PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Quantifying the relative risk of harm to self and others from substance misuse – results from a survey of clinical experts across Scotland
AUTHORS	Taylor, Mark ; Mackay, Kirsty; Murphy, Jen; McIntosh, Andrew; McIntosh, Claire; Anderson, Seonaid; Welch, Killian

VERSION 1 - REVIEW

REVIEWER	Nutt, David University of Bristol, Psychopharmacology
REVIEW RETURNED	23-Jan-2012

GENERAL COMMENTS	this is an interesting follow up to the nutt et al 2007 study Strengths = large number of expert responders Well written - clear and easy to read - Discussion fair and balanced Recommend - accept

REVIEWER	Dr. J.G.C. van Amsterdam, senior scientist RIVM Bilthoven, The Netherlands I have no conflicts of interest.
REVIEW RETURNED	28-Dec-2011

GENERAL COMMENTS	The paper of Taylor et al. describes the risk assessment by a large panel of 292 experts in addiction of the 19 most widely used drugs in the UK. The issue addressed is of high interest for both scientists and policy makers. Major points. 1. The properly evaluate the impact of the survey it is required to describe in the Methods section: 1. the procedure how the experts were invited (selected) to participate in the study, and 2. the response rate of the different groups (nurses, psychiatrists, staff, others). 2. Psychiatric nurses are overrepresented (almost half). Though I have no doubt about their expertise, it should be described at least how high their experience of the nurses was (for instance how many years of experience in drug addiction).

	3. The lowest score for cannabis is remarkable and should therefore be discussed in some more depth. For instance in the Netherlands, a sharp rise in a help requests among young users was noted following the availability of cannabis containing very high levels of THC. Minor points 4. p. 4, bottom: "... for each of the nine parameters." Though the nine parameters are mentioned in Nutt's paper, they should all be mentioned here. 5. Table 3: are the scores expressed as the mean values of the median values? 6. Were there any remarkable differences in scores between nurses and 'others'? 7. For the most prominent drugs: how high was the variation in scores (st. dev.)? Especially the range for cannabis is of interest ! 8. p. 8, line 11-12: I recommand to add here 'the better social embedment' of the legal drugs. Secondly, the legal drugs are far more widely available and used ! 9. p. 8, line 20-21: "…. indicated that 58% of individuals dying by suicide…" Though this may be true, the real cause to commit suicide probably are underlying factors, like social isolation, unemployment, divorce, poverty. This should be highlighted somewhere.

REVIEWER	Tim Stockwell, PhD Director, Centre for Addictions Research of BC Professor, Department of Psychology University of Victoria, BC
REVIEW RETURNED	22-Feb-2012

THE STUDY	Details provided in my review- basically, I think there is a slightly misleading approach to addressing the research question and that it's not clear if the sample is representative of a broader sample of professionals working in the addictions field in Scotland.
RESULTS & CONCLUSIONS	I believe that the question posed is overly simplistic and it is unclear as to exactly how respondents have made comparisons about potential harmful is of different substances. My main criticism is that the question appears to have been posed without reference to level of use - all harms from substance use are in some way dosed dependent and this dimension has not been clarified for the respondents.
GENERAL COMMENTS	This is an interesting and straightforward paper presenting simple descriptive statistics from a survey of 292 "experts" on alcohol and other drugs regarding their ratings of the relative harmfulness of 19 different substances including alcohol and tobacco, the rest being some form of illicit drug. The main interest is in contrasting these ratings of harmfulness with the legal status of different substances including whether they are category A, B or C controlled substances if illicit or uncontrolled i.e. alcohol and tobacco. In keeping with results from well-known studies by Nutt and colleagues as well as a Dutch study the respondents consider alcohol to be the fourth most

