

## Peer Review File

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### Reviewer A

This manuscript is a very well written comprehensive review of e-cigarettes with an emphasis on the use and impact of e-cigs among childhood cancer survivors. This is an extremely important topic with little research in the area.

It is very comprehensive, covering basics of e-cigarette components, how they differ from conventional cigarettes, trends in use of e-cigs among AYA, and covers the limited data available on e-cig use on hematopoiesis and cancer.

The authors thank Reviewer A for reviewing our manuscript and pointing out the importance of the topic. We agree that our review is unique in the topics that it covers and highlights what is known in regard to electronic cigarette use and the impact on leukemogenesis.

I have limited critiques, the only very minor critique:

Line 185 – states 8 out of 10 middle/high school students use flavored e-cig. This is incorrect, the ref says “approximately eight in 10 middle and high school students who used e-cigarettes reported using flavored e-cigarettes”

Thank you for catching this oversight in the text. We have edited the manuscript to cite the reference more accurately. The sentence now states, “In 2020 and 2021, approximately eight out of ten middle/high school students who use electronic cigarettes use a flavored version.”

### Reviewer B

This article examined e-cigarette use among leukemia patients and its effects on long-term outcomes. The study reviewed existing literature and studies that summarizes the current state of research on e-cigarette use and leukemia.

This article provides important findings that can improve the long-term health of patients with leukemia. This study supports the need for future research to be done in this specific patient population. This research can then be used to tailor clinical strategies to a very specific adolescent cancer patient population that is at high risk in regards to e-cigarette use.

Overall this is a well-written and thorough review of the literature, and will provide a very important contribution to the field that can directly inform clinical practices and interventions. I just have a few comments for improvement and consistency.

The authors would like to thank Reviewer B for the thorough review of our manuscript and providing suggestions to strength our statements and clarity. We appreciate that Reviewer B

acknowledges the important findings covered in our review and how they may impact our pediatric and AYA population.

#### Introduction

1. Page 3 Line 69 – Please cite the “few studies” you reference here

Thank you for the suggestion to add in additional references. We have now included 3 new citations and believe this adds strength to our sentence.

2. Page 4 Line 80 – Please cite your statement about the risk for psychosocial disorders

We added in the reference for our statement about the risk for psychosocial disorders. This is now included as reference #7. Thank you for catching this!

3. Page 5 Line 91 – missing the word “cigarette”

Thank you for finding this word to be missing. We have double checked this sentence to make sure the word cigarette is included, and the sentence reads more clearly.

4. Page 5 Line 92 - Can you include a more clear “purpose of this review article” statement at the end of your introduction?

We appreciate the suggestion to revise the wording in our introduction to improve its clarity and have added the suggested sentence.

5. Throughout the introduction (and entire paper), you use youth, YA, AYA, and pediatric and AYA all interchangeably. I would just pick one term/abbreviation and use it throughout the entire manuscript for consistency. Or clearly define what age groups, etc. you mean with each of those terms.

Thank you for pointing out this and suggesting we define the groups more clearly. We have edited the manuscript to state AYA throughout the paper. Also, pediatrics and AYA are now defined in introduction paragraph number 3.

#### Electronic cigarettes

6. Page 8 Line 148 – Please provide citations for each sentence in this paragraph about cigarettes

Thank you for noticing this, we have added the appropriate reference.

#### Trends in electronic cigarette use

7. Page 10 Line 178 – you use “e-cigarette” here for the first time. Keep consistent if you are spelling out “electronic cigarette” throughout the rest of the manuscript

To stay consistent, we have updated the manuscript text to “electronic cigarettes” and removed “e-cigarettes”.

8. Page 11 Line 183 & 185 – Please be consistent with whether you spell out numbers or not throughout the manuscript

A. Numbers up to and including ten should be spelled out in full. Numbers after and including 11 should be written using numerals

Thank you for catching this inconsistency in spelling out numbers compared with writing them numerically. We have gone through the manuscript and updated all numbers less than or equal to 10 to be spelled out, and those greater to be written in numerals. We appreciate this suggestion.

9. Page 11 Line 184 – again be consistent throughout the manuscript with whether your abbreviate or spell out “United States”

We have edited the manuscript text to stay consistent with spelling out United States. Thank you for helping us improve the consistency in our text.

Electronic cigarettes and the potential risk of leukemogenesis

10. No comments here, this is a very interesting review of the literature specific to cancer risk. Thank you for the review of this section. We agree that this information regarding electronic cigarettes and the risk of cancer is very interesting and relevant to our young patients.

Electronic cigarettes, late, effects, and survivorship

11. Page 17 Line 286 – What do you mean by “particularly significant”?

Thank you for noticing this, we have added the appropriate reference.

12. Page 18 Line 303 – “Thus” may not be the right word here

We updated this sentence to read “Preliminary studies show that chronic electronic cigarette use impairs endothelial function and is concerning for late cardiovascular damage.” Thank you for this suggestion to replace the work “thus”.

13. Page 18 Line 305 – should be a comma instead of a period after the [50] citation

Our punctuation mark has been corrected to a comma instead of a period. We are grateful for this correction which improves how the sentence reads.

14. Page 18 Line 308 – Citation for this sentence?

Thank you for noticing this, we have added the appropriate reference.

15. Page 19 Line 317 – Citation for this sentence?

Thank you for noticing this, we have added the appropriate reference.

16. Page 19 Line 320 – Citation for this sentence?

Thank you for noticing this, we have added the appropriate reference.

17. Page 19 Line 321 – Spell out/define “ROS”

Thank you for finding this undefined word in our manuscript. We have now defined ROS as reactive oxygen species at its first mention on page 8 line 149 (or in **Chemical composition of electronic cigarettes** “A complex mixture of combustion products, cigarette smoke can include more than 7,000 different chemicals and up to  $1 \times 10^{17}$  free radicals, including both reactive oxygen species (ROS) and reactive nitrogen species<sup>18, 24</sup>”).

## Conclusion

18. No comments, excellent takeaways from your literature review!

Thanks again for your careful review of our manuscript!