

Final Summary Report

External Letter Peer Review of FDA's

Scientific Assessment of the Impact of Flavors in Cigar Products

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Prepared for:

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I. INTRODUCTION

Versar, Inc. (Versar), an independent Food and Drug Administration (FDA) contractor, coordinated an external letter peer review of FDA's scientific assessment of the impact of flavors in cigar products. The peer review was conducted for FDA's Center for Tobacco Products.

In general, FDA may pursue product standards related to reducing the appeal, toxicity, or addictiveness of tobacco products. Specifically, section 907 of the Federal Food, Drug, & Cosmetic Act (FD&C Act) (Pub. L. 111-31) authorizes FDA to issue tobacco product standards that are appropriate for the protection of the public health, including provisions that would require the reduction or elimination of a constituent (including a smoke constituent), or harmful component of tobacco products and provisions respecting the construction, components, ingredients, additives, constituents (including smoke constituents), and properties of the tobacco product (section 907(a)(3), (a)(4)(A)(ii), and (a)(4)(B)(i) of the FD&C Act).

In accordance with its statutory authority under section 907 of the FD&C Act, FDA completed a scientific assessment evaluating the impact of flavors in cigar products.

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II. CHARGE TO REVIEWERS

FDA has completed a scientific assessment evaluating the impact of flavors in cigar products. The completed document, entitled “Scientific Assessment of the Impact of Flavors in Cigar Products,” presents a synthesis of scientific evidence regarding the role that characterizing flavors play in increasing the appeal and use of tobacco products, particularly cigars, among youth, young adults, and adults in the United States.

Charge Questions

Please provide written responses to the following questions:

1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.
2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.
3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.

III. INDIVIDUAL REVIEWER COMMENTS

A. Reviewer #1

Scientific Support Document(s) for Potential Tobacco Product Standards: Flavored Cigars

Reviewer #1

Scientific Assessment of the Impact of Flavors in Cigar Products

I. GENERAL IMPRESSIONS

The *Scientific Assessment of the Impact of Flavors in Cigar Products* is a comprehensive review of the available literature. Overall, the conclusions stated for each question are sound and supported by the presented evidence. The organizational structure of the document is appropriate and easy to follow. Many studies included in the current review report complex outcomes and analyses from longitudinal surveys with multiple age categories. In general, the review does a good job providing an appropriate level of detail and information about these complex studies.

The prevalence section at the beginning of the document highlights the importance of the three questions being examined in the current review. The disparities section emphasizes the need for policies targeting flavored combusted tobacco products, including cigars, to reduce commercial tobacco use among priority populations like Black and African American persons and members of the LGBTQ+ community. Including both behavioral outcome data and sales data provides converging evidence about the impact of flavored tobacco product restrictions or bans. The section about flavors in food science also contributed meaningful information about how youth and adults differ with respect to flavor appeal.

The review could be improved by adding more detail within the main text about the inclusion and exclusion criteria for studies rather than reporting this information exclusively in the appendices. For example, “studies employing exclusively animal models” should be excluded from the review based on the eligibility criteria listed in Appendix 1. However, there is a subsection on abuse liability for Question 1 that includes studies with animal models. Are these animal studies part of the literature review or providing explanatory information? Additionally, figures displaying the article selection process for each question would also be useful to include.

Finally, throughout the document there are often very long sentences and paragraphs. Many studies report multiple outcomes by flavored tobacco product use, overall tobacco use, cigar use by subtype, age category, etc., so I would recommend trying to simplify sentence structures and breaking up paragraphs to enhance readability. The positive spin to this critique is there is a substantial amount of evidence supporting regulations for flavored tobacco products, including cigars, presented in this review.

II. RESPONSE TO CHARGE QUESTIONS

1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.

Question 1: How Does the Addition of Characterizing Flavors to Tobacco Products, Including Cigars, Impact Product Appeal and Product Use? – The conclusions that characterizing flavors in tobacco products increases appeal and ease of use, especially among youth, is supported by the literature reviewed in this section. This section had an exhaustive

review of the literature ranging from qualitative research to nationally-representative longitudinal surveys. Clinical research supports the conclusion that flavors contribute to increased abuse liability for tobacco products. In focus groups, youth often cite flavors as appealing and the reason for use. Analyses from the PATH survey found that flavors are the primary reason youth use cigars. Finally, four systematic reviews also report that flavors are appealing to youth and contribute to experimentation and progression to regular use. Overall, the review appropriately concludes that flavors in tobacco products appeal to youth.

Question 2: How Do Characterizing Flavors Impact Youth and Young Adult Experimentation with Tobacco Products, Including Cigars, and Do They Make Progression to Regular Tobacco Use More Likely?

– The conclusion that characterizing flavors are associated with increased likelihood of experimentation and progression to regular use is supported by the literature reviewed in this section. Two qualitative studies and one systematic review highlight the appeal of flavors among youth and young adults who use cigars. Several strong, longitudinal studies using nationally-representative samples find that experimentation with flavored tobacco products is associated with subsequent tobacco use. Evidence also suggests that experimenting with cigars can lead to nicotine dependence, which is associated with sustained tobacco use.

Question 3: What Impact Do Local Policies Restricting the Sale of Flavored Cigars and Other Flavored Tobacco Products Have on Cigar Sales and Use? – The conclusion that sales of flavored cigars and cigars overall decreased after flavored tobacco restrictions or bans is supported by the literature. This section reviewed sales data after flavored tobacco policy implementation in several municipalities in the US and Canada. Most studies reported significant reductions in sales of flavored tobacco products, including cigars; however, some studies observed increases in concept flavor sales following the flavored tobacco restrictions or bans, indicating some product switching.

The conclusion that reductions in youth use of flavored tobacco products also decreases after flavored tobacco restrictions or bans is also supported by the literature. Most studies across jurisdictions with flavored tobacco restrictions or bans (NYC, Providence, Lowell, Minneapolis, St. Paul and Canada) reported decreases in youth use after the ban. However, evidence from San Francisco suggests potential product substitution among youth after banning flavored tobacco products. Friedman, 2021 reported increases in cigarette smoking among high school students in San Francisco post-ban. Importantly, the study does not report changes in flavored tobacco use or overall tobacco use, so caution should be used when interpreting these findings with respect to tobacco use behavior among youth.

2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

There are publications about retailer compliance for selling and advertising flavored and menthol tobacco products after flavored tobacco policy restrictions in Minnesota and Massachusetts that could be included under Question 3. Although the studies do not report explicit sales figures for cigar products, they report observed changes in product availability in retail stores in the affected jurisdictions. According to the study eligibility criteria listed in Appendix 1, retailer compliance

studies are not explicitly excluded from the review. However, if such studies are not appropriate for inclusion in this review, then the eligibility criteria should be revised accordingly.

D'Silva et al., 2021 examined sales restrictions for menthol tobacco products in four Minnesota cities (Minneapolis, St. Paul, Duluth, and Falcon Heights). The authors used the Standardized Tobacco Assessment for Retail Settings (STARS) tool to examine sales and advertising of menthol tobacco products in retail stores. They assessed compliance rates of stores in cities with menthol tobacco policies versus comparison cities without menthol tobacco restrictions. They found significant reductions in the availability of menthol tobacco products across grocery/convenience stores and gas stations.

D'Silva J, Moze J, Kingsbury JH, et al. Local sales restrictions significantly reduce the availability of menthol tobacco: Findings from four Minnesota cities. *Tobacco Control* 2021;**30**:492-497.

Brock et al., 2019 examined sales restrictions for flavored tobacco products in Minneapolis and St. Paul. They found reductions in the availability of flavored tobacco products in retail stores with youth-access but the proportion of unflavored tobacco products increased after the policy.

Brock B, Carlson SC, Leizinger A, et al. A tale of two cities: Exploring the retail impact of flavoured tobacco restrictions in the twin cities of Minneapolis and Saint Paul, Minnesota. *Tobacco Control* 2019;**28**:176-180.

Kephart et al., 2020 examined sales restrictions for flavored tobacco products in Boston, Massachusetts. They found most retailers were compliant and access to flavored tobacco products in youth-accessible stores declined significantly after the policy

Kephart L, Setodji C, Pane J, et al Evaluating tobacco retailer experience and compliance with a flavoured tobacco product restriction in Boston, Massachusetts: Impact on product availability, advertisement and consumer demand. *Tobacco Control* 2020;**29**:e71-e77.

3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.

Under Question 1, there is a subsection called “systematic reviews on appeal, use and progression to regular use of tobacco products.” The content reported in this section could also belong under Question 2 since that is addressing experimentation and progression to regular use. It may be worth including another short section under Question 2 briefly restating the findings from the systematic reviews reported under Question 1.

For the Minneapolis and St. Paul, Minnesota flavored tobacco restrictions, the policies allow flavored tobacco product sales to adult-only venues, like tobacco and alcohol retailers (<https://www.publichealthlawcenter.org/sites/default/files/resources/US-sales-restrictions-flavored-tobacco-products.pdf>). This should be explicitly stated in the study description narrative on page 25.

PATH Study Memo and PATH Study Online Tables have placeholders in the reference section. Since I was not able to examine these documents, I cannot verify their content or accuracy.

The citations Palmatier et al., 2013 and Palmatier et al., 2020 are missing from the reference list. Please review all cited to work to ensure they are included in the reference list.

One minor suggestion is to include an abbreviations list at the beginning of the review document.

III. Specific Observations on FDA's *Scientific Assessment of the Impact of Flavors in Cigar Products*

Page	Paragraph	Comment
4	1	Typographical error in the third sentence: "...by non-Hispanic Black high school students as twice as high..." – the first 'as' should be 'is'
4	1	Revise to say 'high school student' instead of "high schooler" in the second sentence.
4	1	Add 'persons' or 'individuals' after Whites or African Americans in this paragraph.
6	2	Add 'persons' or 'individuals' after Whites, Blacks, Hispanics or African Americans in this paragraph
6	2	Black non-Hispanic is used in sentence two but non-Hispanic Black is used elsewhere in the paragraph. Revise for consistency.
6	3	The last sentence on the page has inconsistent reference formatting for the Hinds citation.
7	3	The second sentence has the citation, Johnson et al., 2019, listed twice.
8	2	The second sentence requires a citation.
9	2	Consider revising the two, long sentences in this paragraph into shorter, more concise sentences to enhance readability.
12	5	Consider dropping the Kool Aid brand name for drink mixes since the authors did not include brand names for candy.
13	1	Typographical error in the second sentence: "...flavors area a leading..." should be 'are'.
14	3	The third paragraph is comprised of one long sentence. Consider revising into shorter, more concise sentences to enhance readability.
16	1	Capitalize the 'w' in Wave 2
16	5	Villanti et al., 2020 – Does this paragraph refer to any cigar use or should there be differentiation by cigar subtype?
17	2	Consider separating this paragraph into two shorter paragraphs since the content is quite dense. The break could be before "Youth who first used..."
17	2	Potential typographical error: "Youth who had first used a flavored cigar other than menthol or mint had a significantly higher prevalence of past 30-day cigarillo use compared to those who first used a non-flavored cigarillo (aPR 1.58; 95% CI: 1.02, 2.43)." Should the underlined word be cigarillo rather than cigar?
17	3	Should the word "traditional" be the descriptor included before each instance of cigar in this paragraph?

Page	Paragraph	Comment
18	2	What does “ delayed past 30-day users” mean?
18	3	Consider separating this paragraph into two shorter paragraphs since the content is quite dense. The break could be before “Researchers analyzing data from the...”
18	3	The last sentence in the paragraph is quite long. Consider revising into shorter, more concise sentences to enhance readability.
19	2	The last sentence in the paragraph is quite long. Consider revising into shorter, more concise sentences to enhance readability.
22	1	The last sentence in the paragraph is quite long. Consider revising into shorter, more concise sentences to enhance readability.
24	2	Typographical error in the fifth sentence: “...current user of flavored cigars...” should be ‘use’
24	3	Possible typographical error: Should it be Difference-in-differences with the second difference plural?
25	2	In the second sentence, consider clarifying what products are included in the regulations, such as e-cigarettes and menthol cigarettes (if accurate).
26	2	No limitations are reported for Yang et al., 2020’s manuscript.
26	3	Does active implementation mean policy enforcement? If so, consider revising for clarity.
31	2	Avoid use of contractions: revise to ‘did not’ in the fifth sentence.
32	4	There is an extra parenthesis in the second sentence.
33	2	Why does the 2009 NTYS data have the descriptor of “Spring 2009” when all others are just the year?
35	1	The first sentence has the citation, Rostron et al., 2019, listed twice.
35	1	Typographical error in the third sentence: “...then utilize PATH Study data...” should be ‘utilized’ (past tense).
43	References	<i>[Placeholder for National Youth Tobacco Survey Memo (2021)]</i> - This citation is included in the reference list but I did not see it in the main document.
51	Appendix 2	The citation format for the appendix is different from the main document. Consider revising for consistency.
56	Appendix 3	Effective or Enforcement Year is a more accurate column title than Effective or Enforcement Date.
57	Canada row	Spell out minimum vs min
62	Last row	Capitalize Black

B. Reviewer #2

Scientific Support Document(s) for Potential Tobacco Product Standards: Flavored Cigars

Reviewer #2

Scientific Assessment of the Impact of Flavors in Cigar Products

I. GENERAL IMPRESSIONS

The overall impression of this information is that this is a rigorous literature review. Methodology for the review is appropriate and comprehensively included most relevant documents. The material for each section was presented clearly and comprehensibly. The documents show that the addition of flavors to tobacco products including cigars can reinforce the effects of nicotine, can increase abuse liability, that flavors appeal to youth and that this is consistent with the role of flavors in food. The document also shows that flavors are a reason for youth to start using cigars, and are associated with progression to regular use and nicotine dependence.

The document also presents data from evaluations of local restrictions. The soundness of the conclusions would also be improved by a specific section for a discussion on enforcement and compliance. The effectiveness and impact of a ban will rely on enforcement and compliance and consequently, this should be highlighted and evaluated carefully to make recommendations for policy.

Most conclusions for each document and the underlying data were sound. However, the primary overall concern is the conflation of three different definitions of flavors. While concept flavors are discussed, the issue is broader and affects all sections. Flavors can be characterizing, ingredients (which could, but not necessarily, lead to a characterizing flavor) or labelled. Each of the studies included may be responsive to one or two of these definitions, but not necessarily characterizing flavors. The definitions used by each study are needed and the conclusions associated with that definition.

II. RESPONSE TO CHARGE QUESTIONS

1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.

