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Care centre accessibility

Cases of adolescent cancer may have improved treatment outcomes when they are referred to paediatric centres, making access to such centres crucial to adolescent cancer survivability *(p.26)*

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Precision treatment

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BDD therapy

Future treatment programs for BDD could target cognitive biases in concert with traditional treatments for more effective results *(p.6)*

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Second Issue of the Fifth Volume December 2020

Courtesy of the Undergraduate Research Opportunities, University of British Columbia, Vancouver

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Letter from the editor-in-chief

The Canadian Journal of Undergraduate Research (CJUR) is pleased to present to you Volume 5 Issue II. Over the years, CJUR's mission has been to provide undergraduate students across Canada with the opportunity to share their research with a public audience and gain experience with academic publishing. Our journal understands the value of engaging in research at the undergraduate level, and we strive to provide an arena for multidisciplinary dialogue and support students in their endeavours of becoming researchers.

As 2020 comes to a close, we reflect on this unique year where we watched history being made in front of our very own eyes. As we transitioned online, we made drastic changes to our everyday lives. CJUR believes showcasing students' work is as important as ever during this time. This year, CJUR has recruited over 100 graduate students, post-doctoral fellows, and professors to continue building a credible reviewer database. We have reached out to student organizations across Canada to collaborate on projects and provide workshops on academic writing and publishing. I commend everyone who has persevered during this time, and applaud the students who have continued their research. We look forward to receiving more submissions and expanding our network in 2021.

This issue includes submissions from the University of British Columbia, University of Victoria, University of Ottawa, and Mount Royal University. Eachmanuscript has undergone two extensive review stages by graduate students and professors specializing in the respective field of research.

CJUR recognizes and supports diverse disciplines, and encourages the communication of complex perspectives and methods in the natural and life sciences, social sciences, arts, and humanities. Each manuscript in this issue reflects the efforts undergraduate students put into research, and I hope you join us in celebrating their work.

Thank you for your continued support and I hope you enjoy Volume 5 Issue II.

Yours sincerely,

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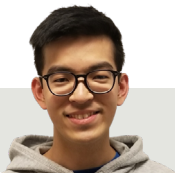

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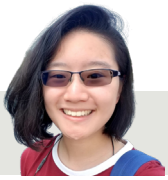

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COVER
Lady Butler, *The remnants of an army, Jellalabad, January 13, 1842* (1879).

Body dysmorphic disorder and face processing

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Abstract Body dysmorphic disorder (BDD) is a mental disorder where an individual becomes so fixated on an exaggerated flaw in their image that it interferes with their daily lives. Current research shows that patients with BDD have deficits in visually processing faces and bodies, such that they rely on local (detail-oriented) processing. By contrast, the typical person processes faces as a whole using global (holistic) processing. This reliance on local processing may be a mechanism through which patients with BDD focus on minute flaws in their appearance, exacerbating their symptomatology. Furthermore, patients with BDD are more likely to incorrectly perceive others' facial expressions as being negative, further contributing to their emotional symptoms. Well-known treatments for BDD, such as cognitive behavioural therapy (CBT) and pharmacotherapy, are effective, but do not target the patient's visual processing deficits. Targeting the visual processing deficits could help alleviate the symptoms of BDD and decrease the chances of relapse. Future research should target BDD's distressing symptoms and visual processing deficits, creating a better treatment program.

Published online
14 September 2020

Citation
Carhoun, J. & Madeleine Topfer (2020), Body dysmorphic disorder and face processing, *CJUR* 5(2), 6-10.

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INTRODUCTION

Body dysmorphic disorder (BDD) is a psychiatric disorder that is defined by such features as an incessant fixation on perceived imperfections in physical appearance and is a relatively common and debilitating disorder (Fang & Wilhelm, 2015). BDD's symptoms in the DSM-5 are described as comprising a distress or impairment in social, occupational, or academic areas of functioning among others, due to intrusive thoughts regarding an imagined flaw in their appearance (American Psychiatric Association, 2013; Phillips et al., 2014). Furthermore, BDD is classified as an obsessive-compulsive and related disorder and diagnosis requires the presence of repetitive behaviours or mental acts (Schieber et al., 2015). A population-based survey performed in the USA found that the prevalence of BDD was 2.4% among adults aged 18 or older (Koran et al., 2008). In addition, BDD is associated with an increased risk of suicidal ideation and attempted suicide (Rief et al., 2006).

Patients diagnosed with BDD are described as having a fear of negative peer-evaluation, which may influence their body image concerns and how they view their social desirability (Buhlmann et al., 2006). Individuals with BDD have delusional or greatly exaggerated thoughts about their body image, which differentiates them from those with image concerns about actual deformities; in a person with BDD, there is no such flaw in their appearance, or the flaw is smaller in proportion to the person's perceptions of it (Phillips et al., 2010). These delusions could be a result of differences in their perceptual mechanisms (Fang & Wilhelm, 2015). For example, studies have hypothesized that participants with BDD, when compared with controls, will stare longer at their faces in a mirror due to a delusion that flaws in their physical appearance are greater than in reality (Veale & Riley, 2001; Möllmann et al., 2020). The consensus in current research is that BDD comprises deficits in visual processing mechanisms, which is observed in their misperceptions about flawed details in their appearances (Stangier et al., 2008; Feusner et al., 2010b; Jefferies et al., 2012; Toh et al., 2017a).

