Reviewer 1:

1. Introduction section: Some sentences are too long in the text. It makes the article difficult to understand. The text should be revised and checked for the grammar.

Reply: We have revised the entire manuscript to ensure it is more understandable. Where we found lengthy sentences, these have been reworded.

2. The contribution of the article to the literature should be written clearly and concisely.

Reply: We have added a paragraph to the end of the Discussions as follows: "Finally, the review of the relevant current literature, combined with the diligence of the consensus Group, has identified the most salient vulnerabilities of individuals with combined ADHD and SU. Furthermore, the consensus statement provides a structure within which the pertinent vulnerabilities can be best identified, treated, and managed by clinical and multi-agency interventions. The statement provides an important readily accessible contribution to the literature for practice, research, and evaluation of treatment effectiveness for adults with combined ADHD and SU/SUD."

Reviewer 2:

3. To be able to arrive at a consensus statement and guidelines valid outside of England and Iceland, the authors should probably include experts from other countries, or they should specify that their views are valid only for those two countries.

Reply: We have added the following underneath the first paragraph in the methods section: "The consensus group incorporated evidence from a broad range of sources. However, this largely reflects clinical practice and legislature in the United Kingdom (UK), which may differ in other countries".

4. Also, the representativity of the authors is not clear. This reader is not familiar with all the abbreviations used in the presentation of the authors, but most of the authors seem to be psychologists, and it is not stated what background (clinical or academic) the various participants have. This would influence the credibility of the statements.

Reply: We have clarified in paragraph one of the methods section that "Meeting attendees included experts from ADHD and/or SUD services across a range of disciplines. Thirteen participants had medical qualifications/appointments, five had psychological qualifications/appointments and nine had academic qualifications/appointments. There was also representation by a service-user and an educational/occupational specialist.

5. The text gives the impression of being at a preliminary stage with respect to organization, clarity, and emphasis. Although eager to learn from colleagues, this reader unfortunately soon became frustrated with the disorganized text. The report has been reviewed only halfway. The authors will have to revise the text thoroughly; this is not the task of a reviewer.

Reply: We have taken on board the reviewer's comments above (which were very helpful) and restructured some parts of the text. We have also reviewed the entire text – see (1) above. This has also meant that some references became obsolete, so the reference list is now shorter.

6. Abstract The authors should distinguish between SU and SUD. From the title, this reader infers that SUD is the topic of the guidelines, not SU.

Reply: We are grateful to the reviewer for pointing this out and we have amended the title to be broader (i.e. substance use).

7. The authors should summarize guidelines in the abstract. Now, the abstract only emphasizes that "it is essential to focus on a lifespan approach and increase inter-organisational working, which is expected to improve outcomes for this complex group." (The latter part of the sentence is rather speculative.)

Reply: The consensus generated 53 specific guidelines. We have removed the last two paragraphs and amended the text to include key issues of concern and need. We then direct the reader that specific guidance can be found within the main body of the text: "Discussions highlighted inter-service barriers and fragmentation of care. It was concluded that a multimodal and multi-agency approach is needed. The consensus concluded with a table of practice recommendations providing guidance on: identification and assessment; pharmacological and psychological treatment; and multi-agency interventions".

8. Introduction L. 152 mentions physical comorbidities only in passing, but these should probably be detailed as they may be an important part of the ADHD-SUD picture. For instance, physical comorbidities (such as cerebral palsy) may severely affect work options/income and social integration.

Reply: Thank you for drawing our attention to this literature. We did not know of the Pahlman manuscript reporting that 30% of children with cerebral palsy were diagnosed with ADHD (and a 30% with autism). This is interesting data and we have added the reference. We are reluctant to include a discussion about the relationship between ADHD and physical comorbidities however as the focus of the paper is on the relationship between ADHD and substance use. The manuscript is already very long.

9. The authors could be more explicit about the patient population they describe. From Table 2 one has to assume that they are disheveled, fatigued, red-eyed etc., but this is not clearly stated anywhere.

Reply: When directing the reader to Table 2 which details this information, we have given greater context: "Typically this is a decline in self-care, physical and/or mental health, and daily functioning, often associated with social and occupational problems. Table 2 details several markers….."

10. L. 165: "Hence individuals with comorbid ADHD and SUD present with a complex presentation, which may complicate identification and treatment…" Change to "Hence,

the presentation of individuals with comorbid ADHD and SUD is complex; this may complicate identification and treatment…" or equivalent.

Reply: Done

11. Methods L. 264: Change the sentence to avoid implying that the consensus reflects the research published by the authors, e.g.: "The consensus is based on published research, but it also reflects the views of the authors based on their practical experience".

Reply: Thank you. Done.

12. State who the medical writer was and who the lead author is.

Reply: The initials of Kelly Cocallis (medical writer) and Susan Young (lead author) have been added to the penultimate paragraph in the methods section.

13. Results The first subheading (l. 271) announces that the following section will be on illicit substances and reasons for their use in ADHD. These topics should be handled in separate sections.

Reply: In response to reviewer's feedback, we have made a lot of changes to this section. Given the changes, as we felt this flowed better as one section. We have amended the title slightly to "Substances and reasons for their use by people with ADHD". These amendments, together with those mentioned below, have also reduced the number of references.

