Migraine and Mental Health in a Population-Based Sample of Adolescents

Serena L. Orr, Beth K. Potter, Jinhui Ma, Ian Colman

ABSTRACT: Objective: To explore the relationship between migraine and anxiety disorders, mood disorders and perceived mental health in a population-based sample of adolescents. Methods: The Canadian Community Health Survey (CCHS) is a cross-sectional health survey sampling a nationally representative group of Canadians. In this observational study, data on all 61,375 participants aged 12-19 years from six survey cycles were analyzed. The relationships between self-reported migraine, perceived mental health, and mood/anxiety disorders were modeled using univariate and multivariate logistic regression. The migraine–depression association was also explored in a subset of participants using the Composite International Diagnostic Interview—Short Form (CIDI–SF) depression scale. Results: The odds of migraine were higher among those with mood disorders, with the strongest association in 2011-2 (adjusted odds ratio [aOR] = 4.59; 95% confidence interval [CI95%] = 3.44-6.12), and the weakest in 2009-10 (aOR = 3.06; CI95% = 2.06-4.55). The migraine–mood disorders association was also significant throughout all cycles, other than 2011-2, when the CIDI–SF depression scale was employed. The odds of migraine were higher among those with anxiety disorders, with the strongest association in 2011-2 (aOR = 4.21; CI95% = 3.31-5.35) and the weakest in 2010 (aOR = 1.87; CI95% = 1.10-3.37). The inverse association between high perceived mental health and the odds of migraine was observed in all CCHS cycles, with the strongest association in 2011-2 (aOR = 0.58; CI95% = 0.48-0.69) and the weakest in 2003-4 (aOR = 0.75; CI95% = 0.62-0.91). Conclusions: This study provides evidence, derived from a large population-based sample of adolescents, for a link between migraine and mood/anxiety disorders.

INTRODUCTION

Migraine is a common presentation encountered in paediatric practice. It has been estimated that the worldwide prevalence of migraine is 7.7% among children and adolescents.1 Migraine is not only very common but also has a significant impact on the lives of those who suffer with it. Children and adolescents with migraine have high levels of disability2-4 and low health-related quality of life.5,7 Research also suggests that school-aged children with migraine tend to have inferior academic performance as compared to their peers.8,9 Many conditions have been found to occur comorbidly with migraine, and the literature on migraine comorbidities is rapidly
expanding. One of the best-studied areas in this body of literature has been the association between migraine and psychiatric comorbidities. Though the link has been relatively firmly established in the adult literature, there is still considerable debate about the association between migraine and psychiatric comorbidities in children and adolescents, with different authors drawing disparate conclusions about the nature and possibility of a true association and investigations in this area yielding heterogeneous results. A deeper understanding of how migraine relates to disorders such as anxiety and depression is imperative to improving clinical practice, as untreated comorbid psychiatric disorders may hamper efforts to optimally treat the migraines.

The purpose of the proposed study was to explore the relationship between migraine and anxiety disorders, mood disorders and perceived mental health in a population-based sample of adolescents. In this analysis, we investigated whether Canadian adolescents with mood and anxiety disorders are more likely to report migraine as compared to their peers.

Materials and Methods

Subjects

The Canadian Community Health Survey (CCHS) is a federally commissioned cross-sectional survey sampling a nationally representative group of Canadians aged 12 years and over through a complex, multistage, probability sampling design. The CCHS uses the sampling frame of the Canadian Labour Force Survey, whereby a multistage stratified cluster design is applied, using the household as the final sampling unit. In this sampling frame, clusters of households are drawn from strata created in a series of stages based on geography, population density (i.e., major urban center vs. rural vs. city regions) and socioeconomic status. The CCHS collects information about a variety of health outcomes, determinants of health and resource utilization patterns using in-person and telephone computer-assisted interviewing. The study participants were all respondents aged 12 to 19 years from six CCHS cycles that included computer-assisted interviewing. The data were analyzed using SAS software (v. 9.4; SAS Institute, Cary, North Carolina, United States). Given that the prevalence of missing data was low, missing data were handled with case-wise deletion, except for total household income, where missing values were imputed by Statistics Canada. We accounted for the complex sampling design of the CCHS by (1) incorporating sampling weights provided by Statistics Canada into all analyses (to account for unequal probability of selection of respondents); and (2) dividing the relative sampling weight for each participant by the square root of the published average design effect (to address cluster sampling). This method has previously been employed to adjust point and variance estimates with CCHS data.

