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### Article

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# 1 'Codeine is my companion': misuse and 2 dependence on codeine containing medicines 3 in Ireland

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9 **Objectives.** Global concern around over the counter availability of codeine containing products and risk of misuse,  
10 dependence and related harms are evident. A phenomenological study of lived experiences of codeine misuse and  
11 dependence was undertaken in Ireland, following the Pharmaceutical Society of Ireland's 2010 guidelines for restricted  
12 supply of non-prescription codeine containing products.

13 **Methods.** In-depth interviews were conducted with a purposive sample of adult codeine misusers and dependents  
14 ( $n = 21$ ), both actively using, in treatment and in recovery. The narratives were analysed using the Empirical Pheno-  
15 menological Psychological five-step method (Karlsson, 1995). A total of 10 themes with 82 categories were identified. Two  
16 concepts at a higher level of abstraction above the theme-level emerged during the final stage of analysis. The concepts  
17 identified were 'emotional pain and user self-legitimization of use' and 'entrapment into habit-forming and invisible  
18 dependent use'. These concepts were reported in different ways by a majority of participants.

19 **Results.** Findings are presented under the following themes: (1) profile and product preferences; (2) awareness of habit  
20 forming use and harm; (3) negotiating pharmacy sales; (4) alternative sourcing routes; (5) the codeine feeling; (6) the daily  
21 routine; (7) acute and chronic side effects; (8) social isolation; (9) withdrawal and dependence and (10) help-seeking and  
22 treatment experiences.

23 **Conclusions.** There is a public health and regulatory imperative to develop proactive responses tackling public  
24 availability of codeine containing medicines, risk minimisation in consumer self-treatment for pain, enhanced patient  
25 awareness of potential for habit forming use and its consequences and continued health professional pharmacovigilance.

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27 **Key words:** Codeine, dependence, opiate.

## 28 Introduction

29 Contemporary research highlights global concerns  
30 around misuse of prescribed and over the counter  
31 codeine as the most commonly consumed opiate  
32 (Van Hout *et al.* 2014). Global demand for codeine  
33 preparations has increased by 27% in the previous decade  
34 (INCB, 2012). Prescription of codeine for pain relief is  
35 increasing in Europe (Fredheim *et al.* 2009). Misuse of  
36 non-prescription codeine containing medicines is  
37 increasing, particularly where available in over the  
38 counter available combination products (McAvoy *et al.*  
39 2011) amid calls for stronger regulatory responses to  
40 tackle over the counter codeine analgesic misuse (Tobin  
41 *et al.* 2013). Quantifying the extent of such misuse centres  
42 on varies by country surveillance and methodological

approaches utilised, and is complicated by public avail- 43  
ability and the hidden and heterogeneous characteristics 44  
of codeine misuse and dependence (UNODC, 2011, 2013). 45

Codeine or 3-methylmorphine is a methylated 46  
morphine derivative occurring naturally with morphine 47  
in the poppy seed. It is a short acting, weak to mid-range 48  
opiate and commonly used to manage mild to moderate 49  
pain in adults as well as for its antitussive and anti- 50  
diarrheal properties (Tremlett *et al.* 2010). Recommended 51  
daily oral dose for adults is between 30 and 60 mg every 52  
4 hours and to a maximum of 240 mg (Derry *et al.* 2013). 53  
Conversion to morphine by endogenous enzymes 54  
causes altered perceptions and emotional responses to 55  
pain (Kelly & Madadi, 2012). Administration of codeine 56  
incurs common opioid-typical side effects, which 57  
include sedation, euphoria and constipation. Of note 58  
is that patient responses to codeine and risk of 59  
intoxication vary due to genetic variations in metabolism 60  
(Ingelman-Sundberg *et al.* 2007; Zhou, 2009). 61

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Codeine has an identified abuse potential evident in drug administration research (Babalonis *et al.* 2013), and multiple reportings of case dependence (Sproule *et al.* 1999; Frei *et al.* 2010). Tolerance develops on repeated administration of codeine within a relatively short time frame, with increasing doses whether legitimate (therapeutic) or intoxicating (non-therapeutic) increasing likelihood of neuro-adaptation and dependence symptomatology (Dobbin & Tobin, 2008; Nielsen *et al.* 2010; Reed *et al.* 2011). Excessive and/or long-term consumption of combination products containing additives (ibuprofen, paracetamol) carries risk of adverse health consequences such as nephro-toxicity, hypokalaemia, gastrointestinal haemorrhage, acute haemorrhagic necrotising pancreatitis and brain damage, often occurring in individuals with no history of substance use disorders or co-morbidity (for a comprehensive review of clinical case presentations see Van Hout *et al.* 2014). Furthermore, misuse of codeine may be an iatrogenic cause of psychiatric disturbances (Manchia *et al.* 2013) with paranoid psychosis frequently associated with codeine cough mixture abuse and symptoms of anxiety and depression occurring with long-term use (Romach *et al.* 1999; Dobbin & Tobin, 2008).

Within trajectories of codeine misuse and dependence, a wide ranging profile of codeine user exists; for example, the elderly (Roumie & Griffin, 2004; Agaba *et al.* 2004); youth (Elwood, 2001; Lam & Shek, 2006; Peters *et al.* 2003, 2007a, 2007b, 2007c; Shek & Lam, 2006, 2008; Ford, 2009; Lao *et al.* 2010; Wilson *et al.* 2010; Tang *et al.* 2012; Agnich *et al.* 2013); parents (Allotey *et al.* 2004); students (Acocella, 2005); pharmacy customers (Sweileh *et al.* 2004; Albsoul-Younes *et al.* 2010); drug and psychiatric treatment patients (Agyapong *et al.* 2013); addiction treatment patients (Akram & Roberts, 2003; Myers *et al.* 2003; Yang & Yuan, 2008; Cohen *et al.* 2009; Thekiso & Farren, 2010; Nielsen *et al.* 2011; Cooper, 2013b) and internet drug forum users (Van Hout, 2015) each with their own motives, patterns and outcomes for use. However, there is a lack of consensus around a definition of misuse of pharmaceutical opioid narcotics (Barrett *et al.* 2008; Casati *et al.* 2012; Cooper, 2013a) with broad misuse of pharmaceutical definitions including incorrect but legitimate use for medical purposes; use outside of acceptable medical guidelines when self-medicating at higher doses and for longer than advised; use for reasons other than for the instructions on the label or the intended purpose; recreational use for intoxication purposes; and where risks and adverse consequences outweigh the benefits (Nielsen *et al.* 2008; Casati *et al.* 2012).

