Title: **The extent that health professionals suspect and address addiction to medicines in primary care: findings from a survey in Northwest England**

Corresponding Author Information

Geoff Bates, MSc. Centre for Public Health, Liverpool John Moores University.
Tel: +44 (0)151 231 4442; Email: g.bates@ljmu.ac.uk.
Address: Centre for Public Health, Faculty of Education, Health and Community, Liverpool John Moores University, Henry Cotton Campus, 15-21 Truman Street, Liverpool, L3 2ET.

Other Author Information:

Madeleine Cochrane, MPH. Centre for Public Health, Liverpool John Moores University.
Adam John Mackridge, PhD. School of Pharmacy and Biomolecular Science, Liverpool John Moores University.

Funding information

This study was funded by The Cheshire and Merseyside Public Health Network who provided support with project development and participant recruitment through the Public Health Directorate at St Helens Council.

Conflict of interest

The authors confirm that they have no conflicts of interest to declare.

Keywords

Substance related disorders; Prescription drug misuse; Nonprescription Drugs; General Practitioners; Pharmacists

Introduction

Medicines, specifically analgesics, are the most commonly misused substances in the US after cannabis and alcohol (1). In the UK, concern around misuse of analgesics has been growing (2), in part owing to a steady rise in the number of deaths related to tramadol (3). Similar concerns exist for other medicines, with an estimated 1.5 million people addicted to benzodiazepines (4) and rising deaths associated with these medicines (3). A series of reviews assert that those with an addiction to medicines (ATM) are gravely underrepresented at UK addiction treatment services (2, 5, 6), although prevalence data are limited. It is likely that a large number of people in the UK with ATM are not receiving the support they need and may be at risk from a range of health concerns. It is suggested that those affected are a diverse group, including those with a history of illicit substance use disorders, psychiatric conditions or a poor knowledge regarding the harms of non-therapeutic use (2, 7).

To increase understanding of the extent and nature of the problem, this study investigates the experiences of health professionals in primary care who are likely to come into contact with people with ATM. This study aimed to explore the experiences of health professionals within General Practice (GP) and community pharmacy settings with respect to patients with ATM.

Methods

An online survey was developed from previous work (8, 9) and disseminated to health professionals in primary care in Northwest England. Eight of nine Local Authorities approached agreed to support snowball recruitment and disseminate the survey to GPs and pharmacies, which was initiated in May 2015. A maximum of one health professional from each site participated in the research. The survey examined the frequency health professionals encounter individuals with ATM and their confidence

and experiences with tackling these addictions. As this was an exploratory study, no statistical analysis was undertaken. The study was approved by the institutional Research Ethics Committee.

Results

Seventy-six health professionals completed the survey, including 35 general practitioners, 19 pharmacists, three nurse prescribers, two pharmacy technicians and one pharmacy dispenser (role missing for 16 participants).

Two thirds of participants (66%, 48/73) reported suspecting a patient (including both patients and customers in the GP and pharmacy setting) has or is developing ATM on a weekly or more frequent basis, and a minority (12%, 9/75) stated that patients admit ATM with the same frequency. Over three quarters of participants reported feeling 'very' or 'fairly' confident in: identifying individuals who are developing an addiction (76%, n= 47/62), initiating a conversation with patients about this (80%, n=50/63) and refusing access to medicines where appropriate (86%, n=54/63) (Figure 1). However, in contrast to the rate that they suspect ATM, only a minority (17%, 27/63) reported initiating a conversation regarding this, or refusing access to medicine (25%, 16/63), on a weekly or more frequent basis.

<<Insert Figure 1 here>>

ATM was suspected on a weekly or more frequent basis for: anxiolytics and hypnotics (53%, n=40/75), weak (47%, n=32/ 68) and strong (39%, n=27/70) opioid analgesics, and anti-epileptics and neuropathic analgesics (26%, n=17, 65) (Figure 2).