The prevalence of migraine and mood/anxiety disorders was estimated using weighted proportions, which were converted into percentages with 95% confidence intervals (CI95%). The associations between migraine and mood, anxiety disorders and perceived mental health were explored using both univariate and multivariate logistic regression. Multivariate models were adjusted for sex, age, socioeconomic status (measured by total household income) and race. The validity of self-reported physician-diagnosed mood disorders was explored by also modeling the relationship between migraine and the CIDI–SF depression scale using both univariate and multivariate logistic regression.

Results

In total, data on 61,375 adolescents were analyzed, and CIDI–SF data were available for a subset of 26,409 participants (see Tables 1 and 3; range of proportions of participants with CIDI–SF data vs. entire participant sample = 16.8% [2011-2 cycle] to 65.6% [2003-4 cycle]). The prevalence of migraine among Canadian adolescents was consistent between cycles, with the highest prevalence found in 2007-8 (10.04%, CI95% = 9.52-10.75) and the lowest in 2010 (8.78%, CI95% = 7.80-9.77) (see Table 1). The odds of migraine were significantly higher among those with mood disorders in both unadjusted and adjusted analyses for all six cycles of the survey (Table 2 and Figure 1). The strongest association was found in 2011-2 (adjusted OR [aOR] = 4.59, CI95% = 3.44-6.12), whereas the weakest was seen in 2009-10

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Table 1: Prevalence of migraine, mood disorders, anxiety disorders and perceived mental health by cycle

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Sample size (sample size of CIDI–SF subset)</th>
<th>Migraine prevalence, n (%; CI 95%)</th>
<th>Mood disorders prevalence, n (%; CI 95%)</th>
<th>CIDI–SF score in depressed range, n (%; CI 95%)</th>
<th>Anxiety disorders prevalence, n (%; CI 95%)</th>
<th>Low perceived mental health, n (%; CI 95%)</th>
<th>High perceived mental health, n (%; CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003-4</td>
<td>11,616 (4,840)</td>
<td>1,113 (9.10; 8.45-9.76)</td>
<td>344 (2.47; 2.11-2.82)</td>
<td>254 (4.98; 4.21-5.75)</td>
<td>256 (2.69; 2.32-3.06)</td>
<td>413 (3.35; 2.94-3.76)</td>
<td>8,838 (76.53; 75.56-77.5)</td>
</tr>
<tr>
<td>2005</td>
<td>11,787 (6,204)</td>
<td>1,121 (9.10; 8.47-9.73)</td>
<td>313 (2.63; 2.27-2.98)</td>
<td>263 (4.08; 3.48-4.68)</td>
<td>356 (2.54; 2.19-2.88)</td>
<td>379 (3.34; 2.95-3.74)</td>
<td>9,156 (78.16; 77.25-79.06)</td>
</tr>
<tr>
<td>2007-8</td>
<td>10,088 (3,599)</td>
<td>1,096 (10.04; 9.32-10.75)</td>
<td>293 (2.69; 2.31-3.08)</td>
<td>209 (5.81; 5.04-6.57)</td>
<td>416 (3.90; 3.44-4.36)</td>
<td>341 (3.57; 3.13-4.01)</td>
<td>7,849 (79.16; 78.19-80.13)</td>
</tr>
<tr>
<td>2009-10</td>
<td>10,037 (4,544)</td>
<td>982 (9.26; 8.55-9.98)</td>
<td>285 (2.39; 2.01-2.76)</td>
<td>245 (4.9; 4.11-5.70)</td>
<td>418 (3.54; 3.08-3.99)</td>
<td>347 (3.22; 2.78-3.65)</td>
<td>7,692 (77.1; 76.06-78.14)</td>
</tr>
<tr>
<td>2010</td>
<td>5,025 (2,293)</td>
<td>466 (8.78; 7.80-9.77)</td>
<td>136 (2.45; 1.91-2.98)</td>
<td>117 (4.23; 3.5-5.26)</td>
<td>205 (3.54; 2.90-4.18)</td>
<td>155 (3.04; 2.44-3.63)</td>
<td>3,841 (76.35; 74.87-77.82)</td>
</tr>
<tr>
<td>2011-2</td>
<td>12,822 (2,188)</td>
<td>1,299 (9.36; 8.72-10.00)</td>
<td>452 (3.02; 2.64-3.40)</td>
<td>143 (7.42; 5.55-9.28)</td>
<td>651 (4.70; 4.23-5.16)</td>
<td>497 (3.59; 3.18-4.0)</td>
<td>9,723 (77.38; 76.46-78.3)</td>
</tr>
</tbody>
</table>