The findings discussed in this review highlight the importance of researching BDD patients' visual processing abnormalities as a target for treatment. The majority of BDD treatments do not attempt to ameliorate these deficits and tend to focus instead on the distressing symptoms (Phillips, 2014). Current treatments for BDD are founded in cognitive behavioural therapy (CBT) programs, such as psychoeducation, motivational and cognitive interventions, prevention of rituals, and perceptual retraining (Fang & Wilhelm, 2015). Although these forms of treatment can be effective, BDD has high rates of comorbidity with disorders such as, major depressive disorder and obsessive compulsive disorder that could affect the treatment response (Grant & Phillips, 2005). Further research is needed to improve treatments that could help prevent or ameliorate the chronicity, morbidity, and mortality associated with BDD (Phillips, 2014).

With future research on BDD, we can more effectively treat, diagnose, and understand the disorder. In this review, we focus on the face processing deficits in BDD revealed by face perception and emotion recognition studies. At the end of the review, we discuss the implications of the literature on face processing for developing innovative intervention programs to treat BDD.

REVIEW

BDD and face perception

Clinical studies have shown that individuals with BDD explicitly attend to a specific feature of their appearance and disregard the rest (Fang & Wilhelm, 2015). This pre-occupation may relate to

altered perceptual processing of faces: most individuals process a face by perceiving it as a whole image, a process called holistic processing (Richler et al., 2009). By contrast, individuals who use local processing perceive a face in terms of its individual features (e.g. nose, mouth, eyes) (Richler et al., 2009). One method of disrupting holistic processing is to turn the image of a face upside-down - although all objects are more difficult to recognize when they are turned upside-down, inversion disproportionately impairs the recognition of faces, a phenomenon known as the face inversion effect (Yin, 1969). Studies have shown that inverting a face forces participants to process the face in terms of its individual parts than as a whole (Rossion, 2008).

Using inversion tasks to compare global and local processing mechanisms, researchers have found that individuals with BDD tend to process faces and objects at a detailed level rather than using holistic processing (Beilharz et al., 2016; Beilharz et al., 2017; Beilharz, 2019; Feusner et al., 2010b). Feusner et al. (2010b) applied the inversion manipulation to observe processing differences between participants with BDD and healthy controls. Their paradigm used a recognition task with upright and inverted faces that were presented for short (500ms) and long (5000ms) durations (Feusner et al., 2010b). The results showed that participants with BDD demonstrated less of an inversion effect compared to controls, which was consistent with their tendency to process faces locally (Feusner et al., 2010b). Although this difference between participants with BDD and controls was found for longer presentation times, none was observed for short durations, which suggests that BDD participants may be processing fast presentations globally/holistically (Feusner et al., 2010b). This could explain why individuals with BDD have distorted perceptions of their faces; specifically, abnormal visual processing contributes to thoughts of perceived flaws in their appearance (Feusner et al., 2010b). Furthermore, longer durations may allow enough time for participants with BDD to process the details of the face, whereas in shorter durations holistic processing capabilities seem to be intact (Monzani et al., 2013). It may therefore be useful to further study how different durations alter the processing of faces and other visual stimuli by individuals with BDD.

Rather than using holistic processing, individuals with BDD exhibit a heightened perception of minute changes in faces (Stangier et al., 2008). In Stangier et al.'s (2008) study, participants with BDD were presented with original faces, followed by an altered version. Alterations included pimples, scars, varying distances between features, different nose sizes, and hair loss. The controls and the BDD group were then asked to rate the degree of change from 0 to 5 (0 indicating no alteration and 5 extremely altered (Stangier et al., 2008). Stangier et al. (2008) found that the BDD group was significantly more accurate than controls in identifying the alterations, which suggests that individuals with BDD are more sensitive to small changes in the face when compared to standard beauty expectations. This study highlights that over-reliance on local processing may affect the symptomatology of BDD such that normal features or small flaws may be misinterpreted as being large defects, resulting in delusions of facial unattractiveness (Stangier et al., 2008). Furthermore, engaging patients with BDD into relying on global processing mechanisms in novel treatment programs may lessen unrealistic perceptions of their appearances (Beilharz et al., 2016).

Monzani et al. (2013) observed global mechanisms in participants with BDD to determine if a failure of holistic processing contributes to the reliance on feature-based processing found in BDD. The researchers used the face inversion task with four conditions (upright faces, upright houses, inverted faces, and inverted houses), presenting each image for 250 ms (Monzani et al., 2013). The participants responded whether the two images were the same or different (Monzani et al., 2013). Accuracy rates and reaction times were recorded; no significant difference between the control and BDD groups were found (Monzani et al., 2013). They concluded that their contrasting results may be due to the short duration of presentation, indicating that holistic processing mechanisms were still intact (Monzani et al., 2013). Monzani et al. (2013) suggest that studies that have found less of an inversion effect in participants with BDD under longer durations could attribute their results to the participants' having had enough time to involve more local processing. Another reason for the conflicting results could be the stimuli used in the experiments: patients with BDD have been reported to compare their facial features with those of famous individuals (Monzani et al., 2013). A study using the famous faces task found that participants with BDD recognized inverted famous faces more accurately than did controls, which was attributed to their reliance on local processing (Jefferies et al., 2012). Due to the variety of results from studies on BDD, observing the differences between processing of famous faces and of anonymous faces is necessary for future investigations, as individuals with BDD frequently compare themselves to famous individuals and may thus be extremely familiar with those used in studies (Monzani et al., 2013).

BDD patients' attention to local rather than global features in viewing faces and other objects is hypothesized to correspond with abnormalities found in neurological studies (Fang & Wilhelm, 2015; Feusner et al., 2007; Feusner et al., 2011). Brain imaging studies indicate a left-hemispheric local bias in individuals with BDD, which is consistent with the behavioural results, demonstrating that BDD's processing abnormalities are not only attributable to the behavioural symptoms associated with BDD – the left hemisphere has been characterized as being more analytical, and the right hemisphere more global (Buchanan et al., 2014; Grace et al., 2017a; Grace et al., 2017b; Fang & Wilhelm, 2015; Feusner et al., 2007; Moody et al., 2015, Bradshaw et al., 1976).

