

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	What is the cost-effectiveness of menu calorie labeling on reducing obesity-associated cancer burdens: an economic evaluation of a federal policy intervention among 235 million adults in the United States
AUTHORS	Du, Mengxi; Griecci, Christina; Cudhea, Frederick; Eom, Heesun; Wong, John; Wilde, Parke; Kim, David; Michaud, Dominique; Wang, Y. Claire; Mozaffarian, Dariush; Zhang, Fang-Fang

VERSION 1 – REVIEW

REVIEWER	Ananthapavan, Jaithri Deakin University, Economics, Cost-effectiveness
REVIEW RETURNED	26-May-2022

GENERAL COMMENTS	<p>This is an important topic that is well researched and modelled, however the reporting of all aspects can be improved. English language editing of the introduction is required. Specific comments below.</p> <p>Abstract: Design: please specify if the model is a Markov model Participants: make it clear that you are talking about a modelled population. What year is the modelled population. The “intervention” section should report more features of the model, rather than only the data inputs. It should also clearly specify the policy being evaluated. The source of the key input related to the effectiveness of the menu labelling on calorie intake should be better explained. Main outcome measure – specify the final health outcome. What threshold is used to report cost-effectiveness? Currency and year should also be specified. Results: page 4, line 56 – not sure you can use the term “observed” as these are modelled findings. A more suitable term may be “predicted”. Introduction: <ul style="list-style-type: none"> • Page 6, line 66 – improve wording...“\$147 billion in healthcare costs each year”. • Page 6, line 67 – report currency and the cost year. • Page 6, line 73 – sentence needs rewording • Page 6, line 75 - sentence needs rewording • Page 7, line 87 – more detail on the prior research is required e.g. types of studies that have demonstrated reduced intake with the intervention, the magnitude of impact, including international literature on cost-effectiveness of menu labelling (see https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0234804 and http://www.aceobesitypolicy.com.au/wp-content/uploads/2018/11/Menu-kilojoule-labelling-FINAL.pdf) • Reference 21 should be discussed further. • Please also provide a rationale for only including cancers rather than other obesity-related diseases. </p>
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	<p>Methods:</p> <ul style="list-style-type: none"> • Page 7, line 98. More detail of the characteristics of the 235 million US adults is required. What is the source of the population data – what population does the model population represent, what is the year of the US population that is simulated? Supplementary figure 1 doesn't provide a reference. Without this data, and an indication that the simulated population is representative of the US population of a specific year, the relevance of the findings to policy is questionable. • Table 1 <ul style="list-style-type: none"> o explanation of the symbols is required o Effect of added sugar on BMI is reported as an input – how about impact of change in calories and subsequent impact on BMI? • Simulated US population <ul style="list-style-type: none"> o This section can be clearer – when you say the baseline, are you suggesting that the population represents the 2016 US population over the age of 20 years? • Calorie consumption from restaurants <ul style="list-style-type: none"> o Please provide stratified data on fast food consumption and BMI in a supplementary file. If this is already provided, please reference it in this section. • Policy association with Calorie Consumption <ul style="list-style-type: none"> o Given that this is the key input for the modelling, more detail on the 7.3% reduction is required i.e. further details of the study. A table within the main text showing the different estimates (as reported in Appendix 1) will help demonstrate that this is a reasonable estimate of policy effect. o Please also clarify that the meta-analysis included the impact on both full service restaurants and fast food o It is also not clear how the calorie reduction per meal (7.3%) was translated to mean calorie consumption reduction from fast food from baseline (as reported in the calorie consumption from restaurants section). o For scenario 1, it states that the impact lasted for the first year. What is the duration of effect for scenario 2? o It is not 100% clear whether in scenario 2 the impact on behaviour change is also included. This would be inappropriate as the 7.3% reduction in calorie consumption may incorporate the impact of reformulation. Please justify if the two scenarios are being combined. • Cancer Incidence, Mortality, and HRQoL <ul style="list-style-type: none"> o Can you please explain what HRQoL measure was used when more than one source reported a relevant measure? Add to limitations the potential issues of using different sources as the basis of utility measurement for the different cancers. Was there a process of ensuring the values were internally consistent? I.e. for some cancers, the “continuous” health state has a higher utility value than the initial health state and for others it is lower. o The cohort of 20-44 year olds could have varied incidence, mortality and costs. Is there a reason for the wide age band? • Policy and related costs: <ul style="list-style-type: none"> o Table of costs would be better in the body of the manuscript rather than the appendix. o Appendix 6 reports the source for healthcare costs – can you please include a table of the cost per health state included in the model? o Were there cost difference by age cohort? • Please add a section reporting costs used in the societal perspective, sources and method of calculation • Cost effectiveness analysis <ul style="list-style-type: none"> o More justification of the WTP threshold is required. Is this a common valued used in the US? • Please add a section on model structure and include supplementary figure 1 within the manuscript. This figure needs to be explained. How is
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	<p>this different from a Markov model? What is the cycle length? What is the validity of the cycle length for transition to the cancer continuing state for each of the cancers?</p> <p>Results:</p> <ul style="list-style-type: none"> • Health Gain <ul style="list-style-type: none"> o Page 15, line 231 – where did the 7.2% come from. Is it the 7.3% reported in the meta-analysis? o Page 15, line 232 – here it looks like scenario 1 and 2 have been combined? Please make clear all the scenarios in your methods and exactly what is changed in the different sensitivity analyses (a table will be good). • Economic impacts <ul style="list-style-type: none"> o Before presenting indirect costs including productivity impacts, the methods used to calculate this need to be better explained o Please present the cost-effectiveness results in a table in the manuscript – i.e. incremental intervention costs, cost-savings, net costs, QALYs gained, ICER <p>Discussion:</p> <ul style="list-style-type: none"> • Page 22, line 300. The societal net costs reported here are different to the results. • In addition to the reporting of CE of screening programs – please also compare the menu labelling CE with other nutrition related interventions e.g. SSB taxes, junk food advertising restrictions etc. <p>Figure 2:</p> <ul style="list-style-type: none"> • Please adjust all figures so that the WTP threshold appear in all images. • Spelling error – Lifetime <p>Supplementary table 2</p> <ul style="list-style-type: none"> • Does the RR change with age? <p>Supplementary table 5</p> <ul style="list-style-type: none"> • How was the end of life utility value used? <p>Supplementary table 9</p> <ul style="list-style-type: none"> • Title says consumption of calories, however the consumption data in the table is in grams – how was this converted to calories? • If this is reported in calories – it doesn't really seem realistic that on average 20-44 consume 425 kcal per day (supplementary table 8) with 84% (357 kcal/day) coming from full-service and fast-food restaurants.
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VERSION 1 – AUTHOR RESPONSE