Prevalence of codeine misuse and dependence is difficult to monitor and quantify, and relies on indicators based on surveillance of treatment cases for

codeine dependence (Pates *et al.* 2002; Skurtveit *et al.* 2011; Roussin *et al.* 2013). Codeine dependence is generally treated in residential detoxification programmes, with opiate substitution therapy (methadone or buprenorphine) or lofexidine in community detoxification (Frei *et al.* 2010; Mattick *et al.* 2008; Kelly & Madadi, 2012). Clinical profiles vary, with majority representation of those in middle to late age, females, poly substance users, alcohol users and those with underlying psychiatric conditions (Myers *et al.* 2003; Johansson *et al.* 2003; Thekiso & Farren, 2010; Robinson *et al.* 2010; Agyapong *et al.* 2013). Other studies report on characteristics of individuals dependent on codeine as young, with lower levels of education and employment, reporting chronic pain, family history of problematic substance use and with greater proportions female when compared with other cohorts of opiate dependent individuals (Nielsen *et al.* 2011). For those seeking treatment for codeine dependence in Australia, primarily older females are reported which distinguish from other groups of opiate dependents, although this trend is now changing to reflect younger males (Nielsen *et al.* 2015).

Recent formal drug treatment data involving codeine misuse and dependence indicates that 1.9% of persons in drug treatment in Ireland (personal communication from the National Drug Treatment Reporting System) reported codeine as a primary or secondary drug of abuse in the time period 2008–2012. Irish studies suggest that misusers of codeine are more likely to be male, older, with co-morbid psychiatric, physical and poly substance illness and with a longer drug dependence history (Cohen *et al.* 2009; Thekiso & Farren, 2010). The covert nature of codeine misuse and dependence with the co-occurrence of serious co-morbidity and complexity of cases highlights the need for further research within an Irish context (Thekiso & Farren, 2010). This is timely given the changes employed by the Irish pharmacy regulator (Pharmaceutical Society of Ireland) in 2010 to regulate safe supply of non-prescription combination products containing codeine and paracetamol, aspirin or ibuprofen for supply only as ‘second line’ products for the treatment of pain relief; with comprehensive patient advice provided around correct use for short-term use (no longer than 3 days and with products in-accessible to the public for self-selection). Arguably, more stringent regulations for safe supply could potentially reduce misuse of codeine medicines among psychiatric patients (Agyapong *et al.* 2013).

Therefore, the aim of this study is to gain an understanding of individual and collective experiences of codeine use, pathways to misuse and dependence and experiences of treatment services in Ireland following the introduction of such guidelines for the safe supply of over the counter codeine-based products.

172 **Methods**

173 In-depth interviews were conducted with a purposive  
 174 sample of adult codeine misusers and dependents  
 175 ( $n = 21$ ), both actively using, in treatment and in  
 176 recovery. In order to distinguish between dependent  
 177 and non-dependent use, participants completed the  
 178 severity of dependence screener (SDS) (Gossop *et al.*  
 179 1995), which is a five-item questionnaire, with scores of  
 180 over five indicating dependence use in the past  
 181 12 months. Each item addresses the psychological  
 182 components of dependence, particularly relating to lack  
 183 of control, preoccupation and anxieties about the drug  
 184 used. Items are scored along a four-point scale, and  
 185 aggregated, with a high score indicating a high level of  
 186 dependence. Nielsen *et al.* (2010) in their research on  
 187 codeine dependence in Australia have suggested a SDS  
 188 cut off of five has reasonable sensitivity and specificity  
 189 in identifying problematic users of codeine containing  
 190 products.

191 Recruitment was facilitated by selected gatekeepers  
 192 (specialist medical doctors) within the National  
 193 Drug Treatment Reporting System. These gatekeepers  
 194 assisted in the recruitment of individuals in the centres  
 195 by identifying codeine misusers and dependent  
 196 patients and providing information on the study to  
 197 these patients before their participation in the study.  
 198 All participants received an information sheet and  
 199 completed a consent form, which was explained  
 200 verbally by the interviewer before the interview. All  
 201 participants were assured of confidentiality and  
 202 anonymity, and that they could withdraw from the  
 203 study if they so wished. Interviews lasted between  
 204 30 and 90 minutes and were audio-recorded with  
 205 permission. Participants' anonymity was protected  
 206 by removal of personal identifiers (Wilkinson &  
 207 Thelwall, 2011).

208 Audio-files were transcribed and transferred to a  
 209 Word document that was password-protected and  
 210 analysed in accordance with the Empirical Pheno-  
 211 menological Psychological (EPP) five-step method  
 212 (Karlsson, 1995) (Table 1). This method is underpinned  
 213 by Husserl's (1970) phenomenology theory and  
 214 strongly aligned with Giorgi's (1997) principles by  
 215 facilitating the interpretation of meaning of lived  
 216 phenomena, in this instance the 'life world' experience  
 217 of codeine misuse and dependence. It is an analytic  
 218 process based on the interpretation of a dialectic  
 219 understanding of the hermeneutical circle and its  
 220 dynamic movement between a sense of the whole  
 221 picture and of its parts in order to achieve an incre-  
 222 mental understanding of the lived phenomenon  
 223 (Karlsson, 1995). The EPP method ensures high validity  
 224 by emphasising an open, non-judgemental and bias  
 225 free attitude in interpretation of the data and respect of