Collectively, these behavioural and neuroimaging findings suggest that the clinical characteristics associated with BDD might be related to a local processing strategy (Buchanan et al., 2014; Grace et al., 2017a; Grace et al., 2017b; Fang & Wilhelm, 2015; Feusner et al., 2007; Moody et al., 2015). If individuals with BDD attend to the details of a face, they might be more prone to fixate on its small imperfections than individuals without BDD who look at a face more holistically (Stangier et al., 2008). Overall, BDD's processing deficits may contribute to their negative symptoms (Feusner et al., 2007; Feusner et al., 2011). Future treatments should target this global perceptual difference to successfully treat BDD (Beilharz, 2019).

BDD and emotion recognition

Current research suggests that people with BDD also have an abnormal mechanism for processing emotional expressions (Grace et al., 2019). Processing emotional expressions is critical for everyday social interactions, and deficits in this area are associated

with significant social impairment (Behere et al., 2008). A study using identity-matching tasks with emotional expressions found that participants with BDD returned slower mean reaction times than controls and that they made more errors matching faces with emotional expressions but not for matching neutral faces (Feusner et al., 2010a). Feusner et al. (2010a) concluded that deficits in emotion recognition are rooted in BDD patients' abnormal visual processing mechanisms.

BDD patients seem to be biased towards interpreting expressions as being negative compared to controls (Buhlmann et al., 2004; Buhlmann et al., 2006; Grace et al., 2019; Johnson et al., 2018). A study on emotion recognition in BDD by Buhlmann et al., (2006) gave participants a photograph and described for them a situation about themselves ("self-referent") or another person ("other-referent"); for example, a self-referent scenario was presented as: "Imagine that the bank teller is looking at you. What is his facial expression?"; an example of other-referent scenario provided was: "Imagine that the bank teller is looking at a friend of yours. What is their facial expression?". Buhlmann et al. (2006) found that participants with BDD identified contemptuous and angry expressions in the self-referent scenarios more often than controls, but not for other-referent scenarios. Buhlmann et al. (2006) concluded that BDD patients generally have poor insight on their own facial features, which also leads to a bias towards interpreting other people's emotional expressions as being negative towards themselves even when this is not the case. Further, their impression of negativity reinforces their own concerns about their appearances, as well as disrupting their view of their personal social desirability, perhaps interpreting negative facial expressions as social rejection (Buhlmann et al., 2006).

Another study researched how participants with BDD processed their own faces using eye-tracking technology (Toh et al., 2017b). Toh et al. (2017b) used black-and-white photographs of six models who displayed six universal facial expressions (anger, disgust, fear, happiness, sadness, and surprise), one neutral facial expression as a control condition, and a photograph of the participant's own face displaying a neutral expression. Each photograph was shown for 8 seconds and was then followed by a 2-second interval for the participant to respond (Toh et al., 2017b). Toh et al. (2017b) found that participants with BDD had fewer fixations and a diminished visual attention to the noticeable features of their face compared to controls. Interestingly, the attention of participants with BDD lingered on other people's faces for longer durations than they did on their own faces (Toh et al., 2017b). Toh et al. (2017b) also found that participants with BDD showed a recognition bias towards angry faces, indicating a susceptibility to misidentifying facial expressions. The results of this study show that BDD patients have limited abilities in scanning their own faces and suffer facial expression recognition deficits (Toh et al., 2017b). Toh et al. (2017b) interpreted their findings as an indication that patients with BDD may be reluctant to analyse their own facial features and suggested that treatment strategies can aid emotion recognition by altering the eye-tracking mechanisms of patients with BDD. Deficits in emotion recognition may be due to negative self-evaluation of their appearances, leading to delusional thoughts of rejection or negative judgement from others (Bjornsson et al., 2010; Buhlmann et al., 2004; Buhlmann et al., 2006; Fang & Wilhelm, 2015; Feusner et al., 2010a; Grace et al., 2019; Stangier et al., 2008). Future interventions for BDD should target negative self-evaluations by focusing on deficits in processing and interpreting emotions (Grace et al., 2019).

Developing perceptual treatments for BDD

The most frequently applied and effective treatment for BDD includes a combination of CBT and pharmacotherapy, like selective serotonin reuptake inhibitors (SSRIs) (Dong et al., 2019). CBT reinforces positive behaviours and emotional patterns of thinking that help the individual cope with personal challenges (Dong et al., 2019; Fang & Wilhelm, 2015). SSRIs are used to improve symptoms of obsessive thinking and compulsive behaviours in BDD (Phillips & Hollander, 2008). In addition, there are non-psychiatric treatments such as cosmetic surgery (Veale, 2000). However, these have not shown significant improvement on BDD symptoms, and have worsened personal concerns and symptomatology in individuals with BDD (Beilharz, 2019; Veale, 2000; Bowyer et al., 2016). Overall, numerous meta-analyses have suggested further research into the long-term efficacy of treating BDD with CBT, pharmacotherapy, and non-psychiatric treatments to target the high rates of relapse associated with BDD (Harrison et al., 2016; Prazeres et al., 2013; Phillipou et al., 2016; Beilharz, 2019). Although current treatments have beneficial aspects for BDD patients, they do not target the visual processing deficits that could be causing the symptoms (Beilharz et al., 2017). Targeting the visual processing deficits of BDD could help prevent relapse while also remediating the distressing symptoms in the long-term (Beilharz et al., 2017).