Comments from Reviewer:

Dr. Jaithri Ananthapavan, Deakin University

This is an important topic that is well researched and modelled, however the reporting of all aspects can be improved. English language editing of the introduction is required. Specific comments below.

Authors' response: We appreciate the reviewer's positive comments and have revised the introduction to improve the readability. Our responses to the specific comments are itemized below.

Abstract:

1. Design: please specify if the model is a Markov model

Authors' response: We have now specified in the Design section that this model is a Markov cohort state-transition model (page 3, line 35).

2. Participants: make it clear that you are talking about a modelled population. What year is the modelled population.

Authors' response: We have now made it clear that participants are a modeled population of 235 million U.S. adults aged 20+ years in 2015-2016 (page 3, line 37).

3. The “intervention” section should report more features of the model, rather than only the data inputs. It should also clearly specify the policy being evaluated. The source of the key input related to the effectiveness of the menu labelling on calorie intake should be better explained.

Authors' response: We have now added descriptions about the policy being evaluated in the first sentence of the “Interventions” section to improve clarity (page 3, line 38) and explained that the key input related to the policy effect estimates was obtained from published literature (line 44). We thank the reviewer for the thoughtful comment for including more features of the model in the abstract; however, due to the word limit, we are unable to expand the abstract further but have included more details about the policy, model features, and data inputs in the Introduction and Methods sections of the manuscript and the Supplementary materials.

4. Main outcome measure – specify the final health outcome. What threshold is used to report cost-effectiveness? Currency and year should also be specified.

Authors' response: The final health outcomes include the number of new cancer cases and cancer deaths being averted. The threshold used to report cost-effectiveness is \$150,000 per quality-adjusted life year (QALY) gained. The costs reported are in 2015 US dollars. We have now added these details to the Main outcome measures.