**Table 1.** Empirical Phenomenological Psychological five-step method (Karlsson, 1995)

Step 1	The data file was read three times so as to familiarise, identify psychological phenomena and achieve an overview of the codeine misuse phenomenon in an unbiased and open manner, and in the absence of any specific hypothesis. Theoretical reflection was withheld at this step
Step 2	The text was then divided into smaller meaning units (MU), without regard to syntax, included whole paragraphs to single words, and each time a new meaning, focus or topic was introduced
Step 3	All MUs were subsequently transformed from the participants wording and restated in order to present the significant and implicit meaning of the codeine misuse phenomena in objectivised terms. In order to obtain interpretative validity (Maxwell, 1992), considerable efforts were made to ensure respect of the participants' experience
Step 4	The restated MUs were categorised by repeated consultation with the raw data, scrutinising that the category itself was maintained, the understanding of what the phenomenon is (noema) and how it is expressed (noesis) and by considering specific characteristics and similarities in this codeine misuse phenomena
Step 5	The generated categories were then part of an abstraction process to create more general and overarching themes through the patterns identified within related categories. A total of 10 themes with 82 categories emerged from the analysis

the experiential perspectives of the individuals 226  
 (Maxwell, 1992). It aims to explore subjective 227  
 experiences by 'describing the meaning-structure of a 228  
 psychological phenomenon. This method yields 229  
 descriptive results, which disclose the intentional 230  
 relationship between the subject and the object of 231  
 experience' (Karlsson, 1995: 78). 232

Table 2 illustrates the emergent 10 themes and 233  
 82 categories. During the final step in the analysis 234  
 process, two concepts at a higher level of abstraction 235  
 above the theme-level (Table 2) emerged. These 236  
 concepts centred on the interplay between 'emotional 237  
 pain and user self-legitimization of use' and 'entrap- 238  
 ment into habit-forming and invisible dependent use'. 239  
 For example 'Pain killers are not just for what is written 240  
 on the back of the pack, muscle pain, period pain, 241  
 toothache, migraine, they should add also pain relief 242  
 from anxiety, depression and heartache'. and 'Codeine 243  
 is my invisible friend It's a very powerful drug, I never 244  
 expected it to take me where it did, which was the 245  
 highest of highs and the lowest of lows'. All raw data 246  
 were re-read with these two concepts described by a 247  
 majority participants in distinct ways. 248

**Table 2.** Themes and categories

Theme	Category
Profile and product preferences	<ol style="list-style-type: none"> <li>1. Minority prior experience of illicit drugs such as heroin, cannabis, cocaine and ecstasy.</li> <li>2. Opinions around combining codeine medicines with alcohol and illicit drugs mixed with regard to desired intoxication outcomes.</li> <li>3. Codeine combined with alcohol, particularly at night time.</li> <li>4. Preference for misuse of Nurofen +<sup>®</sup>, with some displacement during times of unavailability to use of other codeine containing medicines, both non-prescription and prescribed (Solpedeine<sup>®</sup>, Feminex<sup>®</sup>, Solpadol<sup>®</sup>, Tylex<sup>®</sup>, Codinex<sup>®</sup>).</li> <li>5. Use of prescribed distalgesic containing codeine.</li> <li>6. The effect of Nurofen +<sup>®</sup> described as optimal for intoxication.</li> <li>7. Solpedeine<sup>®</sup> observed to contain too much caffeine, with unpleasant symptoms on excessive use.</li> <li>8. Feminex<sup>®</sup> observed to cause nausea.</li> <li>9. Consumption of tablets favoured.</li> </ol>
Awareness of habit forming use and harm	<ol style="list-style-type: none"> <li>1. Lack of awareness of addictive potential of codeine containing medicines and the harms related to additives such as ibuprofen and paracetamol.</li> <li>2. Few read product information leaflet.</li> <li>3. Health professionals (users) aware of additive potential and related harms.</li> <li>4. Lack of public awareness and televised product marketing as painkiller by companies.</li> <li>5. Need for greater information provision around use, and risks of misuse from prescribing doctors relating to codeine containing medicines.</li> <li>6. Low awareness of intoxication potential of codeine containing medicines for recreational purposes.</li> <li>7. Consultation of the internet to learn more about which products contained codeine when actively misusing.</li> <li>8. Low reporting of tablet splicing of Nurofen +<sup>®</sup> and cold water extraction.</li> <li>9. Low reporting of consumption of food before consumption of large amounts of tablets.</li> <li>10. Despite awareness of habit forming use and harm, while actively misusing, denial and inability to stop.</li> </ol>
Negotiating pharmacy sales	<ol style="list-style-type: none"> <li>1. Accessing of pharmacies as primary route to securing codeine containing medicines.</li> <li>2. Accessing multiple pharmacies in different locations and at intervals in order to circumvent suspicion.</li> <li>3. Few purchased over the internet.</li> <li>4. Awareness of deception and overt manipulation of pharmacy and medical staff.</li> <li>5. Intense discomfort relating to the thought processes of seeking and securing sufficient supplies of codeine containing medicines.</li> <li>6. Awareness of regulation for restricted sale of codeine containing medicines.</li> <li>7. Use of pre-rehearsed scripts when responding to pharmacist interrogation.</li> <li>8. Appearances in securing a successful sale varied.</li> <li>9. Asking for a female specific codeine containing medicine (Feminex<sup>®</sup>) sometimes secured a successful sale.</li> <li>10. Instances when pharmacy staff recognised the customer, led to purchasing of alternative products or simply leaving the store.</li> <li>11. Asking friends to purchase on their behalf.</li> <li>12. Pharmacist intervention at point of sale triggering thoughts and realisations around misuse.</li> </ol>
Alternative sourcing routes	<ol style="list-style-type: none"> <li>1. Alternative methods of sourcing codeine containing medicines centred on diversion via prescriber, street and family routes.</li> <li>2. Border travel to jurisdictions with less stringent regulations around pharmacy supply (Spain and Northern Ireland).</li> <li>3. Accessing surplus codeine containing medicines from friends and family, who did not utilise their repeat script.</li> <li>4. Street diversion via purchasing from medical card patient in receipt of repeat scripts and not utilising the medicine.</li> <li>5. Manipulation of doctors for early and repeat prescriptions.</li> <li>6. Consulting multiple doctors and forging of scripts.</li> <li>7. Health service work related theft.</li> </ol>

Table 2: (Continued)