Overall, the conclusions of each of the sections were scientifically supported with the following exceptions below.

The document across all of the sections, even including the section on concept flavors, uses characterizing flavors to describe these. Generally, pre-clinical studies assess ingredients and other types of studies vary. For instance, Chaiton (2018) assessed labelled flavor, not ingredients or presence of characterizing flavor. Or on page 155, tobacco flavored Black and Milds may still have non-characterizing flavor ingredients, but are unlabeled. Relatedly on page 12, for ENDS tobacco flavored are flavored—i.e., have flavor ingredients. For appendix 2, reference to concept flavor can also include the experience in Ontario, in which alcohol labels were used as concept flavors (i.e., wine replacing berry labelling) (Chaiton 2018). I would recommend that the definition of characterizing flavors, ingredients, and labelled flavor be provided upfront and be

clear for each identified study which is being assessed or discussed. Conclusions may depend upon these definitions.

For Question 2, page 19 on the discussion of attention and impulsivity, data on the familial confounding can be cited. For instance: Skoglund C, Chen Q, D' Onofrio BM, Lichtenstein P, Larsson H. Familial confounding of the association between maternal smoking during pregnancy and ADHD in offspring. *Journal of Child Psychology and Psychiatry*. 2014 Jan;55(1):61-8.

2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

Bosma LM, D'Silva J, Moze J, Matter C, Kingsbury JH, Brock B. Restricting Sales of Menthol Tobacco Products: Lessons Learned from Policy Passage and Implementation in Minneapolis, St. Paul, and Duluth, Minnesota. *Health Equity*. 2021 Jun 1;5(1):439-47.

This paper assesses implementation challenges from Minnesota.

Chaiton M, Schwartz R, Cohen JE, Soule E, Zhang B, Eissenberg T. Prior Daily Menthol Smokers More Likely to Quit 2 Years After a Menthol Ban Than Non-menthol Smokers: A Population Cohort Study. *Nicotine & Tobacco Research*. 2021 Mar 10.

Two year data with 6 month abstinence quit definition of effects in Ontario for cigarette but also shows the impact of substitution of other flavored products on likelihood of quit success.

Chaiton MO, Schwartz R, Cohen JE, Soule E, Zhang B, Eissenberg T. The use of flavor cards and other additives after a menthol ban in Canada. *Tobacco control*. 2021 Sep 1;30(5):601-2.

Assesses impact of availability of flavor cards (and other menthol additives) on successful quitting after the ban in Ontario. Flavor cards can also be used for other tobacco products particularly waterpipe.

Denlinger-Apte RL, Cassidy RN, Carey KB, Kahler CW, Bickel WK, O'Connor R, Thussu S, Tidey JW. The impact of menthol flavoring in combusted tobacco on alternative product purchasing: A pilot study using the Experimental Tobacco Marketplace. *Drug and Alcohol Dependence*. 2021 Jan 1;218:108390.

Experimental marketplace study showing that menthol little cigars and vapes were significant substitutes.

Borland T, Dubray J, Chaiton M, Schwartz R. Monitoring and Evaluating Ontario's New Tobacco Policy Measures: Flavored Tobacco Prohibition. Toronto, ON: Ontario Tobacco Research Unit, September 2017. Available at: https://otru.org/wp-content/uploads/2017/08/special_nm_flavors_2017.pdf

Report on the implementation of the flavored cigar ban. Includes assessment of challenges such as relabeling, new products that attempt to find exemptions, and products that are not marked as flavored but appear to be. Also shows lack of public awareness and challenges in enforcement.

Silver KK, Hiscock R. Tobacco industry tactics to circumvent and undermine the TPD menthol ban in the UK. *Tobacco Prevention & Cessation*. 2020 Oct 22;6(Supplement).

Branston JR, Hiscock R, Silver K, Arnott D, Gilmore AB. Cigarette-like cigarillo introduced to bypass taxation, standardized packaging, minimum pack sizes, and menthol ban in the UK. *Tobacco Control*. 2021 Nov 1;30(6):708-11.

These two papers include assessment of the use of menthol flavored cigarillos to circumvent the menthol tobacco ban.

3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.

My primary suggestion would be specifically to discuss the challenges with enforcement as a separate section. Some of this detail can be found occasionally when mentioned by some articles, but there is additional literature (see above) and additional detail within existing studies. The effectiveness and impact of a ban will rely on enforcement and compliance and consequently this should be highlighted and evaluated carefully to make recommendations for policy.

A second issue to highlight is the impact of flavor tobacco bans on the effectiveness of menthol cigarette bans. The Canadian ban and other local bans on menthol were in the context of the flavor cigar bans and availability of menthol cigars may affect the effectiveness of the menthol restrictions in cigarettes so that these issues must be considered in conjunction, particularly for little cigars and cigarillos. Some citations are provided above.

In the methodology it should be clarified that research prior to 2010 was eligible for inclusion.

There should be discrimination between studies that use longitudinal pre-post designs vs cross-sectional re-post designs (e.g. Chaiton 2020 is longitudinal while Chaiton 2018 is a cross sectional time series) as the former allows for control of within-person characteristics especially compared to cross-sectional population surveys.

Product substitution is discussed.

III. Specific Observations on FDA's *Scientific Assessment of the Impact of Flavors in Cigar Products*

Page	Paragraph	Comment
36	3	Final paragraph is missing citation to the discussed study

C. Reviewer #3

Scientific Support Document(s) for Potential Tobacco Product Standards: Flavored Cigars

Reviewer #3

Scientific Assessment of the Impact of Flavors in Cigar Products

I. GENERAL IMPRESSIONS

Overall, the review accurately presents the information of *reviewed* studies and the conclusions are largely in line with my own reading of the literature. Conclusions that flavors in cigars contribute to appeal, initiation, and experimentation and that flavor restrictions on cigars lead to reductions in sales and youth use are generally well supported. In particular, the review of the evaluation literature on flavor policies in various localities is thorough and does a good job of pointing out study limitations given the wide heterogeneity in this literature. However, as a comprehensive review of the published literature in this area there are some significant gaps in the review as detailed extensively below. Inclusion of missing studies and newer studies would strengthen the conclusions of this document. Lack of inclusion of these studies makes the evidence base weaker than would otherwise be the case.

Overall changes that would strengthen the document include the following. Where possible, young adults should be separated out from youth and adults 25+. It would be clearer to understand use patterns if data on use patterns over time by age and race/ethnicity was included as graphs rather than just including prevalence estimates from the most current data wave. Cigar use appears to be increasing over time which is not easily determined from the cross-sectional data. A more nuanced discussion of disparities in cigar use could include literature on gender, mental health, substance use, and medical co-morbidities and a broader discussion of differences by race/ethnicity beyond Black/White differences would provide a fuller picture of the potential health equity impacts of a flavored cigar ban. Where possible, more data on cigar cessation patterns over time would be useful. Discussion of flavored blunt use is missing. The discussion of ‘concept flavors’ should be incorporated into the main document as this is likely to be a significant area where implementation of flavored cigar bans will face challenges in practice. Finally, the impacts of flavored cigar bans should be clearly noted in relation to the comprehensiveness of flavor policies and the extent of compliance with implementation. Additional specific recommendations are listed below.

II. RESPONSE TO CHARGE QUESTIONS

1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.

Conclusions for question 1 and 2 are supported but I suggest breaking out conclusions by youth vs. young adults. Flavors are also used to appeal to young adults and the evidence for this should be separated out from the youth data. The conclusions also state that adolescence is a critical time period for tobacco use experimentation which is true but initiation of tobacco use and experimentation is increasingly moving into the young adult years. This is particularly true for African American young adults who disproportionately use flavored cigars. For this group young adulthood is a time when lower youth substance use patterns “cross over” to higher use prevalence compared with White tobacco users (e.g., Watt, 2008 The race/ethnic age crossover

effect in drug use and heavy drinking. *Journal of Ethnicity in Substance Abuse*). Additional discussion of young adulthood as a time of initiation/experimentation would strengthen this conclusion, particularly in relation to disparities.

Conclusions for question 3 are supported but rely on a limited evidence base – additional potentially relevant papers are listed below. The studies included discuss reduced sales and reduced youth use, but omit papers on reduced retail availability (i.e., retail compliance papers) and policy impact on reduced flavored advertising. As this is a fast-moving area, continuing to monitor the literature will be critical. Additionally, the paper on modeling the effects of this policy (pages 35-36) should be reviewed in more detail to actually detail the main morbidity and prevalence reduction estimates from this study (i.e., number of reduced deaths, number of fewer cigar smokers). The San Francisco studies should also be more clearly noted as the impact of a comprehensive flavor ban and not simply a ban on flavored cigars. For instance, the potential substitution effect with smoking in the Friedman 2021 by the author’s own discussion is likely due to the inclusion of flavored vape products not because of a ban on flavored cigars. Additionally, San Francisco also banned all e-cigarette sales in 2019 with enforcement starting Jan 29 2020 which may have had some effects beyond flavor restrictions. While there is likely to be substitution with existing (non-banned) products, the conclusion is based specifically on San Francisco data and should have these caveats or should be broadened.

2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

1. Additional potential references are shown below (but are not comprehensive). General types of missing information are listed.
2. The focus on only use estimates from the current waves of PATH, NYTS, NSDUH and other national datasets obscures changes over time from recent prior waves especially in longitudinal datasets. Including discussion of the data on cigar and flavor use from prior waves would help to highlight how both the policy environment, secular trends, and changes in the tobacco product marketplace may influence flavor use and cigar use more broadly and provide a fuller picture of how these elements may be changing. Additionally, in addition to a table in appendix 5, a graph of the PATH study prevalence estimates over time would be helpful.
3. Additionally, papers on any tobacco use that separate out flavor use or use patterns by product (including cigar use) are generally not included and could provide good information on cigar use patterns. They should also be used to compare with other tobacco products, since cigars are more likely to be flavored than other products like cigarettes, but less likely than products such as hookah or e-cigarettes.
4. Papers on cigar use appeal more broadly should be reviewed – many of these include discussion of flavors.
5. Including data on race/ethnicity beyond Black non-Hispanic and White non-Hispanic would be useful – these data should exist in the papers already cited. Additionally, where possible disaggregating data for Asian and Hispanic populations is useful. For example, while overall use rates for Asians may be low, use is higher for Filipinos and for those of more than one race. Even if these data do not show higher use rates for some groups it would be good to have a sense of how a flavored cigar policy may affect all sub-populations.

6. Studies of local evaluations of flavored cigar restrictions can be linked to information in the Truth Initiative flavored policy database to have a better comparison between the comprehensiveness of policies <https://truthinitiative.org/research-resources/emerging-tobacco-products/local-restrictions-flavored-tobacco-and-e-cigarette>
7. Studies from relevant journals that are not currently indexed in PubMed should be reviewed for inclusion including Tobacco Regulatory Science and Tobacco Induced Diseases
8. Studies from the recent Tobacco Regulatory Science conference should be reviewed for inclusion as pre-publication materials.

POTENTIAL ADDITIONAL PAPERS FOR REVIEW

1. Alizaga NM, Hartman-Filson M, Elser H, Halpern-Felsher B, Vijayaraghavan M. Alternative flavored and unflavored tobacco product use and cigarette quit attempts among current smokers experiencing homelessness. *Addict Behav Rep.* Dec 2020;12:100280. doi:10.1016/j.abrep.2020.100280
2. Andersen-Rodgers E, Zhang X, Vuong TD, et al. Are California's Local Flavored Tobacco Sales Restrictions Effective in Reducing the Retail Availability of Flavored Tobacco Products? A Multicomponent Evaluation. *Eval Rev.* Oct 25 2021;193841X211051873. doi:10.1177/0193841X211051873
3. Bonhomme, M.G., Holder-Hayes, E., Ambrose, B.K., Tworek, C., Feirman, S.P., King, B.A. and Apelberg, B.J., 2016. Flavoured non-cigarette tobacco product use among US adults: 2013–2014. *Tobacco control*, 25(Suppl 2), pp.ii4-ii13.
4. Bosma LM, D'Silva J, Moze J, Matter C, Kingsbury JH, Brock B. Restricting Sales of Menthol Tobacco Products: Lessons Learned from Policy Passage and Implementation in Minneapolis, St. Paul, and Duluth, Minnesota. *Health Equity.* 2021;5(1):439-447. doi:10.1089/heq.2020.0137
5. Brock B, Carlson SC, Leizinger A, D'Silva J, Matter CM, Schillo BA. A tale of two cities: exploring the retail impact of flavoured tobacco restrictions in the twin cities of Minneapolis and Saint Paul, Minnesota. *Tob Control.* Mar 2019;28(2):176-180. doi:10.1136/tobaccocontrol-2017-054154
6. Brown EM, Gammon DG, Rogers T, et al. Changes in retail sales of tobacco products in Ontario after a menthol sales restriction. *Tob Control.* Jul 13 2021; doi:10.1136/tobaccocontrol-2021-056489
7. Brown EM, Rogers T, Eggers ME, et al. Implementation of the New York City Policy Restricting Sales of Flavored Non-Cigarette Tobacco Products. *Health Educ Behav.* Oct 2019;46(5):782-789. doi:10.1177/1090198119853608
8. Cadham, C.J., Sanchez-Romero, L.M., Fleischer, N.L. et al. The actual and anticipated effects of a menthol cigarette ban: a scoping review. *BMC Public Health* 20, 1055 (2020). <https://doi.org/10.1186/s12889-020-09055-z> (supplemental table reviews flavor ban restrictions that do not include menthol)
9. Chaiton M, Papadhima I, Schwartz R, et al. Product Substitution After A Real-World Menthol Ban: A Cohort Study. *Tob Regul Sci.* May 2020;6(3):205-212. doi:10.18001/trs.6.3.5
10. Cohn A, Cobb CO, Niaura RS, Richardson A. The Other Combustible Products: Prevalence and Correlates of Little Cigar/Cigarillo Use Among Cigarette Smokers. *Nicotine Tob Res.* Dec 2015;17(12):1473-81. doi:10.1093/ntr/ntv022
11. Cohn A, Johnson A, Ehlke S, Villanti AC. Characterizing substance use and mental

- health profiles of cigar, blunt, and non-blunt marijuana users from the National Survey of Drug Use and Health. *Drug Alcohol Depend.* Mar 1 2016;160:105-11. doi:10.1016/j.drugalcdep.2015.12.017
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3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.

