PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	'I Can't be an Addict. I am.' Over-the-Counter Medicine Addiction – a Qualitative Study
AUTHORS	Cooper, Richard

VERSION 1 - REVIEW

REVIEWER	Mackridge, Adam Liverpool John Moores University, Pharmacy & Biomolecular Science
REVIEW RETURNED	02-Apr-2013

THE STUDY	The recruitment strategy used is likely to bias towards codeine dependence owing to one of the sites used being clearly set up for individuals with addiction to codeine products and may, as a consequence, underrepresent those with issues arising from other substances. This does not detract from the value of the study and reflects one of the key difficulties in conducting research to understand this complex problem and this study very usefully explores a key group of people affected by OTC addiction. However, it is important that this possible bias is recognised more clearly in the limitations and appropriate caveats are included in discussion of the implications of the findings. Also, not all people with access to the internet will engage with web-forums and the recruitment strategy would also have been biased against such individuals - this should be acknowledged.
GENERAL COMMENTS	Thank you for allowing me to review this well written and interesting article on the personal perspectives of people affected by over-the-counter medicine addiction. This study usefully explores an under-researched issue and will be useful for a wide range of academic and practitioner audiences. Aside from my comments above relating to clearer statement of limitations, I have few comments regarding the text and these are listed below: 1) Page 1, Line 10, the authors states that OTC pharmacy medicines are considered relatively safe - please clarify this point - considered safe by whom? Patients or professionals? Also, I think the word 'pharmacy' adds confusion in this sentence, particularly for non-UK readers. Whilst the paper discusses OTC medicines that are generally only available from Pharmacies in the UK, Over the Counter medicines is usually taken to mean those that can be purchased without a prescription (from a pharmacy or other outlet). Pharmacy only medicines are defined in UK law as those that can be purchased under the supervision of a pharmacist from registered pharmacy premises. 2) On Page 6, Line 23, the author reports that challenge whilst making purchases may have been linked to recognition of a problem. This may warrant further explanation - if possible from the

	available data - since it might represent an important intervention that could help to address this issue. 3) Could the author expand on what is meant by 'relevant' in relation to the involvement of pharmacists in treatment (Page 9, line 41) - were they simply not mentioned, or were they considered by participants to have no role in treatment or support for OTC addicted individuals? 4) I am unfamiliar with the term 'qua medicines' use on page 10, line29 - could this be reworded? 5) Page 11, Line 13 - there appears to be a reference to a participant name. If this is the case, it should be removed.

REVIEWER	Malcolm Dobbin Senior Medical Advisor (Alcohol and Drugs) Mental Health, Drugs and Regions Division Department of Health Victoria, Australia
REVIEW RETURNED	08-Apr-2013

THE STUDY	This is to supply details about the 'yes' response to the last question about the study. The author could also cite another relevant article that may have been published subsequent to his literature review: Nielsen S, Cameron J, Lee N. Characteristics of a nontreatment-seeking sample of over-the-counter codeine users: implications for intervention and prevention. J Opioid Manag 2011;7:363-70
GENERAL COMMENTS	Was your study conducted subsequent to the labelling changes in the UK, when the prominant warning "Can cause addiction" was included on the front of packs? I suggest that you could include mention of this, and either the response of those interviewed if it was subsequent to your interviews, or whether it may have helped to steer people into treatment if it was not. Do you think it would be worth discussing whether some of these survey participants might have been suited to pharmacotherapy for opioid dependence (methadone or buprenorphine)? Many of the subjects of our study either sought, or were commenced on pharmacotherapy subsequent to experiencing a serious NSAID morbidity such as perforated or haemorrhaging peptic ulcers (Frei M et al, 2010). You describe a number of statements that suggest interviewees describe many of the criteria of the DSM IV criteria for dependence. It might be worthwhile to pull these together at the end of the results, or in the discussion, to draw a conclusion about how these descriptions by subjects suggest or confirm a diagnosis of addiction. There aren't many good descriptions about the behaviour and experience of individuals who've become addicted to OTC codeine-ibuprofen analgesics. Also, it might be worthwhile to summarise those insights from the interviews to inform development of scripted questions for pharmacists interacting with customers requesting OTC codeine analgesics that might best serve to assist the misuser at risk to identify that they may have a problem, and feel able to discuss this

	with the pharmacist. Nielsen et al 2011 identified that those using higher than recommended doses or over a longer period than recommended, were expereiencing psychological distrees, and experiencing chronic pain, were associated with dependence.

