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Complete List of Authors:	Kinnaird, Emma; King's College London, Eating Disorders, Psychological Medicine Kimergård, Andreas; King's College London, Addictions Department Jennings, Stacey Drummond, Colin; Kings College London, Institute of Psychiatry Deluca, Paolo; King's College London, Addictions
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From pain to dependence: A qualitative study of environmental influence on codeine use

Emma Kinnaird[1*], Andreas Kimergård[2*], Stacey Jennings[2], Colin Drummond[2], Paolo Deluca[2]

** Joint first authors*

[1] Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

[2] National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

Correspondence to: Andreas Kimergård, National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 4 Windsor Walk, SE5 8BB, London, United Kingdom, e-mail: Andreas.Kimergard@kcl.ac.uk, telephone: 020 7848 0825

ABSTRACT

Objectives To investigate individual experiences of transitions in codeine use from treatment of acute pain to codeine dependence in order to characterise environmental factors capable of producing and reducing harm.

Design This was a qualitative interview study. Probable codeine dependence was measured using the Severity of Dependence Scale (SDS).

Setting Participants were recruited from a residential rehabilitation service and from an online survey.

Participants 16 adults (13 women and 3 men) from the UK using codeine other than as directed or as indicated and initially using codeine to treat pain. Mean age was 32.7 years (*SD* = 10.1) and mean period of codeine use was 9.1 years (*SD* = 7.6).

Results Participants' experiences indicated that they became dependent on codeine as a result of environmental factors. Medicine review of repeat prescribing of codeine, well-managed dose tapering to reduce codeine consumption, support from social structures in form of friends and online, and access to addiction treatment interacted in the environment to reduce the risk of harm. Micro- and macro- environmental factors capable of producing harm, included unsupervised, long-term codeine prescribing and breakdown in structures to reduce the use of over-the-counter codeine other than as indicated. In the sample, the mean SDS score was 6.5 (*SD* = 4.9) (cut-off score ≥ 5).

Conclusion The study identified micro- and macro- environments capable of producing dependence on codeine, including repeat prescribing and unsupervised use over a longer time period. The economic environment is crucial in its influence upon the available resources for holistic pain therapy in primary care to offer alternative treatments to codeine. Overall, the goal is to create an environment that reduces risk of harm by promoting safe use of codeine for treatment of acute pain, whilst providing effective care for those developing tolerance and dependence.

Keywords

Codeine, dependence, prescribing, over-the-counter, risk environment.

Strengths and limitations of this study

- We present an investigation of the environmental factors producing and reducing harm related to codeine containing medicines to realign the risk environment with practices of codeine use and dependence.
- Understanding micro- and macro- level risk environments enables use of codeine in a way so the benefits outweigh the harms.
- A limitation is the small sample size and findings cannot be generalised to all regions of the UK.
- Environmental factors to reduce or produce harm related to codeine may vary depending on factors such as local funding and health care coverage.

INTRODUCTION

The risk of physical harm and depression associated with long-term use of and dependence upon codeine containing medicines are well-known,[1,2] and in the UK, data from the National Drug Treatment Monitoring System show that codeine was the primary or secondary drug for 2.2% of clients (*N* = 4,248) in structured drug treatment (2013/2014).[3] Daily consumption of 1,250 mg codeine, which is 5 times the maximum daily dose,[4] has successfully been treated with opioid agonist therapy (buprenorphine/naloxone) and tapered dosing over a 4-month period.[2] However, many individuals who are dependent on codeine may not seek help due to a reluctance to explore non-opioid pain treatments.[5,6] Furthermore, regional variability in addiction treatment may act as a barrier against receiving effective care. To improve pain treatment and physical and mental health, concerted efforts are needed at the level of codeine prescribing, dispensing and use to reduce the number of patients who become dependent after treatment of acute pain.

Codeine is widely accessible in the UK: it is one of the most commonly prescribed opioids and can be purchased over-the-counter (OTC) in licensed pharmacies without a medical prescription. In 2016, the UK was the second biggest consumer of codeine in the world at 44.2 tons.[7] According to Prescription Cost Analysis data, more than 15 million items of co-codamol (codeine/paracetamol) were dispensed in the community in England in 2017 − an increase of approximately 15% since 2007.

Therapeutic indications for codeine use are treatment of mild to moderate pain not relieved by non-opioid analgesics such as paracetamol and ibuprofen.[4] Although considered a 'mild opioid',[8] long-term codeine use can lead to tolerance and dependence.[9-11] Use of compound products containing paracetamol or ibuprofen in higher than recommended doses may result in harm from high doses of accompanying non-opioid analgesics, such as gastrointestinal complications attributed to ibuprofen and liver damage with paracetamol.[12] Indications of possible codeine dependence include long-term use for non-cancer pain,[5] use for anxiety and depression,[10] and obtaining codeine from multiple sources, including prescribed, OTC and from the illicit market.[2,13]

With these levels of codeine use in the UK, it is important to consider the factors which impact on the production and reduction of harm. In this article, we utilise the 'risk

environment' framework to understand the environmental factors specific to codeine use. The framework highlights the impact of context on individual risk by considering how environments (physical, social, economic and policy) interact at varying levels (micro and macro) to influence risk.[14] This framework has previously been applied to investigate the production of illicit drug harms,[15,16] but not the development of codeine dependence in a pain treatment context.

Codeine-specific examples illustrate the logic applied in this framework: at the micro level, starting patients on prescribed codeine without a clear plan for stopping again may increase the risk of long-term use and dependence.[6] Conversely, careful and patient-involve dose tapering protect against long-term use. At a macro level, regulation restricts access to high doses of codeine in the form of pure formulations to prescription-only with prescribers deciding if they are appropriate to use. Although formulations of codeine combined with paracetamol or ibuprofen are available OTC, only one packet can be sold at a time and the packet labelling must state: 'Can cause addiction. For three days use only'.

Yet, studies indicate that transitions still occur from short-term codeine use to treat pain to long-term use and dependence.[10,13,17] Reasons why individuals experience harm with, and dependence on codeine include: physical and psychological withdrawal resulting in prolonged use,[1,10,18] poor understanding of the risks of taking codeine,[19] and disengagement from general practitioners (GPs) due to concerns of codeine dependence being recorded in medical notes.[13,20] In an environment where opioids are prescribed more often and for longer periods, despite the lack of evidence of long-term efficacy for chronic pain,[10,21-23] dependence is an increasing problem.

This article investigates the individual experiences of transitions in codeine use from treatment of acute pain to use other than as directed and to codeine dependence to identify salient environmental factors that shape codeine practices.

METHODS

Design

This was a qualitative study that used data from semi-structured interviews with participants reporting use of codeine in the last 12 months and living in England. Inclusion

criteria were: Any individual aged between 18 and 75 who used codeine other than as directed or as indicated, whether wilful or unintentional, and whether it resulted in harm or not.[24] The study was approved by the NHS REC Committee London (London Bridge), REC Reference 15/LO/0107.

Recruitment

Participants were recruited from a residential rehabilitation service and amongst respondents to an online survey.[10] A leaflet was provided to clients in the residential rehabilitation programme informing about the study. All eligible clients in the service at that time were invited to take part, resulting in ten interviews conducted by AK. A question in an online survey[10] invited respondents to take part in an interview by emailing the researcher or providing contact details. AK contacted and interviewed all eligible participants who did so, resulting in an additional eighteen interviews.

Sample

Of the 28 participants, one was excluded as codeine was used according to accepted medical practice or guidelines, whilst 11 participants were excluded from the analysis due to their initial use of codeine not relating to pain treatment. This resulted in a sample of 16 participants who first took codeine for pain treatment purposes.

Data Collection

Participants were given a Participant Information Sheet informing of the reasons for doing the study and the involved researchers and institutions and asked to sign a consent form (Supplementary File). Interviews took place either in the residential rehabilitation service, at a location chosen by the participant or over phone. The first interview was conducted in May 2015, and the last in April 2016. Interviews lasted from 35 minutes to an hour and 35 minutes. Participants were compensated for their time with a £20 gift voucher. Interviews were conducted using a topic guide, covering: demographic information, initial use of codeine, patterns of codeine use, difficulties managing codeine use, sourcing of codeine, use of other drugs or medicines, and views on codeine availability and regulation. New topics brought up by the participants were pursued during the interviews with follow-up questions. Codeine dependence was measured using the 5-item Severity of Dependence

Scale (SDS) during the most recent period of codeine use.[25,26] A score of 5 or above was used to indicate probable codeine dependence.[9]

Data management and analysis

Interviews were audio-recorded then transcribed verbatim by a professional service, with any participant identifying information removed from the transcripts. Data were entered into NVivo 11 for coding. Data was analysed using Framework.[27] A coding framework was developed deductively based on the topic guide and codes that emerged inductively from the data. To address the aims of this article, analyses were confined to experiences with codeine use and factors relevant to understand the risk environment for codeine. This resulted in codes relating to: i) the role of prescribing practices related to codeine and non-opioid treatment, ii) the accessibility and use of OTC codeine, and iii) interventions and treatment for codeine dependence. The goal was to identify factors producing and reducing harm, which may have transferability to other settings.[28] Analyses are presented with supporting quotes (anonymised using participant numbers) and SDS scores.

RESULTS

Participant characteristics

The sample consisted of 3 men and 13 women, with a mean age of 32.7 years (*SD* = 10.1) and a mean period of codeine use of 9.1 years (*SD* = 7.6) (Table 1). In the sample, 3 participants (18.8%) were unemployed, 3 (18.8%) were students, and 10 (62.5%) were employed. Co-morbid anxiety or depression was reported by 4 participants (25%), and 4 (25%) reported concurrent use of codeine and other prescription opioids. A majority of 6 were living in Greater London, 4 in North West England, 2 in East of England and 1 in each of the regions: North East England, West Midlands, Yorkshire and the Humber, and East Midlands. Using the SDS, 10 participants (62.5%) scored 5 or more, indicating probable codeine dependence. The mean score for the sample was 6.5 (*SD* = 4.9). At the time of interview, 4 participants (25%) sourced codeine from a medical prescription, 3 used OTC codeine (18.8%), whereas 9 used both (56.3%). Only 1 participant reported additionally sourcing codeine from the internet, whilst 3 also used codeine obtained from family or friends. In total, 4 participants (25%) had received intervention and treatment for their

codeine use, including addiction treatment, GP led intervention, counselling or from a psychiatrist.

Education of patients on prescribed codeine

Many participants explained that they had not fully understood the potential risks when they first started taking codeine, including its addictive potential. Reflecting on their initial codeine use, many expressed frustrations with their GP and suggested that they wished they had been given more information:

> "If I had had a doctor who possibly just had a little bit more time to say here's what I'm giving you, here's what it is, here's what it does, here's the risks to it. If I had just been a little bit more educated, perhaps it wouldn't have happened [use in excessive doses]." Participant 11, male, dependence score 0.

Participants identified several potential barriers facing health professionals in effectively communicating risks. Specifically, participants felt that the typical 10-minute GP appointment was not enough to fully discuss available options for pain therapy. Of note was that participants who had greater awareness of the risks of codeine, typically from searching for information on the internet, were often more motivated to avoid these risks. However, when participants voiced concerns to their GP, they felt ignored and detached from decisions about their health and care:

> "I kind of had to battle to get my GP to do or say anything about my lower back pain, because they're just like, it's lower back pain, what can you do? They just kind of send you away, say carry on, take the painkillers…It didn't seem like anyone was taking any care in the fact that I could get addicted to this; I didn't bother to go back." Participant 15, female, dependence score 2.

Such encounters with health professionals enhanced the feeling of not being listened to and contributed toward disengagement from health services, distrust in medical opinions, and isolation. In this environment, fewer factors act to protect against unsupervised, long-term codeine use. Consequently, the lack of effective risk communication between prescribers and patients, and a resulting poor education of patients on codeine risk, appeared to facilitate the development of codeine dependence for some participants.

Inappropriate prescribing?

The majority of participants who received prescription codeine did so through a repeat prescription. Individuals robustly reported being able to order their repeat prescription with few restrictions on amounts and frequency, which for some resulted in increasing codeine intake:

> "It wasn't just once a month for my periods, like I went through a period of having really bad back ache, so I took it for that. Then for when I twisted my ankle like four or five times, so I'd take it for that. I started running two years ago, now I've got a knee injury, so I'd take it for that. It was just whatever niggles and pains there were, I'll just pop some tablets because I had them on a repeat prescription and they were basically on tap. That's when it started to really get a grip, because I was taking them for other things on a more or less daily basis." Participant 8, female, dependence score 7.

Within the codeine risk environment, prolonged access to codeine with minimal supervision from a health professional can facilitate use of codeine other than as indicated during the initial consultation, influencing transition to subsequent dependence. This demonstrates how structural factors impact on patients' consumption to influence the practices of codeine use.

Codeine or non-opioid pain treatment?

It was striking that participants using codeine from a medical prescription reported being prescribed codeine as a first resort for pain, even when participants were otherwise motivated to try other types of pain treatments:

> "I went and said I need another bout of physio for my back because it's starting to hurt again. And they [GP] said: 'oh, you've got to be in constant pain for six weeks'. And I said: 'I've been in constant pain for six weeks already, and it's a recurring problem, so please just refer me.' And the doctor said: 'no, go and take these pain medicines [codeine] and come back in six weeks'. And I said: 'I think it's really dangerous that you're telling me to go away and take a pain med that I know is really highly addictive constantly for six weeks, for a problem that you already know

exists.' And they said: 'well, that's just the way it works, I'm sorry." Participant 8, female, dependence score 7.

For some primary care patients in the study, these issues were perceived as a general systematic problem reflecting a lack of treatment resources. They felt like they had been prescribed codeine in order to quickly get rid of them, rather than their GP taking the time to deal with the underlying problem or being referred to specialist services. This did lead to frustration and, in some cases, disengagement from GPs, for example to seek treatment privately:

"…if that's the only advice you're going to give me [take codeine], then I will do what works for me. And I went to an osteopath and that really helped." Participant 15, female, dependence score 2.

In contrast with the negative perceptions of codeine prescribing expressed by some participants, those who were treated with non-opioid pain medicines, physiotherapy and hydrotherapy, indicated that they felt less concerned about continued codeine use:

"Through the doctor they referred me to a hydrotherapy thing, because I just hadn't had any physiotherapy before for the pain. So, I had six sessions with them and they gave me exercises to do at home. I've been trying to keep up with that, which has I guess lessened the pain. I no longer think that I'm going to get dependent on codeine because it's been that long that I don't wake up in the morning and think I have to take a pill." Participant 12, female, dependence score 5.

Participants' accounts therefore highlighted several structural factors in the risk environment influencing codeine harm: having alternative treatments available beyond codeine resulted in better engagement with health services and greater patient satisfaction, whilst minimising chronic codeine therapy. Conversely, treating pain solely with codeine did result in disengagement from health. Clearly, a perceived lack of resources in primary care emerged as an important economic factor in the environment.

Differences in relationships with pharmacists and GPs

Implementation of pharmacist intervention to regulate OTC codeine sales is intended to prevent codeine from being used other than as indicated and is one example of a factor which reduces risk. However, participants were able to circumvent restrictions on sale by

purchasing from multiple pharmacies over the course of a week or even a day. While one participant had been refused codeine in a pharmacy, most OTC codeine users reported rarely being questioned by pharmacists to find out if codeine was a safe choice, even when they regularly came to the same pharmacy and obtained large amounts of codeine:

> "It's the same staff all the time and I've bought it from there many times. And nobody has ever questioned me at all." Participant 7, female, dependence score 14.

Another important outcome of accessing multiple pharmacies in the local area was that participants never established a strong relationship with a single pharmacist, contrasting this to many perceiving a much better relationship with their GP. Even where participants only accessed one pharmacist, they often perceived this relationship as less important to them and therefore less effective in providing risk education, support and interventions than their GP. This appeared to also be related to the short amount of time participants spent interacting with pharmacists when buying codeine:

> "Whenever I go and speak to pharmacists, I've just never felt particularly comfortable speaking to a pharmacist. I find they're a bit… maybe not judgmental, but I find they're a bit short and like they are very kind of medical. I don't find that there's much interaction. I would just prefer to speak to my GP, because I feel I can trust him and I feel I've got a good relationship." Participant 3, female, dependence score 7.

However, participants also emphasised that pharmacists were far easier and quicker to access than scheduling an appointment with their GP, providing a disincentive to wait and consult with their GP about their codeine use. The difference in role perceptions of different groups of health professionals appears to act as a factor which may 'push' codeine dependent patients away from GP led codeine monitoring to unsupervised OTC use:

> "I lied to the doctor once, but that killed me doing that. I was really ashamed of myself at the time. I wouldn't have kept doing that [to continue using codeine]. It's only because I had been able to buy it OTC that I've kept on with that addiction. And even now, when I have a bad week and I really need codeine, I'll go and buy it OTC. I wouldn't do that if I had to go to my GP and explain." Participant 7, female, dependence score 14.

Some participants with personal experience of use other than as indicated and codeine dependence believed that codeine should be restricted to prescription only. In contrast, one participant with a low SDS score suggested that this would not be necessary nor feasible in the context of a wider NHS lack of resources – If everyone self-treating their pain with codeine had to regularly see their GP, primary care would become overwhelmed:

> "I think that it shouldn't be made much more difficult to get hold of because I think most people can go through some acute pain that lasts a couple of days that you might need something like this for, and our NHS is stretched enough without having to go to the GP every time you spring your ankle." Participant 15, female, dependence score 2.

This illustrates the dynamic nature of the risk environment, where multiple factors may influence the production of codeine harm, suggesting that for short term use for acute pain the benefits of OTC codeine outweigh the potential risk of dependence and thus play a significant role in providing access to pain treatment. However, in cases where factors implemented to protect against long-term use fail, such as pharmacist regulation of OTC sales, OTC codeine is associated with a risk of dependence. Here, its availability may to some extent undermine wider public health attempts to promote safe use of opioids.

Support, intervention and treatment of codeine dependence

Four participants had experience with intervention and treatment for codeine dependence, ranging from GP initiated medicine review to addiction treatment. Still, most participants with SDS scores indicating probable codeine dependence did not report any medical supervision or support; for some this spanned several years during which codeine use became an established part of their daily practice.

It is particularly relevant to note the significance of the role GPs played for many dependent participants. Whilst many participants expressed frustration with the perceived lack of resources and alternative treatment options, when participants openly disclosed their difficulties in controlling their use of codeine, GPs played an important role in intervening:

> "I thought I'll just tell him [GP] and I'll just see what he says [about difficulties in managing codeine use]. And I ended up getting signed off work for about four weeks...I really trust my GP…When I tell him that I don't want to take codeine,

> he asks me why, and he kind of tries to look at other options for me, which I really appreciate. I think it was kind of a combination of all those different things, the GP and the counselling, the time off work, everything sort of came together. I think if it had only been one of those things, I don't know how well my recovery would have gone." Participant 3, female, dependence score 7.

Where participants engaged with their GP regarding their codeine use, either due to GP instigated follow-up consultations concerning their use of codeine or to the participant asking for an appointment, their GP was able to help via effective interventions such as tapering codeine and replacing compound products with pure codeine formulations to prevent the risk of physical harm from non-opioid analgesics. This suggests that in an environment where GPs have resources to support the patient, they reduce the likelihood of risks occurring:

> "He wrote me out like a little rota. He said we were going to do it [taper] over a certain period of time. And I had to sign, like he made like a contract for me to sign, and he signed it as well, to say that he was going to help me, and he was going to support me. And he was really understanding and not judgmental at all, it was fabulous. He said he was going to prescribe me a certain amount of just codeine, so not the paracetamol, just codeine on its own." Participant 8, female, dependence score 7.

