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43RD ANNUAL CANADIAN ACADEMY OF CHILD AND ADOLESCENT PSYCHIATRY CONFERENCE

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43E CONGRÈS DE L’ACADÉMIE CANADIENNE DE PSYCHIATRIE DE L’ENFANT ET DE L’ADOLESCENT

S1 Résumés

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EDITORIAL

Clinical relevance

Peter Braunberger MD FRCPC, Clinical Editor

Within any clinical journal, we might ask why we choose to read the articles that we read. Fascination or curiosity or novelty might motivate a second look. A maybe still vague sense of importance might also draw us in. We might also ask what is it about the articles that we choose not to read? The conscious or unconscious filters we apply to the always too long list of articles following a literature search (e.g., PubMed) also warrant reflection. Ultimately, are the articles we have available or choose to read helpful or relevant?

Translational sciences usefully aim to unite basic and clinical and public health research towards common clinical goals (1), but what clinicians and clinician-researchers and researchers need or ask of a clinical journal very likely and fairly varies considerably, even if some overlap is also acknowledged. The pairing of “science and practice” and “research and treatment” in the Aim and Scope statement of the Journal of the American Academy of Child and Adolescent Psychiatry also provides a helpful example for our own Journal (2). However, given that the majority of child and adolescent psychiatrists and other mental health professionals are primarily clinicians, answers to more specific questions about what is clinically relevant or helpful to the clinician are still warranted.

In the National Institutes of Health Toolkit for Patient Focused Therapy Development, “clinical relevance refers to the ability of the therapy to improve how the patient feels, functions, and/or survives. More specifically, a therapy is clinically relevant if it provides a positive benefit from a patient’s perspective and the benefit is statistically significant and outweighs any potential harm or risk of harm” (3). Clinical relevance might also be seen as a matter of timing, bearing on proximal decisions, in contrast to hypothesis-generating or early findings that may still be some years away from the clinic.

If clinical relevance is to be grounded or evaluated in the context of decision making in upcoming appointments, then considering who is making decisions and their valuation of benefits and harms becomes central to a determination of clinical relevance. A patient or parent might ask “Did the information that made it to the appointment reflect my decision-making values?” A clinician might ask “Did what I read (and also what I did not read) reflect my patients’ values or my own values?” Clinical relevance might also then be seen as a dynamic value-informed process with patient feedback.

What could the Journal be doing to enhance clinical relevance? One initiative is expanding the “Clinical Rounds” column which will now include case studies, case series, and program innovations with preliminary data with an expectation of clinical relevance while also acknowledging the state of evidence. See the draft author guidelines for this expanded section at the end of this editorial. Additionally, in establishing a clinical editor position, a lens of clinical relevance is applied more widely, to include, for example, columns such as Recommended Academic Reading, but also research papers. The Journal also anticipates a growing and changing and hopefully maturing discussion of clinical relevance itself.

In this issue find two articles in the Clinical Rounds section. First a practice-informing paper by Halawa et al. on clozapine rechallenge in the context of a myocarditis history (2). Their discussion speaks directly to day-to-day clinical decisions enriched by a thoughtful discussion of the literature and an illustrative case. A second potentially model-of-care
informing paper by Neufeld et al. addresses community physicians’ experiences managing complex child mental health care, framed by self-determination theory (3).

Also in this issue find two research papers, one focused on trajectories of oppositional defiant disorder by Leadbeater et al. (4), followed by a commentary by Andrade (5). Then a second research paper, a scoping review on mood and anxiety symptoms following pediatric mild traumatic brain injury by Sabir & Malhi (6).

Find in the Advocacy column an update on Canadian government practices leading to family separation, and in the Apercevoir column, Dr. Rasasingham’s career reflections through an interview with Dr. Lind Grant-Oyeye.

Finally, find in a supplement to this issue, abstracts from the 43rd Annual Canadian Academy of Child and Adolescent Psychiatry Conference recently held in Calgary.

References

Draft author guidelines for expanded CLINICAL ROUNDS section

The Journal of the Canadian Academy of Child & Adolescent Psychiatry (JCACAP) is now soliciting manuscript submissions for the expanded Clinical Rounds section.

The Clinical Rounds section provides a space for clinically relevant and data-supported articles on child and adolescent mental health practice and policy. This may include presentation of (i) a novel or challenging case with detailed discussion of relevant literature, (ii) a case series examining emerging patterns, or (iii) the rationale and preliminary descriptive data for a service or policy innovation. Although the Journal still expects standardized methodological processes (e.g., for data collection and analysis), it is recognized that the novelty or stage of development may not have allowed for the use of more robust research components (e.g., adequate sample size, experimental design). Practical implications of findings may be proposed but recommendations and promotion of ideas should be grounded in evidence, with clear documentation of limitations.

Specific submission parameters include: (1) maximum word count of 4000 words (not including references or tables/figures), (2) a maximum of six combined tables/figures, and (3) an unstructured abstract (max 250 words). External reviews will be sought for submissions meeting minimal internal journal standards. See other details in the Journal’s author guidelines: https://www.cacap-acpea.org/wp-content/uploads/2021-08-04-Instr-to-authors-EN.pdf

In some cases, JCACAP editors may solicit a commentary to be paired with manuscripts accepted for publication in the Clinical Rounds section.
RESEARCH ARTICLE

Trajectories of oppositional defiant disorder severity from adolescence to young adulthood and substance use, mental health, and behavioral problems

Bonnie J. Leadbeater PhD; Gabriel J. Merrin PhD; Alejandra Contreras BSc; Megan E. Ames, PhD

Abstract

Background: Oppositional Defiant Disorder (ODD) is a disruptive behavioral disorder; however, increasing evidence emphasizes irritable mood as a primary symptom of ODD. Objectives: This study investigated whether heterogeneous groups (classes) of individuals can be differentiated based on ODD sub-dimensions (irritability and defiance) or on overall ODD symptoms longitudinally. We also examine associations between ODD trajectory class and comorbid substance use (heavy episodic drinking, cannabis use), mental health (depression and anxiety) and behavioral symptoms (ADHD, aggression and substance use) in both adolescence and young adulthood (controlling for adolescent levels of each of these concerns). Method: Data were from a randomly recruited community sample of 662 Canadian youth (T1 ages 12-18) followed biennially for 10 years (T6 ages 22-29). Results: Growth mixture models revealed trajectories classes of ODD based on severity of symptoms. A three-class solution provided the best fit with Low (n = 119; 18%), Moderate (n = 473; 71.5%), and High (n = 70; 10.6%) ODD classes. Class trajectory differences were similarity based on symptoms severity (rather than type) for symptom sub-dimensions (irritability defiance). Adolescent and young adult substance use, mental health symptoms, and behavioral problems were significantly higher for the High ODD trajectory class compared to both other classes. Youth in the Moderate ODD trajectory class also showed higher comorbid symptoms in adolescence and young adulthood, compared to the Low ODD trajectory class. Conclusion: Early identification of children and adolescents with high or moderate ODD symptoms and interventions that simultaneously address defiance and irritability are supported by the findings.

Key words: oppositional defiant disorder; irritability; defiance; growth mixture model; transitions

Résumé

Contexte: Le trouble oppositionnel avec provocation (TOP) est un trouble du comportement perturbateur; toutefois, des données probantes croissantes soulignent que l’humeur irritable est un symptôme primaire du TOP. Objectifs: La présente étude a investigué si les groupes (classes) hétérogènes de personnes qui peuvent être différenciées au mieux selon les sous-dimensions (irritabilité et défi) ou selon les symptômes généraux du TOP longitudinalement. Nous
examines également les associations entre la classe de trajectoire du TOP et l’utilisation de substances comorbide (lourde consommation d’alcool épisodique, utilisation de cannabis), la santé mentale (dépression et anxiété) et symptômes comportementaux (TDAH, agression et utilisation de substances) tant chez les adolescents que chez les jeunes adultes (contrôler les niveaux adolescents de chacun de ces problèmes). Méthode: Les données provenaient d’un échantillon communautaire recruté au hasard de 662 jeunes Canadiens (âges T1 2-18) suivis tous les deux ans pendant 10 ans (T6 âges 22-29). Résultats: Des modèles de mélange de croissance ont révélé des classes de trajectoire du TOP basées sur la gravité des symptômes. Une solution en trois classes a fourni le meilleur ajustement avec des classes de TOP faible (n = 119; 18 %), modérée (n = 473; 71,5 %), et élevée (n = 70; 10,6 %). Les différences de classes de trajectoire étaient également basées sur la gravité des symptômes (plutôt que sur le type) des sous-dimensions des symptômes (irritabilité, défi). L’utilisation de substances chez les adolescents et les jeunes adultes, les symptômes de santé mentale et les problèmes de comportement étaient significativement plus élevés pour la classe de la trajectoire élevée du TOP comparé aux deux autres classes. Les jeunes de la classe de trajectoire modérée du TOP présentaient aussi des symptômes comorbidés plus élevés à l’adolescence et au jeune âge adulte, comparé à la classe de trajectoire faible du TOP.

Conclusion: L’identification précoce des enfants et des adolescents présentant des symptômes élevés ou modérés du TOP et les interventions qui prennent en charge simultanément le défi et l’irritabilité sont soutenues par les résultats.

Mots clés: trouble oppositionnel avec provocation; irritabilité; défi; modèle de mélange de croissance; transitions

Lifet ime prevalence of Oppositional Defiant Disorder (ODD) is estimated to be 10% (males = 11%; females = 9%)(1). Of those with lifetime ODD, 92% meet criteria for at least one other lifetime DSM-5 disorder, including mood (45.8%), anxiety (62.3%), impulse-control (68.2%), and substance use (47.2%) disorders (1). ODD is a disruptive behavioral disorder; however, increasing evidence points to irritable mood as a primary symptom in children and youth experiencing ODD (2). Research also suggest that ODD symptoms have effects beyond adolescence and are also associated with disruptions of healthy development of relationships and of educational and occupational success by young adulthood (3-6).

Considerable cross-sectional research using factor analyses with community (7-13) and clinic-referred samples of children and adolescents (14, 15) demonstrate that ODD comprises two important sub-dimensions that have been labeled: irritability and defiance dimensions. Irritable symptoms of ODD (i.e., touchy and easily annoyed, often resentful or angry, often loses temper) typically correlate concurrently and prospectively with mood disorders; whereas defiant symptoms (i.e., argues, blames others, defies authorities) are related more strongly, but not exclusively, to externalizing problems (see reviews 2, 16). A third dimension, hurtful, spiteful, or vindictive, has received somewhat less attention, in part, given assessments of these symptoms are often limited to one item. Research has also shown that by young adulthood irritability symptoms of ODD predict subsequent internalizing problems (anxiety and depression); whereas, defiance symptoms are associated with both internalizing and externalizing symptoms and with substance use by young adulthood (2) ODD, as a severe multi-dimensional concern, can disrupt the course of development for some children and youth, particularly if undiagnosed or untreated (17).

Defiant and irritable symptoms typically co-occur in individuals experiencing ODD and longitudinal research is lacking. It remains unclear whether children and youth can be classified into clinically distinct groups based on the sub-dimensions (e.g., high in defiance or low in irritability) over time (17). The correlation between these two constructs is typically high in samples of children and adolescents (e.g., r = 0.81 to 0.91) (7) and young adults (e.g., r = 0.70 to 0.89) (18). Longitudinal research is needed to distinguish between groups of adolescents and youth with varying levels of defiance and irritability symptoms in order to better understand the thresholds, patterns, and the developmental course of these concerns across the transition from adolescence to young adulthood (17-19).

Past cross sectional research suggest that ODD symptoms in affected individuals do not reflect distinct sub-dimensions. Rather most individuals with ODD report symptoms of both defiance and irritability. In their review of the evidence for the ODD dimensions, Evans et al. (17) conclude that current findings “do not support cleaving ODD into distinct subtypes or disorders (of either defiance or irritability); rather, ODD items include heterogeneous variability that is accounted for by a general ODD factor, as well as dimensions of irritability and defiant behavior” (p. 38). The present study uses longitudinal data from cohorts of Canadian youth who were ages 12 to 18 in 2003. We include six waves of data collected longitudinally over 10 years. We use growth mixture modeling (GMM) to classify the
longitudinal trajectories of ODD symptoms considered together. We also classified youth based on each of the two sub-dimensions, to investigate whether distinct subtype trajectories (of either defiance or irritability) were evident across this transition.

Previous cross-sectional research with children and youth using latent class analysis (LCA) has identified three (or four) class solutions that include a low or no symptoms class, a defiant or irritable symptoms class, and a class experiencing both irritable and defiant symptom (14, 20-26). However, these classes confound symptom numbers (severity) and sub-dimension types (22). For example, in research with male youth from the Zurich Juvenile Detention Centre, Abei et al.(20) identified classes that combine severity and sub-dimensions; including, a no-ODD subtype, a severe ODD subtype, and two moderate ODD subtypes comprised of either defiant or irritable symptoms. Other cross-sectional research identified classes that differ in severity of symptoms (low, moderate, and high), rather than in distinctive sub-dimensions (24, 25). Longitudinal research is needed to assess patterns of ODD symptoms and sub-dimensions across time in order to disentangle the trajectories of ODD and the sub-dimensions as well as their relations with co-morbid problems.

Previous longitudinal research that included five of the six waves of data used in this study (18) examined the trajectories of irritability and defiance variables in growth curve analyses. Defiance symptoms declined over time, whereas irritability remained relatively stable from ages 12 to 25. In addition, the associations of irritability with internalizing were stronger than associations of irritability with conduct problems and defiance was associated with both internalizing and conduct problems in mid-adolescence. However, defiance was more highly related to internalizing than to conduct problems by early adulthood (ages 18 to 25) (18). Our previous research also showed that higher overall ODD symptoms in adolescence predicted lower educational attainment (for males only), lower occupational prestige, higher debt (for females only), and more trouble paying for necessities and medical attention, and greater perceived workplace stress (18). Increases in ODD symptoms across the transition from adolescence to young adulthood also predicted worsening educational attainment and annual income for males, and higher debt and greater perceived personal conflict in the workplace for females, as well as greater job instability for both males and females (4). The current study investigates whether there are heterogeneous groups (classes) of youth in a community sample who can be classified based on their ODD symptoms over time. We also examined trajectory classes for the sub-dimensions, but we did not hypothesize that there would be distinctive trajectory classes for irritability and defiance symptoms given the previous review by Evans et al(17).

We use GMM to classify youth’s reports of ODD symptoms across a decade spanning adolescence to young adulthood (using six waves of data). In addition, we examine the associations of these class trajectories at their onset in adolescence and ten years in young adulthood (controlling for adolescent levels of these comorbid concerns with substance use (cannabis and alcohol), mental health symptoms (depression and anxiety), and behavior problems (Attention-Deficit/Hyperactivity Disorder [ADHD] and aggression).

**Method**

**Participants and Procedure**

The Victoria Healthy Youth Survey (V-HYS) (27) is a 10-year prospective longitudinal study of Canadian youth followed biennially for six assessments (T1; N = 662; 48% male $M_{age} = 15.5$, $SD = 1.9$) to 2013 (T6; N = 478; 45% male; $M_{age} = 26.8$, $SD = 2.0$). Males were slightly more likely to be lost to follow-up compared to females (i.e., males comprised 48% of the sample at T1 and 45% at T6; $\chi^2 (1, 662) = 8.77$, $p = .003$). Participants from higher socio-economic status (SES) families (T1: $M = 6.79$, $SD = 1.66$; $F(1, 636) = 19.39$, $p < .001$) were more likely to be retained in the study than participants from lower SES families ($M = 6.05$, $SD = 1.94$).

In 2003, participants were recruited from a random sample of 9,500 telephone listings; 1,036 households with an eligible youth (ages 12 to 18 years) were identified. Of these, 662 agreed to participate in the study. The sample was representative of the Greater Victoria Areas population surveyed (27). Youth and the parent or guardian for youth under age 18 gave written consent for participation at each wave, and youth received a gift certificate at each interview. A trained interviewer administered the V-HYS individually in the youth’s home or another private place. To enhance privacy, the portion of the V-HYS questionnaire dealing with private topics (i.e., sexual experiences) was self-administered and placed in a sealed envelope not accessible to the interviewer. Retention rates were high at all assessments: 87% (T2), 81% (T3), 69% (T4), 70% (T5), and 72% (T6). The university’s research ethics board approved the research protocol.
Measures

Dimensions of ODD were measured using six items from the Brief Child and Family Phone Interview (BCFPI) (28) which assesses DSM-5 criteria for child and adolescent psychiatric disorders, including ODD symptoms (irritability and defiance symptoms). Items were rated on a three-point Likert scale (0 = never, 1 = sometimes, or 2 = often) in response to the question, “Do you notice that you are [...item].” Items for the irritability subscale (three items) are “easily annoyed by others?” “angry and resentful?” and “cranky or irritable?” Items for the defiance subscale (three items) are “argue a lot with others?” “defiant or talk back to people?” and “blame others for your own mistakes?” Scores ranged from 0 to 12 for ODD total symptoms (six items). Reliability estimates (alphas) for these ordinal scales were obtained using polychoric correlations. Alphas ranged from 0.79 to 0.84 for symptoms of ODD (total score), 0.74 to 0.81 for irritability, and 0.69 to 0.79 for defiance, with the exception of Wave 4 (alpha = 0.61) for defiance. The ODD subscale has been shown to be invariant across sex and time in previous studies using the V-HYS data.17 Within-time correlations between the irritability and defiance subdimensions were moderate at each time point (r’s = 0.47 to 0.58).

Demographic variables. Participants self-reported their gender and age at T1. As an estimate of socioeconomic status (SES), participants reported parent occupations were coded from 1 to 9 using the Hollingshead Occupational Status Scale (29). The highest level of occupational prestige for either parent was used as a measure of SES.

Substance use. In order to assess heavy episodic drinking (HED), participants were asked how often they had five or more drinks on one occasion in the past year: 0 = never, 1 = a few times a year, 2 = a few times a month, 3 = once a week, and 4 = more than once a week. The definition of a standard drink was provided (30). To assess the frequency of cannabis use, participants were asked: “how often marijuana (pot, hash) was used in the past 12 months.” Responses were given on a five-point scale: 0 = never, 1 = a few times a year, 2 = a few times a month, 3 = once a week, and 4 = more than once a week.

Depressive and anxiety symptoms. The BCFPI (28) assesses DSM-IV criteria for child and adolescent psychiatric disorders, including internalizing symptoms (i.e., depressive symptoms and anxiety). The BCFPI uses six items for each disorder and has demonstrated strong psychometric properties with the present sample.27 Items for each domain are rated on a three-point Likert scale (0 = never, 1 = sometimes, or 2 = often). Sum totals are used for this study (ranges = 0 to 12). Polychoric alphas were good for both depression and anxiety at T1 and T6, respectively: 0.87 and 0.92 for depression and 0.81 and 0.88 for anxiety.