5. Results: page 4, line 56 – not sure you can use the term “observed” as these are modelled findings. A more suitable term may be “predicted”.

Authors' response: We have changed the term “observed” to “predicted” as suggested by the reviewer (page 4, line 59).

6. Introduction:

- Page 6, line 66 – improve wording...“\$147 billion in healthcare costs each year”.
- Page 6, line 67 – report currency and the cost year.
- Page 6, line 73 – sentence needs rewording
- Page 6, line 75 - sentence needs rewording

Authors' response: We have updated the costs to direct cancer care expenditures based on a more recently published article and added the currency and the cost year (page 6, lines 88-89). We have rephrased the sentences to improve the clarity.

- Page 7, line 87 – more detail on the prior research is required e.g. types of studies that have demonstrated reduced intake with the intervention, the magnitude of impact, including international literature on cost-effectiveness of menu labelling
(see <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0234804> and <http://www.aceobesitypolicy.com.au/wp-content/uploads/2018/11/Menu-kilojoule-labeling-FINAL.pdf>)
- Reference 21 should be discussed further.
- Please also provide a rationale for only including cancers rather than other obesity-related diseases.

Authors' response: We have now added more details on the prior research including reference 21 (Pages 6-7, lines 107-111). We have also included evidence from the international literature on the cost-effectiveness of menu calorie labeling as suggested (Page 7, lines 113-121, references 22-23). Prior studies have evaluated the cost-effectiveness of menu-calorie labeling on obesity and obesity-related outcomes. Despite obesity-related cancers being diagnosed disproportionately at a younger age, no prior studies have specifically evaluated the policy's impact on preventing obesity-related cancers. Our study aimed to address this knowledge gap. We have provided the rationale in lines 121-122.

7. Methods:

- *Page 7, line 98. More detail of the characteristics of the 235 million US adults is required. What is the source of the population data – what population does the model population represent, what is the year of the US population that is simulated? Supplementary figure 1 doesn't provide a reference. Without this data, and an indication that the simulated population is representative of the US population of a specific year, the relevance of the findings to policy is questionable.*

Authors' response: We appreciate the reviewer's thoughtful comments and have added more details about the population. We would like to clarify that this section is to provide a brief overview of the modeling study and model structure, and we have provided more detailed descriptions of the US adult population in "Simulated US Population" in the Methods and "Population Characteristics" in the Results sections of the manuscript.

- *Table 1*

- o *explanation of the symbols is required*

- o *Effect of added sugar on BMI is reported as an input – how about impact of change in calories and subsequent impact on BMI?*

Authors' response: We thank the reviewer's careful review and have changed the symbols to texts and corrected the typos.

- *Simulated US population*

- o *This section can be clearer – when you say the baseline, are you suggesting that the population represents the 2016 US population over the age of 20 years?*

Authors' response: Considering that some restaurants have taken actions to label calories on their menus or menu boards prior to the date when FDA published the final rules whereas others implemented the policy during 2016-2018, we decided to use 2015-2016 as the baseline of the policy intervention. The projected population size (235 million) of US adults in 2015-2016 was obtained from the 2017 National Population Projections Tables published by the US Census. We have added these details to the revised manuscript for more clarity.

- *Calorie consumption from restaurants*

- o *Please provide stratified data on fast food consumption and BMI in a supplementary file. If this is already provided, please reference it in this section.*

Authors' response: Our study modeled the impact of menu calorie labeling on BMI change through the reduction of calories consumed from fast-food or full-service restaurants rather than the consumption of fast foods. The stratified data on calorie intake have been presented in Supplementary Tables 8-9 and referred in the Results section of the manuscript (page 17, lines 282-283).

- *Policy association with Calorie Consumption*

- o *Given that this is the key input for the modelling, more detail on the 7.3% reduction is required i.e. further details of the study. A table within the main text showing the different estimates (as reported in Appendix 1) will help demonstrate that this is a reasonable estimate of policy effect.*

- o *Please also clarify that the meta-analysis included the impact on both full service restaurants and fast food*

Authors' response: We have added more details about the systematic review and meta-analysis in the main text (page 12, lines 167-170) and added a table to summarize the designs and estimates from prior studies. Because only up to 5 tables/figures can be included in the main text, we have included the summary table in the Supplemental materials (Appendix Table 1).