1. More longitudinal studies examining cessation (and not just initiation) or switching outcomes would also be useful if these exist.
2. General information about morbidity and mortality from cigar smoking as a combustible tobacco product should be briefly added to the introduction. This would help to contextualize the particular harms of use of these products as well as how cigar use disparities translate into health disparities.
3. There is some discussion of flavor use differences by cigar product type (e.g., traditional cigar, little filtered cigars, cigarillos), but there is not much discussion of flavor differences by brand use (e.g., Delnevo, et al. *Tobacco Control* 2015). About half of the cigars sold are flavored and some brands such as White Owl have a much higher proportion of flavored sales than other brands. If available, papers examining specific

brands that are highly flavored should also be reviewed as contributing to the literature on flavor use.

4. Studies of exposure to cigar marketing should be added to the section on appeal.
5. Studies of cigarillo packaging perceptions (e.g., experimental studies, behavioral economics studies) including differences in perceptions by color should be added to the section on appeal.
6. Studies of harm perceptions of cigars and cigar flavors are largely missing from this review and should have their own section.
7. Discussion of Blunt use is missing as a reason for flavored cigar use. Those using blunts often use flavored blunt wrappers. Use of blunts still has the issues of tobacco use and nicotine dependence and leaving out these studies/estimates may under report cigar use patterns and the impact of flavored cigar restrictions.
8. Discussion of dual/poly use of cigars with other tobacco products is limited. Given that most cigar users also use other products, discussion of broader risk patterns is important to fully understand the additional risk of these products. This is also important to contextualize the potential for substitution with alternative products in flavored cigar policies.
9. Papers discussing flavored vape restrictions and menthol bans should also be more broadly reviewed for substitution with flavored cigars (i.e., for unintended consequences of other flavor tobacco restrictions) but information on these types of policies should be included in their own sections.
10. If available, studies of behavioral intentions (e.g., survey studies asking about hypothetical bans, behavioral economic studies) of what those who smoke flavored cigars would do if flavored cigars were unavailable should be included to better estimate the potential policy impacts. Several studies from the recent TRS meeting addressed these issues and should be considered as pre-publication materials.
11. Separating out the youth and young adult literature would be helpful. Both of these age groups are important for initiation and progression to regular use. With Tobacco 21 as a national policy (including young adults) and increases of tobacco initiation into the young adult years, young adults are a critical age group for flavored cigar use. The current literature combines studies of both age groups and conclusions to question 1 and 2 do not clearly call out the impacts on young adults. General literature on how patterns of tobacco initiation have expanded into the young adult years should be more fully examined.
12. Gender differences should also be discussed more fully. Cigars are used more frequently by males but flavored cigar use is typically higher among women including pregnant women.
13. Where possible, issues of intersectionality should be more clearly addressed (e.g., racial/ethnic disparities in flavored cigar use among sexual and gender minority populations).
14. There are several studies of flavor use and mental health/substance use/medical comorbidities/homelessness and should be included to assess disparities.
15. Studies on retail availability of flavored tobacco after policy change should be included. These include studies on compliance/adherence with flavor restrictions from store audits or littered packs can help to determine why some policies may or may not have had adequate impacts (i.e., if compliance/enforcement was poor). Examination of reduced flavor advertising should also be included.

III. Specific Observations on FDA's *Scientific Assessment of the Impact of Flavors in Cigar Products*

Page	Paragraph	Comment
5	2	Our study Rose SW, Johnson AL, Glasser AM, et al. Flavour types used by youth and adult tobacco users in wave 2 of the Population Assessment of Tobacco and Health (PATH) Study 2014-2015. <i>Tob Control</i> . Jul 2020;29(4):432-446. doi:10.1136/tobaccocontrol-2018-054852 included tables on concordance between self-report and brand assessed flavors including for cigars which may help with the discussion of self-reported flavors assessment.
9	1	“They also found that abuse liability can differ with cigar flavor (Bono et al 2020)” Please clarify in which direction and which flavor(s).
13	1	“... showing that flavors are a leading...”
16	1	Paragraph is about adults 25+ but last sentence is about youth and should be moved to the discussion of youth. This entire section should be reorganized to discuss the findings for youth, young adults, and then adults 25+ separately. Currently the discussion goes back and forth making it hard to follow.
20	2	“...consumers did not appear to completely substitute non-flavored cigars or concept flavored cigars for flavored cigars.”
24	3 rd	The section is titled Lowell, Massachusetts but also includes review studies based in Attleboro and Salem
27	2 nd	Discussion of the Yang study repeats discussion of articles already reviewed on page 26. This information should be put together or deleted since including the same study more than once makes it seem like there is more evidence than actually exists.
29	2 nd	Paragraph repeats discussion of articles already reviewed as part of the discussion of each city policy. Including this information more than once makes it seem like there is more evidence than actually exists.
34	1 st	Discussion of Courtemanche article is duplicated from page 33
35	2 nd	“...estimate the potential range of cigar...”
35-36	1st	Add specific mortality decrease and prevalence decrease estimates to this discussion. It seems that the Rostron 2019 study referenced on pages 35-36 is miscited in the reference list (L Rostron, B., G Corey, C., Holder-Hayes, E., & K Ambrose, B. (2019). Estimating the Potential Public Health Impact of Prohibiting Characterizing Flavors in Cigars throughout the US. <i>International journal of environmental research and public health</i> , 16(18), 3234. https://doi.org/10.3390/ijerph16183234 instead of Rostron BL, Corey CG, Gindi RM. Cigar smoking prevalence and morbidity among US adults, 2000–2015. <i>Preventive Medicine Reports</i> . 2019/06/01/ 2019;14:100821. doi:

Page	Paragraph	Comment
5	2	Our study Rose SW, Johnson AL, Glasser AM, et al. Flavour types used by youth and adult tobacco users in wave 2 of the Population Assessment of Tobacco and Health (PATH) Study 2014-2015. <i>Tob Control</i> . Jul 2020;29(4):432-446. doi:10.1136/tobaccocontrol-2018-054852 included tables on concordance between self-report and brand assessed flavors including for cigars which may help with the discussion of self-reported flavors assessment.
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20	2	“...consumers did not appear to completely substitute non-flavored cigars or concept flavored cigars for flavored cigars.”
24	3 rd	The section is titled Lowell, Massachusetts but also includes review studies based in Attleboro and Salem
		https://doi.org/10.1016/j.pmedr.2019.100821 which is in the references)
36	Last sentence	Add “The study did not account for tobacco product...”

D. Reviewer #4

Scientific Support Document(s) for Potential Tobacco Product Standards: Flavored Cigars

Reviewer #4

Scientific Assessment of the Impact of Flavors in Cigar Products

I. GENERAL IMPRESSIONS

Overall, the literature review presents accurate, timely, and wide-reaching evidence that flavored cigars are commonly used, that they are appealing to young people, that flavors are one of the main reasons those products are appealing to young people, and that community interventions to restrict or eliminate flavored cigars have been effective to reduce the appeal and use of these products especially to young people. The conclusions in the literature review are supported by the data presented, and the data is presented in a fair and objective manner.

There are three points that I believe were not adequately addressed, which serve to underestimate the adverse public health impact of flavored cigars. These include:

- Studies that do not assess the use of different types of cigars may be systematically underestimating cigar use compared to studies that do. In order to assess the prevalence of each type of cigar, studies should make use of both pictures and descriptive text. More details could be provided in the literature review on these measurement issues.
- The use of cigars for the purpose of blunts was generally not considered in this review. Exclusive blunt use is more than a trivial behavior and by not including it in the review the scope of cigar use in the population is systematically underestimated.
- More careful attention to studies that examine ‘youth’ cigar use should be taken to define ‘youth’ as those 20 years of age and younger because in today’s regulatory environment, nationally it is illegal to sell tobacco products to those under the age of 21. Failure to consider those under 21 years of age as ‘youth’ systematically underestimates the scope of underage cigar use.

None of these issues detracts from the conclusions made in the report, but rather addressing these points should lend even greater support to those conclusions.

In addition to the comments above, several comments are provided to improve the flow and clarity of the literature review including providing more evidence on the health risks from cigar smoking, defining ‘characterizing flavor’, and presenting the literature on relevant cigar use progression transition points more clearly, among other feedback provided elsewhere.

II. RESPONSE TO CHARGE QUESTIONS

1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.

Yes, each section of the literature on flavored cigars was thorough and had conclusions that were supported by the studies described in the report. If anything, I believe the literature review is conservative with its conclusions because it does not consider the following three points in

sufficient detail:

- *Type of Cigar.* Studies that do not assess the use of different types of cigars may be systematically underestimating cigar use compared to studies that do. In order to assess the prevalence of each type of cigar, studies should make use of both pictures and descriptive text. More details could be provided in the literature review on these measurement issues.
- *Blunts.* The use of cigars for the purpose of blunts was generally not considered in this review. Exclusive blunt use is more than a trivial behavior and by not including it in the review the scope of cigar use in the population is systematically underestimated.
- *Define ‘youth’ as under 21.* More careful attention to studies that examine ‘youth’ cigar use should be taken to define ‘youth’ as those 20 years of age and younger because in today’s regulatory environment, nationally it is illegal to sell tobacco products to those under the age of 21. Failure to consider those under 21 years of age as ‘youth’ systematically underestimates the scope of underage cigar use.

2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

Generally, I believe the literature review captures the totality of evidence that is publicly available on the topics explored. In my detailed comments below there are a limited number of places I suggest additional review is undertaken to determine if added data sources might be available.

For example, data from the PATH Study may be available to assess blunt use in more detail as well as to assess the prevalence of flavored cigar use by demographics, especially those age 20 and under. I do not believe this information is currently publicly available, but I do believe the data is being collected that could be analyzed to address these points.

3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.

I have no methodological concerns that diminish my confidence in the conclusions drawn from the literature review, and the review is done in an objective manner. I do believe that addressing the three points raised in response to Charge Question #1 - considering the type of cigar for all studies when possible, including blunt users, and including those under 21 years of age as ‘youth’ - will further expand the scope of cigar use in the population. Specific comments are provided in the table below for FDA’s consideration.

III. Specific Observations on FDA's *Scientific Assessment of the Impact of Flavors in Cigar Products*

Page	Paragraph	Comment
3	Purpose and Scope section	Recommend adding sections on 1) health risks from cigar use; and 2) the evidence that cigars are smoking cessation aids

Page	Paragraph	Comment
		<p>I believe the data will show that cigars pose significant health risks and NCI Monograph 6 among other review documents describe this in detail. Linking the behavior to health outcomes is needed in this Review to make that case that cigars pose a risk to individual and public health.</p> <p>The 2nd point about whether cigars are a cessation aid, which I don't believe there is any evidence to indicate that, simply makes the case that there is no upside benefit to public health from the use of cigars.</p> <p>Walk the reader through the full spectrum: from cigars being harmful, to they are commonly used, and part of that is due to the appealing flavors, and there's no benefit to having appealing cigars for public health...or something like that, of course, guided by what the <u>summary of the literature in each area indicates.</u></p>
3	Purpose and Scope section, bullet #1	<p>Define 'characterizing flavor' and how does this differ from a flavor that is not 'characterizing'. How is characterizing flavors defined for the purposes of this review and the studies that comprise it, which I believe make assumptions that certain brand names have characterizing flavors, but is there evidence to link the product names to the product formulations that produce the characterizing flavor?</p>
3	Prevalence of Cigar Use Among Youth section	<p>Three general comments about methods for assessing cigar use among youth. The first is that the PATH Study demonstrates that assessment of the different types of cigars is necessary to better estimate cigar prevalence. Many past studies assess cigar use as a single question, which yields lower estimates of cigar use. The PATH Study and some more recent studies use better methods to show pictures and provide a description of different types of cigars, which provide a more detailed, and in my opinion, superior method for assessing cigar use. The importance of this is that studies that assess cigar use with a single item and does not differentiate between the different types of cigars are likely underestimating the true prevalence of cigar use.</p> <p>The 2nd comment is that blunt use is a common behavior that involves the use of cigars for cannabis intake. Relatively few studies capture cigar use in the context of blunts and, thus, those studies will underestimate cigar use. The methods for this review indicate that studies primarily of blunt users are excluded, which is a condition I believe should be reconsidered because regardless of blunt use, by definition, is the use of cigars and omitting blunt use will systematically bias the results, particularly with respect to certain minority populations. Results from the PATH Study may be available to assess this in more detail.</p> <p>The 3rd comment is that past studies of 'youth' are</p>

Page	Paragraph	Comment
		underestimating the number of underage cigar smokers in the population. The minimum sales age for tobacco products is 21 years of age, therefore, all those age 20 and below are underage users to whom it is illegal to sell tobacco. The literature review should be clearer on this point and what the definition of ‘youth’ is. The takeaway point is that virtually all of the studies cited in this review define youth as <18 year of age; therefore, they underestimate the number of underage cigar smokers in the current policy setting where 21 is the minimum sales age.
4	Disparities in Cigar Use Among Youth section	Assessment of blunt use may differ by race/ethnicity and other factors, so it is particularly important to include an assessment of cigar use in the context of blunting for this review.
8	Addition of Characterizing Flavors in Tobacco Products section	Confirm this refers to ‘characterizing flavors’. It probably does, but the term ‘characterizing’ is subjective, but the point made here addresses the chemistry of the product.
8	Addition of Characterizing Flavors in Tobacco Products section	Recommend using the term ‘cigar manufacturers’ instead of ‘tobacco industry’ throughout when referring specifically to cigars as it is more precise and doesn’t pin practices necessarily for certain types of manufacturers on other types (i.e., vaping product manufacturers that are not involved in work with smoke chemistry, bitter tobacco leaves, etc.).
8	Abuse Liability of Flavored Tobacco Products	<p>I found this section to be under-developed and suggest incorporating it with the more compelling studies in the following section. There are just a limited number of studies with some of them using hypothetical purchase tasks, which are a great method, without a lot of empirical evidence.</p> <p>Consider framing this new section that describes the literature on the appeal and abuse liability of flavored cigars in the following way:</p> <p>There are two relevant issues – initial trial and progression to more regular use.</p> <p>For initial trial, appealing flavors can promote trying the flavored cigars, which studies show will greatly increase the likelihood of becoming a current or regular user in the future. This can work both through the marketing and advertising angle as well as making the first experience with the flavored product appealing and then the nicotine takes over to promote dependence. In other words, the flavors themselves don’t need to produce dependence directly, but just their making the product worth trying, it can produce dependence indirectly.</p>

