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

87 Within trajectories of codeine misuse and depen-
 88 dence, a wide ranging profile of codeine user exists; for
 89 example, the elderly (Roumie & Griffin, 2004; Agaba
 90 *et al.* 2004); youth (Elwood, 2001; Lam & Shek, 2006;
 91 Peters *et al.* 2003, 2007a, 2007b, 2007c; Shek & Lam, 2006,
 92 2008; Ford, 2009; Lao *et al.* 2010; Wilson *et al.* 2010; Tang
 93 *et al.* 2012; Agnich *et al.* 2013); parents (Allotey *et al.*
 94 2004); students (Acocella, 2005); pharmacy customers
 95 (Sweileh *et al.* 2004; Albsoul-Younes *et al.* 2010); drug
 96 and psychiatric treatment patients (Agyapong *et al.*
 97 2013); addiction treatment patients (Akram & Roberts,
 98 2003; Myers *et al.* 2003; Yang & Yuan, 2008; Cohen *et al.*
 99 2009; Thekiso & Farren, 2010; Nielsen *et al.* 2011;
 100 Cooper, 2013b) and internet drug forum users (Van
 101 Hout, 2015) each with their own motives, patterns and
 102 outcomes for use. However, there is a lack of consensus
 103 around a definition of misuse of pharmaceutical opioid
 104 narcotics (Barrett *et al.* 2008; Casati *et al.* 2012; Cooper,
 105 2013a) with broad misuse of pharmaceutical definitions
 106 including incorrect but legitimate use for medical
 107 purposes; use outside of acceptable medical guidelines
 108 when self-medicating at higher doses and for longer
 109 than advised; use for reasons other than for the
 110 instructions on the label or the intended purpose;
 111 recreational use for intoxication purposes; and where
 112 risks and adverse consequences outweigh the benefits
 113 (Nielsen *et al.* 2008; Casati *et al.* 2012).

114 Prevalence of codeine misuse and dependence is
 115 difficult to monitor and quantify, and relies on indica-
 116 tors based on surveillance of treatment cases for

codeine dependence (Pates *et al.* 2002; Skurtveit *et al.* 117
 2011; Roussin *et al.* 2013). Codeine dependence is 118
 generally treated in residential detoxification 119
 programmes, with opiate substitution therapy (metha- 120
 done or buprenorphine) or lofexidine in community 121
 detoxification (Frei *et al.* 2010; Mattick *et al.* 2008; Kelly 122
 & Madadi, 2012). Clinical profiles vary, with majority 123
 representation of those in middle to late age, females, 124
 poly substance users, alcohol users and those with 125
 underlying psychiatric conditions (Myers *et al.* 2003;
 Johansson *et al.* 2003; Thekiso & Farren, 2010; Robinson 127
et al. 2010; Agyapong *et al.* 2013). Other studies 128
 report on characteristics of individuals dependent on 129
 codeine as young, with lower levels of education 130
 and employment, reporting chronic pain, family 131
 history of problematic substance use and with greater 132
 proportions female when compared with other cohorts 133
 of opiate dependent individuals (Nielsen *et al.* 2011). 134
 For those seeking treatment for codeine dependence in 135
 Australia, primarily older females are reported which 136
 distinguish from other groups of opiate dependents, 137
 although this trend is now changing to reflect younger 138
 males (Nielsen *et al.* 2015). 139