When two participants, who had attended addiction treatment, were asked why they had started treatment they generally described lengthy and complicated pathways which did require significant level of self-motivation. One male participant who was currently a client in a residential rehabilitation programme described the social, economic and physical factors that motivated him to eventually seek treatment and detoxification for codeine dependence. These included transitions from single to multiple codeine containing medicine use (OTC and prescribed), breakdown in family relationships, dropping out of university, social isolation, being fired from work and physical adverse effects from high doses of compounded ibuprofen:

> "I think when I had the stomach ulcer, I started realizing then that this will actually kill me. I cut down the Nurofen Plus [codeine/ibuprofen] because it was what kept me going really, but I couldn't put it down…I just couldn't stop. I

> hadn't got a job, I'd dropped out of uni. Just living at home doing nothing and it kind of dawned on me you know, I've really got a problem. At first, I went to the local drug services, and they said that they don't deal with codeine so there wasn't any help there, and someone gave the number for there [residential rehabilitation service], a family friend or something…It was quite quick, about after two weeks [starting in treatment]." Participant 1, male, dependence score 15.

For some of the participants, disengagement from medical professionals, and the placing of responsibility on the patient to self-manage their dependence, created situations where participants reported that they instead used the internet to find out more information about codeine, pain treatments, and advice on how to manage the use of codeine.

> "When I was first diagnosed with depression and anxiety, when I was just being pushed and pulled from different doctors, different psychiatrists, I looked to the internet to do my own research and just understand what these medicines were [codeine]. I didn't know what I was taking, and I didn't know what the risks of abusing it was, so I felt that I should really start understanding what I'm being prescribed." Participant 11, male, dependence score 0.

Support structures in form of family and friends also played an important role to some participants as a source of information about codeine. For this participant, an encounter with a friend facilitated personal reflection as to her own use of codeine:

> "One of my best friends was going for a job interview and I said to her: 'do you want to take a codeine like an hour before you leave the house? You'll feel so very relaxed.' And although she took the tablets, she said to me: 'I don't feel comfortable with this and I don't think that I should' A few months later she asked me if I used to take them for reasons other than pain, and I said to her no, but in my heart, I knew that I did. I asked her why. She said: 'because it's a very addictive drug…it's something that can basically change the chemicals in your brain and you'll be addicted forever.' She suggested a few articles for me to read, which I did, and then I was very worried because then I learned that codeine was connected to morphine." Participant 10, female, dependence score 2.

Such relationships played an important role for participants to gain more confidence in their ability to manage their use of codeine, especially for those using codeine other than as indicated, but not experiencing codeine dependence. However, over-reliance on inaccurate online sources and advice from friends and family may also delay or prevent patients from seeking support from health professionals until they experience severe dependence that is much more complicated to treat. As such, the social environment has the capacity to both produce and reduce codeine-related harm.

DISCUSSION

This qualitative study explored individual transitions in codeine use from treatment of acute pain to dependence, in order to unpack the key elements of this specific risk environment. These findings add to existing literature that suggest that some patients who use codeine for acute pain become dependent as a result of environmental factors.[10,20] We identified a number of environmental factors that reduced the risk of dependence: medicine review of repeat codeine prescribing, interventions in primary care (such as tapering), social support (friends and online), and access to addiction treatment (Table 2). We also identified several micro- and macro- environmental factors capable of producing harm, especially unsupervised, long-term codeine prescribing and breakdown in structures to stop sales of OTC codeine for use other than as indicated (Table 2). These findings indicate the importance of re-aligning codeine practices with situational reduction of harm to enable safer use of codeine in pain therapy.

Amongst micro-level barriers, participants spoke of perceived limitations of pain therapy in primary care resulting in overreliance on codeine. Codeine prescribing often occurred in the context of poor utilisation of non-opioid therapies, including nonsteroidal anti-inflammatory drugs, graduated exercise, and cognitive behavioural therapy, which may achieve similar levels of improvement in pain[29,30] without risk of dependence.[31] Lack of psychological, social community and pain specialist resources and the services of physiotherapists, occupational therapists and social workers thus appeared to hinder a holistic approach in pain therapy that incorporates prevention, active treatment and rehabilitation. Overcoming these impediments most likely require amending the economic environment that regulates the availability of these resources.

A policy environment dictates procedures for OTC codeine sale in the UK to prevent use other than as indicated.[32] However, lack of trust in the relationship between pharmacists and participants using OTC codeine, confirmed concerns previously raised about OTC codeine sale, including inabilities to effectively monitor OTC codeine consumption and intervene to halt escalating use.[33] OTC medicines play an important role given the increasing acceptance of self-care to promote patient empowerment and reduce the burdens for health care. However, drawing on knowledge of engagement between pharmacists and patients at the point of an OTC codeine sale is important to realign OTC sales of codeine with environmental factors to reduce harm.

Comprehensive assessment of codeine dependence, support delivered in primary care, and access to addiction treatment is required and should be available for those who need it.[5] Although participants viewed the uptake of primary care intervention and addiction treatment positively, they also found them difficult to access. Where engagement and resources permitted, GPs proved to be an effective source of monitoring and reducing harm when concerns had been communicated. Increased awareness of the potential for codeine dependence amongst GPs is likely to improve treatment of codeine dependence further.[19] Easy-to-access addiction services capable of handling individuals with codeine as the primary drug may also be important here.

Implications for the codeine risk environment

Considering the negative consequences of prolonged opioid use for chronic pain, which include paralysis of the endogenous opioid system, depression and ineffective pain control,[23] alternative management of patients with chronic codeine use is warranted.[22,34] The findings of this study suggest that GPs are well-placed to communicate risk, monitor and, if necessary, intervene in codeine use. However, their ability to do so may be limited by a lack of resources and subsequent patient disengagement. Training and funding must be provided, including more time to spend with patients, effective ways to monitor codeine prescriptions, access to non-opioid treatments, and ability to refer to secondary services.

Although pharmacists are empowered by current UK regulations to restrict individual access to OTC codeine by refusing sales and limiting the amounts sold, this study found that having codeine available OTC acts to produce harm due to break-down of protecting barriers. With

Australia recently joining countries like the US, Germany and Japan in restricting codeine to prescription-only,[35] it is necessary to review UK OTC regulation to reduce the risk of excessive use of codeine. There is also a need to explore how to improve patient/pharmacist communication.

Using codeine only for its intended indications of mild to moderate pain on a short-term basis would most likely go a long way in preventing dependence. However, this requires effective and acceptable alternatives to manage pain to ensure that pain patients receive the care they need. The goal is to create a system where patients understand their options for pain therapy and the risks of taking codeine. Finally, ending codeine prescriptions in cases of dependence should not be done abruptly, and only under close monitoring to prevent relapse or use of other opioids (sourced online or from the illicit market).

Strengths and limitations

A strength of this study is that it illustrates the risk environment surrounding codeine use in the UK, an area previously unexplored in the literature. Specifically, this study highlights how different environmental factors intended to facilitate safe use of codeine can potentially act to increase risks without proper utilisation and sufficient funding. This is important in implementing change to ensure that benefits of codeine use in pain therapy outweighs harm. Most obviously, a limitation of the study is the small sample size. Findings cannot be generalised to all regions of the UK. As such, a reduction or production of harm related to codeine containing medicines will depend on many factors, such as the nature and funding of local primary care. The inclusion criteria enabled us to study factors contributing to codeine dependence, whilst limiting our ability to identify protective factors in the environment, which may have stopped dependence from occurring. Had we recruited from primary care instead of from an online survey, our findings may have been different in that we had recruited more patients with experience of factors that stopped codeine use other than as indicated.

CONCLUSION

This study highlights environmental factors that produce and reduce harm related to codeine containing medicines among participants with recent use of codeine other than as indicated. The study identified micro- and macro- environments capable of producing harm,

unless realigned with current risks of codeine use and provided with adequate funding. The economic environment is often crucial in reducing drug harm and facilitating effective treatment of dependence. We echo calls for funding to facilitate a more holistic approach to pain therapy to reduce prescribing to patients who may not benefit from opioids.[22,34] Whilst alternative non-opioid therapies may go a long way to reduce codeine dependence, we also emphasis regular review of patient prescribed codeine. Providing interventions and treatment designed for patients with chronic use that facilitate enabling environments to change practices of individuals who are codeine dependent should be explored.

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Author contributions

PD and AK designed and planned the study. AK recruited and collected the data. EK performed the literature research and undertook data analysis with input from AK. EK and AK contributed to theoretical implications of study analysis. EK and AK led on writing the paper. All authors had access to the data used and provided final approval of the manuscript to be published.

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Disclaimer

The views expressed are those of the authors and not necessarily those of the NIHR, SLaM NHS Foundation Trust and the BRC.

Competing Interests

None.

Patient consent

Participants provided written consent. Personal details were removed from the collected data to ensure anonymity.

Ethics Approval

This qualitative study was imbedded in the CODEMISUSED project approved by King's College London, Psychiatry, Nursing & Midwifery Research Ethics Sub-Committee and the NRES Committee London - London Bridge.

Data sharing statement

No additional data are available.

Patient Involvement

Patients were not involved in the design and conduct of the study.

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TABLES

Table 1. Participant characteristics and codeine use.

Participant	Gender (F/M)	Initial type of pain	Subsequent reasons for codeine use	Time between first and last use	Source of obtaining codeine	Severity of Dependence Scale (SDS) score	Intervention and treatment
1	M	Headache	To reduce stress	7 years	Prescription, OTC, obtained from family	15*	Residential rehabilitation programme
2	F	Dysentery	Recreational purposes, to reduce stress	1 year	Prescription, OTC	4	None
3	F	Pain after an operation	To sleep, to reduce stress, for depression	1 month	Prescription	7*	GP support, counselling
4	F	Period pain		15 years	Prescription	12*	GP support
5	F	Injury	To sleep, recreational purposes	15 years	Prescription, OTC	8*	None
6	F	Deep vein thrombosis from heroin use	Used when heroin unavailable	8 years	Prescription, OTC	11*	Previously in residential rehabilitation. At time of interview none

7	F	Pain after an operation	For anxiety	10 years	Prescription, OTC	14*	None
8	F	Back pain		20 years	Prescription	7*	None
9	F	Head injury	To reduce stress, to sleep	2 years	Prescription, OTC	10*	None
10	F	Migraines	To reduce stress, to sleep	25 years	Prescription	2	None
11	M	Migraines and back pain	For anxiety, for depression	14 years	Prescription, OTC, internet	0	Private psychiatry, private pain specialist
12	F	Arthritis		2 years	Prescription, OTC	5*	None
13	M	Headache, later osteoarthritis	For anxiety, recreational purposes	15 years	Prescription, OTC, obtained from family	1	None
14	F	Arthritis		3 years	OTC	6*	None
15	F	Migraines, back pain, irritable bowel syndrome	To sleep	8 years	OTC, obtained from a friend	2	None
16	F	Ulcers	Sleep	4 months	OTC	0	None

* Scores of 5 and above indicate probable codeine dependence.

Table 2. The codeine risk environment in the context of pain treatment: examples of factors producing and reducing harm.*

	Micro-environment		Macro-environment	
	Risk	*Intervention*	*Risk*	*Intervention*
Physical	Prolonged codeine use Excessive codeine use Codeine dependence		Diversion of codeine containing medicines (obtaining codeine from friends and family)	
Social	Community pharmacy service access and poor engagement Ineffective risk communication between GPs and patients to inform of codeine risks	Social and peer groups norms surrounding codeine use	Codeine's dominant role in contemporary pain treatment Stigmatisation of codeine dependence Anonymised information sourcing on the internet from unreliable sources	Anonymised information sourcing on the internet from reliable sources
Economic	Lack of resources available for non-opioid pain treatment (e.g. physical therapy) Low use of medicine review of repeat prescription		Funding for NHS primary care Funding for local drug addiction treatment services	
Policy	Nature of GP appointments (long waiting times, short duration)	Primary care interventions, including codeine tapering Access to structured drug addiction treatment for codeine dependence		Laws and regulation governing OTC sales of codeine containing medicines

* Factors may overlap physical, social, economic and policy environments and change place between environments over time.

INFORMATION SHEET FOR PARTICIPANTS

REC Reference Number: PNM/14/15-110

Version: 2 - 20 April 2015

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of study

Understanding codeine use: exploring the experiences and characteristics of codeine users

Invitation Paragraph

You are being invited to take part in a research study. Before you decide we would like to explain why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you have any other questions. Take time to decide if you want to take part or not.

What is the purpose of the study?

This interview study is being conducted by King's College London as part of an EU funded project about codeine misuse, related health harms, characteristics of users, and dependence. There is limited evidence available on the factors associated with and outcomes of use. The aim of the interview study is to collect qualitative data to explore codeine users' choices and decision-making when using codeine (prescribed or otherwise), codeine use patterns, favoured route of administration, recreational use and tampering with codeine pharmaceuticals, adverse health consequences (including codeine related problems and dependence), characteristics of dependent and non-dependent codeine users, sourcing of codeine, use of other drugs and medication, opinions around medical prescribing, and pharmacy dispensing and internet based retail.

During the interview you will be asked questions about which codeine products you use, how and why. You will be asked about from where you get your codeine and any problems you have experienced as a result of using codeine. We will also ask if you have used any other drugs or any other medicines. We will ask how you first got introduced to

using codeine. This will help to increase the evidence base, which will be of potential benefit to people who decide to use codeine and in the development of public health responses.

If you would like to read more about our research about codeine use, then go to: www.codemisused.org

Do I have to take part?

No. It is up to you to decide whether or not you want to take part. If you do we will ask that you give your consent to take part. You are still free to withdraw up until the point of publication of results without giving a reason. If you wish to do so you must inform the researcher in writing. A decision to withdraw will not affect your rights to any health care you receive.

What will happen to me if I take part?

If you decide to take part we will ask you to take part in an interview that will last about 1 hour and that will be audio recorded. In this interview we will ask you questions about your use of codeine, what products you use, and your experiences with any problems you may have encountered. When taking part in an interview you will receive a £20 gift voucher in reward of your time.

What are the possible risks of taking part?

We understand that answering questions about substance use and dependence can be stressful. We know from experience that talking about these issues as part of an interview can sometimes make participants feel worse. Should you become distressed during the interview, the interview will terminate immediately. We will advice you to seek help from GP.

Will my taking part be kept confidential?

Yes. All the information that we collect will be kept strictly confidential. Any identifying information about you will not be disclosed to anyone outside the research team. You do not have to give us your full name or date of birth.

Once the audio recording of your interview has been transcribed, the audio recording is deleted. Any details that might be used to identify who you are will be erased from the transcription of your interview. All transcriptions are safely stored at King's College London to make sure that no one other than the research team can look at it. We do this by storing it on a computer that can only be accessed with a password.

Researchers work under the same rules of confidentiality as doctors and nurses, which can only be broken, without your consent, in very exceptional circumstances. **Usually this is if the researcher sees or is told something which raises serious concern for your personal safety.**

How is the project being funded?

The research is funded by the European Commission — 7th Framework Programme (reference number: FP7-PEOPLE-2013-IAPP-611736) and is sponsored by King's College London.

What will happen to the results of the study?

The results of the study will be published in reports, articles and conference presentations.

Who should I contact for further information?

Ask us if there is anything that is not clear or if you would like more information. Please contact the researcher using the following contact details:

Dr Andreas Kimergård, Addictions Department, King's College London, T: 020 7848 0446, @: Andreas.Kimergard@kcl.ac.uk

What if I have further questions, or if something goes wrong?

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you can contact King's College London using the details below for further advice and information: The Chair, PNM Research Ethics Subcommittee (RESC), rec@kcl.ac.uk

What else do I need to know?

You must be 18 years or older to take part in this study. If you are interested in receiving the final results of this study please get in contact with Andreas Kimergård. However, remember that data from studies such as these often take many months to prepare for publication.

Thank you for reading this information sheet and for considering taking part in this research.

REC ref.: 15/LO/0107
Short Title: Codeine Interview Study
Document name: Annex D: Consent form A
Version: 2
Date: 24/02/15

Consent form

Codeine interview study: benefits of codeine use, side effects and use of treatment services

Researcher: Andreas Kimergård, King's College London

Email: Andreas.Kimergard@kcl.ac.uk

Please tick box

☐ I confirm that I have read and understand the information provided for this study. I have had the opportunity to consider the information and ask questions.

☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care being affected.

☐ I understand that personal information collected during the study will be anonymised and remain confidential.

☐ I understand that I can choose not to answer questions which I feel uncomfortable about answering.

☐ I agree to the digital recording of this interview.

☐ I agree that quotes from my interview may be reported in published documents but that this will be anonymous and no-one will be able to identify me from this.

☐ I agree to take part in the study.

Name of participant:

Date:

Signature:

Name of researcher:

Date:

Signature:

Note: This form must be completed in 2 copies, one for the participant and one for the researcher.

From pain to dependence: A qualitative study of environmental influence on codeine use

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Inter viewer/facilitator	Which author/s conducted the inter view or focus group?	*Page 6*
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	*PhD* *Not reported in manuscript*
3. Occupation	What was their occupation at the time of the study?	*Page 1*
4. Gender	Was the researcher male or female?	*Page 1*
5. Experience and training	What experience or training did the researcher have?	*Page 1*
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	*Page 6-7*
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	*Page 6-7* *Supplementary File*
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	*Page 6-7* *Supplementary File*

Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	*Page 7*
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	*Page 6 - 7*
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	*Page 6 - 7*
12. Sample size	How many participants were in the study?	*Page 6*
13. Non-participation	How many people refused to participate or dropped out? Reasons?	*Page 6*
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	*Page 6*
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	*Page 6*
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	*Page 6 - 8*
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	*Page 6*
18. Repeat interviews	Were repeat inter views carried out? If yes, how many?	*No* *Page 6 - 7*

19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	*Page 7*
20. Field notes	Were field notes made during and/or after the inter view or focus group?	*No* *Page 6 - 7*
21. Duration	What was the duration of the inter views or focus group?	*Page 6*
22. Data saturation	Was data saturation discussed?	*N/A* *Not reported*
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	*No* *Not reported*
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	*Page 18*
25. Description of the coding tree	Did authors provide a description of the coding tree?	*Page 7*
26. Derivation of themes	Were themes identified in advance or derived from the data?	*Page 7*
27. Software	What software, if applicable, was used to manage the data?	*Page 7*
28. Participant checking	Did participants provide feedback on the findings?	*No* *Not reported*
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	*Page 8 - 15*
30. Data and findings	Was there consistency between the data	*Page 8 - 16*

consistent	presented and the findings?	
31. Clarity of major themes	Were major themes clearly presented in the findings?	*Page 8 - 15*
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	*Page 8 - 15*

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From pain treatment to opioid dependence: A qualitative study of the environmental influence on codeine use

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From pain treatment to opioid dependence: A qualitative study of the environmental influence on codeine use

Emma Kinnaird[1*], Andreas Kimergård[2*], Stacey Jennings[2], Colin Drummond[2,3], Paolo Deluca[2]

* Joint first authors

[1] Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

[2] National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

[3] National Institute for Health Research Biomedical Research Centre for Mental Health, South London and Maudsley NHS Foundation Trust, London, UK.

Correspondence to: Andreas Kimergård, National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 4 Windsor Walk, SE5 8BB, London, United Kingdom, e-mail: Andreas.Kimergard@kcl.ac.uk, telephone: 020 7848 0825

ABSTRACT

Objectives To investigate the views and experiences of people who use codeine in relation to pain treatment in order to describe the environments capable of producing and reducing harm.

Design This was a qualitative interview study. Psychological dependence upon codeine was measured using the Severity of Dependence Scale (SDS). A cut-off score of five or higher indicates probable codeine dependence.

Setting Participants were recruited from an online survey and one residential rehabilitation service.

Participants 16 adults (13 women and 3 men) from the UK using codeine other than as directed or as indicated and initially using codeine to treat physical pain. Mean age was 32.7 years (*SD* = 10.1) and mean period of codeine use was 9.1 years (*SD* = 7.6).

Results Participants' experiences indicated that they became dependent on codeine as a result of various environmental factors present in a 'risk environment'. The environments to reduce risk included: Medicine review of repeat prescribing of codeine, well-managed dose tapering to reduce codeine consumption, support from social structures in form of friends and online, and access to addiction treatment. Environments capable of producing harm included: Unsupervised, long-term codeine prescribing, poor access to non-pharmacological pain treatments and breakdown in structures to reduce the use of over-the-counter codeine other than as indicated.

