

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Prevalence and Incidence of Alcohol Dependence: Cross-sectional primary care analysis in Liverpool, UK.
AUTHORS	Montgomery, Catharine; Schoetensack, Christine; Saini, Pooja; Owens, Lynn; Van Ginneken, Nadja; Rice, Melissa; Young, Ryan; Jones, Andrew

VERSION 1 – REVIEW

REVIEWER	Geert Dom University of Antwerp, CAPRI
REVIEW RETURNED	29-Dec-2022

GENERAL COMMENTS	<p>This is an interesting study on different levels. Its focus on primary care within a regional context allows for the findings to guide healthcare policy changes in a dedicated region. In addition, the focus on AUD and its associations with socially deprived individuals within a given region is important. In spite of these clear positive points I have the following comments:</p> <p>Methodology:</p> <ul style="list-style-type: none">- The authors identify two categories: Alcohol Dependence (SNOMED Code) and Hazardous alcohol (HA) use. However, the latter is (unless I missed it) not clearly defined in the method section. So please provide a clear definition of HA and provide a reference to support the choice of definition.- Results: Table 2 would benefit from indications of whether the prevalences/incidences decrease or increase as to the year/to/year comparisons.- Association between IMD and prevalence rates: although interesting I am not sure whether the results presented can be interpreted. Did the authors take into account (correlate for) possible (demographic) differences between practices that are themselves related to AUD/HA risk (e.g. ratio men/women, ethnicity)? Please specify. In addition, why only report on the relation between alcohol dependence and social deprivation and not hazardous alcohol use?
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REVIEWER	Miroslav Barták Charles University and General University Hospital in Prague, Department of Addictology
REVIEW RETURNED	30-Jan-2023

GENERAL COMMENTS	<p>Dear authors, thank you for the opportunity to review your interesting and relevant article.</p> <p>In the abstract, I recommend including the number of practices (now just in the Figure 1) from which the data was obtained. For now, we</p>
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	<p>can only learn about the excluded practices. Please also specify the number of practices in the methodology section. The list of variables could be part of an appendix, or just written in a line. Patient and public involvement is very nicely described, but we do not learn how it was accomplished outside the presence of the author, given that all co-authors seem to have local knowledge. Authors may have to consider to adjust Table 1, given that the most common ethnicity was White British or Irish and the second most common answer was Missing. In total, therefore, 81% of respondents gave that option and together with those who did not give an answer represent 92% of respondents. Similarly, frequencies below 0.1% need not be reported in the table and can be reported elsewhere if relevant to the analysis. In general, I like the analysis made. However, I would give the authors some consideration in the supplementary material to further describe the methodology of dataset construction, which is probably understandable to readers in the UK, but in other countries around the world the approach to patient data is different in some ways. Figure 1 does not provide all the information needed, and some of the abbreviations may not be understandable to readers whose first language is not English. The IMD score is used correctly, however, many readers may not be familiar with the Index of Multiple Deprivation and it would be helpful for the authors to add this information. I also suggest that the authors pay more attention to the generalizability of their findings. In the version presented, generalisability is (logically) related to the city under study, or the UK, which is fine. However, in my opinion, the paper also draws conclusions for a wider international readership that should be more fully elaborated. The authors conclude the paper with a number of certainly valid implications of their research. On the other hand, these implications are not based on research per se, but on knowledge of the local environment, which should be part of the discussion rather than the conclusion of the paper.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1	Response	Location
<p>This is an interesting study on different levels. Its focus on primary care within a regional context allows for the findings to guide healthcare policy changes in a dedicated region. In addition, the focus on AUD and its associations with socially deprived individuals within a given region is important.</p>	<p>We thank Reviewer 1 for these comments.</p>	-
<p>Methodology:</p> <p>The authors identify two categories: Alcohol Dependence (SNOMED Code) and Haradous alcohol (HA) use. However, the latter is (unless I missed it) not clearly defined in the method section. So please provide a clear definition of HA and provide a reference to support the choice of definition.</p>	<p>In our database, individuals were defined as hazardous drinkers if they had a SNOMED code that indicated a “mental and behavioural disorder due to the use of alcohol: harmful use” according to the ICD-10 criteria. These individuals had various SNOMED and free text codes entered by GPs (Alcohol – problem drinking; Alcohol abuse; ALCOHOL DRINKING EXCESSIVE; Alcohol misuse; Alcohol Misuse; ALCOHOL PROBLEM; Alcohol problem drinking; ALCOHOL PROBLEM DRINKING;</p>	<p>Please see readme file accompanying open access dataset and Page 6-7 of data analysis section.</p>