	dangerous substance and cannabis the least harmful. There are some minor differences in the results e.g. Nutt et al ranked cannabis has 11th or 12th which are discussed. Otherwise, the only differences are that the group of experts used is much larger than the previous studies and that they were all drawn from Scotland. The sample is dominated by community psychiatric nurses who account for almost half the total sample. No analysis is provided of whether rankings varied according to broad professional groups e.g. medical versus nursing and allied health professions. Another analysis might have contrasted numbers of years experience with specialist addiction services or in general health care to see if this variable predicted different results. The method used replicates Nutt et al (2007, The Lancet) with minor modifications. Summary scores are given for three dimensions of personal harm to self, a rating of social harms including those to other people and a total harmfulness score. There is no information about how participants were approached or selected and how many refused which is a weakness. The deceptively simple and straightforward approach employed makes the powerful point that current drug classifications do not reflect expert opinion. A major issue glossed over in the paper and perhaps in the survey is how one actually makes contrasts about harmfulness when degree of harm is entirely dose-dependent. We do not know whether for example participants were comparing recreational use of one drug versus dependent use of another? A commonsense approach would be to define level of use before asking the questions and repeat questions for contrasting patterns and levels of use e.g. (i) occasional light use (ii) regular light use (iii) occasional heavy use (iv) regular heavy use. Another contrast would be injection versus non-injection use. Given the much greater prevalence of use of alcohol than heroin for example might lead some participants in the survey to give extra weight to the fact that the overall burden of harm to society from alcohol was greater simply because 90% of the population use it as opposed to 2 or 3% the heroin. My preference would have been to see a much more nuanced discussion of this issue in more detailed analyses controlling the variables of level of use and also exploring how responses varied by different professional groups and/or length of experience. I think it's also important to justify the nature of the sampling strategy as to whether this could be considered to result in a representative sample of addiction experts.

VERSION 1 – AUTHOR RESPONSE

Reviewer: –Dr Amsterdam; RIVM Bilthoven

Comments from Dr Amsterdam
1) The properly evaluate the impact of the survey it is required to describe in the Methods section: 1. the procedure how the experts were invited (selected) to participate in the study, and 2) the response rate of the different groups (nurses, psychiatrists, staff, others).

Authors response:

We agree with the reviewer's comments and have added explanatory text in the methods section

Comments from Dr Amsterdam

2) Psychiatric nurses are overrepresented (almost half). Though I have no doubt about their expertise, it should be described at least how high their experience of the nurses was (for instance how many years of experience in drug addiction).

Authors response:

We do not accept that the specialist addiction community psychiatric nurses are over-represented as they constitute the largest single discipline numerically in any addictions service. They thus dominate the sample as the vast majority of responses were obtained via face-to-face interview. Precise detail on experience is unknown but the average is > 5 years (added in text)

Comments from Dr Amsterdam
The lowest score for cannabis is remarkable and should therefore be discussed in some more depth. For instance in the Netherlands, a sharp rise in a help requests among young users was noted following the availability of cannabis containing very high levels of THC.

Authors response:
This is an important & interesting point, and we have added discussion on this – it may be that at the time of survey the high potency THC had not yet become widely available in Scotland.

Comments from Dr Amsterdam
4. p. 4, bottom: "... for each of the nine parameters." Though the nine parameters are mentioned in Nutt's paper, they should all be mentioned here.
5. Table 3: are the scores expressed as the mean values of the median values?
6. Were there any remarkable differences in scores between nurses and 'others'?
7. For the most prominent drugs: how high was the variation in scores (st. dev.)? Especially the range for cannabis is of interest !
8. p. 8, line 11-12: I recommand to add here 'the better social embedment' of the legal drugs. Secondly, the legal drugs are far more widely available and used !
9. p. 8, line 20-21: "…. indicated that 58% of individuals dying by suicide…" Though this may be true, the real cause to commit suicide probably are underlying factors, like social isolation, unemployment, divorce, poverty. This should be highlighted somewhere

Authors response:
The nine parameters are now explicitly listed. Table 3 values are means, as stated. Non-medical staff (mostly nurses) had precisely the same pattern of harm ratings although their mean values were marginally higher across the board. The score variations are low. The availability and social / cultural embedment are specifically noted in paragraphs 1 & 2 of discussion. A cautionary statement on cause & effect re suicide has been added to discussion.

