

Article details: 2016-0154	
Title	Adverse effects of caffeinated energy drinks among youth and young adults in Canada: a web-based survey
Authors	David Hammond PhD, Jessica Reid MSc, Sara Zukowski BSc
Reviewer 1	Dr. Jamie Falk
Institution	University of Manitoba, Rady Faculty of Health Sciences, College of Pharmacy, Winnipeg, Man.
General comments (author response in bold)	<p>Thank you for this evaluation of caffeinated energy drinks. It was a pleasure to read and provided an effective analysis of a difficult-to-study area of importance. A few comments and suggestions:</p> <p>Background:</p> <p>1. Page 4, line 27 "consistent with potential adverse outcomes": unsure what this means. Consistent with other reports? Consistent with caffeine-related CV outcomes? If so, which ones? The phrase is referring to the adverse outcomes listed in the following sentence: "A variety of case reports have linked energy drink consumption with serious adverse events, such as stroke, seizures, and serious cardiac effects." We have removed this phrase to avoid potential confusion.</p> <p>2. Page 4, line 43: I don't find 3 cases based on ref: Toronto Star reporting compelling and doesn't fit well with the more rigorous methods of the other references. Consider removing. We agree that it would be helpful to have more validated sources of information on case reports. Unfortunately, the investigation referenced in the citation is one of the only public sources of Canadian data on adverse events from energy drinks. In addition, the data reported in the article is based on cases reported to Health Canada. We have clearly noted the source of this evidence so that readers are aware of the source and can interpret the data accordingly. We can remove this citation if the editor wishes; however, we think it helps to illustrate the lack of validated data and the need for additional evidence on this topic.</p> <p>Methods:</p> <p>3. Page 5, line 37-38 is a repeated sentence "All respondents were provided with information about the study and asked to give consent before participating" Thank you, the repeated text has been deleted.</p> <p>4. Page 5, lines ~45-49: 2181 respondents completed the survey. What is the denominator (i.e. what is the % that did respond out of the entire population that could have)? Additional information on response has been added, as per the editor's request.</p> <p>5. Results:</p> <p>6. Page 6, lines ~40-45: no stats reported for comparison between energy drinks and coffee consumers adverse events We have added the results of new analyses that test the prevalence of adverse events between coffee and energy drinks, among users of each product. Please see page 6, as well as a description of the tests under the Analyses section on page 5.</p> <p>7. Page 6, line ~50-51: Please provide what the recommended maximum is. You cite ref 7 in the background section, but since this is a measured outcome, the maximum reference point you are using should be stated/mentioned in the methods. The recommended maximum printed on the container is either one or two (depending on the size of the container). This detail has been added to the revised manuscript.</p> <p>8. Page 7, lines 3-14: Could you comment on whether there was a trend in adverse events requiring/considering medical attention and consuming below or above the maximum recommended beverages (i.e. were the more serious adverse events associated with higher consumption?) We are reluctant to test such comparisons among subgroups, as few respondents sought medical attention (n=49 [unweighted] respondents who sought/considered seeking medical attention for side effects of energy drinks; n=24 [unweighted] respondents who sought/considered seeking medical attention for side effects of coffee). As noted in the manuscript, the majority of those who experienced adverse effects had consumed less than the maximum guidance (i.e., 2 or fewer); this was true of both those who sought medical attention and those who did not. Of the energy drink consumers who reported side effects but did NOT seek/consider medical attention, 76.9% had consumed 2 or less and 23.1% had consumed more than 2 (n=82 missing excluded); of those who DID seek/consider medical attention, 64.9% had consumed 2 or less and 35.1% had consumed more than 2 (n=2 missing excluded). For coffee, the comparable figures are 74.2%/25.8% (58 missing) and 82.1%/17.9% (1 missing). These additional results have not been added to the manuscript for the reason noted above and due to restrictions on length, but this addition could be made should the editor recommend it.</p> <p>9. Page 7, lines ~17-19: Is this referring to consumers and non-consumers? If so, please state, but ideally, summarizing the consumers proportions and stats from the previous paragraphs would be more meaningful (5.9% vs. 4.2%). This is "overall" (i.e., consumers and non-consumers); revised to say "among all respondents" to make this more clear. As noted above, we have added analyses that are restricted to consumers only.</p> <p>Discussion:</p> <p>10. Page 7: I don't feel the Supplemental file is necessary. The reference is adequate. As noted above in our response to the Editor (response #5), the data included in the Supplemental file are contained in the Canada Vigilance Online Database, however they can only be accessed by entering search terms, which requires a familiarity with the database. If we were only to provide a reference to the database, we anticipate that few, if any, readers would be able to access the results. We believe that a summary of the data contained in the Database will provide readers with the necessary information.</p> <p>11. Page 8, lines 3-6: As for previous comment from page 7 lines 17-19, if this statement</p>

