve pain post-surgical interventions, alleviation of emotional distress, self-medication of anxiety and social isolation; and for the numbing of trauma tied to life events. This so called 'blurring' of self-medication for therapeutic and legitimate reasons (pain) and misuse pathways toward iatrogenic dependence is described elsewhere (Sproule et al., 1999; Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008; Nielsen et al., 2011; Roussin et al., 2013) and in this study appeared fuelled by the presence of underlying psychiatric co-morbidity (depression, anxiety disorders), and the causal relationship with negative social and environmental circumstances of the codeine addict, and social consequences of addiction. Self-detoxification attempts as a result for the most part appeared unsuccessful. Treatment given these unique characteristics required psycho-social intervention, and opiate substitution modalities for optimal outcomes.

### Conclusion

In this study a unique illustration of the codeine use, misuse and dependence phenomena in South Africa emerged. Whilst the South African 'Codeine Care' initiative represents an important and unique effort to counter misuse and inadvertent and intentional forms of dependence on codeine containing medicines, there remains a public health and medicines regulatory imperative in South Africa to consider up-scheduling, promotion of non-opioid analgesics, enhance patient awareness of abuse risk and dependence, and the related harms from excessive or long term use of combination products, ensure national pharmacy and medical surveillance and monitoring of misuse of medicines, and develop appropriate treatment protocols both within existing treatment services and as adjunct community based detoxification in pharmacies. Optimal treatment outcomes will require tapering of medication with long term and top-up cognitive behavioural based supports (Darker, Sweeney, Barry, Farrell, & Donnelly-Swift, 2015) given the interplay between the presence of physical

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or emotional pain, maladaptive coping mechanisms, destruction of social connectivity for addicts, stigma and particular needs of this distinct treatment cohort (Fishbain et al., 2008; Otto et al., 2009; Zahradnik et al., 2009; McAvoy, Dobbin & Tobin, 2011; Reed et al., 2011).

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For Peer Review

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'Codeine is my Helper': Misuse of and dependence on codeine containing medicines in South

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Tables

Table 1 Themes and Categories

<i>Participant Profile and Product Preferences</i>	<ol style="list-style-type: none"> <li>1. Stilpane®, Syndol®, Myprodol® and Adcodol® most common.</li> <li>2. Codeine cough mixtures included Benylin® .</li> <li>3. Some history of using illicit drugs such as heroin, cannabis, cocaine and ecstasy.</li> <li>4. Some use of codeine containing medicines in combination with alcohol.</li> <li>5. Minority female combining codeine containing medicines with diet pills.</li> <li>6. Some use of codeine based cough mixtures on their own or with codeine containing tablets.</li> </ol>
<i>Motives for Codeine Use</i>	<ol style="list-style-type: none"> <li>7. Bio-psycho-social motives identified as central to initial use and pathways toward misuse and dependence.</li> <li>8. Management of physical pain (arthritis, migraine, post surgery and severe headaches)</li> <li>9. Used to suppress psychological (depression, anxiety) and stress related conditions.</li> <li>10. Social issues contributed to and a consequence of codeine use and misuse.</li> <li>11. Emotional and tangible support from family and friends sustained patients through difficult times related to use, misuse and dependence.</li> <li>12. Poor social support contributed to stressful life factors underpinning initial and continued misuse and dependence.</li> <li>13. Consequences of misuse were loss of social support networks.</li> </ol>
<i>Transitioning from Codeine Use to Misuse and Dependence</i>	<ol style="list-style-type: none"> <li>14. Initial use was appropriate and used for legitimate therapeutic reasons.</li> <li>15. Lack of awareness of codeine’s addictive potential and the harms related to additives.</li> <li>16. Lack of awareness of personal actual addiction to codeine despite increase in their use; desire to continue to misuse and not being able to stop.</li> <li>17. Awareness of habit forming use and related tolerance was a gradual and subtle process underpinned by tolerance and withdrawal.</li> <li>18. Pattern of use would ‘escalate’ as a result of on-going life events.</li> <li>19. Daily use progressed within several weeks.</li> <li>20. Daily use helped support coping.</li> <li>21. Use for pre-empting of physical pain.</li> <li>22. Use characterised by intense craving and the need to consume in order to function throughout the day.</li> </ol>