Page	Paragraph	Comment
		<p>The progression to more regular use issue would include some of the studies that are in this section here on abuse liability in the area of transition from occasional to more regular use.</p>
9	Appeal of Flavored Tobacco Products	<p>The studies described here are strong and a compelling case is made.</p> <p>However, I think it is preferable to organize the section according to behavioral transitions and include the studies across the current subsections. I see now that question #2 addresses the issue of progression in use so that in large part addresses my comment; however, there may be opportunities to be clearer with the presentation that question 1 and question 2 are connected and flow sequentially.</p> <p>Transitions include initial trial – what is the evidence that flavored cigars promote trying the product?</p> <p>Then the transition from trial to occasional use – evidence like Villanti’s recent PATH Study paper showing, I think, that those who start with a flavored cigar were more likely to be a past 30 day user at follow-up.</p> <p>Then transition to frequent/regular/daily use, which gets it to the issues of dependence and abuse liability... and this is the pattern of use that has most of the evidence of harm to health.</p>
9	Appeal of Flavored Tobacco Products	<p>To what extent has the marketing of flavored cigars been shown to be associated with these measures of use/progression? Consider adding this component to make a stronger case for accompanying conditions to limit marketing to those under 21 as part of any rule making process. The marketing component is very important to incorporate.</p>
13	Last paragraph on this page	<p>Great to see this is being considered elsewhere. It’s necessary to document the literature on health risks of cigars.</p>
13	Last paragraph on this page	<p>Is it also appropriate to cite appropriate rules/regulations that limit the use of characterizing flavors in other types of tobacco products under FDA/CTPs authority?</p>
20	Local and National Policy Evaluation Studies section	<p>Somewhere in here I recommend considering the difference between a local and a nationally implemented policy. Local policy effects are likely a lower bound of their impact because it’s easier to circumvent the policy by traveling outside the jurisdiction; however, this is generally not practical for nationally implemented policies and this is particularly true for young people.</p>
28	Last full paragraph on	<p>I believe there is a Letter to the Editor and response by Dr. Friedman recently published that identifies and addresses some</p>

Page	Paragraph	Comment
	this page	<p>of the criticisms raised, which should be checked out.</p> <p>The main conclusion in this paper is that cigarette smoking increased in San Francisco where there was a policy, compared to other locations where no flavored policy was present. I don't believe any data on cigar use or vaping is reported. As such this study is not a direct evaluation of the flavor policy with respect to cigars. However, it does speak to potential unintended consequences of a broad flavor policy.</p> <p>The literature review should address whether any of the other local policy evaluations found evidence of unintended consequences including pushing people to use cigarettes, increasing contraband product, increasing use of third party product add-ons for flavor enhancement, or cross-border sales.</p>

IV. PEER REVIEWER COMMENT TABLES

Flavored Cigars
Scientific Assessment of the Impact of Flavors in Cigar Products

I. General Impressions		
REVIEWER	COMMENT	RESPONSE
Reviewer #1	The <i>Scientific Assessment of the Impact of Flavors in Cigar Products</i> is a comprehensive review of the available literature. Overall, the conclusions stated for each question are sound and supported by the presented evidence. The organizational structure of the document is appropriate and easy to follow. Many studies included in the current review report complex outcomes and analyses from longitudinal surveys with multiple age categories. In general, the review does a good job providing an appropriate level of detail and information about these complex studies.	
Reviewer #1	The prevalence section at the beginning of the document highlights the importance of the three questions being examined in the current review. The disparities section emphasizes the need for policies targeting flavored combusted tobacco products, including cigars, to reduce commercial tobacco use among priority populations like Black and African American persons and members of the LGBTQ+ community. Including both behavioral outcome data and sales data provides converging evidence about the impact of flavored tobacco product restrictions or bans. The section about flavors in food science also contributed meaningful information about how youth and adults differ with respect to flavor appeal.	
Reviewer #1	The review could be improved by adding more detail within the main text about the inclusion and exclusion criteria for studies rather than reporting this information exclusively in the appendices. For example, “studies employing exclusively animal models” should be excluded from the review based on the eligibility criteria listed in Appendix 1. However, there is a subsection on abuse liability for Question 1 that includes studies with animal models. Are these animal studies part of the literature review or providing explanatory information? Additionally, figures displaying the article selection process for each question would also be useful to include.	
Reviewer #1	Finally, throughout the document there are often very long sentences and paragraphs. Many studies report multiple outcomes by flavored tobacco product use, overall tobacco use, cigar use by subtype, age category, etc., so I would recommend trying to simplify sentence structures and breaking up paragraphs to enhance readability. The positive spin to this critique is there is a substantial amount of evidence supporting regulations for flavored tobacco products, including cigars, presented in this review.	
Reviewer #2	The overall impression of this information is that this is a rigorous literature review. Methodology for the review is appropriate and comprehensively included most relevant	

I. General Impressions		
REVIEWER	COMMENT	RESPONSE
	documents. The material for each section was presented clearly and comprehensibly. The documents show that the addition of flavors to tobacco products including cigars can reinforce the effects of nicotine, can increase abuse liability, that flavors appeal to youth and that this is consistent with the role of flavors in food. The document also shows that flavors are a reason for youth to start using cigars, and are associated with progression to regular use and nicotine dependence.	
Reviewer #2	The document also presents data from evaluations of local restrictions. The soundness of the conclusions would also be improved by a specific section for a discussion on enforcement and compliance. The effectiveness and impact of a ban will rely on enforcement and compliance and consequently, this should be highlighted and evaluated carefully to make recommendations for policy.	
Reviewer #2	Most conclusions for each document and the underlying data were sound. However, the primary overall concern is the conflation of three different definitions of flavors. While concept flavors are discussed, the issue is broader and affects all sections. Flavors can be characterizing, ingredients (which could, but not necessarily, lead to a characterizing flavor) or labelled. Each of the studies included may be responsive to one or two of these definitions, but not necessarily characterizing flavors. The definitions used by each study are needed and the conclusions associated with that definition.	
Reviewer #3	Overall, the review accurately presents the information of <i>reviewed</i> studies and the conclusions are largely in line with my own reading of the literature. Conclusions that flavors in cigars contribute to appeal, initiation, and experimentation and that flavor restrictions on cigars lead to reductions in sales and youth use are generally well supported. In particular, the review of the evaluation literature on flavor policies in various localities is thorough and does a good job of pointing out study limitations given the wide heterogeneity in this literature. However, as a comprehensive review of the published literature in this area there are some significant gaps in the review as detailed extensively below. Inclusion of missing studies and newer studies would strengthen the conclusions of this document. Lack of inclusion of these studies makes the evidence base weaker than would otherwise be the case.	
Reviewer #3	Overall changes that would strengthen the document include the following. Where possible, young adults should be separated out from youth and adults 25+. It would be clearer to understand use patterns if data on use patterns over time by age and race/ethnicity was included as graphs rather than just including prevalence estimates from the most current data wave. Cigar	

I. General Impressions		
REVIEWER	COMMENT	RESPONSE
	<p>use appears to be increasing over time which is not easily determined from the cross-sectional data. A more nuanced discussion of disparities in cigar use could include literature on gender, mental health, substance use, and medical co-morbidities and a broader discussion of differences by race/ethnicity beyond Black/White differences would provide a fuller picture of the potential health equity impacts of a flavored cigar ban. Where possible, more data on cigar cessation patterns over time would be useful. Discussion of flavored blunt use is missing. The discussion of ‘concept flavors’ should be incorporated into the main document as this is likely to be a significant area where implementation of flavored cigar bans will face challenges in practice. Finally, the impacts of flavored cigar bans should be clearly noted in relation to the comprehensiveness of flavor policies and the extent of compliance with implementation. Additional specific recommendations are listed below.</p>	
Reviewer #4	<p>Overall, the literature review presents accurate, timely, and wide-reaching evidence that flavored cigars are commonly used, that they are appealing to young people, that flavors are one of the main reasons those products are appealing to young people, and that community interventions to restrict or eliminate flavored cigars have been effective to reduce the appeal and use of these products especially to young people. The conclusions in the literature review are supported by the data presented, and the data is presented in a fair and objective manner.</p>	
Reviewer #4	<p>There are three points that I believe were not adequately addressed, which serve to underestimate the adverse public health impact of flavored cigars. These include:</p> <ul style="list-style-type: none"> • Studies that do not assess the use of different types of cigars may be systematically underestimating cigar use compared to studies that do. In order to assess the prevalence of each type of cigar, studies should make use of both pictures and descriptive text. More details could be provided in the literature review on these measurement issues. 	
Reviewer #4	<ul style="list-style-type: none"> • The use of cigars for the purpose of blunts was generally not considered in this review. Exclusive blunt use is more than a trivial behavior and by not including it in the review the scope of cigar use in the population is systematically underestimated. 	
Reviewer #4	<ul style="list-style-type: none"> • More careful attention to studies that examine ‘youth’ cigar use should be taken to define ‘youth’ as those 20 years of age and younger because in today’s regulatory environment, nationally it is illegal to sell tobacco products to those under the age of 21. Failure to consider those under 21 years of age as ‘youth’ systematically underestimates the scope of underage cigar use. 	

I. General Impressions		
REVIEWER	COMMENT	RESPONSE
Reviewer #4	<p>None of these issues detracts from the conclusions made in the report, but rather addressing these points should lend even greater support to those conclusions.</p> <p>In addition to the comments above, several comments are provided to improve the flow and clarity of the literature review including providing more evidence on the health risks from cigar smoking, defining ‘characterizing flavor’, and presenting the literature on relevant cigar use progression transition points more clearly, among other feedback provided elsewhere.</p>	

II. Response to Charge Questions

CHARGE QUESTION 1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.		
REVIEWER	COMMENT	RESPONSE
Reviewer #1	<p>Question 1: How Does the Addition of Characterizing Flavors to Tobacco Products, Including Cigars, Impact Product Appeal and Product Use? – The conclusions that characterizing flavors in tobacco products increases appeal and ease of use, especially among youth, is supported by the literature reviewed in this section. This section had an exhaustive review of the literature ranging from qualitative research to nationally-representative longitudinal surveys. Clinical research supports the conclusion that flavors contribute to increased abuse liability for tobacco products. In focus groups, youth often cite flavors as appealing and the reason for use. Analyses from the PATH survey found that flavors are the primary reason youth use cigars. Finally, four systematic reviews also report that flavors are appealing to youth and contribute to experimentation and progression to regular use. Overall, the review appropriately concludes that flavors in tobacco products appeal to youth.</p>	
Reviewer #1	<p>Question 2: How Do Characterizing Flavors Impact Youth and Young Adult Experimentation with Tobacco Products, Including Cigars, and Do They Make Progression to Regular Tobacco Use More Likely? – The conclusion that characterizing flavors are associated with increased likelihood of experimentation and progression to regular use is supported by the literature reviewed in this section. Two qualitative studies and one systematic review highlight the appeal of flavors among youth and young adults who use cigars. Several strong, longitudinal studies using nationally-representative samples find that experimentation with flavored tobacco products is associated with subsequent tobacco use. Evidence also suggests</p>	

CHARGE QUESTION 1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.		
REVIEWER	COMMENT	RESPONSE
	that experimenting with cigars can lead to nicotine dependence, which is associated with sustained tobacco use.	
Reviewer #1	Question 3: What Impact Do Local Policies Restricting the Sale of Flavored Cigars and Other Flavored Tobacco Products Have on Cigar Sales and Use? – The conclusion that sales of flavored cigars and cigars overall decreased after flavored tobacco restrictions or bans is supported by the literature. This section reviewed sales data after flavored tobacco policy implementation in several municipalities in the US and Canada. Most studies reported significant reductions in sales of flavored tobacco products, including cigars; however, some studies observed increases in concept flavor sales following the flavored tobacco restrictions or bans, indicating some product switching.	
Reviewer #1	The conclusion that reductions in youth use of flavored tobacco products also decreases after flavored tobacco restrictions or bans is also supported by the literature. Most studies across jurisdictions with flavored tobacco restrictions or bans (NYC, Providence, Lowell, Minneapolis, St. Paul and Canada) reported decreases in youth use after the ban. However, evidence from San Francisco suggests potential product substitution among youth after banning flavored tobacco products. Friedman, 2021 reported increases in cigarette smoking among high school students in San Francisco post-ban. Importantly, the study does not report changes in flavored tobacco use or overall tobacco use, so caution should be used when interpreting these findings with respect to tobacco use behavior among youth.	
Reviewer #2	Overall, the conclusions of each of the sections were scientifically supported with the following exceptions below. The document across all of the sections, even including the section on concept flavors, uses characterizing flavors to describe these. Generally, pre-clinical studies assess ingredients and other types of studies vary. For instance, Chaiton (2018) assessed labelled flavor, not ingredients or presence of characterizing flavor. Or on page 155, tobacco flavored Black and Milds may still have non-characterizing flavor ingredients, but are unlabeled. Relatedly on page 12, for ENDS tobacco flavored are flavored—i.e., have flavor ingredients. For appendix 2, reference to concept flavor can also include the experience in Ontario, in which alcohol labels were used as concept flavors (i.e., wine replacing berry labelling) (Chaiton 2018). I would recommend that the definition of characterizing flavors, ingredients, and labelled flavor be provided upfront and be	

CHARGE QUESTION 1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.		
REVIEWER	COMMENT	RESPONSE
	clear for each identified study which is being assessed or discussed. Conclusions may depend upon these definitions	
Reviewer #2	For Question 2, page . 19 on the discussion of attention and impulsivity, data on the familial confounding can be cited. For instance: Skoglund C, Chen Q, D' Onofrio BM, Lichtenstein P, Larsson H. Familial confounding of the association between maternal smoking during pregnancy and ADHD in offspring. <i>Journal of Child Psychology and Psychiatry</i> . 2014 Jan;55(1):61-8.	
Reviewer #3	Conclusions for question 1 and 2 are supported but I suggest breaking out conclusions by youth vs. young adults. Flavors are also used to appeal to young adults and the evidence for this should be separated out from the youth data. The conclusions also state that adolescence is a critical time period for tobacco use experimentation which is true but initiation of tobacco use and experimentation is increasingly moving into the young adult years. This is particularly true for African American young adults who disproportionately use flavored cigars. For this group young adulthood is a time when lower youth substance use patterns “cross over” to higher use prevalence compared with White tobacco users (e.g., Watt, 2008 The race/ethnic age crossover effect in drug use and heavy drinking. <i>Journal of Ethnicity in Substance Abuse</i>). Additional discussion of young adulthood as a time of initiation/experimentation would strengthen this conclusion, particularly in relation to disparities.	
Reviewer #3	Conclusions for question 3 are supported but rely on a limited evidence base – additional potentially relevant papers are listed below. The studies included discuss reduced sales and reduced youth use, but omit papers on reduced retail availability (i.e., retail compliance papers) and policy impact on reduced flavored advertising. As this is a fast-moving area, continuing to monitor the literature will be critical. Additionally, the paper on modeling the effects of this policy (pages 35-36) should be reviewed in more detail to actually detail the main morbidity and prevalence reduction estimates from this study (i.e., number of reduced deaths, number of fewer cigar smokers). The San Francisco studies should also be more clearly noted as the impact of a comprehensive flavor ban and not simply a ban on flavored cigars. For instance, the potential substitution effect with smoking in the Friedman 2021 by the author’s own discussion is likely due to the inclusion of flavored vape products not because of a ban on flavored cigars. Additionally, San Francisco also banned all e-cigarette sales in 2019 with enforcement starting Jan 29 2020 which may have had some effects beyond flavor restrictions. While there is likely to	