CIDI–SF = Composite International Diagnostic Interview–Short Form. CI 95% = 95% confidence interval.

Table 2: Results of logistic regression analyses describing migraine–mental health associations in CCHS adolescents

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Association with mood disorders, OR (CI 95%)</th>
<th>Association with anxiety disorders, OR (CI 95%)</th>
<th>Association with low perceived mental health, OR (CI 95%)</th>
<th>Association with high perceived mental health, OR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted</td>
<td>Unadjusted</td>
<td>Adjusted</td>
</tr>
<tr>
<td>2003-4</td>
<td>4.53 (3.26-6.30)**</td>
<td>4.05 (2.90-5.66)**</td>
<td>4.31 (3.13-5.94)**</td>
<td>3.96 (2.87-5.47)**</td>
</tr>
<tr>
<td>2005</td>
<td>4.18 (3.07-5.71)**</td>
<td>3.52 (2.56-4.84)**</td>
<td>5.05 (3.73-6.86)**</td>
<td>3.52 (2.56-4.84)**</td>
</tr>
<tr>
<td>2007-8</td>
<td>4.32 (3.13-5.98)**</td>
<td>3.74 (2.68-5.22)**</td>
<td>3.01 (2.24-4.04)**</td>
<td>2.66 (1.97-3.60)**</td>
</tr>
<tr>
<td>2009-10</td>
<td>3.51 (2.38-5.18)**</td>
<td>3.06 (2.06-4.55)**</td>
<td>2.45 (1.72-3.49)**</td>
<td>2.26 (1.58-3.24)**</td>
</tr>
<tr>
<td>2010</td>
<td>4.09 (2.45-6.85)**</td>
<td>3.32 (1.94-5.66)**</td>
<td>2.02 (1.20-3.39)**</td>
<td>1.87 (1.10-3.17)**</td>
</tr>
<tr>
<td>2011-2</td>
<td>5.14 (3.88-6.82)**</td>
<td>4.59 (3.44-6.12)**</td>
<td>4.61 (3.64-5.85)**</td>
<td>4.21 (3.31-5.35)**</td>
</tr>
</tbody>
</table>

Adjusted analyses comprised multivariate models, which included age, sex, race and socioeconomic status. CCHS = Canadian Community Health Survey; OR = odds ratio; CI 95% = 95% confidence interval.

*Significance at \( p < 0.05 \) level.

**Significance at \( p < 0.0001 \) level.
The migraine–mood disorders association was also significant throughout all cycles, with the exception of 2011-2, when using the CIDI–SF depression scale score to ascertain mood disorder status rather than the self-reported variable (Table 3 and Figure 1). The odds of migraine were consistently higher among those with anxiety disorders, with the strongest association seen in 2011-2 (aOR = 4.21, CI95% = 3.31-5.35) and the weakest in 2010 (aOR = 1.87, CI95% = 1.10-3.37). The association between low perceived mental health and migraine was less consistent, with only three of the six CCHS cycles revealing a statistically significant association between the two variables. Interestingly, the inverse association between high perceived mental health and the odds of migraine was consistently observed in all CCHS cycles, with the strongest association seen in 2011-2 (aOR = 0.58, CI95% = 0.48-0.69) and the weakest in 2003-4 (OR = 0.75, CI95% = 0.62-0.91).

**DISCUSSION**

In this study, we found a strong and consistent association between physician-diagnosed migraine and mood and anxiety disorders. The vertical dashed line on the forest plot indicates an OR=1.