<<Insert Figure 2 here>>

Participants were asked to describe patients in whom they identified ATM. Amongst responses (n=55), common themes were that ATM relating to anxiolytics and hypnotics, opioid analgesics, anti-epileptic and neuropathic analgesics tended to

involve middle-aged or older individuals with a history of chronic pain or mental health issues such as depression and anxiety. Addiction to antihistamines was also commonly associated with this population and linked with sleep disorders. Addiction to anxiolytics and hypnotics, opioid analgesics and stimulants were linked to younger people who were also using illicit substances or engaging in pleasure seeking behaviour.

Discussion

This study contributes further evidence that ATM is a significant public health issue in the UK, and highlights that there is likely to be a significant population of individuals with untreated ATM amongst those prescribed or purchasing medicines. In line with recent evidence (5) the most frequently suspected addictions in this study include anxiolytics and hypnotics (e.g. benzodiazepines and z-drugs), strong and weak opioid analgesics (e.g. tramadol & codeine), and anti-epileptic/neuropathic analgesics (e.g. pregabilin) suggesting that medicines containing codeine are likely to be of concern. This study adds to the international evidence base suggesting that the frequency with which health professionals take action when they suspect ATM is suboptimal and affected individuals may be at risk of harm through continued non-therapeutic use of these substances without diagnosis, support or treatment (6).

Respondents identified ATM amongst a diverse range of individuals supporting prior work that reported populations at risk to include those using medication to manage chronic pain and psychological problems (7), young people intentionally using medications for recreational purposes (10) and individuals with other substance use problems including with alcohol and/or illicit drugs (2). Evidence suggests that many individuals affected by ATM may not typically identify as a ‘drug user’ (6) with implications for diagnosis and treatment as individuals may not view their medicines

use as harmful or requiring treatment, or may be unwilling to seek support in drug treatment settings.

The main limitation of this study is the number and geographic spread of the survey participants. However, the diverse health professionals included in the survey, and inclusion of both Community Pharmacy and General Medical Practice, provide confidence that the findings are not isolated to one locality/setting. Also, as ATM issues have been documented in a multiple studies from other parts of the UK and beyond, it is not unreasonable to conclude that the experiences reported are representative.

Conclusion

Findings from this study suggest that health professionals frequently suspect ATM amongst patients including a range of individuals, but in many cases suspected addiction goes unchallenged. Further research is needed to identify effective approaches to support health professionals to tackle ATM and to enable effective delivery of treatment services to this diverse group of individuals for whom traditional addiction services may not be attractive or suitable.

Funding

This study was funded by The Cheshire and Merseyside Public Health Network who provided support with project development and participant recruitment through the Public Health Directorate at St Helens Council.

References

1. National Institute on Drug Abuse (US). Drug facts: Prescription and over-the-counter medications. US Department of Health and Human Services; 2000 Nov. 4 p.

2. National Treatment Agency for Substance Misuse (UK). Addiction to Medicine: An investigation into the configuration and commissing of treatment

services to support those who develop problems with prescription-only or over-the-counter medicine. London: NHS; 2011 May. 32 p.

3. Office for National Statistics (UK). Deaths Related to Drug Poisoning in England and Wales, 2014 registrations. London: Office for National Statistics; 2015 Sep. 30 p.

4. Reay G. An Inquiry into physical dependence and addiction to prescription and over-the-counter medication: All-Party Parliamentary Drugs Misuse Group (UK); 2008 May.67 p.

5. Reed K, Bond A, Witton J, Cornish R, Hickman M, Strang J. The changing use of prescribed benzodiazepines and z-drugs and of over-the-counter codeine-containing products in England: a structured review of published English and international evidence and available data to inform consideration of the extent of dependence and harm. In: National Addictions Centre (UK). 2011. London: Kings College London. 122 p.

6. Cooper RJ. Over-the-counter medicine abuse - a review of the literature. J Subst Use. 2013 Apr;18(2):82-107.

7. Sehgal N, Manchikanti, L., Smith HS. Prescription opioid abuse in chronic pain: A review of opioid abuse predictors and strategies to curb opioid abuse. Pain Physician. 2012 Jul;15(3):ES67-ES92.

8. Mackridge AJ, McKenny C. Abuse of over the counter medicines: the pharmacists' perspective. International J Pharm Pract. 2007 Jan;15(2):B70.