ADHD and aggression. The BCFPI (28) also assessing symptoms of inattention and hyperactivity (i.e., ADHD). Total scores (six items; range 0 to 12) are used and polychoric alphas were 0.74 and 0.82 for T1 and T6, respectively. Aggression was assessed using nine items from Buss and Perry (31). Participants were asked to rate nine items (e.g., “once in a while I can’t control the urge to strike another person”) on a five-point Likert scale (1 = extremely uncharacteristic of me to 5 = extremely uncharacteristic of me, range 1 to 36). This was not assessed at T1 or T2, so T3 scores were used as baseline scores, when youth were in the 16- to 22-years-old cohort. Cronbach’s alphas were 0.85 at T3 and 0.85 at T6.

Statistical Analyses

All analyses were fit using Mplus version 8.7 (32) using full-information maximum likelihood to address missing data and with the robust maximum likelihood estimator that adjusts for potential non-normality in the data by estimating robust standard errors using a Huber White Sandwich estimator. GMM was used to assess whether a given population is composed of multiple subpopulations across time (33). The observed variables were the ODD total symptom scores (a composite of both irritability and defiance symptoms) for each of six assessments. We also fit growth mixtures for irritability and defiance symptoms separately; however, given their similarities in classifying youth, we use the combined ODD trajectories to classify youth. Cross tabulation of the three defiant and irritable classes showed only one youth was high in defiance and low in irritability only four were high in irritability and low in defiance.

The ODD scores for the six time points were used to identify ODD growth trajectories (classes). First, we determined the number of distinct classes to retain through a class enumeration process. We used standard fit indices and the theoretical meaningfulness of the classes to select the number of latent classes to retain. Fit indices included the Bayesian Information Criterion (BIC) and the Aikake Information Criteria (AIC), where lower values indicate a better-fitting model, the significance on the Lo–Mendell–Rubin Adjusted Likelihood Ratio Test (LMR-LRT), Bootstrap Likelihood Ratio Test (BLRT) as well as the usefulness of the latent classes given the number of individuals in each class.34 Entropy, the quality of class separation is reported but was not
used to determine the number of classes to retain because it is not a fit index. We examined the functional form of the data and determined that a quadratic function fit the data best. For example, for ODD symptoms using a likelihood ratio test the linear functional form fit the data significantly worse than the quadratic ($\Delta -2LL = 53.85, \Delta DF = 6, p < .001$).

We used the standard three-step approach (34) to fit the mixture models and examine adolescent (T1; ages 12-18) predictors (i.e., substance use, mental health, and behavioral problems) of the classes using multinomial logistic regression. Then, linear regression was used to examine differences in the same young adult (T6; ages 22-29) outcomes (i.e., substance use, mental health, and behavior problems). All models controlled for demographic variables including age, sex, and SES. Young adult models (T6) also accounted for T1 levels of the outcome variables. We examined these predictors and outcomes in three separate models grouped by concern (substance use, mental health, and behavioral problems).

### Results

**Descriptive Statistics**

Correlations between irritability and defiance were moderate at each time point (T1 $r = 0.47$; T2 $r = 0.51$; T3 $r = 0.57$; T4 $r = 0.49$; T5 $r = 0.54$; T6 $r = 0.58$), Correlations between ODD symptoms and the substance use, mental health, and behavioral problem variables were also in the expected directions (see Supplemental Table S1, available from the authors).

**Growth Mixture Models of Classes of ODD and the Sub dimensions**

Using separate GMMs for ODD, irritability, and defiance, we tested an increasing number of class solutions iteratively to determine the best fitting model see (Table 2 and Figure 1). Model testing ceased when the additional class provided a poorer fit and was not different qualitatively from the more parsimonious model. A three-class solution provided the best fit for the ODD variable reflecting differences in the severity of ODD symptoms across each assessment Low ($n = 119, 18.0\%$), Moderate ($n = 473; 71.5\%$), and High ($n = 70, 10.6\%$) classes (Table 1 and Figure 1). Similarly, three-class solutions provided the best fit reflecting severity of symptoms for irritability symptoms: Low ($n = 209, 31.6\%$), Moderate ($n = 350; 52.9\%$), and High ($n = 103, 15.6\%$) classes and for defiance symptoms: Low ($n = 207; 31.3\%$), Moderate ($n = 346; 52.3\%$), and High ($n = 109, 16.5\%$). Given the moderately high positive correlations between irritability and defiance at T1 and T6, the three-class solutions for each, and the similar trajectories for irritability and defiance, all subsequent analyses focus on the three overall ODD classes only.

Mean differences and standard errors for irritability and defiance at T1 and T6 for each of the classes are presented in Table 3. Significantly, from both a clinically meaningful and statistical perspective at T1, symptoms of defiance were approximately two times greater in the High compared to the Moderate class, and symptoms of irritability were approximately two times greater in the High versus Moderate class. Similarly, at T6 symptoms of defiance were 1.5 times greater in the High compared to the Moderate class, and symptoms of irritability were 1.6 times greater in the High versus Moderate class.

**Mental Health, Substance Use, and Behavioral Problems as Predictors of Class Severity**

As shown in Table 4, adolescent levels of HED, cannabis use, depression and anxiety, and behavioral problems were all significantly higher for youth in the High ODD trajectory class compared to those in both the Low and Moderate ODD classes. In addition, youth in the moderate ODD class had significantly higher symptoms of depression, ADHD.

Table 1. Cross-tabulation of modal class assignments for irritability and defiance growth mixture classes

<table>
<thead>
<tr>
<th></th>
<th>Defiance Low Class</th>
<th>Defiance Medium Class</th>
<th>Defiance High Class</th>
<th>Row Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritability Low Class</td>
<td>128 (61%)</td>
<td>80</td>
<td>1</td>
<td>209</td>
</tr>
<tr>
<td>Irritability Medium Class</td>
<td>75</td>
<td>222 (63%)</td>
<td>53</td>
<td>350</td>
</tr>
<tr>
<td>Irritability High Class</td>
<td>4</td>
<td>44</td>
<td>55 (53%)</td>
<td>103</td>
</tr>
<tr>
<td>Column Totals</td>
<td>207</td>
<td>346</td>
<td>109</td>
<td>662</td>
</tr>
</tbody>
</table>

Note: Percentages indicate class overlap for low/low, medium/medium and high/high irritability and defiance classes using row totals for irritability.
and aggression compared to youth in the Low ODD class (but not for HED, cannabis and anxiety).

Using assessments collected in young adulthood (T6) and controlling for adolescent levels of each variable, significant differences between the High ODD trajectory class and the other two classes were evident for each of the mental health, substance use, and behavioral problem variables assessed (see Table 5). The Moderate ODD class also had significantly greater increases in symptoms of depression, anxiety, ADHD and aggression than youth in the Low ODD class, but not for the substance use variables.

Discussion

This study examines ODD symptom across the transition from adolescence to young adulthood in a large longitudinal Canadian sample. Given ODD symptoms are often thought to dissipate after adolescence, our findings of continuity in symptom classes based on seriousness of symptoms across the ten years show the need to advocate for and undertake both early and ongoing treatment of ODD. The study also raises attention to the need for treating symptoms of irritability, as well as defiance, in youth with ODD to prevent further negative mental health and behavioral consequences.

The goal of this study was to examine of the heterogeneity in the trajectories of ODD symptoms in a community representative sample of youth across ten years, across the transition from adolescence (ages 12 to 18) to young adulthood (ages 22 to 29). We found trajectory differences that reflected the severity of ODD symptoms (for defiance and irritability and for the combined symptoms) across this salient life transition. Subgroup classes for youth with combined ODD symptoms of defiance and irritability showed that Low (18.0%), Moderate (71.5%), and High (10.6%) levels of overall ODD symptoms best characterized the ODD class trajectories over time. In assessments of comorbid symptoms, the High ODD class had higher levels for all predictors of substance use (cannabis use), mental health (depression and anxiety), and behavioral problems (ADHD and aggression) in adolescence and young adulthood (also

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Table 2. Model fit indices for latent class models examined for ODD, Irritability, and Defiance Symptoms.

<table>
<thead>
<tr>
<th></th>
<th>AIC</th>
<th>BIC</th>
<th>LMR</th>
<th>BLRT</th>
<th>entropy</th>
<th>Class 1</th>
<th>Class 2</th>
<th>Class 3</th>
<th>Class 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ODD total symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>one-class</td>
<td>13025.91</td>
<td>13093.34</td>
<td></td>
<td></td>
<td>0.671</td>
<td>107 (16%)</td>
<td>555 (84%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>two-class</td>
<td>12966.81</td>
<td>13085.70</td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.001</td>
<td>0.574</td>
<td>119 (18%)</td>
<td>473 (71%)</td>
<td>70 (11%)</td>
<td></td>
</tr>
<tr>
<td>three-class</td>
<td>12963.93</td>
<td>13094.29</td>
<td>p = 0.04</td>
<td>p &lt; 0.001</td>
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<td>four-class</td>
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<tr>
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<td>10966.97</td>
<td></td>
<td></td>
<td>0.672</td>
<td>409 (62%)</td>
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<td></td>
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<tr>
<td>two-class</td>
<td>10228.99</td>
<td>10287.42</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>0.712</td>
<td>209 (32%)</td>
<td>350 (53%)</td>
<td>103 (15%)</td>
<td></td>
</tr>
<tr>
<td>three-class</td>
<td>10014.25</td>
<td>10090.67</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>0.716</td>
<td>207 (31%)</td>
<td>346 (52%)</td>
<td>109 (17%)</td>
<td></td>
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<tr>
<td>four-class</td>
<td>9973.992</td>
<td>10068.39</td>
<td>p = 0.11</td>
<td>p &lt; 0.001</td>
<td>0.669</td>
<td>40 (6%)</td>
<td>151 (23%)</td>
<td>154 (23%)</td>
<td>317 (48%)</td>
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<td><strong>Defiance symptoms</strong></td>
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<tr>
<td>one-class</td>
<td>10380.381</td>
<td>10420.838</td>
<td></td>
<td></td>
<td>0.708</td>
<td>227 (34%)</td>
<td>435 (66%)</td>
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<td></td>
</tr>
<tr>
<td>two-class</td>
<td>9773.94</td>
<td>9832.38</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>0.642</td>
<td>207 (31%)</td>
<td>346 (52%)</td>
<td>109 (17%)</td>
<td></td>
</tr>
<tr>
<td>three-class</td>
<td>9645.671</td>
<td>9722.09</td>
<td>p = 0.008</td>
<td>p &lt; 0.001</td>
<td>0.67</td>
<td>346 (52%)</td>
<td>32 (5%)</td>
<td>182 (28%)</td>
<td>102 (15%)</td>
</tr>
<tr>
<td>four-class</td>
<td>9607.22</td>
<td>9701.07</td>
<td>p = 0.35</td>
<td>p &lt; 0.001</td>
<td></td>
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</tr>
</tbody>
</table>

Note: *p < 0.05; **p < 0.01; ***p < 0.001; BIC= Bayesian information criterion, AIC= Akaike Information Criteria, LMR Lo–Mendell–Rubin Adjusted Likelihood Ratio Test, BLRT = Bootstrap Likelihood Ratio Test
including HED) compared to the Moderate and Low ODD classes. The Moderate ODD class reported more depressive symptoms and behavioral problems (ADHD and aggression) than the Low ODD class in adolescence and more symptoms of both mental health (depression and anxiety) and behavioral problems (ADHD and aggression) in young adulthood (but not more substance use concerns).

Our findings also showed trajectory class differences based on severity of symptoms for irritability and defiance. Consistent with a review of this research by Evans et al. (2), the findings did not distinguish separate groups of youth by sub-dimensions. Specifically, cross tabulations of the defiance and irritability subclasses classes did not reveal youth in high irritability/low defiance or low irritability/high defiance classes. Cross-sectional studies, with predominately children and adolescents have identified three- or four-class solutions based on the severity of symptoms as well as irritable and defiant subtypes (21-22,35-36). However, the frequency of youth experiencing defiance without irritability was low and the current study is among few examining...
Table 4. Multinomial regression analysis showing ODD symptoms trajectories class differences in adolescents (T1; ages 12-18) predicted by age, sex, SES, substance use, mental health, and behavioral problem indicators. The Low ODD class (n=199) is the reference group

<table>
<thead>
<tr>
<th>Substance use</th>
<th>2. Moderate ODD class (n = 473)</th>
<th>3. High ODD class (n = 70)</th>
<th>Pairwise comparison*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Est (SE)</td>
<td>OR</td>
<td>Est (SE)</td>
</tr>
<tr>
<td>Sex (male = 0)</td>
<td>0.15 (0.38)</td>
<td>1.16</td>
<td>-0.66 (0.37)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.12 (0.17)</td>
<td>0.89</td>
<td>-0.25 (0.15)</td>
</tr>
<tr>
<td>SES</td>
<td>-0.05 (0.12)</td>
<td>0.95</td>
<td>-0.23 (0.11)</td>
</tr>
<tr>
<td>HED</td>
<td>0.03 (0.28)</td>
<td>1.03</td>
<td>0.01 (0.27)</td>
</tr>
<tr>
<td>Cannabis</td>
<td>0.28 (0.29)</td>
<td>1.33</td>
<td>0.81 (0.25)</td>
</tr>
</tbody>
</table>

Mental health

<table>
<thead>
<tr>
<th></th>
<th>2. Moderate ODD class (n = 473)</th>
<th>3. High ODD class (n = 70)</th>
<th>Pairwise comparison*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Est (SE)</td>
<td>OR</td>
<td>Est (SE)</td>
</tr>
<tr>
<td>Sex (male = 0)</td>
<td>-0.04 (0.29)</td>
<td>0.96</td>
<td>-0.41 (0.37)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.17 (0.08)</td>
<td>0.85</td>
<td>-0.11 (0.10)</td>
</tr>
<tr>
<td>SES</td>
<td>-0.05 (0.08)</td>
<td>0.96</td>
<td>-0.16 (0.10)</td>
</tr>
<tr>
<td>Depression</td>
<td>0.22 (.09)</td>
<td>1.24</td>
<td>0.47 (0.10)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.08 (0.06)</td>
<td>1.09</td>
<td>0.38 (0.08)</td>
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</tbody>
</table>

Conduct problems

<table>
<thead>
<tr>
<th></th>
<th>2. Moderate ODD class (n = 473)</th>
<th>3. High ODD class (n = 70)</th>
<th>Pairwise comparison*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Est (SE)</td>
<td>OR</td>
<td>Est (SE)</td>
</tr>
<tr>
<td>Sex (male = 0)</td>
<td>1.28 (0.46)</td>
<td>3.61</td>
<td>-0.12 (0.58)</td>
</tr>
<tr>
<td>Age</td>
<td>0.16 (0.10)</td>
<td>0.86</td>
<td>-0.18 (0.13)</td>
</tr>
<tr>
<td>SES</td>
<td>-0.04 (0.10)</td>
<td>0.96</td>
<td>-0.19 (0.13)</td>
</tr>
<tr>
<td>ADHD</td>
<td>0.47 (0.12)</td>
<td>1.60</td>
<td>0.71 (0.14)</td>
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<tr>
<td>Aggression (T3)</td>
<td>0.24 (0.08)</td>
<td>1.27</td>
<td>0.36 (0.09)</td>
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</tbody>
</table>

SES = socioeconomic status; HED = Heavy episodic drinking; ADHD = Attention-deficit/hyperactivity disorder. *p < 0.05; **p < 0.01; ***p < 0.001
* 1=Low, 2=Moderate, 3=High ODD class.

Table 5. Linear regression was used to examine differences in young adult substance use, mental health, and conduct problem outcome means and comparisons by ODD growth mixture classes. All models control for the outcome measures at T1, sex, age, and socioeconomic status.

<table>
<thead>
<tr>
<th></th>
<th>1. Low ODD class (n = 99)</th>
<th>2. Moderate ODD class (n = 428)</th>
<th>3. High ODD class (n = 133)</th>
<th>Group comparisons Wald test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SE</td>
<td>M</td>
<td>SE</td>
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<tr>
<td>HED T6</td>
<td>1.04</td>
<td>0.32</td>
<td>1.40</td>
<td>0.13</td>
</tr>
<tr>
<td>Cannabis T6</td>
<td>1.40</td>
<td>0.21</td>
<td>1.54</td>
<td>0.08</td>
</tr>
<tr>
<td>Depression T6</td>
<td>0.70</td>
<td>0.11</td>
<td>2.65</td>
<td>0.19</td>
</tr>
<tr>
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<td>0.22</td>
<td>5.34</td>
<td>0.22</td>
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<tr>
<td>ADHD T6</td>
<td>2.04</td>
<td>0.16</td>
<td>4.12</td>
<td>0.19</td>
</tr>
<tr>
<td>Aggression T6</td>
<td>3.41</td>
<td>0.43</td>
<td>5.54</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Note: HED = Heavy episodic drinking; ADHD = Attention-deficit/hyperactivity disorder. *p < 0.05; **p < 0.01; ***p < 0.001.
the longitudinal trajectories in symptoms which may be a more accurate representation of symptom experiences over time. It is possible that within the large percentage of youth classified in the Moderate class (71.5%), there may be additional classes that are not captured here due to low numbers of youth. In adolescence, the Moderate ODD class did not differ from the Low class on HED, cannabis use, and anxiety; however, on average, they did have more symptoms of depression, ADHD, and aggression. Consistent with Copeland et al. (19), some level of ODD symptoms and substance use may be normative and intermittent at ages 9 to 18. However, here, as young adults, youth in the Moderate ODD class showed higher levels of depression, anxiety, ADHD, and aggression compared to the Low ODD class suggesting further refinements are needed to distinguish youth at-risk for young adult problems within the Moderate ODD class. Continuation of ODD symptoms into the transition to young adulthood and the cumulative impact of moderate levels of both irritability and defiance may also cascade into comorbid mental health and behavioral problems. Early identification and treatment of even moderate levels of ODD symptoms may prevent these negative outcomes.

In some previous research, irritable (angry) mood appears to occur without the behavioral manifestations of ODD (6); however, defiance rarely occurred without irritable mood (19, 37). Increasing research suggests that irritability may be a trans-diagnostic symptom that characterizes many mental health and behavioral disorders (19, 37, 38). In addition, there is some evidence that irritability may be distinguishable from other concerns that have irritability as one component (e.g., ODD, depression, bipolar disorder) (2, 37, 38). Irritability may also be a multidimensional construct reflecting mood or emotional regulation problems (angry, grouchy, grumpy) rather than behavioral problems (behavioral expressions of intense anger, temper outbursts, screaming) as well as chronic and episodic phases. Following DSM-5, symptoms of ODD-irritability in the current study (i.e., easily annoyed, cranky, angry, and resentful) tap mood disruptions that may not be similar to irritability that characterizes other disorders (tense, dysthmic, moody, cranky). In contrast, ODD-defiance items (argues a lot, defiant, talks back and blame others for mistakes) are observable behavioral symptoms, but are not the same as severe manifestations of intense anger by breaking things or temper outbursts. Further research into the quality and functional impairments related to irritability experienced by individuals with ODD may reveal additional differences from other diagnoses.