<p><i>Process of Pharmacy Purchasing</i></p>	<p>23. Without regular daily use sleep patterns were disrupted.</p> <p>24. View that over the counter codeine containing medicines were not drug[s] per se due to their free availability to purchase without any real regulations or protocols guiding their sale.</p> <p>25. Pharmacies were the primary source for purchasing codeine containing medicines.</p> <p>26. Majority purchasing over the counter with a few using scripts from their doctors.</p> <p>27. Accessing of multiple pharmacies in different locations and at various times in order to avoid suspicion.</p> <p>28. Identification of pharmacies within an area and use intentionally to build up supply.</p> <p>29. Purchasing with relative ease and little or no questioning by pharmacy staff.</p> <p>30. Computer monitoring systems appeared to act as deterrent.</p> <p>31. Being prepared to answer queries in a deceitful manner was a regular occurrence.</p> <p>32. Manipulative behaviour when negotiating a script from the doctor or when purchasing codeine containing medicines.</p> <p>33. Corruption in pharmacy sales viewed to underpin codeine misuse.</p>
<p><i>Diverse Alternative Sourcing Routes</i></p>	<p>34. Alternative methods for sourcing centred on internet purchasing and diversion via prescriber, street and family routes.</p> <p>35. Travel to other jurisdictions with less stringent regulations around pharmacy supply.</p> <p>36. Online access favoured due to its accessibility with little or no questioning with regards to purchase transactions.</p> <p>37. Purchasing on the 'black market'.</p> <p>38. Consulting several doctors when away from their home territory and facilitated by exaggerating pain symptoms.</p> <p>39. Health care work facilitated access.</p>
<p><i>The Codeine Effect</i></p>	<p>40. Initial use of codeine containing medicines centred on physical pain with recognition of codeine's pleasurable effects, as well as its relief of some negative emotional symptoms related to stress, anxiety or depression.</p> <p>41. Consumption of codeine containing medicines was a coping mechanism.</p> <p>42. Use of codeine with alcohol and marijuana for optimal effect.</p> <p>43. Consumption of codeine based cough syrup as well as misusing codeine tablets caused gross disturbances of perception leading to various types visual and auditory coupled with suspicious or paranoid thought processes.</p> <p>44. Common side effects; dry mouth, loss of appetite and weight, vomiting, nausea, stomach cramps and constipation.</p>

	<p>45. Common adverse effects; headaches, dizziness, excessive perspiration, 'goose bumps', tachycardia and palpitations.</p> <p>46. Some awareness of long term effects such as liver and kidney damage, delirium and personality change.</p>
<i>Withdrawal Experiences</i>	<p>47. Experiences of unpleasant withdrawal symptoms; pain (physical and psychological), fear, crying, self-pity, irritability, anxiety, aggression, disturbed sleep patterns, perspiration, tremors and goose bumps.</p> <p>48. Such experiences often contributed to their continued use of codeine products.</p> <p>49. Difficulties were described in trying to cease use.</p> <p>50. Use of other illicit drugs (cannabis) or engaging a hobby as time diversion as a means for managing the cravings for codeine.</p> <p>51. One report of successful detoxification.</p>
<i>Help-seeking and Treatment Experiences</i>	<p>52. Help-seeking and treatment for dependency involved detoxification, rehabilitation and counselling interventions.</p> <p>53. Importance of dealing with underlying issues</p> <p>54. Acceptance of being an addict and the impact this had both psychologically and socially (family and work) motivated many to seek help.</p> <p>55. Some preference for psychological interventions to help cope with depression, anxiety or stressful situations.</p> <p>56. Some references to Suboxone® as very effective substitute.</p> <p>57. Integrated pharmacy led detoxification treatment approach can complement existing treatment services or offer an alternative to mainstream drug treatment clinics.</p>
<i>Strategies for Prevention</i>	<p>58. Codeine containing medicines regarded as effective Strategies highlighted to promote more responsible use and minimise the risk of misuse and dependence.</p> <p>59. Legislative changes and the up scheduling of codeine products;</p> <p>60. Greater awareness and education of consumers by professionals that prescribe and dispense the medicines;</p> <p>61. Enhanced implementation of strategies already in place, the 'Codeine Care' project;</p> <p>62. Greater enforcement of regulations governing the sales of codeine products and marketing strategies by manufacturers that clearly highlight to consumers addiction potential.</p> <p>63. Provision of information leaflets alone regarded as ineffective as most people tend not to read them.</p>

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For Peer Review

**Table 2 Codeine products most frequently reported as misused or causing dependence**

<b>Product</b>	<b>Quantity of codeine per tablet, capsule (mg)</b>	<b>Other components and their quantities</b>
Stilpane®	8	Caffeine 32mg; paracetamol (acetaminophen) 320mg; meprobamate 150mg.
Adcodo®	10	Caffeine 45mg; doxylamine 5mg; paracetamol (acetaminophen) 450mg
Myprodol®	10	Ibuprofen 200mg; paracetamol(acetaminophen) 250mg
Syndol®	10	Paracetamol (acetaminophen) 450mg; doxylamine succinate 5mg; caffeine 30mg