CHARGE QUESTION 1. For each section that you reviewed, were the conclusions scientifically supported given the available evidence? If not, provide specific examples as to where conclusions are not supported.		
REVIEWER	COMMENT	RESPONSE
	be substitution with existing (non-banned) products, the conclusion is based specifically on San Francisco data and should have these caveats or should be broadened.	
Reviewer #4	<p>Yes, each section of the literature on flavored cigars was thorough and had conclusions that were supported by the studies described in the report. If anything, I believe the literature review is conservative with its conclusions because it does not consider the following three points in sufficient detail:</p> <ul style="list-style-type: none"> • <i>Type of Cigar.</i> Studies that do not assess the use of different types of cigars may be systematically underestimating cigar use compared to studies that do. In order to assess the prevalence of each type of cigar, studies should make use of both pictures and descriptive text. More details could be provided in the literature review on these measurement issues. 	
Reviewer #4	<ul style="list-style-type: none"> • <i>Blunts.</i> The use of cigars for the purpose of blunts was generally not considered in this review. Exclusive blunt use is more than a trivial behavior and by not including it in the review the scope of cigar use in the population is systematically underestimated. 	
Reviewer #4	<ul style="list-style-type: none"> • <i>Define 'youth' as under 21.</i> More careful attention to studies that examine 'youth' cigar use should be taken to define 'youth' as those 20 years of age and younger because in today's regulatory environment, nationally it is illegal to sell tobacco products to those under the age of 21. Failure to consider those under 21 years of age as 'youth' systematically underestimates the scope of underage cigar use. 	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.		
REVIEWER	COMMENT	RESPONSE
Reviewer #1	There are publications about retailer compliance for selling and advertising flavored and menthol tobacco products after flavored tobacco policy restrictions in Minnesota and Massachusetts that could be included under Question 3. Although the studies do not report explicit sales figures for cigar products, they report observed changes in product availability in retail stores in the affected jurisdictions. According to the study eligibility criteria listed in Appendix 1, retailer compliance studies are not explicitly excluded from the review. However, if such studies are not appropriate for inclusion in this review, then the eligibility criteria should be revised accordingly.	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.		
REVIEWER	COMMENT	RESPONSE
Reviewer #1	<p>D'Silva et al., 2021 examined sales restrictions for menthol tobacco products in four Minnesota cities (Minneapolis, St. Paul, Duluth, and Falcon Heights). The authors used the Standardized Tobacco Assessment for Retail Settings (STARS) tool to examine sales and advertising of menthol tobacco products in retail stores. They assessed compliance rates of stores in cities with menthol tobacco policies versus comparison cities without menthol tobacco restrictions. They found significant reductions in the availability of menthol tobacco products across grocery/convenience stores and gas stations.</p> <p>D'Silva J, Moze J, Kingsbury JH, et al. Local sales restrictions significantly reduce the availability of menthol tobacco: Findings from four Minnesota cities. <i>Tobacco Control</i> 2021;30:492-497.</p>	
Reviewer #1	<p>Brock et al., 2019 examined sales restrictions for flavored tobacco products in Minneapolis and St. Paul. They found reductions in the availability of flavored tobacco products in retail stores with youth-access but the proportion of unflavored tobacco products increased after the policy.</p> <p>Brock B, Carlson SC, Leizinger A, et al. A tale of two cities: Exploring the retail impact of flavoured tobacco restrictions in the twin cities of Minneapolis and Saint Paul, Minnesota. <i>Tobacco Control</i> 2019;28:176-180.</p>	
Reviewer #1	<p>Kephart et al., 2020 examined sales restrictions for flavored tobacco products in Boston, Massachusetts. They found most retailers were compliant and access to flavored tobacco products in youth-accessible stores declined significantly after the policy</p> <p>Kephart L, Setodji C, Pane J, et al Evaluating tobacco retailer experience and compliance with a flavoured tobacco product restriction in Boston, Massachusetts: Impact on product availability, advertisement and consumer demand. <i>Tobacco Control</i> 2020;29:e71-e77.</p>	
Reviewer #2	<p>Bosma LM, D'Silva J, Moze J, Matter C, Kingsbury JH, Brock B. Restricting Sales of Menthol Tobacco Products: Lessons Learned from Policy Passage and Implementation in Minneapolis, St. Paul, and Duluth, Minnesota. <i>Health Equity</i>. 2021 Jun 1;5(1):439-47.</p> <p>This paper assesses implementation challenges from Minnesota.</p>	

CHARGE QUESTION 2. <i>Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.</i>		
REVIEWER	COMMENT	RESPONSE
Reviewer #2	<p>Chaiton M, Schwartz R, Cohen JE, Soule E, Zhang B, Eissenberg T. Prior Daily Menthol Smokers More Likely to Quit 2 Years After a Menthol Ban Than Non-menthol Smokers: A Population Cohort Study. <i>Nicotine & Tobacco Research</i>. 2021 Mar 10.</p> <p>Two year data with 6 month abstinence quit definition of effects in Ontario for cigarette but also shows the impact of substitution of other flavored products on likelihood of quit success.</p>	
Reviewer #2	<p>Chaiton MO, Schwartz R, Cohen JE, Soule E, Zhang B, Eissenberg T. The use of flavor cards and other additives after a menthol ban in Canada. <i>Tobacco control</i>. 2021 Sep 1;30(5):601-2.</p> <p>Assesses impact of availability of flavor cards (and other menthol additives) on successful quitting after the ban in Ontario. Flavor cards can also be used for other tobacco products particularly waterpipe.</p>	
Reviewer #2	<p>Denlinger-Apte RL, Cassidy RN, Carey KB, Kahler CW, Bickel WK, O'Connor R, Thussu S, Tidey JW. The impact of menthol flavoring in combusted tobacco on alternative product purchasing: A pilot study using the Experimental Tobacco Marketplace. <i>Drug and Alcohol Dependence</i>. 2021 Jan 1;218:108390.</p> <p>Experimental marketplace study showing that menthol little cigars and vapes were significant substitutes.</p>	
Reviewer #2	<p>Borland T, Dubray J, Chaiton M, Schwartz R. Monitoring and Evaluating Ontario's New Tobacco Policy Measures: Flavored Tobacco Prohibition. Toronto, ON: Ontario Tobacco Research Unit, September 2017. Available at: https://otru.org/wp-content/uploads/2017/08/special_nm_flavors_2017.pdf</p> <p>Report on the implementation of the flavored cigar ban. Includes assessment of challenges such as relabeling, new products that attempt to find exemptions, and products that are not marked as flavored but appear to be. Also shows lack of public awareness and challenges in enforcement.</p>	
Reviewer #2	<p>Silver KK, Hiscock R. Tobacco industry tactics to circumvent and undermine the TPD menthol ban in the UK. <i>Tobacco Prevention & Cessation</i>. 2020 Oct 22;6(Supplement).</p>	

CHARGE QUESTION 2. <i>Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.</i>		
REVIEWER	COMMENT	RESPONSE
	<p>Branston JR, Hiscock R, Silver K, Arnott D, Gilmore AB. Cigarette-like cigarillo introduced to bypass taxation, standardized packaging, minimum pack sizes, and menthol ban in the UK. Tobacco Control. 2021 Nov 1;30(6):708-11.</p> <p>These two papers include assessment of the use of menthol flavored cigarillos to circumvent the menthol tobacco ban.</p>	
Reviewer #3	1. Additional potential references are shown below (but are not comprehensive). General types of missing information are listed.	
Reviewer #3	2. The focus on only use estimates from the current waves of PATH, NYTS, NSDUH and other national datasets obscures changes over time from recent prior waves especially in longitudinal datasets. Including discussion of the data on cigar and flavor use from prior waves would help to highlight how both the policy environment, secular trends, and changes in the tobacco product marketplace may influence flavor use and cigar use more broadly and provide a fuller picture of how these elements may be changing. Additionally, in addition to a table in appendix 5, a graph of the PATH study prevalence estimates over time would be helpful.	
Reviewer #3	3. Additionally, papers on any tobacco use that separate out flavor use or use patterns by product (including cigar use) are generally not included and could provide good information on cigar use patterns. They should also be used to compare with other tobacco products, since cigars are more likely to be flavored than other products like cigarettes, but less likely than products such as hookah or e-cigarettes.	
Reviewer #3	4. Papers on cigar use appeal more broadly should be reviewed – many of these include discussion of flavors.	
Reviewer #3	5. Including data on race/ethnicity beyond Black non-Hispanic and White non-Hispanic would be useful – these data should exist in the papers already cited. Additionally, where possible disaggregating data for Asian and Hispanic populations is useful. For example, while overall use rates for Asians may be low, use is higher for Filipinos and for those of more than one race. Even if these data do not show higher use rates for some groups it would be good to have a sense of how a flavored cigar policy may affect all sub-populations.	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.		
REVIEWER	COMMENT	RESPONSE
Reviewer #3	6. Studies of local evaluations of flavored cigar restrictions can be linked to information in the Truth Initiative flavored policy database to have a better comparison between the comprehensiveness of policies https://truthinitiative.org/research-resources/emerging-tobacco-products/local-restrictions-flavored-tobacco-and-e-cigarette	
Reviewer #3	7. Studies from relevant journals that are not currently indexed in PubMed should be reviewed for inclusion including Tobacco Regulatory Science and Tobacco Induced Diseases	
Reviewer #3	8. Studies from the recent Tobacco Regulatory Science conference should be reviewed for inclusion as pre-publication materials.	
Reviewer #3	<p>POTENTIAL ADDITIONAL PAPERS FOR REVIEW</p> <ol style="list-style-type: none"> 1. Alizaga NM, Hartman-Filson M, Elser H, Halpern-Felsher B, Vijayaraghavan M. Alternative flavored and unflavored tobacco product use and cigarette quit attempts among current smokers experiencing homelessness. <i>Addict Behav Rep.</i> Dec 2020;12:100280. doi:10.1016/j.abrep.2020.100280 2. Andersen-Rodgers E, Zhang X, Vuong TD, et al. Are California's Local Flavored Tobacco Sales Restrictions Effective in Reducing the Retail Availability of Flavored Tobacco Products? A Multicomponent Evaluation. <i>Eval Rev.</i> Oct 25 2021:193841X211051873. doi:10.1177/0193841X211051873 3. Bonhomme, M.G., Holder-Hayes, E., Ambrose, B.K., Tworek, C., Feirman, S.P., King, B.A. and Apelberg, B.J., 2016. Flavoured non-cigarette tobacco product use among US adults: 2013–2014. <i>Tobacco control</i>, 25(Suppl 2), pp.ii4-ii13. 4. Bosma LM, D'Silva J, Moze J, Matter C, Kingsbury JH, Brock B. Restricting Sales of Menthol Tobacco Products: Lessons Learned from Policy Passage and Implementation in Minneapolis, St. Paul, and Duluth, Minnesota. <i>Health Equity.</i> 2021;5(1):439-447. doi:10.1089/heq.2020.0137 5. Brock B, Carlson SC, Leizinger A, D'Silva J, Matter CM, Schillo BA. A tale of two cities: exploring the retail impact of flavoured tobacco restrictions in the twin cities of Minneapolis and Saint Paul, Minnesota. <i>Tob Control.</i> Mar 2019;28(2):176-180. doi:10.1136/tobaccocontrol-2017-054154 	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.		
REVIEWER	COMMENT	RESPONSE
	<p>6. Brown EM, Gammon DG, Rogers T, et al. Changes in retail sales of tobacco products in Ontario after a menthol sales restriction. <i>Tob Control</i>. Jul 13 2021; doi:10.1136/tobaccocontrol-2021-056489</p> <p>7. Brown EM, Rogers T, Eggers ME, et al. Implementation of the New York City Policy Restricting Sales of Flavored Non-Cigarette Tobacco Products. <i>Health Educ Behav</i>. Oct 2019;46(5):782-789. doi:10.1177/1090198119853608</p> <p>8. Cadham, C.J., Sanchez-Romero, L.M., Fleischer, N.L. <i>et al</i>. The actual and anticipated effects of a menthol cigarette ban: a scoping review. <i>BMC Public Health</i> 20, 1055 (2020). https://doi.org/10.1186/s12889-020-09055-z (supplemental table reviews flavor ban restrictions that do not include menthol)</p> <p>9. Chaiton M, Papadhima I, Schwartz R, et al. Product Substitution After A Real-World Menthol Ban: A Cohort Study. <i>Tob Regul Sci</i>. May 2020;6(3):205-212. doi:10.18001/trs.6.3.5</p> <p>10. Cohn A, Cobb CO, Niaura RS, Richardson A. The Other Combustible Products: Prevalence and Correlates of Little Cigar/Cigarillo Use Among Cigarette Smokers. <i>Nicotine Tob Res</i>. Dec 2015;17(12):1473-81. doi:10.1093/ntr/ntv022</p> <p>11. Cohn A, Johnson A, Ehlke S, Villanti AC. Characterizing substance use and mental health profiles of cigar, blunt, and non-blunt marijuana users from the National Survey of Drug Use and Health. <i>Drug Alcohol Depend</i>. Mar 1 2016;160:105-11. doi:10.1016/j.drugalcdep.2015.12.017</p> <p>12. Coleman-Cowger, V. H., Pickworth, W. B., Lordo, R. A., & Peters, E. N. (2018). Cigar and Marijuana Blunt Use Among Pregnant and Nonpregnant Women of Reproductive Age in the United States, 2006-2016. <i>American journal of public health</i>, 108(8), 1073–1075. https://doi.org/10.2105/AJPH.2018.304469</p> <p>13. Conway KP, Green VR, Kasza KA, et al. Co-occurrence of tobacco product use, substance use, and mental health problems among youth: Findings from wave 1 (2013-2014) of the population assessment of tobacco and health (PATH) study. <i>Addict Behav</i>. Jan 2018;76:208-217. doi:10.1016/j.addbeh.2017.08.009</p> <p>14. Conway KP, Green VR, Kasza KA, et al. Co-occurrence of tobacco product use, substance use, and mental health problems among adults: Findings from Wave 1 (2013-2014) of the Population Assessment of Tobacco and Health (PATH) Study. <i>Drug Alcohol Depend</i>. Aug 1 2017;177:104-111. doi:10.1016/j.drugalcdep.2017.03.032</p>	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