Similar to findings by Copeland et al. (19) the parallel trajectories of irritability and defiant symptoms of ODD found in the current research suggest these mood and behavioral dimensions may be distinguishable variables but they co-occur in youth with ODD. Variable centered research that demonstrates the associations of irritability and defiance with specific comorbid concerns may suggest that one subtype may occur without the other. The current study adds to the growing number of studies (2) that do support subgroups of ODD youth who manifest as defiance without irritability or of irritability without defiance.

A majority of youth in the current study (71.5%) were classified in the Moderate ODD class across adolescence and young adulthood; however, the persistence of these negative feelings may be particularly difficult for adolescents to regulate and may be dismissed as normative changes accompanying adolescence and go untreated. By young adulthood, even the moderate levels of persistent ODD symptoms may disrupt functioning as they are not tolerated in work, community, and school settings. Thresholds of symptoms related to pathology may be difficult to establish with the brief screening tool used here; however, consistent with Copeland et al. (19), the current research makes clear that persistently moderate levels detected in even a short screening measure may be implicated in the development of young adult mental health problems and behavioral concerns.

**Implications**

Our findings show that youth’s experiences of moderate and high levels of symptoms of ODD are typically characterized by both irritability and defiance. ODD levels persisted from adolescence to young adulthood. Moreover, experiences of ODD were associated, in adolescences and young adulthood, with risks for comorbid depression, anxiety, behavioral problems, and cannabis use.

A combination of genetic, temperament, and parenting or other contextual factors lie at the basis of high levels of ODD symptoms and may sustain these over time. Research on the etiology and development of ODD suggests that adolescents with ODD showed difficulties in self-regulation and anger as children and that their parents may have had difficulties in attachments and child management (39). By adolescence and young adulthood, high levels of ODD symptoms are increasingly non-normative and annoying to parents, teachers, employers, and peers. This may lead to conflicts in relationships that, in turn, exacerbate perceptions that others are to blame for their problems in youth.
with ODD. The persistence of symptoms into young adulthood suggest early identification and treatments are needed.

Evidence-based treatments for ODD commonly focus on behavioral and anger management (often with a parenting behavior management component) or alternatively, on problem solving or cognitive interventions that target social information processing errors and disruptive interactions with peers (41, 42). Given the severity and persistence of both irritability and defiance symptoms found here, support for parents and treatments of children’s irritability, emotional regulation, and attachment disruptions may also be needed (39, 43). Pharmacotherapeutic treatment options of both aggression and chronic irritability in youth with ODD has begun to be assessed but conclusions are preliminary (44). Our findings do not support treatment options that based on the unsubstantiated view there are distinguishable subgroups of youth with ODD who experience irritability with or without defiance manifestations (40).

Limitations
Our data are generalizable to Canadian youth comprising predominately Caucasian samples. All data were reported by the youth themselves, which may contribute to shared reporter variance. Outcome data were collected in face-to-face structured interviewers and coded by trained research assistants (i.e., educational attainment, occupational prestige, income, work characteristics). Consistency across multiple assessments spaced two years apart (18) increase our confidence in the findings. Slightly more males and youth from lower income families were lost to follow-up. While the effects of family SES are included in our models to adjust for potential bias due to missing data for low-income participants, our models may underestimate these youth. Our analyses also focused on the symptom levels in this community-based sample rather than clinical diagnoses. However, our findings concur with previous research on depressive symptoms (45), suggesting that subclinical symptoms of mental health problems in adolescence can have long term negative outcomes.

Conclusion
While there is a tendency to view ODD symptoms of irritability and defiance as evidence of bad temper or moodiness, consistently high levels of these concerns can compromise the achievement of developmental task appropriate to later adolescence and young adulthood. Early identification and interventions is needed to address both mood regulation and anger management. More research into the etiology of comorbid irritable mood and behavioral manifestations of this serious disorder is needed. Costs to families trying to manage these concerns can be high. Defiance, anger, and touchiness may be responded to by repeated school suspensions that further impede development. Risks for substance use and deviant behavior and depression in young adulthood also suggest early intervention is important.

Conflict of Interests
The authors have no conflicts of interest related to this research.

Acknowledgments
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References


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Trajectories of oppositional defiant disorder severity from adolescence to young adulthood and substance use, mental health, and behavioral problems


Discussant: Distilling symptom heterogeneity in youth with ODD: a commentary on Leadbeater et al., 2023

Brendan F. Andrade, Ph.D., C.Psych.¹

Approximately 1-12% of children and youth are estimated to meet criteria for Oppositional Defiant Disorder (ODD) and ODD constitutes a major reason for referral to mental health centers [1,2]. Effective and targeted interventions are necessary to reduce and prevent significant morbidities.

A number of well-established psychosocial interventions exist that show on average, low to moderate treatment effect sizes [3-8]. Although promising, these evidence-based interventions do not meet the needs of a substantial proportion of youth with ODD [7,9]. One possible explanation for these sub-optimal intervention effects may be due to the considerable heterogeneity in symptoms of ODD. DSM-5 criteria for ODD allow diagnosis based on four out of eight possible symptoms from any of the three clusters of symptoms (angry/irritable mood; argumentative/defiant behavior; vindictiveness). Thus, a child with ODD may be diagnosed based on many distinct combinations of symptoms, making it difficult to design treatment for ODD per se. As such, clinicians commonly recommend that children with ODD, and their parents, receive best-practice psychosocial interventions based on diagnostic cutoffs or symptom severity [10]. What is missing from this widely used and mostly generic approach is specificity based on symptom domains, or key aspects of psychopathology that may underlie symptom presentation and severity.

A more personalized approach to intervention may be needed. One perspective emphasizes differences in mental health outcomes based on symptoms that comprise the angry/irritable and argumentative/defiance dimensions. For example, symptoms on the angry/irritable dimension, such as “often loses temper,” “often touchy and easily annoyed” and “often angry and resentful,” may be more associated with internalizing difficulties such as mood and anxiety disorders [11,12,13]. In contrast, symptoms on the argumentative/defiant dimension, such as “often argues with authority figures,” “often actively defies or refuses to comply with requests” and “often deliberately annoys others” may be more associated with outcomes such as Conduct Disorder and delinquency [11,12]. Although not independent, based solely on an ODD diagnosis, children and adolescents with these two somewhat distinct clinical presentations may be placed in the same psychosocial intervention, regardless of differences in their symptom presentation or underlying psychological and/or neurobiological bases of these clinical presentations. This relatively non-specific form of treatment selection should be revisited within mental health care.

In their longitudinal study of ODD, Leadbeater et. al. [19], determined symptom trajectory classes within a community sample of adolescents and emerging adults that they then associate with comorbid substance use, other mental health and behavioral symptoms. A key finding was their

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identification of trajectories based on overall ODD symptom severity (i.e., low, moderate, and high). They did not identify distinct trajectories for defiance and irritability symptoms (e.g., in which one increases or decreases over time while the other did not). This finding may be consistent with some who propose that there are not clear subtypes based on these symptom groups, but that heterogeneity is accounted for by a general ODD factor (18). Further longitudinal studies with clinical samples or those populations enriched for ODD symptoms may be important to potentially uncover symptom differences.

Leadbeater et al.’s study is an important contribution to the literature in a number of ways. First, the authors highlight the continuity in the three trajectory classes identified (i.e., low, moderate and high) across development. Current best-practice and widely used interventions for ODD often focus on the pre-adolescent period. Findings from this study are consistent with other studies showing evidence of enduring and broad impacts of ODD. The persistence of ODD symptom severity trajectories may necessitate developmentally informed and tailored intervention approaches that target not only ODD symptoms but also co-occurring challenges such as substance use and comorbid mental health challenges.

Another strength of the study is the use of person-centered methods to study ODD trajectories and associated impairments. These methods identify subgroups based on patterns of multiple characteristics [15,16]. This type of research is needed to distill the heterogeneity and non-specific nature of an ODD diagnosis in order to move towards more personalized and tailored approaches to interventions. Determination of patterns may enable development of approaches to best target subgroups of children and youth with ODD. Most studies to date have used variable centered approaches that explain associations between variables of interest within this population and compare groups. Although these approaches have provided a wealth of important information, they are likely not sufficient as they do not take into account the impact of specific combinations of symptoms or characteristics that jointly influence the type and severity of problems experienced by children with ODD [14,15].

Findings from Leadbeater et al.’s study also raise a number of important questions and avenues for further study. First, application of longitudinal person-centered methods within clinical samples of children and youth with elevated symptoms may be necessary to advance understanding and improve interventions. Second, further consideration of environmental factors, such as caregiver and sibling influences on ODD trajectories and symptom severity, is needed to inform prevention and intervention. Third, the importance of conceptualizing irritability that is characteristic of ODD and how this may be similar or different than irritability within other mental health disorders is in need of clarification. Fourth, additional work is needed to understand the biopsychosocial domains, including learning, cognitive, and aspects of psychopathology, that may underlie ODD and low, moderate and high symptom severity trajectories that were identified. This information may be important in order to meaningfully subgroup children and potentially provide more tailored intervention. Finally, consideration of diversity factors and engaging youth, caregivers and other clinical stakeholders in unpacking findings from these and other studies, may be key to build on and contextualize findings from studies such as these.

References


Mood and anxiety symptoms following pediatric mild traumatic brain injury: a scoping review

Seemab Sabir, B.A.¹ and Rebecca Malhi, PhD²

Abstract

Background: Thousands of children sustain mild traumatic brain injuries (mTBI) worldwide each year. Multiple physical and somatic symptoms can occur following pediatric mTBI, including new-onset mood symptoms, headaches, and pain.

Objective: This scoping review examined the existing literature pertaining to mood and anxiety symptoms following pediatric mTBI, in order to summarize the current evidence and identify areas for future research.

Methods: The Pubmed, EMBase, and APA PsycINFO databases were searched to identify articles that examined mood and anxiety symptoms in children and adolescents following mTBI.

Results: A total of 20 published articles were included in the review. The existing research suggests that mood and anxiety symptoms are more common in children and adolescents with mTBI, when compared to orthopedically injured or healthy controls. Several factors may contribute to the development of these symptoms: injury characteristics, older age at injury, female sex, and psychosocial variables including lower socioeconomic status and family history of psychiatric disorders.

Conclusion: The findings of this review highlight the need for additional research on the relationship between pediatric mTBI and subsequent mood and anxiety symptoms. We particularly recommend long-term prospective cohort studies which include appropriate control groups as well as a neuroimaging component to distinguish complicated from uncomplicated mTBI.

Key Words: concussion, pediatric, mood disorder, anxiety, review

Résumé

Contexte: Des milliers d’enfants subissent des traumatismes crâniens légers (TCI) dans le monde entier chaque année. De multiples symptômes physiques et somatiques peuvent se produire par suite d’un TCI pédiatrique, y compris des symptômes de l’humeur nouvellement apparus, des maux de tête et des douleurs. Objectif: Cet examen de la portée a examiné la littérature existante concernant les symptômes de l’humeur et d’anxiété suivant un TCI pédiatrique, afin de résumer les données probantes actuelles et d’identifier les domaines de la future recherche. Méthodes: Les bases de données Pubmed, EMBase, et APA PsycINFO ont été recherchées pour identifier les articles qui examinaient les symptômes de l’humeur et d’anxiété chez les enfants et les adolescents après le TCI. Résultats: Un total de 20 articles publiés a été inclus dans la revue. La recherche existante suggère que les symptômes de l’humeur et d’anxiété sont plus communs chez les enfants et les adolescents qui ont un TCI, lorsque comparés avec les blessés orthopédiquement ou les témoins en santé. Plusieurs facteurs peuvent contribuer au développement de ces symptômes: caractéristiques de la blessure, plus âgé lors de la blessure, sexe féminin, et variables psychosociales dont un statut socio-économique plus faible, et antécédents familiaux de troubles psychiatriques. Conclusion: Le résultats de cette revue mettent en valeur le besoin de recherche additionnelle sur la relation entre le TCI pédiatrique et les symptômes de l’humeur et d’anxiété subséquents. Nous recommandons particulièrement les études de cohorte à long terme qui incluent des groupes témoins appropriés ainsi qu’une composante de neuroimagerie pour distinguer la forme compliquée de la forme non compliquée du TCI.

Mots clés: commotion cérébrale, pédiatrique, trouble de l’humeur, anxiété, revue
Introduction

Traumatic brain injury occurs in 69 million people worldwide per year, including over 3 million children (1). Of these cases, an estimated 80% were classified as mild traumatic brain injury (mTBI), also known as concussion (2). An estimated 692 out of 100,000 children present to emergency departments annually with pediatric mTBI in the United States alone (3). However, a study by Powell et al (4) found that over 56% of mTBI cases go undiagnosed. Patients with untreated mTBIs could potentially have lengthened recovery times due to a lack of post-discharge management education (4). As well, compared to healthy controls, patients with a history of mTBI have an increased risk for the development of long-term medical and behavioral comorbidities (5).

The definition of mTBI is often disputed, with different organizations reporting different qualifying criteria. Some of the key issues in contention include the use of the Glasgow Coma Scale, the duration of altered consciousness, and the presence of neurological symptoms following injury. The lack of consensus on mTBI diagnostic criteria fosters a situation in which many cases of mTBI are left undiagnosed, even when patients report symptoms consistent with an mTBI diagnosis. This is illustrated by the results from a 2019 study of patients presenting to a trauma and emergency care centre in the United States. Koval et al (6) found that an evaluation for mTBI was conducted in less than 50% of patients with a head injury, and only 41% of patients who were diagnosed with mTBI received post-discharge mTBI education.

Research shows that most adults will recover from mTBI within 12 months of injury (7). However, a significant minority will still experience persistent post-concussive symptoms (also known as post-concussion syndrome; PCS), such as fatigue and headaches (7). There is also an increased risk for psychiatric disorders (8).

Pediatric mTBI can cause physical, affective, and cognitive symptoms (9-11). Resolution of symptoms to premorbid levels occurs one month following mTBI in most children, but 13-16% of symptoms can persist several months post-injury (9). Changes in mood, including irritability and other symptoms of anxiety and depression, as well as new-onset mood disorders (also referred to as novel psychiatric disorders; NPD), can also occur after TBI in children (12-14). These symptoms can negatively impact patients’ quality of life and recovery (15).

Mood disorders including depression are common in children and adolescents in the general population, with 17% of adolescents in the US reporting a major depressive episode in 2020 (16). Anxiety and depressive symptoms are often comorbid in pediatric populations. Between 25-50% of children and adolescents with depression also have comorbid anxiety (17). If left undiagnosed or untreated, anxiety and pediatric depression can lead to many negative consequences that can persist into adulthood including disability, a loss of productivity, a high risk for suicide (18), criminal behavior, and dysfunctional interpersonal relationships (19).

Although it is a significant medical issue, few studies have been conducted in children on the effects of pediatric mTBI. One exception is a literature review by Laliberte et al (20) which examined the relationship between pediatric TBI and depression. However, this review only considered depression as an outcome and was not restricted to mTBI. The aim of this study is to examine the occurrence of mood and anxiety disorders following mTBI in children and identify any potential gaps in the research using a scoping review.

Methods

This review followed Arksey and O’Malley’s methodological framework for scoping reviews (21). The steps for the framework are: (a) identifying the research question, (b) identifying relevant studies, (c) study selection, (d) charting the data, and (e) collating, summarizing, and reporting results.

The databases Pubmed, EMBase, and APA PsycINFO were searched in April 2022 for relevant studies published in peer-reviewed academic journals since 2002. The timeframe of twenty years was arbitrary but was selected with the assumption that older high-quality studies would be cited and their findings incorporated into newer published research. We reasoned that more recent studies would include updated information that supersedes older findings. The database search (see Appendix A for search terms) identified 3107 papers: 1105 from APA PsycInfo, 1267 from EMBase, and 735 from Pubmed. One additional article was found after a hand-search of citing articles.

Results from the database search were imported into a Microsoft Excel spreadsheet. After duplicate records were removed, article titles and abstracts were reviewed for relevance. This scan resulted in 1,940 articles being excluded. The remaining 143 articles were selected for full-text review and assessed for eligibility. Abstracts of these articles were reviewed using the following inclusion criteria: (a) Study participants must be below the age of 18 at the time of injury and (b) the study must assess mood disorders or symptoms as an outcome following mTBI. For the purpose of this review, concussion and mTBI were used synonymously. Review papers, articles without abstracts, and non-English language studies were excluded. Of the 143 articles
reviewed, 123 articles did not meet inclusion criteria and were excluded from further analysis. Twenty studies, therefore, met the inclusion criteria. A diagram of the search process is shown in Figure 1.

Both authors independently appraised each of the 20 included articles for study quality using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies (22). Items assessed included selection bias, study design, confounders, blinding, reliability/validity of data collection tools, and study withdrawals. Based on these item assessments, each study was given an overall global quality assessment rating (Weak, Moderate, and Strong). Each article was also reviewed for quality of evidence, using items that are pertinent to the topic of pediatric mTBI: prospective versus retrospective study design, chart review versus in-person assessments, consecutively treated for mTBI versus referred/clinic sample, symptom checklists versus standardized interviews, and the presence of a control group.