Treatments concerning eye movements combined with cognitive behavioural programs show promise as an effective treatment for BDD (Toh et al., 2017b). Understanding an individual's eye movements could identify differences in visual processing from controls, which could help create a new treatment program targeting inaccuracies in facial processing and emotion recognition (Toh et al., 2017b). More specifically, introducing new eye movement mechanisms to target overreliance on local processing and train individuals with BDD to rely on holistic processing could be an effective treatment (Toh et al., 2017b). An eye tracking training program could incorporate a top-down strategy emphasizing the global qualities of a face, as well as a bottom-up approach that focuses on the processing of finer details (Beilharz at al., 2017).

Alternative treatment strategies could also involve aspects of mirror-checking behaviour in people with BDD, such as mirror exposure therapy (MET) (Griffen et al., 2018; Möllman et al., 2020). MET is a methodical and repetitive treatment strategy that helps individuals view themselves in a mirror (Griffen et al., 2018). Therapists direct the patient's gaze and modify the amount of time they spend looking into a mirror to create a healthier self-image (Griffen et al., 2018). Some individuals with BDD tend to concentrate on precise areas of their face and body when viewing themselves in the mirror, magnifying the concerns about their appearance (Beilharz, 2019; Silver & Farrants, 2016; Veale & Riley, 2001). By contrast, some individuals with BDD avoid the features that preoccupy them when viewing themselves in a mirror but continue to obsessively look at themselves (Griffen et al., 2018). Other individuals may find their reflections aversive and avoid mirrors in general (Beilharz, 2019). MET has been used as an effective treatment strategy for individuals with eating disorders or immense disapproval of their own body or face (Griffen et al., 2018). MET can be combined with CBT to alter the perceptual abilities of individuals with BDD, retraining them using photographs of themselves or extending mirror exposure times (Möllmann et al., 2020). The potential benefits of MET

are evident, however, further research on how it can be applied in combination with CBT and pharmacotherapy needs to be explored (Griffen et al., 2018; Möllmann et al, 2020).

CONCLUSIONS

The research discussed in this paper demonstrate the differences in visual processing strategies between participants with BDD and controls. Patients with BDD have deficits in processing faces holistically and focus on the details of their faces (Stangier et al., 2008; Toh et al., 2017a). Emotion recognition studies have shown that patients with BDD have deficits in recognizing emotions that may be a result of negative self-evaluations of their appearances, leading to manifestations of the disorder (Buhlmann et al., 2006; Fang & Wilhelm, 2015). Additionally, neurological studies have shown differences in the processing and structure of the left cerebral hemisphere of participants with BDD compared to controls (Grace et al., 2017a; Buchanan et al., 2014). Understanding the perceptual aspects of BDD and its symptoms can help ameliorate an individual's symptomatology and body image concerns. In turn, this could help decrease suicidal ideation and the prevalence of BDD in general (Rief et al., 2006). The studies involving face perception and emotion recognition deficits provide evidence for the delusional perceptions found in patients with BDD. Future research should consider each one of these differences to find a more effective perceptual treatment strategy, such as targeting BDD's bias towards local processing (Beilharz et al., 2016) and treating BDD's irregular processing of negative emotions (Grace et al., 2019).

The authors would like to thank* Dr Jim Tanaka *"for all his help with the writing process for this paper, from the many Zoom meetings and discussions, to the encouragements to finishing this paper".

REFERENCES

[1] American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: Author.

[2] Behere, R, Raghunandan, V., Venkatasubramanian, G., Subbakrishna, D., Jayakumar, P., Gangadhar, B. (2008). Trends-a tool for recognition of emotions in neuropsychiatric disorders. *Indian Journal of Psychological Medicine 30*(1), 32-38.

[3] Beilharz, F. (2019). *Visual Processing in Body Dysmorphic Disorder: Investigating Eye Movements and Piloting a Novel Training Program* [Doctoral dissertation submitted for publication]. Department of Psychology, Swinburne University of Technology.

[4] Beilharz, F., Atkins, K., Duncum, A., & Mundy, M. E. (2016). Altering visual perception abnormalities: A marker for body image concern. *PLoS One 11*(3) doi: 10.1371/journal.pone.0151933

[5] Beilharz, F., Castle, D.J., Grace, S., & Rossell, S.L. (2017). A systematic review of visual processing and associated treatments in body dysmorphic disorder. *Acta Psychiatrica Scandinavica 136*(1), 16-36. doi: 10.1111/acps.12705

[6] Bjornsson, A. S., Didie, E. R., & Phillips, K. A. (2010). Body dysmorphic disorder. *Dialogues in Clinical Neuroscience 12*(2), 221.

[7] Bowyer, L., Krebs, G., Mataix-Cols, D., Veale, D., & Monzani, B. (2016). A critical review of cosmetic treatment outcomes in body dysmorphic disorder. *Body Image 19*, 1-8.

[8] Bradshaw, J. L., Gates, A., & Patterson, K. (1976). Hemispheric differences in processing visual patterns. *The Quarterly Journal of Experimental Psychology 28*(4), 667-681. doi: 10.1080/14640747608400593

[9] Buchanan, B., Rossell, S., Maller, J. J., Toh, W. L., Brennan, S., & Castle, D. (2014). Regional brain volumes in body dysmorphic disorder compared to controls. *Australian & New Zealand Journal of Psychiatry 48*(7), 654-662. doi: 10.1177/0004867413520253

[10] Buhlmann, U., Etcoff, N. L., & Wilhelm, S. (2006). Emotion recognition bias for contempt and anger in body dysmorphic disorder. *Journal of Psychiatric Research 40*(2), 105-111. doi: 10.1016/j.jpsychires.2005.03.006

[11] Buhlmann, U., McNally, R. J., Etcoff, N. L., Tuschen-Caffier, B., & Wilhelm, S. (2004). Emotion recognition deficits in body dysmorphic disorder. *Journal of Psychiatric Research 38*(2), 201-206. doi: 10.1016/S0022-3956(03)00107-9

[12] Dong, N., Nezgovorova, V., Hong, K., & Hollander, E. (2019). Pharmacotherapy in body dysmorphic disorder: Relapse prevention and novel treatments. *Expert Opinion on Pharmacotherapy 20*(10), 1211-1219.