9. Mackridge AJ, Harvey M. Qualitative evaluation of the experiences of people with dependency issues with over-the-counter and prescription medicines. International Harm Reduction Association Conference; 2010 Apr; Liverpool (UK).

10. Benotsch EG, Koester S, Martin, AM, Ceijka A, Luckman D, Jeffers, AJ. Intentional misuse of over the counter medications, mental health and polysubstance use in young adults. Journal Community Health. 2014 Aug;39(4):688-95.

Responses to reviewer comments

We thank the reviewers for their thoughtful and detailed comments and have attempted to address each of them in the table below. We have highlighted the altered text in the resubmitted manuscript, but quite a lot of additional text was revised to remain within word limits. We believe that the revised version is much improved and reports our findings in a clear and concise manner, which we hope will be of interest to the readers of the Journal of Addictive Diseases.

Comment #	Reviewer comment	Detail of amendment/ response
REVIEWER 1		
1	Little more about why experiences of GPs are needed?	We have added the following text in lines 16-17 to make this clear: "Experiences of GP and Pharmacy staff were sought due to their role as gatekeepers to medicines".
2	Also, aim was to "...explore the experiences of health professionals…". This is vague.	Updated in lines 14-16 to make the study aims clearer: "This study aimed to explore the frequency that health professionals within General Practice (GP) and community pharmacy settings suspect and respond to ATM and their perceptions about patients with ATM"
3	The survey measure was not described. Without a more thorough description of the measure and its development, it is difficult to know the validity of the results. I would suggest listing sample items from the main domains of the survey (e.g., frequency of health professional contact with individuals with ATM; confidence and experience addressing ATM).	Added detail regarding topics covered in the survey in lines 22-26. "…the survey, which examined: how frequently health professionals suspect patients to have addiction to different medicines; how frequently action is taken following such suspicion; and confidence in identifying and responding to ATM. Participants were also asked in open questions regarding characteristics of patients they suspected of ATM, and the medicines involved".
4	What was the total possible N for the study? If 76 individuals, each from a different site, completed the survey, how many possible sites were there?	We are unable to report the total possible N. Each local authority public health team disseminated the survey to GPs and pharmacies in their region (clarified in line 21) but owing to an error in the protocol, data were not collected on how many sites they had disseminated the survey to and this information is not available. In the limitations (lines 87-88) we have highlighted this to the reader.
5	The statement, "As this was an exploratory study, no statistical analysis was undertaken", is insufficient. Better to describe what was done and why such an approach was appropriate to the research aims.	The text has been modified in lines 27-28 to now read: "Frequencies and valid proportions of responses are reported, but the sample size precluded subgroup analysis by role"
6	This sentence is unclear: "Two-thirds of participants reported suspecting a patient has or is developing ATM on a weekly or more frequent basis…". Does this mean that two-thirds of participants suspect at least 1 patient they interacted with in the past week has ATM?	To clarify, the text has been updated in line 34-35 to read: "Two thirds of participants (66%, 48/73) reported suspecting ATM in one or more patients on a weekly or more frequent basis"
7	The results in lines 38-44 (and other places as well) report an N of 62 and 63 - why are the other 13 or 14 participants not included?	To clarify this, the following text has been added in line 27. "Frequencies and valid proportions of responses are reported".