REVIEWER	COMMENT	RESPONSE
	<p>15. Corey CG, Holder-Hayes E, Nguyen AB, et al. US Adult Cigar Smoking Patterns, Purchasing Behaviors, and Reasons for Use According to Cigar Type: Findings From the Population Assessment of Tobacco and Health (PATH) Study, 2013-2014. <i>Nicotine Tob Res.</i> Nov 15 2018;20(12):1457-1466. doi:10.1093/ntr/ntx209</p> <p>16. Cullen J, Mowery P, Delnevo C, et al. Seven-year patterns in US cigar use epidemiology among young adults aged 18-25 years: a focus on race/ethnicity and brand. <i>Am J Public Health.</i> Oct 2011;101(10):1955-62. doi:10.2105/AJPH.2011.300209</p> <p>17. Dai H, Hao J. Flavored Tobacco Use Among U.S. Adults by Age Group: 2013-2014. <i>Subst Use Misuse.</i> 2019;54(2):315-323. doi:10.1080/10826084.2018.1521428</p> <p>18. Dai H. Changes in Flavored Tobacco Product Use Among Current Youth Tobacco Users in the United States, 2014-2017. <i>JAMA Pediatr.</i> Mar 1 2019;173(3):282-284. doi:10.1001/jamapediatrics.2018.4595</p> <p>19. Dai H. Single, Dual, and Poly Use of Flavored Tobacco Products Among Youths. <i>Prev Chronic Dis.</i> Jun 28 2018;15:E87. doi:10.5888/pcd15.170389</p> <p>20. Delnevo CD, Bover-Manderski MT, Hrywna M. Cigar, marijuana, and blunt use among US adolescents: Are we accurately estimating the prevalence of cigar smoking among youth? <i>Prev Med.</i> Jun 2011;52(6):475-6. doi:10.1016/j.ypmed.2011.03.014</p> <p>21. Delnevo CD, Giovenco DP, Miller Lo EJ. Changes in the Mass-merchandise Cigar Market since the Tobacco Control Act. <i>Tob Regul Sci.</i> Apr 2017;3(2 Suppl 1):S8-S16. doi:10.18001/trs.3.2(suppl1).2</p> <p>22. Delnevo CD, Giovenco DP, Miller Lo EJ. Changes in the Mass-merchandise Cigar Market since the Tobacco Control Act. <i>Tob Regul Sci.</i> Apr 2017;3(2 Suppl 1):S8-S16. doi:10.18001/trs.3.2(suppl1).2</p> <p>23. Delnevo CD, Hrywna M. Clove cigar sales following the US flavoured cigarette ban. <i>Tob Control.</i> Dec 2015;24(e4):e246-50. doi:10.1136/tobaccocontrol-2013-051415</p> <p>24. Delnevo CD, Jeong M, Ganz O, Giovenco DP, Miller Lo E. The Effect of Cigarillo Packaging Characteristics on Young Adult Perceptions and Intentions: An Experimental Study. <i>Int J Environ Res Public Health.</i> Apr 19 2021;18(8)doi:10.3390/ijerph18084330</p> <p>25. Denlinger-Apte, R.L., Cassidy, R.N., Carey, K.B., Kahler, C.W., Bickel, W.K., O'Connor, R., Thussu, S. and Tidey, J.W., 2021. The impact of menthol flavoring in combusted tobacco on alternative product purchasing: A pilot study using the Experimental Tobacco Marketplace. <i>Drug and Alcohol Dependence</i>, 218, p.108390.</p>	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

REVIEWER	COMMENT	RESPONSE
	<p>26. D'Silva J, Moze J, Kingsbury JH, et al. Local sales restrictions significantly reduce the availability of menthol tobacco: findings from four Minnesota cities. <i>Tob Control</i>. Sep 2021;30(5):492-497. doi:10.1136/tobaccocontrol-2019-055577</p> <p>27. Dunn, D.S., Johnson, A.L., Sterling, K.L. and Cohn, A.M., 2021. Differences in reasons for little cigar/cigarillo use across white and black/African American young adult users. <i>Addictive Behaviors</i>, 118, p.106884.</p> <p>28. Erinoso, O., Smith, K.C., Iacobelli, M., Saraf, S., Welding, K. and Cohen, J.E., 2021. Global review of tobacco product flavour policies. <i>Tobacco control</i>, 30(4), pp.373-379.</p> <p>29. Farley SM, Sisti J, Jasek J, Schroth KRJ. Flavored Tobacco Sales Prohibition (2009) and Noncigarette Tobacco Products in Retail Stores (2017), New York City. <i>Am J Public Health</i>. May 2020;110(5):725-730. doi:10.2105/AJPH.2019.305561</p> <p>30. Feld AL, Rogers T, Gaber J, et al. Impact of Local Flavored Tobacco Sales Restrictions on Policy-Related Attitudes and Tobacco Product Access. <i>Health Educ Behav</i>. Aug 16 2021;10901981211027520. doi:10.1177/10901981211027520</p> <p>31. Fishbein, H., Bauer, D., Yu, Q., Mermelstein, R., Jones, D., Miller, A., Harrell, M., Loukas, A., Sterling, K., Colip, B. and Mittl, B., 2021. Harmonizing Cigar Survey Data Across Tobacco Centers of Regulatory Science, Center for Tobacco Products, and Population Assessment of Tobacco and Health Studies: The Cigar Collaborative Research Group. <i>Nicotine and Tobacco Research</i>, 23(1), pp.212-218.</p> <p>32. Freitas-Lemos R, Stein JS, Tegge AN, et al. The Illegal Experimental Tobacco Marketplace I: Effects of Vaping Product Bans. <i>Nicotine Tob Res</i>. Aug 29 2021;23(10):1744-1753. doi:10.1093/ntr/ntab088</p> <p>33. Gaiha SM, Henriksen L, Halpern-Felsher B, et al. Sources of flavoured e-cigarettes among California youth and young adults: associations with local flavoured tobacco sales restrictions. <i>Tob Control</i>. Apr 13 2021;doi:10.1136/tobaccocontrol-2020-056455</p> <p>34. Gammon DG, Rogers T, Coats EM, et al. National and state patterns of concept-flavoured cigar sales, USA, 2012-2016. <i>Tob Control</i>. Jul 2019;28(4):394-400. doi:10.1136/tobaccocontrol-2018-054348</p> <p>35. Ganz O, Cohn AM, Goodwin RD, et al. Internalizing problems are associated with initiation and past 30-Day use of flavored tobacco products. <i>Addictive behaviors</i>. 2022/02/01/ 2022;125:107162. doi: https://doi.org/10.1016/j.addbeh.2021.107162</p>	

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REVIEWER	COMMENT	RESPONSE
	<p>36. Ganz O, Hrywna M, Schroth KRJ, Delnevo CD. Innovative promotional strategies and diversification of flavoured mass merchandise cigar products: a case study of Swedish match. <i>Tob Control</i>. Feb 1 2021;doi:10.1136/tobaccocontrol-2020-056145</p> <p>37. Ganz O, King JL, Giovenco DP, Hrywna M, Strasser AA, Delnevo CD. Associations between Black and Mild Cigar Pack Size and Demographics and Tobacco Use Behaviors among US Adults. <i>Int J Environ Res Public Health</i>. Jun 20 2021;18(12)doi:10.3390/ijerph18126628</p> <p>38. Giovenco DP, Miller Lo EJ, Lewis MJ, Delnevo CD. "They're Pretty Much Made for Blunts": Product Features That Facilitate Marijuana Use Among Young Adult Cigarillo Users in the United States. <i>Nicotine Tob Res</i>. Nov 1 2017;19(11):1359-1364. doi:10.1093/ntr/ntw182</p> <p>39. Giovenco DP, Spillane TE, Mauro CM, Martins SS. Cigarillo sales in legalized marijuana markets in the U.S. <i>Drug Alcohol Depend</i>. Apr 1 2018;185:347-350. doi:10.1016/j.drugalcdep.2017.12.011</p> <p>40. Harrell MB, Loukas A, Jackson CD, Marti CN, Perry CL. Flavored Tobacco Product Use among Youth and Young Adults: What if Flavors Didn't Exist? <i>Tob Regul Sci</i>. Apr 2017;3(2):168-173. doi:10.18001/TRS.3.2.4</p> <p>41. Hefner K, Valentine G, Sofuoglu M. Electronic cigarettes and mental illness: Reviewing the evidence for help and harm among those with psychiatric and substance use disorders. <i>Am J Addict</i>. Jun 2017;26(4):306-315. doi:10.1111/ajad.12504</p> <p>42. Henriksen, L., Schleicher, N.C., Ababseh, K., Johnson, T.O. and Fortmann, S.P., 2018. Marijuana as a 'concept' flavour for cigar products: availability and price near California schools. <i>Tobacco control</i>, 27(5), pp.585-588.</p> <p>43. Kephart, L., Setodji, C., Pane, J., Shadel, W., Song, G., Robertson, J., Harding, N., Henley, P. and Ursprung, W.W.S., 2020. Evaluating tobacco retailer experience and compliance with a flavoured tobacco product restriction in Boston, Massachusetts: impact on product availability, advertisement and consumer demand. <i>Tobacco control</i>, 29(e1), pp.e71-e77.</p> <p>44. King, Brian A., Michael A. Tynan, Shanta R. Dube, and Rene Arrazola. "Flavored-little-cigar and flavored-cigarette use among US middle and high school students." <i>Journal of Adolescent Health</i> 54, no. 1 (2014): 40-46.</p>	

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REVIEWER	COMMENT	RESPONSE
	<p>45. Kong G, Bold KW, Simon P, Camenga DR, Cavallo DA, Krishnan-Sarin S. Reasons for Cigarillo Initiation and Cigarillo Manipulation Methods among Adolescents. <i>Tob Regul Sci.</i> Apr 2017;3(2 Suppl 1):S48-S58. doi:10.18001/TRS.3.2(Suppl1).6</p> <p>46. Kong G, Cavallo DA, Bold KW, LaVallee H, Krishnan-Sarin S. Adolescent and Young Adult Perceptions on Cigar Packaging: A Qualitative Study. <i>Tob Regul Sci.</i> Jul 2017;3(3):333-346. doi:10.18001/TRS.3.3.9</p> <p>47. Kong G, Cavallo DA, Goldberg A, LaVallee H, Krishnan-Sarin S. Blunt Use among Adolescents and Young Adults: Informing Cigar Regulations. <i>Tob Regul Sci.</i> Sep 2018;4(5):50-60. doi:10.18001/TRS.4.5.5</p> <p>48. Kuiper NM, Gammon D, Loomis B, et al. Trends in Sales of Flavored and Menthol Tobacco Products in the United States During 2011-2015. <i>Nicotine Tob Res.</i> May 3 2018;20(6):698-706. doi:10.1093/ntr/ntx123</p> <p>49. Kurti MK, Schroth KRJ, Delnevo C. A discarded cigar package survey in New York City: indicators of non-compliance with local flavoured tobacco restrictions. <i>Tob Control.</i> Sep 2020;29(5):585-587. doi:10.1136/tobaccocontrol-2019-055035</p> <p>50. Lawyer GR, Jackson M, Prinz M, et al. Classification of flavors in cigarillos and little cigars and their variable cellular and acellular oxidative and cytotoxic responses. <i>PLoS One.</i> 2019;14(12):e0226066. doi:10.1371/journal.pone.0226066</p> <p>51. Levy, D.T., Meza, R., Yuan, Z., Li, Y., Cadham, C., Sanchez-Romero, L.M., Travis, N., Knoll, M., Liber, A.C., Mistry, R. and Hirschtick, J.L., 2021. Public health impact of a US ban on menthol in cigarettes and cigars: a simulation study. <i>Tobacco Control.</i></p> <p>52. Liu, Jessica, Divya Ramamurthi, and Bonnie Halpern-Felsher. "Inside the adolescent voice: A qualitative analysis of the appeal of different tobacco products." <i>Tobacco induced diseases</i> 19 (2021).</p> <p>53. Meernik C, Ranney LM, Lazard AJ, et al. The effect of cigarillo packaging elements on young adult perceptions of product flavor, taste, smell, and appeal. <i>PLoS One.</i> 2018;13(4):e0196236. doi:10.1371/journal.pone.0196236</p> <p>54. Nali MC, Purushothaman V, Xu Q, Cuomo RE, Mackey TK. Characterizing and assessing compliance of online vendors to the state of Massachusetts ENDS product sales ban. <i>Tob Induc Dis.</i> 2021;19:05. doi:10.18332/tid/131199</p> <p>55. Nguyen AB. Disaggregating Asian American and Native Hawaiian and Other Pacific Islander (AANHOP) Adult Tobacco Use: Findings from Wave 1 of the Population</p>	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