Theme	Category
261	The codeine feeling
262	<ol style="list-style-type: none"> <li>1. Physical reasons for initial use centred on physical pain (migraine, dental, back, menstrual, joint, postoperative, child birth).</li> <li>2. Recognition of appreciation and 'liking' the effect of codeine, which contributed to development of inappropriate 'misuse' patterns for other emotive reasons.</li> </ol>
263	<ol style="list-style-type: none"> <li>3. Low initial use for recreational intoxication purposes.</li> <li>4. Initial perspectives around the codeine intoxication feeling centred on its euphoric, warm, fuzzy feeling, pleasurable effect and ability to assist sleep.</li> </ol>
264	<ol style="list-style-type: none"> <li>5. Use generally occurred privately and at home (to a lesser extent at work).</li> <li>6. Buffer mechanism or 'crutch' in negotiating daily tasks and stressors.</li> <li>7. Codeine's capacity to reduce stress and enhance relaxation.</li> </ol>
265	<ol style="list-style-type: none"> <li>8. Codeine to enhance motivation and confidence within normal daily activity.</li> <li>9. Development of daily use appeared to cement codeines psychological role in the reduction of and distancing from depression and anxiety.</li> </ol>
266	<ol style="list-style-type: none"> <li>10. Legitimised use in serving a perceived therapeutic need and availability in pharmacies appeared to enhance user solitary and covert habitual use.</li> <li>11. Despite generally consuming codeine products in private homes, commonly alone, codeine intoxication assisted with social communication.</li> </ol>
267	<ol style="list-style-type: none"> <li>12. Low reporting of partner use.</li> <li>13. On consistent use over time codeine intoxication was described as changing from having a sedative numbing effect to energising the user.</li> </ol>
268	The daily routine
269	<ol style="list-style-type: none"> <li>14. Codeine addiction contributing to depression itself.</li> <li>1. Daily use progressed within several weeks and grounded in the users' appreciation of the opiate effect and rising tolerance.</li> <li>2. Thought processes around consumption of codeine on awakening.</li> </ol>
270	<ol style="list-style-type: none"> <li>3. Use characterised by intense craving and need to consume in order to 'feel normal' and operate throughout the day.</li> <li>4. Maximum daily doses ranging between 24 and 115 tablets/day (e.g. between three and four boxes of Nurofen +<sup>®</sup>).</li> </ol>
271	<ol style="list-style-type: none"> <li>5. High dose daily consumption occurring within 6–12 months.</li> <li>6. Staggered use of high dose amounts throughout the day.</li> <li>7. Consciously never exceeding over the recommended daily guidelines for use but misusing products over the long term.</li> </ol>
272	Acute and chronic side effects
273	<ol style="list-style-type: none"> <li>8. Financial and time related cost in supporting a daily 'codeine habit'</li> <li>1. Reported acute side effects centred on opiate urticarial itching, distorted vision and respiratory depression.</li> <li>2. Chronic health consequences centred on weight loss, rebound headache, nausea, constipation, liver, bowel and kidney failure, anaemia, seizures, ulcers and swollen stomach.</li> </ol>
274	Social isolation
275	<ol style="list-style-type: none"> <li>3. Symptoms of withdrawal centred on emesis, diarrhoea, sweating, agitation, insomnia, seizures and cramps.</li> <li>1. Loss of social support networks due to the isolating and pre-occupating nature of codeine dependence.</li> <li>2. Codeine dependence itself negatively impacted on family relationships, contributing to child neglect and ability to sustain employment.</li> </ol>
276	Withdrawal and dependence
277	<ol style="list-style-type: none"> <li>3. Trauma centring on abuse, loss of children, spouses and family homes.</li> <li>4. Failed attempts to cease use additionally contributed to family dysfunction.</li> <li>1. Craving and unpleasant withdrawal symptoms supported continued use.</li> <li>2. Fears around existing pain conditions underpinned difficulties in ceasing use.</li> </ol>
278	<ol style="list-style-type: none"> <li>3. Consumption of sufficient codeine to keep withdrawals at bay in order to sustain normal social functioning and employment.</li> <li>4. Necessity to develop a new daily routine and alternate coping mechanisms underpinned difficulties in self-detoxing.</li> <li>5. Self-detoxification attempts common but unsuccessful, and often resulting in greater amounts consumed when resuming use.</li> </ol>

**Table 2:** (Continued)

Theme	Category
	6. Few sourced street methadone to assist in withdrawals.
Help-seeking and treatment experiences	<ol style="list-style-type: none"> <li>1. Help-seeking efforts overall positive and grounded in pharmacist and treatment service intervention.</li> <li>2. Realisation of being an addict and loss of employment contributed to decisions to attempt detoxification.</li> <li>3. Barriers to treatment access and retention centred on stigma and labelling as drug addict, particularly in the case of supervised methadone consumption in pharmacies.</li> <li>4. Supportive medical care and a slow approach to tapering of codeine products themselves, or substitution agents to avoid unpleasant withdrawals optimal.</li> <li>5. Relapse with codeine phosphate tapering universal due to lack of effect on cravings, and instances of 'topping up' with Nurofen +<sup>®</sup>.</li> <li>6. Difference in effect between prescribed codeine phosphate and Nurofen +<sup>®</sup> complicated successful withdrawal attempts.</li> <li>7. Adopting a new daily routine was deemed important in stabilisation.</li> <li>8. Suboxone<sup>®</sup> viewed very positively in removal of craving and withdrawal effects.</li> <li>9. Integrated pharmacy led detoxification can offer an alternative to accessing mainstream drug treatment centres.</li> </ol>

279 **Results**280 *Profile and product preferences*

281 A total of 57% ( $n = 12$ ) of the sample were female and  
 282 43% ( $n = 9$ ) male. Participants ranged from 26 to 62  
 283 years old (mean age = 39) with 71% ( $n = 15$ ) aged  
 284 between 30 and 49 years. A total of 52% ( $n = 11$ ) of  
 285 participants were unemployed. A total of 15 partici-  
 286 pants admitted to using codeine within the last  
 287 12 months and with a majority scored 10 or above (80%,  
 288  $n = 12$ ) in the SDS. A total of 18 of the 20 participants  
 289 reported codeine-based medications (e.g. Solpadol<sup>®</sup>,  
 290 Nurofen Plus<sup>®</sup> or Solpadeine<sup>®</sup>) as their primary  
 291 problematic drug, with the remainder reporting heroin  
 292 ( $n = 1$ ) and distalgesic ( $n = 1$ ) as primary. A total of  
 293 62% ( $n = 13$ ) reported Nurofen Plus<sup>®</sup> was their  
 294 primary drug of use with 67% ( $n = 14$ ) of participants  
 295 reporting that they were currently on methadone  
 296 maintenance treatment and 14% ( $n = 3$ ) on Suboxone<sup>®</sup>.