VERSION 1 – AUTHOR RESPONSE

Reviewer – AM
Comment #1: The recruitment strategy used is likely to bias towards codeine dependence owing to one of the sites used being clearly set up for individuals with addiction to codeine products and may, as a consequence, underrepresent those with issues arising from other substances. This does not detract from the value of the study and reflects one of the key difficulties in conducting research to understand this complex problem and this study very usefully explores a key group of people affected by OTC addiction.
However, it is important that this possible bias is recognised more clearly in the limitations and appropriate caveats are included in discussion of the implications of the findings. Also, not all people with access to the internet will engage with web-forums and the recruitment strategy would also have been biased against such individuals - this should be acknowledged.

Response: I agree, this is a possible limitation and I have revised the limitations section further to include the following:

“However, related study limitations are that the sample reflected only those individuals who had internet access and already recognised they had a problem and that those who had not engaged with these support groups were not represented. In addition, the dominance of codeine amongst participants may be related to one of the internet support groups targeting only those affected by opiates.”

Comment #2: Page 1, Line 10, the authors states that OTC pharmacy medicines are considered relatively safe - please clarify this point - considered safe by whom? Patients or professionals This was ambiguous and a helpful comment, and I have now added the phrase “by the public” to clarify and used this word instead of patients, as both the papers I cite draw on public samples and not those from patients. There are other papers I could cite to support this view, but felt 2 was enough.
Also, I think the word 'pharmacy' adds confusion in this sentence, particularly for non-UK readers. Whilst the paper discusses OTC medicines that are generally only available from Pharmacies in the UK, Over the Counter medicines is usually taken to mean those that can be purchased without a prescription (from a pharmacy or other outlet). Pharmacy only medicines are defined in UK law as those that can be purchased under the supervision of a pharmacist from registered pharmacy premises.

Response: I agree that this is a possible source of confusion in the literature and in relation to medicines supply internationally. I wanted to retain mention of the primary focus on the physical pharmacy premises but to capture the wider range have added the following text:
“ Such non-prescription, or over-the-counter (OTC) medicines as they are also known, are typically those purchased from non-medical outlets such as pharmacies and increasingly the internet [3] and have enabled individuals to be active participants in their own health.”
I suppose it is debatable if the metonymic ‘counter’ in over-the-counter’ is only that in a pharmacy or a convenience store or supermarket and whilst traditionally capturing pharmacy I suspect it does cover all!

Comment #3: On Page 6, Line 23, the author reports that challenge whilst making purchases may have been linked to recognition of a problem. This may warrant further explanation - if possible from

the available data - since it might represent an important intervention that could help to address this issue.

Response: I agree that adding additional evidence would be helpful and have added two relevant quotes from patients, that capture how being challenged might prompt reflection although I still wanted to capture the view that, overall, this study suggests such challenges were not percieved effective overall, and in one further quote, it merely made him more selective! The quotes are:
"I've only ever been challenged once and it was quite a confrontational challenge and…but that was back in the days when I was taking eight a day and […] that one experience kind of altered how I did things. I started pharmacy shopping, I started varying where I went and I started to notice you know the shop workers' routines. P18
However, several participants considered these challenges to have influenced their attempts to seek help:
I knew it would come sometime but you know to actually face it, that she had actually confronted me with it and that was really a wakeup call for me. P19"

I also add further discussion points about questions to ask, but indicate the enduring tension in this (see comments below).

Comment #4: Could the author expand on what is meant by 'relevant' in relation to the involvement of pharmacists in treatment (Page 9, line 41) - were they simply not mentioned, or were they considered by participants to have no role in treatment or support for OTC addicted individuals?

Response: Apologies, this has now been re-worded to confirm that it was the absence of any reference to pharmacists in relation to participants' discussion of treatment or support, rather than an active mentioning of them. However, I still consider this omission quite telling. New wording is as follows:
"However, it is also of note that pharmacists were not referred to by participants at allin relation to treatment or support in the present study, and this not only reflects previous omissions in the literature [5] but also concerns around difficulties in implementing harm-reduction strategies in this setting [7, 11, 22]."

Comment #5: I am unfamiliar with the term 'qua medicines' use on page 10, line29 - could this be reworded?

Response: This has now been less pretentiously worded as : "Treatment options involving specific medicines…" Sorry!

Comment #6: Page 11, Line 13 - there appears to be a reference to a participant name. If this is the case, it should be removed.

Response: Michelle was a pseudonym used so there were no threats to anonymity but this has been changed to the nomenclature of the paper, and words 'as one participant (P25)...'