[13] Fang, A., & Wilhelm, S. (2015). Clinical features, cognitive biases, and treatment of body dysmorphic disorder. *Annual Review of Clinical Psychology 11*(1), 187-212. doi: 10.1146/annurev-clinpsy-032814-112849

[14] Feusner, J. D., Bystritsky, A., Hellemann, G., & Bookheimer, S. (2010a). Impaired identity recognition of faces with emotional expressions in body dysmorphic disorder. *Psychiatry Research 179*(3), 318-323. doi: 10.1016/j.psychres.2009.01.016

[15] Feusner, J. D., Hembacher, E., Moller, H., & Moody, T. D. (2011). Abnormalities of object visual processing in body dysmorphic disorder. *Psychological Medicine 41*(11), 2385-2397. doi: 10.1017/S0033291711000572

[16] Feusner, J. D., Moller, H., Altstein, L., Sugar, C., Bookheimer, S., Yoon, J., & Hembacher, E. (2010b). Inverted face processing in body dysmorphic disorder. *Journal of Psychiatric Research 44*(15), 1088-1094. doi: 10.1016/j.jpsychires.2010.03.015

[17] Feusner, J. D., Townsend, J., Bystritsky, A., & Bookheimer, S. (2007). Visual information processing of faces in body dysmorphic disorder. *Archives of General Psychiatry 64*(12), 1417-1425. doi: 10.1001/archpsyc.64.12.1417

[18] Frey, R. J., & Harmon, A. (2016). Body Dysmorphic Disorder. In D. S. Blanchfield (Ed.), *The Gale Encyclopedia of Children's Health: Infancy through Adolescence* (3rd ed., Vol. 1, pp. 385-389). Farmington Hills, MI: Gale. Retrieved from http://link.galegroup.com.ezproxy.library.uvic.ca/apps/doc/CX3630900119/GVRL?u=uvictoria&sid=GVRL&xid=0160d74a

[19] Grace, S. A., Buchanan, B., Maller, J. J., Toh, W. L., Castle, D. J., & Rossell, S. L. (2017a). Reduced cortical thickness in body dysmorphic disorder. *Psychiatry Research: Neuroimaging 259*, 25-28. doi: 10.1016/j.pscychresns.2016.11.004

[20] Grace, S. A., Labuschagne, I., Kaplan, R. A., & Rossell, S. L. (2017b). The neurobiology of body dysmorphic disorder: A systematic review and theoretical model. *Neuroscience and Biobehavioral Reviews 83*, 83-96. doi: 10.1016/j.neubiorev.2017.10.003

[21] Grace, S. A., Toh, W. L., Buchanan, B., Castle, D. J., & Rossell, S. L. (2019). Impaired Recognition of Negative Facial Emotions in Body Dysmorphic Disorder. *Journal of the International Neuropsychological Society 25*(8), 884-889.

[22] Grant, J., & Phillips, K. (2005) Recognizing and treating body dysmorphic disorder. *Annals of Clinical Psychiatry 17*(4), 205-210. doi: 10.3109/10401230500295313

[23] Griffen, T., Naumann, E., & Hildebrandt, T. (2018). Mirror exposure therapy for body image disturbances and eating disorders: a review. *Clinical Psychology Review 65*, 163-174. https://doi.org/10.1016/j.cpr.2018.08.006

[24] Harrison, A., de la Cruz, L. F., Enander, J., Radua, J., & Mataix-Cols, D. (2016). Cognitive-behavioral therapy for body dysmorphic disorder: A systematic review and meta-analysis of randomized controlled trials. *Clinical Psychology Review 48*, 43-51.

[25] Jefferies, K., Laws, K. R., & Fineberg, N. A. (2012). Superior face recognition in body dysmorphic disorder. *Journal of Obsessive-Compulsive and Related Disorders 1*(3), 175-179. doi: 10.1016/j.jocrd.2012.03.002

[26] Johnson, S., Williamson, P., & Wade, T. D. (2018). A systematic review and meta-analysis of cognitive processing deficits associated with body dysmorphic disorder. *Behaviour research and therapy 107*, 83-94.

[27] Koran, L., Abujaoude, E., Large, M., & Serpe, R. (2008). The Prevalence of Body Dysmorphic Disorder in the United States Adult Population. *CNS Spectrums 13*(4), 316-322. doi: 10.1017/S1092852900016436

[28] Möllmann, A., Hunger, A., Schulz, C., Wilhelm, S., & Buhlmann, U. (2020). Gazing rituals in body dysmorphic disorder. *Journal of Behavior Therapy and Experimental Psychiatry 68*, 101522.

[29] Monzani, B., Krebs, G., Anson, M., Veale, D., & Mataix-Cols, D. (2013). Holistic versus detailed visual processing in body dysmorphic disorder: Testing the inversion, composite and global precedence effects. *Psychiatry Research 210*(3), 994-999. doi: 10.1016/j.psychres.2013.08.009

[30] Moody, T. D., Sasaki, M. A., Bohon, C., Strober, M. A., Bookheimer, S. Y., Sheen, C. L., & Feusner, J. D. (2015). Functional connectivity for face processing in individuals with body dysmorphic disorder and anorexia nervosa. *Psychological Medicine 45*(16), 3491-3503. doi: 10.1017/S0033291715001397

[31] Phillips, K. A. (2014). Body dysmorphic disorder: common, severe, and in need of treatment research. *Psychotherapy and Psychosomatics 83*, 325-329. https://doi.org/10.1159/000366035

[32] Phillips, K. A., & Hollander, E. (2008). Treating body dysmorphic disorder with medication: evidence, misconceptions, and a suggested approach. *Body image 5*(1), 13-27.

