

Reviewer 1 v.1

#### Comments to the Author

This manuscript addresses a review for a randomized placebo-controlled trial regarding the pharmacological intervention with among patients with nicotine dependence. Generally, I have several major concerns listed as following:

1. To date, there are several reviews regarding as the efficacy of medications for nicotine use disorder, so you should point out the novelty or new information provided in your review.
2. The searching strategy is entirely missing in the text. Please add one section to address it. The sentence “we describe the molecular basis of nicotine addiction and review approved drugs and currently investigated clinically relevant agents based on the Cochrane Database of Systemic Reviews, PubMed, Ovid, and Clinical-Trials.gov to aid understanding” is insufficient for readers to understand if your searching strategy is appropriate.
3. In order to fit the scope of this journal, I suggest authors add additional paragraph to address the hazardous effect of smoking on respiratory disease, such as COPD, asthma....,etc. Maybe authors can shorten the description of other medical conditions, such as gastro-intestinal disease.
4. There are several vague statements repeatedly shown, such as the phrases “abstinence prevalence”. Please have somebody familiar with English grammar and spelling edit the manuscript.

The remaining minor concerns are as following:

1. Provide more updated data about the prevalence of nicotine use in the first paragraph of introduction
2. The second paragraph of introduction is too short, and I suggest to combine into the first paragraph.
3. Cite the reference for the sentence “The World Health Organization (WHO) estimates that, worldwide, tobacco accounts for 9%....”.
4. Cite the reference for the sentence “Prochaska et al. proposed a “stage model of behavioral change”....” in the second paragraph of Guidance for smoking cessation.
5. Since your topic is “pharmacological treatments”, I suggest authors should simplify the sentences of psychological intervention at page 8 to 10.
6. Add “nicotine replacement therapy” at the first abbreviation of “NRT” at page 11.
7. Cite the reference for the sentence “NRT is contraindicated in nonsmokers as well as in people with unstable angina, acute myocardial infarction, severe arrhythmias....” at page 11.
8. Cite the reference for the sentence “Side-effects of intraoral problems, sore throat, and stomach pain have....” at page 12.
9. Replace phrase of “smoking desire” into “craving” in the page 12.

10. Again, at page 12, I am confused about the sentence “If the symptoms of acute nicotine addiction appear”. Do you mean “acute nicotine intoxication”?
11. Add additional paragraph to address the efficacy of nicotine inhaler. It`s also commonly used during clinical practice.
12. Cite the reference for the sentence “Bupropion has been approved for the treatment of major depressive disorder and seasonal affective disorder” at page 13.