Codeine Use, Misuse and Dependence

Marie Claire Van Hout, Ph.D
Principal Investigator
CODEMISUSED
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Marie Claire Van Hout, PhD
M.Sc International Programme in Addiction Studies (IPAS)
M.Sc Health Promotion.

Coordinator, Substance Misuse Research, School of Health Sciences,
Waterford Institute of Technology, Ireland

Registered on the European Network of Centres for Pharmaco-epidemiology
and Pharmaco-vigilance (European Medicines Agency).

Associate Staff Member, Alcohol, Tobacco and Other Drug Research Unit,
Medical Research Council, Cape Town, South Africa.

Visiting Research Fellow, Centre for Public Health, Liverpool John Moore’s
University, Liverpool, United Kingdom

Visiting Research Fellow, Glyndwr University, Wales, United Kingdom
• **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 € 2.04 million.

• 6 Partners, 3 countries, 27 Marie Curie Fellows.

• Registered as EC funded study on the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) register of the European Medicines Agency.
CODEMISUSED Expert Panel

Dr Kevin Blake, European Medicines Agency
Dr Richard Cooper, University of Sheffield

David Bayever
University of Witwatersrand Medical School

Dr Michael Evans Brown
European Monitoring Centre for Drugs and Drug Addiction

European Monitoring Centre for Drugs and Drug Addiction
Research objectives of CODEMISUSED

CODEMISUSED aimed to explore the nature of *codeine use, misuse and dependence* in Ireland, United Kingdom and South Africa from the perspectives of:

- National stakeholders
- Consumers
- Medical, pharmacy & addiction treatment professionals
- Addiction treatment patients
- Internet monitoring of online pharmacies and drug forum activity
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TOK-transfer of knowledge, RTD – Research to Dissemination
• **Misuse of opioid pharmaceuticals** is emerging as a global public health concern, amid calls for revised scheduling and increased pharmacovigilance.

• **Codeine**, or 3-methylmorphine, is the most commonly consumed opiate worldwide, widely used for its analgesic, anti-diarrhoeal and antitussive properties.

• There is a global shift toward availability of non-prescription codeine-containing products and promotion of **patient self-management**.

• Misuse of non-prescription codeine-containing products, particularly combination codeine analgesics, is on the **increase** in countries where available.
• Codeine has an **identified abuse potential** which centres on its opiate effect and development of tolerance within a short timeframe on regular or excessive use.

• Risk of tolerance is increased through increasing the dose for **therapeutic and non-medical or recreational purposes**.

• **Physical dependency and withdrawal symptoms** mimic those of morphine and, whilst less severe, include cravings, preoccupation with obtaining and taking codeine, lack of control of consumption despite negative side effects, insomnia, restlessness, runny nose, stomach pains, diarrhoea and chills.
Misuse of Codeine

- 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 other than for the instructions on the label or the intended purpose;
- recreational use for mind altering effects;
- and where risks and adverse consequences outweigh the benefits.

(Casati et al., 2012).
Consequences

Prolonged use of codeine is strongly associated with depression and dysphoric mood states.

Codeine can interact with other medications and substances such as alcohol, leading to respiratory depression and other central nervous system effects.

Long term use of combination analgesic products containing ibuprofen and paracetamol can lead to gastric ulcers, gastrointestinal bleeding, hepatotoxicity, hypokalaemia, inflammatory bowel conditions, and profound hypokalaemia associated with a severe myopathy.
Consequences

**Impairment** (driving and neurological damage).

**Injury** (trauma, fractures and lacerations in falls/accidents).

**Injecting harms** (abscess, necrosis and BBV transmission).

**Dependence** (often in users with no history of substance use disorders and co-morbidity).

**Overdose.**
Extent of the Issue

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 therapeutic and non therapeutic use.
Identified Wide Ranging Profile of Individuals who misuse codeine

- Parental medication of children
- Drug users
- Adolescents and youth
- University students
- Pharmacy customers
- Drug treatment patients
- Psychiatric patients
- Older people
- Health professionals
The available evidence also suggests that many codeine dependent people regret their dependence and associated work and social problems and also reject a ‘drug identity’, seeing themselves different from other illicit drug users because of

- their **continued work and social activity** and;
- because they are **reassured about its safety through its legal status and availability over the counter from community pharmacies.**
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
Displacement Patterns between OTC and Prescribed Supply
A total of 938 medical professionals involved in the prescribing of medicines completed the survey, 398 in Ireland, 300 in the UK and 238 in South Africa

**Key Medical Prescriber Findings**

- Patients do not fully understand the potential risks of codeine use.
- Patients are not provided with sufficient information when purchasing OTC medicines from pharmacies.
- Communication platforms should be examined:
  - namely those from pharmacists and counter staff and from prescribing professionals including patient information leaflets contained in both dispensed and OTC medicines
  - role of information obtained on the internet and through the advertisement of the products should also be examined in the context of purchasing power and influence in the decision to use codeine for self-medication purposes
  - labelling and packaging of products sold OTC should be examined in the context not only of addiction but the dangers of excess use of paracetamol or ibuprofen
  - toxicity information must be clear to all those prescribed codeine by a professional.
A total of 716 pharmacists completed the survey, Ireland, n=464, South Africa n=123, United Kingdom n=129

