



CODEMISUSED

CODEINE USE MISUSE DEPENDENCE



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Coordinator



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- **Principal Investigator** Dr Marie Claire Van Hout
- Marie Skłodowska Curie Actions-Industry-Academia Partnerships and Pathways (IAPP).
- Scored Highest in Life Sciences Division 96/100.
- Commenced 9/13 and funded for 36 months € 2.04ml.
- 6 Partners, 25 Marie Curie Fellows.
- Expert Advisory Panel with representative experts from the European Medicines Agency, European Monitoring Centre for Drugs and Drug Addiction, Royal Pharmaceutical Society UK and Pharmaceutical Society of South Africa.
- Registered as EC funded study on the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) register of the European Medicines Agency.



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- CODEMISUSED aims to investigate extent and nature of codeine use, misuse and dependence in Ireland, United Kingdom and South Africa from perspectives of:
 - Users
 - Medical, pharmacy & treatment professionals
 - Customers
 - Treatment patients
 - National stakeholders
- Data will be used to inform:
 - Design of pharmacy screening & brief interventions
 - Risk management
 - Monitoring and surveillance
 - CPD training
 - Specific clinical/community pharmacy treatment protocols



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| Work package No | Work package title | Lead Beneficiary | Type of activity | Start-End month |
|-----------------|--|------------------|------------------|-----------------|
| WP1 | Project management and co-ordination | 1 | MGN | 1-48 |
| WP 2 | Systematic Review of Literature | 1 | TOK RTD | 2-6 |
| WP 3 | Web Survey of Medical Professionals | 1 | TOK RTD | 7-11 |
| WP 4 | Web Survey of Pharmacy staff | 3 | TOK RTD | 12-16 |
| WP 5 | Web Survey of Addiction Treatment Providers | 2 | TOK RTD | 17-21 |
| WP 6 | Sweep Survey of Customers | 3 | TOK RTD | 20-25 |
| WP 7 | Internet Survey of Codeine Users | 2 | RTD | 5-26 |
| WP 8 | Interviews with Codeine Users, Misusers and Dependents. | 1 | TOK RTD | 14-25 |
| WP 9 | Innovation | 2 | TOK TR | 26-29 |
| WP 10 | Networking Support | ALL | TOK | 6-29 |
| WP 11 | Liaising, co-ordinating and linking to other European projects and programmes' | ALL | DISS | 17-29 |
| WP 12 | Sustainability | ALL | DISS | 28-30 |

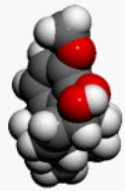


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- **WP 10-12 CODEMISUSED Networking Support, Liaising with other EC projects and Project Sustainability**
- ENCePP Research Centres and Networks
- Database of Research Resources
- Partners forum
- Working and Special Interest Groups
- E-Register of Studies
- ENCePP Code of Conduct
- ENCePP Checklist for Study Protocols
- ENCePP Guide on Methodological Standards in Pharmacoepidemiology



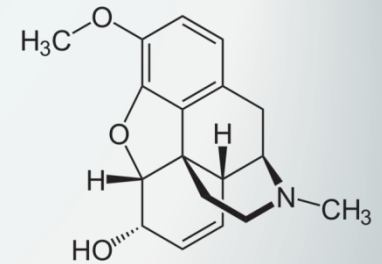
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- Van Hout, MC. Bergin, M. Foley, M. Rich, E. Rapca, Al. Harris, R. Norman I. (2014) **A Scoping Review of Codeine Use, Misuse and Dependence**, final report. CODEMISUSED Project European Commission 7th Framework Programme, EU. Brussels.
- Codeine or 3-methylmorphine is the most commonly consumed opiate in the world, and is used for its analgesic, anti tussive and anti-diarrhoeal properties.
- Globally, the demand for codeine remains high and has risen by approximately 27% over the last decade (INCB 2012).
- Codeine is available in over the counter combination preparations with caffeine, paracetamol or ibuprofen.
- Mild to moderate pain (prescribed).
- Moderate pain after unsuccessful treatment with paracetamol, ibuprofen or aspirin (over the counter).



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Misuse is defined as:

'The problematic consumption of codeine where risks and adverse consequences outweigh the benefits, and which includes use of codeine with or without prescription, outside of acceptable medical practice or guidelines, for recreational reasons, when self-medicating, with higher doses and for longer than advisable.'

Prevalence

Difficulties in estimating the scale of misuse centre on codeine product availability in pharmacies and online, and the heterogeneous and hidden nature of misuse and dependent use.



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Consequences of Misuse

- Impairment (driving and neurological damage).
- Injury risk (trauma, fractures and lacerations in falls/accidents).
- Excessive, long term or dependent use of codeine and combination codeine products causing chronic headache, perforated gastric ulcers, gastrointestinal bleeding, hepatotoxicity, inflammatory bowel conditions, pancreatitis and profound hypokalaemia associated with a severe myopathy, and often in users with no history of substance use disorders and co-morbidity .
- Neonate mortality and neonatal abstinence syndrome.
- Psychological harm and psychiatric disturbances.
- Dependence.
- Overdose.
- Injecting harms such as abscess, necrosis and BBV transmission.



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Types of Misuse

Use based on quantity of consumption.

- I. users that never exceed the maximum dose;
- i. users who sometimes consume slightly higher than the recommended dose;
- ii. users who consume significantly higher doses than recommended.