297 Some participants had prior experience of illicit  
 298 drugs such as heroin, cannabis, cocaine and ecstasy.  
 299 Opinions around mixing codeine medicines with  
 300 alcohol and illicit drugs were mixed with regard to  
 301 desired intoxication outcomes. Many combined  
 302 codeine with alcohol, particularly at night time.

303 Every weekend I would combine my codeine use  
 304 with alcohol and or weed for the extra 'buzz'.  
 305 I really liked mixing the diazepam with the codeine,  
 306 it made the high more intense or lasted longer.

307 Displacement to more serious opioids ('Oxycontin<sup>®</sup>  
 308 and heroin) was reported by two participants.

The majority of participants reported preference for  
 misuse of Nurofen Plus<sup>®</sup>, with some displacement  
 during times of unavailability to use of other codeine  
 containing medicines, both over the counter and pre-  
 scribed (Solpadeine<sup>®</sup>, Feminex<sup>®</sup>, Solpadol<sup>®</sup>, Tylex<sup>®</sup>,  
 Codinex<sup>®</sup>). A minority reported use of prescribed  
 distalgesic containing codeine.

I have used them [Solpadeine] as a last resort. If  
 I was going to be sick and if I couldn't get  
 Nurofen Plus<sup>®</sup>. Just to stop the withdrawal,  
 I would take the cough syrup and the Solpadeine.

The effect of Nurofen Plus<sup>®</sup> was described by many  
 participants as optimal for intoxication purposes.  
 Solpadeine<sup>®</sup> was observed to contain too much  
 caffeine, with unpleasant symptoms on excessive  
 use while Feminex<sup>®</sup> was reported to cause nausea.  
 Consumption of tablets was favoured.

*Awareness of habit forming use and harm*

The majority of participants were not aware of the  
 addictive potential of codeine containing medicines  
 and the harms related to additives such as ibuprofen  
 and paracetamol. A minority (two) reported reading  
 the product information leaflet. Two participants were  
 health professionals and were aware of addictive  
 potential and related harms.

You were never told. Now you know that it's not  
 the codeine that is the problem, it's the Ibuprofen  
 that is the problem.

- 337 One participant commented on a lack of public  
338 awareness and televised product marketing as pain-  
339 killer by companies.
- 340 I really don't think people know the danger of  
341 codeine, but the ads are back on the television now.
- 342 The majority of participants commented on the need  
343 for greater information provision around use, and risks  
344 of misuse from prescribing doctors relating to codeine  
345 containing medicines.
- 346 If it was explained to me properly by the doctor  
347 what the risks could be, I may not have even gone  
348 down that road in the first place, the predict-  
349 ability and how quickly it would take for you to  
350 get addicted on it. I think patients should be told  
351 more about what the symptoms are and what can  
352 happen.
- 353 A minority of participants were aware of intoxication  
354 potential of codeine containing medicines for recrea-  
355 tional purposes, but were unaware of addiction risk.
- 356 My cousin said that we could get it [codeine]  
357 from Nurofen Plus<sup>®</sup>. At that time we didn't know  
358 it was addictive.
- 359 Nearly all participants reported consulting the inter-  
360 net to learn more about which products contained  
361 codeine when actively misusing. In terms of optimising  
362 the effect and reduction of harm by removal of additives,  
363 two participants reported tablet splicing of Nurofen  
364 Plus<sup>®</sup> and cold water extraction. One reported eating  
365 food before consumption of large amounts of tablets.
- 366 The best part was that the paracetamol would  
367 freeze and all the rest of the water was just golden  
368 heaven to drink off.
- 369 Despite becoming aware of habit forming use and  
370 harm, while actively misusing, participants described  
371 denial and were unable to stop.
- 372 ... to be honest I don't think it would have chan-  
373 ged, I knew what was in them, I knew they were  
374 addictive.
- 375 *Negotiating pharmacy sales*
- 376 All reported accessing pharmacies as their primary  
377 route to securing codeine containing medicines. All  
378 described accessing multiple pharmacies in different  
379 locations and at various intervals in order to circum-  
380 vent suspicion. One participant described purchasing  
381 over the internet.
- 382 ... you would have to travel wider, and just go to  
383 pharmacies less frequently. An addiction will
- find a way, there's always a way. When you want  
something you will always find a way to get it.
- Awareness of deception and overt manipulation of  
pharmacy and medical staff was described.
- In my time of addiction, I knew what pharmacist  
was on and in what place and what name/s  
I used last time. Addiction teaches you master  
manipulation. No matter what barriers you build  
an addicts mind goes far beyond it.
- Many described intense discomfort relating to the  
thought processes of seeking and securing sufficient  
supplies of codeine containing medicines.
- I get so worked up that I am going to get them ...  
and something pulls me back coz I really don't  
really want to get them ... I'm emotionally  
drained.
- All participants were aware of PSI 2010 regulation  
for restricted sale of codeine containing medicines, and  
employed pre-rehearsed scripts when responding to  
pharmacist interrogation. Opinions around appear-  
ances varied, from 'looking dishevelled and in pain' to  
appearing "professional" (particularly relating to  
health professional attire, I would go in there with my  
nurses uniform and they would never refuse.)
- I probably looked like I let go of my appearance,  
I really didn't care. I got up in the morning and  
the first thing on my mind was where was I going  
to go today to get the codeine.
- Asking for a female specific codeine containing  
medicine (Feminexs<sup>®</sup>) sometimes secured a successful  
sale.
- When it was men, I would deliberately embarrass  
them so that I'd get them (Nurofen Plus<sup>®</sup>), and if  
he tried to make me elaborate, he wasn't long  
blushing and going behind and getting the box  
for me.
- Instances when pharmacy staff recognised the  
customer, led to purchasing of alternative products or  
simply leaving the store. Some described asking friends  
to purchase on their behalf. Pharmacist intervention at  
point of sale was described by many as triggering  
thoughts and realisations around misuse.
- Alternative sourcing routes*
- Alternative methods of sourcing codeine containing  
medicines centred on diversion via prescriber, street  
and family routes. Border travel to jurisdictions with  
less stringent regulations around pharmacy supply was  
reported by two participants (Spain and Northern  
Ireland).



