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Title	**Association between salt substitutes/enhancers and changes in sodium levels in fast-food restaurants: a cross-sectional analysis**
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Reviewer 1	Dr. hasanain Faisal Ghazi
Institution	Management and science University, Community Medicine, International Medical School, Shah Alam, Selangor, Malaysia
General comments (author response in bold)	1. As the study examined salt substitutes in restaurant menu of specific database MENU-FLIP , it is better to include in the study title findings from MENU-FLIP database.. as results include only online published informations from restaurant. **We have respectfully chosen not to include MENU-FLIP in the title, however, we have been very clear in the methods and upfront in the abstract explaining that this data is based on the MENU-FLIP database.** 2. The database include restaurant with more than 20 locations nationwide, are they considered as fast food chains? should it be included in the title? **The title has been changed to include "fast-food"** **New title = Association between salt substitutes/enhancers and the change in sodium levels in fast-food restaurants: a cross-sectional analysis**
Reviewer 2	Dr. Hsing-yi Chang
Institution	National Health Research Institutes, Center for Health Policy Research and Development, Zhunan township, Maoli, Taiwan
General comments (author response in bold)	This manuscript set out to find the replacement of sodium from Canadian chain restaurant foods. It is good to document the replacement of sodium in restaurants. Authors took samples from chain restaurant foods. The database is valuable. It must take a lot of work to collect the information. **There were no questions from reviewer 2. Thank you for your comments.**
Reviewer 3	Dr. Yoni Freedhoff
Institution	Bariatric Medical Institute, Ottawa, Ont.
General comments (author response in bold)	Enjoyed the paper. I would have been curious too whether or not sodium reduction efforts had an impact on meal calories. Given public health push to reduce both, I think good to know if sodium reduction efforts were calorie neutral, or if they had an impact. **Thank you for these comments. The effect of sodium reductions on calorie levels was explored in our previous publication in CMAJ in 2013 "Changes in sodium levels in chain restaurant foods in Canada (2010-2013):a longitudinal study". At the time we found no effect of sodium reduction on calorie levels. Thank you for this comment, we do continue to investigate the interplay between calories and sodium in our current research.**
Reviewer 4	Dr. Jacqui Webster
Institution	The George Institute for Global Health, Food Policy Division, Camperdown, New South Wales, Australia
General comments (author response in bold)	Thanks for the opportunity to review this paper. It is well-written and it is very interesting to consider the use of salt substitutes in restaurant foods. However, I think the paper would need to be re-written, including re-doing the analysis, to make it suitable for publication. **We have re-focused and re-written substantial components of the manuscript. In addition, we have clarified the analysis error/typo that was brought to our attention.** 1. Firstly, at the moment the paper seems to be written from the premise that salt substitutes are inherently bad when there is a wealth of literature highlighting the potential benefits of salt substitutes (potassium chloride) as an effective way of reducing sodium and blood pressure (http://ajcn.nutrition.org/content/early/2014/10/15/ajcn.114.089235). The UK government is currently reviewing the use of potassium chloride in the food supply as a way of reducing salt and is expected to issue new recommendations shortly. It would be helpful if this study could be presented in the context of salt substitutes (KCl) potentially being a very effective way of reducing salt intake, with reference to the benefits of increased potassium consumption as well as the potentially dangerous health risks to a very small minority (mainly patients with end stage kidney disease who should be avoiding high salt foods anyway). **We do not intend to suggest that substitutes are bad. However, it surprised us to find that the most prevalent substitutes/enhancers being used are "glutamate containing substitutes/enhancers". Therefore, because of the controversy that surrounds orally consumed glutamate, we framed some of the discussion around these substitutes and their "potential" health effects in some individuals.** **In the introduction we try to introduce substitutes as being a good thing:** **"It has been recommended that the best strategy to lower sodium is to gradually reduce levels across the food supply to enable consumers' taste-buds to re-sensitize to less salt. Salt substitutes (such as potassium chloride) and salt enhancers (such as monosodium glutamate and yeast extracts) are one means by which sodium can be removed without reducing the perceived salty taste (line 63-68)... Furthermore, when compared to table salt, MSG contains one-third the**

amount of sodium, thus enabling sodium reductions as high as 40%, with no loss of palatability. (line 69-72)
Surprisingly, we did not find potassium chloride to be present in many foods, only 12%, and it was only the fourth most common substitute. That is why we focused our discussion on the more prevalent substitutes (glutamate containing substitutes ie yeast extracts and msg).