Conclusion The study identified micro- and macro- environments capable of producing dependence on codeine, including repeat prescribing and unsupervised use over a longer time period. The economic environment was important in its influence upon the available resources for holistic pain therapy in primary care in order to offer alternative treatments to codeine. Overall, the goal is to create an environment that reduces risk of harm by promoting safe use of codeine for treatment of pain, whilst providing effective care for those developing withdrawal and dependence.

Keywords

Codeine, dependence, prescribing, over-the-counter, risk environment.

Strengths and limitations of this study

- Adds to a relatively small body of qualitative research investigating codeine dependence.
- Presents an investigation of environmental factors producing and reducing harm related to codeine containing medicines through the adoption of the 'risk environment' approach.
- A limitation is the small sample size and findings cannot be generalised to all regions of the UK.
- The study recruited a higher proportion of women compared to men which reduces the generalizability of the findings.
- The risk environment approach focuses on a particular part of the social world and may overlook individual circumstances.

INTRODUCTION

The risk of codeine dependence and physical harm associated with long-term use of codeine containing medicines are well-known.[1,2] In the UK, data from the National Drug Treatment Monitoring System show that codeine was the primary or secondary drug for 2.2% of clients (*N* = 4,248) in structured drug treatment (2013/2014).[3] Daily consumption of 1,250 mg codeine, which is 5 times the maximum daily dose,[4] has successfully been treated with opioid agonist therapy (buprenorphine/naloxone) and tapered dosing over a 4-month period.[2] However, many individuals who are dependent on codeine (experiencing withdrawal symptoms when codeine is removed) may not seek help due to a reluctance to explore other types of pain treatments.[5,6] Furthermore, regional variability in addiction treatment may act as a barrier against receiving effective care. To improve pain treatment and physical and mental health, concerted efforts are needed at the level of codeine prescribing, dispensing and use to reduce the number of patients who become dependent after starting on codeine.

Codeine is widely accessible in the UK: It is one of the most commonly prescribed opioids and can be purchased over-the-counter (OTC) in licensed pharmacies without a medical prescription. In 2016, the UK was the second biggest consumer of codeine in the world at 44.2 tons.[7] According to Prescription Cost Analysis data, more than 15 million items of co-codamol (codeine/paracetamol) were dispensed in the community in England in 2017 – an increase of approximately 15% since 2007.

Therapeutic indications for codeine use are treatment of mild to moderate pain not relieved by non-opioid analgesics such as paracetamol and ibuprofen.[4] Although considered a 'mild opioid',[8] long-term codeine use can lead to tolerance and dependence.[9-11] Use of compound products containing paracetamol or ibuprofen in higher than recommended doses may result in harm from high doses of accompanying non-opioid analgesics, such as renal and gastrointestinal complications attributed to ibuprofen and liver damage attributed to paracetamol.[12] Indications of possible codeine dependence include long-term use for non-cancer pain,[5] use for anxiety and depression,[10] and obtaining codeine from multiple sources, including prescribed, OTC and from the illicit market.[2,13]

With the high level of codeine use in the UK, it is important to consider which factors impact on the production and reduction of codeine related harm. In this article, we adopt the 'risk environment' framework as an approach to investigate social situations and environments which are specific to codeine use. The risk environment can be seen as a space where multiple factors affect individual risk by considering how different types of environments (physical, social, economic and policy) interact at different levels (micro and macro).[14] This framework has previously been applied to explore the risk environments of illicit drug harms, including in relation to HIV transmissions [15] and overdose [16], but not the development of codeine dependence in a pain treatment context.

In the risk environment, micro-environments involve physical risks from substance use and social- and financial circumstances, whereas macro-environments relate to wider structural influences such as laws, health service revenue and spend and national policies.[14] Codeine-specific examples illustrate the logic applied in this framework: at the micro level, starting patients on prescribed codeine without a clear plan for stopping again may increase the risk of long-term use and subsequently dependence.[6] Conversely, careful and patient-involved dose tapering protect against long-term use. At a macro level environment, regulation restricts access to high doses of codeine in the form of pure formulations to prescription-only with prescribers deciding if they are appropriate to use. Whilst compound codeine formulations (combined with paracetamol or ibuprofen) are available OTC, regulations state that only one packet can be sold at a time and the packet labelling must state: 'Can cause addiction. For three days use only'.

However, studies indicate that transitions still occur from short-term codeine use to treat pain into long-term use and dependence.[10,13,17] Reasons why individuals experience dependence on codeine include: Physical and psychological withdrawal resulting in prolonged use,[1,10,18] poor understanding of the risks of taking codeine,[19] and disengagement from general practitioners (GPs) due to concerns of codeine dependence being recorded in medical notes.[13,20] In a pain treatment setting where opioids are prescribed more often and for longer periods, despite the lack of evidence of long-term efficacy for chronic pain,[10,21-23] investigating the risk environment can offer a better understanding of the social and political institutions that play a role in reducing codeine harm.

As such, our aim of the article is to explore the risk environment that influence codeine harm from the perspective of people who use or have used codeine recently for pain treatment.

METHODS

Design

This was a qualitative study that used data from semi-structured interviews with participants living in England who reported use of codeine in the last 12 months. Inclusion criteria were: Any individual aged 18 or over who used codeine other than as directed or as indicated, whether wilful or unintentional, and whether it resulted in harm or not.[24] The study was approved by the NHS REC Committee London (London Bridge), REC Reference 15/LO/0107.

Recruitment

Participants were recruited amongst respondents to an online survey (*N* = 14) and from a residential rehabilitation service (*N* = 2) in order to capture individual experiences across the spectrum from initial misuse to dependence which required structured addiction treatment.[10] A question in an online survey[10] invited respondents to take part in an interview by emailing the researcher or providing contact details. AK contacted and interviewed all eligible participants who did so, resulting in eighteen interviews. A leaflet was provided to clients in the residential rehabilitation programme informing about the study. All eligible clients in the service at that time were invited to take part, resulting in an additional ten interviews conducted by AK.

Sample

Of the 28 participants, one was excluded as codeine was used according to accepted medical practice or guidelines. Another 11 participants were excluded from the analysis as codeine was predominantly sourced as substitution for illicit opioids (heroin). This resulted in a sample of 16 participants who first took codeine for pain treatment, which allows for an investigation of influential factors that have an effect on codeine harm.

Data Collection

Participants were given a Participant Information Sheet informing of the reasons for doing the study and the involved researchers and institutions and asked to sign a consent form (Supplementary File). Interviews took place either in the residential rehabilitation service, at a location chosen by the participant or over the phone. The first interview was conducted in May 2015, and the last in April 2016. Interviews lasted from 35 minutes to an hour and 35 minutes. Participants were compensated for their time with a £20 gift voucher. Interviews were conducted using a topic guide, covering: demographic information, initial use of codeine, patterns of codeine use, difficulties managing codeine use, sourcing of codeine, use of other drugs or medicines, and views on codeine availability and regulation. New topics brought up by the participants were pursued during the interviews with follow-up questions. Codeine dependence was measured using the 5-item Severity of Dependence Scale (SDS) during the most recent period of codeine use.[25,26] A score of 5 or above, out of a maximum score of 15, was used to indicate probable psychological dependence on codeine.[9]

Data management and analysis

Interviews were audio-recorded and then transcribed verbatim by a professional service, with any participant identifying information removed from the transcripts. Data analyses were completed by three researchers on the project (AK, EK, SJ) and coded using the qualitative software NVivo (Version 11). A coding framework was developed deductively from the topic guide and from codes that emerged inductively from the data.[27] For this paper, all coded data were analysed using Framework.[28] In the first stage, the coded data were reviewed to describe aspects of each factor which influenced codeine use in the risk environment. Since similar factors were identified as being important to the production and reduction of harm amongst the participants, the analyses were merged and then grouped into more inductive categories. We organised these under four headings: i) patient education on the risk of codeine, ii) the role of prescribing practices related to codeine and non-pharmacological pain treatment, iii) the accessibility and use of OTC codeine and the differences between relationships with GPs and pharmacists, and iv) access to interventions and treatment for codeine dependence. These categories are used to structure the results below. Emergent factors that appeared to have an impact on the harms of using codeine use that may have transferability to other settings[29] were categorised into micro- and

macro-environments (physical, social, economic and policy) and used for mapping the various domains of the risk environment.[14] A risk environment for codeine is presented in Table 1. Analyses are presented with supporting quotes (anonymised using participant numbers) and SDS scores.

RESULTS

Participant characteristics

The sample consisted of 3 men and 13 women, with a mean age of 32.7 years (*SD* = 10.1) and a mean period of codeine use of 9.1 years (*SD* = 7.6) (Table 2). In the sample, 3 participants (18.8%) were unemployed, 3 (18.8%) were students, and 10 (62.5%) were employed. Co-morbid anxiety or depression was self-reported by 4 participants (25%), and 4 (25%) reported concurrent use of codeine and other prescription opioids. Using the SDS, 10 participants (62.5%) scored 5 or more, indicating probable codeine dependence. At the time of interview, 4 participants (25%) sourced codeine from a medical prescription, 3 used OTC codeine (18.8%), whereas 9 used both (56.3%). Only 1 participant reported additionally sourcing codeine from the internet, whilst 3 also used codeine obtained from family or friends. In total, 4 participants (25%) had received intervention and treatment for their codeine use, including addiction treatment, GP led intervention, counselling or from a psychiatrist.

Education of patients on prescribed codeine

Many participants explained that they had not fully understood the potential risks when they first started taking codeine, including its addictive potential. Reflecting on their initial codeine use, many expressed frustrations with their GP and suggested that they wished they had been given more information:

> "If I had had a doctor who possibly just had a little bit more time to say here's what I'm giving you, here's what it is, here's what it does, here's the risks to it. If I had just been a little bit more educated, perhaps it wouldn't have happened [use in excessive doses]." Participant 11, male, dependence score 0.

Participants identified several potential barriers facing health professionals in effectively communicating risks. Specifically, participants felt that the typical 10-minute GP

appointment was not enough to fully discuss available options for pain therapy. Of note was that participants who had greater awareness of the risks of codeine, typically from searching for information on the internet, were often more motivated to avoid these risks. However, when participants voiced concerns to their GP, they felt ignored and detached from decisions about their health and care:

> "I kind of had to battle to get my GP to do or say anything about my lower back pain, because they're just like, it's lower back pain, what can you do? They just kind of send you away, say carry on, take the painkillers…It didn't seem like anyone was taking any care in the fact that I could get addicted to this; I didn't bother to go back." Participant 15, female, dependence score 2.

Such encounters with health professionals enhanced the feeling of not being listened to and contributed toward disengagement from health services, distrust in medical opinions, and isolation. In this environment, fewer factors acted to protect against unsupervised, long-term codeine use. Consequently, the lack of effective communication between prescribers and patients, and a resulting poor education of patients on codeine risk, appeared to facilitate the development of codeine dependence for some participants.

Prescribing practices and the use of non-pharmacological pain therapies

The majority of participants who received prescription codeine did so through a repeat prescription. Individuals robustly reported being able to order their repeat prescription with few restrictions on amounts and frequency, which for some resulted in increasing codeine intake:

> "It wasn't just once a month for my periods, like I went through a period of having really bad back ache, so I took it for that. Then for when I twisted my ankle like four or five times, so I'd take it for that. I started running two years ago, now I've got a knee injury, so I'd take it for that. It was just whatever niggles and pains there were, I'll just pop some tablets because I had them on a repeat prescription and they were basically on tap. That's when it started to really get a grip, because I was taking them for other things on a more or less daily basis." Participant 8, female, dependence score 7.

Within the risk environment, prolonged access to codeine with minimal supervision from a health professional can facilitate use of codeine other than as indicated during the initial consultation, influencing transition to subsequent dependence.

It was striking that participants using codeine from a medical prescription reported being prescribed codeine as a first resort for pain, even when participants were otherwise motivated to try other types of pain treatments:

> "I went and said I need another bout of physio for my back because it's starting to hurt again. And they [GP] said: 'oh, you've got to be in constant pain for six weeks'. And I said: 'I've been in constant pain for six weeks already, and it's a recurring problem, so please just refer me.' And the doctor said: 'no, go and take these pain medicines [codeine] and come back in six weeks'. And I said: 'I think it's really dangerous that you're telling me to go away and take a pain med that I know is really highly addictive constantly for six weeks, for a problem that you already know exists.' And they said: 'well, that's just the way it works, I'm sorry." Participant 8, female, dependence score 7.

For some primary care patients in the study, these issues were perceived as a general systematic problem reflecting a lack of treatment resources. They felt like they had been prescribed codeine in order to quickly get rid of them, rather than their GP taking the time to deal with the underlying problem or being referred to specialist services. This did lead to frustration and, in some cases, disengagement from GPs, for example to seek treatment privately:

> "…if that's the only advice you're going to give me [take codeine], then I will do what works for me. And I went to an osteopath and that really helped." Participant 15, female, dependence score 2.

In contrast with the negative perceptions of codeine prescribing expressed by some participants, those who were treated with non-opioid pain medicines, physiotherapy and hydrotherapy, indicated that they felt less concerned about continued codeine use:

> "Through the doctor they referred me to a hydrotherapy thing, because I just hadn't had any physiotherapy before for the pain. So, I had six sessions with them and they gave me exercises to do at home. I've been trying to keep up with that, which has I

guess lessened the pain. I no longer think that I'm going to get dependent on codeine because it's been that long that I don't wake up in the morning and think I have to take a pill." Participant 12, female, dependence score 5.

Participants' accounts therefore highlighted several structural factors in the risk environment influencing codeine harm: having alternative treatments available beyond codeine resulted in better engagement with health services and greater patient satisfaction, whilst minimising chronic codeine therapy. Conversely, treating pain solely with codeine did result in disengagement from health services.

Differences in relationships with pharmacists and GPs

Implementation of pharmacist intervention to regulate OTC codeine sales is intended to prevent codeine from being used other than as indicated and is one example of a factor which reduces harm. However, participants were able to circumvent restrictions on sale by purchasing from multiple pharmacies over the course of a week or even a day. While one participant had been refused codeine in a pharmacy, most OTC codeine users reported rarely being questioned by pharmacists to find out if codeine was a safe choice, even when they regularly came to the same pharmacy and obtained large amounts of codeine:

"It's the same staff all the time and I've bought it from there many times. And nobody has ever questioned me at all." Participant 7, female, dependence score 14.

Another important outcome of accessing multiple pharmacies in the local area was that participants never established a strong relationship with a single pharmacist, contrasting this to those who described a better relationship with their GP. Even where participants only accessed one pharmacist, they often perceived this relationship as less important to them and therefore less effective in regulating use and providing risk education, support and interventions than their GP. This appeared to also be related to the short amount of time participants spent interacting with pharmacists when buying codeine:

"Whenever I go and speak to pharmacists, I've just never felt particularly comfortable speaking to a pharmacist. I find they're a bit… maybe not judgmental, but I find they're a bit short and like they are very kind of medical. I don't find that there's much interaction. I would just prefer to speak to my GP, because I feel I can

trust him and I feel I've got a good relationship." Participant 3, female, dependence score 7.

However, participants also emphasised that pharmacists were far easier and quicker to access than scheduling an appointment with their GP, providing a disincentive to wait and consult with their GP about their codeine use. For participants with a positive and trusting relationship with their GP, a reluctance to be dishonest in their communication with the GP appeared to reduce the risk of dependence occurring; however, this appeared, in some cases, to be undermined by the convenience of OTC availability:

> "I lied to the doctor once, but that killed me doing that. I was really ashamed of myself at the time. I wouldn't have kept doing that [to continue using codeine]. It's only because I had been able to buy it OTC that I've kept on with that addiction. And even now, when I have a bad week and I really need codeine, I'll go and buy it OTC. I wouldn't do that if I had to go to my GP and explain." Participant 7, female, dependence score 14.

Some participants believed that codeine should be restricted to prescription only. In contrast, one participant with a low SDS score suggested that this would not be necessary nor feasible in the context of a wider NHS lack of resources – If everyone self-treating their pain with codeine had to regularly see their GP, primary care would become overwhelmed:

> "I think that it shouldn't be made much more difficult to get hold of because I think most people can go through some acute pain that lasts a couple of days that you might need something like this for, and our NHS is stretched enough without having to go to the GP every time you spring your ankle." Participant 15, female, dependence score 2.

This illustrates the dynamic nature of the risk environment, suggesting that for short term use for acute pain the benefits of OTC codeine outweigh the potential risk of dependence and thus play a significant role in providing access to pain treatment. However, in cases where factors implemented to protect against long-term use fail, such as pharmacist regulation of OTC sales, OTC codeine is associated with a risk of dependence.

Support, intervention and treatment of codeine dependence

Four participants had experience with intervention and treatment for codeine dependence, ranging from GP initiated medicine review to addiction treatment. Still, most participants with SDS scores indicating probable codeine dependence did not report any medical supervision or support; for some this spanned several years during which codeine use became an established part of their daily practice.

It is relevant to note the significance of the influence GPs possessed for some dependent participants in influencing their codeine use. Whilst most participants expressed negative GP experiences which led to disengagement and overreliance on poor information sources, those participants who openly disclosed difficulties in controlling their use of codeine, in the context of a positive and trusting relationship with their GP, were able to receive useful interventions:

> "I thought I'll just tell him [GP] and I'll just see what he says [about difficulties in managing codeine use]. And I ended up getting signed off work for about four weeks...I really trust my GP…When I tell him that I don't want to take codeine, he asks me why, and he kind of tries to look at other options for me, which I really appreciate. I think it was kind of a combination of all those different things, the GP and the counselling, the time off work, everything sort of came together. I think if it had only been one of those things, I don't know how well my recovery would have gone." Participant 3, female, dependence score 7.

Where participants engaged with their GP regarding their codeine use, either due to GP instigated follow-up consultations concerning their use of codeine or to the participant asking for an appointment, their GP was able to help via effective interventions such as tapering codeine and replacing compound products with pure codeine formulations to prevent the risk of physical harm from non-opioid analgesics. This suggests that in an environment where GPs have resources to support the patient, they reduce the likelihood of harm occurring:

> "He wrote me out like a little rota. He said we were going to do it [taper] over a certain period of time. And I had to sign, like he made like a contract for me to sign, and he signed it as well, to say that he was going to help me, and he was going to support me. And he was really understanding and not judgmental at all, it was fabulous. He said he was going to prescribe me a certain amount of just codeine, so

not the paracetamol, just codeine on its own." Participant 8, female, dependence score 7.

When two participants, who had attended addiction treatment, were asked why they had started treatment they generally described lengthy and complicated pathways which did require significant level of self-motivation. One male participant who was currently a client in a residential rehabilitation programme described the social, economic and physical circumstances that motivated him to eventually seek treatment and detoxification for codeine dependence. These included transitions from single to multiple codeine containing medicine use (OTC and prescribed), breakdown in family relationships, dropping out of university, social isolation, being fired from work and physical adverse effects from high doses of compounded ibuprofen:

"I think when I had the stomach ulcer, I started realizing then that this will actually kill me. I cut down the Nurofen Plus [codeine/ibuprofen] because it was what kept me going really, but I couldn't put it down…I just couldn't stop. I hadn't got a job, I'd dropped out of uni. Just living at home doing nothing and it kind of dawned on me you know, I've really got a problem. At first, I went to the local drug services, and they said that they don't deal with codeine so there wasn't any help there, and someone gave the number for there [residential rehabilitation service], a family friend or something…It was quite quick, about after two weeks [starting in treatment]." Participant 1, male, dependence score 15.

For some of the participants, disengagement from medical professionals, and the placing of responsibility on the patient to self-manage their dependence, created situations where participants reported that they instead used the internet to find out more information about codeine, pain treatments, and advice on how to manage the use of codeine.

"When I was first diagnosed with depression and anxiety, when I was just being pushed and pulled from different doctors, different psychiatrists, I looked to the internet to do my own research and just understand what these medicines were [codeine]. I didn't know what I was taking, and I didn't know what the risks of abusing it was, so I felt that I should really start understanding what I'm being prescribed." Participant 11, male, dependence score 0.