Results

Study Characteristics

An overview of the study designs, populations, and relevant findings from each of the 20 included articles can be found in Table 1. The final set of papers had a variety of study designs, including retrospective, cross-sectional, and prospective cohort studies, as well as randomized controlled trials and case series. Of the 20 included articles, there were 2 retrospective chart reviews, 1 cross-sectional study, 14 prospective cohort studies, 1 retrospective cohort study, 1 randomized controlled trial, and 1 retrospective survey. Seven articles included a non-mTBI control group while 10 articles did not. A variety of assessment tools were used including questionnaires, symptom checklists, and standardized interviews. In 9 studies, participants were treated immediately after injury (consecutively treated) for mTBI, 4 used samples of patients referred to clinics, 2 used both

![Figure 1. Literature Review Process](image-url)
<table>
<thead>
<tr>
<th>Author(s), Year of publication</th>
<th>Study design</th>
<th>Study population</th>
<th>Measured variables</th>
<th>Relevant Findings</th>
<th>Author EPHP Quality Rating</th>
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</thead>
<tbody>
<tr>
<td>Chrisman and Richardson, 2014 (13)</td>
<td>Retrospective cohort</td>
<td>Adolescents aged 12-17 (N = 36,060)</td>
<td>Age, sex, parental mental health, history of concussion, diagnosis of depression</td>
<td>2.7% of participants had a history of concussion and 3.4% had a current diagnosis of depression; 7.8% of currently depressed subjects had a history of concussion. History of concussion was associated with a 3.3-fold greater risk for depression.</td>
<td>Moderate</td>
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<tr>
<td>Luis and Mittenberg, 2002 (14)</td>
<td>Prospective cohort</td>
<td>Children (N = 96) with mTBI (n = 45), moderate/severe TBI (n = 19), and orthopedic controls</td>
<td>DISC-IV Modules A and C, DSM-IV criteria, SRRQ, age, gender, race, parental level of education and parental occupation</td>
<td>The TBI group reported significantly more psychiatric disorders at the 6-month follow up than the controls (46% versus 14%). 38.1% of the mTBI group developed a new-onset disorder (NOD).</td>
<td>Moderate</td>
</tr>
<tr>
<td>Tham et al., 2015 (27)</td>
<td>Prospective cohort</td>
<td>Adolescents (N = 100) with mTBI (n = 50), and healthy controls (n = 50)</td>
<td>Age, sex, race, ethnicity, household income, pain intensity (NRS), CES-D, ASWS, PSA, Actigraphy sleep assessment</td>
<td>36% of the mTBI group met criteria for depressive illness compared to 12% of the healthy control group. Greater depressive symptoms were associated with poorer sleep quality in both groups.</td>
<td>Moderate</td>
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<tr>
<td>Ho et al., 2020 (28)</td>
<td>Cross-sectional</td>
<td>Children and adolescents (N = 30) with a diagnosis of concussion and symptomatic at time of recruitment</td>
<td>PCSI, CDI 2, ImPACT</td>
<td>Heightened emotionality, irritability, and nervousness were commonly reported by subjects with post-concussive depression. Sadness and fatigue were reported by patients with and without post-concussive depression.</td>
<td>Strong</td>
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<tr>
<td>Connolly and McCormick, 2019 (29)</td>
<td>Longitudinal cohort</td>
<td>Children and adolescents aged 10-18 (N = 1827)</td>
<td>History of mTBI, CBCL/4-18, parent-child conflict, victimization, Vocabulary subtest of the Wechsler Intelligence Scale for Children-Revised, race, sex</td>
<td>mTBI was positively associated with an increase in anxiety/depression, aggressive behaviour, and delinquency.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Macartney et al., 2021 (30)</td>
<td>Retrospective chart review</td>
<td>Concussion clinic patients aged 6-18 (N = 155)</td>
<td>PCSI, KAD-6, GAD-7</td>
<td>Low overall mean depression and anxiety scores were reported. There is a statistically significant association between PCSI scores and KAD-6 scores as well as GAD-7 scores in males and females.</td>
<td>Moderate</td>
</tr>
<tr>
<td>O’Connor et al., 2012 (31)</td>
<td>Prospective cohort</td>
<td>(n = 35) moderate/severe TBI (n = 31), and arm-injured controls (n = 39)</td>
<td>Preinjury functioning, PHQ-9, DSM-IV criteria, PedsQL, FAD General Functioning Scale</td>
<td>No significant differences were found between TBI groups and the arm-injured groups for depressive symptoms.</td>
<td>Moderate</td>
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<td>Hammer et al., 2020 (32)</td>
<td>Prospective cohort</td>
<td>High school athletes (N = 2160)</td>
<td>Demographics, PHQ-9, SCAT5</td>
<td>5.8% of participants sustained an SRC over the course of two years. PHQ-9 scores returned to normal by return to sport, and there was no significant difference in PHQ-9 scores between</td>
<td>Moderate</td>
</tr>
<tr>
<td>Max et al., 2021 (33)</td>
<td>Prospective Cohort</td>
<td>Children and adolescents who sustained an mTBI (N = 220) or OI (N = 110) and were seen at the emergency department</td>
<td>ISS, AIS, K-SADS-PL, NPRS, TRF, DSM-IV, Vineland Adaptive Behavior Scales, WASI, CRS, WRAT-4, McSIFF, FAD, Family History Research Diagnostic Criteria</td>
<td>NPD occurred in a higher rate of children with mTBI than with OI (mean ratio [MR] 3.647, 95% confidence interval [CI95] (1.264, 15.405), p = 0.014).</td>
<td>Strong</td>
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<tr>
<td>Chrisman et al., 2021 (34)</td>
<td>Randomized controlled trial</td>
<td>Children diagnosed with a sports-related or recreation-related concussion (N = 200)</td>
<td>Demographics, injury characteristics, history of mental health or chronic pain, ASWS-28, UCLA Trauma History Profile, National Comorbidity Trauma History Screen, PHQ-9, GAD-7</td>
<td>40% of the sample reported significant depressive symptoms, 25% significant anxiety symptoms, 14% thoughts of death/self-harm, and 8% thoughts of suicide.</td>
<td>Weak</td>
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<tr>
<td>Max et al., 2013 (35)</td>
<td>Prospective cohort</td>
<td>Children who sustained mTBI (N = 79)</td>
<td>K-SADS-PL, DSM-IV criteria, NPRS, lesions on MRI, GCS score, Survey Diagnostic Instrument, AIS, ISS, Family History Research Diagnostic Criteria, FAD General Functioning Scale, Four-Factor Index, psychosocial adversity, Vineland Adaptive Behavior Scale, Woodcock-Johnson Revised Letter-Word Identification, WISC-III, Rapid Automatized Naming task, CVLT-C, CELF-3</td>
<td>23% of subjects developed NPD by the 12-month assessment, including generalized anxiety disorder (n = 3), major depressive disorder (n = 2), and separation anxiety disorder (n =1)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Gillie et al., 2022 (36)</td>
<td>Observational cohort</td>
<td>Children who presented to a concussion specialty clinic (N = 129)</td>
<td>VOMS, ImPACT, PCSS, SCARED-C, GAD-7</td>
<td>21.7% of subjects displayed levels of anxiety consistent with a diagnosis of anxiety disorder. 13.2% met or exceeded clinical cutoffs for post-injury anxiety.</td>
<td>Strong</td>
</tr>
<tr>
<td>Max et al., 2013 (37)</td>
<td>Prospective cohort</td>
<td>Children who sustained mTBI (N = 87)</td>
<td>DSM-IV criteria, K-SADS-PL, NPRS, GCS score, AIS, ISS, lesions on MRI, Family History Research Diagnostic Criteria, FAD general functioning scale, Four-Factor Index, psychosocial adversity, Vineland Adaptive Behavior Scale, Woodcock-Johnson Revised Calculation and Letter–Word Identification, WISC-III, WASI, CELF-3, Stroop Color-Word Inference Task, SSRT</td>
<td>36% of subjects developed NPD by the 12-month assessment, including major depressive disorder (n = 3), generalized anxiety disorder (n = 2), and separation anxiety disorder (n = 2)</td>
<td>Moderate</td>
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### Table 1. Continued

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<tr>
<td>Max et al., 2015 (38)</td>
<td>Prospective cohort</td>
<td>Children who sustained mTBI (N = 87)</td>
<td>DSM-IV criteria, K-SADS-PL, NPRS, GCS score, AIS, ISS, lesions on MRI, Family History Research Diagnostic Criteria, FAD general functioning scale, Four-Factor Index, psychosocial adversity, Vineland Adaptive Behavior Scale, Woodcock-Johnson Revised Calculation and Letter–Word Identification, WISC-III, WASI, CELF-3, Stroop Color-Word Inference Task, SSRT</td>
<td>19% of subjects who returned for the 24-month assessment developed NPD, including depressive disorders (n = 3) and anxiety disorders (n = 3).</td>
<td>Moderate</td>
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<tr>
<td>Ellis et al., 2015 (39)</td>
<td>Retrospective chart review</td>
<td>Pediatric patients referred to a concussion program between September 2013 and October 2014 (N = 174)</td>
<td>Demographic information, sport played at time of injury, medical history, past concussion history, family history, PCSS</td>
<td>49.4% of participants reported at least one emotional symptom. 11.5% of participants met the criteria for a postinjury psychiatric outcome, including NPD (n = 14), isolated suicidal ideation (n = 2), and worsening symptoms of a preinjury psychiatric disorder (n = 4).</td>
<td>Weak</td>
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<tr>
<td>Massagli et al., 2004 (40)</td>
<td>Prospective cohort</td>
<td>Children (N = 1960) with mTBI (n = 490) and unexposed controls (N = 1470)</td>
<td>ICD-9-CM codes for psychiatric diagnosis, filling of prescription for psychiatric medication, or utilization of psychiatric services</td>
<td>Psychiatric illness was found in a greater percentage of children with mTBI compared to unexposed controls (30% versus 20%) in the three years post-injury. An estimated 3% of children with mTBI are predicted to develop affective disorders including depression and anxiety disorders.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Brooks et al., 2019 (41)</td>
<td>Prospective cohort</td>
<td>Children and adolescents who sustained a concussion within the past 48 hours and presented to the emergency department (N = 311)</td>
<td>Demographics, past medical, developmental, and psychiatric histories, injury characteristics, PCSI, SAC, M-BESS, SCAT, CBCL, SDQ</td>
<td>Psychological distress was experienced by 19.4% of participants at the 4-week follow-up and 24.1% at the 12-week follow-up.</td>
<td>Weak</td>
</tr>
<tr>
<td>McKinlay et al., 2009 (42)</td>
<td>Longitudinal birth cohort</td>
<td>Children (N = 1265) who were admitted to a hospital for mTBI (n = 19), who were sent home</td>
<td>Premorbid and post-injury functioning, DSM-III-R criteria, Revised Behavior</td>
<td>Children who were hospitalized for mTBI were significantly more likely to display symptoms of mood disorder, substance abuse, and CD/ODD but not anxiety disorder.</td>
<td>Strong</td>
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Definition of mTBI

The World Health Organization (WHO) defines mTBI as a Glasgow Coma Scale (GCS) score of 13 to 15 out of 15 that is accompanied by at least one of the following symptoms: loss of consciousness (LOC) less than 30 minutes, post-traumatic amnesia (PTA) less than 24 hours, impaired mental state at the time of injury, or transient neurological deficit (23). The Zurich consensus statement defines concussion as a brain injury with “a complex pathophysiological process affecting the brain, induced by biomechanical forces” (24, pp1). Several studies also use International Classification of Diseases (ICD)-9 codes to define mTBI. Relevant ICD-9 codes include: skull fracture (800.0, 800.5, 801.0, 801.5, 803.0, 803.5, 804.0, or 804.5), concussion (850.0, 850.1, 850.5, or 850.9), intracranial injury of other and unspecified nature (854.0), or head injury, unspecified (959.01) (25).

The included studies used several different criteria to determine exposure to mTBI. Two studies used the Zurich Consensus Statement on Concussion in Sport (24). One study used diagnostic categories from the Centers for Disease Control and Prevention (CDC), which encompass multiple ICD-9 codes. Six papers used a combination of diagnostic criteria, including GCS scores, length of time where there was a loss of consciousness, and neuroimaging.

Table 1. Continued

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</thead>
<tbody>
<tr>
<td>Chendrasekhar et al., 2020 (43)</td>
<td>Retrospective survey</td>
<td>Children and adolescents (N = 100) who sustained mTBI</td>
<td>ISS, AIS-H, RTS, GCS score, vital signs, pre-existing conditions, post-injury symptoms</td>
<td>33% of participants reported residual effects following injury; 21% of participants who reported sequelae had anxiety/depression issues.</td>
<td>Weak</td>
</tr>
<tr>
<td>Starkey et al., 2018 (44)</td>
<td>Prospective cohort</td>
<td>Children and adolescents (N = 184) with mTBI (n = 117) and TBI free controls (n = 67)</td>
<td>Demographics, injury characteristics, pre-injury health, RPQ, BASC-2, Hospital Anxiety and Depression Scale</td>
<td>mTBI group reported more PCSs and behavioural problems than the control group. The proportion of children with clinically significant internalizing problems increased over time in the mTBI group.</td>
<td>Weak</td>
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</table>

Abbreviations: AIS, Abbreviated Injury Scale; ASWS, Adolescent Sleep Wake Scale; CBCL/4-18, Child Behavior Checklist for Ages 4-18; CD, conduct disorder; CDI 2, Children’s Depression Inventory; CELF-3, Clinical Evaluation of Language Fundamentals, 3rd Edition; CES-D, Center for Epidemiological Studies Depression Scale; CRN, Clinical Rating Scale; CVLT-C, California Verbal Learning Test-Children’s Version; DISC-V, Diagnostic Interview Schedule for Children - 4th edition; DSM-III-R, Diagnostic & Statistical Manual of Mental Disorders—3rd Edition Revised; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; FAD, Family Assessment Device; GAD-7, Generalized Anxiety Disorder 7-item; GCS, Glasgow Coma Scale; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ImPACT, Immediate Post-Concussion Assessment and Cognitive Test; ISS, Injury Severity Score; KAD-6, 6-item Kutcher Adolescent Depression Scale; K-SADS-PL, Schedule for Affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime Version; M-BESS, Modified Balance Error Scoring System; McSIFF Mcmaster Structured Interview of Family Functioning; MRI, magnetic resonance imaging; NOD, new-onset disorder; NPD, new-onset (novel) psychiatric disorder; NPRS, Neuropsychiatric Rating Schedule; NRS, Numeric Rating Scale; ODD, oppositional defiant disorder; PCSI, Post-Concussion Symptom Inventory; PCSS, Post-Concussion Symptom Scale; PSA, Pre-Sleep Arousal; RPQ, Rivermead Post-Concussion Symptoms Questionnaire; RTS, Revised Trauma Score; SAC, Standardized Assessment of Concussion; SCARED-C, Screening for Child Anxiety Related Disorders—Child Report; SCAT, Child-Sport Concussion Assessment Tool; SDQ, Strengths and Difficulties Questionnaire; SRC, sports-related concussion; SRRQ, Social Readjustment Rating Questionnaire; TRF, Teacher’s Report Form; VOMS, Vestibular Ocular-Motor Screening; WASI, Wechsler Abbreviated Scale of Intelligence; WISC-III, Wechsler Intelligence Scale for Children—III; WRAT-4, Wide Range Achievement Test—Fourth Edition

consecutively treated and clinically referred patient samples, and 5 were unknown or not applicable.

The majority of the included studies included participants from North America including 11 studies with participants from the United States, 4 from Canada, and 3 from both the United States and Canada. Another 2 studies included participants from New Zealand.

Using the EPHP Quality Assessment Tool, 4 included articles were rated as “Strong”, 11 as “Moderate”, and 5 as “Weak”. We had an initial inter-rater reliability of 85% agreement. Disagreements were discussed by the authors until consensus was reached.
studies did not specify diagnostic criteria as participants were recruited from either concussion specialty clinics or hospitals following injury. The remainder of the articles (n = 8) used an array of measures, including chart reviews, parental reports, self-reports, the WH0 Task Force definition of mTBI, the Abbreviated Injury Scale - Head, and Injury Severity Scores. Despite the use of different criteria, there was general agreement that mTBI is a closed-head injury resulting from blunt-force trauma. Some articles discussed mTBI cases with abnormalities on neuroimaging, known as complicated mTBI (26).

**Depression and Depressive Symptoms**

The studies in the scoping review reported rates of depression following pediatric mTBI ranging from 0% to 40%, depending on the assessment interval and instrument. Tham et al (27) reported that in the first 12 months following injury, 36% of children with mTBI met the Center for Epidemiologic Studies Depression Scale (CES-D) measure for depressive symptoms, compared to 12% of healthy controls. Chrisman and Richardson (13) found that a history of concussion was associated with a 3.3-fold greater risk for depression in patients (95% CI: 2.0–5.5), compared to patients with no history of concussion. Ho et al (28) reported that 83.3% of adolescents experienced at least one depressive symptom on the Children’s Depression Inventory 2 (CDI 2) after concussion, with sadness and irritability being the most commonly reported symptoms. Connolly and McCormick (29) found that when compared to individuals without mTBI, participants with mTBI are significantly more likely to report symptoms of depression (95% CI: 0.10-0.41) in the 2.5 years following injury, even after controlling for prior histories of depression.

The remaining studies, however, did not find an association between pediatric mTBI and depression. For example, Macartney et al (30) reported a mean 6-item Kutcher Adolescent Depression Scale depression score of 4.7 (range 0-18), indicating low levels of depression post-injury. Similarly, O’Connor et al (31) found no significant differences in rates of depressive symptoms between head injury and arm injury groups in the first 24 months post-injury. According to Hammer et al (32), mood symptoms only slightly worsened after injury but returned to baseline within a few months. Max et al (33) reported no difference in rates of new-onset depressive disorders between children with mTBI and children with orthopedic injury (OI), with neither group reporting depressive symptoms at 3 months post-injury.

**Anxiety**

Clinically significant anxiety and associated symptoms following pediatric mTBI were noted by several studies included in the review. Christman et al (34) found that 25% of youth with concussions met the guidelines for clinically significant anxiety. A variety of anxiety disorders as defined by DSM-IV criteria, including generalized anxiety disorder and separation anxiety disorder, were reported by Max et al (35) in 6% of subjects aged 5-14 years old in the first 12 months post-injury. Using a combination of DSM-IV diagnostic criteria and the Screen for Child Anxiety Related Disorders, Gillie and colleagues (36) found that over 13% of concussed youths met or exceeded clinical cutoffs for anxiety, noting that clinically significant anxiety appeared to be associated with non-sports related concussion injuries as well as pre-injury panic symptoms. Connolly and McCormick (29) also found elevated incidences of anxiety after mTBI in participants aged 10-18 years old. New-onset anxiety disorders were reported by Max et al (33) as 2.1% and 1.1% in the mTBI and OI groups at 3 months post-injury, respectively.

Of the articles reviewed, only one article did not find a significant association between mTBI and post-injury anxiety symptoms. Participants in the Macartney et al (30) study only had a mean General Anxiety Disorder-7 score of 7.4 (range 0-24), indicating low levels of anxiety overall.

**New-onset mood disorders and psychiatric outcomes**

Several studies analyzed general rates of new-onset mood disorders or new-onset psychiatric disorders that occurred following mTBI. Luis and Mittenberg (14) found that over 38% of pediatric mTBI subjects developed a new-onset mood disorder, compared to 14% of controls. These disorders included social phobia, separation anxiety, panic attacks, agoraphobia, obsessive-compulsive disorder, post-traumatic stress disorder, and major depressive disorder. Across several prospective cohort studies, Max and colleagues (33, 35, 37, 38) found that between 19% and 36% of children and adolescents with mTBI presented with new-onset (novel) psychiatric disorders (NPD) in the first two years following injury. Ellis et al (39) noted that emotional symptoms, including sadness, irritability, and/or nervousness, were found in 49.4% of concussion patients, as well as NPD in 8% of patients.

Massagli et al (40) also found significantly higher rates of psychiatric illness in mTBI patients compared to OI patients, estimating 30% in the mTBI group and 20% in the OI group (p = 0.0001). In that study, psychiatric illness was operationalized as psychiatric diagnosis, the filling of a prescription for a psychiatric medication, or use of psychiatric...
services post-injury. A study by Brooks et al (41) reported that one in five children presented with elevated levels of psychological distress within the first three months after injury. McKinlay et al (42) found that up to 58% of adolescents who sustained mTBI had behaviors consistent with one or more psychiatric disorders, compared to 43% of non-mTBI controls.

Chrisman et al (34) noted that thoughts of death or self-harm as well as thoughts of suicide were reported in 14% and 8% of subjects with persistent post-concussive symptoms after mTBI, respectively. Anxiety and depression issues were described by Chendrasekhar et al (43) as long-term sequelae in 20% of mTBI patients. Similarly, Starkey et al (44) reported higher internalizing symptoms including anxiety, depression, and other somatization issues over time in the mTBI group versus uninjured controls, noting up to 14.1% and 6.2% in the first 12 months of the study, respectively.