8	The following is mentioned in the Results: "Participants were asked to describe patients in whom they identified ATM." Was this an open-ended question? If so, more detail is needed about how the results were derived.	This has been addressed in the additional detail provided regarding the nature of the questionnaire, as described in the response to comment #3.
9	The most compelling finding of the study is that health professionals frequently suspect but do not address possible ATM. This should be emphasized in the Results and Discussion, and the overall manuscript would be much stronger if this became the focal point.	We agree that this finding is particularly of interest and had become lost slightly. We have updated the title of the paper and emphasised this finding through additional text in the discussion and re-ordering the results.
10	This section (discussion) needs to be reduced so that the measure can be better described. The Discussion extends beyond the scope of the survey in line 71 when the authors state, "Respondents identified ATM amongst a diverse range of individuals…". In reality, ATM was only suspected, and it cannot me be known whether any of the individuals actually suspected of ATM actually had it.	We have amended the text in line 70 to read: "Respondents **suspected** ATM amongst…" A number of amendments have been made to the text in response to this and other comments to make clear that the article is examining suspected addiction rather than any attempt to identify a firm diagnosis.
11	The limitations paragraph should be extended. For example, the role (e.g., GP, pharmacist) was not known for 21% of the sample. Also, it should be emphasized that these results are for individuals suspected of ATM, and that actual ATM could be more or less frequent.	The limitations are now discussed in more detail (lines 75-88) to address both these points and others raised elsewhere.
REVIEWER 2		
12	the sentence beginning on line 35 should be reworded to remove any ambiguity as to its intent (eg, was the suspicion of ATM on a weekly or more frequent basis or was the development of ATM on a weekly or more frequent basis?)	To clarify, the text has been updated in line 34-35 to read: "Two thirds of participants (66%, 48/73) reported suspecting ATM in one or more patients on a weekly or more frequent basis"
13	I would suggest replacing reference 1 with something a bit more current than 16-year-old citation, especially when referencing a contemporaneous phenomenon.	The reference was from 2015 – this was our mistake. This particular reference has now been removed and all references have now been checked for accuracy.
REVIEWER 3		
14	While ATM may be an accepted abbreviation in Europe it is not in the United States, and in fact searching the internet for "ATM" and "addiction" the most frequent hits are for an "addiction" to using ATMs (automated teller machines). Thus, I suggest coming up with a different terminology so that the article is more globally understood.	Despite extensive literature review, we were unable to find an accepted wide-spread term for this phenomenon and believe that we have described the term 'addiction to medicine' and its meaning clearly, along with defining the abbreviation in the article abstract and introduction. If the reviewer is able to suggest a more appropriate term or abbreviation that is in wide use, we would be happy to revisit this point.
15	the title includes "and over the counter medicines", yet which medicines are OTC is not clarified in the article. What is OTC in the EU is likely far different from what is OTC in the US.	We agree that this distinction may cause confusion to an international readership and have removed the terms 'prescription medicine' and 'over the counter medicines' from the article title and text as the focus on this work was any medicine to which the respondents were acting as gatekeepers. We have further clarified in the study aims

		that the survey examined medicines that were prescribed or purchased over the counter medicine (as detailed in the response to comment #2).
16	Line 5: Abbreviation should be spelled out the first time they are used, e.g., US and UK in the first paragraph of the article.	The text has been updated to address this (lines 5 & 8).
17	references that are more than 4-5 years old should rarely be used for making an argument about current additions s much has changed in the past few years. Using s reference from 2000 (16 years ago), which is likely referring to data from 1999 or earlier is completely inappropriate for supporting a statement about the "most commonly misused substances" as is a 2011 reference as the sole reference for supporting the growing concern about the misuse of analgesics.	The references have been reviewed and additional contemporary work is now cited. As described in comment #13, this reference was mistakenly detailed as being from 2000, but is no longer used owing to reference number limits.
18	Consistency is important for understanding the article - individuals are referred to as "patients" and "people" e.g., lines 17-18: health professional in primary care who are likely to come in contact with people" - are these "people" not "patients", and lines 19-20, "community pharmacy settings with regard to patients with ATM." And later on line 27 where "individuals" is used	For consistency, all references to individuals have been updated to patients throughout the article
19	Line 24: define "snowball recruitment"	On reflection we feel 'snowball recruitment' was a misleading term as dissemination was via public health teams within local authorities, who distributed the survey to General Practices and Pharmacies in their area. We have changed the text in lines 21-22 to describe the recruitment process: "…via Local Authority (LA) Public Health teams. Eight of the nine LAs approached agreed to do this.".
20	Line 29-30: the actual name and location for the institutional review board should be included.	We have amended the text accordingly in line 28-29: "The study was approved by the Liverpool John Moores University Research Ethics Committee.
21	Line 60-61: the word "significant" should be reserved for issues that are statistically significant, and not simply for issues that the authors believe are important.	We have amended the text as suggested to remove the word significant to read: Lines 56-57: "This study contributes further evidence that ATM is an **important** public health issue in the UK" Line 57: "findings suggest that there is a **sizeable** population…"
22	Line 64: define "z-drugs"	To avoid confusion we have updated the text in line 59 to read: "hypnotics (e.g. benzodiazepines and similar drugs)"
23	Line 66: the following statement does not appear supported by the data, "suggesting that medicines containing codeine are likely to be of concern". Why is codeine singled out? Figure 2 shows more suspected	We thank the reviewer for highlighting this and have removed the line from the manuscript.