Support structures in form of family and friends also played an important role to some participants as a source of information about codeine. For this participant, an encounter with a friend facilitated personal reflection as to her own use of codeine:

> "One of my best friends was going for a job interview and I said to her: 'do you want to take a codeine like an hour before you leave the house? You'll feel so very relaxed.' And although she took the tablets, she said to me: 'I don't feel comfortable with this and I don't think that I should' A few months later she asked me if I used to take them for reasons other than pain, and I said to her no, but in my heart, I knew that I did. I asked her why. She said: 'because it's a very addictive drug…it's something that can basically change the chemicals in your brain and you'll be addicted forever.' She suggested a few articles for me to read, which I did, and then I was very worried because then I learned that codeine was connected to morphine." Participant 10, female, dependence score 2.

Such relationships played an important role for participants to gain more confidence in their ability to manage their use of codeine, especially for those using codeine other than as indicated, but not experiencing codeine dependence. However, over-reliance on inaccurate online sources and advice from friends and family may also delay or prevent patients from seeking support from health professionals until they experience severe dependence that is much more complicated to treat. As such, the social environment has the capacity to both produce and reduce codeine-related harm.

DISCUSSION

This qualitative study explored codeine use from the perspective of people who use or have used codeine to treat pain in order to unpack the key factors of the risk environment. These findings add to existing literature that suggest that some patients who use codeine for treatment of pain become dependent as a result of environmental factors.[10,20] We identified a number of environmental factors that reduced the risk of dependence: medicine review of repeat codeine prescribing, interventions in primary care (such as tapering), social support (friends and online), and access to addiction treatment (Table 1). We also identified several micro- and macro- environmental factors capable of producing harm, especially

unsupervised, long-term codeine prescribing and breakdown in structures to stop sales of OTC codeine for use other than as indicated (Table 1).

Amongst micro-level barriers, participants spoke of perceived limitations of pain therapy in primary care resulting in overreliance on codeine. Codeine prescribing often occurred in the context of poor utilisation of nonsteroidal anti-inflammatory drugs, graduated exercise, and cognitive behavioural therapy, which may achieve similar levels of improvement in pain[30,31] without risk of dependence.[32] Lack of psychological, social community and pain specialist resources and the services of physiotherapists, occupational therapists and social workers thus appeared to hinder a holistic approach in pain therapy that incorporates prevention, active treatment and rehabilitation. Overcoming these impediments most likely require amending the economic environment that regulates the availability of these resources.

A policy environment dictates procedures for OTC codeine sale in the UK to prevent use other than as indicated.[33] However, lack of trust in the relationship between pharmacists and participants using OTC codeine, confirmed concerns previously raised about OTC codeine sale, including inabilities to effectively monitor OTC codeine consumption and intervene to halt escalating use.[34] OTC medicines play an important role given the increasing acceptance of self-care to promote patient empowerment and reduce the burdens for health care. However, drawing on knowledge of engagement between pharmacists and patients at the point of an OTC codeine sale is important to realign OTC sales of codeine with environmental factors to reduce harm.

Comprehensive assessment of codeine dependence, support delivered in primary care, and access to addiction treatment is required and should be available for those who need it.[5] Although some participants viewed the uptake of primary care intervention and addiction treatment positively, they also found them difficult to access. Where engagement and resources permitted, GPs proved to be an effective source of monitoring and reducing harm when concerns had been clearly communicated. Increased awareness of the potential for codeine dependence amongst GPs is likely to improve treatment of codeine dependence further.[19] Easy-to-access addiction services capable of handling individuals with codeine as the primary drug may also be important here.

Implications for the risk environment

Considering the negative consequences of prolonged opioid use for chronic pain, which include paralysis of the endogenous opioid system, depression and ineffective pain control,[23] alternative management of patients with chronic codeine use is warranted.[22,35] The findings of this study suggest that GPs are well-placed to communicate risk, monitor and, if necessary, intervene in codeine use. However, their ability to do so may be limited by a lack of resources and subsequent patient disengagement. Training and funding must be provided, including more time to spend with patients, effective ways to monitor codeine prescriptions, access to other types of treatments, and ability to refer to secondary services.

Although pharmacists are empowered by current UK regulations to restrict individual access to OTC codeine by refusing sales and limiting the amounts sold, this study found that having codeine available OTC acts to produce harm due to break-down of protecting barriers. With Australia recently joining countries like the US, Germany and Japan in restricting codeine to prescription-only,[36] it is necessary to review UK OTC regulation to reduce the risk of excessive use of codeine. There is also a need to explore how to improve patient/pharmacist communication.

Using codeine only for its intended indications of mild to moderate pain on a short-term basis would most likely go a long way in preventing dependence. However, this requires effective and acceptable alternatives to manage pain to ensure that pain patients receive the care they need. The goal is to create a system where patients understand their options for pain therapy and the risks of taking codeine. Finally, ending codeine prescriptions in cases of dependence should not be done abruptly, and only under close monitoring to prevent relapse or use of other opioids (sourced online or from the illicit market).

Strengths and limitations

A strength of this study is that it illustrates the risk environment surrounding codeine use in the UK, an area previously unexplored in the literature. Specifically, this study highlights how different environmental factors intended to facilitate safe use of codeine can potentially act to increase risk without proper utilisation and sufficient funding. This is important in implementing change to ensure that benefits of codeine use in pain therapy outweighs harm. Most obviously, a limitation of the study is the small sample size. Findings cannot be generalised to all regions of the UK. As such, a reduction or production of harm

related to codeine containing medicines will depend on many factors, such as the nature and funding of local primary care. The majority of participants in this study were female, whereas two previous studies have managed to recruit a more evenly distributed sample.[13,20] The advertisement for the online survey was designed to attract both men and women, however more women responded creating a multiplying effect. The inclusion criteria enabled us to study factors contributing to codeine dependence, whilst limiting our ability to identify protective factors in the environment, which may have stopped dependence from occurring. Had we recruited from primary care instead of from an online survey, our findings may have been different in that we had recruited more patients with experience of factors that stopped codeine use other than as indicated. The risk environment approach has a limitation in its ability to understand codeine-related risks. This is because this approach focuses on a particular part of the social world and may not capture individual perspectives which influence codeine dependence, such as co-morbidities and specific types of pain. Furthermore, overlaps between different environments (physical, social, economic and policy) are likely when mapping the risk environment. While this is useful for understanding the complicated nature of how drug harms are generated, it can also make it difficult to determine how to implement effective change.

CONCLUSION

This study identifies environments that produce and reduce harm related to codeine containing medicines among participants with recent use of codeine. The study highlights micro- and macro- environments capable of producing harm, particularly in regard to long-term prescribing, unless realigned with current risks of codeine use and provided with adequate funding. The economic environment is often crucial in reducing drug harm and facilitating effective treatment of dependence. We echo calls for funding to facilitate a more holistic approach to pain therapy to reduce prescribing to patients who may not benefit from opioids.[22,35] The study found evidence to support regular review of patients prescribed codeine. Alternative non-pharmacological therapies may also go a long way to reduce codeine dependence.

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Author contributions

PD and AK designed and planned the study. Ak wrote the research protocol. AK recruited and collected the data. EK performed the literature research and undertook data analysis with AK and SJ. EK and AK contributed to theoretical implications of study analysis. EK and AK led on writing the paper with input from CD, SJ and PD. All authors had access to the data used and provided final approval of the manuscript to be published.

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Disclaimer

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Competing Interests

None.

Patient consent

Participants provided written consent. Personal details were removed from the collected data to ensure anonymity.

Ethics Approval

This qualitative study was imbedded in the CODEMISUSED project approved by King's College London, Psychiatry, Nursing & Midwifery Research Ethics Sub-Committee and the NRES Committee London - London Bridge.

Data sharing statement

No additional data are available.

Patient Involvement

Patients were not involved in the design and conduct of the study.

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TABLES

Table 1. The codeine risk environment in the context of pain treatment: examples of environments producing and reducing harm

	Micro-environment		Macro-environment	
	Risk	*Intervention*	*Risk*	*Intervention*
Physical	Prolonged codeine use Excessive codeine use Codeine dependence	Increased education for peers on diversion of medications	Diversion of codeine containing medicines (obtaining codeine from friends and family)	Review of regulation on prescription and monitoring
Social	Ineffective risk communication between GPs and patients to inform of codeine risks Disengagement from healthcare providers Limited engagement between patient and pharmacist Overreliance on inaccurate internet and peer information	Increased information provision on codeine risk and alternative pain therapies in primary care GPs receptive to reviewing patient concerns Improving patient attitudes towards GP consultations and pain management. Improving healthcare provider attitudes to pain management and codeine misuse. Clinician-led assertive engagement strategies in primary care Provision of social support via peer group and online Explore pharmacist-patient communication strategies	Codeine's dominant role in contemporary pain treatment Stigmatisation of codeine dependence Anonymised information sourcing on the internet from unreliable sources	Improved access to alternative non-pharmacological pain management therapies Increased awareness and opportunity for early intervention for codeine dependence across community, employment and health services

		Effective strategies targeting peer education and awareness of codeine misuse		
Economic			Lack of resources available for non-pharmacological pain treatments in primary care (e.g. physical therapy)	Funding and reform for NHS primary care and local drug addiction treatment services
Policy	Low utilisation of medicine review of repeat prescription of codeine Ineffective implementation of pharmacy OTC restrictions Ease of circumventing pharmacy restrictions	Timely prescription monitoring and review of concerns GP instigated follow up consultations and interventions Assertive and active review from primary care Continued provision of effective interventions in primary care such as tapering and pure codeine replacement Training of pharmacy staff to ensure consistent implementation of pharmacy OTC risk reduction policy	Nature of GP appointments (long waiting times, short duration) Ineffective laws and regulation governing OTC sales of codeine containing medicines	More time to spend with codeine dependent patients. Increased availability and convenience in securing appointment and access to screening and brief intervention Review of legal and regulatory governance surrounding OTC codeine

Factors may overlap physical, social, economic and policy environments and change place between environments over time.

Table 2. Participant characteristics and codeine use

Participant	Gender (F/M)	Initial type of pain	Subsequent reasons for codeine use	Time between first and last use	Source of obtaining codeine	Severity of Dependence Scale (SDS) score	Intervention and treatment
1	M	Headache	To reduce stress	7 years	Prescription, OTC, obtained from family	15*	Residential rehabilitation programme
2	F	Dysentery	Recreational purposes, to reduce stress	1 year	Prescription, OTC	4	None
3	F	Pain after an operation	To sleep, to reduce stress, for depression	1 month	Prescription	7*	GP support, counselling
4	F	Period pain		15 years	Prescription	12*	GP support
5	F	Injury	To sleep, recreational purposes	15 years	Prescription, OTC	8*	None
6	F	Deep vein thrombosis from heroin use	Used when heroin unavailable	8 years	Prescription, OTC	11*	Previously in residential rehabilitation. At time of interview none
7	F	Pain after an operation	For anxiety	10 years	Prescription, OTC	14*	None
8	F	Back pain		20 years	Prescription	7*	None

9	F	Head injury	To reduce stress, to sleep	2 years	Prescription, OTC	10*	None
10	F	Migraines	To reduce stress, to sleep	25 years	Prescription	2	None
11	M	Migraines and back pain	For anxiety, for depression	14 years	Prescription, OTC, internet	0	Private psychiatry, private pain specialist
12	F	Arthritis		2 years	Prescription, OTC	5*	None
13	M	Headache, later osteoarthritis	For anxiety, recreational purposes	15 years	Prescription, OTC, obtained from family	1	None
14	F	Arthritis		3 years	OTC	6*	None
15	F	Migraines, back pain, irritable bowel syndrome	To sleep	8 years	OTC, obtained from a friend	2	None
16	F	Ulcers	Sleep	4 months	OTC	0	None

* Scores of 5 and above indicate probable psychological dependence upon codeine.

INFORMATION SHEET FOR PARTICIPANTS

REC Reference Number: PNM/14/15-110

Version: 2 - 20 April 2015

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of study

Understanding codeine use: exploring the experiences and characteristics of codeine users

Invitation Paragraph

You are being invited to take part in a research study. Before you decide we would like to explain why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you have any other questions. Take time to decide if you want to take part or not.

What is the purpose of the study?

This interview study is being conducted by King's College London as part of an EU funded project about codeine misuse, related health harms, characteristics of users, and dependence. There is limited evidence available on the factors associated with and outcomes of use. The aim of the interview study is to collect qualitative data to explore codeine users' choices and decision-making when using codeine (prescribed or otherwise), codeine use patterns, favoured route of administration, recreational use and tampering with codeine pharmaceuticals, adverse health consequences (including codeine related problems and dependence), characteristics of dependent and non-dependent codeine users, sourcing of codeine, use of other drugs and medication, opinions around medical prescribing, and pharmacy dispensing and internet based retail.

During the interview you will be asked questions about which codeine products you use, how and why. You will be asked about from where you get your codeine and any problems you have experienced as a result of using codeine. We will also ask if you have used any other drugs or any other medicines. We will ask how you first got introduced to

using codeine. This will help to increase the evidence base, which will be of potential benefit to people who decide to use codeine and in the development of public health responses.

If you would like to read more about our research about codeine use, then go to: www.codemisused.org

Do I have to take part?

No. It is up to you to decide whether or not you want to take part. If you do we will ask that you give your consent to take part. You are still free to withdraw up until the point of publication of results without giving a reason. If you wish to do so you must inform the researcher in writing. A decision to withdraw will not affect your rights to any health care you receive.

What will happen to me if I take part?

If you decide to take part we will ask you to take part in an interview that will last about 1 hour and that will be audio recorded. In this interview we will ask you questions about your use of codeine, what products you use, and your experiences with any problems you may have encountered. When taking part in an interview you will receive a £20 gift voucher in reward of your time.

What are the possible risks of taking part?

We understand that answering questions about substance use and dependence can be stressful. We know from experience that talking about these issues as part of an interview can sometimes make participants feel worse. Should you become distressed during the interview, the interview will terminate immediately. We will advice you to seek help from GP.

Will my taking part be kept confidential?

Yes. All the information that we collect will be kept strictly confidential. Any identifying information about you will not be disclosed to anyone outside the research team. You do not have to give us your full name or date of birth.

Once the audio recording of your interview has been transcribed, the audio recording is deleted. Any details that might be used to identify who you are will be erased from the transcription of your interview. All transcriptions are safely stored at King's College London to make sure that no one other than the research team can look at it. We do this by storing it on a computer that can only be accessed with a password.

Researchers work under the same rules of confidentiality as doctors and nurses, which can only be broken, without your consent, in very exceptional circumstances. **Usually this is if the researcher sees or is told something which raises serious concern for your personal safety.**

How is the project being funded?

The research is funded by the European Commission — 7th Framework Programme (reference number: FP7-PEOPLE-2013-IAPP-611736) and is sponsored by King's College London.

What will happen to the results of the study?

The results of the study will be published in reports, articles and conference presentations.

Who should I contact for further information?

Ask us if there is anything that is not clear or if you would like more information. Please contact the researcher using the following contact details:

Dr Andreas Kimergård, Addictions Department, King's College London, T: 020 7848 0446, @: Andreas.Kimergard@kcl.ac.uk

What if I have further questions, or if something goes wrong?

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you can contact King's College London using the details below for further advice and information: The Chair, PNM Research Ethics Subcommittee (RESC), rec@kcl.ac.uk

What else do I need to know?

You must be 18 years or older to take part in this study. If you are interested in receiving the final results of this study please get in contact with Andreas Kimergård. However, remember that data from studies such as these often take many months to prepare for publication.

Thank you for reading this information sheet and for considering taking part in this research.

REC ref.: 15/LO/0107
Short Title: Codeine Interview Study
Document name: Annex D: Consent form A
Version: 2
Date: 24/02/15

Consent form

Codeine interview study: benefits of codeine use, side effects and use of treatment services

Researcher: Andreas Kimergård, King's College London

Email: Andreas.Kimergard@kcl.ac.uk

Please tick box

☐ I confirm that I have read and understand the information provided for this study. I have had the opportunity to consider the information and ask questions.

☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care being affected.

☐ I understand that personal information collected during the study will be anonymised and remain confidential.

☐ I understand that I can choose not to answer questions which I feel uncomfortable about answering.

☐ I agree to the digital recording of this interview.

☐ I agree that quotes from my interview may be reported in published documents but that this will be anonymous and no-one will be able to identify me from this.

☐ I agree to take part in the study.

Name of participant:

Date:

Signature:

Name of researcher:

Date:

Signature:

Note: This form must be completed in 2 copies, one for the participant and one for the researcher.

From pain treatment to opioid dependence: A qualitative study of environmental influence on codeine use

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Inter viewer/facilitator	Which author/s conducted the inter view or focus group?	*Page 6*
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	*PhD* *Not reported in manuscript*
3. Occupation	What was their occupation at the time of the study?	*Page 1*
4. Gender	Was the researcher male or female?	*Page 1*
5. Experience and training	What experience or training did the researcher have?	*Page 1*
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	*Page 6-7*
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	*Page 6-7* *Supplementary File*
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	*Page 6-7* *Supplementary File*

Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	*Page 7 - 8*
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	*Page 6*
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	*Page 6*
12. Sample size	How many participants were in the study?	*Page 8*
13. Non-participation	How many people refused to participate or dropped out? Reasons?	*None* *Not reported* *Page 6 - 7*
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	*Page 7*
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	*No* *Not reported* *Page 7*
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	*Page 8*
Data collection		

17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	*Page 7*
18. Repeat interviews	Were repeat inter views carried out? If yes, how many?	*No* *Page 6 - 7*
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	*Page 7*
20. Field notes	Were field notes made during and/or after the inter view or focus group?	*No* *Page 6 - 7*
21. Duration	What was the duration of the inter views or focus group?	*Page 7*
22. Data saturation	Was data saturation discussed?	*The applied methodology did not rely on data saturation* *Not reported*
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	*No* *Not reported*
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	*Page 7, 18*
25. Description of the coding tree	Did authors provide a description of the coding tree?	*Page 7 - 8*
26. Derivation of themes	Were themes identified in advance or derived from the data?	*Page 7 - 8*
27. Software	What software, if applicable, was used to manage the data?	*Page 7*
28. Participant checking	Did participants provide feedback on the findings?	*No* *Not reported*
Reporting		

29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	*Page 8 - 15*
30. Data and findings consistent	Was there consistency between the data presented and the findings?	*Page 8 - 15*
31. Clarity of major themes	Were major themes clearly presented in the findings?	*Page 8 - 15*
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	*Page 8 - 15*

BMJ Open

From pain treatment to opioid dependence: A qualitative study of the environmental influence on codeine use

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From pain treatment to opioid dependence: A qualitative study of the environmental influence on codeine use

Emma Kinnaird[1*], Andreas Kimergård[2*], Stacey Jennings[2], Colin Drummond[2,3], Paolo Deluca[2]

* Joint first authors

[1] Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

[2] National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

[3] National Institute for Health Research Biomedical Research Centre for Mental Health, South London and Maudsley NHS Foundation Trust, London, UK.

Correspondence to: Andreas Kimergård, National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 4 Windsor Walk, SE5 8BB, London, United Kingdom, e-mail: Andreas.Kimergard@kcl.ac.uk, telephone: 020 7848 0825

ABSTRACT

Objectives To investigate the views and experiences of people who use codeine in order to describe the 'risk environment' capable of producing and reducing harm.

Design This was a qualitative interview study. Psychological dependence upon codeine was measured using the Severity of Dependence Scale (SDS). A cut-off score of five or higher indicates probable codeine dependence.

Setting Participants were recruited from an online survey and one residential rehabilitation service.

Participants 16 adults (13 women and 3 men) from the UK who had used codeine in the last 12 months other than as directed or as indicated. All participants began using codeine to treat physical pain. Mean age was 32.7 years (*SD* = 10.1) and mean period of codeine use was 9.1 years (*SD* = 7.6).

Results Participants' experiences indicated that they became dependent on codeine as a result of various environmental factors present in a risk environment. Supporting environments to reduce risk included: Medicine review of repeat prescribing of codeine, well-managed dose tapering to reduce codeine consumption, support from social structures in form of friends and online, and access to addiction treatment. Environments capable of producing harm included: Unsupervised and long-term codeine prescribing, poor access to non-pharmacological pain treatments, barriers to provision of risk education of codeine related harm and breakdown in structures to reduce the use of over-the-counter codeine other than as indicated.