Pre-injury Psychiatric History
The presence of a pre-injury psychiatric diagnosis was associated with an increased risk of developing a new-onset mood disorder (33). Chrisman et al (34) reported a higher risk for suicidality and self-harm in children with a history of depression and anxiety. Preinjury anxiety was also associated with post-injury psychological distress, anxiety, and lingering post-concussive problems. Max et al (33) found that the presence of a pre-injury psychiatric disorder was significantly associated with higher NPD counts following injury.

Interestingly, Massagli et al (40) found higher occurrences of novel diagnoses in uninjured children with psychiatric histories when compared to children with mTBI and psychiatric histories. Research is needed to further explicate this finding and determine if pre-injury psychiatric histories significantly increase the risk of novel diagnoses post-injury.

Discussion
This scoping review examined the current literature on the relationship between pediatric mild traumatic brain injury and mood disorders and their symptoms. There is some evidence to suggest that mood symptoms are commonly seen following mTBI in children. However, the distinction between increased mood symptomology versus a formal diagnosis of a mood disorder is not clear. Five studies used DSM-IV diagnostic criteria, and one study used DSM-III-R criteria. The remaining studies used a variety of methods including structured interviews, self-reports, parental reports, and symptom rating questionnaires. Although these assessment tools aid in analyzing the prevalence of mood and anxiety symptoms in a pediatric population, they may not always provide benchmarks for clinically significant levels of reported symptoms. The use of self-reports and questionnaires raises the question of whether all the mood symptoms that a patient may be experiencing are accounted for when making a clinical diagnosis.

Additionally, few studies assessed long-term mood-related outcomes. The majority of studies conducted follow-up between 3 and 6 months after injury, and only one paper analyzed the incidence of psychiatric illness 3 years after mTBI in children. Though it is generally accepted that many post-injury outcomes resolve within a few weeks (9), some evidence suggests that psychiatric outcomes may carry on well after 6 months post-injury (35, 37, 38, 40) In addition to increased rates of psychiatric outcomes, pediatric mTBI patients may be at risk for long-term behavioural outcomes, including being more likely to be arrested and involved with violent offences (42). There is a need for prospective cohort studies in order to assess the longitudinal outcomes of mTBI in children.

Another issue highlighted by this review was the lack of consistency between control groups. Many studies included non-injured subjects as controls, whereas others included an OI control group. The inclusion of an uninjured control group rather than an OI group does not take into account outcomes that can be attributed to acute injury to the body, regardless of anatomical location.

Although this review focused on mood disorders and symptoms, several non-mood related outcomes were also observed across the included studies. For example, reduced adaptive functioning (35), decrements in expressive functioning and expressive language (37), memory loss (43), learning disability (43), and sleep disturbance (27, 43) were all found to be associated with mTBI. However, such symptoms and their associated mental and physical outcomes are beyond the scope of this review and warrant further investigation.

Other Confounders
There were several non-injury factors that appeared to be associated with mood disturbances following mTBI. These potential confounders include family psychiatric history, socioeconomic status, age, sex, and parent mental health.

There is little concurrence on the true extent of the confounding effect of these variables, as findings from multiple studies contradict one another. One study noted that older adolescence is associated with a 1.5-fold greater risk for depression compared to younger adolescence (13), while others found that age is not associated with the occurrence of new-onset psychiatric disorders after injury (33, 35, 37).
Female sex was observed in several instances to be associated with psychiatric outcomes (30, 38, 39) such as higher rates of anxiety and depression. There also appeared to be a correlation between the incidence of NPDs and psychosocial factors. These factors included family functioning (33, 35), lower SES (13), family psychiatric history (33, 39), vestibular dysfunction (33, 36), parent mental health (13), and neurocognitive deficits (35), but they were not analyzed in depth. Due to this, it is undetermined whether the increase in psychiatric outcomes can be attributed to any psychosocial variables, or if the outcomes resulted solely due to the injury and not influenced by any other variable.

Complicated mTBI was examined in several studies. Two studies by Max et al (37, 38) found that frontal white matter lesions were associated with NPD. Contrarily, Max et al (35) also reported in a 2013 study that the location of lesions was not associated with NPD. It is imperative that future studies include a complicated mTBI group and assess lesion location as a potential confounder for the development of NPD post-injury.

**Limitations of this review**

As this article is a scoping review, no meta-analysis was conducted. The exclusion of non-English articles as well as the exclusion of articles published before 2002 may have resulted in selection bias.

Another limitation of this review concerns complicated mTBI. Of the 20 selected articles, 11 did not include neuroimaging, which is the method for distinguishing between complicated and uncomplicated mTBI. Due to this, it cannot be determined whether instances of new-onset mood disorders and symptoms following concussion can be attributed solely to exposure to mTBI or if the results are confounded by the presence of intracranial lesions.

Only five of the included articles were rated as “strong”. Several studies featured weaker study designs such as retrospective chart reviews or a lack of appropriate control groups. However, the articles do represent the state of the current literature and highlight the need for high-quality medical research in this subject area.

**Recommendations**

Additional research is needed on the relationship between pediatric mTBI and mood disorders. These studies should be long-term (>24 months post-injury) prospective cohort studies in nature and include an orthopedic injury control group. Generally, mTBI and complicated mTBI are assessed as separate categories, but the inclusion of a complicated mTBI group in future studies may provide insight on subsequent symptoms that may be correlated to lesion location. DSM-IV or DSM-V diagnostic criteria should be utilized, as well as in-depth analysis on psychosocial and neurocognitive risk factors. It is crucial to control for potential confounders and the presence of pre-injury psychiatric disorders and symptoms as a risk factor for new-onset symptomatology. It is also imperative to conduct further research on non-mood related and somatic PCS including sleep disturbances, pain, memory loss, and vestibular dysfunction.

Within the scope of mTBI, there is evidence to suggest that NPD is associated with more serious cases (i.e., mTBI cases requiring inpatient hospitalization) and the type of injury (sports-related concussion or not). Current literature regarding sports-related concussion (SRC) and its connection to mood outcomes is inconclusive, and very few studies have focused on inpatient mTBI. Future studies on the relationship between new-onset mood disorders and inpatient status following injury as well as studies which consider injury type should be conducted.

**Conclusion**

Sequelae of pediatric mTBI can include the development of new-onset mood and anxiety disorders or symptomatology. Our recommendations for future research may aid in the detection of mood and anxiety outcomes following pediatric mTBI, ultimately resulting in early management and fewer long-term symptoms.

**Conflicts of Interest**

The authors have no financial relationships or other ties to disclose.

**Acknowledgements**

We thank Dr. Meadow Schroeder of the University of Calgary and Ms. Inayah Nurur-Rahman, B.A. of Wayne State University for their insights, expertise, and assistance with editing.

**References**


Mood and anxiety symptoms following pediatric mild traumatic brain injury: a scoping review


### Appendix A: Pediatric mTBI Scoping Review – Database Searches

<table>
<thead>
<tr>
<th>Terms</th>
<th>EMBASE</th>
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<td>S3: (depress* or anxi* or «mood disorder*» or «mood symptom*» or «low mood*» or «mood outcome*» or «psychiatric disorder*» or «psychiatric symptom*» or «psychiatric ill*» or sequelae).mp.</td>
<td>S3: (depress* or anxi* or «mood disorder*» or «mood symptom*» or «low mood*» or «mood outcome*» or «psychiatric disorder*» or «psychiatric symptom*» or «psychiatric ill*» or sequelae)</td>
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Clozapine-induced myocarditis and subsequent rechallenge: a narrative literature review and case report

Nadine Halawa PharmD, BCPS¹; Mackenzie Armstrong MD, FRCPC²; Sarah Fancy, MD, FRCP³; Sabina Abidi MD, FRCPC⁴

Abstract

Clozapine is an antipsychotic medication that has been proven effective for the management of treatment-resistant schizophrenia (TRS). For some patients, it is the only medication that can improve disease burden and quality of life. Clozapine comes with various potentially serious adverse effects which may dissuade physicians from prescribing it despite its well-documented efficacy. One of these adverse effects is clozapine-induced myocarditis (CIM). Due to these risks, patients who undergo a clozapine rechallenge after CIM require close monitoring. Myocardial damage can be reversible if CIM is promptly identified, and clozapine is discontinued appropriately. The gold-standard for diagnosing myocarditis is an endomyocardial biopsy but there are no clear recommendations for how to use less invasive screening assessments to monitor for CIM during a clozapine rechallenge. This review article aims to increase awareness of CIM and provide guidance on monitoring and management. The accompanying case report presents a proposed strategy, including biomarkers that were used to identify inflammation and cardiac injury which guided the treatment of an adolescent patient who had a successful clozapine rechallenge. Further research is necessary to validate the proposed monitoring protocol and to further advance guidance for clinicians.

Key Words: clozapine, clozapine-induced myocarditis, rechallenge, CIM, adolescents, protocol

Résumé

La clozapine est une médication antipsychotique qui s’est révélée efficace pour la prise en charge de la schizophrénie résistante au traitement (SRT). Pour certains patients, c’est le seul médicament qui peut améliorer le fardeau de la maladie et la qualité de vie. La clozapine s’accompagne de divers effets secondaires potentiellement sérieux qui peuvent empêcher les médecins de la prescrire, malgré son efficacité bien documentée. L’un de ces effets indésirables est la myocardite induite par la clozapine (MIC). En raison de ces risques, les patients qui subissent une nouvelle provocation à la clozapine après une MIC demandent une surveillance étroite. Les lésions myocardiques peuvent être réversibles si la MIC est rapidement identifiée et que la clozapine est interrompue de façon appropriée. La référence en matière de diagnostic
Clozapine-induced myocarditis and subsequent rechallenge: a narrative literature review and case report

Introduction

Schizophrenia is a mental disorder characterized by disturbances in thought, perception, and behavior (1). Roughly one-third of patients diagnosed with schizophrenia have treatment-resistant schizophrenia (TRS). TRS is defined when patients do not have adequate response to at least two trials of different antipsychotics, with sufficient dose and duration (2). Compared to individuals with treatment-responsive schizophrenia, those with TRS spend significantly more days per year in hospital (75 versus 5.3 days) and score 20% lower on quality-of-life scales (3). Patients with TRS also have higher rates of suicide (4). Clozapine is a second-generation antipsychotic that has proven efficacy for the treatment of TRS, including evidence for decreased suicidality and mood stabilization (5,6).

Approximately 5% of patients with schizophrenia are diagnosed before the age of 18 (7). Since early-onset schizophrenia (EOS) occurs during crucial years of neurodevelopment, it is a predictor of worse prognosis, with greater chronicity and clinical morbidity (1). Response rates to antipsychotics are lower in patients with EOS relative to other individuals (8). Hence, this population is more commonly treatment-resistant and eligible for clozapine treatment (7). In Canada, clozapine is recommended as first-line treatment in youth with TRS (9). Although the data are limited compared to adult populations, clozapine’s superior efficacy in TRS has also been demonstrated in youth. Tolerability is comparable to adult populations, with low discontinuation rates (3-6%) (7).

Unfortunately, initiation is often delayed in youth who meet criteria for TRS despite availability of guidelines which may be due to prescriber discomfort and inherent risks (10,11). This may be particularly true in the pediatric population where literature is limited. Clozapine’s restricted use in TRS is in part due to the risk for rare but severe adverse effects, some of which include agranulocytosis, seizures, and myocarditis (2).

In Canada, all patients that are on clozapine treatment are registered under a national network to monitor for agranulocytosis (12). The cumulative incidence of agranulocytosis associated with clozapine treatment was reported to be 0.8% over a one-year period (13). Myocarditis associated with clozapine has a estimated incidence, ranging from 0.7% to 1.2%, over a ten-year period (14) and laboratory monitoring is not mandated in Canada (12). Since myocarditis can be life-threatening, vigilance and close monitoring should be recommended with clozapine treatment where a history of clozapine-induced myocarditis (CIM) is present (15,16).

This article reviews the definition, rates, and pathophysiology of CIM, as well as recommendations for monitoring, diagnosing, and treating CIM. This is followed by a case report of a successful clozapine rechallenge in an adolescent who had a history of CIM, along with an accompanied proposed monitoring protocol that was implemented. This review and case presentation may serve to aid clinicians when considering clozapine rechallenge by providing a potential framework for monitoring in the context of a rechallenge.

Clozapine-Induced Myocarditis (CIM)

Myocarditis is an inflammatory disease of the cardiac muscle, which can be caused by infectious and non-infectious conditions (17). In adults, the absolute risk of CIM has been reported to be low at 0.01% to 0.19% (18) with true risk estimated to be higher than that given potential underreporting (17). The incidence of CIM ranged from 0.7% to 1.2% of treated patients in a 10-year period (14) with one inpatient study identifying 10 of 316 patients as meeting criteria for CIM during their hospitalization (19). CIM has been reported to occur primarily in the first two to eight weeks of clozapine treatment (17,20). The mortality rate of CIM ranged from 10 to 30%, with the highest risk occurring in the first month of treatment (19). In children and adolescents, the epidemiology of CIM is unknown given the small number of studies published.

Mots clés: clozapine, myocardite induite par la clozapine, provocation, MIC, adolescents, protocole
The exact pathophysiology of CIM is unknown. Some hypothesize clozapine has a direct myotoxic effect (21) while others suspect it triggers a type I immunoglobulin E (IgE)-mediated hypersensitivity reaction (15). In the review of cases of CIM, the development of eosinophilia has been observed. This suggests an IgE mediated hypersensitivity reaction as far as mechanism (21,22). A rise in proinflammatory cytokines has been found to be dose-dependent and leads to increased oxidative stress and cardiotoxicity (23). Several pathways are involved including immune modulation and proinflammation including an IgE-mediated response, catecholamine activation, induction of free radicals and oxidative stress, and activation of cardiomyocyte cell death pathways (24). Furthermore, sympathetic hyperactivity and blockade of cholinergic and adrenergic receptors are also attributed to myocarditis (25). A full appreciation of the mechanisms remains unclear but observed to be multifactorial.

The course of CIM has been described in the literature (26). It involves a benign increase in heart rate (HR) of 10-20 beats per minute (bpm) around 10-19 days after clozapine initiation, followed by onset of respiratory, gastrointestinal, and urinary symptoms and/or a mild C-reactive protein (CRP) rise. This is then followed by further rise in HR of 20 to 30 bpm (higher than previous), with subsequent troponin-I elevation greater than two times the upper limit of normal, CRP greater than 100 mg/L, and abnormalities in left ventricular (LV) function on echocardiogram. Commonly, nonspecific symptoms are experienced including malaise, myalgia, pleuritic chest pain, tachypnea, low-grade fever, fatigue, and hypotension.

The onset of CIM typically occurs 10 to 30 days after clozapine is started, with 88% of cases occurring during the first three weeks (26). CIM that begins beyond three weeks could represent a delayed hypersensitivity reaction (type II or IV) where clozapine forms an antigen complex with cardiac myocytes (27). This complex attracts monocytes and promotes inflammation, resulting in myocardial damage. Hence, clozapine-induced cardiomyopathy can occur much later with a median onset of 9 months (28). Furthermore, the presentation of CIM overlaps with other types of myocarditis, other viral infections, and medical conditions therefore alternative causes must be excluded.

Five cases of suspected CIM in youth have been published (29,30,31,32). The cases range in age from 15-18 with multiple presenting symptoms suspicious for CIM including fever, chest pain, dyspnea, tachycardia, myalgias and lethargy as well as abnormalities on bloodwork. Four of the patients developed cardiac symptoms at daily clozapine doses between 125-200mg two weeks after starting treatment (30,31,31). All five patients stabilized following clozapine discontinuation (29,30,31,32).

A systematic review of reported CIM in youth as an adverse drug reaction (ADR) from the Word Health Organization (WHO) pharmacovigilance database was published by Les Cuevas and colleagues in 2022 (33). The authors identified 19 possible, and 22 probable cases of CIM based on symptom presentation and the ADR scale confirming that CIM does occur in youth. Roughly two thirds of patients were on clozapine monotherapy, and most cases of CIM occurred in the first month of treatment often associated with up-titration. Fatal outcomes were lower in children and increased by age in this sample. The characteristics observed in these cases was deemed similar to adults, including heterogeneity of symptom presentation.

Monitoring Recommendations for CIM

In Canada, the clozapine product monograph details signs and symptoms of myocarditis but only recommends discontinuation of clozapine and to obtain an urgent cardiac evaluation upon suspicion of CIM (12,34). A 2018 systematic review summarized clozapine monitoring recommendations from 27 studies (35). At baseline, a physical exam, history, and interval electrocardiograms (EKGs) are consistently suggested (17,36,37). If the patient has any cardiac risk factors, a cardiology consult is indicated (35). The recommendations for baseline echocardiograms are inconsistent, with some reviews cautioning against its use unless the patient has significant cardiac risk factors (17,38). Others recommend a baseline echocardiogram for all clozapine patients, with a repeat scan in either two or six months (37,39). Prolonged QTc (QT corrected for heart rate) on EKG may also be observed and should be monitored (40). Caution and vigilance should be observed for patients with a known history of cardiovascular or conduction abnormalities (12).

After clozapine is initiated, the recommendations include monitoring for clinical signs of myocarditis, including cardiac distress [i.e., chest pain, palpitations, dyspnea] and immune response [e.g., fever, fatigue, myalgia] (28). Recommendations for laboratory testing are varied, but several studies recommend baseline and weekly troponin-I, creatine kinase (CK), and CRP for the first three to four weeks of clozapine therapy (41,42,43). The evidence is mixed as to the role of measuring white blood cells (WBCs), erythrocyte sedimentation rate (ESR), B-type Natriuretic Peptide (BNP) and eosinophils to screen for myocarditis.

CIM may be difficult to detect based upon specific signs, symptoms, and echocardiogram alone. Left ventricular
impairment is observed in approximately two-thirds of patients and early symptoms are often nonspecific (19).

**Diagnosing CIM**

Endomyocardial biopsy is the gold standard for diagnosing myocarditis but in practice, it is more frequently diagnosed using a combination of less invasive assessments, including clinical, biochemical, electrocardiographic, and echocardiographic tests (19,31). Experts also suggest Cardiovascular Magnetic Resonance (CV-MRI) as part of the assessment (19,44).

An Australian team developed an evidence-based monitoring protocol for adults based on the analysis of 75 CIM cases, which details laboratory thresholds for when clozapine should be stopped (26). Their monitoring protocol recommends baseline troponin-I/T, CRP and echocardiography, and monitoring troponin-I/T and CRP on days 7, 14, 21 and 28 of treatment; hence, active monitoring for at least four weeks when reintroducing clozapine in cases with a history of CIM. They suggest that clozapine administration should cease if CRP is greater than 100 mg/L or if troponin-I/T is more than two times the upper limit of normal. If CRP is between 50-100 mg/L or if troponin-I/T is elevated but less than two times the upper limit of normal, they recommend continuing clozapine with increased monitoring. Elevated WBC, CK, ESR, and BNP would also be concerning and warrant further work-up. Investigating both CRP and troponin-I together was found to have a sensitivity of 100% for the detection of myocarditis in patients that are symptomatic. It is important to note that troponin I/T can be monitored and a high sensitivity troponin value above the 99th percentile upper reference limit at any time is also suggestive of early myocarditis (45), alongside other parameters such as N-terminal pro b-type natriuretic peptide (NT-proBNP) (19).