Recent formal drug treatment data involving codeine 140
 misuse and dependence indicates that 1.9% of persons 141
 in drug treatment in Ireland (personal communication 142
 from the National Drug Treatment Reporting System) 143
 reported codeine as a primary or secondary drug of 144
 abuse in the time period 2008–2012. Irish studies 145
 suggest that misusers of codeine are more likely to be 146
 male, older, with co-morbid psychiatric, physical and 147
 poly substance illness and with a longer drug depen- 148
 dence history (Cohen *et al.* 2009; Thekiso & Farren, 149
 2010). The covert nature of codeine misuse and depen- 150
 dence with the co-occurrence of serious co-morbidity 151
 and complexity of cases highlights the need for further 152
 research within an Irish context (Thekiso & Farren, 2010). 153
 This is timely given the changes employed by the Irish 154
 pharmacy regulator (Pharmaceutical Society of Ireland) 155
 in 2010 to regulate safe supply of non-prescription 156
 combination products containing codeine and para- 157
 cetamol, aspirin or ibuprofen for supply only as ‘second 158
 line’ products for the treatment of pain relief; with 159
 comprehensive patient advice provided around correct 160
 use for short-term use (no longer than 3 days and with 161
 products in-accessible to the public for self-selection). 162
 Arguably, more stringent regulations for safe supply 163
 could potentially reduce misuse of codeine medicines 164
 among psychiatric patients (Agyapong *et al.* 2013). 165

Therefore, the aim of this study is to gain an under- 166
 standing of individual and collective experiences of 167
 codeine use, pathways to misuse and dependence and 168
 experiences of treatment services in Ireland following 169
 the introduction of such guidelines for the safe supply 170
 of over the counter codeine-based products. 171

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

Table 2: (Continued)

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

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"> 1. Help-seeking efforts overall positive and grounded in pharmacist and treatment service intervention. 2. Realisation of being an addict and loss of employment contributed to decisions to attempt detoxification. 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. 4. Supportive medical care and a slow approach to tapering of codeine products themselves, or substitution agents to avoid unpleasant withdrawals optimal. 5. Relapse with codeine phosphate tapering universal due to lack of effect on cravings, and instances of 'topping up' with Nurofen +[®]. 6. Difference in effect between prescribed codeine phosphate and Nurofen +[®] complicated successful withdrawal attempts. 7. Adopting a new daily routine was deemed important in stabilisation. 8. Suboxone[®] viewed very positively in removal of craving and withdrawal effects. 9. Integrated pharmacy led detoxification can offer an alternative to accessing mainstream drug treatment centres.

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[®],
 290 Nurofen Plus[®] or Solpadeine[®]) 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[®] 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[®].

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[®]
 308 and heroin) was reported by two participants.

The majority of participants reported preference for
 misuse of Nurofen Plus[®], with some displacement
 during times of unavailability to use of other codeine
 containing medicines, both over the counter and pre-
 scribed (Solpadeine[®], Feminex[®], Solpadol[®], Tylex[®],
 Codinex[®]). 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[®]. Just to stop the withdrawal,
 I would take the cough syrup and the Solpadeine.