	<p>ALCOHOL RELATED DISTURBANCES; Alcohol; Problem Drinking; EXCESSIVE DRINKING ALCOHOL; INTOXICATION ALCOHOL CHRONIC; Problem drinker; Alcohol consumption; Persistent alcohol abuse), but did not meet the case definition for dependence developed by Thompson and co-workers.</p> <p>We have included these codes and a clearer definition of how the patients were identified and the read codes used in the readme file accompanying the dataset, and added some descriptive text in the data analysis part of the method section (p 6-7). Please note it can take our institution up to 72 hours to process a new dataset request, so this data will be available by Friday 3rd March at the address specified in the manuscript.</p> <p><i>“For a more detailed description of database construction and SNOMED and free text codes for hazardous drinking, please see readme file accompanying open access dataset (URL). All alcohol codes were reviewed by two researchers (CM; CK) and confirmed to indicate either alcohol dependence (using the case definition in Thompson and co-workers [13]), or harmful drinking [15]. Where there was uncertainty, the clinical opinion of LO and CK was used assign cases.”</i></p>	
<p>Results:</p>		
<p>Table 2 would benefit from indications of whether the prevalences/incidences decrease or increase as to the year/to/year comparisons.</p>	<p>We have edited Table 2 to include arrows indicating whether the flagged significant prevalence/incidence comparisons indicate an increase or decrease from year to year.</p>	<p>P 12</p>
<p>- Association between IMD and prevalence rates: although interesting I am not sure whether the results presented can be interpreted. Did the authors take into account (correlate for) possible (demographic) differences between practices that are themselves related to AUD/HA risk (e.g. ratio men/women, ethnicity)? Please specify. In addition, why only report on the relation between alcohol dependence and social deprivation and not hazardous alcohol use?</p>	<p>This was an interesting point and we have rerun all of our main analyses to include both sex and ethnicity. For patient level analyses, we have also include mean age of patients. We have also performed the same analyses for hazardous drinking in addition to the dependent drinking analyses.</p> <p>These analyses and respective figures can be found on pages 12-14 of the results section.</p> <p>In summary:</p> <p>For both dependence and hazardous drinking, there is a significant association between IMD and prevalence, but no significant effects of gender or ethnicity.</p>	<p>Pages 12-15. Figures 3 – 5.</p>

	<p>For pharmacotherapy, there was no significant association between GP surgery IMD and prescribing, and a weak association between patient level IMD and prescribing.</p> <p>We have also noted on p8 in our statistical analysis section that <i>“We also examined the % of males and females who identified as ‘British or Mixed British’ as their ethnicity (vs other possible ethnicities). We chose this as it was the most commonly reported ethnicity. However, this analysis is exploratory as the quality of ethnicity reporting was poor (many surgeries reported missing ethnicity data).”</i> While we have left this analysis in for the revision, we do not think it adds to the manuscript as the reporting of ethnicity was variable, so we are happy to remove this again at Reviewer 1’s request.</p>	P8
Reviewer: 2		
Dear authors, thank you for the opportunity to review your interesting and relevant article.	Thank you for reviewing the article!	
In the abstract, I recommend including the number of practices (now just it the Figure 1) from which the data was obtained. For now, we can only learn about the excluded practices. Please also specify the number of practices in the methodology section.	<p>This information is now displayed in the setting section of the abstract and in the method:</p> <p><i>“Setting: NHS Liverpool CCG primary care. Sixty-two of 86 GP practices agreed to share their anonymised EMIS data from 01/01/2017 – 31/12/2021.”</i></p> <p><i>“Practices were excluded if they opted out (N = 2) or did not respond to the data sharing request (N = 22), resulting in data being shared by 62 practices in total.”</i></p>	<p>Page 2, Abstract, Setting.</p> <p>Page 5, Design, Setting and Study Population</p>
The list of variables could be part of an appendix, or just written in a line.	<p>We have collapsed the numbered list so variables are now written in the text:</p> <p><i>“Variables extracted from the EMIS system were: Anonymised identifier; Sex; Age; Ethnicity; Postcode of registered GP practice; Occupation; Alcohol use metrics (related diagnoses e.g. Wernicke’s encephalopathy, alcohol consumption, Alcohol Brief Interventions, onwards referrals); Medications to treat alcohol dependence (Disulfiram; Topiramate; Acamprosate; Baclofen; Naltrexone); Major psychiatric and physical comorbidities.”</i></p>	Page 6, Design, Setting and Study Population.
Patient and public involvement is very nicely described, but we do not learn	We have attempted to further clarify the role of Ms. Rice and the nature of our	P6