(aOR = 3.06, CI95% = 2.06-4.55). The migraine–mood disorders association was also significant throughout all cycles, with the exception of 2011-2, when using the CIDI–SF depression scale score to ascertain mood disorder status rather than the self-reported variable (Table 3 and Figure 1). The odds of migraine were consistently higher among those with anxiety disorders, with the strongest association seen in 2011-2 (aOR = 4.21, CI95% = 3.31-5.35) and the weakest in 2010 (aOR = 1.87, CI95% = 1.10-3.37). The association between low perceived mental health and migraine was less consistent, with only three of the six CCHS cycles revealing a statistically significant association between the two variables. Interestingly, the inverse association between high perceived mental health and the odds of migraine was consistently observed in all CCHS cycles, with the strongest association seen in 2011-2 (aOR = 0.58, CI95% = 0.48-0.69) and the weakest in 2003-4 (OR = 0.75, CI95% = 0.62-0.91).

**Table 3: Results of logistic regression analyses describing migraine–CIDI–SF depression association in CCHS adolescents**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Sample size</th>
<th>Association in unadjusted model, OR (CI95%)</th>
<th>Association in adjusted model, OR (CI95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003-4</td>
<td>7,621</td>
<td>2.37 (1.56-3.61)**</td>
<td>2.12 (1.38-3.27)*</td>
</tr>
<tr>
<td>2005</td>
<td>6,204</td>
<td>4.15 (2.91-5.92)**</td>
<td>3.69 (2.54-5.37)**</td>
</tr>
<tr>
<td>2007-8</td>
<td>3,599</td>
<td>3.76 (2.48-5.71)**</td>
<td>3.14 (2.03-4.84)**</td>
</tr>
<tr>
<td>2009-10</td>
<td>4,544</td>
<td>2.79 (1.78-4.32)**</td>
<td>2.25 (1.42-3.54)*</td>
</tr>
<tr>
<td>2010</td>
<td>2,293</td>
<td>3.15 (1.66-5.95)*</td>
<td>2.48 (1.29-4.78)*</td>
</tr>
<tr>
<td>2011-12</td>
<td>2,148</td>
<td>2.13 (1.05-4.32)*</td>
<td>1.99 (0.95-4.16)</td>
</tr>
</tbody>
</table>

Adjusted analyses comprised multivariate models, which included age, sex, race and socioeconomic status. CIDI–SF = Composite International Diagnostic Interview–Short Form; CCHS = Canadian Community Health Survey, OR = odds ratio; CI95% = 95% confidence interval.

*Significance at p < 0.05 level.

**Significance at p < 0.0001 level,
disorders in a sample of 61,375 Canadian adolescents derived from six waves of a population-based survey. The strong association between migraine and mood disorders was replicated in a subset of participants who completed the CIDI–SF depression scale, which is a structured and validated depression screening instrument. In addition, we found consistent prevalence rates for migraine and mood/anxiety disorders across cycles.

It is well known that migraine is associated with a range of comorbid psychiatric disorders in adults.10-13 It appears that children and adolescents seen in clinical settings for migraine also have a higher prevalence of mood and anxiety symptoms, though it is not clear as to whether population-based samples of paediatric migraine patients differ from their peers in this regard. In fact, based on similar observations, a recent review concluded that there is no definite link between migraine and clinical anxiety and depression.14 A view that has been expressed in the past by other authors.15,16

Four systematic reviews have explored the relationship between psychiatric symptoms and migraine in the paediatric population. A 2008 meta-analysis uncovered 11 studies examining the association between migraine, anxiety and depression. Three of the studies were population-based and found no differences between respondents with migraine as compared to controls on a variety of depression and anxiety scales. However, most of the remaining studies, which were all conducted among clinical samples of migraine patients, found that children and adolescents with migraine had more symptoms of anxiety and depression than controls.16 A systematic review published in 2010 examined seven studies of psychological and psychiatric symptoms among clinical samples of migraine patients and concluded that there was insufficient evidence to establish a relationship between migraine and psychological functioning and psychiatric comorbidity in children and adolescents.15 A meta-analysis published in 2011 found that children and adolescents with chronic migraine were more likely to report depressive symptoms than controls.24 Finally, 10 studies were pooled together in a 2013 meta-analysis examining the association between migraine and psychopathological symptoms as measured by the Child Behavior Checklist (CBCL). Only one of the studies was population-based, with the remaining studies being carried out in clinical populations. Participants with migraine had higher total CBCL scores, as well as higher scores on the “internalizing” and “externalizing” scales, as compared to their peers.17 Results from published studies examining the relationship between psychological and psychiatric symptoms in children and adolescents with migraine are thus quite heterogeneous, based on pooled results described in systematic reviews.