The effect of Nurofen Plus[®] was described by many
 participants as optimal for intoxication purposes.
 Solpadeine[®] was observed to contain too much
 caffeine, with unpleasant symptoms on excessive
 use while Feminex[®] 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[®]. 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[®] 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[®]) sometimes secured a successful
sale.
- When it was men, I would deliberately embarrass
them so that I'd get them (Nurofen Plus[®]), 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 appreci-	system.	520
475	ation 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
536	<i>The daily routine</i>	flush; the typical Codeine symptoms. As in go to	582
537	Daily use for all progressed within several weeks and	sleep and not breath and then wake up. That's	583
538	grounded in the user's appreciation of the opiate effect	why you can't really take too much. You realise	584
539	and rising tolerance. The majority of participants	you're so short of breath.	585
540	described thought processes around consumption of	Chronic health consequences centred on nausea,	586
541	codeine on awakening.	constipation, liver, bowel and kidney failure, anaemia,	587
542	I took four and I got a little feeling off of them and	seizures, ulcers and swollen stomach.	588
543	I liked it, so then I gradually increased to six and		
544	then I just kept going up and up, I just kept taking	The real physical affect codeine has had on me is	589
545	them all the time.	bowel failure. I now take 3 different types of	590
546	It slowly expanded pace really rapidly were I was	medications for my bowels alone.	591
547	taking three boxes in the morning. I would get all		
548	the usual feelings.	Several participants described loss of appetite and	592
549	Use was characterised by intense craving and need to	weight. Rebound headaches were described by half	593
550	consume in order to 'feel normal' and operate	of participants. Symptoms of withdrawal centred	594
551	throughout the day.	on emesis, diarrhoea, sweating, agitation, insomnia,	595
552	I was taking 28 tablets a day. I was taking them to	seizures and cramps.	596
553	feel normal initially and then the more you take		
554	the worse you feel, you end up feeling sick from	I'd get withdrawals, I'd get very, very agitated	597
555	them but yet you couldn't be without them.	and pains in my legs and my arms and my	598
556	Maximum daily doses were reported to range	stomach. I'd get blinding head aches and loss of	599
557	between 24 and 115 tablets/day (e.g. between three	appetite, restlessness, couldn't sleep, I wasn't	600
558	and four boxes of Nurofen Plus [®]) and with high	eating, complete shutdown.	601
559	dose daily consumption occurring within 6–12	<i>Social isolation</i>	602
560	months. Staggered use of high dose amounts	Loss of social support networks due to the isolating and	603
561	throughout the day was common. One participant	pre-occupating nature of codeine dependence was	604
562	reported use of 96 tablets of Nurofen Plus [®] in one go.	described by some participants.	605
563	I'd take 24 at once and then at lunch time take the	I don't really have friends any more. My friends	606
564	other 24 and then in the evening then take the	are gone and it's more a companion addiction. It	607
565	other 24 so that was a ritual of things, gradually	feels like it has its arm around you. That's how	608
566	I had to take more because I'd take 24 and	it is for me now. It gives me that sense of security	609
567	I wouldn't feel anything.	and that's what I'm struggling with at the	610
568	Some reported consciously never exceeding over	moment, it's to break that cycle.	611
569	the recommended daily guidelines for use but misusing	Codeine dependence itself was viewed by many	612
570	products over the long term, and recognising	as negatively impacting on family relationships,	613
571	dependence within 3 months.	contributing to child neglect and ability to sustain	614
572	Never took more than eight, always within	employment. Trauma centring on abuse, loss of	615
573	recommended guidelines, but dependent within	children, spouses and family homes were common.	616
574	three months.	Failed attempts to cease use additionally contributed	617
		to family dysfunction.	618
		My life has become unmanageable, every penny	619
		I have has gone to this tablets, I've lost my job,	620
		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 [®] 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 [®] 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 [®] .	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 [®] 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 [®] .	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.

842 References

843 **Acocella CM** (2005). Using diaries to assess non prescription
 844 drug use among university students. *Journal of Drug*
 845 *Education* **35**, 267–274.
 846 **Agaba EI, Agaba PA, Wigwe CM** (2004). Use and abuse of
 847 analgesics in Nigeria: a community survey. *Nigerian Journal*
 848 *of Medicine* **13**, 379–382.
 849 **Agnich L, Stogner JM, Miller BL, Marcum C** (2013).
 850 Purple drank prevalence and characteristics of misusers
 851 of codeine cough syrup mixtures. *Addictive Behaviors* **38**,
 852 2445–2449.
 853 **Agyapong VIO, Singh K, Savage M, Thekiso BT, Finn M,**
 854 **Farren CK, McLoughlin DM** (2013). Use of codeine-
 855 containing medicines by Irish psychiatric in-patients before
 856 and after regulatory limitations on their supply. *Irish Journal*
 857 *of Psychological Medicine* **30**, 7–12.
 858 **Akram G, Roberts K** (2003). Pharmacists' management of over-
 859 the-counter medication requests from methadone patients.
 860 *Journal of Substance Use* **8**, 215–222.
 861 **Albsoul-Younes A, Wazaify M, Yousef AM, Tahaineh L**
 862 (2010). Abuse and misuse of prescription and non
 863 prescription drugs sold in community pharmacies in Jordan.
 864 *Substance Use and Misuse* **45**, 1319–1329.
 865 **Allotey P, Reidpath DD, Elisha D** (2004). "Social medication"
 866 and the control of children: a qualitative study of over-
 867 the-counter medication among Australian children.
 868 *Pediatrics* **114**, e378–e383.