- o *It is also not clear how the calorie reduction per meal (7.3%) was translated to mean calorie consumption reduction from fast food from baseline (as reported in the calorie consumption from restaurants section).*

o For scenario 1, it states that the impact lasted for the first year. What is the duration of effect for scenario 2?

o It is not 100% clear whether in scenario 2 the impact on behaviour change is also included. This would be inappropriate as the 7.3% reduction in calorie consumption may incorporate the impact of reformulation. Please justify if the two scenarios are being combined.

Authors' response: We have now added two sentences to describe how the reduction in mean calories consumed from fast-food or full-service restaurants was computed among the simulated population (page 13, lines 196-198). We have also added the assumptions about the policy duration in this section (pages 12-13, lines 186-189). These assumptions are provided in Table 1. We have specified that scenario 2 combined the impact on behavior change and the impact of reformulation, the total effect size is 7.3% plus 5% = 12.3%.

- *Cancer Incidence, Mortality, and HRQoL*

o Can you please explain what HRQoL measure was used when more than one source reported a relevant measure? Add to limitations the potential issues of using different sources as the basis of utility measurement for the different cancers. Was there a process of ensuring the values were internally consistent? I.e. for some cancers, the “continuous” health state has a higher utility value than the initial health state and for others it is lower.

Authors' response: The inclusion criteria and process of selecting HRQoL are reported in the supplemental material (Appendix 4). When more than one source reported a relevant measure, the EQ-5D instrument conducted among US samples was chosen to keep consistency and match with our simulated population. The chosen values were based on the best available data, and we have two researchers independently extracted the data with the consensus being reached after having multiple rounds of discussions with senior researchers.

o The cohort of 20-44 year olds could have varied incidence, mortality and costs. Is there a reason for the wide age band?

Authors' response: We acknowledge that the cohort of 20-44 years old could have different incidence, mortality, and costs, but in general, most people in this group are healthy, and the differences in cancer statistics and healthcare-related costs are relatively small compared with other age groups. To improve the model efficiency and save computing time, we decided to categorize people into this age group.

- *Policy and related costs:*

o Table of costs would be better in the body of the manuscript rather than the appendix.

o Appendix 6 reports the source for healthcare costs – can you please include a table of the cost per health state included in the model?

o Were there cost difference by age cohort?

Authors' response: We thank the reviewer's helpful comments. Because only up to 5 tables/figures are allowed in the main manuscript, we kept the cost tables in the supplementary materials (policy costs were reported in Appendix Table 5, healthcare costs by age, sex, and phases of cancer care were reported in Supplementary Table 6, and healthcare costs by age, sex, and race/ethnicity for the general population were reported in Supplementary Table 7).

- *Please add a section reporting costs used in the societal perspective, sources and method of calculation*

Authors' response: We would like to clarify that the calculations for net costs from the societal perspective are described in the “Cost-Effectiveness Analysis” section (page 15, lines 254-256). “Net costs from the societal perspective were assessed as the difference between total policy costs (including both government and industry costs) and health-related costs saved (including direct and indirect costs of cancer care).” The sources for each cost component are reported in both the main text and the supplementary materials.

- *Cost effectiveness analysis*

- o *More justification of the WTP threshold is required. Is this a common value used in the US?*

Authors' response: The WTP threshold is the common value used in the US as cited in the main text (references 49-50).

- *Please add a section on model structure and include supplementary figure 1 within the manuscript. This figure needs to be explained. How is this different from a Markov model? What is the cycle length? What is the validity of the cycle length for transition to the cancer continuing state for each of the cancers?*

Authors' response: We have added a description of the model structure in the "Study overview" section. The description is also included in the figure legend of Supplementary Figure 1. Due to the space limitation, we would like to keep the figure as a supplementary figure. The model that we used is a Markov model. As specified in the description, the model integrated the annual likelihood of changes in health, meaning that the cycle length is 1 year, and people may change their health state or remain in the same state at the end of each year. To ensure the validity of the cycle length for transition to cancer continuing state, cancer- and state-specific health costs and HRQoLs used were modeled.