2. Secondly, yeast and MSG are not salt substitutes, they are salt enhancers. This distinctions is made clearly in Appendix D of the NHI report on Strategies to Reduce Sodium in the United States which is referenced by the authors: https://www.ncbi.nlm.nih.gov/books/NBK50965/ It does not help t to classify them as the same when we are talking about potential harms and benefits when this topic is such an important area of scientific debate and the potential harms and benefits are different for each product.

We have changed the wording throughout the entire manuscript to refer to these as being substitutes and enhancers.

3. Also, MSG has been used by the food industry as an alternative to salt for many years and I don't think it is correct to imply that restaurants are using MSG to reduce salt in foods. It is the sodium in salt that is bad for health so MSG is just a different form of sodium in the diet that we should be trying to reduce. It is useful to know that restaurants are using MSG in meals but I'm not sure it is really accurate to suggest they are doing this as a way of reducing sodium in the food supply are they?

You're right, MSG has been used for many years. However, we showed an association between foods with decreased levels of sodium and the presence of salt substitutes. We have been very clear in the manuscript that this is an association and does not prove causation. Furthermore, MSG is currently being marketed as a tool to help the food industry decrease sodium levels in the food supply. Therefore, our findings aligned with data which shows that market share for MSG and glutamate ingredients is increasing. This implies that MSG and glutamate ingredients are being used more often by manufacturers. We are clear that we did not prove that salt substitutes have been used to achieve reductions:
"Hence, this study demonstrates an association between salt substitutes/enhancers and change in sodium levels (per serving), but does not prove that salt substitutes/enhancers have been added to achieve sodium reductions" (line 232-234)
We hope that this association will stimulate future research which can investigate this, that is why we are publishing this data. At this point in time, we do not have longitudinal data to prove causation.
Please note, while MSG contains sodium, its intense flavor enables less sodium from MSG to be used. This is stated in the paper (lines 70-72) "when compared to table salt, MSG contains one-third the amount of sodium, thus enabling sodium reductions as high as 40%, with no loss of palatability."

4. Lines 72-74 "MSG and other ingredients …….. are potentially desirable" This should be reworded to say desirable to the food industry as MSG is not desirable to consumers or for public health.

"for food manufacturers" has been added to this sentence: "MSG and other ingredients that could contain free glutamates (such as yeast extracts and hydrolyzed vegetable protein) are desirable for food manufacturers because they stimulate the fifth taste bud—umami" (line 69-70)

5. Yeast extracts are a flavour enhancer not a salt substitute. I wasn't aware of any potential negative health impacts of using yeast extracts so any new evidence on this would be useful. However, at the moment the section on hydrolyzed vegetable proteins and yeast extracts seems a bit speculative and lacks any references with supporting evidence.

We have removed the section on yeast extracts and hydrolyzed vegetable proteins from the discussion.

6. In relation to calcium chloride, I'm not aware of this being used as a salt substitute in itself. Most commercially available salt substitutes and those that I've known be manufactured for trials contain a mixture of sodium, potassium, magnesium and calcium chloride. Both potassium and calcium are essential for health and so the potential benefits of increasing amounts of potassium and calcium in the food supply need to be further considered in the paper. There is currently no discussion about potassium chloride or calcium chloride in the interpretation of the results which is an important omission which needs to be addressed.

Calcium chloride was listed in the IOM report as being a substitute. That is why we included it in our analysis. We do recognize that some food additives may serve multiple functions and may not only be present because of their usefulness as salt substitute/enhancer. We chose not to discuss potassium chloride in the discussion in detail because it was only the fourth most common substitute. We considered adding some discussion around it, however, we are nearly exceeding the two paragraph limit for the "explanation and comparison with other studies" therefore, we have not added any discussion of potassium chloride.