Babalonis S, Lofwall MR, Nuzzo PA, Siegel AJ, Walsh SL 869
 (2013). Abuse liability and reinforcing efficacy of oral tramadol 870
 in humans. *Drug and Alcohol Dependence* **129**, 116–124. 871
Barrett SP, Meisner JR, Stewart SH (2008). What constitutes 872
 prescription drug misuse? Problems and pitfalls of current 873
 conceptualizations. *Current Drug Abuse Reviews* **1**, 255–262. 874
Bendtsen L, Birk S, Kasch H, Aegidius K, Sorensen PS, 875
Thomsen LL, Poulsen L, Rasmussen MJ, Kruuse C, 876
Jensen R, Danish Headache Society (2012). Reference 877
 programme: diagnosis and treatment of headache disorders 878
 and facial pain. Danish Headache Society. *Journal of Headache* 879
and Pain **13**, 1–29. 880
Brands B, Blake J, Sproule B, Gourley D, Busto U (2004). 881
 Prescription opioid abuse in patients presenting for 882
 methadone maintenance treatment. *Drug and Alcohol* 883
Dependence **73**, 199–207. 884
Casati A, Sedefov R, Pfeiffer-Gerschel T (2012). Misuse of 885
 medicines in the European union: a systematic review of the 886
 literature. *European Addiction Research* **18**, 228–245. 887
Cohen DP, Unoh E, Barry H, O'Connor JJ (2009). Codeine 888
 misuse among service users on a methadone treatment 889
 programme. *Irish Journal of Medical Science* **179**, 465. 890
Comments on the Reported Statistics on Narcotic Drugs 891
Austria: 73-93 – International Narcotics Controls Board 892
 (INCB) (<https://www.incb.org/>). Accessed October 2013. 893
Cooper RJ (2011). Respectable addiction – a qualitative study 894
 of over the counter medicine abuse in the UK. Sheffield, UK: 895
 School of Health and Related Research (ScHARR), 896
 University of Sheffield. 897
Cooper RJ (2013a). I can't be an addict. I am.' Over-the-counter 898
 medicine abuse: a qualitative study. *BMJ Open Online* **3**, 899
 e002913. 900
Cooper RJ (2013b). Over-the-counter medicine abuse: a review 901
 of the literature. *Journal of Substance Use* **18**, 82–107. 902
Derry S, Karlin SM, Moore RA (2013). Single dose oral 903
 ibuprofen plus codeine for acute postoperative pain in adults. 904
The Cochrane Database Systematic Review **3**, CD010107. 905
Dobbin M, Tobin C (2008). *Over-the-Counter (OTC) Ibuprofen/* 906
Codeine Analgesics: Misuse and Harm. Drugs Policy and 907
 Services Branch, Department of Human Services: 908
 Melbourne, Vic, Australia. 909
Elwood W (2001). Sticky business: patterns of procurement 910
 and misuse of prescription cough syrup in houston. *Journal of* 911
Psychoactive Drugs **33**, 121–133. 912
Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS 913
 (2008). What percentage of chronic non malignant pain 914
 patients exposed to chronic opioid analgesic therapy develop 915
 abuse/addiction and/or aberrant drug-related behaviors? 916
 A structured evidence-based review. *Pain Medicine* **9**, 917
 444–459. 918
Ford JA (2009). Misuse of over-the-counter cough or cold 919
 medications among adolescents: prevalence and correlates 920
 in a national sample. *Journal of Adolescent Health* **44**, 505–507. 921
Fredheim OMS, Skurtveit S, Moroz A, Breivik H, 922
Borchgrevink PC (2009). Prescription pattern of codeine 923
 for non-malignant pain: a pharmacoepidemiological 924
 study from the Norwegian Prescription Database. 925
Acta Anaesthesiologica Scandinavica **53**, 627–633. 926
Frei MY, Nielsen S, Dobbin MD, Tobin CL (2010). Serious 927
 morbidity associated with misuse of over-the-counter 928