Results:

- *Health Gain*

- o *Page 15, line 231 – where did the 7.2% come from. Is it the 7.3% reported in the meta-analysis?*

Authors' response: Thank you for the careful review. The number should be 7.3%. We have removed this sentence to avoid redundancy.

- o *Page 15, line 232 – here it looks like scenario 1 and 2 have been combined? Please make clear all the scenarios in your methods and exactly what is changed in the different sensitivity analyses (a table will be good).*

Authors' response: We would like to confirm that in scenario 2, the effects on consumer behavior and industry reformulation were combined. We have specified this in the Methods section (page 13, lines 189-191). In sensitivity analyses, only one parameter was changed at a time (one-way sensitivity analysis). Each specific change is included in the main text, Supplementary Figure 6 and its footnotes.

- *Economic impacts*

- o *Before presenting indirect costs including productivity impacts, the methods used to calculate this need to be better explained*

Authors' response: We would like to clarify that indirect costs were costs that fall outside of the formal healthcare section.¹ In our analysis, the indirect costs included productivity loss and patient time costs. The productivity costs reflect the value of time in society and productivity loss can be attributable to patients' disability to work or missed workdays that patients used to receive medical care.¹ Patient time costs refer to the time a patient spends to access care (e.g., travel waiting time) and participate in or undergo an intervention as well as the time spent by informal (unpaid) caregivers in caring for patients.¹ These were the common terms used in cost-effectiveness analysis evaluations in health and medicine in the US.

- o *Please present the cost-effectiveness results in a table in the manuscript – i.e. incremental intervention costs, cost-savings, net costs, QALYs gained, ICER*

Authors' response: The net costs, QALYs gained, and ICERs are presented in table 2. The negative net costs suggested that this policy scenario is cost-saving. The incremental intervention costs are the "policy implementation costs" in table 2 as we compared the policy impact with the status quo (no policy).

Discussion:

- *Page 22, line 300. The societal net costs reported here are different to the results.*
- *In addition to the reporting of CE of screening programs – please also compare the menu labelling CE with other nutrition related interventions e.g. SSB taxes, junk food advertising restrictions etc.*

Authors' response: We have corrected the values in the result section (page 21, lines 321-324) and added discussions on other nutrition-related policy interventions for cancer prevention, including SSB tax, added sugar labeling, and tax on processed meat (page 25, lines 379-385).

Figure 2:

- *Please adjust all figures so that the WTP threshold appear in all images.*
- *Spelling error – Lifetime*

Authors' response: We appreciate the reviewer's thoughtful comments. We have tried to adjust the figures, but due to the wide range of the y-axis, the adjusted figures were less visual-friendly. We will keep the figures as is for now but seek the editor's help on this.

Supplementary table 2

- *Does the RR change with age?*

Authors' response: There is no strong evidence to suggest that RR changes with age per the expert panel review conducted by the World Cancer Research Fund/American Institute for Cancer Research Continuous Update Project. We assumed that the association between change in BMI and change in cancer risk remained consistent across different age groups.

Supplementary table 5

- *How was the end of life utility value used?*

Authors' response: We assumed that the end of life was the last year of their life for cancer patients or survivors. The corresponding value was used to calculate the quality-adjusted life year for the last year of their life. We also applied a half-cycle correction to account for the different timing of death. We have added the definition for each phase of care in the main text to improve clarity (page 15, lines 241-242).

Supplementary table 9

- *Title says consumption of calories, however the consumption data in the table is in grams – how was this converted to calories?*
- *If this is reported in calories – it doesn't really seem realistic that on average 20-44 consume 425 kcal per day (supplementary table 8) with 84% (357 kcal/day) coming from full-service and fast-food restaurants.*

Authors' response: We appreciate the reviewers' careful review and have now corrected the typo. We would like to clarify that the 425 kcal/day reported in the main text (page 17, line 282) was the mean intake of calories from full-service or fast-food restaurants for people aged 20-44 years old, while the 357 kcal/day is the mean intake of calories from full-service or fast-food restaurants for people who are non-Hispanic white and aged 20-44 years old.

We appreciated the comments from the reviewer and the editors and the opportunity of submitting the revised manuscript. Thank you for considering our paper for publication in *BMJ Open*.