<p>how it was accomplished outside the presence of the author, given that all co-authors seem to have local knowledge.</p>	<p>engagement with her:</p> <p><i>“The research team are active members of Liverpool Centre for Alcohol Research (LCAR). Through our engagement with local patients and stakeholders in LCAR, we invited Melissa Rice to join our team as an expert-by-experience. Through steering group meetings and project development updates, Melissa has been involved in the design of the study (offering expertise on the personal experience of accessing treatment in primary care and associated factors), has reviewed the manuscript and will be the PPI chair on our future work.”</i></p>	
<p>Authors may have to consider to adjust Table 1, given that the most common ethnicity was White British or Irish and the second most common answer was Missing. In total, therefore, 81% of respondents gave that option and together with those who did not give an answer represent 92% of respondents. Similarly, frequencies below 0.1% need not be reported in the table and can be reported elsewhere if relevant to the analysis.</p>	<p>We have deleted the percentages for Disulfiram and Naltrexone which were both below 0.1% from Table 1.</p>	<p>Page 11, Table 1.</p>
<p>In general, I like the analysis made. However, I would give the authors some consideration in the supplementary material to further describe the methodology of dataset construction, which is probably understandable to readers in the UK, but in other countries around the world the approach to patient data is different in some ways.</p>	<p>We have included a supplementary file including a brief readme which is available with the publicly available data used in the study (available on the institutional data repository). The readme file describes the dataset and how it was constructed by LCCG from the available data in Egton Medical Information Systems, and how items were recoded and curated within that dataset.</p>	<p>See URL:</p>
<p>Figure 1 does not provide all the information needed, and some of the abbreviations may not be understandable to readers whose first language is not English.</p>	<p>We have edited Figure 1 to fully define the abbreviations the first time they are used.</p>	<p>Figure 1.</p>
<p>The IMD score is used correctly, however, many readers may not be familiar with the Index of Multiple Deprivation and it would be helpful for the authors to add this information.</p>	<p>This was a really useful suggestion. We have included definition of the in the data analysis part of the method section:</p> <p><i>“GP postcode was recoded to reflect the 2019 Indices of Multiple Deprivation for England (IMD) deciles, based on the Lower Layer Super Output Area (LSOA) of the GP postcode. The IMD gives a single weighted score for the relative deprivation of a small geographical area (the LSOA) based on seven domains (income, employment, education, health, crime, barriers to housing and services, living environment). We also received patient level LSOA codes, which were recoded to reflect the IMD decile of</i></p>	<p>Page 7-8, Data analysis.</p>