On EKG, no specific abnormality is pathognomonic for myocarditis, but concerning findings include ST elevation or depression, T wave inversions, arrhythmia, or bundle branch block (46,47). Approximately 25-50% of patients develop sinus tachycardia upon starting clozapine; it is one of the most common reasons for discontinuation (28,48). Although tachycardia with clozapine is typically transient and benign, it should prompt additional assessments (e.g., EKG, cardiovascular exam) to rule out underlying pathology, such as myocarditis (28). Clozapine-induced tachycardia is a result of direct effects on the sympathetic nervous system and clozapine's anticholinergic properties and likely resulting from rapid dose titration (48).

A systematic review identified 58 patients with diagnosed clozapine-induced myocarditis whose echocardiogram findings were published (49). Of these, 57% had at least mild ventricular dysfunction and dilatation, while 10% had “unremarkable” echocardiograms, presenting an argument for further research on diagnostic criteria.

**Treatment of CIM**

If CIM is identified and no other causes are found, clozapine should be stopped immediately, and cardiology should be consulted (47). The individual will require hospital admission and supportive care. If all other causes are ruled out, early clozapine discontinuation should lead to the relevant symptoms and abnormal investigations returning to normal (19,31) and myocardial damage is typically reversible (2). Beyond discontinuation, a cardiology consultant may start steroids or other medications to specifically manage heart failure, such as beta-blockers, angiotensin-converting enzyme inhibitors, and diuretics in addition to supportive care (19,49). Refraining from exercise during this period is critical given the increased risk of arrhythmias and sudden death in the acute phase (50). Other treatments and transfer to a critical care unit may also be warranted (19).

**Clozapine Rechallenge Following CIM**

There is no consensus for how to safely rechallenge patients with clozapine after it has been stopped due to CIM (51). In deciding to rechallenge, the potential psychiatric benefit must outweigh the potential risk involved. To better inform this decision, a 2012 case-control study looked at eight adult patients who underwent a clozapine rechallenge after CIM (52). Of the eight cases, four had successful rechallenges. Of the four unsuccessful rechallenges, only one was diagnosed with myocarditis. The other three failed rechallenges developed non-specific, non-cardiac adverse effects during the first two to seven days after restarting clozapine. Based on these cases, they were not able to make any firm conclusions, but the authors proposed that the severity index of the myocarditis episode and the speed of clozapine upitation during the rechallenge are crucial factors for predicting a successful rechallenge.

With regards to the severity of an index myocarditis episode, levels of CRP and LV function on echocardiogram could be predictive (53). For the four individuals who had successful clozapine rechallenges, their average peak CRP was 120 mg/L during the index myocarditis episode. This contrasts with the four patients who had unsuccessful rechallenges, with an average peak CRP of 211 mg/L during the index myocarditis episode. With regards to echocardiogram, 75% of the successful rechallenge cases had normal LV function during the index myocarditis episode, whereas
100% of the unsuccessful rechallenge cases previously had LV dysfunction. Ronaldson and colleagues analyzed 10 fatal cases in comparison with 66 surviving cases and found no difference regarding age, gender, smoking status, dose at onset or concomitant valproate; however, obesity and duration of clozapine was significantly longer for fatal cases, in addition to elevated CK over 1000 U/L after excluding one outlier (54).

When considering titration speed, 75% of successful rechallenges had relatively slow up-titrations (52). The one patient who was diagnosed with myocarditis after the rechallenge had been given a one-time 400 mg dose of clozapine, without any preceding up-titration. The authors suggested that clozapine rechallenge should not be contraindicated in patients with a history of CIM, but that rechallenge should be done with the patient’s informed consent, careful monitoring, and with slow up-titration in cases of mild-moderate CIM (53).

Shivakumar and colleagues also recommended slow up-titration to minimize the risk of cardiotoxicity, speculating that this approach gives the body more time to become “desensitized” to clozapine’s hypothesized IgE-mediated hypersensitivity reaction (27). While no threshold of increase was provided, the authors recommend that if CRP is elevated, clozapine up-titration should be held, and bloodwork should be repeated twice over two days. If CRP normalizes, the up-titration can re-start, but if CRP remains elevated, other causes for the inflammation should be investigated. If troponin-I is elevated at any time, they recommend discontinuing clozapine and consulting cardiology to help guide next steps.

To evaluate the risk associated with clozapine rechallenge after CIM, a systematic review identified 19 patients who were rechallenged with clozapine (49). The start date of these rechallenges ranged between several weeks to 25 months after discontinuation of clozapine. There were no deaths and 63% of the rechallenges were successful.

There are only two case reports of patients under age 19 who underwent a clozapine rechallenge after CIM (29,31). One of these rechallenges was unsuccessful, where clozapine was stopped in a 15-year-old patient after they developed nausea and vomiting on clozapine 12.5 mg (4 to 5 days after starting), with an elevated troponin-I (29). No other details were provided in the report which limits the ability to interpret the findings. The other rechallenge was successful with slow up-titration, where clozapine was restarted in a 15-year-old patient, initially at 6.25 mg and gradually increased by 6.25 mg every two days (31). The up-titration was accompanied by regular medical monitoring, including clinical (e.g., heart rate, blood pressure, temperature), biochemical (e.g., CBC with differential, troponin-I, CRP, BNP) and EKG assessments. These evaluations were combined with follow-up cardiology appointments.

At six months, a CV-MRI showed unchanged chronic scarring from the previous episode of myocarditis, with no new abnormalities. At twelve months, the patient was tolerating clozapine 325 mg twice daily with no further evidence of myocarditis.

**Case report**

An 18-year-old female with a history of TRS since the age of 15 was admitted to hospital with a relapse of psychotic symptoms. The patient presented in distress, expressing suicidal ideation secondary to command auditory hallucinations. The patient was well-known to the inpatient medical team, and her decline was deemed significant and observable. When considering precipitants for her deterioration, the team found no evidence of substance use or medication non-adherence.

The patient was admitted for a third trial of clozapine on the following medications: pimozide 10 mg total daily dose; quetiapine extended release 900 mg at bedtime; loxapine 40 mg total daily dose, divalproex sodium 1250 mg at bedtime, and metformin 750 mg. The patient has a past medical history of iron deficiency anemia, previously documented CIM (resolved), metabolic syndrome, sinus tachycardia, and mild sleep apnea.

The patient has a complex history, with multiple hospital admissions as well as medication trials with minimal sustained clinical response to antipsychotics apart from clozapine. Previous medication trials consisted of both monotherapy and combination therapy of various antipsychotics including olanzapine, aripiprazole, larusidone, loxapine, quetiapine, asenapine, zuclopenthixol, divalproex sodium, pimozide, and clozapine.

During this admission, a third trial (second rechallenge) of clozapine was assessed and implemented given that the patient responded well previously but had developed suspected CIM. A comprehensive medication review of the previous two trials of clozapine was conducted. The cardiologist at The Clozapine Support and Assistance Network (CSAN) a national centralized monitoring system for clozapine in Canada, was consulted alongside the hospital cardiologist. A review of these two previous clozapine trials is summarized below.

**Clozapine Trial # 1**

Before clozapine was started, the patient’s CRP and troponin-I were within normal limits. Baseline EKG and chest x-ray showed no abnormalities. Clozapine was initiated and titrated by 25-50 mg every one to two days. The patient was asymptomatic during the up-titration and had significant observable improvement in her psychiatric symptoms. CRP and troponin-I were not routinely ordered. On day 18, at a clozapine dose of 300mg daily, the patient reported general fatigue and had a low-grade fever but no other reported
symptoms suggestive of myocarditis. A troponin-I was ordered and found to be significantly elevated at 8.05 µg/L. An EKG was also ordered and was found to show sinus tachycardia and non-specific T-wave flattening. The hospital cardiologists’ impression was that this was probable CIM and recommended discontinuation. An echocardiogram performed 2 days later showed mild hypokinesis and a small pericardial effusion; overall function was normal, and the patient suffered no cardiac structural consequence. The troponin-I and CRP returned to normal within four days after clozapine discontinuation. Refer to Table 1 for details around timeline post up-titration. Troponin-I was used for this case; nevertheless, both high sensitivity Troponin I/T indicates myocardial injury when at least one value is above the 99th percentile of the upper reference limit (55).

**Clozapine Trial # 2 (first rechallenge)**

Six months later the patient was readmitted for ongoing psychotic symptoms and suboptimal response to interventions. The patients’ medications were titrated down: loxapine was decreased to 20 mg once daily (admission dose of 40mg total daily), quetiapine XR was decreased to 800 mg total daily dose (admission dose of 1200 mg total daily dose), metformin continued. At baseline, notable findings included sinus tachycardia on EKG and trivial pericardial effusion on echocardiogram (LV ejection fraction of 79%).

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Dose of clozapine</th>
<th>CRP (mg/L)</th>
<th>Troponin-I (ug/L)*</th>
<th>EKG/ECHO/Chest X-Ray</th>
</tr>
</thead>
</table>
| Day 18      | Clozapine discontinued  
(last administered dose was 300 mg at bedtime) | 11:05 AM → 8.050  
12:35 AM → 6.190 | EKG - QTc 431 msec; normal |
| Day 19      | No clozapine       | 08:25 AM → 1.510 | EKG - QTc 425 msec; normal  
Chest X-ray – normal; lungs clear; no pneumonia |
| Day 20      |                   | 07:58 AM → 0.570  
10:40 AM → 0.420 | ECHO - normal structures; mild hypokinesis but overall normal function; small pericardial fluid; no mitral valve regurgitation. |
| Day 22      |                   | 07:41 AM → 0.119 | EKG - QTc 427 msec; normal sinus rhythm; nonspecific T wave flattening |
| Day 23      |                   | 08:08 AM → 0.103 | EKG - QTc 422 msec; normal sinus rhythm |
| Day 24      |                   | 3.5          | EKG - QTc 448 msec; borderline sinus tachycardia; otherwise normal |
| ~ three months post discontinuation | | | EKG - QTc 435 msec; sinus tachycardia; T wave abnormality; consider inferior ischemia [Abnormal] |
| ~ three months post discontinuation | | | EKG - QTc – 454 msec; sinus tachycardia; T wave abnormality ECHO - limited imaging; function normal; no effusion |

*Local laboratory limits: Troponin I - 0.034 µg/L upper limit; normal <0.012 µg/L  
CRP = C-reactive protein; ECHO = Echocardiogram; EKG = Electrocardiogram
CRP was 6.9 mg/L and normal troponin-I (<0.012 ug/L). This first rechallenge involved a slower up-titration of clozapine by 25 mg per day every two days and a general split dosing of clozapine every 12 hours to minimize side effects. CRP and troponin-I were also monitored every one to two days. Troponin-I levels did not increase. By day six clozapine was 25 mg twice daily and CRP was elevated to 47.7 mg/L. The patient had no clinically significant physical complaints and troponin-I remained normal. Due to the elevated CRP within less than a week of clozapine exposure, the hospital cardiologist was consulted and again recommended discontinuation. Refer to Table 2 for more details around the timeline.

### Clozapine Trial # 3 (second rechallenge)

During the most recent admission triggered once again by severe symptoms of the TRS and associated morbidity and risk, the course of the first and second trials of clozapine were thoroughly reviewed by the team along with the CSAN cardiologist. Since there was no elevation in troponin-I and no symptoms of clinical significance despite the elevated CRP, the team deemed the second trial (first rechallenge) an inadequate rechallenge of clozapine, with premature discontinuation.

In the effort to mitigate risk with the second clozapine rechallenge, all potential risk factors were minimized. The
patient was titrated off all medications, including divalproex sodium, with exception of quetiapine extended release which was reduced to 600 mg daily and metformin which was continued and used to mitigate symptoms of metabolic syndrome. A strict protocol was set forth by the team based on literature review to inform the course of treatment. A cut-off of two times the upper limit of normal was chosen for troponin-I based upon Ronaldson and colleagues’ findings to allow for flexibility in management (26). This protocol is presented in Figure 1.

The hospital Ethics Board was consulted regarding the risk and benefit of a second clozapine rechallenge. The benefits included it being the best chance for symptoms remission, improved quality of life for the patient and a potential decrease in physical risks associated with polypharmacy. The risks included the known potential for CIM and the possibility of treatment resistance to clozapine. The team and substitute decision maker felt that another clozapine challenge would give the patient the best possibility for positive life outcomes.

The third trial (second rechallenge) of clozapine occurred 1.5 years after the second trial. The baseline echocardiogram demonstrated normal LV and right ventricular (RV) function, a left ventricular ejection fraction (LVEF) of 79%, trivial pericardial effusion and mild septal hypokinesis. Baseline CBC, CRP, and troponin-I were within normal

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**Figure 1: Proposed Protocol for Mitigating Clozapine-Induced Myocarditis During a Rechallenge**

<table>
<thead>
<tr>
<th>General considerations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase clozapine by 12.5 mg to 25 mg every five days as tolerated with split dosing twice daily</td>
</tr>
<tr>
<td>CRP and troponin-I twice weekly in initial phase of protocol until lab parameters have been stabilized for a period of time. Daily if CRP or Troponin rise, return to once or twice weekly when values have normalized.</td>
</tr>
<tr>
<td>EKG weekly or q2weeks for one month. ECHO monthly for 1-2 months and consider CMR if there are signs/symptoms of myocarditis</td>
</tr>
<tr>
<td>Monitor vitals daily and increase monitoring of myocarditis if HR ≥ 120 bpm or increased by &gt; 30 bpm from baseline</td>
</tr>
</tbody>
</table>

**Specific parameters:**

| If CRP < 10 AND troponin-I is less than 2 x ULN |
| CONTINUE slow titration of clozapine and monitor vitals daily, and CRP/Troponin weekly |

| If CRP is > 10 and < 100 AND troponin-I is less than 2 x ULN |
| CONTINUE clozapine at the same dose, monitor CRP and troponin-I daily. Increase clozapine cautiously once CRP < 10 |

| If CRP > 100 and < 150 AND troponin-I less than 2 x ULN |
| DECREASE dose of clozapine to previously ordered dose and CONTINUE clozapine monitor CRP and troponin-I daily; repeat ECHO |

| CRP > 150 AND/OR troponin-I greater than 2 x ULN |
| DISCONTINUE clozapine Monitor CRP, troponin-I, EKG and ECHO; consult cardiology |

---

*This protocol was not otherwise validated.

1 Troponin-I was used for this case per local laboratory requirements; however, high sensitivity Troponin I or T can be utilized.

CRP = C-reactive protein; CMR = Cardiovascular Magnetic Resonance; EKG = electrocardiogram; ECHO = echocardiogram; bpm = beats per minute; ULN= upper limit of normal
limits. The titration was slow, with a total weekly dose increase of 25 mg (divided into two 12.5 mg increases on subsequent days). Troponin-I and CRP were checked weekly, unless there was a rise, in which case they were checked every one to two days (with no clozapine dose change) until normalized. An echocardiogram was completed at the one-month mark.

By day 4 of the trial, the CRP peaked at 48.8 mg/L with no associated clinical symptoms; and then subsequently gradually decreased remaining under 10 mg/L from day 21 onwards. An echocardiogram was completed on day 10 (6 days post-CRP spike) which demonstrated a decrease in LVEF to 63% and the trivial pericardial effusion remained the same. On day 14, the LVEF improved to 67% with mild reduced septal motion. On day 18 the echocardiogram showed a spontaneously improved LVEF fraction of 73% and an exceedingly small anterior pericardial effusion. At that time, cardiology verbalized that given the improvements no further echocardiograms were required unless CRP spiked again. At no point during the trial did troponin I increase. The total length of the trial was a little over three months, with the clozapine dose reaching 300 mg daily and a dramatic clinical improvement in both positive and negative symptoms of schizophrenia. Table 3 includes the first 21 days of this trial where most major changes were experienced. One year later the patient continues clozapine with no evidence of cardiac compromise and positive clinical outcomes.

**Discussion**

With regards to the case presented, in the first clozapine trial, the up-titration of clozapine was 25 mg to 50 mg every one to two days, reaching 300 mg daily in 18 days; and the dose was not split twice daily. There was no scheduled

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Dose of clozapine</th>
<th>CRP (mg/L)</th>
<th>Troponin-I (ug/L)*</th>
<th>EKG/ECHO/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>12.5 mg at bedtime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>12.5 mg twice daily</td>
<td>6.3</td>
<td>&lt;0.012</td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td>12.5 mg twice daily</td>
<td>31.5</td>
<td>&lt;0.012</td>
<td></td>
</tr>
<tr>
<td>Day 4</td>
<td>12.5 mg twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 5</td>
<td>12.5 mg twice daily</td>
<td>48.8</td>
<td>&lt;0.012</td>
<td></td>
</tr>
<tr>
<td>Day 6</td>
<td>12.5 mg twice daily</td>
<td></td>
<td></td>
<td>HR 140 bpm</td>
</tr>
<tr>
<td>Day 7</td>
<td>12.5 mg twice daily</td>
<td>31.1</td>
<td>&lt;0.012</td>
<td></td>
</tr>
<tr>
<td>Day 8</td>
<td>12.5 mg twice daily</td>
<td>25.7</td>
<td>&lt; 0.012</td>
<td></td>
</tr>
<tr>
<td>Day 9</td>
<td>12.5 mg in the morning and 25 mg at bedtime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 10</td>
<td>12.5 mg in the morning and 25 mg at bedtime</td>
<td>22.2</td>
<td>&lt; 0.012</td>
<td>ECHO - Left ventricular function at 63%, septal wall hypokinesis HR 140 bpm</td>
</tr>
<tr>
<td>Day 11-13</td>
<td>12.5 mg in the morning and 25 mg at bedtime</td>
<td>Slowly decreased</td>
<td>&lt;0.012</td>
<td></td>
</tr>
<tr>
<td>Day 14</td>
<td>12.5 mg in the morning and 25 mg at bedtime</td>
<td>&lt;10</td>
<td>&lt; 0.012</td>
<td>ECHO - Left ventricular function increased to 69%, mild septal wall hypokinesis HR 140 bpm</td>
</tr>
<tr>
<td>Day 21</td>
<td>25 mg in the morning and 37.5 mg at bedtime</td>
<td>&lt; remained below 10 for the rest of the titration</td>
<td>&lt;0.012</td>
<td>ECHO - Left ventricular function increased to 73%, no septal wall hypokinesis HR - 110-120 bpm</td>
</tr>
</tbody>
</table>

*Local laboratory limits: Troponin I - 0.034 ug/L upper limit; normal <0.012 ug/L.
bpm = beats per minute; CRP = C-reactive protein; ECHO = Echocardiogram; EKG = Electrocardiogram; HR = heart rate
monitoring of CRP and troponin-I throughout the titration process. In retrospect, checking CRP and troponin-I may have better guided decision-making regarding up-titration of clozapine dose thereby reducing the risk of CIM. Specifically, when the initial rise in troponin-I began, holding the dose until troponin-I normalized may have allowed the trial to continue. Furthermore, a slower titration may have been beneficial given the patient’s medical comorbidities. This first trial presents a probable case of CIM. A consideration of the severity of myocarditis was lacking, which could have better informed the rechallenge.