REVIEWER	COMMENT	RESPONSE
	<p>Assessment of Tobacco and Health (PATH) Study, 2013-2014. <i>J Racial Ethn Health Disparities</i>. Apr 2019;6(2):356-363. doi:10.1007/s40615-018-00532-1 1. Jeong M, Wackowski OA, Schroth KRJ, Strasser AA, Delnevo CD. Influence of cigarillo packaging characteristics on young adults' perceptions and intentions: findings from three online experiments. <i>Tob Control</i>. Oct 28 2021;doi:10.1136/tobaccocontrol-2021-056785</p> <p>56. Nyman AL, Sterling KL, Weaver SR, Majeed BA, Eriksen MP. Little Cigars and Cigarillos: Users, Perceptions, and Reasons for Use. <i>Tob Regul Sci</i>. Jul 2016;2(3):239-251. doi:10.18001/TRS.2.3.4</p> <p>57. Posner H, Romm K, Henriksen L, Bernat D, Berg CJ. Reactions to sales restrictions on flavored vape products or all vape products among young adults in the US. <i>Nicotine Tob Res</i>. Jul 31 2021;doi:10.1093/ntr/ntab154</p> <p>58. Printz C. JUUL sales recovered after self-imposed flavor ban. <i>Cancer</i>. Nov 1 2020;126(21):4629. doi:10.1002/cncr.33250</p> <p>59. Rao M, Bar L, Yu Y, et al. Disaggregating Asian American Cigarette and Alternative Tobacco Product Use: Results from the National Health Interview Survey (NHIS) 2006-2018. <i>J Racial Ethn Health Disparities</i>. Apr 28 2021;doi:10.1007/s40615-021-01024-5</p> <p>60. Ribisl KM, D'Angelo H, Feld AL, et al. Disparities in tobacco marketing and product availability at the point of sale: Results of a national study. <i>Preventive medicine</i>. 2017/12/01/ 2017;105:381-388. doi: https://doi.org/10.1016/j.ypmed.2017.04.010</p> <p>61. Rogers T, Brown EM, McCrae TM, et al. Compliance with a Sales Policy on Flavored Non-cigarette Tobacco Products. <i>Tob Regul Sci</i>. 2017;3(2 Suppl 1):S84-S93. doi:10.18001/TRS.3.2(Suppl1).9</p> <p>62. Rose SW, Amato MS, Anesetti-Rothermel A, et al. Characteristics and Reach Equity of Policies Restricting Flavored Tobacco Product Sales in the United States. <i>Health Promot Pract</i>. Jan 2020;21(1_suppl):44S-53S. doi:10.1177/1524839919879928</p> <p>63. Rose SW, Anesetti-Rothermel A, Westneat S, et al. Inequitable distribution of FTP marketing by neighborhood characteristics: further evidence for targeted marketing. <i>Nicotine Tob Res</i>. Oct 23 2021;doi:10.1093/ntr/ntab222</p> <p>64. Rose SW, Johnson AL, Glasser AM, et al. Flavour types used by youth and adult tobacco users in wave 2 of the Population Assessment of Tobacco and Health (PATH) Study 2014-2015. <i>Tob Control</i>. Jul 2020;29(4):432-446. doi:10.1136/tobaccocontrol-2018-054852</p>	

CHARGE QUESTION 2. Are you aware of additional publicly available information that should have been included? If so, please specify what that information is and discuss its relevance to the scientific assessment.

REVIEWER	COMMENT	RESPONSE
	<p>65. Rostron BL, Cheng YC, Gardner LD, Ambrose BK. Prevalence and Reasons for Use of Flavored Cigars and ENDS among US Youth and Adults: Estimates from Wave 4 of the PATH Study, 2016-2017. <i>Am J Health Behav.</i> Jan 1 2020;44(1):76-81. doi:10.5993/AJHB.44.1.8</p> <p>66. Rostron, B, C GC, Holder-Hayes E, B KA. Estimating the Potential Public Health Impact of Prohibiting Characterizing Flavors in Cigars throughout the US. <i>Int J Environ Res Public Health.</i> Sep 4 2019;16(18)doi:10.3390/ijerph16183234</p> <p>67. Safi Z, Ganz O, Giovenco DP, Delnevo C, Lewis MJ. White Owl launches sweepstakes to promote new dessert-flavoured cigar. <i>Tob Control.</i> May 24 2021;doi:10.1136/tobaccocontrol-2021-056590</p> <p>68. Schneller LM, Li D, Tavarez ZQ, et al. Flavor Inconsistencies between Flavored Tobacco Products among US Adults. <i>Am J Health Behav.</i> Sep 1 2020;44(5):617-630. doi:10.5993/AJHB.44.5.6</p> <p>69. Schroth KRJ, Kurti M, Delnevo CD. Flavored cigar availability in Oakland after a partial ban. <i>Addict Behav.</i> Oct 12 2021;125:107150. doi:10.1016/j.addbeh.2021.107150</p> <p>70. Shang, C., Nonnemaker, J., Sterling, K., Sobolewski, J. and Weaver, S.R., 2021. Impact of Little Cigars and Cigarillos Packaging Features on Product Preference. <i>International Journal of Environmental Research and Public Health</i>, 18(21), p.11443.</p> <p>71. Simuzingili M, Hoetger C, Garner W, et al. What influences demand for cigars among African American adult cigar smokers? Results from a hypothetical purchase task. <i>Exp Clin Psychopharmacol.</i> Jun 10 2021;doi:10.1037/pha0000491</p> <p>72. Stanton CA, Keith DR, Gaalema DE, et al. Trends in tobacco use among US adults with chronic health conditions: National Survey on Drug Use and Health 2005-2013. <i>Prev Med.</i> Nov 2016;92:160-168. doi:10.1016/j.yjpm.2016.04.008</p> <p>73. Sterling KL, Fryer CS, Nix M, Fagan P. Appeal and Impact of Characterizing Flavors on Young Adult Small Cigar Use. <i>Tob Regul Sci.</i> Apr 2015;1:42-53. doi:10.18001/TRS.1.1.5</p> <p>74. Sterling KL, Jones DM, Majeed B, Nyman AL, Weaver SR. Affect Predicts Small Cigar Use in a National Sample of US Young Adults. <i>Tob Regul Sci.</i> May 2019;5(3):253-263. doi:10.18001/TRS.5.3.4</p> <p>75. Sterling KL, Vishwakarma M, Ababseh K, Henriksen L. Flavors and Implied Reduced-Risk Descriptors in Cigar Ads at Stores Near Schools. <i>Nicotine Tob Res.</i> Oct 7 2021;23(11):1895-1901. doi:10.1093/ntr/ntab136</p>	

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REVIEWER	COMMENT	RESPONSE
	<p>76. Sterling, K.L., Fryer, C.S., Pagano, I. and Fagan, P., 2017. Flavored cigar misperceptions and uncertainty: identifying at-risk smokers. <i>Tobacco Regulatory Science</i>, 3(2), pp.17-30.</p> <p>77. Stokes, A.C., Wilson, A.E., Lundberg, D.J., Xie, W., Berry, K.M., Fetterman, J.L., Harlow, A.F., Cozier, Y.C., Barrington-Trimis, J.L., Sterling, K.L. and Benjamin, E.J., 2021. Racial/Ethnic Differences in Associations of Non-cigarette Tobacco Product Use With Subsequent Initiation of Cigarettes in US Youths. <i>Nicotine and Tobacco Research</i>, 23(6), pp.900-908.</p> <p>78. Timberlake DS, Rhee J, Silver LD, et al. Impact of California's tobacco and cannabis policies on the retail availability of little cigars/cigarillos and blunt wraps. <i>Drug Alcohol Depend</i>. Sep 24 2021;228:109064. doi:10.1016/j.drugalcdep.2021.109064</p> <p>79. Villanti AC, Johnson AL, Ambrose BK, et al. Flavored Tobacco Product Use in Youth and Adults: Findings From the First Wave of the PATH Study (2013-2014). <i>Am J Prev Med</i>. Aug 2017;53(2):139-151. doi:10.1016/j.amepre.2017.01.026</p> <p>80. Yingst JM, Bordner CR, Hobkirk AL, et al. Response to Flavored Cartridge/Pod-Based Product Ban among Adult JUUL Users: "You Get Nicotine However You Can Get It". <i>Int J Environ Res Public Health</i>. Dec 30 2020;18(1)doi:10.3390/ijerph18010207</p> <p>81. Zhu, Y., Pasch, K.E., Loukas, A., Sterling, K.L. and Perry, C.L., 2021. Exposure to cigar Point-of-Sale marketing and use of cigars and cigarettes among young adults. <i>Addictive Behaviors</i>, 116, p.106821.</p>	
Reviewer #4	Generally, I believe the literature review captures the totality of evidence that is publicly available on the topics explored. In my detailed comments below there are a limited number of places I suggest additional review is undertaken to determine if added data sources might be available.	
Reviewer #4	For example, data from the PATH Study may be available to assess blunt use in more detail as well as to assess the prevalence of flavored cigar use by demographics, especially those age 20 and under. I do not believe this information is currently publicly available, but I do believe the data is being collected that could be analyzed to address these points.	

CHARGE QUESTION 3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.		
REVIEWER	COMMENT	RESPONSE
Reviewer #1	Under Question 1, there is a subsection called “systematic reviews on appeal, use and progression to regular use of tobacco products.” The content reported in this section could also belong under Question 2 since that is addressing experimentation and progression to regular use. It may be worth including another short section under Question 2 briefly restating the findings from the systematic reviews reported under Question 1.	
Reviewer #1	For the Minneapolis and St. Paul, Minnesota flavored tobacco restrictions, the policies allow flavored tobacco product sales to adult-only venues, like tobacco and alcohol retailers (https://www.publichealthlawcenter.org/sites/default/files/resources/US-sales-restrictions-flavored-tobacco-products.pdf). This should be explicitly stated in the study description narrative on page 25.	
Reviewer #1	PATH Study Memo and PATH Study Online Tables have placeholders in the reference section. Since I was not able to examine these documents, I cannot verify their content or accuracy.	
Reviewer #1	The citations Palmatier et al., 2013 and Palmatier et al., 2020 are missing from the reference list. Please review all cited to work to ensure they are included in the reference list.	
Reviewer #1	One minor suggestion is to include an abbreviations list at the beginning of the review document.	
Reviewer #2	My primary suggestion would be specifically to discuss the challenges with enforcement as a separate section. Some of this detail can be found occasionally when mentioned by some articles, but there is additional literature (see above) and additional detail within existing studies. The effectiveness and impact of a ban will rely on enforcement and compliance and consequently this should be highlighted and evaluated carefully to make recommendations for policy.	
Reviewer #2	A second issue to highlight is the impact of flavor tobacco bans on the effectiveness of menthol cigarette bans. The Canadian ban and other local bans on menthol were in the context of the flavor cigar bans and availability of menthol cigars may affect the effectiveness of the menthol restrictions in cigarettes so that these issues must be considered in conjunction, particularly for little cigars and cigarillos. Some citations are provided above.	
Reviewer #2	In the methodology it should be clarified that research prior to 2010 was eligible for inclusion.	
Reviewer #2	There should be discrimination between studies that use longitudinal pre-post designs vs cross-sectional re-post designs (e.g. Chaiton 2020 is longitudinal while Chaiton 2018 is a cross sectional time series) as the former allows for control of within-person characteristics especially compared to cross-sectional population surveys.	
Reviewer #2	Product substitution is discussed.	

CHARGE QUESTION 3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.		
REVIEWER	COMMENT	RESPONSE
Reviewer #3	1. More longitudinal studies examining cessation (and not just initiation) or switching outcomes would also be useful if these exist.	
Reviewer #3	2. General information about morbidity and mortality from cigar smoking as a combustible tobacco product should be briefly added to the introduction. This would help to contextualize the particular harms of use of these products as well as how cigar use disparities translate into health disparities.	
Reviewer #3	3. There is some discussion of flavor use differences by cigar product type (e.g., traditional cigar, little filtered cigars, cigarillos), but there is not much discussion of flavor differences by brand use (e.g., Delnevo, et al. Tobacco Control 2015). About half of the cigars sold are flavored and some brands such as White Owl have a much higher proportion of flavored sales than other brands. If available, papers examining specific brands that are highly flavored should also be reviewed as contributing to the literature on flavor use.	
Reviewer #3	4. Studies of exposure to cigar marketing should be added to the section on appeal.	
Reviewer #3	5. Studies of cigarillo packaging perceptions (e.g., experimental studies, behavioral economics studies) including differences in perceptions by color should be added to the section on appeal.	
Reviewer #3	6. Studies of harm perceptions of cigars and cigar flavors are largely missing from this review and should have their own section.	
Reviewer #3	7. Discussion of Blunt use is missing as a reason for flavored cigar use. Those using blunts often use flavored blunt wrappers. Use of blunts still has the issues of tobacco use and nicotine dependence and leaving out these studies/estimates may under report cigar use patterns and the impact of flavored cigar restrictions.	
Reviewer #3	8. Discussion of dual/poly use of cigars with other tobacco products is limited. Given that most cigar users also use other products, discussion of broader risk patterns is important to fully understand the additional risk of these products. This is also important to contextualize the potential for substitution with alternative products in flavored cigar policies.	
Reviewer #3	9. Papers discussing flavored vape restrictions and menthol bans should also be more broadly reviewed for substitution with flavored cigars (i.e., for unintended consequences	

CHARGE QUESTION 3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.		
REVIEWER	COMMENT	RESPONSE
	of other flavor tobacco restrictions) but information on these types of policies should be included in their own sections.	
Reviewer #3	10. If available, studies of behavioral intentions (e.g., survey studies asking about hypothetical bans, behavioral economic studies) of what those who smoke flavored cigars would do if flavored cigars were unavailable should be included to better estimate the potential policy impacts. Several studies from the recent TRS meeting addressed these issues and should be considered as pre-publication materials.	
Reviewer #3	11. Separating out the youth and young adult literature would be helpful. Both of these age groups are important for initiation and progression to regular use. With Tobacco 21 as a national policy (including young adults) and increases of tobacco initiation into the young adult years, young adults are a critical age group for flavored cigar use. The current literature combines studies of both age groups and conclusions to question 1 and 2 do not clearly call out the impacts on young adults. General literature on how patterns of tobacco initiation have expanded into the young adult years should be more fully examined.	
Reviewer #3	12. Gender differences should also be discussed more fully. Cigars are used more frequently by males but flavored cigar use is typically higher among women including pregnant women.	
Reviewer #3	13. Where possible, issues of intersectionality should be more clearly addressed (e.g., racial/ethnic disparities in flavored cigar use among sexual and gender minority populations).	
Reviewer #3	14. There are several studies of flavor use and mental health/substance use/medical co-morbidities/homelessness and should be included to assess disparities.	
Reviewer #3	15. Studies on retail availability of flavored tobacco after policy change should be included. These include studies on compliance/adherence with flavor restrictions from store audits or littered packs can help to determine why some policies may or may not have had adequate impacts (i.e., if compliance/enforcement was poor). Examination of reduced flavor advertising should also be included.	
Reviewer #4	I have no methodological concerns that diminish my confidence in the conclusions drawn from the literature review, and the review is done in an objective manner. I do believe that addressing the three points raised in response to Charge Question #1 - considering the type of cigar for all studies when possible, including blunt users, and including those under 21 years of age as 'youth'	

CHARGE QUESTION 3. Provide any additional comments, such as methodological concerns, objectivity and strength of the data, limitations, or outcomes not discussed.