- codeine-ibuprofen analgesics: a series of 27 cases. *Medical Journal Australia* **193**, 294–296.
- Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W, Strang J** (1995). The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction* **90**, 607–614.
- Hamer A, Spark J, Wood P, Roberts E** (2013). The upscheduling of combination analgesics containing codeine: the impact on the practice of pharmacists. *Research in Social and Administrative Pharmacy* **10**, 669–678.
- Giorgi A** (1997). The theory, practice, and evaluation of the phenomenological method as a qualitative research procedure. *Journal of Phenomenological Psychology* **28**, 235–260.
- Husserl E** (1970). *Logical Investigation*. New York: Humanities Press.
- INCB (International Narcotics Controls Board)** (2012). Comments on the Reported Statistics on Narcotic Drugs Austria, 73–93 (<https://www.incb.org/>). Accessed October 2013.
- Inciardi JA, Surratt HL, Cicero TJ, Rosenblum A, Ahwah C, Bailey JE, Dart RC, Burke JJ** (2010). Prescription drugs purchased through the internet: who are the end users? *Drug and Alcohol Dependence* **110**, 21–29.
- Ingelman-Sundberg M, Sim SC, Gomez A, Rodriguez-Antona C** (2007). Influence of cytochrome P450 polymorphisms on drug therapies: pharmacogenetic, pharmacoeconomic and clinical aspects. *Pharmacology and Therapeutics* **116**, 496–526.
- Johansson BA, Berglund M, Hanson M, Pohlen C, Persson I** (2003). Dependence on legal psychotropic drugs among alcoholics. *Alcohol and Alcoholism: International Journal of the Medical Council on Alcoholism* **38**, 613–618.
- Karlsson G** (1995). *Psychological Qualitative Research from a Phenomenological Per-Spective*. Almqvist & Wiksell International: Stockholm, Sweden.
- Katsarava Z, Jensen R** (2007). Medication-overuse headache: where are we now? *Current Opinion in Neurology* **20** 326–330.
- Kelly LE, Madadi P** (2012). Is there a role for therapeutic drug monitoring with codeine? *Therapeutic Drug Monitoring* **34**, 249–256.
- Lam CM, Shek D** (2006). A qualitative study of cough medicine abuse among Chinese young people in Hong Kong. *Journal of Substance Abuse* **11**, 233–244.
- Lao YZ, Jiang ZY, Tong ZS, Pang ZT, Xu JX** (2010). Clinical features and defense styles in patients with cough medicine abuse. *Medical Journal of Chinese People's Health* **22**, 272–274.
- Lincoln YS, Guba EG** (1985). *Naturalistic Inquiry*. Sage: Beverly Hills, CA.
- Manchia M, Alda M, Clakin C** (2013). Repeated erythromycin/codeine-induced psychotic mania. *Clinical Neuropharmacology* **36**, 177–178.
- Mattick RP, Kimber J, Breen C, Davoli M** (2008). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews* **2**.
- Maxwell JA** (1992). Understanding and validity in qualitative research. *Harvard Educational Review* **62**, 279–301.
- McAvoy BR, Dobbin M, Tobin C** (2011). Over-the-counter codeine analgesic misuse and harm: characteristics of cases in Australia and New Zealand. *New Zealand Medical Journal* **124**, 29–33.