	<i>that LSOA. In the current study IMD deciles were used in the main analyses with 1 = most deprived – 10 = least deprived.”</i>	
I also suggest that the authors pay more attention to the generalizability of their findings. In the version presented, generalisability is (logically) related to the city under study, or the UK, which is fine. However, in my opinion, the paper also draws conclusions for a wider international readership that should be more fully elaborated.	We have reviewed the discussion and have attempted to weave the implications of the research nationally and globally into our narrative by reflecting on trends in alcohol use and dependence worldwide, and alcohol treatment processes and pathways in other countries. Sections are highlighted throughout the discussion where we have made those changes, for example: <i>“While nationally, prevalence of alcohol use disorders has increased with subsequent increases in alcohol-related mortality and disease [2, 10], a trend which has also been observed globally [17], we have demonstrated local decreases in the incidence of diagnoses identified in primary care over a 5-year period.”</i>	P15 - 18
The authors conclude the paper with a number of certainly valid implications of their research. On the other hand, these implications are not based on research per se, but on knowledge of the local environment, which should be part of the discussion rather than the conclusion of the paper.	We agree with Reviewer 2 and have revised the end of the manuscript to provide a stronger concluding statement. <i>“In conclusion, this research highlights the association between social deprivation and prevalence and incidence of hazardous and dependent alcohol drinking. Future research should seek to identify perceived barriers and facilitators of access to treatment in primary care from both patient and practitioner perspectives, to identify specific local, national and international need for different treatment pathways for hazardous and dependent drinkers.”</i>	P17 - 18

VERSION 2 – REVIEW

REVIEWER	Geert Dom University of Antwerp, CAPRI
REVIEW RETURNED	15-Mar-2023
GENERAL COMMENTS	the authors responded very well to my comments - many thanks - great paper
REVIEWER	Miroslav Barták Charles University and General University Hospital in Prague, Department of Addictology
REVIEW RETURNED	07-Mar-2023
GENERAL COMMENTS	Thank you for the opportunity to re-evaluate the submitted article after incorporating the changes. I can conclude that the authors have incorporated all the comments made during the first round of review. As part of the data are related to the COVID-19 period, I suggest that the authors discuss this fact and assess the potential impact of this "variable" on their dataset.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1	Response	Location
<p>Thank you for the opportunity to re-evaluate the submitted article after incorporating the changes. I can conclude that the authors have incorporated all the comments made during the first round of review.</p> <p>As part of the data are related to the COVID-19 period, I suggest that the authors discuss this fact and assess the potential impact of this "variable" on their dataset.</p>	<p>We agree with Reviewer 1 that the final 2 years of data collection during our period were during the pandemic and that this may have affected the incidence and prevalence levels. This is potentially more worrying, as we know that drinking increased during the pandemic, and the lower levels of identification would therefore mean that there are more patients requiring support who are not being identified in a timely manner. Indeed, we have discussed this in the introduction, Page 4, Paragraph 2 and also the discussion, Page 15, paragraph 2 (see text below and highlighted in the manuscript). We have also analysed incidence and prevalence data by year, with data from 2020 and 2021 being during the pandemic. The trends that we observed in 2017, 2018 and 2019 of decreasing incidence are also evident in 2020 and 2021. We have tried to make this even clearer by adding a statement to the summary and also additional text to the discussion to highlight this.</p> <p><i>Introduction:</i> <i>“The COVID-19 pandemic is likely to have further exacerbated social inequalities in access to AD treatment as services were forced to cancel face-to-face contact for individuals with AD, and the proportion of individuals drinking at higher risk levels reportedly increased over the course of the 12 months between March 2020 -2021 [10].”</i></p> <p><i>And</i></p> <p><i>“a clear picture of the incidence and prevalence of alcohol presentations in primary care, as well as associated sociodemographic variables, is needed to understand the impact of the COVID-19 pandemic on identification of alcohol use disorders but also to elucidate local inequalities in AUD presentations.”</i></p> <p><i>Discussion:</i> <i>“Changes in prevalence were more subtle with significant decreases in 2020 due to the COVID-19 pandemic, but not other years during the analysis period.”</i></p> <p><i>Article summary:</i> <i>“It should also be noted that the final 2 years in the analyses were during the COVID-19 pandemic, and changes in identification during this period could be affected by restrictions in health care settings.”</i></p>	<p>Page 4 paragraph 2</p> <p>Page 15, paragraph 2</p> <p>Page 3, bullet point 4</p>

	<p><i>Discussion:</i> <i>“Finally, the final two years of primary care data were for incidence and prevalence of alcohol diagnoses during the COVID-19 pandemic. It is likely that due to the increases in drinking during this time, these figures are an especially low reflection of actual prevalence and incidence.”</i></p>	<p>Page 16, paragraph 1.</p>
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