433	A minority reported accessing surplus codeine	with anyone and I truly believe I became an	481
434	containing medicines from friends and family, who did	addict straight after feeling its effects.	482
435	not utilise their repeat script.		
436	Easy enough to come by, I know a friend who got	One participant described initial use for recreational	483
437	boxes and boxes of it, so she never used to take them.	intoxication purposes.	484
438	One participant described street diversion via	I used to look forward to it throughout the week	485
439	purchasing from a medical card patient who was in	... to treat myself on Friday.	486
440	receipt of repeat scripts and not utilising the medicine.		
441	The only place you can get it is from somebody	Initial perspectives around the codeine intoxication	487
442	who has a medical card, you can buy it off them.	feeling centred on its euphoric, warm, fuzzy feeling,	488
443	I think they give out medicines too freely on a	pleasurable effect and ability to assist sleep. Use	489
444	medical card.	generally occurred privately and at home (to a lesser	490
445	The manipulation of doctors for early and repeat	extent at work), and appeared to act as buffer mechan-	491
446	prescriptions was described by several participants.	ism or 'crutch' in negotiating daily tasks and stressors.	492
447	After going through a monthly prescription in a	Back then it was simply for the feeling of the drug	493
448	week, I decided it was time to manipulate some	alone, not for what the drug gave me.	494
449	doctors about the "pain" I was in.	I wasn't in any pain, I would take them to make	495
450	Consulting multiple doctors and forging of scripts	me in better form, get through the day, just purely	496
451	was described by one participant.	for buzz, just to give me a feeling of euphoria.	497
452	This is when I was cunning and had an addictive	Comments emphasised codeine's capacity to reduce	498
453	mind, I would go to different doctors and I would	stress and enhance relaxation, and enhance motivation	499
454	come with everything and all sorts to get them.	and confidence within normal daily activity.	500
455	I would have 5 or 6 doctors at a time and the scripts	For more of a normal feeling, it gave me that	501
456	I would get, I would copy them at least 5 times.	sense of de-stressing the body, emotional relief	502
457	Two health professionals described stealing at work	from emotional stress.	503
458	when having access to secured storage for medicines.	Development of daily use appeared to cement	504
459	I just thought about codeine all day long, I stole a	codeines psychological role in the reduction of and	505
460	few from work but soon it was noticed and	distancing from depression and anxiety.	506
461	I never took from work again [nurse].	I had really no treatment [for depression] but	507
462	<i>The codeine feeling</i>	I was totally dependent on the codeine, codeine	508
463	Physical reasons for initial use centred on physical pain	was my treatment, codeine was my life.	509
464	(migraine, dental, back, menstrual, joint, postoperative,	Legitimised use in serving a perceived therapeutic	510
465	child birth). Displacement toward recognition of	need and availability in pharmacies appeared to	511
466	codeine's pleasurable effect and administration for	enhance user solitary and covert habitual use.	512
467	emotional distress and as a coping mechanism (in some	It's very socially acceptable because nobody	513
468	instances postnatal depression) was reported by a	knows you're doing it.	514
469	majority.	Despite generally consuming codeine products in	515
470	Very quickly it was not enough in the morning to	private homes, commonly alone, some participants	516
471	have me floating, feeling euphoric, and care free	observed how codeine intoxication assisted with social	517
472	really. I was numb and I liked that. Nothing	communication.	518
473	stressed me when it worked, codeine filled a void.	I wouldn't be sociable if I didn't have them in my	519
474	Several participants described recognition of appre-	system.	520
475	ciation and 'liking' the effect of codeine, which	Two participants described using with a partner.	521
476	contributed to development of inappropriate 'misuse'	We [husband] did do it together but it wasn't a	522
477	patterns for other emotive reasons.	shared thing, it was a need.	523
478	I wasn't expecting the high I got but I was very	With consistent use over time codeine intoxication	524
479	happy with its effects, it felt like the missing piece	was described as changing from having a sedative	525
480	to my life. I didn't share my codeine addiction	numbing effect to energising the user.	526

527	The drug itself, started to change, it was no	Participants commented on financial and time	575
528	longer giving me a downer; it was giving me a	related cost in supporting a daily 'codeine habit'.	576
529	booster. That's why it has been so hard; it lifts		
530	your spirit.	It's an expensive little endeavour.	577
531	Codeine addiction was also viewed by some as	<i>Acute and chronic side effects</i>	578
532	contributing to depression itself.	Reported acute side effects centred on opiate urticarial	579
533	It gave me direct depression ... from coming off	itching, distorted vision and respiratory depression.	580
534	such a euphoric feeling to just living in the		
535	real world.	We got really itchy, the blotchy skin and the heat	581
		flush; the typical Codeine symptoms. As in go to	582
536	<i>The daily routine</i>	sleep and not breath and then wake up. That's	583
537	Daily use for all progressed within several weeks and	why you can't really take too much. You realise	584
538	grounded in the user's appreciation of the opiate effect	you're so short of breath.	585
539	and rising tolerance. The majority of participants	Chronic health consequences centred on nausea,	586
540	described thought processes around consumption of	constipation, liver, bowel and kidney failure, anaemia,	587
541	codeine on awakening.	seizures, ulcers and swollen stomach.	588
542	I took four and I got a little feeling off of them and	The real physical affect codeine has had on me is	589
543	I liked it, so then I gradually increased to six and	bowel failure. I now take 3 different types of	590
544	then I just kept going up and up, I just kept taking	medications for my bowels alone.	591
545	them all the time.	Several participants described loss of appetite and	592
546	It slowly expanded pace really rapidly were I was	weight. Rebound headaches were described by half	593
547	taking three boxes in the morning. I would get all	of participants. Symptoms of withdrawal centred	594
548	the usual feelings.	on emesis, diarrhoea, sweating, agitation, insomnia,	595
549	Use was characterised by intense craving and need to	seizures and cramps.	596
550	consume in order to 'feel normal' and operate	I'd get withdrawals, I'd get very, very agitated	597
551	throughout the day.	and pains in my legs and my arms and my	598
552	I was taking 28 tablets a day. I was taking them to	stomach. I'd get blinding head aches and loss of	599
553	feel normal initially and then the more you take	appetite, restlessness, couldn't sleep, I wasn't	600
554	the worse you feel, you end up feeling sick from	eating, complete shutdown.	601
555	them but yet you couldn't be without them.	<i>Social isolation</i>	602
556	Maximum daily doses were reported to range	Loss of social support networks due to the isolating and	603
557	between 24 and 115 tablets/day (e.g. between three	pre-occupating nature of codeine dependence was	604
558	and four boxes of Nurofen Plus <sup>®</sup> ) and with high	described by some participants.	605
559	dose daily consumption occurring within 6–12	I don't really have friends any more. My friends	606
560	months. Staggered use of high dose amounts	are gone and it's more a companion addiction. It	607
561	throughout the day was common. One participant	feels like it has its arm around you. That's how	608
562	reported use of 96 tablets of Nurofen Plus <sup>®</sup> in one go.	it is for me now. It gives me that sense of security	609
563	I'd take 24 at once and then at lunch time take the	and that's what I'm struggling with at the	610
564	other 24 and then in the evening then take the	moment, it's to break that cycle.	611
565	other 24 so that was a ritual of things, gradually	Codeine dependence itself was viewed by many	612
566	I had to take more because I'd take 24 and	as negatively impacting on family relationships,	613
567	I wouldn't feel anything.	contributing to child neglect and ability to sustain	614
568	Some reported consciously never exceeding over	employment. Trauma centring on abuse, loss of	615
569	the recommended daily guidelines for use but misusing	children, spouses and family homes were common.	616
570	products over the long term, and recognising	Failed attempts to cease use additionally contributed	617
571	dependence within 3 months.	to family dysfunction.	618
572	Never took more than eight, always within	My life has become unmanageable, every penny	619
573	recommended guidelines, but dependent within	I have has gone to this tablets, I've lost my job,	620
574	three months.	I've lost my partner and kids, I had a nice	621