Misuse Characteristics

- I. exceeding recommended doses and treatment duration;
- II. becoming dependent on codeine for medical reasons (ie. pain);
- III. using codeine to manage opiate withdrawals;
- IV. using codeine for its euphoric effects;
- V. tampering with codeine preparations.



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Types of Dependence

- **Therapeutic dependence**

Not exceeding therapeutic doses but still demonstrating features of codeine dependence and often with worsening pain. Some are consistent with descriptions of medication overuse headache.

- **Non-medical dependence**

Use for intoxicating purposes. Often seeking and sharing knowledge and indigenous harm reduction (peer drug user and Internet forums).

- **High dose dependence:**

Use of high doses (multiple packets per day) and experiencing serious adverse effects from their use.

Almost always stemming from therapeutic use, with users often having limited insight into their dependence for an extended period of time.

In some cases, use begins for therapeutic use and escalates rapidly once euphoric effects of codeine were experienced.



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DSM-V Criteria Substance Use Disorder

- Taking the substance in larger amounts or for longer than intended.
 - Wanting to cut down or stop but cannot.
 - Spending a lot of time getting, using, or recovering from use of the substance
 - Cravings and urges to use the substance.
 - Not managing to do what you should at work, home or school.
 - Continuing to use, even when it causes problems in relationships.
 - Giving up important activities because of substance use.
 - Using substances again and again, even when it puts you in danger.
 - Continuing to use, even when the you know you have a physical or psychological problem that could have been caused or made worse by the substance.
 - Needing more of the substance to get the effect you want (tolerance).
 - Development of withdrawal symptoms
- ***1 – 2 indicate a mild substance use disorder. 6 - 7 symptoms indicate a severe substance use disorder.***



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Wide ranging profile of individuals who misuse codeine

- parental medication of children.
- youth
- drug users.
- adolescents
- university students.
- pharmacy customers.
- drug treatment patients.
- psychiatric patients.
- older people.



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Aberrant Behaviours

- Doctor 'hopping'
- Pharmacy 'shopping'
- Selling prescription codeine
- Forging prescriptions for codeine
- Obtaining prescriptions from non-medical sources
- Repeated episodes of lost and/or stolen prescriptions
- Aggressively demanding increased dosages of codeine
- Requesting specific products by name
- Repeated requests
- Tampering with codeine formulations



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- Van Hout, MC (2014). **Kitchen Chemistry: A scoping review of the diversionary use of pharmaceuticals for non-medical use and home production of drug solutions.** *Drug Testing and Analysis.* 6, 7-8, 778-87

Types of Formulation Tampering

- Cold Water Extraction Methods and Nurofen Plus splicing.
- Oral misuse of codeine cough syrups (i.e Purple Drank, Lemon Drop)
- Home-made solutions containing codeine cough mixture with alcohol, benzodiazepines, caffeine, kratom and soft drinks (Kratom Cocktails).
- Home-made solutions for injecting purposes using over the counter codeine products, with morphine (Braun, Home Bake) or by generation of desomorphine (Russian Magic)



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Van Hout, MC (2014). Nod and Wave: an Internet study of the codeine intoxication phenomenon. *International Journal of Drug Policy*. E-Pub Ahead of Print. June 30th 2014.

Codeine Intoxication

- Dulling of emotional and/or physical pain, opiate withdrawal management and for intoxication.
- Appeal centres on access via family medicine cabinets, prescribers and over the counter in pharmacies.
- Oral and rectal use, optimal codeine dose per session 250mg.
- Online indigenous harm reduction; learning to appreciate codeine's effect via moderated use in optimal settings, avoidance of tolerance by use of informed dosing schedules, cold water extraction of codeine, and using codeine as an alternative to stronger opioids.
- Dissociation, synaesthesia, and out of body experiences.
- Potentiating practices (i.e. grapefruit) and using over-the-counter medications (anti histamine, antacids) to improve intoxication experiences and reduce unpleasant side effects.



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Treatment of Codeine Dependence

Clinical profiles of codeine dependents vary but are over represented by females, those in middle to late age, poly substance users, alcohol users, opioid dependents and those with underlying psychiatric conditions.

The majority of codeine dependent individuals do not view themselves as needing help and do not identify themselves as 'drug addicts'.

The literature in relation to treatment and management of codeine misuse lacks specificity to codeine protocols.

Poor long term outcomes for codeine dependents at 12 month follow up.



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Recommendations for Practice and Policy

- Public and professional awareness campaigns around safe use of medicines containing codeine, particularly in terms of patient aberrance, the risks of dependence and associated health consequences on excessive and / or long term use.
- Integrated monitoring and surveillance in pharmacies , national recording of prevalence of use, misuse and dependence.
- Coordinated responses in the form of patient or customer education, screening for risk of abuse and patient agreements are warranted to address drug compliance.
- Pharmacy precaution and protocols for sales and refusal to supply, training and support of staff.
- ‘Universal precautions’ approach for all codeine sales is warranted rather than the current selective type methods based upon suspicion.
- Screening and brief interventions at point of sale along with supported detoxification in pharmacies.



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Evidence and understanding of codeine misuse will inform promotion of safer public use of codeine, innovative public health interventions, clinical and pharmacy practice guidance, risk management and drug surveillance, and effective enforcement policies.

Recommendations for Research

Gaps in knowledge centre on prevalence of misuse and dependence, therapeutic and non therapeutic pathways and trajectories to misuse and dependence, risk profiles and characteristics of users, poly pharming practices, adverse health and social consequences, treatment and interventions, and displacement between legitimate pharmacy supply and illicit sourcing.



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