	<p>applies to all responders, suggest adding wording to indicate this, but again, ideally the consumer data denominator would provide the primary comparison of proportions of energy drink serious events to coffee serious events</p> <p>Thank you for this suggestion. We have revised the description, as noted above. We have also provided the additional analysis among consumers only, as noted above.</p> <p>Page 8, Strengths and Limitations section:</p> <p>12. Since this population was 43% from Quebec and 75% white, I would suggest including this as a limitation in generalizability, specifically regarding the former as it is uncertain if the dynamics of energy drink consumption would be similar in other areas of the country. The sample was weighted so that Quebec responses were proportional to population size (i.e., 23% of people this age, rather than 43%), but it has been mentioned in the limitations. Regarding the sample being 75% White, this is comparable to the overall population and not a limitation of the sample; only 19% of Canadians are visible minorities, according to national statistics (http://www12.statcan.gc.ca/nhs-enm/2011/as-sa/99-010-x/99-010-x2011001-eng.cfm#a4).</p> <p>13. Another difficulty with surveys of consumption are determining what defines a dose, so there is a limitation of the uncertainty around the amount of caffeine consumed beyond simply 1-2 beverages, unless this was specified in the questions asked. But even so, the caffeine content especially in coffee varies significantly. Suggest providing a statement addressing this. The caffeine content in both energy drinks and coffee varies, and it is not possible from the survey data to precisely estimate how much caffeine each individual consumed when experiencing adverse effects. It is reasonable to assume that anyone who consumed 3 or more beverages (of either coffee or energy drinks) was exceeding the daily recommendation. This has been noted in the Limitations section of the revised manuscript.</p>
Reviewer 2	Dr. Andrew Bulloch
Institution	University of Calgary, Community Health Sciences, Calgary, Alta
General comments (author response in bold)	<p>This is the first population based survey of energy drinks in Canada that makes comparisons with the adverse effects of coffee. This is a timely and thorough report that encompasses all 10 provinces (but not the Territories) and provides weighted estimates. It is timely because the public generally views energy drinks as safe (as cannabis is viewed) and this will provide an important warning (press releases should be considered). Limitations have been acknowledged and the results backed up by use of data from Health Canada's Adverse Reaction Reporting for Specific Products. Methodology is appropriate. Attention should be paid to the following points:</p> <ol style="list-style-type: none"> Intro paragraph 1: what is the maximum recommended caffeine intake for children < 13; how many drinks does this represent (say of Red Bull)? The maximum recommended intake varies by age: 45 mg/day for 4-6 years; 62.5 mg/day for 7-9 years; 85 mg/day for 10-12 years; no more than 2.5mg/kg body weight for adolescents; 400mg for adults. Details for the relevant age groups have been added to the Background. Intro paragraph3: what country was ref 35 carried out in? The survey was conducted with medical students in Italy. This information has been added to the study description in the paper. Methods: I suggest inclusion of the survey as a supplementary file. The survey has been added as a supplementary file. If the editors wish, we could also post a copy of the survey on a study website. Results: please add some more McNemar's tests: e.g., in paragraph beginning Table 2 shows. As noted above, we have provided additional analysis, as described on pages 5 and 6. Discussion: clarify throughout the paper that the population surveyed has non-consumers, the first sentence confused me at first. The first sentence of the Results for Adverse events notes, "The overall proportions of young people (including consumers and non-consumers)..." This wording has been repeated in the first sentence of the Discussion and we have made other revisions to clarify the respondents included in each analysis, as noted above. Page 8 para 2: sentence: the association between energy drinks and alcohol...needs at least one reference. Thank you for this suggestion: we have cited a review article on this topic in the revised manuscript. Table 3 shows 22.5% were also consuming alcohol whereas this figure is 6.6% in the supplementary data, please comment. The difference is most likely due to differences in age: the current sample is restricted to youth and young adults, whereas there are no age restrictions on the data included in the Canada Vigilance Online Database. Given that consuming alcohol mixed with energy drinks is more common among young people, this likely accounts for the difference. Supplementary data: what is the age range? Please see response to comment immediately above: there is no age limit to the data included in the Canada Vigilance Online Database. Supplementary data: why no Discussion? As noted in our response to the Editor, the purpose of the Supplemental data was to provide readers with a summary of data, but not to provide any additional comment or interpretation, other than in reference to the current findings, contained in the Discussion section on pages 7 and 8 of the manuscript.