622	home, its actually destroyed my life, it's taken	Barriers to treatment access and retention centred	667
623	everything, it's taken away my self-respect.	on stigma and being labelling as a drug addict,	668
		particularly in the case of supervised methadone	669
		consumption in pharmacies.	670
624	<i>Withdrawal and dependence</i>		
625	Craving and unpleasant withdrawal symptoms were	It made me feel very shameful and my picture	671
626	described as supporting continued use. Fears around	was on the wall with methadone, I just felt very	672
627	existing pain conditions underpinned difficulties in	ashamed.	673
628	ceasing use for some participants.		
629	It causes horrible dependence, physical and	Supportive medical care and a slow approach to	674
630	mental dependence. It just destroys your life	tapering of codeine products themselves or substitution	675
631	basically.	agents to avoid unpleasant withdrawals were advised.	676
632	Many tried to consume sufficient codeine to keep	If you are taking four boxes it would take you two	677
633	withdrawals at bay in order to sustain normal social	and a half years to come down. You can't go	678
634	functioning and employment.	down too fast, the body needs time to catch up.	679
635	I was taking it almost to work because of the		
636	withdrawal symptoms. Once I realised I was	For a minority of participants with experience (all	680
637	addicted to something, I realised I'd have to take	unsuccessful) of codeine phosphate withdrawal, the	681
638	too much time off work. So it would end up being	sedative effect of codeine phosphate tapering treatment	682
639	a vicious circle.	form contrasted with the Nurofen Plus <sup>®</sup> energising effect,	683
		which patients found complicated their successful detox.	684
640	The necessity to develop a new daily routine and	There is a huge difference. The over the counter	685
641	in many instances alternate coping mechanisms	codeine phosphate makes you feel down and	686
642	underpinned difficulties in self-detoxing.	sleepy, Nurofen Plus <sup>®</sup> makes you the opposite,	687
643	When I used to get up and feel crap, I'll take it and	gives you uplift.	688
644	feel instantly better. Now it has become part of		
645	my daily routine in my daily life. Trying to break	Relapse with codeine phosphate tapering was	689
646	that is really hard.	universal due to lack of effect on cravings, and instan-	690
647	Self-detoxification attempts were common but	ces of 'topping up' with Nurofen Plus <sup>®</sup> .	691
648	unsuccessful, and often more excessive in amounts	I wouldn't even say I lasted a day or two on that.	692
649	consumed thereafter. One participant described	I felt a huge overwhelming need, even when	693
650	sourcing street methadone to assist in withdrawals.	I was taking them [codeine phosphate].	694
651	I tried to cut down on it, gradually cut down, and		
652	then I'd just have a bad day and I'd be straight	Particularly for those on methadone, while mana-	695
653	back up to 24 [tablets].	ging unpleasant withdrawals, adopting a new daily	696
		routine was deemed important.	697
654	<i>Help-seeking and treatment experiences</i>	I realised that routine is very important in my	698
655	Help-seeking efforts were overall positive and	addiction, so I had to start my own new routines.	699
656	grounded in pharmacist and treatment service		
657	intervention. Realisation of being an addict and loss of	Suboxone <sup>®</sup> in particular was viewed very positively	700
658	employment was described by several as contributing	in removal of craving and withdrawal effects.	701
659	to decisions to attempt detoxification.		
660	The person who becomes addicted to pain killers	From the very first day I put a Suboxone in my	702
661	and over the counter drugs wouldn't necessary	body, I have no jitter, I have no side effects,	703
662	see themselves as a drug addict.	I never ever took a codeine since the first day	704
663		I took Suboxone.	705
664	There is no difference between a heroin addict		
665	and some who's been taking Nurofen Plus <sup>®</sup> .	It was a miracle, a door was opened for me, I was	706
666	Because at the end of the day, it's not the	able to function, I was on no codeine. I actually	707
	substance they're treating, it's the person.	walked into the chemist and I apologized to	708
		everyone who I had fooled.	709
		Some participants suggested that the pharmacist	710
		could support them in tapering down from over the	711
		counter codeine containing products, as an alternative	712
		to accessing mainstream drug treatment centres.	713

714 I think they would appreciate a different  
715 approach, if there was in the middle place where  
716 people using over the counter drug could go,  
717 instead of going to the main drug centres.