It is clear that the evidence supporting an association between migraine and psychiatric comorbidities is derived largely from clinical samples of migraine patients, and that population-based studies on this association are less numerous and less consistent. Anttila et al.25 randomly selected a subset of children participating in a population-based study of schoolchildren to explore this association. Children with migraine and tension-type headaches and children without headaches were compared in terms of their scores on the Children’s Depression Inventory (CDI) and the CBCL. No significant differences in CDI scores were found when comparing children with migraine to control children; and although total CBCL scores were higher in children with migraine, they did not differ from control scores on the anxiety/depression subscale.25 In a small case-control study drawing on a sample of children recruited from local schools, Kowal and Pritchard26 found no significant differences comparing children with headaches (including migraine) to children without headaches in terms of anxiety and depression scores, as measured by the self-reported anxiety scale called “what I think and feel” and the self-reported depression scale called “the children’s depression scale.” Laurell et al.27 randomly selected 130 children and adolescents from a representative sample of Swedish schoolchildren participating in a questionnaire on headache prevalence to participate in further evaluations with interviews. The selected sample was stratified by age, gender and headache diagnosis, and 42 of the participants suffered from migraine. The CBCL was used to measure psychological symptoms. As in the Anttila et al. study,25 scores on the anxiety/depression subscale of the CBCL did not differ when comparing participants with migraine and tension-type headache and controls.27

Although the three studies described above found no association between anxiety and depression symptoms in non-clinical samples of children and adolescents with migraine, other studies have contradicted these conclusions. Carlsson et al.28 randomly selected school districts and schools from a Swedish city for participation in a case-control study on the link between headache and psychosocial functioning in children and adolescents. Participants with primary headaches reported higher anxiety symptoms though no difference was found in mood symptoms, and anxiety symptoms did not differ significantly within the different primary types of headache. A recent longitudinal study in Norway showed that anxiety and depression symptoms, as measured by the Symptom Checklist 5, were significantly associated with migraine four years later in a sample of 12- to 20-year-old secondary school students.18 A few years prior to this study, the same group published a cross-sectional analysis using the first iteration of the same data set and showed that participants with migraine had more anxiety and depression symptoms as compared to controls.20 In a large Turkish population-based study recruiting school-aged children from randomly selected schools and school districts, children with migraine were more likely to have high depression and anxiety scores on a validated Turkish depression score and the Turkish version of the Beck Anxiety Inventory score, respectively.30 Thus, when assessing the association between migraine and mood/anxiety disorders in non-clinical population-based samples, the results are heterogeneous and conclusions contradictory.

In our analysis, we found a consistent and strong association between migraine and mood/anxiety disorders, as well as an inverse association between migraine and high perceived mental health. Our study adds to the body of literature investigating the migraine–mental health association in children and adolescents in that it provides further evidence for a link between migraine and mood/anxiety disorders outside of clinical samples, which are inherently limited by a high risk of selection bias. There are important clinical implications to be drawn from the associations among migraine, depression and anxiety. Although there is presently no evidence with which to assess the direct impact of treating comorbid depression and anxiety on migraine, addressing comorbidities is an important task for the treating paediatrician. A randomised controlled trial carried out in children and adolescents with chronic migraine showed that amitriptyline plus cognitive behavioural therapy (CBT), a treatment modality also employed in the treatment of depression and anxiety, was superior to amitriptyline plus headache education in reducing headache frequency.31,32 Although mental health outcomes were not measured in this trial, one could hypothesize that some of the benefit of the CBT in terms of the
observed reduction in disability scores was derived from coping strategies learned during therapy sessions that can be equally applied to management of the symptoms of depression and anxiety. In addition, inadequately treated comorbid psychiatric conditions may be associated with higher migraine severity and burden: one study found that adult patients with migraine were more likely to visit the emergency department for migraine if they had a comorbid psychiatric disorder.\textsuperscript{33} It has also been shown that both adult and paediatric patients with migraine and comorbid anxiety or depression have significantly higher medical costs as compared to patients with migraine alone.\textsuperscript{34} Therefore, given the association between migraine and mood/anxiety disorders in the paediatric population, and given preliminary evidence to suggest a high clinical burden in patients with these comorbidities, paediatricians should consistently screen for depression and anxiety symptoms in migraine patients, and make referrals as appropriate.