[33] Phillips, K.A, Hart, A., Simpson, H., & Stein, D. (2014). Delusional versus nondelusional body dysmorphic disorder: Recommendations for DSM-5. *CNS Spectrums 19*(1), 10-20. doi: 10.1017/S1092852913000266

[34] Phillips, K. A., Wilhelm, S., Koran, L. M., Didie, E. R., Fallon, B. A., Feusner, J., & Stein, D. J. (2010). Body dysmorphic disorder: Some key issues for DSM-V. *Depression and anxiety 27*(6), 573-591.

[35] Phillipou, A., Rossell, S. L., Wilding, H. E., & Castle, D. J. (2016). Randomised controlled trials of psychological & pharmacological treatments for body

dysmorphic disorder: A systematic review. *Psychiatry research 245*, 179-185.
[36] Prazeres, A. M., Nascimento, A. L., & Fontenelle, L. F. (2013). Cognitive-behavioral therapy for body dysmorphic disorder: a review of its efficacy. *Neuropsychiatric disease and treatment 9*, 307.
[37] Rief, W., Buhlmann, U., Wilhelm, S., Borkenhagen, A., & Brähler, E. (2006). The prevalence of body dysmorphic disorder: A population-based survey. *Psychological Medicine 36*(6), 877-885. doi: 10.1017/S0033291706007264
[38] Richler, J., Mack, M., Gauther, I., & Palmeri, T.(2009). Holistic processing of faces happens at a glance. *Vision Research 49*, 2856-2861. https://doi.org/10.1016/j.visres.2009.08.025
[39] Rossion, B. (2008). Picture-plane inversion leads to qualitative changes of face perception. *Acta Psychol (Amst) 128*(2), 274–289.
[40] Silver, J., & Farrants, J. (2016). 'I Once Stared at Myself in the Mirror for Eleven Hours.' Exploring mirror gazing in participants with body dysmorphic disorder. *Journal of Health Psychology 21*(11), 2647-2657.
[41] Schieber, K., Kollei, I., de Zwaan M., & Martin, A. (2015). Classification of body dismorphic disorder-what is the advantage of the new DSM-5 criteria? *Journal of Psychosomatic Research 78*(3), 223-227. https://doi.org/10.1016/j.jpsychores.2015.01.002
[42] Stangier, U., Adam-Schwebe, S., Müller, T., & Wolter, M. (2008). Discrimination of facial appearance stimuli in body dysmorphic disorder. *Journal of Abnormal Psychology 117*(2), 435-443. doi: 10.1037/0021-843X.117.2.435
[43] Toh, W.L., Castle, D.J., & Rossell, S.L. (2017a). Face and object perception in body dysmorphic disorder versus obsessive-compulsive disorder: the mooney faces task. *Journal of the International Neuropsychological Society 23*(6), 471-480. doi: 10.1017/S1355617717000327
[44] Toh, W. L., Castle, D. J., & Rossell, S. L. (2017b). How individuals with body dysmorphic disorder (BDD) process their own face: A quantitative and qualitative investigation based on an eye-tracking paradigm. *Cognitive Neuropsychiatry 22*(3), 213-232. doi: 10.1080/13546805.2017.1300090
[45] Veale, D. (2000). Outcome of cosmetic surgery and 'DIY' surgery in patients with body dysmorphic disorder. *Psychiatric Bulletin 24*(6), 218-221.
[46] Veale, D., & Riley, S. (2001). Mirror, mirror on the wall, who is the ugliest of them all? The psychopathology of mirror gazing in body dysmorphic disorder. *Behaviour research and therapy 39*(12), 1381-1393.
[47] Yin, R. K. (1969). Looking at upside-down faces. *Journal of Experimental Psychology 81*(1), 141–145).

Variation in the efficacy of remote cameras used to monitor wildlife

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Abstract Wildlife cameras allow conservation scientists to monitor wildlife. However, there are performance limitations associated with wildlife cameras that must be understood prior to their use. This study compared two wildlife camera models, the Spypoint Solar Trail and the Reconyx Hyperfire 2, on behalf of Calgary Captured, a collaborative project between the Miistakis Institute and the City of Calgary to determine wildlife occupancy in Calgary's Natural Area Parks. The camera models were set up in pairs at 10 sites. There was no significant difference in detections of white-tailed deer (*Odocoileus virginianus*) or coyotes (*Canis latrans*) by either model, but the Reconyx cameras successfully captured two species that the Spypoint model failed to detect: bobcat (*Lynx rufus*) and deer mouse (*Peromyscus maniculatus*). The Reconyx cameras had fewer trap days because the Nickel Metal Hydride (NiMH) batteries supplied by Calgary Captured consistently failed in cold weather, whereas the Spypoint cameras' solar panels continued to function through the duration of the study. Despite having had fewer trap days, the Reconyx cameras captured more species than did the Spypoint cameras. There was no significant difference in the number of false positives and false negatives produced by the two models, but only the Spypoint cameras produced malfunctioned images. For projects like Calgary Captured, the Reconyx Hyperfire 2 is a more effective camera model than the Spypoint Solar Trail because it captures more species and is less prone to malfunction. The results of this study also highlight the importance of choosing appropriate batteries and settings for the camera model in question to ensure successful use.

Published online
17 November 2020

Citation
Pizante, R. (2020), Variation in the efficacy of remote cameras used to monitor wildlife, *CJUR 5*(2), 11-19.