The second trial of clozapine was deemed an inadequate rechallenge upon review of the trial details. The CRP increased to 47.7 mg/L by day 6 at clozapine 25 mg twice daily and the hospital cardiologist recommended discontinuation out of caution given the history of CIM. A barrier to this trial continuing may have been lack of experience with clozapine and clozapine rechallenge amongst hospital cardiology and the psychiatric team. There was a lack of transparent agreement on thresholds for discontinuation prior to initiation of treatment. In hindsight, given the pathophysiology discussed previously, it would be expected to see an elevation in CRP with clozapine re-exposure, as was observed during this second trial. Having predetermined thresholds for how to manage dosing in the face of a rising CRP is valuable to consider.

In the third trial all efforts to mitigate risk of myocarditis were implemented including discontinuation of medications that can elevate risk, such as divalproex sodium (53). The up-titration of clozapine was slow, with a weekly 25 mg increase divided as two separate 12.5 mg increases, frequent monitoring of CRP and troponin-I, and monthly echocardiograms. The trial was considered successful as the patient’s symptoms stabilized at clozapine 300 mg daily.

For this rechallenge it was most helpful to consult a cardiologist with more expertise in clozapine rechallenges, specifically the cardiologist that worked with CSAN. It was also helpful to have pre-determined protocols informed by existing literature for monitoring and titration thresholds for the team to consider. Throughout the trial, there was ongoing discussion and collaboration between psychiatry, pharmacy, cardiology, the patient, and the substitute decision maker to ensure consistency in approach and mitigation of risks.

The protocol set forth in Figure 1 is more rigorous than what has been previously described in the literature; however, this protocol is not validated. A review conducted by Knoph and colleagues suggested monitoring CRP and troponin twice weekly, slower re-titration of clozapine than the generally recommended increment of 25 mg per day and monitoring of echocardiography (35). The protocol we propose in Figure 1 based its thresholds for discontinuation on the Australian monitoring protocol previously described which focuses on monitoring during the first four weeks of treatment including CRP and Troponin I/T and echocardiography (26). In this monitoring protocol, clozapine is discontinued only when CRP is greater than 100 mg/L or when troponin-I or -T is two times the upper limit of the reference range. The protocol we present in this case report suggest monitoring CRP and troponin-I/T more frequently than once weekly, particularly after any dosage changes until the patient is stabilized, which is beyond the three-to-four-week monitoring period described in the literature (41,42,43). For this patient, the up-titration took a little over three months where monitoring of CRP and troponin I/T continued. Investigating both CRP and troponin-I/T together remains critical as it provides for more sensitive detection of myocarditis in symptomatic patients. In an analysis of 10 fatal cases of CIM, a CK greater than 1000 U/L was associated with death (p=0.0004) (55). Given this data, including CK monitoring as part of a monitoring protocol may be of additive value and consideration can be done in consult with cardiology.

Recommendations in the literature have been inconsistent regarding monitoring other indices outside of CRP and Troponin-I/T during clozapine rechallenge, thus routine monitoring of indices such as ESR, BNP or eosinophils (37) are not included in this protocol. Our protocol agrees with the continuation of clozapine in the presence of mild physical illness as described by Ronaldson and colleagues (26). Daily measurement of vitals including temperature, heart rate and blood pressure helps to identify any clinical symptoms of concern (37), and while they are not included in the proposed protocol, they were part of ongoing vital assessment for the patient during the inpatient admission. The protocol highlights measures outside of routine assessment.

While the proposed protocol reflects a successful rechallenge of clozapine following CIM, there are limitations. Identifying pathognomonic symptoms and laboratory investigations needed to confirm cases of CIM is challenging given the paucity of documented case reports and lack of guidance around managing CIM, especially in youth (33). Our protocol is guided by these few reports and specific to the patient in question. At this point given the heterogeneity of presentation of CIM, and without further published experiences, clozapine rechallenge protocols remain case specific. Furthermore, the decision to move forward with a clozapine rechallenge should be weighed against potential risks to the individual patient.
A further limitation of this work included a lack of incorporating patient and family goals in terms of quality of life. Outcome measurements along with self-report would allow for more valid determination of effectiveness of the intervention for the patient and family.

We report this case to raise awareness of CIM, emphasizing that developed protocols to mitigate risks can inform a decision towards clozapine rechallenge. Youth with TRS are vulnerable to poor outcomes without the option of clozapine. Approved protocols can assist in mitigating risks and optimizing options for rechallenge should risk occur. Future research directions should focus on the evaluation of such protocols. Validated protocols will enhance physician comfort in prescribing this potentially lifesaving intervention for young patients.

**Conclusion**
To increase prescriber and team comfort with clozapine-use and rechallenge, protocols are not only useful but essential. Without this guidance, treatment teams might avoid trials or a rechallenge of clozapine. Young patients with TRS may then suffer from psychiatric morbidity and mortality that could have been otherwise successfully treated with clozapine. Previously published literature has outlined how a clozapine rechallenge may be successful post-CIM. This review and case report builds upon the existing literature, providing a protocol developed from a successful experience with the intention of increasing clinician confidence in prescribing clozapine for adolescents with TRS and monitoring/mitigating the risk of CIM.

**Conflict of Interest**
The authors of this manuscript have no conflicts of interest to disclose.

**References**


Community physician perceptions of managing complex child and adolescent psychiatric patients: a self-determination theory perspective

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Abstract

Children and adolescents with complex mental health needs often require a level of care that is unsustainable in tertiary settings. Yet, the psychological impact of this on community physicians, who are tasked with providing quality care to this population, is not well understood. Grounded in Self-Determination Theory (SDT), the present study explores how the challenges of caring for these patients is affecting community physicians' basic psychological needs (autonomy, competence, and relatedness) and intrinsic motivation. Participants from Calgary, Alberta, Canada, were invited to complete an anonymous online survey containing questions about managing complex child and adolescent psychiatric patients. We used SDT's needs-based framework and 22-item Intrinsic Motivation Inventory as a component of our pilot study, to explore and understand their ideas. Community physicians reported moderate-high interest/enjoyment and moderate perceived competence in managing complex child and adolescent patients, but little perceived choice and high tension/pressure in carrying out this task. Physician remarks provided meaningful insights into how these clinical experiences are impacting them, psychologically, and where opportunities may exist for interventions to support them and their patients. Findings from this study suggest that the participating community physicians feel interested and adequately skilled to manage complex child and adolescent psychiatric patients, but that systemic barriers are hindering their basic psychological needs and intrinsic motivation to do so. Potential explanations and implications for these findings are discussed.

Key Words: complex mental health, complex child & adolescent psychiatric patients, physician perceptions, basic psychological needs, intrinsic motivation

Résumé

Les enfants et les adolescents dont les besoins de santé mentale sont complexes nécessitent souvent un niveau de soins insoutenable dans les milieux tertiaires. Et pourtant, l’impact psychologique de ce fait sur les médecins communautaires, qui sont chargés de procurer des soins de qualité à cette population, n’est pas bien compris. Ancrée dans la théorie de l’autodétermination (TAD), la présente étude explore comment les difficultés de soigner ces patients affectent les
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Introduction

Many children and adolescents with complex mental health needs present to primary care (1, 2). However, they often require much more care than what community physicians can manage, owing largely to systemic barriers, such as lack of resources and access to specialists and allied health workers (3, 4). At the same time, psychiatrists working in both inpatient and outpatient specialty settings are faced with pressures to discharge these patients to create capacity for others, who are often waiting months to years to be seen (5). Thus, an inherent tension exists between the needs of patients, community physicians, and specialists working in hospitals and specialty outpatient-based mental health services. Grounded in Self-Determination Theory (6), the present study explores how this tension is impacting the motivation of community physicians. Examining this issue is important because it can shed new light on how community physicians are dealing with the challenges of supporting child and adolescent psychiatric patients, and where opportunities may exist to support them.

Researchers have investigated the pressures that primary care physicians face in managing complex child and adolescent psychiatric patients. Loeb et al. (7) identified that type and severity of mental illness, acuity of presentation, and communication style (e.g., having a personality disorder, a confrontational manner, and/or use of abusive language) were main patient factors, while level of clinical training was a strong determinant of physician comfort in managing these patients. There are also serious concerns raised by physicians, however, about the state of the mental healthcare system and the urgent need for interventions that promote better integration of care and collaboration between primary care providers and mental health specialists (4, 7).

In other words, primary care physician efforts alone are unlikely to meet the needs of these complex patients, and effective systems solutions need to be considered (8, 9, 10). That said, one gap in addressing this conundrum is the lack of application of a sound psychological framework. Such an approach would help us to better understand how community physicians are managing, psychologically, and how best to support them and the quality of their patient care.

A Brief Overview of Self-Determination Theory (SDT)

SDT is a well-supported theory of human motivation, development, and wellness (6). It posits that people universally require satisfaction of three basic psychological needs to function optimally and thrive—autonomy (sense of volition), competence (sense of efficacy), and relatedness (sense of belongingness). Thus, environments which support these needs (e.g., work settings) will promote engagement, performance, and well-being, while environments that hinder these needs will promote disengagement, stress, and maladjustment (6).

Research in healthcare supports these principles. For example, studies have shown that satisfaction of practicing physicians’ basic psychological needs was associated with more autonomous (and less controlled) motivation for work and lifelong learning (11), higher life satisfaction and work engagement, lower work exhaustion, and greater professional well-being (12). Studies have also shown that intrinsically motivating factors (e.g., sense of professional calling, personally rewarding work hours, and meaningful relationships with patients) were strong predictors of physician well-being, whereas extrinsic factors (e.g., salary and work environment), which are more often studied and...
discussed in the literature, tend not to be (13). According to SDT, this is because motivation and goals that are more intrinsic (e.g., personal growth, good health, community service, and relationships) are inherently need satisfying, whereas motivation and goals that are more extrinsic and superficial (e.g., wealth, social status, and fame) will only indirectly satisfy, if not perpetually frustrate, one’s basic psychological needs (14). Importantly, meeting the psychological needs of physicians, in turn, influences the motivation of their patients. Studies show that when primary care physicians provide their patients with more autonomy support (by being warm and non-judgmental, adopting a positive and unconditional regard, taking their perspective, offering meaningful rationales, and providing them with choices), it stimulates their intrinsic motivation and promotes a host of beneficial health and wellness outcomes. Examples include but are not limited to: improved weight loss and maintenance (15), better glycemic control and dietary changes in diabetes (16), higher success rates with smoking cessation and abstinence (17), and better adherence to medication prescriptions (18). While these studies came from adult populations and similar work would need to be conducted with pediatric populations to compare outcomes, results point to the importance of physician motivation in promoting not only their own engagement and well-being but also that of their psychiatric patients.

SDT outlines different dimensions of intrinsic motivation, four of which are most relevant in this study: interest/enjoyment, perceived competence, perceived choice, and pressure/tension (6). Interest/enjoyment (interest and pleasure in performing an activity), perceived competence (sense of being able to learn, master, and apply certain skills) and perceived choice (sense of having decision-making flexibility and opportunities to choose what to do) are positive predictors of intrinsic motivation, and felt pressure/tension (pressure to succeed in an activity) is a negative predictor of intrinsic motivation (6).

**Current Study**

Having a better understanding of the quality of motivation and needs-based experiences of community physicians is key for guiding interventions that support them and their patients. The present study therefore collected preliminary data on this, to explore: 1) the degree that Calgary-based family physicians and pediatricians are intrinsically motivated towards managing these patients in the community, 2) how they feel that current healthcare system barriers are negatively impacting them and their ability to provide quality patient care, and 3) what aspects they think could be improved to facilitate a better patient-doctor relationship. Using SDT as a lens, we hypothesize that aspects of community physicians’ intrinsic motivation towards managing complex child and adolescent psychiatric patients will be hindered (with increased tension/pressure, reduced perceived choice and perceived competence, etc.), due to the aforementioned challenges they face in performing this task. And, these hindrances will ultimately reflect frustrations of basic psychological needs, which will be reflected in the community physicians’ responses to our open-ended questions.

**Method**

**Procedure**

Community family physicians and pediatricians were invited to complete an online survey, containing one scale and three open-ended questions (see Measures). Invitations were sent via two list-serves: one through the Department of Family Medicine, to approx. 1,000 family physicians affiliated with the University of Calgary, and the other through the Department of Pediatrics, to approx. 200 pediatricians with the same affiliation. To maintain confidentiality and minimize response bias, survey responses were anonymous. Participants received a brief email invitation, an consent form containing information about the study, and a link to the online survey tool. All were advised that their participation implied their free and informed consent. This study was approved by the University of Calgary Human Research Ethics Board (REB # 21-1321).

**Participants**

In total, 41 physicians participated in the survey. However, 7 surveys were excluded from analysis due to being < 50% complete, which left 34 full responses: 11 by family doctors (31%) and 23 by pediatricians (69%). All participants practiced in an urban setting, except one family doctor who practiced rurally.

**Measures**

The electronic survey asked about speciality (“family medicine” or “pediatrics”) and primary work setting (“Calgary” or “Rural”). No other demographic information was collected. Participants then completed the Intrinsic Motivation Inventory, which is freely available online, before answering three questions designed by the authors (see below).

**Intrinsic Motivation**

**Intrinsic Motivation Inventory (IMI):** The 22-item IMI measures peoples’ intrinsic motivation towards performing a specific task. It has shown convergent validity in studies on motivation in healthcare (19, 20, 21). It has four
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subcales: interest/enjoyment, perceived competence, perceived choice, and pressure/tension. We adapted the wording of the scale to measure physician motivation towards “caring for complex child and adolescent psychiatric patients and their unique needs in the community”. Participants responded to items on a scale from 1 (not true at all) to 7 (very true), based on their experiences. Examples were: “I found the task very interesting” (interest/enjoyment), “I think I am pretty good at this task” (perceived competence), “I didn’t really have a choice about doing this task” (perceived choice), and “I felt pressured while doing this task” (pressure/tension). We calculated mean scores for each subscale, where higher scores indicate stronger perceptions of that type.

Needs-Based Experiences
To enrich the quantitative data, we developed and included three open-ended questions: 1) In your experience, what are the main issues you see in managing the care of complex child and adolescent psychiatric patients in the community? 2) How do you think these issues or barriers might affect you personally and/or the quality of care you can provide to these patients? 3) What, if anything, do you wish existed that could improve care for complex psychiatric patients in the community, and/or alleviate constraints on the patient-doctor relationship? We designed these items based on our professional experiences in seeing and managing complex child and adolescent psychiatric patients in the community, and our knowledge of SDT and related hypotheses.

Table 1. Descriptive statistics and Pearson correlations based on the Intrinsic Motivation Inventory subscales

<table>
<thead>
<tr>
<th>Variables</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>INT/ENJ</td>
<td>(.92)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-COMP</td>
<td></td>
<td>.35*</td>
<td>(.90)</td>
<td></td>
</tr>
<tr>
<td>P-CHOICE</td>
<td></td>
<td>.60**</td>
<td></td>
<td>(.86)</td>
</tr>
<tr>
<td>TEN/PRE</td>
<td></td>
<td>-.55**</td>
<td>-.18</td>
<td>-.64**</td>
</tr>
</tbody>
</table>

INT/ENJ, interest/enjoyment; P-COMP, perceived competence; P-CHOICE, perceived choice; TEN/PRE, tension/pressure. Cronbach’s alphas along the diagonal. * p < .05 and ** p < .01

Statistical Analyses
The software SPSS version 25.0 (SPSS Inc, Chicago, IL) was used for statistical analyses for the quantitative data. All variables were checked for normal distribution and linearity of relationships. Cronbach’s alpha coefficients were computed for all scales (see Table 1). Descriptive statistics (mean and standard deviation) were computed for each IMI subscale and variable relationships were then assessed with Pearson correlation. Open-ended responses were examined, and quotes that best captured the physicians’ overall sentiments and experiences were selected and presented (see Tables 2, 3, and 4).

Results / Discussion
Sample Characteristics and Variable Relationships
We first assessed the mean scores and Cronbach alpha reliability values for each IMI subscale, which were determined to be satisfactory (see Table 1). Family physicians reported moderate interest/enjoyment ($M = 4.1$, $SD = 1.2$), tension/pressure ($M = 3.9$, $SD = 1.4$), and perceived competence ($M = 4.4$, $SD = .5$), and low perceived choice ($M = 2.6$, $SD = 1.3$). Pediatricians reported low to moderate interest/enjoyment ($M = 3.2$, $SD = 1.3$), moderate tension/pressure ($M = 4.4$, $SD = .6$) and perceived competence ($M = 4.3$, $SD = .9$), and very low perceived choice ($M = 2.2$, $SD = .9$).

As seen in Table 1, there was a positive association between the physicians’ interest/enjoyment, perceived competence, and perceived choice, in managing complex child and adolescent psychiatric patients in the community. Conversely, there was a negative association between their tension/pressure, interest/enjoyment, and perceived choice, in
performing this task. The strength and direction of these relationships are in line with the SDT literature (22, 23). Together, results suggest that with more perceived choice and competence in carrying out this work, community physicians’ intrinsic motivation will increase. Conversely, with greater pressure/tension in performing their job, their sense of agency and interest/enjoyment will decrease. That there was no direct relationship between pressure/tension and perceived competence makes sense, since feeling pressured does not reduce one’s knowledge or skills – only one’s intrinsic motivation and mental energy to use them.

**Physician Responses to Open-Ended Questions**

For question #1 *(In your experience, what are the main issues you see in managing the care of complex child and adolescent psychiatric patients in the community?)*, most physicians focused on the detrimental lack of resources and supports (e.g., access to timely care and allied health services), fragmented care and lack of collaboration between those working in community and hospital (e.g., with lack of continuity and disconnected care), and inevitable pressures it places on them as community physicians (see Table 2). The overarching sentiment was that they felt deeply frustrated, overwhelmed, and unable to perform their jobs effectively (competence), disconnected, unsupported, and alone (relatedness), and essentially helpless, resentful, and burned out in being forced to assume these unsustainable responsibilities (autonomy).

For question #2 *(How do you think these issues or barriers might affect you personally and/or the quality of care you can provide to these patients?)*, almost all the physicians described feeling helpless, alone, and finding the work exhausting and unrewarding, due to lack of supports and system inadequacies (see Table 3). Many also described feeling impaired in their ability to help their patients, who need far more access to timely, comprehensive, outpatient supports than what Alberta Health Services (AHS; provincial health care authority in Alberta) is providing.