Conclusion The study identified micro- and macro- environments capable of producing dependence on codeine, including repeat prescribing and unsupervised use over a longer time period. The economic environment was important in its influence upon the available resources for holistic pain therapy in primary care in order to offer alternative treatments to codeine. Overall, the goal is to create an environment that reduces risk of harm by promoting safe use of codeine for treatment of pain, whilst providing effective care for those developing withdrawal and dependence.

Keywords

Codeine, dependence, prescribing, over-the-counter, risk environment.

Strengths and limitations of this study

- Adds to a relatively small body of qualitative research investigating codeine dependence.
- Presents an investigation of environmental factors producing and reducing harm related to codeine containing medicines through the adoption of the 'risk environment' approach.
- A limitation is the small sample size and findings cannot be generalised to all regions of the UK.
- The study recruited a higher proportion of women compared to men potentially ignoring certain experiences of pain, codeine use and dependence specific to men.
- The risk environment approach focuses on a particular aspect of the social world and may overlook individual circumstances.

INTRODUCTION

The risk of codeine dependence and physical harm associated with long-term use of codeine containing medicines are well-known.[1,2] In the UK, data from the National Drug Treatment Monitoring System show that codeine was the primary or secondary drug for 2.2% of clients (*N* = 4,248) in structured drug treatment (2013/2014).[3] Escalating use to a daily dose of 1,250 mg codeine, which is 5 times the maximum daily dose,[4] has successfully been treated with opioid agonist therapy (buprenorphine/naloxone) and tapered dosing over a 4-month period.[2] However, many individuals who are dependent on codeine (experiencing withdrawal symptoms when codeine is removed) may not seek help due to a reluctance to explore other types of pain treatments.[5,6] Furthermore, regional variability in addiction treatment may act as a barrier against receiving effective care. To improve pain treatment and physical and mental health, concerted efforts are needed at the level of codeine prescribing, dispensing and use to reduce the number of patients who become dependent after starting on codeine.

Codeine is widely accessible in the UK: It is one of the most commonly prescribed opioids and can be purchased over-the-counter (OTC) in licensed pharmacies without a medical prescription. Codeine is available in pure formulations with a medical prescription and as compound products available OTC or with a medical prescription depending on the codeine dose. In 2016, the UK was the second biggest consumer of codeine in the world at 44.2 tons.[7] According to Prescription Cost Analysis data, more than 15 million items of co-codamol (codeine/paracetamol) were dispensed in the community in England in 2017 – an increase of approximately 15% since 2007.

Therapeutic indications for codeine use are treatment of mild to moderate pain not relieved by non-opioid analgesics such as paracetamol and ibuprofen.[4] Although considered a 'mild opioid',[8] long-term codeine use can lead to tolerance and dependence.[9-11] Use of compound products containing paracetamol or ibuprofen in higher than recommended doses may result in harm from high doses of accompanying non-opioid analgesics, such as renal and gastrointestinal complications attributed to ibuprofen and liver damage attributed to paracetamol.[12] Indications of possible codeine dependence include long-term use for

non-cancer pain,[5] use for anxiety and depression,[10] and obtaining codeine from multiple sources, including prescribed, OTC and from the illicit market.[2,13]

With the high level of codeine use in the UK, it is important to consider which factors impact on the production and reduction of codeine related harm. In this article, we adopt the 'risk environment' framework as an approach to investigate social situations and environments which are specific to codeine use. The risk environment can be seen as a space where multiple factors affect individual risk by considering how different types of environments (physical, social, economic and policy) interact at different levels (micro and macro).[14] This framework has previously been applied to explore the risk environments of illicit drug harms, including in relation to HIV transmissions [15] and overdose [16], but not the development of codeine dependence in a pain treatment context.

In the risk environment, micro-environments involve physical risks from substance use and social- and financial circumstances, whereas macro-environments relate to wider structural influences such as laws, health service revenue and spend, and national policies.[14] Codeine-specific examples illustrate the logic applied in this framework: at the micro level, starting patients on prescribed codeine without a clear plan for stopping again may increase the risk of long-term use and subsequently dependence.[6] Conversely, careful and patient-involved dose tapering protect against long-term use. At a macro level environment, regulation restricts access to high doses of codeine in the form of pure formulations to prescription-only with prescribers deciding if they are appropriate to use. Whilst compound codeine formulations (combined with paracetamol or ibuprofen) are available OTC, regulations state that only one packet can be sold at a time and the packet labelling must state: 'Can cause addiction. For three days use only'.

However, studies indicate that transitions still occur from short-term codeine use to treat pain into long-term use and dependence.[10,13,17] Reasons why individuals experience dependence on codeine include: Physical and psychological withdrawal resulting in prolonged use,[1,10,18] poor understanding of the risks of taking codeine,[19] and disengagement from general practitioners (GPs) due to concerns of codeine dependence being recorded in medical notes.[13,20] In a pain treatment setting where opioids are prescribed more often and for longer periods, despite the lack of evidence of long-term efficacy for chronic pain,[10,21-23] investigating the risk environment can offer a better

understanding of the social and political institutions that play a role in reducing codeine harm.

As such, our aim of the article is to explore the risk environment that influence codeine harm from the perspective of people who use or have used codeine recently for pain treatment.

METHODS

Design

This was a qualitative study that used data from semi-structured interviews with participants living in England who reported use of codeine in the last 12 months. Inclusion criteria were: Any individual aged 18 or over who used codeine other than as directed or as indicated, whether wilful or unintentional, and whether it resulted in harm or not.[24] The study was approved by the NHS REC Committee London (London Bridge), REC Reference 15/LO/0107.

Recruitment

Participants were recruited amongst respondents to an online survey (*N* = 14) and from a residential rehabilitation service (*N* = 2) in order to capture individual experiences across the spectrum from initial misuse to dependence which required structured addiction treatment.[10] A question in an online survey[10] invited respondents to take part in an interview by emailing the researcher or providing contact details. The researcher (AK) contacted and interviewed all eligible participants who did so, resulting in eighteen interviews. A leaflet was provided to clients in the residential rehabilitation programme informing about the study. All eligible clients in the service at that time were invited to take part, resulting in an additional ten interviews conducted by AK.

Sample

Of the 28 participants, one was excluded as codeine was used according to accepted medical practice or guidelines. Another 11 participants were excluded from the analysis as codeine was predominantly sourced as substitution for illicit opioids (heroin). This resulted in a sample of 16 participants who first took codeine for pain treatment, which allows for an investigation of influential factors that have an effect on codeine harm.

Data Collection

Participants were given a Participant Information Sheet informing them of the reasons for doing the study and the involved researchers and institutions (Supplementary File). They were then asked to sign a consent form to ensure their informed consent to the research (Supplementary File). Interviews took place either in the residential rehabilitation service, at a location chosen by the participant or over the phone. The first interview was conducted in May 2015, and the last in April 2016. Interviews lasted from 35 minutes to an hour and 35 minutes. Participants were compensated for their time with a £20 gift voucher. Interviews were conducted using a topic guide, covering: demographic information, initial use of codeine, patterns of codeine use, difficulties managing codeine use, sourcing of codeine, use of other drugs or medicines, and views on codeine availability and regulation. New topics brought up by the participants were pursued during the interviews with follow-up questions. Codeine dependence was measured using the 5-item Severity of Dependence Scale (SDS) during the most recent period of codeine use.[25,26] A score of 5 or above, out of a maximum score of 15, was used to indicate probable psychological dependence on codeine.[9]

Data management and analysis

Interviews were audio-recorded and then transcribed verbatim by a professional service, with any participant identifying information removed from the transcripts. Data analyses were completed by three researchers on the project (AK, EK, SJ) and coded using the qualitative software NVivo (Version 11). A coding framework was developed deductively from the topic guide and from codes that emerged inductively from the data.[27] For this paper, all coded data were analysed using Framework.[28] In the first stage, the coded data were reviewed to describe aspects of each factor which influenced codeine use in the risk environment. Since similar factors were identified as being important to the production and reduction of harm amongst the participants, the analyses were merged and then grouped into more inductive categories. We organised these under four headings: i) patient education on the risk of codeine, ii) the role of prescribing practices related to codeine and non-pharmacological pain treatment, iii) the accessibility and use of OTC codeine and the differences between relationships with GPs and pharmacists, and iv) access to interventions

and treatment for codeine dependence. These categories are used to structure the results below. Emergent factors that appeared to have an impact on the harms of using codeine use that may have transferability to other settings[29] were categorised into micro- and macro-environments (physical, social, economic and policy) and used for mapping the various domains of the risk environment.[14] A risk environment for codeine is presented in Table 1. Analyses are presented with supporting quotes (anonymised using participant numbers) and SDS scores.

RESULTS

Participant characteristics

The sample consisted of 3 men and 13 women, with a mean age of 32.7 years (*SD* = 10.1) and a mean period of codeine use of 9.1 years (*SD* = 7.6) (Table 2). In the sample, 3 participants (18.8%) were unemployed, 3 (18.8%) were students, and 10 (62.5%) were employed. Co-morbid anxiety or depression was self-reported by 4 participants (25%), and 4 (25%) reported concurrent use of codeine and other prescription opioids. Using the SDS, 10 participants (62.5%) scored 5 or more, indicating probable codeine dependence. At the time of interview, 4 participants (25%) sourced codeine from a medical prescription, 3 used OTC codeine (18.8%), whereas 9 used both (56.3%). Only 1 participant reported additionally sourcing codeine from the internet, whilst 3 also used codeine obtained from family or friends. In total, 4 participants (25%) had received intervention and treatment for their codeine use, including addiction treatment, GP led intervention, counselling or from a psychiatrist.

Education of patients on prescribed codeine

Many participants explained that they had not fully understood the potential risks when they first started taking codeine, including its addictive potential. Reflecting on their initial codeine use, many expressed frustrations with their GP and suggested that they wished they had been given more information:

> "If I had had a doctor who possibly just had a little bit more time to say here's what I'm giving you, here's what it is, here's what it does, here's the risks to it. If I had just

been a little bit more educated, perhaps it wouldn't have happened [use in excessive doses]." Participant 11, male, dependence score 0.

Participants identified several potential barriers facing health professionals in effectively communicating risks. Specifically, participants felt that the typical 10-minute GP appointment was not enough to fully discuss available options for pain therapy. Of note was that participants who had greater awareness of the risks of codeine, typically from searching for information on the internet, were often more motivated to avoid these risks. However, when participants voiced concerns to their GP, they felt ignored and detached from decisions about their health and care:

"I kind of had to battle to get my GP to do or say anything about my lower back pain, because they're just like, it's lower back pain, what can you do? They just kind of send you away, say carry on, take the painkillers…It didn't seem like anyone was taking any care in the fact that I could get addicted to this; I didn't bother to go back." Participant 15, female, dependence score 2.

Such encounters with health professionals enhanced the feeling of not being listened to and contributed toward disengagement from health services, distrust in medical opinions, and isolation. In this environment, fewer factors acted to protect against unsupervised, long-term codeine use. Consequently, the lack of effective communication between prescribers and patients, and a resulting poor education of patients on codeine risk, appeared to facilitate the development of codeine dependence for some participants.

Prescribing practices and the use of non-pharmacological pain therapies

The majority of participants who received prescription codeine did so through a repeat prescription. Individuals robustly reported being able to order their repeat prescription with few restrictions on amounts and frequency, which for some resulted in increasing codeine intake:

"It wasn't just once a month for my periods, like I went through a period of having really bad back ache, so I took it for that. Then for when I twisted my ankle like four or five times, so I'd take it for that. I started running two years ago, now I've got a knee injury, so I'd take it for that. It was just whatever niggles and pains there were, I'll just pop some tablets because I had them on a repeat prescription and they were

> basically on tap. That's when it started to really get a grip, because I was taking them for other things on a more or less daily basis." Participant 8, female, dependence score 7.

Within the risk environment, prolonged access to codeine with minimal supervision from a health professional can facilitate use of codeine other than as indicated during the initial consultation, influencing transition to subsequent dependence.

It was striking that participants using codeine from a medical prescription reported being prescribed codeine as a first resort for pain, even when participants were otherwise motivated to try other types of pain treatments:

> "I went and said I need another bout of physio for my back because it's starting to hurt again. And they [GP] said: 'oh, you've got to be in constant pain for six weeks'. And I said: 'I've been in constant pain for six weeks already, and it's a recurring problem, so please just refer me.' And the doctor said: 'no, go and take these pain medicines [codeine] and come back in six weeks'. And I said: 'I think it's really dangerous that you're telling me to go away and take a pain med that I know is really highly addictive constantly for six weeks, for a problem that you already know exists.' And they said: 'well, that's just the way it works, I'm sorry." Participant 8, female, dependence score 7.

For some primary care patients in the study, these issues were perceived as a general systematic problem reflecting a lack of treatment resources. They felt like they had been prescribed codeine in order to quickly get rid of them, rather than their GP taking the time to deal with the underlying problem or being referred to specialist services. This did lead to frustration and, in some cases, disengagement from GPs, for example to seek treatment privately:

> "…if that's the only advice you're going to give me [take codeine], then I will do what works for me. And I went to an osteopath and that really helped." Participant 15, female, dependence score 2.

In contrast with the negative perceptions of codeine prescribing expressed by some participants, those who were treated with non-opioid pain medicines, physiotherapy and hydrotherapy, indicated that they felt less concerned about continued codeine use:

> "Through the doctor they referred me to a hydrotherapy thing, because I just hadn't had any physiotherapy before for the pain. So, I had six sessions with them and they gave me exercises to do at home. I've been trying to keep up with that, which has I guess lessened the pain. I no longer think that I'm going to get dependent on codeine because it's been that long that I don't wake up in the morning and think I have to take a pill." Participant 12, female, dependence score 5.

Participants' accounts therefore highlighted several structural factors in the risk environment influencing codeine harm: having alternative treatments available beyond codeine resulted in better engagement with health services and greater patient satisfaction, whilst minimising chronic codeine therapy. Conversely, treating pain solely with codeine did result in disengagement from health services.

Differences in relationships with pharmacists and GPs

Implementation of pharmacist intervention to regulate OTC codeine sales is intended to prevent codeine from being used other than as indicated and is one example of a factor which reduces harm. However, participants were able to circumvent restrictions on sale by purchasing from multiple pharmacies over the course of a week or even a day. While one participant had been refused codeine in a pharmacy, most OTC codeine users reported rarely being questioned by pharmacists to find out if codeine was a safe choice, even when they regularly came to the same pharmacy and obtained large amounts of codeine:

> "It's the same staff all the time and I've bought it from there many times. And nobody has ever questioned me at all." Participant 7, female, dependence score 14.

Another important outcome of accessing multiple pharmacies in the local area was that participants never established a strong relationship with a single pharmacist, contrasting this to those who described a better relationship with their GP. Even where participants only accessed one pharmacist, they often perceived this relationship as less important to them and therefore less effective in regulating use and providing risk education, support and interventions than their GP. This appeared to also be related to the short amount of time participants spent interacting with pharmacists when buying codeine:

> "Whenever I go and speak to pharmacists, I've just never felt particularly comfortable speaking to a pharmacist. I find they're a bit… maybe not judgmental,

> but I find they're a bit short and like they are very kind of medical. I don't find that there's much interaction. I would just prefer to speak to my GP, because I feel I can trust him and I feel I've got a good relationship." Participant 3, female, dependence score 7.

However, participants also emphasised that pharmacists were far easier and quicker to access than scheduling an appointment with their GP, providing a disincentive to wait and consult with their GP about their codeine use. For participants with a positive and trusting relationship with their GP, a reluctance to be dishonest in their communication with the GP appeared to reduce the risk of dependence occurring; however, this appeared, in some cases, to be undermined by the convenience of OTC availability:

> "I lied to the doctor once, but that killed me doing that. I was really ashamed of myself at the time. I wouldn't have kept doing that [to continue using codeine]. It's only because I had been able to buy it OTC that I've kept on with that addiction. And even now, when I have a bad week and I really need codeine, I'll go and buy it OTC. I wouldn't do that if I had to go to my GP and explain." Participant 7, female, dependence score 14.

Some participants believed that codeine should be restricted to prescription only. In contrast, one participant with a low SDS score suggested that this would not be necessary nor feasible in the context of a wider NHS lack of resources – If everyone self-treating their pain with codeine had to regularly see their GP, primary care would become overwhelmed:

> "I think that it shouldn't be made much more difficult to get hold of because I think most people can go through some acute pain that lasts a couple of days that you might need something like this for, and our NHS is stretched enough without having to go to the GP every time you spring your ankle." Participant 15, female, dependence score 2.

This illustrates the dynamic nature of the risk environment, suggesting that for short term use for acute pain the benefits of OTC codeine outweigh the potential risk of dependence and thus play a significant role in providing access to pain treatment. However, in cases where factors implemented to protect against long-term use fail, such as pharmacist regulation of OTC sales, OTC codeine is associated with a risk of dependence.

Support, intervention and treatment of codeine dependence

Four participants had experience with intervention and treatment for codeine dependence, ranging from GP initiated medicine review to addiction treatment. Still, most participants with SDS scores indicating probable codeine dependence did not report any medical supervision or support; for some this spanned several years during which codeine use became an established part of their daily practice.

It is relevant to note the significance of the influence GPs possessed for some dependent participants in influencing their codeine use. Whilst most participants expressed negative GP experiences which led to disengagement and overreliance on poor information sources, those participants who openly disclosed difficulties in controlling their use of codeine, in the context of a positive and trusting relationship with their GP, were able to receive useful interventions:

> "I thought I'll just tell him [GP] and I'll just see what he says [about difficulties in managing codeine use]. And I ended up getting signed off work for about four weeks...I really trust my GP…When I tell him that I don't want to take codeine, he asks me why, and he kind of tries to look at other options for me, which I really appreciate. I think it was kind of a combination of all those different things, the GP and the counselling, the time off work, everything sort of came together. I think if it had only been one of those things, I don't know how well my recovery would have gone." Participant 3, female, dependence score 7.

Where participants engaged with their GP regarding their codeine use, either due to GP instigated follow-up consultations concerning their use of codeine or to the participant asking for an appointment, their GP was able to help via effective interventions such as tapering codeine and replacing compound products with pure codeine formulations. This suggests that in an environment where GPs have resources to support the patient, they reduce the likelihood of harm occurring:

> "He wrote me out like a little rota. He said we were going to do it [taper] over a certain period of time. And I had to sign, like he made like a contract for me to sign, and he signed it as well, to say that he was going to help me, and he was going to support me. And he was really understanding and not judgmental at all, it was

fabulous. He said he was going to prescribe me a certain amount of just codeine, so not the paracetamol, just codeine on its own." Participant 8, female, dependence score 7.

When two participants, who had attended addiction treatment, were asked why they had started treatment they generally described lengthy and complicated pathways which did require significant level of self-motivation. One male participant who was currently a client in a residential rehabilitation programme described the social, economic and physical circumstances that motivated him to eventually seek treatment and detoxification for codeine dependence. These included transitions from single to multiple codeine containing medicine use (OTC and prescribed), breakdown in family relationships, dropping out of university, social isolation, being fired from work and physical adverse effects from high doses of compounded ibuprofen:

"I think when I had the stomach ulcer, I started realizing then that this will actually kill me. I cut down the Nurofen Plus [codeine/ibuprofen] because it was what kept me going really, but I couldn't put it down…I just couldn't stop. I hadn't got a job, I'd dropped out of uni. Just living at home doing nothing and it kind of dawned on me you know, I've really got a problem. At first, I went to the local drug services, and they said that they don't deal with codeine so there wasn't any help there, and someone gave the number for there [residential rehabilitation service], a family friend or something…It was quite quick, about after two weeks [starting in treatment]." Participant 1, male, dependence score 15.

For some of the participants, disengagement from medical professionals, and the placing of responsibility on the patient to self-manage their dependence, created situations where participants reported that they instead used the internet to find out more information about codeine, pain treatments, and advice on how to manage the use of codeine.

"When I was first diagnosed with depression and anxiety, when I was just being pushed and pulled from different doctors, different psychiatrists, I looked to the internet to do my own research and just understand what these medicines were [codeine]. I didn't know what I was taking, and I didn't know what the risks of

abusing it was, so I felt that I should really start understanding what I'm being prescribed." Participant 11, male, dependence score 0.