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INTRODUCTION

Determining the distribution of wildlife through wildlife surveys is essential to conservation (Ahumada, Hurtado, & Lizcano, 2013; O'Brien, Baillie, Krueger, & Cuke, 2010). Traditional wildlife survey methods such as scat and track transects can be expensive and time-consuming, and often result in misidentification or failure to detect species, hampering conservation efforts (Mackenzie, 2005). It is therefore important to select appropriate survey methods that avoid these biases (Miller, Nichols, McClintock, Campbell Grant, Bailey, & Weir, 2011). Wildlife cameras overcome some of these shortcomings by collecting data continuously over a long period of time and by easing photographic identification of wildlife, thereby increasing the survey period and reducing the probability of detection error (Vine, Crowther, Lapige, Dickman, Mooney, Piggot, & English, 2009). Vine *et al.* (2009) compared camera traps, hair traps, scat from bait stations, and spotlighting to determine the best survey method for a low-density red fox (*Vulpes vulpes*) population and found that camera traps provided the most consistent and univocal results, minimizing bias.

Despite these benefits, wildlife cameras have performance limitations and not all wildlife cameras perform equally (Meek, Ballard, & Fleming, 2015). Broadly speaking, there are performance disparities between "professional" and "recreational" camera models. Professional models are designed for research and incorporate higher-quality components (e.g.: sensors, camera lens, etc.), have more customization options, and are thus more expensive, whereas recreational models are intended for use by the general public and have limited features, resulting in a more affordable and user-friendly product (Newey, Davidson, Nazir, Fairhurst, Verdicchio, Irvine, & van der Wal, 2015). One study completed by Newey *et al.* (2015) found that recreational camera models are less reliable than professional models and produced a greater number of false positive (blank) images and false negative (missed detection) data. A false positive occurs when a camera takes a photo in the absence of wildlife. False positives can present issues because they consume memory, batteries, and time processing images (Heiniger & Gillespie, 2018). Newey *et al.* (2015) also note that recreational cameras are prone to malfunction, which also take up memory and drain batteries, possibly leading to data loss. For the purposes of this study, a malfunction is defined as an image that is colour-stained (Figure 1). Sometimes, wildlife can be identified from malfunctioned images, but in more serious malfunctions, the colour stain completely blocks the image, making identification impossible, as seen in Figure 1B.

Researchers also need to consider the specifications of wildlife cameras as differing specifications can result in highly variable data (Meek *et al.*, 2015, p. 3). While countless studies have used wildlife cameras, few have considered the differences between models (Rovero, Zimmermann, Berzi, & Meek, 2013; Trolliet *et al.*, 2013; Meek et al., 2015). A study will typically use only one model,

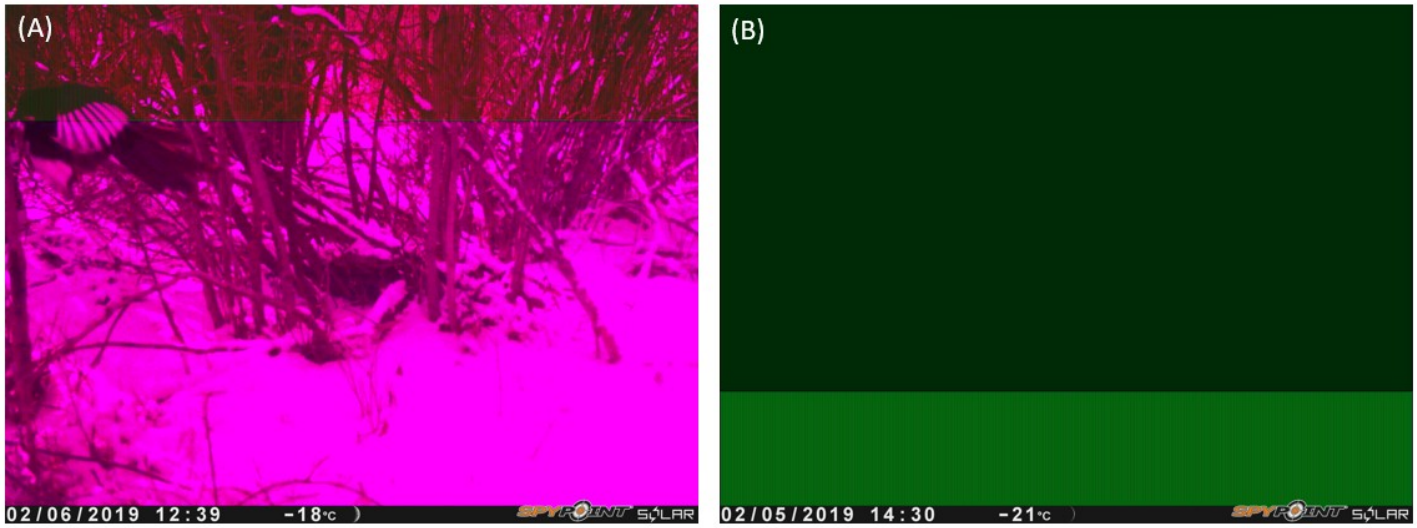

Fig. 1: two examples of a malfunction image collected from a Spypoint Solar Trail camera. No Reconyx camera collected a malfunction image. (A, left) Malfuction image in which identification is still possible. (B, right) Malfuction image in which identification is not possible.

so it is imperative that the selected camera has the minimum specifications required to fulfil the study's needs. There can also be substantial variation between different units of the same model (Hughson, Darby, & Dungan, 2010), as camera set-up, settings, and the quantity of cameras used can alter the likelihood of detecting certain species (Rovero et al., 2013; Wellington, Bottom, Merrill, & Litvaitis, 2014; Meek, Ballard, & Falzon, 2016). Therefore, it is crucial that researchers consider not only which model, but also which settings to use (Driessen, Jarman, Troy, & Callander, 2017).