- Myers B, Siegfried N, Parry CD** (2003). Over-the-counter and prescription medicine misuse in Cape Town – findings from specialist treatment centres. *South African Medical Journal* **93**, 367–370.
- Nielsen S, Bruno R, Carruthers S, Fischer J, Lintzeris N, Stooze M** (2008). *Investigation of Pharmaceutical Misuse Amongst Drug Treatment Clients*. Turning Point Alcohol and Drug Centre: Melbourne, Australia.
- Nielsen S, Cameron J, Lee N** (2011). Characteristics of a nontreatment-seeking sample of over-the-counter codeine users: implications for intervention and prevention. *Journal of Opioid Management* **7**, 363–370.
- Nielsen S, Cameron J, Pahoki S** (2010). *Over the Counter Codeine Dependence*. Turning Point Drug and Alcohol Centre: Vic, Australia.
- Nielsen S, Cameron J, Pahokia S** (2013). Opportunities and challenges: Over-the-counter codeine supply from the codeine consumer's perspective. *International Journal of Pharmacy Practice* **21**, 161–168.
- Nielsen S, Murnion B, Dunlop A, Degenhardt L, Demirkol A, Muhleisen P, Lintzeris N** (2014). Comparing treatment-seeking codeine users and strong opioid users: findings from a novel case series. *Drug and Alcohol Review* **34**, 304–311.
- Nielsen S, Roxburgh A, Bruno R, Lintzeris N, Jefferson A, Degenhardt L** (2015). Changes in non-opioid substitution treatment episodes for pharmaceutical opioids and heroin from 2002 to 2011. *Drug Alcohol Depend* **149**, 212–219.
- Pates R, McBride AJ, Li S, Ramadan R** (2002). Misuse of over-the-counter medicines: a survey of community pharmacies in a South Wales health authority. *Pharmaceutical Journal* **268**, 179–182.
- Peters R, Yacoubian GS, Rhodes W, Forsythe KJ, Bowers KS, Eulian VM, Mangum CA, O'Neal JD, Martin Q, Essien EJ** (2007a). Beliefs and social norms about codeine and promethazine hydrochloride cough syrup (CPHCS) use and addiction among multi-ethnic college students. *Journal of Psychoactive Drugs* **39**, 277–282.
- Peters RJ, Williams M, Ross MW, Atkinson J, Yacoubian GS** (2007b). Codeine cough syrup use among African-American crack cocaine users. *Journal of Psychoactive Drugs* **39**, 97–102.
- Peters RJ, Amos C, Meshack A, Savage C, Sinclair MM, Williams LT, Markham C** (2007c). Codeine cough syrup use among sexually active, African-American high school youths: why southern males are down to have sex. *The American Journal on Addictions* **16**, 144–145.
- Peters RJ, Kelder SH, Markham CM, Yacoubian GS, Peters LA, Ellis A** (2003). Beliefs and social norms about codeine and promethazine hydrochloride cough syrup (CPHCS) onset and perceived addiction among urban Houstonian adolescents: an addiction trend in the city of lean. *Journal of Drug Education* **33**, 415–425.
- Reed K, Bond A, Witton J, Cornish R, Hickman M, Strang J** (2011). *The Changing Use of Prescribed Benzodiazepines and*