	"addiction issues" with anxiolytics and hypnotics and with strong opioid analgesics than with weak opioids (which is where I assume codeine fits), and I assume in the group of weak opioids there are opioids in addition to codeine in this category.	
24	how much training do GPs and Pharmacists in the UK receive regarding addiction, in particular accurate diagnosis, and for treating pain. If it is as limited as it is in US medical schools then there is no reason to put much significance at all on these results. Addition is not an easy issue to diagnosis without appropriate training, and without some compassion for population. It is easy to assess a patient taking any of these medications as an "addict", especially if they are difficult or problematic in any way. And how is "addiction" seen in the general population - what do patients (or people or individuals) interpret as an addiction. In the US anything done frequently is often labeled as an addiction (see reference to "automatic teller machine (ATM) addiction" mentioned earlier).	The underpinning premise for this work is around examining the need for additional support for patients and healthcare professionals in respect of addiction to medicines – a phenomenon that is increasingly being recognised as problematic in the UK and elsewhere. Education and training on addiction for health professionals in the UK is varied and depends very much on the postgraduate training that individuals have undertaken. However, we feel that the key message from this work is that health professionals are relatively frequently suspecting addiction to medicines, but in many cases they report feeling unable to respond to this. Therefore, while we accept the point the reviewer is making regarding the potential inaccuracy of diagnosis, and the possibly unwarranted labelling of some behaviours as an addiction, the value that this paper adds is around highlighting the need for improving core education for healthcare professionals around understanding risks of addiction with respect to medicines, how to identify it and how it might be tackled. In revising the manuscript, we have further emphasised this point while recognising a limitation of the study being that addiction is only suspected and not diagnosed by the health professionals involved.
25	The abuse of anti-epileptics and neuropathic analgesics are limited in the US; there is no justification given in this article for their inclusion in this study, and their inclusion likely skews the results.	Questions about antiepileptic and neuropathic agents (such as gabapentinoids) were included in the questionnaire owing to numerous suggestions regarding misuse and addiction issues relating to these (Schifano F, D'Offizi S, Piccione M, *et al.* Is there a recreational misuse potential for pregabalin? Analysis of anecdotal online reports in comparison with related gabapentin and clonazepam data. *Psychotherapy and psychosomatics* 2011; **80**: 118–22 and Kapil V, Green JL, Le Lait M-C, Wood DM, Dargan PI. Misuse of the γ-aminobutyric acid analogues baclofen, gabapentin and pregabalin in the UK. *British Journal of Clinical Pharmacology* 2014; **78**: 190–1.), as evidenced in a recent review article – Smith R V., Havens JR, Walsh SL. Gabapentin misuse, abuse and diversion: a systematic review. *Addiction* 2016; **111**: 1160–74. We have now made explicit reference to this in the introduction. Further, we believe that the fact that substantial numbers of health professionals surveyed reported that they suspected addiction to these substances justifies their inclusion.
26	And what about OTC and prescribed stimulants; they are included in figure 2, but not discussed,other than being linked to younger individuals. And abuse issues associate with their use appears to be the	As this is a short report, with limited space available, and the study being focussed on the broader issues around the overall frequency that addiction to medicine is suspected and how this is responded to by health professionals, we have not been able to discuss in detail individual substance groups in great depth.