Regarding question #3 *(What, if anything, do you wish existed that could improve care for complex psychiatric patients in the community, and/or alleviate constraints on the patient-doctor relationship?)*, responses largely centered around the need for greater access to psychiatric care and outpatient supports (see Table 4). However, most also emphasized the need for better closed-loop communication (e.g., timely, clear, accessible discharge summaries), better collaboration between community physicians, allied...
Table 3. Physician responses to survey Q2 (selected): How do you feel these issues are affecting you and the quality of your patient care?

<table>
<thead>
<tr>
<th>Response</th>
<th>Physician</th>
</tr>
</thead>
<tbody>
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<td>“I am feeling overwhelmed with the volume and intensity of patients and their needs. There is just not enough time in the day to see and help them. I feel alone as a sole practitioner and wish I had more interaction with the therapists that the kids are seeing. Waiting for therapy or help upon discharge can take a long time. There is also always a sense of urgency when the child/teen is discharged, and the parents can be very insistent and desperate when they call for an appointment.”</td>
<td>Pediatrician #3</td>
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<td>“It is impossible to know what happened during an inpatient stay without a discharge summary. It is not abnormal to see a patient after a hospital admission and have no idea which medications they are on, yet we are expected to provide refills. This causes stress for me, and the families, and it results in extra work for office staff. Having to tell parents that supports are not available for 6+ months, or that we can offer only short term supports through AHS (Alberta Health Service; provincial health care authority in Alberta), and they will need to fund the rest, is very hard.”</td>
<td>Family Physician #3</td>
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<td>“I was not trained to do this quantity or depth of psychiatric care and it is one reason that I do not plan on staying in this field long term.”</td>
<td>Family Physician #4</td>
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<td>“I have done some extra training because of the difficulties accessing resources. However, sometimes I am stuck and would like a consult with a psychiatrist. I find that access to mental health often does not follow my requests when I make referrals and I find it infuriating.”</td>
<td>Family Physician #5</td>
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<td>“These patients require a lot of time. You may have to contact social workers, group homes, parents if they are involved, teachers, school counsellors. In addition to psychiatric care, they may need housing, food. A lot to accomplish in a 15 minute GP visit.”</td>
<td>Family Physician #6</td>
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<td>“It’s stressful for me. I fit in a ton of mental health patients into my over-filled schedule. Financially if it’s done over the phone, I don’t feel it is adequate compensation for what I do as I often spend 30 minutes with these patients over the phone. If I had more psychiatric help, it would feel like there was less pressure on me to keep these kids alive!”</td>
<td>Pediatrician #4</td>
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<td>“Leads to significant burnout. Feelings that you cannot control the outcome because this isn’t an area that I was trained in. At times, difficult to be compassionate when a lot of the issues are parent/child relationships and chaotic families.”</td>
<td>Pediatrician #5</td>
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Table 4. Physician responses to survey Q3 (selected): What do you feel could be improved to facilitate better patient care and promote the patient-doctor relationship?

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<th>Response</th>
<th>Physician</th>
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<td>“…a central website with available resources that patients can access, as this would streamline attention to appropriately defined issues for the complex adolescent psychiatric patient and strengthen the doctor patient relationship.”</td>
<td>Family Physician #7</td>
</tr>
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<td>“…improved counselling, psychology follow up, and provision of neuropsychiatric testing are needed, as so many of our patients have neurocognitive deficits and learning disorders which greatly compound their mental health. … In many circumstances, we also see patients at a fiscal loss to our practice. For example, a 45-minute visit with a suicidal teenager, who just showed up at the office, results in the pediatrician spending more money to see the patient than what they bring in through billing.”</td>
<td>Pediatrician #6</td>
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<td>“We already follow many of these children with limited supports. Community practices generally do a lot of mental health care but having limited access to counseling, and other supports for these patients is difficult (very long waitlists, especially for funded options) and access to specialty support is incredibly limited (very long wait lists for Peds Psych support if needed and then usually discharged back to us after one visit). Generally, it is hard because we feel quite unsupported. It’s not that we’re not following these children - we already are. There is just so much need right now that everyone’s resources are strained.”</td>
<td>Pediatrician #7</td>
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<tr>
<td>“Case management. Better communication from psychiatry to community providers. Better documentation from psychiatry to community providers. Psychiatry contacting community providers to discuss a plan and use the expertise of community providers. Longitudinal access to psychiatry. Analysis of what recommendations there are for management of this population and striving to implement this. Less barriers in community pediatricians being able to access care for their patients.”</td>
<td>Pediatrician #4</td>
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<td>“It would be nice to have more “bodies” (more Psychiatrists, Psychologists, Therapists) … but that’s not going to happen anytime soon. I would like more communication, especially with the “therapy” team. I really like the CanReach model. Empowering our Primary Care Physicians to help manage psychiatric patients really helps.”</td>
<td>Family Physician #6</td>
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services, and psychiatrists, and the need for better transition services, to support patients and their families.

**Conclusions, Limitations, and Future Directions**

This pilot study explored the motivation and unique challenges community family physicians and pediatricians face in managing complex psychiatric child and adolescent patients.

Both groups of physicians reported moderate to high interest/enjoyment and perceived competence in managing complex child and adolescent psychiatric patients. In line with hypotheses, however, they also reported little perceived choice and high tension/pressure when performing this task. This suggests that while community physicians may be interested in and capable of managing these patients, the current system is creating stress and hindering their intrinsic motivation to do so. These findings point to the potential benefit of interventions that support the basic psychological needs and intrinsic motivation of community physicians (24). Research shows that professional culture tends to undermine these things by prioritizing extrinsic (e.g., pay for performance) over intrinsic (e.g., competence, values, and interest) motivators (25).

In terms of limitations, this was a pilot study, and the survey response rate was low. There were also more pediatricians than family physicians in the study. Both of these limitations reduce the generalizability of our findings. Additionally, the survey was electronic and based on self-report data, which precludes a specific response rate, and creates potential for response bias. And, there is typically only a moderate correlation between self-report and behavioural measures of intrinsic motivation. Results should thus be interpreted with caution. Nonetheless, preliminary findings shed new light on community physicians’ intrinsic motivation towards managing complex child and adolescent patients. They also raise new and important questions about how this task is hindering community physicians’ basic psychological needs for self-determination and well-being, and where opportunities might exist to support them, in an evidence-informed way.

From a SDT perspective, the physicians’ responses appear to indicate frustration of autonomy (i.e., in perceiving little choice and feeling forced to assume responsibilities beyond their time availability and scope of practice), competence (i.e., in feeling ill-prepared, pressured, and unable to do a good job by their patients), and relatedness (i.e., in feeling disconnected, alone, and resentful about systemic barriers and injustices). Future studies ought to test these hypotheses and explore how basic psychological need frustrations, in trying to manage complex child and adolescent psychiatric patients, relates to community physicians’ job satisfaction and risk for burnout and career change. Studies could also explore whether added training would improve their work-related need satisfaction, since results from this study suggest that a focus on systems (and not individuals) would be more fruitful for community physicians and their well-being.

Importantly, the majority of community physicians discussed the inadequate availability and access to community resources and supports for their patients, the need for better prevention-focused resources, and how the current medical system relies on processes that lend to fragmented care and poor communication between inpatient and outpatient providers. Additionally, many emphasized the lack of structured guidance and support they receive when re-assuming care for their patients following a hospital admission—for example, due to unavailable discharge summaries and care plans. For example, some identified being unaware of which medications had been discontinued and started, yet they would be expected to take over the management. These issues highlight the potential benefit of quality improvement studies and interventions that focus on creating successful transitions from inpatient to outpatient settings, and vice versa, that directly involve the full medical care team, the child/adolescent, and their parents (26, 27, 28).

**Conflict of Interest**

The authors have no financial relationships to disclose.

**Contributions**

Nneka Orakwue-Ononye and Adam Neufeld designed the research project, and she and Abdul Rahman facilitated departmental and ethical approval. Nneka Orakwue-Ononye and Adam Neufeld were each involved in the data collection phase. Adam Neufeld handled the statistical analysis and wrote the first draft of the manuscript. All authors reviewed initial and subsequent versions, including the final submission.

**Ethical Considerations**

All research participants provided informed consent prior to taking part. The authors of the present study have no conflicts of interest or financial interests in the research.
References


APERCEVOIR: THE PEOPLE OF CHILD AND ADOLESCENT PSYCHIATRY

Dr. Raj Rasasingham

Lind Grant-Oyeye

Raj Rasasingham, the Vice President of the Canadian Academy of Child Psychiatry, has held multiple leadership roles within the Academy and the University of Toronto. He chaired the Advocacy Committee and the Global Psychiatry Committee for CACAP, as well as the CACAP Conference Committee. Collaborating with colleagues worldwide, he has contributed to workshops and policy statements on mental health advocacy. Dr. Rasasingham has actively advocated for children’s mental health, driving system change in psychiatry. Additionally, he serves as the National Chair of CPD Directors in Canada, promoting Continuous Professional Development. He has received notable awards, including the Council on Psychiatric Continuing Education Award, Colin Woolf Continuing Education Award, and the Ivan Silver Award for Innovation. He is a co-principal investigator and collaborator on various grants in postgraduate and public education. Recently, he was honored as a Fellow of the American Psychiatric Association.

LIND GRANT-OYEYE (LGO): Thank you for agreeing to this interview with JCACAP.

Raj Rasasingham (RR): I really liked this new initiative. The interview column is a really nice thing to get to know people in a different way, right. It is wonderful.

LGO: Thank you. Could you please tell us about your background?

RR: Sure! You know, I have had an interesting background. I was born in Sri Lanka, and I left when I was about three years old. It was a war-torn country, with lots of challenges, so it shaped my life in so many ways. Then I moved to Africa. I spent about three to four years in Nigeria in the late ‘70s. In Nigeria, I was in Kaduna for some time. I have very fond memories of my time there. After that, I moved to Southern Africa, to Botswana. I spent seven to eight years in Botswana. Again, it was an interesting experience, and I have profound memories from there. Botswana’s people were very welcoming, and many things shaped my subsequent life because of my time there. Botswana is a neighbouring country to South Africa. This was a time when Nelson Mandela was in Robben Island, which was a different time in terms of equity, diversity, and inclusiveness in that region. It shaped a lot of my later work in this area. Then we moved to Canada at age 12. Canada and Toronto had a diverse group of people, and it helped in so many ways. The beauty of Canada is that it’s a melting pot. We have all the communities together. I had a lot of diversity in terms of my friends, that really helped me understand different cultures. It’s all part of the Canadian mix.

LGO: I am familiar with the Nigerian landscape having lived there. Your background is indeed fascinating! Tell me a little more about your transition to Canada?

RR: I moved to Canada in the seventh grade, and it was quite a transition. It really shaped my work with advocacy because I understood inequality as a new immigrant growing up in Toronto at that time. Even though our family was educated, we had to start from the bottom here. But it really shaped my understanding of social determinants of health, looking at housing and other factors. So, the way I look at clinical care and the world of child psychiatry is through this lens, and I continue to do that. I primarily work in a disadvantaged neighborhood. Then I attended the University of Toronto for undergraduate studies, following which I went to medical school and did my clinical training in the US. I committed myself to do a lot of volunteer work, such as helping with tsunami relief and post-9/11 work. I did a fellowship in child psychiatry at Harvard, which changed my career and understanding of many things. I came back to Toronto to work and gradually got more involved in
different activities, including the Canadian Academy of Child and Adolescent Psychiatry. So that’s a little peek into my background.

**LGO:** Thank you. You have unpacked a lot regarding social issues. It is interesting that you address advocacy from a lived experience perspective. Looking back, what were the main challenges integrating following your move to Canada?

**RR:** That’s a great question. As a child psychiatrist, this is a fundamental question, right? I think I had some social advantage. I’ll be honest with you because I could speak English, and I have been speaking English since I was very young. So, in that sense, I could assimilate to some degree. But culturally, there were many things that were different. Culturally, there were many things that were different in several ways. You know, growing up in Africa and South Asia, we were into soccer, cricket, and different types of sports, where you connect. And then when I came to Canada, connecting with young people was different, but I don’t know. For me, at least, I was really involved in sports and activities, so I was able to connect that way and get involved with a lot of people. I went to a school called Vaughan Road Collegiate in Toronto. A very diverse school at that time.

**LGO:** What factors influenced your decision to choose child psychiatry as your field of specialization?

**RR:** One of my turning points was witnessing the impact of 9/11, while being a medical student during a psychiatry rotation in New York. It made me realize the importance of mental health. 9/11 really impacted the people of New York. I wished to help, so I volunteered at Pier 94 during the crisis. That event had a big impact on my life. I realized the importance of psychiatry. Moreover, through residency, I developed a passion for working with young individuals, being fascinated by their potential. Child psychiatry offered a combination of biological and psychotherapeutic approaches. My early training with exceptional mentors in the field further fueled my growth. I haven’t looked back since. It is truly the most wonderful profession, as every day we wake up to help young people improve their mental health and achieve their full potential.

**LGO:** You seem to have acquired significant lived experience. Would you have a favorite life quote?

**RR:** When I was younger, I wrote down quotes; when social media emerged, that became my thing. Looking back, I realize the profound influence figures like Gandhi and Mandela had on me. Gandhi’s famous quote, “You must be the change you wish to see in the world,” still resonates today amidst the current global circumstances.

**LGO:** Can we assume that Nelson Mandela and Mahatma Gandhi were your heroes?

**RR:** Certainly! Gandhi’s was a little before my time, but I’ve always been inspired by how he diplomatically changed the world. Mandela’s influence is immense, and most of us living on the continent have a deep fondness for him. Our work would be significant if we could embody just a fraction of their greatness.

**LGO:** What was your desired career path as a child, if not psychiatry?

**RR:** My family has a lot of accountants. My father and sister are accountants, and my wife is one too. So, it made sense for me to enter the business field. My maternal grandfather was a lawyer and my mother felt I had good communication skills to become one. However, my interests shifted in high school when I developed a strong passion for biology and understanding the workings of the human body and mind. This led me towards a career in medicine.

**LGO:** In terms of advocacy, are you currently undertaking any specific advocacy work?

**RR:** There are concerns regarding the lack of consideration for the best interests of children in the refugee and immigration process. For example, problems can arise for children born in Canada whose foreign-born parents are still navigating the Canadian immigration system. There are some Canadian-born children during the immigration process of their parents. Sometimes these parents are deported. They must decide whether to take their children with them and face uncertainties in the country where they are being deported to, or given the risk, decide to leave the child behind in Canada. The child’s well-being when returning to the parent’s home country or the emotional distress caused by separation is very concerning. Advocacy efforts are being made to raise awareness and support for this issue.

Also, our committee has published position statements on child psychiatry and advocacy, addressing topics such as world events, social determinants of health, marginalized populations, and cultural perspectives in care. Moving forward, we aim to raise awareness and integrate these principles, including culturally sensitive care in child psychiatry, to better support vulnerable children and their families. Integrating those principles into child psychiatry is important and raising awareness about them will be one of my future focuses.

**LGO:** In the context of advocacy and practice, and the current global interest in Artificial intelligence, what is your view on the role of technology, specifically Artificial Intelligence?
RR: The rapid advancement of technology has transformed healthcare, particularly during the pandemic, enabling virtual care and reaching more people. Child psychiatry faces a workforce shortage but integrating technology and innovation into care models can help bridge the gap. Transferring knowledge to allied health and other providers can expand access to care, especially in low-income countries. Addressing these challenges requires robust programming, education, and the potential use of AI and other technologies.

LGO: Do you have any parting thoughts for the JCACAP readership?

RR: As the Vice President of the Academy, I am grateful for the Academy’s wonderful community of clinicians, physicians, and allied health professionals. Together, there is nothing we cannot achieve. It has been a privilege and honor to serve in various capacities, and I hope to continue doing so. Being part of this organization is a true privilege.

LGO: Thank you for your service and all the best in your advocacy journey.

RR: I want to thank you and the Journal for supporting the efforts of the committee in promoting advocacy initiatives for the Academy and the profession. My heartfelt thanks go to the editorial board as well.

LGO: Thank you once again on behalf of JCACAP.
ADVOCACY

A follow-up on the “Best Interests of the Child”

John D. McLennan, MD, MPH, PhD

This journal’s inaugural Advocacy Column, published in the May 2023 issue, raised concerns about the seeming failure of the Canadian government to prioritize the principles of the “Best Interests of the Child” when considering deportation of parents (1). The principles of the “Best Interests of the Child” are detailed in the United Nations’ Convention on the Rights of the Child, of which Canada is a signatory (2). This same Advocacy Column included a CACAP Advocacy statement focused on this very concern as it relates to the deportation of parents of Canadian children (3).

A letter of concern was also then written to the Honorable Marco Mendicino, the then Minister of Public Safety, as this ministry is responsible for the Canada Border Service Agency (CBSA) which manages and enforces deportation. No response was received. The next step involved meetings with two sympathetic Senators from the Canadian Senate to solicit advice on how to advance this concern. Several recommendations were made including writing to the Minister of Families, Children and Social Development. A prompt response was received from this Minister’s office indicating that given the nature of the concern, they were forwarding my letter to the Ministry of Public Safety. A direct response from the office of the Minister of Public Safety to this second communication was not received, however the Vice-President of the Intelligence and Enforcement Branch of the CBSA, on behalf of Minister Mendicino, replied. This letter, received March 23, 2023, included the following: “At all times, the best interests of the child are taken into account when persons are facing removal from Canada, and this means keeping families together. Canada recognizes the importance of promoting and safeguarding the rights of children, both in Canada and abroad, and works closely with other levels of government, law enforcement authorities, and intergovernmental organizations to ensure that decisions on behalf of children are made in consideration of their best interests and in accordance with Canadian laws and regulations.”

Unfortunately, no additional information was included on how exactly the “best interests of the child” are served in cases where a deportation leads to family separation or forces a Canadian child to leave Canada in order to remain with their parent, incurring major life disruptions and other potential risks outside of Canada. This had been the crux of our original expression of concern. However, without additional information on the process as to how the best interests of the child are actually assessed and protected, this attempt at reassurance that children are in such proceedings protected is woefully inadequate. The process ought to be transparent and available for scrutiny by experts in child health and development.

Since that first Advocacy Column, updates have been published in the news about an Edmonton family, mentioned...
in the original advocacy statement, who have continued to face the prospect of family separation, prompting the mother to go into hiding (4), and then, at the 11th hour, obtain a reprieve (5). Similar threats of family separation are also experienced by immigrant and refugee families as exemplified in a report about a family in Trois-Rivières (6) and discussed by Kronick in that last Advocacy Column (7). Even prior to a final deportation decision, families in such situations can face chronic uncertainty from the often prolonged deportation proceedings (8). This chronic stress entails its own risks of adverse impacts, even in cases where a deportation order may eventually be stayed. How many children and families in Canada are facing the consequence of this Canadian policy and practice is not publicly known. We have been told that such statistics are not routinely collected.

There is now a new Minister of Public Safety (the Honorable Dominic LeBlanc), so a third inquiry will be sent to this office in an attempt to move this advocacy concern forward. Efforts to help advance this concern are welcome.

References