## 718 Discussion

719 This study presents unique qualitative insights around  
720 codeine misuse and dependence within an Irish context  
721 following the PSI's regulatory restrictions in 2010 to  
722 promote safe supply of non-prescription codeine  
723 containing products in Ireland. 'Trustworthiness' of  
724 the data (Lincoln & Guba, 1985) is promoted by  
725 verification of extensive similarities across the lived  
726 experience of participants, along with horizontal and  
727 vertical consistency in the interpretation of the data,  
728 and partial phenomenological psychological reduction  
729 (Karlsson, 1995).

730 The study builds on findings reported in earlier  
731 qualitative studies with codeine dependents in the  
732 United Kingdom (Cooper, 2011, 2013a), Australia  
733 (Nielsen *et al.* 2010, 2011, 2013) and active online drug  
734 users (Van Hout, 2015). Given the covert nature of this  
735 issue, confounded by withdrawals, emotional distress  
736 and potential for serious co-morbidity, this study  
737 presents novel and meaningful illustration of the  
738 codeine misuse phenomenon, particularly within the  
739 Irish context. Multiple routes to access centred on  
740 the easy availability of codeine-based products within  
741 pharmacies, when prescribed via repeat or through the  
742 forging of scripts, over the counter and diversionary  
743 means. All contributed to the misuse of codeine in  
744 individuals largely unaware of potential for habit  
745 forming use, craving and withdrawals. Two way  
746 displacements between prescribed codeine for physical  
747 pain management and over the counter sourcing were  
748 observed and similar to that illustrated in Cooper's  
749 study in the United Kingdom (2013a). Similar to extant  
750 research (Inciardi *et al.* 2009, 2010; Wilsey *et al.* 2010;  
751 Hamer *et al.* 2013) online sourcing of codeine rarely  
752 occurred in preference for pharmacies, and prescribers.

753 This study supports the distinction of three  
754 broad categories of codeine misuse identified in  
755 Australia (Nielsen *et al.* 2010) and the United Kingdom  
756 (Cooper, 2011): (1) use which never exceeds the  
757 maximum recommended dose, but in terms of duration  
758 and nature of use meets criteria for dependence,  
759 (2) consumption of slightly higher than the recom-  
760 mended dose (for therapeutic or non-therapeutic  
761 reasons) and (3) consumption of doses which sub-  
762 stantially exceed recommended doses (generally in the  
763 context of serious opioid dependence). Daily doses  
764 were described as over the recommended daily dose of  
765 240 mg, and higher than other studies reporting ranges

of 21–65 tablets daily (Brands *et al.* 2004; McAvoy *et al.* 766  
2011; Van Hout, 2015). Adverse health consequences on 767  
sustained long-term codeine use were similar to those 768  
reported earlier in the literature, with withdrawal- 769  
based medication overuse headache (Katsarava & 770  
Jensen, 2007; Bendtsen *et al.* 2012) common. 771

The phenomenon of codeine misuse appeared 772  
closely situated within the 'blurring' of therapeutic 773  
self-medication for legitimate medical reasons (chronic 774  
pain), and misuse for iatrogenic dependence (Sproule 775  
*et al.* 1999; Nielsen *et al.* 2010; Hamer *et al.* 2013; Roussin 776  
*et al.* 2013; Nielsen *et al.* 2014), alongside individual 777  
difficulties in self-identifying problematic use along 778  
their own trajectory of use (Pates *et al.* 2002; Nielsen 779  
*et al.* 2010). Of note were the invisible and covert 780  
characteristics of dependent use, combined with social 781  
isolation over time. Use of codeine products was 782  
described as facilitating the individuals' capacity to 783  
operate quasi-normally within life and work stressors 784  
and relationships. The research supports that indivi- 785  
duals dependent on codeine largely differ from other 786  
population's dependent on prescription opioids by 787  
higher employment rates (Nielsen *et al.* 2011, 2014). 788  
Recognition of needing help for codeine dependence or 789  
identification as 'drug addict' (Dobbin & Tobin, 2008; 790  
Nielsen *et al.* 2010; Cooper, 2013a, 2013b) occurred 791  
when adverse effects and socio-economic problems 792  
relating to codeine misuse became intolerable. Help 793  
seeking was positive, despite some reporting of stigma 794  
relating to methadone maintenance treatment. Use of 795  
Suboxone (buprenorphine and naloxone) showed 796  
promise in stabilisation and recovery. 797

## Conclusion 798

This study highlights the unique and hidden nature of 799  
the codeine misuse phenomenon and with trajectories 800  
of habit forming use and dependence particularly 801  
underpinned by presence of emotional distress and 802  
self-medication. Interventions for referral, treatment 803  
and management of codeine misuse remain limited 804  
given it's heterogeneous nature, over the counter 805  
availability and lack specificity for this distinct group of 806  
opiate dependents despite extrapolation from extant 807  
evidence-based opioid policies and protocols (Myers 808  
*et al.* 2003; Thekiso & Farren, 2010; Cooper, 2011, 2013a; 809  
Reed *et al.* 2011). Access to existing treatment systems 810  
is hampered by stigma and poor consideration of 811  
needs, with pathways and outcomes complicated by 812  
requirements for the co-existing management of 813  
physical pain (Dobbin & Tobin, 2008; Fishbain *et al.* 814  
2008; Reed *et al.* 2011). There is a public health and 815  
regulatory imperative to develop proactive responses 816  
tackling public availability of codeine containing 817  
medicines, risk minimisation in consumer self- 818

819 treatment for physical and emotional pain, need for  
820 enhanced patient awareness of habit forming use and  
821 its consequences, and continued health professional  
822 screening and pharmacovigilence (Casati *et al.* 2012;  
823 Cooper, 2013b; Agnich *et al.* 2013; Van Hout *et al.* 2014).

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## 831 Conflicts of Interest

832 None.

## 833 Ethical Standards

834 The authors assert that all procedures contributing to  
835 this work comply with the ethical standards of the  
836 relevant national and institutional committee on  
837 human experimentation with the Helsinki Declaration  
838 of 1975, as revised in 2008. The study protocol was  
839 approved by the institutional review board of each  
840 participating institution. Written informed consent was  
841 obtained from all participating patients.

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