	lowest of all the drugs investigated. This is contrary to what we are seeing in the US, and should be discussed.	
REVIEWER 4		
27	In the first paragraph of results and Figures 1 and 2 it needs to be made clearer that the frequencies listed ("Weekly or more", "Monthly or more" and "Less than Monthly") refer to the frequency of occurrence reported by the participants of the item noted (e.g. patient admitting addiction) and not to the frequency of drug use by the patient. I assume that "Monthly or more" means occurrence at least once/month, but not as frequently as once/week. If so, that needs to be stated. If not, why does that category not include "Weekly or more"?	For clarity, frequency categories have been updated in the text and figures to indicate that, as the reviewer assumed, “monthly or more” meant occurrence at least once per month but not as frequently as once per week.
28	The numbers referred to in lines 38-42 are referenced to Figure 1. However, they do not seem to agree with numbers in the figure (e.g. in line 42, 27/63 are reported to have initiated a conversation; however, Fig. 1 appears to show that 11 initiated a conversation at least once/wk, 25 initiated a conversation at least once/month and 27 initiated a conversation less than once/month). If the numbers reported in Results refer to numbers different from those shown in Fig. 1, that needs to be explained.	We thank the reviewer for highlighting this discrepancy, the number of participants reporting initiating a conversation on a less than monthly basis rather than a weekly or more frequent basis was reported in the text in lines 36-38. This has now been updated and data in the text matches data in figures. “However, just (17%, **11**/63) reported initiating a conversations, or refusing access to medicines (25%, 16/63), on a weekly or more frequent basis”
29	Were there any guidelines for participants in items to consider in making their judgments concerning "Participant suspects addiction" or was this just an "opinion" with no qualifiers?	We have made changes to the text regarding the survey items (lines 23-36) and discussion of study limitations (lines 75-88) to address this point.
30	Is there any information on how many participants were identified in each category and perhaps approximately what percentage of the patients seen by that participant fell into each category?	We have now added text to make clear that the sample size precluded subgroup analysis by job role (lines 27-28).

Figure 1: Frequency of participants reporting patient's admission and personal suspicion of addiction alongside frequency that action is taken

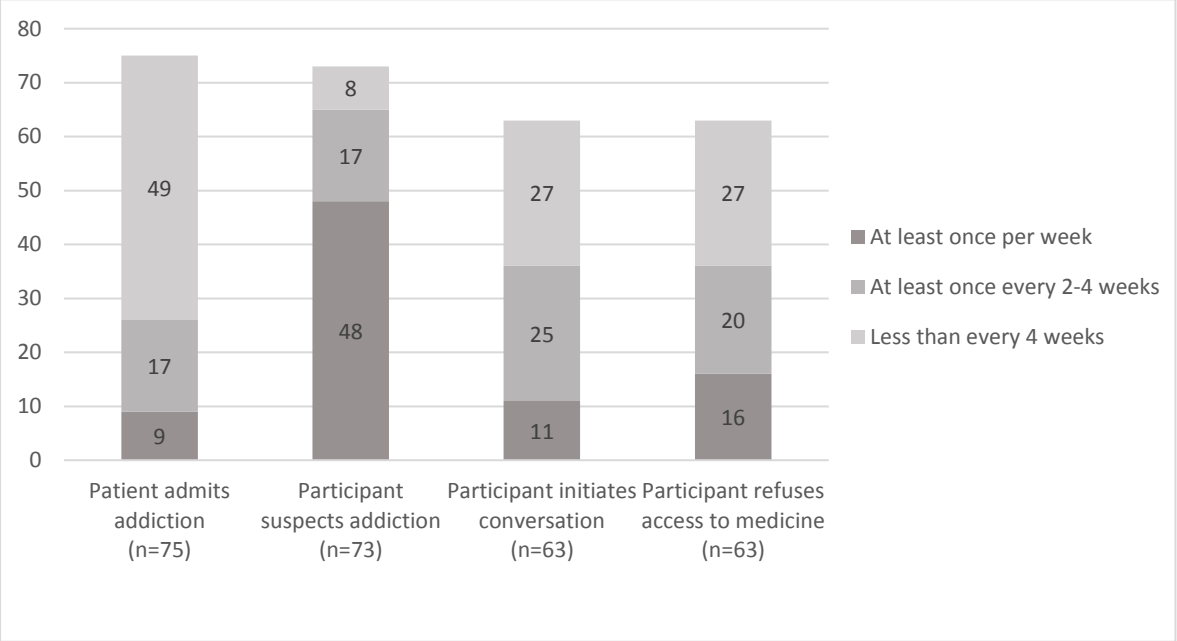

Figure 2: Frequency of suspected addiction in patients by medicine group (n=75)