The greatest strengths of the present investigation lie in the size of the sample and the sampling methodology utilized in our survey. The sampling frame used in the CCHS survey involves a multistage process where samples of households are systematically selected from clusters of households, which are in turn drawn from strata defined based on geography, population density and socioeconomic status.\textsuperscript{19} This probability sampling method yields a population-based representative sample of the Canadian population, making results generalizable to all Canadian adolescents. In addition, because participants were asked to report on physician-diagnosed migraine and mood/anxiety disorders, our study was not simply measuring self-reported symptoms, which are often subclinical. Therefore, the associations seen are presumably clinically relevant. However, there are several limitations to our analysis. First, ascertainment of migraine and mood/anxiety disorder status was limited to self-report, thereby introducing a significant risk of misclassification bias. It is also possible that the misclassification was differential; for example, adolescents diagnosed with mood or anxiety disorders may also have a higher likelihood of being diagnosed with migraine given that they have presented for medical attention, and this could have resulted in overestimation of the association between migraine and mood/anxiety disorders. However, in order to validate the migraine–mood disorders link, we were able to assess the association using CIDI–SF scores in a subset of participants in addition to the self-reported mood disorders variable, and the association was reproduced in these analyses. Furthermore, self-reported migraine has previously been shown to be a valid measure of physician-diagnosed migraine\textsuperscript{35} and of migraine diagnosed using the International Classification of Headache Disorders criteria.\textsuperscript{36} Given that participation in the CCHS is voluntary, it is also possible that selection bias was at play, with adolescents suffering from migraine and mood/anxiety disorders being less likely to participate. However, we would expect that this type of selection bias would skew the results toward the null. Finally, the CCHS data do not distinguish between episodic and chronic migraine, and we were therefore unable to make inferences about any differences in these two subgroups in the present study.

**CONCLUSIONS**

In the present investigation, which is the largest population-based study to date to explore the association between migraine and mood/anxiety disorders in the paediatric population, we found a strong and consistent association between migraine and mood/anxiety disorders in adolescents. This study further strengthens the view that these associations are not only present in highly selected samples of paediatric migraineurs seen in clinical settings, but also in more general, population-based samples. This evidence, along with evidence from similar previous work, highlights the importance of screening for symptoms of anxiety and depression in children and adolescents presenting with migraines. Future studies should address the impact of treating comorbid mood and anxiety disorders on outcomes related to migraine. It will be important to clarify whether or not addressing anxiety and depression symptoms can mitigate migraine-related symptoms, given that this could lead to both new clinical insights and insights into potential areas of shared aetiology between migraine and mood/anxiety disorders.

**ABBREVIATIONS**

CCHS = Canadian Community Health Survey; \( OR = \) odds ratio; CIDI–SF = Composite International Diagnostic Interview—Short Form; \( CI_{95\%} = 95\% \) confidence interval.

**FUNDING**

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**DISCLOSURES**

Serena L. Orr, Ian Colman, Beth Potter and Jinhui Ma hereby state that they have nothing to disclose.

**CONFLICTS OF INTEREST**

Serena L. Orr, Ian Colman, Beth Potter and Jinhui Ma hereby state that they have no conflicts of interest to declare.

**STATEMENT OF AUTHORSHIP**

Serena L. Orr conceptualized the study, ran the data analyses, wrote the first draft of the manuscript, and edited and approved the final manuscript. Beth Potter and Jinhui Ma assisted Dr. Orr with the data analyses, interpreted the results, edited the manuscript and approved the final manuscript. Ian Colman assisted Dr. Orr with conceptualizing the study, assisted Dr. Orr with data analyses, interpreted the results, edited the manuscript and approved the final manuscript.

**REFERENCES**