However, the approach needs to deal with the four different substitutes/enhancers separately and discuss the potential pros and cons of each (health impacts are important but consumer acceptability and cost to the

	industry could also be usefully discussed). **Thank you for this suggestion. We recognize that different substitute sand enhancers have varying pros and cons. Currently the objective of this study was to determine what substitutes/enhancers are out there and to see if there is an association between their presence and sodium changes. While we would love to include further details about each of the substitutes and enhancers, there is limited room in this manuscript. Our discussion is already too long and we have been asked by the editors to shorten it, therefore, we have not added info on the pros and cons of each. Thank you for this suggestion, we agree that there needs to be more discussion on this topic!**
Reviewer 5	Dr. Richard Lewanczuk
Institution	University of Alberta, Endocrinology, University of Alberta, Edmonton, Alta.
General comments (author response in bold)	1. The title is misleading and better suited to an opinion article or editorial. The title should be factual, describing the study and its main finding or subject e.g. "The association between the introduction of salt substitutes and the change in total sodium content…" In terms of being misleading, the study, as I understand it, cannot comment on the presence of salt substitutes before 2016 and therefore cannot comment as to whether salt substitutes replaced salt, if they were added for other purposes, or whether they may have been present and their amounts adjusted over time. **Thank you for your suggested title. The title has been changed to "Association between salt substitutes/enhancers and the change in sodium levels in fast-food restaurants: a cross-sectional analysis"** 2. The purpose and objectives (L 88 onwards) seem to be at odds. It seems the objectives are more in line with what is reported and discussed in the paper whereas the purpose cannot be addressed by database analysis – it would require determining intent on the part of the restaurant(s) **We have rewritten the objectives:** **"The first objective of this study was to investigate the prevalence of salt substitutes/enhancers in restaurant foods. The second objective was to understand if there is an association between containing a salt substitute/enhancer and the magnitude of decrease in sodium between 2010 and 2016.The third objective was to determine if the presence of glutamate-containing enhancers (MSG, yeast extracts and hydrolyzed vegetable proteins) is associated with decreased sodium levels in restaurant foods between 2010 and 2016." (lines 83-88)** 3. A minor point, but somewhere in the introduction, purpose or title, it should be clarified that the study applies to typical fast food. **This has been added to the title:** **"Association between salt substitutes/enhancers and the change in sodium levels in fast-food restaurants: a cross-sectional analysis"** 4. In the background or discussion, some mention of the controversy between sodium and sodium chloride should be acknowledged. That is, some proponents suggest that it is sodium chloride that has adverse health consequences, and that sodium per se, is not harmful. Others link health consequences to sodium regardless of its associated anion. **This is an interesting point, thank you for raising it. However, we are struggling to keep the word count below 2500 and thus we have respectfully chosen not to add any discussion of this controversy as it does not directly pertain to our findings.** 5. The authors should consult a statistician. A Chi-square test typically tests observed vs expected results and I'm not sure how that was applied in these circumstances. I gather that proportions are being compared and a Chi-square would not be the correct test in those circumstances. Similarly, the Wilcoxon-Mann-Whitney compares non-parametric distributions and again I'm not sure that was the correct test to use, nor how it was applied. At a minimum, the statistical section, and possibly analyses, needs to be strengthened. **Thank you for spotting this error! We inappropriately indicated that we did "Wilcoxon-Mann-Whitney" tests when in fact, we computed "Wilcoxon Signed Rank" tests. This was simply a typo! The Wilcoxon signed-rank test is appropriate for comparing two non-parametric samples and is a substitute for a t-test when data are non-parametric. That is why we chose to use this test. We have used this test in the past and this test was recommended to our lab by a statistician. Chi-Square tests were used because in a sense, we are comparing observed and expected values. For example, if containing a salt substitute was random, we would expect that 50% of foods would have decreased and 50% would not have decreased. Therefore, 50:50 would have been the expected values, assuming randomness among those that decreased versus didn't decrease. Hence we were comparing our observed proportions in relation to our expected (random distribution would have been 50%). Thus, we feel that chi-square tests were applicable here.** 6. To the authors' point, in line 183, if 64% of foods with a salt substitute showed a decrease in sodium content, what about the other 36%? Does that imply the salt substitutes used in those foods were for purposes other than to reduce sodium? By extension then, perhaps the use of salt substitutes and the