- 1047 Z-Drugs and of Over-the-Counter Codeine-Containing Products
1048 in England: A Structured Review of Published English and
1049 International Evidence and Available Data to Inform
1050 Consideration of the Extent of Dependence and Harm. The
1051 National Addiction Centre, Kings College London and
1052 School of Social and Community Medicine, University of
1053 Bristol, United Kingdom: London and Bristol.
- 1054 **Robinson GM, Robinson S, McCarthy P, Cameron C** (2010).
1055 Misuse of over-the-counter codeine-containing analgesics:
1056 dependence and other adverse effects. *New Zealand Medical*
1057 *Journal* **123**, 59–64.
- 1058 **Romach MK, Sproule BA, Sellers EM, Somer G, Busto UE**
1059 (1999). Long-term codeine use is associated with depressive
1060 symptoms. *Journal of Clinical Psychopharmacology* **19**, 373–376.
- 1061 **Roumie CL, Griffin MR** (2004). Over-the-counter analgesics in
1062 older adults, a call for improved labelling and consumer
1063 education. *Drugs and Aging* **21**, 485–498.
- 1064 **Roussin A, Bouyssi A, Pouche L, Pourcel L, Lapeyre-Mestre M**
1065 (2013). Misuse and dependence on non-prescription codeine
1066 analgesics or sedative H1 antihistamines by adults: a cross-
1067 sectional investigation in France. *PLoS One* **8**, e76499.
- 1068 **Shek DT, Lam CM** (2006). Adolescent cough medicine abuse
1069 in Hong Kong: implications for the design of positive youth
1070 development programs in Hong Kong. *International Journal*
1071 *of Adolescent Medicine and Health* **18**, 493–503.
- 1072 **Shek DTL, Lam CM** (2008). Beliefs about cough medicine
1073 abuse among Chinese young people in Hong Kong. *Social*
1074 *Behavior and Personality* **36**, 135–144.
- 1075 **Skurtviet S, Faru K, Borchgrevink P, Handal M, Fredheim O**
1076 (2011). To what extent does a cohort of new users of weak
1077 opioids develop persistent or probable problematic
1078 opioid use? *International Association for the Study of Pain* **152**,
1079 1555–1561.
- 1080 **Sproule BA, Busto UE, Somer G, Romach MK, Sellers EM**
1081 (1999). Characteristics of dependent and nondependent
1082 regular users of codeine. *Journal of Clinical Psychopharmacology*
1083 **19**, 367–372.
- 1084 **Sweileh WM, Arafat RT, Al-Khyat LS, Al-Masri DM, Jaradat NA**
1085 (2004). A pilot study to investigate over-the-counter drug abuse
1086 and misuse in Palestine. *Saudi Medical Journal* **25**, 2029–2032.
- 1087 **Tang AK, Tang WK, Liang HJ, Chan F, Mak SC, Ungvari GS**
1088 (2012). Clinical characteristics of cough mixture abusers referred
1130 to three substance abuse clinics in Hong Kong: a
1089 retrospective study. *East Asian Archives of Psychiatry* **22**, 154–159. 1090
- Thekiso B, Farren C** (2010). Over the counter' (over the
1091 counter) opiate abuse treatment. *Irish Journal of Psychological*
1092 *Medicine* **27**, 189–191. 1093
- Tobin C, Dobbin M, McAvoy B** (2013). Regulatory responses
1094 to over-the-counter codeine analgesic misuse in Australia,
1095 New Zealand and the United Kingdom. *Australian and New*
1096 *Zealand Journal of Public Health* **37**, 483–488. 1097
- Tremlett M, Anderson BJ, Wolf A** (2010). Pro-con debate: is
1098 codeine a drug that still has a useful role in pediatric
1099 practice? *Paediatric Anaesthesia* **20**, 183–194. 1100
- UNODC** (2011). The non medicinal use of prescription drugs.
1101 Discussion paper. United Nations Publication: Vienna. 1102
- UNODC** (2013). World drug report 2013. United Nations
1103 Publication: Vienna. 1104
- Van Hout MC** (2015). Nod and wave: an internet study of the
1105 codeine intoxication phenomenon. *International Journal of*
1106 *Drug Policy* **26**, 67–77. 1107
- Van Hout MC, Bergin M, Foley M, Rich E, Rapca AI, Harris R,**
1108 **Norman I** (2014). A Scoping review of codeine use, misuse and
1109 dependence, final report. CODEMISUSED Project European
1110 Commission 7th Framework Programme, EU. Brussels. 1111
- Wilkinson D, Thelwall M** (2011). Researching personal
1112 information on the public web: methods and ethics. *Social*
1113 *Science Computer Review* **29**, 387–401. 1114
- Wilsey BL, Fishman SM, Gilson AM, Casamalhuapa C,**
1115 **Baxi H, Zhang H, Li CS** (2010). Profiling multiple provider
1116 prescribing of opioids, benzodiazepines, stimulants, and
1117 anorectics. *Drug and Alcohol Dependence* **112**, 99–106. 1118
- Wilson KM, Singh P, Blumkin AK, Dallas L, Klein JD** (2010).
1119 Knowledge gaps and misconceptions about over-the-
1120 counter analgesics among adolescents attending a hospital-
1121 based clinic. *American Academy of Pediatrics* **10**, 228–232. 1122
- Yang Y, Yuan QY** (2008). Investigation and analysis on
1123 personalities of male – codeine phosphate addicts by MMPI. 1124
Chinese Journal of Drug Abuse Prevention and Treatment **14**,
1125 143–145. 1126
- Zhou S** (2009). Polymorphism of human cytochrome P450 2D6
1127 and its clinical significance. Part 1. *Clinical Pharmacokinetics*
1128 **48**, 689–723. 1129