14. Additionally, instead of focusing on the substances themselves, this section begins with a distinction between illicit use of prescribed and non-prescribed substances (including energy drinks), which this reader found confusing and not wholly fluent (energy drinks as SU?). The two first sentences (l. 273-278) could be removed or reused in a separate section further down.

Reply: We decided to delete this section.

15. This also goes for the discussion of nicotine (+ Fig. 1), which is not an illicit drug, prescribed by an MD or not, and it applies to vaping, which could be a health issue, but is not relevant to SUD.

Reply: We amended the title to 'substances' rather than 'illicit substances'. We therefore mention that alcohol and nicotine are the most commonly used recreational substances before going on to state that cannabis and stimulants are commonly used illicit substances. We therefore did not exclude nicotine from Figure 1. We have deleted mention of vaping.

16. L. 283: The sentence "Stimulant use such as cocaine, amphetamines and metamphetamine (Ice) has also been reported;" is awkward, and so is the continuation:

"among adults with ADHD a recent meta-analysis of studies from several countries found the prevalence of cocaine use to be around 26% and cocaine use disorder 10%."

Reply: This has been revised to "Stimulants such as cocaine, amphetamines and metamphetamine (Ice) are also common [59,60]; a meta-analysis reported the prevalence of cocaine use in adults with ADHD to be around 26%. Ten percent had cocaine use disorder[61]"

17. How "cultural factors" (L. 288) translates into "high rates of sedative use among young people with ADHD (…) in France and Iceland", whereas "in Turkey (…) the most frequently used substance" is amphetamine/ methamphetamine remains obscure. Geographical differences in substance use could be a separate section.

Reply: We have deleted this text.

18. Beginning on l. 294, an argumentative streak appears: self medication is unlikely to explain SUD in ADHD.

Reply: In order to not appear argumentative, we have amended this text to clarify that many people with ADHD provide this feedback and state there is no robust empirical evidence to support this stance. "Various reasons have been proposed for SU among individuals with ADHD. Individuals with ADHD often claim that, prior to their diagnosis, they used substances as a form of self-medication to attenuate ADHD symptoms and associated impairments. However, there is no robust empirical evidence to support this proposal [64-66]"

19. Beginning on l. 306, the association between ADHD per se and SUD is severely doubted: conduct/oppositional defiant disorder explains the association.

Reply: We have revised the text to clarify this point. "Adolescents and adults with ADHD have high rates of comorbidity with other conditions, many of which are associated with increased risk of SU. Conduct disorder (CD) and oppositional defiant disorder (ODD) may explain the association [70-72]."

20. And, beginning on l. 318, "one theory explaining the link between ADHD and SU/SUD that gained a lot of interest" is presented, namely "sensitisation through the use of stimulant medication (77)". The authors fail to mention that this is a study done by themselves. These various points are discussed in a manner that render them obsolete, e.g. (l. 324): "There is little evidence from human studies to support the sensitisation hypothesis; most studies either demonstrate a protective effect or no effect of early stimulant use on later SU among those with ADH." Why then forward a "sensitization hypothesis" or "theory"? L. 298:

Reply: The reference given (77) is not the correct reference, it should be reference 66 (Young and Sedgwick), which is still led by the lead author. but it is a review of the literature reporting causal hypotheses. However, the reviewer makes a helpful point and we have removed this paragraph from the section.

21. Is ref 65 (Hall & Queener) relevant for ADHD?

Reply: We have deleted this from the reference list.

22. Compare the statement on l. 294 (self medication is unlikely to explain SUD) to l. 428: "Substances may have a countering effect for individuals with ADHD which should be taken into consideration…"

Reply: The first statement has now been amended (see 18 above) and we have amended the second statement to "Some individuals report that substances have a countering effect on their ADHD symptoms….". The statements are now more consistent.

23. And compare the statement on l 318 (sensitization theory) to l. 524: "Historically there have been concerns regarding prescribed stimulant medications' abuse potential, addictive nature, or that they may worsen a pre-existing SUD. These concerns are unfounded."

Reply: We believe that the point being made above (at the beginning of the pharmacological section) is important to acknowledge. Historically there have been concerns that stimulant medication is a pathway to increased SU, addiction and abuse. We go on to refute these concerns. The sensitisation hypothesis paragraph has been removed from the manuscript (see 20 above).

24. See also l. 554ff.

Reply: We have rewritten this sentence to state "It is essential that individuals with ADHD and SU/SUD are not deprived of effective treatments with medication".

25. L. 440: Rewrite difficult sentence: "Considering the elevated prevalence of ADHD and SUD comorbidity, when the individual already has a primary diagnosis of ADHD, they should be carefully monitored for SU."

Reply: This has been revised to "Individuals who already have a primary diagnosis of ADHD should be carefully monitored for SU".

26. L. 416 "diagnosis" is missing: "may be lower in females) which may result in missed or misdiagnosis."

Reply: Done.

27. Please scrutinize and revise the rest of the manuscript.

Reply : See response to (1) and (5) above