	reduction in sodium are not causally linked, but two separate processes – one of reducing salt, and one of adding e.g. MSG for flavor enhancement (e.g. stimulating the 5th taste bud). **We agree, in this paper the use of salt substitutes and reductions in sodium are not causally linked. We have been clear in the discussion that this data depicts associations using the data that was available. There was insufficient data to demonstrate causation. In the discussion we are very clear that this data is only depicting associations:** **"this study demonstrates an association between salt substitutes/enhancers and change in sodium levels (per serving), but does not prove that salt substitutes/enhancers have been added to achieve sodium reductions" (line 233-235)** 7. Starting in line 190, it's not clear what is being compared - is it foods that decreased in salt with glutamate vs non-glutamate substitutes or is it glutamate substitutes vs the whole category where salt decreased? **We added some text to help clarify this: "70% of foods that had a glutamate-containing enhancer decreased in sodium between 2010 and 2016. Furthermore, foods that had glutamate-containing enhancers were significantly more likely to have decreased in sodium (p=0.0345) compared to foods that did not have a glutamate-containing enhancers." (line 237-241)** 8. In the overall Interpretation, the authors need to be specific, factual and not presume. For example, the first line of the Interpretation is speculative, not factual. **We have removed the first line of the interpretation.** 9. It is unclear why there is so much emphasis and discussion on glutamate-containing salt substitutes. Given the title and objectives, most discussion should be on the associations between salt substitute presence and changes in sodium content. **We chose to focus a lot of our discussion on glutamate containing substitutes for two reasons: First, they were the most prevalence substitutes/enhancers in the restaurant food supply. Second, they are the substitute with the greatest amount of controversy surrounding them and with potential adverse effects for some consumers. Therefore, because of their potential effect on human health we wanted to ensure that the research investigating them was thoroughly discussed in our paper so that readers will understand what is and is not known about these additives. Particularly, we wanted to shed light on the conditions that may mitigate their effects ie dose, and food context with a full literature review on this topic.** 10. One very major point in the design – and perhaps its just poorly explained – is how do the authors know that salt substitutes were introduced between 2010 and 2016? In other words, how do they know that salt substitutes may not have been present in 2010 and just the salt content reduced during that time? **You are correct. This is a design issue due to the fact that ingredient information was not collected in 2010 or 2013. Hence, we have investigated an association because that is the best that can be done using the data that is available. In the limitations we clearly explain that this is only an association:** **"this study demonstrates an association between salt substitutes/enhancers and change in sodium levels (per serving), but does not prove that salt substitutes/enhancers have been added to achieve sodium reductions. Many restaurant foods are constantly introduced or removed from menus, therefore, the results of this study only include foods that have persisted on menus between 2010 and 2016. Ingredient data was not collected in 2010 or 2013, therefore, longitudinal comparisons to prove that substitutes were added while sodium levels simultaneously decreased were not possible" (line 233-239)** 11. I found it very difficult to interpret Figure 1. **We put some thought into ways to reconfigure this figure. We clarified the figure title, however, ultimately, because this was the only comment we received regarding this figure, we have chosen to leave it as is.** 12. In Figure 3, the use of SE vs SD bars is not justified or explained. Thus, it would appear that some comparisons should be statistically significant whereas they are not noted to be so. We chose to use standard errors because standard errors are more appropriate when reporting the results of non-parametric Wilcoxon-sign tests. Therefore, for consistency, we used SE throughout the paper. **We assume you are referring to the "breakfast" data from figure 3. Indeed, the SE bar does suggest that this comparison is significant. From what we can ascertain, it appears that because the "n" among breakfast foods that do not contain a salt substitute is so low that there is insufficient power to make this significant. According to our data, the p value here is 0.06.**