Key Pharmacist Findings

• Pharmacists described popular codeine containing products, and the need for improved patient medicine information & warning labels.
• Issues raised around legitimate availability of non-prescription codeine, retail focus, presence of therapeutic need, difficulties in customer–pharmacist communication, and merits of up-scheduling.
• Identification of customers who misused codeine, pharmacy ‘hopping’, & problematic relationships between pharmacists and prescribers.
• Specialist training, reimbursement for customer consultation, screening brief interventions, visible referral structures & assisted community pharmacy detoxification were also discussed.
Key Pharmacist Findings

- A “centralised system” to record and restrict codeine sales where customers would have to provide identification when they purchased codeine-containing products.
- Upscheduling
- Need for inter-agency care in identification, referral and support of customers experiencing problematic use.
- Changes to packaging of codeine products
- Reducing the size of codeine products (for example, reducing the number of tablets that are sold in one packet of codeine combination products),
- Increasing the price of these products
- Removal of certain products from the market completely, such as Solpadeine and Nurofen Plus.
- In Ireland and the UK, a few participants also mentioned that they thought that the level of control of codeine was fine in their jurisdiction, and that it is important to “treat people like adults. They felt that an increase in control could undermine the genuine “therapeutic need” for these products in Ireland.
Types of Formulation Tampering and Home manufacture of drug solutions

- 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)
Drug Users: The Codeine Intoxication Phenomenon

- 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.
- 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.
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 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.
Key Addiction Treatment Findings

- Formal drug treatment data involving codeine misuse and dependence were retrieved from the United Kingdom (UK) National Drug Treatment Monitoring System (NDTMS), the Irish National Drug Treatment Reporting System (NDTRS), and the South African Community Epidemiology Network on Drug Use (SACENDU).
- 1.9% of persons in drug treatment in Ireland (2008-12) had codeine as a primary or secondary drug of abuse compared to 2.2% in the UK (2013/14) and 2.5% in South Africa (2014).
- Survey of Addiction Treatment providers ongoing.
CODEMISUSED will inform

- Manufacture and product formulation;
- Monitoring and surveillance of sales;
- Consumer medicine information, packaging and warning labels;
- Responsible prescribing;
- Pharmacy dispensing practice, risk management and clinical audit;
- Pharmacy screening and brief interventions;
- Road and workplace safety interventions;
- Internet supply and drug forum monitoring;
- CPD training and E-Learning modules for health professionals;
- Specific clinical and community pharmacy treatment protocols.
Sources

ENCEPP circular request for innovation across the EU.
Conversational interviews with information rich national
key stakeholder key informants from across the 3
participating countries of the Codemisused Project
A search of literature retrieved for the Scoping Review
(WP2) for examples of innovations.
Inclusion of a single item within questionnaire surveys of
medical practitioners, pharmacy staff and addiction
treatment providers in CODEMISUSED.
Challenges for CODEMISUSED

Complexity of inter-relations between the different pharmacological, social, economic, legal and individual factors which shape patterns of use and misuse.

Thin dividing line between therapeutic use and misuse of codeine.

Unsystematic and poorly integrated drug and pharmaceutical monitoring systems making it difficult to know the true extent of the codeine misuse problem and the profile of codeine users.

Potential for use of unregulated internet retail sites to purchase codeine and access networks of codeine users.
Scientific Outputs

- 5 peer reviewed journal publications to date (August 9th 2015);
- Accepted title on Cochrane Review registry investigating efficacy of di-hydro-codeine in the opiate dependence;
- 2 scoping reports on Codeine and submitted to the European Medicines Agency Pharmacovigilence and Risk Assessment Committee (PRAC);
- 4 reports presenting national medical prescriber, pharmacy, addiction treatment provider and addict perspectives;
- 3 clinical audits for pharmacy training and safe supply of non-prescription codeine containing medicines for use by national pharmacy regulators;
- 1 report (in draft) on Innovation to manage and address misuse of codeine medicines;
- 2 patient and health professional factsheets;
- 1 European EURODURG bulletin;
- 1 European Research Directorate publication (EU-Africa);
- One National Primary Health Care Award for Best Conference Poster;
- Dissemination at 10 national and international conferences;
- Delivery of 27 workshops and seminars in each partner country;
- 6 journal publications under review.
Scientific Highlights

- Acceptance of CODEMISUSED onto the Pharmacovigilance (ENCePP) registry of research projects approved by the European Medicines Agency (EMA) for research in the EU - Official reference number is ENCEPP/SDPP/4708.
- CODEMISUSED was selected as success story for inclusion in the upcoming publication by the Directorate General "Research and Innovation" of the European Commission. This publication highlights the results of EU-Africa collaboration on science, technology and innovation funded by the EU's 7th Research Framework program.
Further Information

See http://www.codemisused.org

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Thanking you, the CODEMISUSED Team.

Correspondence: Dr Marie Claire Van Hout - mcvanhout@wit.ie