Support structures in form of family and friends also played an important role to some participants as a source of information about codeine. For this participant, an encounter with a friend facilitated personal reflection as to her own use of codeine:

> "One of my best friends was going for a job interview and I said to her: 'do you want to take a codeine like an hour before you leave the house? You'll feel so very relaxed.' And although she took the tablets, she said to me: 'I don't feel comfortable with this and I don't think that I should' A few months later she asked me if I used to take them for reasons other than pain, and I said to her no, but in my heart, I knew that I did. I asked her why. She said: 'because it's a very addictive drug…it's something that can basically change the chemicals in your brain and you'll be addicted forever.' She suggested a few articles for me to read, which I did, and then I was very worried because then I learned that codeine was connected to morphine." Participant 10, female, dependence score 2.

Such relationships played an important role for participants to gain more confidence in their ability to manage their use of codeine, especially for those using codeine other than as indicated, but not experiencing codeine dependence. However, over-reliance on potentially inaccurate online sources and advice from friends and family may also delay or prevent patients from seeking support from health professionals until they experience severe dependence that is much more complicated to treat. As such, the social environment has the capacity to both produce and reduce codeine-related harm.

DISCUSSION

This qualitative study explored codeine use from the perspective of people who use or have used codeine to treat pain in order to unpack the key factors of the risk environment. These findings add to existing literature that suggest that some patients who use codeine for treatment of pain become dependent as a result of environmental factors.[10,20] We identified a number of environmental factors that reduced the risk of dependence: medicine review of repeat codeine prescribing, interventions in primary care (such as tapering), social

support (friends and online), and access to addiction treatment (Table 1). We also identified several micro- and macro- environmental factors capable of producing harm, especially unsupervised, long-term codeine prescribing and breakdown in structures to stop sales of OTC codeine for use other than as indicated (Table 1).

Amongst micro-level barriers, participants spoke of perceived limitations of pain therapy in primary care resulting in overreliance on codeine. Codeine prescribing often occurred in the context of poor utilisation of nonsteroidal anti-inflammatory drugs, graduated exercise, and cognitive behavioural therapy, which may achieve similar levels of improvement in pain[30,31] without risk of dependence.[32] Lack of psychological, social community and pain specialist resources and the services of physiotherapists, occupational therapists and social workers thus appeared to hinder a holistic approach in pain therapy that incorporates prevention, active treatment and rehabilitation. Overcoming these impediments most likely require amending the economic environment that regulates the availability of these resources.

A policy environment dictates procedures for OTC codeine sale in the UK to prevent use other than as indicated.[33] However, lack of trust in the relationship between pharmacists and participants using OTC codeine, confirmed concerns previously raised about OTC codeine sale, including inabilities to effectively monitor OTC codeine consumption and intervene to halt escalating use.[34] OTC medicines play an important role given the increasing acceptance of self-care to promote patient empowerment and reduce the pressure on local GP practices. However, drawing on knowledge of engagement between pharmacists and patients at the point of an OTC codeine sale is important to realign OTC sales of codeine with environmental factors to reduce harm.

Comprehensive assessment of codeine dependence, support delivered in primary care, and access to addiction treatment is required and should be available for those who need it.[5] Although some participants viewed the uptake of primary care intervention and addiction treatment positively, they also found them difficult to access. Where engagement and resources permitted, GPs proved to be an effective source of monitoring and reducing harm when concerns had been clearly communicated. Increased awareness of the potential for codeine dependence amongst GPs is likely to improve treatment of codeine dependence

further.[19] Easy-to-access addiction services capable of handling individuals with codeine as the primary drug may also be important here.

Implications for the risk environment

Considering the negative consequences of prolonged opioid use for chronic pain, which include paralysis of the endogenous opioid system, depression and ineffective pain control,[23] alternative management of patients with chronic codeine use is warranted.[22,35] The findings of this study suggest that GPs are well-placed to communicate risk, monitor and, if necessary, intervene in codeine use. However, their ability to do so may be limited by a lack of resources and subsequent patient disengagement. Training and funding must be provided, including more time to spend with patients, effective ways to monitor codeine prescriptions, access to other types of treatments, and ability to refer to secondary services.

Although pharmacists are empowered by current UK regulations to restrict individual access to OTC codeine by refusing sales and limiting the amounts sold, this study found that having codeine available OTC may produce harm due to limited effectiveness of these interventions. With Australia recently joining countries like the US, Germany and Japan in restricting codeine to prescription-only,[36] it is necessary to review UK OTC regulation to reduce the risk of excessive use of codeine. There is also a need to explore how to improve patient/pharmacist communication.

Using codeine only for its intended indications of mild to moderate pain on a short-term basis and only if they help would most likely go a long way in preventing dependence. However, this requires effective and acceptable alternatives to manage pain to ensure that pain patients receive the care they need. The goal is to create a system where patients understand their options for pain therapy and the risks of taking codeine. Finally, ending codeine prescriptions in cases of dependence should not be done abruptly, and only under close monitoring to prevent relapse or use of other opioids (sourced online or from the illicit market).

Strengths and limitations

A strength of this study is that it helps understand individual experiences in their broader context of the risk environment surrounding codeine use in the UK, an area previously

unexplored in the literature. Specifically, this study highlights how different environmental factors intended to facilitate safe use of codeine can potentially act to increase risk without proper utilisation and sufficient funding. This is important in implementing change to ensure that benefits of codeine use in pain therapy outweighs harm. Most obviously, a limitation of the study is the small sample size. Findings cannot be generalised to all regions of the UK. As such, a reduction or production of harm related to codeine containing medicines will depend on many factors, such as the nature and funding of local primary care. The majority of participants in this study were female, whereas two previous qualitative studies recruited a more evenly distributed sample.[13,20] The advertisement for the online survey was designed to attract both men and women, however more women responded (67%)[10] creating a multiplying effect when recruiting for interviews. Although the gender distribution could potentially introduce bias, this is consistent with previous research where opioid utilisation in GP practices in the UK increased with greater proportion of female registrants.[37] As such, the sample in the online survey[10] and in this interview study may reflect the type of individual most likely to receive treatment with opioids. Future qualitative studies should explore the differences between pain, opioid use and dependence in men and women. The inclusion criteria enabled us to study factors contributing to codeine dependence, whilst limiting our ability to identify protective factors in the environment, which may have stopped dependence from occurring. Had we recruited from primary care instead of from an online survey, our findings may have been different in that we had recruited more patients with experience of factors that stopped codeine use other than as indicated. The risk environment approach has a limitation in its ability to understand codeine-related risks. This is because this approach focuses on a particular part of the social world and may not capture individual circumstances which inform codeine dependence, such as co-morbidities and specific types of pain. Furthermore, overlaps between different environments (physical, social, economic and policy) are likely when mapping the risk environment. While this is useful for understanding the complicated nature of how drug harms are generated, it can also make it difficult to determine how to implement effective change.

CONCLUSION

This study identifies environments that produce and reduce harm related to codeine containing medicines among participants with recent use of codeine. The study highlights micro- and macro- environments capable of producing harm, particularly in regard to long-term prescribing, unless realigned with current risks of codeine use and provided with adequate funding. The economic environment is often crucial in reducing drug harm and facilitating effective treatment of dependence. We echo calls for funding to facilitate a more holistic approach to pain therapy to reduce prescribing to patients who may not benefit from opioids.[22,35] The study found evidence to support regular review of patients prescribed codeine. Alternative non-pharmacological therapies may also go a long way to reduce codeine dependence.

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Author contributions

PD and AK designed and planned the study. Ak wrote the research protocol. AK recruited and collected the data. EK performed the literature research and undertook data analysis with AK and SJ. EK and AK contributed to theoretical implications of study analysis. EK and AK led on writing the paper with input from CD, SJ and PD. All authors had access to the data used and provided final approval of the manuscript to be published.

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Disclaimer

The views expressed are those of the authors and not necessarily those of the NIHR, SLaM NHS Foundation Trust and the BRC.

Competing Interests

None.

Patient consent

Participants provided written consent. Personal details were removed from the collected data to ensure anonymity.

Ethics Approval

This qualitative study was imbedded in the CODEMISUSED project approved by King's College London, Psychiatry, Nursing & Midwifery Research Ethics Sub-Committee and the NRES Committee London - London Bridge.

Data sharing statement

No additional data are available.

Patient Involvement

Patients were not involved in the design and conduct of the study.

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TABLES

Table 1. The codeine risk environment in the context of pain treatment: examples of environments producing and reducing harm

	Micro-environment		Macro-environment	
	Risk	*Intervention*	*Risk*	*Intervention*
Physical	Prolonged codeine use Excessive codeine use Codeine dependence	Increased education for peers on diversion of medications	Diversion of codeine containing medicines (obtaining codeine from friends and family)	Review of regulation on prescription and monitoring
Social	Ineffective risk communication between GPs and patients to inform of codeine risks Disengagement from healthcare providers Limited engagement between patient and pharmacist Overreliance on potentially inaccurate internet and peer information	Increased information provision on codeine risk and alternative pain therapies in primary care GPs receptive to reviewing patient concerns Improving patient attitudes towards GP consultations and pain management. Improving healthcare provider attitudes to pain management and codeine misuse. Clinician-led assertive engagement strategies in primary care Provision of social support via peer group and online Explore pharmacist-patient communication strategies	Codeine's dominant role in contemporary pain treatment Stigmatisation of codeine dependence Anonymised information sourcing on the internet from unreliable sources	Improved access to alternative non-pharmacological pain management therapies Increased awareness and opportunity for early intervention for codeine dependence across community, employment and health services

		Effective strategies targeting peer education and awareness of codeine misuse		
Economic			Lack of resources available for non-pharmacological pain treatments in primary care (e.g. physical therapy)	Funding and reform for NHS primary care and local drug addiction treatment services
Policy	Low utilisation of medicine review of repeat prescription of codeine Ineffective implementation of pharmacy OTC restrictions Ease of circumventing pharmacy restrictions	Timely prescription monitoring and review of concerns GP instigated follow up consultations and interventions Assertive and active review from primary care Continued provision of effective interventions in primary care such as tapering and pure codeine replacement Training of pharmacy staff to ensure consistent implementation of pharmacy OTC risk reduction policy	Nature of GP appointments (long waiting times, short duration) Ineffective laws and regulation governing OTC sales of codeine containing medicines	More time to spend with codeine dependent patients. Increased availability and convenience in securing appointment and access to screening and brief intervention Review of legal and regulatory governance surrounding OTC codeine

Factors may overlap physical, social, economic and policy environments and change place between environments over time.

Table 2. Participant characteristics and codeine use

Participant	Gender (F/M)	Initial type of pain	Subsequent reasons for codeine use	Time between first and last use	Source of obtaining codeine	Severity of Dependence Scale (SDS) score	Intervention and treatment
1	M	Headache	To reduce stress	7 years	Prescription, OTC, obtained from family	15*	Residential rehabilitation programme
2	F	Dysentery	Recreational purposes, to reduce stress	1 year	Prescription, OTC	4	None
3	F	Pain after an operation	To sleep, to reduce stress, for depression	1 month	Prescription	7*	GP support, counselling
4	F	Period pain		15 years	Prescription	12*	GP support
5	F	Injury	To sleep, recreational purposes	15 years	Prescription, OTC	8*	None
6	F	Deep vein thrombosis from heroin use	Used when heroin unavailable	8 years	Prescription, OTC	11*	Previously in residential rehabilitation. At time of interview none
7	F	Pain after an operation	For anxiety	10 years	Prescription, OTC	14*	None
8	F	Back pain		20 years	Prescription	7*	None

9	F	Head injury	To reduce stress, to sleep	2 years	Prescription, OTC	10*	None
10	F	Migraines	To reduce stress, to sleep	25 years	Prescription	2	None
11	M	Migraines and back pain	For anxiety, for depression	14 years	Prescription, OTC, internet	0	Private psychiatry, private pain specialist
12	F	Arthritis		2 years	Prescription, OTC	5*	None
13	M	Headache, later osteoarthritis	For anxiety, recreational purposes	15 years	Prescription, OTC, obtained from family	1	None
14	F	Arthritis		3 years	OTC	6*	None
15	F	Migraines, back pain, irritable bowel syndrome	To sleep	8 years	OTC, obtained from a friend	2	None
16	F	Ulcers	Sleep	4 months	OTC	0	None

* Scores of 5 and above indicate probable psychological dependence upon codeine.

INFORMATION SHEET FOR PARTICIPANTS

REC Reference Number: PNM/14/15-110

Version: 2 - 20 April 2015

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of study

Understanding codeine use: exploring the experiences and characteristics of codeine users

Invitation Paragraph

You are being invited to take part in a research study. Before you decide we would like to explain why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you have any other questions. Take time to decide if you want to take part or not.

What is the purpose of the study?

This interview study is being conducted by King's College London as part of an EU funded project about codeine misuse, related health harms, characteristics of users, and dependence. There is limited evidence available on the factors associated with and outcomes of use. The aim of the interview study is to collect qualitative data to explore codeine users' choices and decision-making when using codeine (prescribed or otherwise), codeine use patterns, favoured route of administration, recreational use and tampering with codeine pharmaceuticals, adverse health consequences (including codeine related problems and dependence), characteristics of dependent and non-dependent codeine users, sourcing of codeine, use of other drugs and medication, opinions around medical prescribing, and pharmacy dispensing and internet based retail.

During the interview you will be asked questions about which codeine products you use, how and why. You will be asked about from where you get your codeine and any problems you have experienced as a result of using codeine. We will also ask if you have used any other drugs or any other medicines. We will ask how you first got introduced to

using codeine. This will help to increase the evidence base, which will be of potential benefit to people who decide to use codeine and in the development of public health responses.

If you would like to read more about our research about codeine use, then go to: www.codemisused.org

Do I have to take part?

No. It is up to you to decide whether or not you want to take part. If you do we will ask that you give your consent to take part. You are still free to withdraw up until the point of publication of results without giving a reason. If you wish to do so you must inform the researcher in writing. A decision to withdraw will not affect your rights to any health care you receive.

What will happen to me if I take part?

If you decide to take part we will ask you to take part in an interview that will last about 1 hour and that will be audio recorded. In this interview we will ask you questions about your use of codeine, what products you use, and your experiences with any problems you may have encountered. When taking part in an interview you will receive a £20 gift voucher in reward of your time.

What are the possible risks of taking part?

We understand that answering questions about substance use and dependence can be stressful. We know from experience that talking about these issues as part of an interview can sometimes make participants feel worse. Should you become distressed during the interview, the interview will terminate immediately. We will advice you to seek help from GP.

Will my taking part be kept confidential?

Yes. All the information that we collect will be kept strictly confidential. Any identifying information about you will not be disclosed to anyone outside the research team. You do not have to give us your full name or date of birth.

Once the audio recording of your interview has been transcribed, the audio recording is deleted. Any details that might be used to identify who you are will be erased from the transcription of your interview. All transcriptions are safely stored at King's College London to make sure that no one other than the research team can look at it. We do this by storing it on a computer that can only be accessed with a password.

Researchers work under the same rules of confidentiality as doctors and nurses, which can only be broken, without your consent, in very exceptional circumstances. **Usually this is if the researcher sees or is told something which raises serious concern for your personal safety.**

How is the project being funded?

The research is funded by the European Commission — 7th Framework Programme (reference number: FP7-PEOPLE-2013-IAPP-611736) and is sponsored by King's College London.

What will happen to the results of the study?

The results of the study will be published in reports, articles and conference presentations.

Who should I contact for further information?

Ask us if there is anything that is not clear or if you would like more information. Please contact the researcher using the following contact details:

Dr Andreas Kimergård, Addictions Department, King's College London, T: 020 7848 0446, @: Andreas.Kimergard@kcl.ac.uk

What if I have further questions, or if something goes wrong?

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you can contact King's College London using the details below for further advice and information: The Chair, PNM Research Ethics Subcommittee (RESC), rec@kcl.ac.uk

What else do I need to know?

You must be 18 years or older to take part in this study. If you are interested in receiving the final results of this study please get in contact with Andreas Kimergård. However, remember that data from studies such as these often take many months to prepare for publication.

Thank you for reading this information sheet and for considering taking part in this research.

REC ref.: 15/LO/0107
Short Title: Codeine Interview Study
Document name: Annex D: Consent form A
Version: 2
Date: 24/02/15

Consent form

Codeine interview study: benefits of codeine use, side effects and use of treatment services

Researcher: Andreas Kimergård, King's College London

Email: Andreas.Kimergard@kcl.ac.uk

Please tick box

☐ I confirm that I have read and understand the information provided for this study. I have had the opportunity to consider the information and ask questions.

☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care being affected.

☐ I understand that personal information collected during the study will be anonymised and remain confidential.

☐ I understand that I can choose not to answer questions which I feel uncomfortable about answering.

☐ I agree to the digital recording of this interview.

☐ I agree that quotes from my interview may be reported in published documents but that this will be anonymous and no-one will be able to identify me from this.

☐ I agree to take part in the study.

Name of participant:

Date:

Signature:

Name of researcher:

Date:

Signature:

Note: This form must be completed in 2 copies, one for the participant and one for the researcher.

From pain treatment to opioid dependence: A qualitative study of environmental influence on codeine use

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Inter viewer/facilitator	Which author/s conducted the inter view or focus group?	*Page 6*
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	*PhD* *Not reported in manuscript*
3. Occupation	What was their occupation at the time of the study?	*Page 1*
4. Gender	Was the researcher male or female?	*Page 1*
5. Experience and training	What experience or training did the researcher have?	*Page 1*
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	*Page 6-7*
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	*Page 6-7* *Supplementary File*
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	*Page 6-7* *Supplementary File*

Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	*Page 7 - 8*
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	*Page 6*
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	*Page 6*
12. Sample size	How many participants were in the study?	*Page 8*
13. Non-participation	How many people refused to participate or dropped out? Reasons?	*None* *Not reported* *Page 6 - 7*
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	*Page 7*
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	*No* *Not reported* *Page 7*
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	*Page 8*
Data collection		

17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	*Page 7*
18. Repeat interviews	Were repeat inter views carried out? If yes, how many?	*No* *Page 6 - 7*
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	*Page 7*
20. Field notes	Were field notes made during and/or after the inter view or focus group?	*No* *Page 6 - 7*
21. Duration	What was the duration of the inter views or focus group?	*Page 7*
22. Data saturation	Was data saturation discussed?	*The applied methodology did not rely on data saturation* *Not reported*
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	*No* *Not reported*
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	*Page 7, 18*
25. Description of the coding tree	Did authors provide a description of the coding tree?	*Page 7 - 8*
26. Derivation of themes	Were themes identified in advance or derived from the data?	*Page 7 - 8*
27. Software	What software, if applicable, was used to manage the data?	*Page 7*
28. Participant checking	Did participants provide feedback on the findings?	*No* *Not reported*
Reporting		

29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	*Page 8 - 15*
30. Data and findings consistent	Was there consistency between the data presented and the findings?	*Page 8 - 15*
31. Clarity of major themes	Were major themes clearly presented in the findings?	*Page 8 - 15*
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	*Page 8 - 15*

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From pain treatment to opioid dependence: A qualitative study of the environmental influence on codeine use in UK adults

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From pain treatment to opioid dependence: A qualitative study of the environmental influence on codeine use in UK adults

Emma Kinnaird[1*], Andreas Kimergård[2*], Stacey Jennings[2], Colin Drummond[2,3], Paolo Deluca[2]

* Joint first authors

[1] Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

[2] National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.

[3] National Institute for Health Research Biomedical Research Centre for Mental Health, South London and Maudsley NHS Foundation Trust, London, UK.

Correspondence to: Andreas Kimergård, National Addiction Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 4 Windsor Walk, SE5 8BB, London, United Kingdom, e-mail: Andreas.Kimergard@kcl.ac.uk, telephone: 020 7848 0825

ABSTRACT

Objectives To investigate the views and experiences of people who use codeine in order to describe the 'risk environment' capable of producing and reducing harm.

Design This was a qualitative interview study. Psychological dependence upon codeine was measured using the Severity of Dependence Scale (SDS). A cut-off score of five or higher indicates probable codeine dependence.