Reviewer MD

Comment #1:The author could also cite another relevant article that may have been published subsequent to his literature review: Nielsen S, Cameron J, Lee N. Characteristics of a nontreatment-seeking sample of over-the-counter codeine users: implications for intervention and prevention. J Opioid Manag 2011;7:363-70

Response: Thank you, this paper is very helpful and has now been added and cited in the introduction

and discussion part of the paper. Thank you for bringing it to my attention. Revised citation and wording, for example, as follows:
"This also applies to pharmacists and particularly since research suggests that they may experience uncertainty about how to support those affected [16] coupled with concerns around implementing harm-reduction strategies in this setting [11]."

Comment #2: Was your study conducted subsequent to the labelling changes in the UK, when the prominant warning "Can cause addiction" was included on the front of packs? I suggest that you could include mention of this, and either the response of those interviewed if it was subsequent to your interviews, or whether it may have helped to steer people into treatment if it was not.

Response: The study was undertaken around the time of this change and participants were asked for both their experiences and views. However, since the aim of the study was to capture past and current OTC problems, it was inherent in the design of the study that some would have experienced purchases after this and some before. Revised wording in the methods is as follows:
“[...] and since recruitment occurred around the time addiction warnings were introduced in the UK, participants were asked for either experiences or views of this change. [10]”
Also in the results, the section originally referring to this has been changed as follows:
This view was held by those interviewed both before and after the addiction warnings were introduced and for those still taking OTC medicines at the time of the study, there was a lack of awareness, which one participant (P5) summed up as: ‘I’ve not noticed, but then again I’m not looking’. There was little awareness of regulatory changes relating to pack sizes in the UK from those interviewed after the changes, but a view that, like warnings, these may have some benefit, but only to those who did not already have a problem

Comment #3: Do you think it would be worth discussing whether some of these survey participants might have been suited to pharmacotherapy for opioid dependence (methadone or buprenorphine)? Many of the subjects of our study either sought, or were commenced on pharmacotherapy subsequent to experiencing a serious NSAID morbidity such as perforated or haemorrhaging peptic ulcers (Frei M et al, 2010).

Response: Yes, and the original paper did actually include reference to this in the section on treatment but this has been further clarified as follows:

“However, the accounts provided from those consuming more significant amounts of opiates suggested that such services, and the use of buprenorphine and methadone, often led to positive outcomes – either on maintenance doses or opiate free - even if concerns were initially apparent about such treatments being inappropriate and suited only for illicit substance misusers”

Comment #4 You describe a number of statements that suggest interviewees describe many of the criteria of the DSM IV criteria for dependence. It might be worthwhile to pull these together at the end of the results, or in the discussion, to draw a conclusion about how these descriptions by subjects suggest or confirm a diagnosis of addiction. There aren't many good descriptions about the behaviour and experience of individuals who've become addicted to OTC codeine-ibuprofen analgesics.

Response: This is an aspect of the study and paper that I have considered on many occasions. I decided not to produce a list and also not to link to the overtly clinical literature (such as DSM-IV) as my study specifically sought self-reported abuse/addiction status and so I felt it would be inappropriate to then discuss if my participants did or did not match this in a comprehensive way. However, I did explore this concern in the more general context of the levels of medicines taken and in the more qualitative aspects of experiences expressed. I feel that a clinical reader would be able to identify the relevant aspects and make their own judgements and comparisons to a clinical criteria. I

hope this reasoning is acceptable but would be happy to discuss further.

Comment #5: Also, it might be worthwhile to summarise those insights from the interviews to inform development of scripted questions for pharmacists interacting with customers requesting OTC codeine analgesics that might best serve to assist the misuser at risk to identify that they may have a problem, and feel able to discuss this with the pharmacist. Nielsen et al 2011 identified that those using higher than recommended doses or over a longer period than recommended, were expereiencing psychological distrees, and experiencing chronic pain, were associated with dependence.
Response: Thank you for this helpful suggstion, and in the discussion several new passages are included to reflect this, and as Adam the other reviewer suggested too. However, I did also want to reiterate the clear finding that participants did not think of pharmacist in relation to support and this remains a concern, and I indicate where other studies refer to this too.
“This study offers suggestions about possible questions for health-care professionals such as pharmacists and prescribers, particularly in relation to those experiencing more severe self-reported problems. For example, asking if individuals had ever taken more than the recommended maximum dose, if their medicine use had affected their work or social life, or if they felt they had lost control over their medicined use have all emerged from this study. However, it is also of note that pharmacists were not referred to by participants in relation to treatment or support in the present study, and this not only reflects previous omissions in the literature [5] but also concerns around difficulties in implementing harm-reduction strategies in this setting [7, 11, 22].