Comments from Prof Nutt

No response required

Reviewer: Dr Stockwell, BC

Comments to the Author
My main criticism is that the question appears to have been posed without reference to level of use - all harms from substance use are in some way dosed dependent and this dimension has not been clarified for the respondents.

A commonsense approach would be to define level of use before asking the questions and repeat

questions for contrasting patterns and levels of use e.g. (i) occasional light use (ii) regular light use (iii) occasional heavy use (iv) regular heavy use. Another contrast would be injection versus non-injection use.

Authors response:
It is correct that dosing has not been specifically allowed for, but harms relating to intoxication; dependence; chronic versus acute use were all specifically questioned. As the reviewer will no doubt appreciate, a true estimate of dosing can often be impossible, even to the user.
A future survey might well attempt to qualify the results via dose (eg occasional; light regular; binge; heavy regular) as suggested, but our aim was to attempt to replicate Nutt et al. Furthermore, we felt the nine parameter questionnaire for 19 substances was already complex and onerous for respondents, and we wished to minimise respondent drop-out / fatigue.

Comments to the Author
No analysis is provided of whether rankings varied according to broad professional group.

There is no information about how participants were approached or selected and how many refused which is a weakness.

I think it's also important to justify the nature of the sampling strategy as to whether this could be considered to result in a representative sample of addiction experts.

Authors response:
Important points. See responses to same points from Dr Amsterdam, above

Comments to the Author
……..might lead some participants in the survey to give extra weight to the fact that the overall burden of harm to society from alcohol was greater simply because 90% of the population use it as opposed to 2 or 3% the heroin. My preference would have been to see a much more nuanced discussion of this issue…

Authors response:
The availability and legality of alcohol (& tobacco) clearly contribute to the estimation of its harm potential, and we have added text in discussion enlarging on these complexities.

VERSION 2 – REVIEW

REVIEWER	Tim Stockwell, PhD Director, Centre for Addictions Research of BC Professor, Department of Psychology University of Victoria, BC
REVIEW RETURNED	11-Mar-2012

THE STUDY	I think the paper is a little improved but I still have reservations regarding a) response rates and possible selection biases in sampling b) how well the actual questions differentiate between asking how harmful different drugs are in relation to each other independently of their prevalence of use i.e. alcohol may get a higher ranking because of its widespread prevalence.
RESULTS & CONCLUSIONS	While this is a very clear and potentially useful study I would like some reassurance in the paper that respondents were comparing different psychoactive substances independently of current prevalence of use and also as to how the problem of responses being conditional on intensity of personal use were factored in. If one

	imagines light occasional use then potentially nearly all substances are equally harm free. If one imagines regular moderate use some differentiation would appear. If one is concerned about risk of dependence from a particular level of use then that will be partly contingent on mode of administration etc etc. It's very hard to really deconstruct and interpret these responses.
GENERAL COMMENTS	I think including the specific generic wording of the questionnaire in the paper itself to see the exact guidance and context respondents were given followed by some justification would satisfy me. An indication of response rate (if known) would satisfy me on the other point.

VERSION 2 – AUTHOR RESPONSE

The authors thank the BMJ open and Dr Stockwell for their continued interest in our paper.

In particular, the paper has been amended (and hopefully improved) with the addition of material in response to the reviewer.

1. A copy of scale used has been placed as an appendix to the paper.
2. Text on the guidance given to respondents including the instructions that the harm ratings were to be based on their clinical experience within addictions rather than more general societal estimations.
3. Detail (as much as is known) on the response rate of the sample has been added to the method.
4. Further caveats or notes on the limitations of the study has been added to the discussion. Specifically, there is extra comment on the availability and cost of a substance (eg alcohol) affecting its harm potential, as well as a note on the possibility of selection and / or observer bias within the sample.

Yours sincerely,

Dr Mark Taylor