Setting Participants were recruited from an online survey and one residential rehabilitation service.

Participants 16 adults (13 women and 3 men) from the UK who had used codeine in the last 12 months other than as directed or as indicated. All participants began using codeine to treat physical pain. Mean age was 32.7 years (*SD* = 10.1) and mean period of codeine use was 9.1 years (*SD* = 7.6).

Results Participants' experiences indicated that they became dependent on codeine as a result of various environmental factors present in a risk environment. Supporting environments to reduce risk included: Medicine review of repeat prescribing of codeine, well-managed dose tapering to reduce codeine consumption, support from social structures in form of friends and online, and access to addiction treatment. Environments capable of producing harm included: Unsupervised and long-term codeine prescribing, poor access to non-pharmacological pain treatments, barriers to provision of risk education of codeine related harm and breakdown in structures to reduce the use of over-the-counter codeine other than as indicated.

Conclusion The study identified micro- and macro- environments capable of producing dependence on codeine, including repeat prescribing and unsupervised use over a longer time period. The economic environment was important in its influence upon the available resources for holistic pain therapy in primary care in order to offer alternative treatments to codeine. Overall, the goal is to create an environment that reduces risk of harm by promoting safe use of codeine for treatment of pain, whilst providing effective care for those developing withdrawal and dependence.

Keywords

Codeine, dependence, prescribing, over-the-counter, risk environment.

Strengths and limitations of this study

- Adds to a relatively small body of qualitative research investigating codeine dependence.
- Presents an investigation of environmental factors producing and reducing harm related to codeine containing medicines through the adoption of the 'risk environment' approach.
- A limitation is the small sample size and findings cannot be generalised to all regions of the UK.
- The study recruited a higher proportion of women compared to men potentially ignoring certain experiences of pain, codeine use and dependence specific to men.
- The risk environment approach focuses on a particular aspect of the social world and may overlook individual circumstances.

INTRODUCTION

The risk of codeine dependence and physical harm associated with long-term use of codeine containing medicines are well-known.[1,2] In the UK, data from the National Drug Treatment Monitoring System show that codeine was the primary or secondary drug for 2.2% of clients (*N* = 4,248) in structured drug treatment (2013/2014).[3] Escalating use to a daily dose of 1,250 mg codeine, which is 5 times the maximum daily dose,[4] has successfully been treated with opioid agonist therapy (buprenorphine/naloxone) and tapered dosing over a 4-month period.[2] However, many individuals who are dependent on codeine (experiencing withdrawal symptoms when codeine is removed) may not seek help due to a reluctance to explore other types of pain treatments.[5,6] Furthermore, regional variability in addiction treatment may act as a barrier against receiving effective care. To improve pain treatment and physical and mental health, concerted efforts are needed at the level of codeine prescribing, dispensing and use to reduce the number of patients who become dependent after starting on codeine.

Codeine is widely accessible in the UK: It is one of the most commonly prescribed opioids and can be purchased over-the-counter (OTC) in licensed pharmacies without a medical prescription. Codeine is available in pure formulations with a medical prescription and as compound products available OTC or with a medical prescription depending on the codeine dose. In 2016, the UK was the second biggest consumer of codeine in the world at 44.2 tons.[7] According to Prescription Cost Analysis data, more than 15 million items of co-codamol (codeine/paracetamol) were dispensed in the community in 2017 (England only) – an increase of approximately 15% since 2007.

Therapeutic indications for codeine use are treatment of mild to moderate pain not relieved by non-opioid analgesics such as paracetamol and ibuprofen.[4] Although considered a 'mild opioid',[8] long-term codeine use can lead to tolerance and dependence.[9-11] Use of compound products containing paracetamol or ibuprofen in higher than recommended doses may result in harm from high doses of accompanying non-opioid analgesics, such as renal and gastrointestinal complications attributed to ibuprofen and liver damage attributed to paracetamol.[12] Indications of possible codeine dependence include long-term use for

non-cancer pain,[5] use for anxiety and depression,[10] and obtaining codeine from multiple sources, including prescribed, OTC and from the illicit market.[2,13]

With the high level of codeine use in the UK, it is important to consider which factors impact on the production and reduction of codeine related harm. In this article, we adopt the 'risk environment' framework as an approach to investigate social situations and environments which are specific to codeine use. The risk environment can be seen as a space where multiple factors affect individual risk by considering how different types of environments (physical, social, economic and policy) interact at different levels (micro and macro).[14] This framework has previously been applied to explore the risk environments of illicit drug harms, including in relation to HIV transmissions [15] and overdose [16], but not the development of codeine dependence in a pain treatment context.

In the risk environment, micro-environments involve physical risks from substance use and social- and financial circumstances, whereas macro-environments relate to wider structural influences such as laws, health service revenue and spend, and national policies.[14] Codeine-specific examples illustrate the logic applied in this framework: at the micro level, starting patients on prescribed codeine without a clear plan for stopping again may increase the risk of long-term use and subsequently dependence.[6] Conversely, careful and patient-involved dose tapering protect against long-term use. At a macro level environment, regulation restricts access to high doses of codeine in the form of pure formulations to prescription-only with prescribers deciding if they are appropriate to use. Whilst compound codeine formulations (combined with paracetamol or ibuprofen) are available OTC, regulations state that only one packet can be sold at a time and the packet labelling must state: 'Can cause addiction. For three days use only'.

However, studies indicate that transitions still occur from short-term codeine use to treat pain into long-term use and dependence.[10,13,17] Reasons why individuals experience dependence on codeine include: Physical and psychological withdrawal resulting in prolonged use,[1,10,18] poor understanding of the risks of taking codeine,[19] and disengagement from general practitioners (GPs) due to concerns of codeine dependence being recorded in medical notes.[13,20] In a pain treatment setting where opioids are prescribed more often and for longer periods, despite the lack of evidence of long-term efficacy for chronic pain,[10,21-23] investigating the risk environment can offer a better

understanding of the social and political institutions that play a role in reducing codeine harm.

As such, our aim of the article is to explore the risk environment that influence codeine harm from the perspective of people who use or have used codeine recently for pain treatment.

METHODS

Design

This was a qualitative study that used data from semi-structured interviews with participants living in the UK who reported use of codeine in the last 12 months. Inclusion criteria were: Any individual aged 18 or over who used codeine other than as directed or as indicated, whether wilful or unintentional, and whether it resulted in harm or not.[24] The study was approved by the NHS REC Committee London (London Bridge), REC Reference 15/LO/0107.

Recruitment

Participants were recruited amongst respondents to an online survey (N = 14) and from a residential rehabilitation service (N = 2) in order to capture individual experiences across the spectrum from initial misuse to dependence which required structured addiction treatment.[10] A question in an online survey[10] invited respondents to take part in an interview by emailing the researcher or providing contact details. The researcher (AK) contacted and interviewed all eligible participants who did so, resulting in eighteen interviews. A leaflet was provided to clients in the residential rehabilitation programme informing about the study. All eligible clients in the service at that time were invited to take part, resulting in an additional ten interviews conducted by AK.

Sample

Of the 28 participants, one was excluded as codeine was used according to accepted medical practice or guidelines. Another 11 participants were excluded from the analysis as codeine was predominantly sourced as substitution for illicit opioids (heroin). This resulted in a sample of 16 participants who first took codeine for pain treatment, which allows for an investigation of influential factors that have an effect on codeine harm.

Data Collection

Participants were given a Participant Information Sheet informing them of the reasons for doing the study and the involved researchers and institutions (Supplementary File). They were then asked to sign a consent form to ensure their informed consent to the research (Supplementary File). Interviews took place either in the residential rehabilitation service, at a location chosen by the participant or over the phone. The first interview was conducted in May 2015, and the last in April 2016. Interviews lasted from 35 minutes to an hour and 35 minutes. Participants were compensated for their time with a £20 gift voucher. Interviews were conducted using a topic guide, covering: demographic information, initial use of codeine, patterns of codeine use, difficulties managing codeine use, sourcing of codeine, use of other drugs or medicines, and views on codeine availability and regulation. New topics brought up by the participants were pursued during the interviews with follow-up questions. Codeine dependence was measured using the 5-item Severity of Dependence Scale (SDS) during the most recent period of codeine use.[25,26] A score of 5 or above, out of a maximum score of 15, was used to indicate probable psychological dependence on codeine.[9]

Data management and analysis

Interviews were audio-recorded and then transcribed verbatim by a professional service, with any participant identifying information removed from the transcripts. Data analyses were completed by three researchers on the project (AK, EK, SJ) and coded using the qualitative software NVivo (Version 11). A coding framework was developed deductively from the topic guide and from codes that emerged inductively from the data.[27] For this paper, all coded data were analysed using Framework.[28] In the first stage, the coded data were reviewed to describe aspects of each factor which influenced codeine use in the risk environment. Since similar factors were identified as being important to the production and reduction of harm amongst the participants, the analyses were merged and then grouped into more inductive categories. We organised these under four headings: i) patient education on the risk of codeine, ii) the role of prescribing practices related to codeine and non-pharmacological pain treatment, iii) the accessibility and use of OTC codeine and the differences between relationships with GPs and pharmacists, and iv) access to interventions

and treatment for codeine dependence. These categories are used to structure the results below. Emergent factors that appeared to have an impact on the harms of using codeine use that may have transferability to other settings[29] were categorised into micro- and macro-environments (physical, social, economic and policy) and used for mapping the various domains of the risk environment.[14] A risk environment for codeine is presented in Table 1. Analyses are presented with supporting quotes (anonymised using participant numbers) and SDS scores.

Patient and Public Involvement

Patients were not involved in the design and conduct of the study.

RESULTS

Participant characteristics

The sample consisted of 3 men and 13 women, with a mean age of 32.7 years (*SD* = 10.1) and a mean period of codeine use of 9.1 years (*SD* = 7.6) (Table 2). In the sample, 3 participants (18.8%) were unemployed, 3 (18.8%) were students, and 10 (62.5%) were employed. Co-morbid anxiety or depression was self-reported by 4 participants (25%), and 4 (25%) reported concurrent use of codeine and other prescription opioids. Using the SDS, 10 participants (62.5%) scored 5 or more, indicating probable codeine dependence. At the time of interview, 4 participants (25%) sourced codeine from a medical prescription, 3 used OTC codeine (18.8%), whereas 9 used both (56.3%). Only 1 participant reported additionally sourcing codeine from the internet, whilst 3 also used codeine obtained from family or friends. In total, 4 participants (25%) had received intervention and treatment for their codeine use, including addiction treatment, GP led intervention, counselling or from a psychiatrist.

Education of patients on prescribed codeine

Many participants explained that they had not fully understood the potential risks when they first started taking codeine, including its addictive potential. Reflecting on their initial codeine use, many expressed frustrations with their GP and suggested that they wished they had been given more information:

> "If I had had a doctor who possibly just had a little bit more time to say here's what I'm giving you, here's what it is, here's what it does, here's the risks to it. If I had just been a little bit more educated, perhaps it wouldn't have happened [use in excessive doses]." Participant 11, male, dependence score 0.

Participants identified several potential barriers facing health professionals in effectively communicating risks. Specifically, participants felt that the typical 10-minute GP appointment was not enough to fully discuss available options for pain therapy. Of note was that participants who had greater awareness of the risks of codeine, typically from searching for information on the internet, were often more motivated to avoid these risks. However, when participants voiced concerns to their GP, they felt ignored and detached from decisions about their health and care:

> "I kind of had to battle to get my GP to do or say anything about my lower back pain, because they're just like, it's lower back pain, what can you do? They just kind of send you away, say carry on, take the painkillers…It didn't seem like anyone was taking any care in the fact that I could get addicted to this; I didn't bother to go back." Participant 15, female, dependence score 2.

Such encounters with health professionals enhanced the feeling of not being listened to and contributed toward disengagement from health services, distrust in medical opinions, and isolation. In this environment, fewer factors acted to protect against unsupervised, long-term codeine use. Consequently, the lack of effective communication between prescribers and patients, and a resulting poor education of patients on codeine risk, appeared to facilitate the development of codeine dependence for some participants.

Prescribing practices and the use of non-pharmacological pain therapies

The majority of participants who received prescription codeine did so through a repeat prescription. Individuals robustly reported being able to order their repeat prescription with few restrictions on amounts and frequency, which for some resulted in increasing codeine intake:

> "It wasn't just once a month for my periods, like I went through a period of having really bad back ache, so I took it for that. Then for when I twisted my ankle like four or five times, so I'd take it for that. I started running two years ago, now I've got a

knee injury, so I'd take it for that. It was just whatever niggles and pains there were, I'll just pop some tablets because I had them on a repeat prescription and they were basically on tap. That's when it started to really get a grip, because I was taking them for other things on a more or less daily basis." Participant 8, female, dependence score 7.

Within the risk environment, prolonged access to codeine with minimal supervision from a health professional can facilitate use of codeine other than as indicated during the initial consultation, influencing transition to subsequent dependence.

It was striking that participants using codeine from a medical prescription reported being prescribed codeine as a first resort for pain, even when participants were otherwise motivated to try other types of pain treatments:

"I went and said I need another bout of physio for my back because it's starting to hurt again. And they [GP] said: 'oh, you've got to be in constant pain for six weeks'. And I said: 'I've been in constant pain for six weeks already, and it's a recurring problem, so please just refer me.' And the doctor said: 'no, go and take these pain medicines [codeine] and come back in six weeks'. And I said: 'I think it's really dangerous that you're telling me to go away and take a pain med that I know is really highly addictive constantly for six weeks, for a problem that you already know exists.' And they said: 'well, that's just the way it works, I'm sorry." Participant 8, female, dependence score 7.

For some primary care patients in the study, these issues were perceived as a general systematic problem reflecting a lack of treatment resources. They felt like they had been prescribed codeine in order to quickly get rid of them, rather than their GP taking the time to deal with the underlying problem or being referred to specialist services. This did lead to frustration and, in some cases, disengagement from GPs, for example to seek treatment privately:

"…if that's the only advice you're going to give me [take codeine], then I will do what works for me. And I went to an osteopath and that really helped." Participant 15, female, dependence score 2.

In contrast with the negative perceptions of codeine prescribing expressed by some participants, those who were treated with non-opioid pain medicines, physiotherapy and hydrotherapy, indicated that they felt less concerned about continued codeine use:

> "Through the doctor they referred me to a hydrotherapy thing, because I just hadn't had any physiotherapy before for the pain. So, I had six sessions with them and they gave me exercises to do at home. I've been trying to keep up with that, which has I guess lessened the pain. I no longer think that I'm going to get dependent on codeine because it's been that long that I don't wake up in the morning and think I have to take a pill." Participant 12, female, dependence score 5.

Participants' accounts therefore highlighted several structural factors in the risk environment influencing codeine harm: having alternative treatments available beyond codeine resulted in better engagement with health services and greater patient satisfaction, whilst minimising chronic codeine therapy. Conversely, treating pain solely with codeine did result in disengagement from health services.

Differences in relationships with pharmacists and GPs

Implementation of pharmacist intervention to regulate OTC codeine sales is intended to prevent codeine from being used other than as indicated and is one example of a factor which reduces harm. However, participants were able to circumvent restrictions on sale by purchasing from multiple pharmacies over the course of a week or even a day. While one participant had been refused codeine in a pharmacy, most OTC codeine users reported rarely being questioned by pharmacists to find out if codeine was a safe choice, even when they regularly came to the same pharmacy and obtained large amounts of codeine:

> "It's the same staff all the time and I've bought it from there many times. And nobody has ever questioned me at all." Participant 7, female, dependence score 14.

Another important outcome of accessing multiple pharmacies in the local area was that participants never established a strong relationship with a single pharmacist, contrasting this to those who described a better relationship with their GP. Even where participants only accessed one pharmacist, they often perceived this relationship as less important to them and therefore less effective in regulating use and providing risk education, support

and interventions than their GP. This appeared to also be related to the short amount of time participants spent interacting with pharmacists when buying codeine:

> "Whenever I go and speak to pharmacists, I've just never felt particularly comfortable speaking to a pharmacist. I find they're a bit… maybe not judgmental, but I find they're a bit short and like they are very kind of medical. I don't find that there's much interaction. I would just prefer to speak to my GP, because I feel I can trust him and I feel I've got a good relationship." Participant 3, female, dependence score 7.

However, participants also emphasised that pharmacists were far easier and quicker to access than scheduling an appointment with their GP, providing a disincentive to wait and consult with their GP about their codeine use. For participants with a positive and trusting relationship with their GP, a reluctance to be dishonest in their communication with the GP appeared to reduce the risk of dependence occurring; however, this appeared, in some cases, to be undermined by the convenience of OTC availability:

> "I lied to the doctor once, but that killed me doing that. I was really ashamed of myself at the time. I wouldn't have kept doing that [to continue using codeine]. It's only because I had been able to buy it OTC that I've kept on with that addiction. And even now, when I have a bad week and I really need codeine, I'll go and buy it OTC. I wouldn't do that if I had to go to my GP and explain." Participant 7, female, dependence score 14.

Some participants believed that codeine should be restricted to prescription only. In contrast, one participant with a low SDS score suggested that this would not be necessary nor feasible in the context of a wider NHS lack of resources – If everyone self-treating their pain with codeine had to regularly see their GP, primary care would become overwhelmed:

> "I think that it shouldn't be made much more difficult to get hold of because I think most people can go through some acute pain that lasts a couple of days that you might need something like this for, and our NHS is stretched enough without having to go to the GP every time you spring your ankle." Participant 15, female, dependence score 2.

This illustrates the dynamic nature of the risk environment, suggesting that for short term use for acute pain the benefits of OTC codeine outweigh the potential risk of dependence and thus play a significant role in providing access to pain treatment. However, in cases where factors implemented to protect against long-term use fail, such as pharmacist regulation of OTC sales, OTC codeine is associated with a risk of dependence.

Support, intervention and treatment of codeine dependence

Four participants had experience with intervention and treatment for codeine dependence, ranging from GP initiated medicine review to addiction treatment. Still, most participants with SDS scores indicating probable codeine dependence did not report any medical supervision or support; for some this spanned several years during which codeine use became an established part of their daily practice.

It is relevant to note the significance of the influence GPs possessed for some dependent participants in influencing their codeine use. Whilst most participants expressed negative GP experiences which led to disengagement and overreliance on poor information sources, those participants who openly disclosed difficulties in controlling their use of codeine, in the context of a positive and trusting relationship with their GP, were able to receive useful interventions:

> "I thought I'll just tell him [GP] and I'll just see what he says [about difficulties in managing codeine use]. And I ended up getting signed off work for about four weeks...I really trust my GP…When I tell him that I don't want to take codeine, he asks me why, and he kind of tries to look at other options for me, which I really appreciate. I think it was kind of a combination of all those different things, the GP and the counselling, the time off work, everything sort of came together. I think if it had only been one of those things, I don't know how well my recovery would have gone." Participant 3, female, dependence score 7.

Where participants engaged with their GP regarding their codeine use, either due to GP instigated follow-up consultations concerning their use of codeine or to the participant asking for an appointment, their GP was able to help via effective interventions such as tapering codeine and replacing compound products with pure codeine formulations. This

suggests that in an environment where GPs have resources to support the patient, they reduce the likelihood of harm occurring:

> "He wrote me out like a little rota. He said we were going to do it [taper] over a certain period of time. And I had to sign, like he made like a contract for me to sign, and he signed it as well, to say that he was going to help me, and he was going to support me. And he was really understanding and not judgmental at all, it was fabulous. He said he was going to prescribe me a certain amount of just codeine, so not the paracetamol, just codeine on its own." Participant 8, female, dependence score 7.

When two participants, who had attended addiction treatment, were asked why they had started treatment they generally described lengthy and complicated pathways which did require significant level of self-motivation. One male participant who was currently a client in a residential rehabilitation programme described the social, economic and physical circumstances that motivated him to eventually seek treatment and detoxification for codeine dependence. These included transitions from single to multiple codeine containing medicine use (OTC and prescribed), breakdown in family relationships, dropping out of university, social isolation, being fired from work and physical adverse effects from high doses of compounded ibuprofen:

> "I think when I had the stomach ulcer, I started realizing then that this will actually kill me. I cut down the Nurofen Plus [codeine/ibuprofen] because it was what kept me going really, but I couldn't put it down…I just couldn't stop. I hadn't got a job, I'd dropped out of uni. Just living at home doing nothing and it kind of dawned on me you know, I've really got a problem. At first, I went to the local drug services, and they said that they don't deal with codeine so there wasn't any help there, and someone gave the number for there [residential rehabilitation service], a family friend or something…It was quite quick, about after two weeks [starting in treatment]." Participant 1, male, dependence score 15.