REVIEWER	COMMENT	RESPONSE
	- will further expand the scope of cigar use in the population. Specific comments are provided in section III Specific Observations for FDA’s consideration.	

III. Specific Observations

REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
Reviewer #1	4	1	Typographical error in the third sentence: “...by non-Hispanic Black high school students <u>as</u> twice as high...” – the first ‘as’ should be ‘is’	
Reviewer #1	4	1	Revise to say ‘high school student’ instead of “high schooler” in the second sentence.	
Reviewer #1	4	1	Add ‘persons’ or ‘individuals’ after Whites or African Americans in this paragraph.	
Reviewer #1	6	2	Add ‘persons’ or ‘individuals’ after Whites, Blacks, Hispanics or African Americans in this paragraph	
Reviewer #1	6	2	Black non-Hispanic is used in sentence two but non-Hispanic Black is used elsewhere in the paragraph. Revise for consistency.	
Reviewer #1	6	3	The last sentence on the page has inconsistent reference formatting for the Hinds citation.	
Reviewer #1	7	3	The second sentence has the citation, Johnson et al., 2019, listed twice.	
Reviewer #1	8	2	The second sentence requires a citation.	
Reviewer #1	9	2	Consider revising the two, long sentences in this paragraph into shorter, more concise sentences to enhance readability.	
Reviewer #1	12	5	Consider dropping the Kool Aid brand name for drink mixes since the authors did not include brand names for candy.	
Reviewer #1	13	1	Typographical error in the second sentence: “...flavors <u>area</u> a leading...” should be ‘are’.	
Reviewer #1	14	3	The third paragraph is comprised of one long sentence. Consider revising into shorter, more concise sentences to enhance readability.	
Reviewer #1	16	1	Capitalize the ‘w’ in Wave 2	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
Reviewer #1	16	5	Villanti et al., 2020 – Does this paragraph refer to any cigar use or should there be differentiation by cigar subtype?	
Reviewer #1	17	2	Consider separating this paragraph into two shorter paragraphs since the content is quite dense. The break could be before “Youth who first used...”	
Reviewer #1	17	2	Potential typographical error: “Youth who had first used a flavored cigar other than menthol or mint had a significantly higher prevalence of past 30-day cigarillo use compared to those who first used a non-flavored cigarillo (aPR 1.58; 95% CI: 1.02, 2.43).” Should the underlined word be cigarillo rather than cigar?	
Reviewer #1	17	3	Should the word “traditional” be the descriptor included before each instance of cigar in this paragraph?	
Reviewer #1	18	2	What does “ delayed past 30-day users” mean?	
Reviewer #1	18	3	Consider separating this paragraph into two shorter paragraphs since the content is quite dense. The break could be before “Researchers analyzing data from the...”	
Reviewer #1	18	3	The last sentence in the paragraph is quite long. Consider revising into shorter, more concise sentences to enhance readability.	
Reviewer #1	19	2	The last sentence in the paragraph is quite long. Consider revising into shorter, more concise sentences to enhance readability.	
Reviewer #1	22	1	The last sentence in the paragraph is quite long. Consider revising into shorter, more concise sentences to enhance readability.	
Reviewer #1	24	2	Typographical error in the fifth sentence: “...current user of flavored cigars...” should be ‘use’	
Reviewer #1	24	3	Possible typographical error: Should it be Difference-in-differences with the second difference plural?	
Reviewer #1	25	2	In the second sentence, consider clarifying what products are included in the regulations, such as e-cigarettes and menthol cigarettes (if accurate).	
Reviewer #1	26	2	No limitations are reported for Yang et al., 2020’s manuscript.	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
Reviewer #1	26	3	Does active implementation mean policy enforcement? If so, consider revising for clarity.	
Reviewer #1	31	2	Avoid use of contractions: revise to 'did not' in the fifth sentence.	
Reviewer #1	32	4	There is an extra parenthesis in the second sentence.	
Reviewer #1	33	2	Why does the 2009 NTYS data have the descriptor of "Spring 2009" when all others are just the year?	
Reviewer #1	35	1	The first sentence has the citation, Rostron et al., 2019, listed twice.	
Reviewer #1	35	1	Typographical error in the third sentence: "...then utilize PATH Study data..." should be 'utilized' (past tense).	
Reviewer #1	43	References	[Placeholder for National Youth Tobacco Survey Memo (2021)]- This citation is included in the reference list but I did not see it in the main document.	
Reviewer #1	51	Appendix 2	The citation format for the appendix is different from the main document. Consider revising for consistency.	
Reviewer #1	56	Appendix 3	Effective or Enforcement Year is a more accurate column title than Effective or Enforcement Date.	
Reviewer #1	57	Canada row	Spell out minimum vs min	
Reviewer #1	62	Last row	Capitalize Black	
Reviewer #2	36	3	Final paragraph is missing citation to the discussed study	
Reviewer #3	5	2	Our study Rose SW, Johnson AL, Glasser AM, et al. Flavour types used by youth and adult tobacco users in wave 2 of the Population Assessment of Tobacco and Health (PATH) Study 2014-2015. <i>Tob Control</i> . Jul 2020;29(4):432-446. doi:10.1136/tobaccocontrol-2018-054852 included tables on concordance between self-report and brand assessed flavors including for cigars which may help with the discussion of self-reported flavors assessment.	
Reviewer #3	9	1	"They also found that abuse liability can differ with cigar flavor (Bono et al 2020)" Please clarify in which direction and which flavor(s).	
Reviewer #3	13	1	"... showing that flavors are a leading..."	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
Reviewer #3	16	1	Paragraph is about adults 25+ but last sentence is about youth and should be moved to the discussion of youth. This entire section should be reorganized to discuss the findings for youth, young adults, and then adults 25+ separately. Currently the discussion goes back and forth making it hard to follow.	
Reviewer #3	20	2	“...consumers did not appear to completely substitute non-flavored cigars or concept flavored cigars for flavored cigars.”	
Reviewer #3	24	3 rd	The section is titled Lowell, Massachusetts but also includes review studies based in Attleboro and Salem	
Reviewer #3	27	2 nd	Discussion of the Yang study repeats discussion of articles already reviewed on page 26. This information should be put together or deleted since including the same study more than once makes it seem like there is more evidence than actually exists.	
Reviewer #3	29	2 nd	Paragraph repeats discussion of articles already reviewed as part of the discussion of each city policy. Including this information more than once makes it seem like there is more evidence than actually exists.	
Reviewer #3	34	1 st	Discussion of Courtemanche article is duplicated from page 33	
Reviewer #3	35	2 nd	“...estimate the potential range of cigar...”	
Reviewer #3	35-36	1st	Add specific mortality decrease and prevalence decrease estimates to this discussion. It seems that the Rostron 2019 study referenced on pages 35-36 is miscited in the reference list (L Rostron, B., G Corey, C., Holder-Hayes, E., & K Ambrose, B. (2019). Estimating the Potential Public Health Impact of Prohibiting Characterizing Flavors in Cigars throughout the US. International journal of environmental research and public health, 16(18), 3234. https://doi.org/10.3390/ijerph16183234 instead of Rostron BL, Corey CG, Gindi RM. Cigar smoking prevalence and morbidity among US adults, 2000–2015. Preventive Medicine Reports. 2019/06/01/	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
			2019;14:100821. doi: https://doi.org/10.1016/j.pmedr.2019.100821 which is in the references)	
Reviewer #3	36	Last sentence	Add “The study did not account for tobacco product...”	
Reviewer #4	3	Purpose and Scope section	<p>Recommend adding sections on 1) health risks from cigar use; and 2) the evidence that cigars are smoking cessation aids.</p> <p>I believe the data will show that cigars pose significant health risks and NCI Monograph 6 among other review documents describe this in detail. Linking the behavior to health outcomes is needed in this Review to make that case that cigars pose a risk to individual and public health.</p> <p>The 2nd point about whether cigars are a cessation aid, which I don’t believe there is any evidence to indicate that, simply makes the case that there is no upside benefit to public health from the use of cigars. Walk the reader through the full spectrum: from cigars being harmful, to they are commonly used, and part of that is due to the appealing flavors, and there’s no benefit to having appealing cigars for public health...or something like that, of course, guided by what the summary of the literature in each area indicates.</p>	
Reviewer #4	3	Purpose and Scope section, bullet #1	Define ‘characterizing flavor’ and how does this differ from a flavor that is not ‘characterizing’. How is characterizing flavors defined for the purposes of this review and the studies that comprise it, which I believe make assumptions that certain brand names have characterizing flavors, but is there evidence to link the product names to the product formulations that produce the characterizing flavor?	
Reviewer #4	3	Prevalence of Cigar Use Among Youth section	Three general comments about methods for assessing cigar use among youth. The first is that the PATH Study demonstrates that assessment of the different types of cigars is necessary to better estimate cigar prevalence. Many past studies assess cigar use as a single question, which yields lower estimates of cigar use. The PATH Study and some more recent studies use better methods to show	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
			<p>pictures and provide a description of different types of cigars, which provide a more detailed, and in my opinion, superior method for assessing cigar use. The importance of this is that studies that assess cigar use with a single item and does not differentiate between the different types of cigars are likely underestimating the true prevalence of cigar use.</p> <p>The 2nd comment is that blunt use is a common behavior that involves the use of cigars for cannabis intake. Relatively few studies capture cigar use in the context of blunts and, thus, those studies will underestimate cigar use. The methods for this review indicate that studies primarily of blunt users are excluded, which is a condition I believe should be reconsidered because regardless of blunt use, by definition, is the use of cigars and omitting blunt use will systematically bias the results, particularly with respect to certain minority populations. Results from the PATH Study may be available to assess this in more detail.</p> <p>The 3rd comment is that past studies of ‘youth’ are underestimating the number of underage cigar smokers in the population. The minimum sales age for tobacco products is 21 years of age, therefore, all those age 20 and below are underage users to whom it is illegal to sell tobacco. The literature review should be clearer on this point and what the definition of ‘youth’ is. The takeaway point is that virtually all of the studies cited in this review define youth as <18 year of age; therefore, they underestimate the number of underage cigar smokers in the current policy setting where 21 is the minimum sales age.</p>	
Reviewer #4	4	Disparities in Cigar Use Among Youth section	Assessment of blunt use may differ by race/ethnicity and other factors, so it is particularly important to include an assessment of cigar use in the context of blunting for this review.	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
Reviewer #4	8	Addition of Characterizing Flavors in Tobacco Products section	Confirm this refers to ‘characterizing flavors’. It probably does, but the term ‘characterizing’ is subjective, but the point made here addresses the chemistry of the product.	
Reviewer #4	8	Addition of Characterizing Flavors in Tobacco Products section	Recommend using the term ‘cigar manufacturers’ instead of ‘tobacco industry’ throughout when referring specifically to cigars as it is more precise and doesn’t pin practices necessarily for certain types of manufacturers on other types (i.e., vaping product manufacturers that are not involved in work with smoke chemistry, bitter tobacco leaves, etc.).	
Reviewer #4	8	Abuse Liability of Flavored Tobacco Products	<p>I found this section to be under-developed and suggest incorporating it with the more compelling studies in the following section. There are just a limited number of studies with some of them using hypothetical purchase tasks, which are a great method, without a lot of empirical evidence.</p> <p>Consider framing this new section that describes the literature on the appeal and abuse liability of flavored cigars in the following way:</p> <p>There are two relevant issues – initial trial and progression to more regular use.</p> <p>For initial trial, appealing flavors can promote trying the flavored cigars, which studies show will greatly increase the likelihood of becoming a current or regular user in the future. This can work both through the marketing and advertising angle as well as making the first experience with the flavored product appealing and then the nicotine takes over to promote dependence. In other words, the flavors themselves don’t need to produce dependence directly, but just their making the product worth trying, it can produce dependence indirectly.</p>	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
			The progression to more regular use issue would include some of the studies that are in this section here on abuse liability in the area of transition from occasional to more regular use.	
Reviewer #4	9	Appeal of Flavored Tobacco Products	<p>The studies described here are strong and a compelling case is made.</p> <p>However, I think it is preferable to organize the section according to behavioral transitions and include the studies across the current subsections. I see now that question #2 addresses the issue of progression in use so that in large part addresses my comment; however, there may be opportunities to be clearer with the presentation that question 1 and question 2 are connected and flow sequentially.</p> <p>Transitions include initial trial – what is the evidence that flavored cigars promote trying the product?</p> <p>Then the transition from trial to occasional use – evidence like Villanti’s recent PATH Study paper showing, I think, that those who start with a flavored cigar were more likely to be a past 30 day user at follow-up.</p> <p>Then transition to frequent/regular/daily use, which gets it to the issues of dependence and abuse liability... and this is the pattern of use that has most of the evidence of harm to health.</p>	
Reviewer #4	9	Appeal of Flavored Tobacco Products	To what extent has the marketing of flavored cigars been shown to be associated with these measures of use/progression? Consider adding this component to make a stronger case for accompanying conditions to limit marketing to those under 21 as part of any rule making process. The marketing component is very important to incorporate.	
Reviewer #4	13	Last paragraph on this page	Great to see this is being considered elsewhere. It’s necessary to document the literature on health risks of cigars.	

III. Specific Observations				
REVIEWER	Page	Paragraph/ Line	Comment	RESPONSE
Reviewer #4	13	Last paragraph on this page	Is it also appropriate to cite appropriate rules/regulations that limit the use of characterizing flavors in other types of tobacco products under FDA/CTPs authority?	
Reviewer #4	20	Local and National Policy Evaluation Studies section	Somewhere in here I recommend considering the difference between a local and a nationally implemented policy. Local policy effects are likely a lower bound of their impact because it's easier to circumvent the policy by traveling outside the jurisdiction; however, this is generally not practical for nationally implemented policies and this is particularly true for young people.	
Reviewer #4	28	Last full paragraph on this page	<p>I believe there is a Letter to the Editor and response by Dr. Friedman recently published that identifies and addresses some of the criticisms raised, which should be checked out.</p> <p>The main conclusion in this paper is that cigarette smoking increased in San Francisco where there was a policy, compared to other locations where no flavored policy was present. I don't believe any data on cigar use or vaping is reported. As such this study is not a direct evaluation of the flavor policy with respect to cigars. However, it does speak to potential unintended consequences of a broad flavor policy.</p> <p>The literature review should address whether any of the other local policy evaluations found evidence of unintended consequences including pushing people to use cigarettes, increasing contraband product, increasing use of third party product add-ons for flavor enhancement, or cross-border sales.</p>	