For some of the participants, disengagement from medical professionals, and the placing of responsibility on the patient to self-manage their dependence, created situations where

participants reported that they instead used the internet to find out more information about codeine, pain treatments, and advice on how to manage the use of codeine.

> "When I was first diagnosed with depression and anxiety, when I was just being pushed and pulled from different doctors, different psychiatrists, I looked to the internet to do my own research and just understand what these medicines were [codeine]. I didn't know what I was taking, and I didn't know what the risks of abusing it was, so I felt that I should really start understanding what I'm being prescribed." Participant 11, male, dependence score 0.

Support structures in form of family and friends also played an important role to some participants as a source of information about codeine. For this participant, an encounter with a friend facilitated personal reflection as to her own use of codeine:

> "One of my best friends was going for a job interview and I said to her: 'do you want to take a codeine like an hour before you leave the house? You'll feel so very relaxed.' And although she took the tablets, she said to me: 'I don't feel comfortable with this and I don't think that I should' A few months later she asked me if I used to take them for reasons other than pain, and I said to her no, but in my heart, I knew that I did. I asked her why. She said: 'because it's a very addictive drug…it's something that can basically change the chemicals in your brain and you'll be addicted forever.' She suggested a few articles for me to read, which I did, and then I was very worried because then I learned that codeine was connected to morphine." Participant 10, female, dependence score 2.

Such relationships played an important role for participants to gain more confidence in their ability to manage their use of codeine, especially for those using codeine other than as indicated, but not experiencing codeine dependence. However, over-reliance on potentially inaccurate online sources and advice from friends and family may also delay or prevent patients from seeking support from health professionals until they experience severe dependence that is much more complicated to treat. As such, the social environment has the capacity to both produce and reduce codeine-related harm.

DISCUSSION

This qualitative study explored codeine use from the perspective of people who use or have used codeine to treat pain in order to unpack the key factors of the risk environment. These findings add to existing literature that suggest that some patients who use codeine for treatment of pain become dependent as a result of environmental factors.[10,20] We identified a number of environmental factors that reduced the risk of dependence: medicine review of repeat codeine prescribing, interventions in primary care (such as tapering), social support (friends and online), and access to addiction treatment (Table 1). We also identified several micro- and macro- environmental factors capable of producing harm, especially unsupervised, long-term codeine prescribing and breakdown in structures to stop sales of OTC codeine for use other than as indicated (Table 1).

Amongst micro-level barriers, participants spoke of perceived limitations of pain therapy in primary care resulting in overreliance on codeine. Codeine prescribing often occurred in the context of poor utilisation of nonsteroidal anti-inflammatory drugs, graduated exercise, and cognitive behavioural therapy, which may achieve similar levels of improvement in pain[30,31] without risk of dependence.[32] Lack of psychological, social community and pain specialist resources and the services of physiotherapists, occupational therapists and social workers thus appeared to hinder a holistic approach in pain therapy that incorporates prevention, active treatment and rehabilitation. Overcoming these impediments most likely require amending the economic environment that regulates the availability of these resources.

A policy environment dictates procedures for OTC codeine sale in the UK to prevent use other than as indicated.[33] However, lack of trust in the relationship between pharmacists and participants using OTC codeine, confirmed concerns previously raised about OTC codeine sale, including inabilities to effectively monitor OTC codeine consumption and intervene to halt escalating use.[34] OTC medicines play an important role given the increasing acceptance of self-care to promote patient empowerment and reduce the pressure on local GP practices. However, drawing on knowledge of engagement between pharmacists and patients at the point of an OTC codeine sale is important to realign OTC sales of codeine with environmental factors to reduce harm.

Comprehensive assessment of codeine dependence, support delivered in primary care, and access to addiction treatment is required and should be available for those who need it.[5]

Although some participants viewed the uptake of primary care intervention and addiction treatment positively, they also found them difficult to access. Where engagement and resources permitted, GPs proved to be an effective source of monitoring and reducing harm when concerns had been clearly communicated. Increased awareness of the potential for codeine dependence amongst GPs is likely to improve treatment of codeine dependence further.[19] Easy-to-access addiction services capable of handling individuals with codeine as the primary drug may also be important here.

Implications for the risk environment

Considering the negative consequences of prolonged opioid use for chronic pain, which include paralysis of the endogenous opioid system, depression and ineffective pain control,[23] alternative management of patients with chronic codeine use is warranted.[22,35] The findings of this study suggest that GPs are well-placed to communicate risk, monitor and, if necessary, intervene in codeine use. However, their ability to do so may be limited by a lack of resources and subsequent patient disengagement. Training and funding must be provided, including more time to spend with patients, effective ways to monitor codeine prescriptions, access to other types of treatments, and ability to refer to secondary services.

Although pharmacists are empowered by current UK regulations to restrict individual access to OTC codeine by refusing sales and limiting the amounts sold, this study found that having codeine available OTC may produce harm due to limited effectiveness of these interventions. With Australia recently joining countries like the US, Germany and Japan in restricting codeine to prescription-only,[36] it is necessary to review UK OTC regulation to reduce the risk of excessive use of codeine. There is also a need to explore how to improve patient/pharmacist communication.

Using codeine only for its intended indications of mild to moderate pain on a short-term basis and only if they help would most likely go a long way in preventing dependence. However, this requires effective and acceptable alternatives to manage pain to ensure that pain patients receive the care they need. The goal is to create a system where patients understand their options for pain therapy and the risks of taking codeine. Finally, ending codeine prescriptions in cases of dependence should not be done abruptly, and only under

close monitoring to prevent relapse or use of other opioids (sourced online or from the illicit market).

Strengths and limitations

A strength of this study is that it helps understand individual experiences in their broader context of the risk environment surrounding codeine use in the UK, an area previously unexplored in the literature. Specifically, this study highlights how different environmental factors intended to facilitate safe use of codeine can potentially act to increase risk without proper utilisation and sufficient funding. This is important in implementing change to ensure that benefits of codeine use in pain therapy outweighs harm. Most obviously, a limitation of the study is the small sample size. Findings cannot be generalised to all regions of the UK. As such, a reduction or production of harm related to codeine containing medicines will depend on many factors, such as the nature and funding of local primary care. The majority of participants in this study were female, whereas two previous qualitative studies recruited a more evenly distributed sample.[13,20] The advertisement for the online survey was designed to attract both men and women, however more women responded (67%)[10] creating a multiplying effect when recruiting for interviews. Although the gender distribution could potentially introduce bias, this is consistent with previous research where opioid utilisation in GP practices in the UK increased with greater proportion of female registrants.[37] As such, the sample in the online survey[10] and in this interview study may reflect the type of individual most likely to receive treatment with opioids. Future qualitative studies should explore the differences between pain, opioid use and dependence in men and women. The inclusion criteria enabled us to study factors contributing to codeine dependence, whilst limiting our ability to identify protective factors in the environment, which may have stopped dependence from occurring. Had we recruited from primary care instead of from an online survey, our findings may have been different in that we had recruited more patients with experience of factors that stopped codeine use other than as indicated. The risk environment approach has a limitation in its ability to understand codeine-related risks. This is because this approach focuses on a particular part of the social world and may not capture individual circumstances which inform codeine dependence, such as co-morbidities and specific types of pain. Furthermore, overlaps between different environments (physical, social, economic and policy) are likely when mapping the risk

environment. While this is useful for understanding the complicated nature of how drug harms are generated, it can also make it difficult to determine how to implement effective change.

CONCLUSION

This study identifies environments that produce and reduce harm related to codeine containing medicines among participants with recent use of codeine. The study highlights micro- and macro- environments capable of producing harm, particularly in regard to long-term prescribing, unless realigned with current risks of codeine use and provided with adequate funding. The economic environment is often crucial in reducing drug harm and facilitating effective treatment of dependence. We echo calls for funding to facilitate a more holistic approach to pain therapy to reduce prescribing to patients who may not benefit from opioids.[22,35] The study found evidence to support regular review of patients prescribed codeine. Alternative non-pharmacological therapies may also go a long way to reduce codeine dependence.

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Author contributions

PD and AK designed and planned the study. Ak wrote the research protocol. AK recruited and collected the data. EK performed the literature research and undertook data analysis with AK and SJ. EK and AK contributed to theoretical implications of study analysis. EK and AK led on writing the paper with input from CD, SJ and PD. All authors had access to the data used and provided final approval of the manuscript to be published.

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Disclaimer

The views expressed are those of the authors and not necessarily those of the NIHR, SLaM NHS Foundation Trust and the BRC.

Competing Interests

None.

Patient consent

Participants provided written consent. Personal details were removed from the collected data to ensure anonymity.

Ethics Approval

This qualitative study was imbedded in the CODEMISUSED project approved by King's College London, Psychiatry, Nursing & Midwifery Research Ethics Sub-Committee and the NRES Committee London - London Bridge.

Data sharing statement

No additional data are available.

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TABLES

Table 1. The codeine risk environment in the context of pain treatment: examples of environments producing and reducing harm

	Micro-environment		Macro-environment	
	Risk	*Intervention*	*Risk*	*Intervention*
Physical	Prolonged codeine use Excessive codeine use Codeine dependence	Increased education for peers on diversion of medications	Diversion of codeine containing medicines (obtaining codeine from friends and family)	Review of regulation on prescription and monitoring
Social	Ineffective risk communication between GPs and patients to inform of codeine risks Disengagement from healthcare providers Limited engagement between patient and pharmacist Overreliance on potentially inaccurate internet and peer information	Increased information provision on codeine risk and alternative pain therapies in primary care GPs receptive to reviewing patient concerns Improving patient attitudes towards GP consultations and pain management. Improving healthcare provider attitudes to pain management and codeine misuse. Clinician-led assertive engagement strategies in primary care Provision of social support via peer group and online Explore pharmacist-patient communication strategies	Codeine's dominant role in contemporary pain treatment Stigmatisation of codeine dependence Anonymised information sourcing on the internet from unreliable sources	Improved access to alternative non-pharmacological pain management therapies Increased awareness and opportunity for early intervention for codeine dependence across community, employment and health services

		Effective strategies targeting peer education and awareness of codeine misuse		
Economic			Lack of resources available for non-pharmacological pain treatments in primary care (e.g. physical therapy)	Funding and reform for NHS primary care and local drug addiction treatment services
Policy	Low utilisation of medicine review of repeat prescription of codeine Ineffective implementation of pharmacy OTC restrictions Ease of circumventing pharmacy restrictions	Timely prescription monitoring and review of concerns GP instigated follow up consultations and interventions Assertive and active review from primary care Continued provision of effective interventions in primary care such as tapering and pure codeine replacement Training of pharmacy staff to ensure consistent implementation of pharmacy OTC risk reduction policy	Nature of GP appointments (long waiting times, short duration) Ineffective laws and regulation governing OTC sales of codeine containing medicines	More time to spend with codeine dependent patients. Increased availability and convenience in securing appointment and access to screening and brief intervention Review of legal and regulatory governance surrounding OTC codeine

Factors may overlap physical, social, economic and policy environments and change place between environments over time.

Table 2. Participant characteristics and codeine use

Participant	Gender (F/M)	Initial type of pain	Subsequent reasons for codeine use	Time between first and last use	Source of obtaining codeine	Severity of Dependence Scale (SDS) score	Intervention and treatment
1	M	Headache	To reduce stress	7 years	Prescription, OTC, obtained from family	15*	Residential rehabilitation programme
2	F	Dysentery	Recreational purposes, to reduce stress	1 year	Prescription, OTC	4	None
3	F	Pain after an operation	To sleep, to reduce stress, for depression	1 month	Prescription	7*	GP support, counselling
4	F	Period pain		15 years	Prescription	12*	GP support
5	F	Injury	To sleep, recreational purposes	15 years	Prescription, OTC	8*	None
6	F	Deep vein thrombosis from heroin use	Used when heroin unavailable	8 years	Prescription, OTC	11*	Previously in residential rehabilitation. At time of interview none
7	F	Pain after an operation	For anxiety	10 years	Prescription, OTC	14*	None
8	F	Back pain		20 years	Prescription	7*	None

9	F	Head injury	To reduce stress, to sleep	2 years	Prescription, OTC	10*	None
10	F	Migraines	To reduce stress, to sleep	25 years	Prescription	2	None
11	M	Migraines and back pain	For anxiety, for depression	14 years	Prescription, OTC, internet	0	Private psychiatry, private pain specialist
12	F	Arthritis		2 years	Prescription, OTC	5*	None
13	M	Headache, later osteoarthritis	For anxiety, recreational purposes	15 years	Prescription, OTC, obtained from family	1	None
14	F	Arthritis		3 years	OTC	6*	None
15	F	Migraines, back pain, irritable bowel syndrome	To sleep	8 years	OTC, obtained from a friend	2	None
16	F	Ulcers	Sleep	4 months	OTC	0	None

* Scores of 5 and above indicate probable psychological dependence upon codeine.

INFORMATION SHEET FOR PARTICIPANTS

REC Reference Number: PNM/14/15-110

Version: 2 - 20 April 2015

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of study

Understanding codeine use: exploring the experiences and characteristics of codeine users

Invitation Paragraph

You are being invited to take part in a research study. Before you decide we would like to explain why the research is being done and what it involves. Please take time to read the following information. Ask us if there is anything that is not clear or if you have any other questions. Take time to decide if you want to take part or not.

What is the purpose of the study?

This interview study is being conducted by King's College London as part of an EU funded project about codeine misuse, related health harms, characteristics of users, and dependence. There is limited evidence available on the factors associated with and outcomes of use. The aim of the interview study is to collect qualitative data to explore codeine users' choices and decision-making when using codeine (prescribed or otherwise), codeine use patterns, favoured route of administration, recreational use and tampering with codeine pharmaceuticals, adverse health consequences (including codeine related problems and dependence), characteristics of dependent and non-dependent codeine users, sourcing of codeine, use of other drugs and medication, opinions around medical prescribing, and pharmacy dispensing and internet based retail.

During the interview you will be asked questions about which codeine products you use, how and why. You will be asked about from where you get your codeine and any problems you have experienced as a result of using codeine. We will also ask if you have used any other drugs or any other medicines. We will ask how you first got introduced to

using codeine. This will help to increase the evidence base, which will be of potential benefit to people who decide to use codeine and in the development of public health responses.

If you would like to read more about our research about codeine use, then go to: www.codemisused.org

Do I have to take part?

No. It is up to you to decide whether or not you want to take part. If you do we will ask that you give your consent to take part. You are still free to withdraw up until the point of publication of results without giving a reason. If you wish to do so you must inform the researcher in writing. A decision to withdraw will not affect your rights to any health care you receive.

What will happen to me if I take part?

If you decide to take part we will ask you to take part in an interview that will last about 1 hour and that will be audio recorded. In this interview we will ask you questions about your use of codeine, what products you use, and your experiences with any problems you may have encountered. When taking part in an interview you will receive a £20 gift voucher in reward of your time.

What are the possible risks of taking part?

We understand that answering questions about substance use and dependence can be stressful. We know from experience that talking about these issues as part of an interview can sometimes make participants feel worse. Should you become distressed during the interview, the interview will terminate immediately. We will advice you to seek help from GP.

Will my taking part be kept confidential?

Yes. All the information that we collect will be kept strictly confidential. Any identifying information about you will not be disclosed to anyone outside the research team. You do not have to give us your full name or date of birth.

Once the audio recording of your interview has been transcribed, the audio recording is deleted. Any details that might be used to identify who you are will be erased from the transcription of your interview. All transcriptions are safely stored at King's College London to make sure that no one other than the research team can look at it. We do this by storing it on a computer that can only be accessed with a password.

Researchers work under the same rules of confidentiality as doctors and nurses, which can only be broken, without your consent, in very exceptional circumstances. **Usually this is if the researcher sees or is told something which raises serious concern for your personal safety.**

How is the project being funded?

The research is funded by the European Commission — 7th Framework Programme (reference number: FP7-PEOPLE-2013-IAPP-611736) and is sponsored by King's College London.

What will happen to the results of the study?

The results of the study will be published in reports, articles and conference presentations.

Who should I contact for further information?

Ask us if there is anything that is not clear or if you would like more information. Please contact the researcher using the following contact details:

Dr Andreas Kimergård, Addictions Department, King's College London, T: 020 7848 0446, @: Andreas.Kimergard@kcl.ac.uk

What if I have further questions, or if something goes wrong?

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you can contact King's College London using the details below for further advice and information: The Chair, PNM Research Ethics Subcommittee (RESC), rec@kcl.ac.uk

What else do I need to know?

You must be 18 years or older to take part in this study. If you are interested in receiving the final results of this study please get in contact with Andreas Kimergård. However, remember that data from studies such as these often take many months to prepare for publication.

Thank you for reading this information sheet and for considering taking part in this research.

REC ref.: 15/LO/0107
Short Title: Codeine Interview Study
Document name: Annex D: Consent form A
Version: 2
Date: 24/02/15

Consent form

Codeine interview study: benefits of codeine use, side effects and use of treatment services

Researcher: Andreas Kimergård, King's College London

Email: Andreas.Kimergard@kcl.ac.uk

Please tick box

☐ I confirm that I have read and understand the information provided for this study. I have had the opportunity to consider the information and ask questions.

☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care being affected.

☐ I understand that personal information collected during the study will be anonymised and remain confidential.

☐ I understand that I can choose not to answer questions which I feel uncomfortable about answering.

☐ I agree to the digital recording of this interview.

☐ I agree that quotes from my interview may be reported in published documents but that this will be anonymous and no-one will be able to identify me from this.

☐ I agree to take part in the study.

Name of participant:

Date:

Signature:

Name of researcher:

Date:

Signature:

Note: This form must be completed in 2 copies, one for the participant and one for the researcher.

From pain treatment to opioid dependence: A qualitative study of environmental influence on codeine use

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Inter viewer/facilitator	Which author/s conducted the inter view or focus group?	*Page 6*
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	*PhD* *Not reported in manuscript*
3. Occupation	What was their occupation at the time of the study?	*Page 1*
4. Gender	Was the researcher male or female?	*Page 1*
5. Experience and training	What experience or training did the researcher have?	*Page 1*
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	*Page 6-7*
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	*Page 6-7* *Supplementary File*
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	*Page 6-7* *Supplementary File*

Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	*Page 7 - 8*
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	*Page 6*
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	*Page 6*
12. Sample size	How many participants were in the study?	*Page 8*
13. Non-participation	How many people refused to participate or dropped out? Reasons?	*None* *Not reported* *Page 6 - 7*
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	*Page 7*
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	*No* *Not reported* *Page 7*
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	*Page 8*
Data collection		

17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	*Page 7*
18. Repeat interviews	Were repeat inter views carried out? If yes, how many?	*No* *Page 6 - 7*
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	*Page 7*
20. Field notes	Were field notes made during and/or after the inter view or focus group?	*No* *Page 6 - 7*
21. Duration	What was the duration of the inter views or focus group?	*Page 7*
22. Data saturation	Was data saturation discussed?	*The applied methodology did not rely on data saturation* *Not reported*
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	*No* *Not reported*
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	*Page 7, 18*
25. Description of the coding tree	Did authors provide a description of the coding tree?	*Page 7 - 8*
26. Derivation of themes	Were themes identified in advance or derived from the data?	*Page 7 - 8*
27. Software	What software, if applicable, was used to manage the data?	*Page 7*
28. Participant checking	Did participants provide feedback on the findings?	*No* *Not reported*
Reporting		

29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	*Page 8 - 15*
30. Data and findings consistent	Was there consistency between the data presented and the findings?	*Page 8 - 15*
31. Clarity of major themes	Were major themes clearly presented in the findings?	*Page 8 - 15*
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	*Page 8 - 15*