The purpose of this study is to examine differences between two wildlife camera models, the Spypoint Solar Trail and Reconyx Hyperfire 2, on behalf of Calgary Captured. Calgary Captured is a collaborative project between the City of Calgary and the Miistakis Institute to determine wildlife occupancy in Calgary's Natural Area Parks using wildlife cameras (Miistakis Institute, 2017). Initially, Calgary Captured used Spypoint Solar Trail cameras, a recreational model as stated by its manual. However, after a period of two years, Calgary Captured began using the Reconyx Hyperfire 2, a professional model, following concerns from Calgary Captured over potential false negatives produced by the Spypoint models (Nicole Kahal, pers. comm.). It is important to understand the variation in performance between these different camera models to avoid making inaccurate conclusions about their results (Heiniger & Gillespie, 2018). Therefore, this study quantifies the difference in detection efficacy between the two models so that the Calgary Captured project can compare the data collected by the Spypoint cameras with those collected by the Reconyx cameras.

METHODS

Study area

10 Spypoint and 10 Reconyx wildlife cameras were placed in pairs at 10 sites: four sites in Weaselhead Flats (Figure 2A), one site in North Glenmore Park (Figure 2A), and five sites in Fish Creek Provincial Park (Figure 2B). Weaselhead Flats and North Glenmore Park are adjacent to each other, and Fish Creek Provincial Park is located approximately 15 km southeast of Weaselhead Flats. All the parks used in this study have similar habitats consisting of riparian zones and aspen poplar, balsam poplar, and white spruce forest. The sites used for this experiment are 10 of the existing 69 Calgary Captured camera sites, which are systematically located near game trails and away from human trails in a 1km by 1km grid, except in Weaselhead Flats, where additional cameras were placed by Calgary Captured, resulting in a higher camera density (N. Kahal, pers. comm.).

Camera set-up

One Spypoint Solar Trail camera and one Reconyx Hyperfire 2 camera were placed together at each site. An ideal setup would place both cameras within 1 m directly next to each other (Hughson *et al.*, 2010; Meek *et al.*, 2015). However, there was rarely a pair of neighbouring trees close enough to allow for this setup. As a consequence, both cameras were placed on the same tree at nine sites, with the Spypoint camera placed above the Reconyx camera so that the Spypoint's solar panel would not be obstructed by the Reconyx camera (Figure 3A). Site 62 was the exception and the cameras there were placed on neighbouring trees (Figure 3B). Camera height was measured by distance from the centre of the Fresnel lens to the ground (Table 1). Information on the specifications and settings of the cameras used in this study can be found in Table 2.

Camera set-up

Memory card collection took place once a week, alternating between the Fish Creek Provincial Park sites and the Weaselhead Flats/North Glenmore Park sites. As a control measure, and to quantify false negatives, "walk-bys" were performed each time a camera was checked, during which the principal researcher walked past each camera three times, each time at three different speeds: slow (0.5m/s-0.6m/s), medium (0.9m/s-1.3m/s), and fast (1.5m/s-3.1m/s). This procedure was not performed at sites 43, 44, and 61 due to safety concerns.

The images captured by the cameras were processed using Microsoft Access and sorted into trap events, which consist of all the photos taken of an animal during its time in front of the cameras (Meek, Ballard, Claridge, Kays, Moseby, O'Brien, O'Connell, ..., & Townsend, 2014). The Reconyx cameras captured three pictures for every detection while the Spypoint cameras took one picture for every detection, so the two models' performances were compared using the number of events instead of the number of detections. Animals were identified by species for each event.

Fig. 2: (A, left) Google Earth image of camera sites in Weaselhead Flats (61, 62, 63, and 64) and North Glenmore Park (66). (B, right) Google Earth image of cameras sites in Fish Creek Provincial Park (39, 43, 44, 45, and 46).

Image processing was conducted on a secure computer at the Miistakis Institute office in compliance with the Alberta Freedom of Information and Protection of Privacy (FOIP) Act (Province of Alberta, 2019).

The cameras in Weaselhead Flats/North Glenmore Park were active from 15 January 2019 to 3 March 2019, and those in Fish Creek Provincial Park were active from 27 January 2019 to 8 March 2019. Due to the cold weather, the NiMH batteries in some Reconyx units repeatedly lost power, reducing the number of trap nights for those cameras (Table 1). Initially, one Spypoint camera was not working and had to be replaced with a different unit (site 64), reducing its number of trap nights (Table 1). To control for these differences in trap nights, the data were standardized to the number of trap events per 100 trap nights (Kelly & Holub, 2008):

$$\frac{\#\text{ of events} \times 100}{\#\text{ of trap nights}}$$

This is the same standard used by the Miistakis Institute and is referred to in their documents as the relative abundance index, or RAI (Miistakis Institute, 2017). Throughout this paper, the number of trap events per 100 trap nights will be abbreviated to RAI.

Microsoft Excel was used to calculate RAI values for each species. To increase sample size, all bird species were placed into one category ("bird"). Because the data were not normally distributed, the non-parametric Wilcoxon signed-rank test was used for all comparisons. JMP (version 14.1.0) was used for statistical analyses and graphing.

RESULTS

Throughout the study, nighttime temperatures often fell below the -18° operating limit specified for the NiMH batteries used in the Reconyx models. Consequently, only four of the ten Reconyx cameras functioned for the entire duration of the study. Furthermore, the camera locks were often frozen, which made changing the Reconyx cameras' batteries impossible, exacerbating the problem. As a result, a substantial amount of Reconyx data were lost, which may have impacted the study.

Species detected

Nine species were detected during the study (Table 3). White-tailed deer was the most commonly detected species. Bobcat and deer mouse were detected only by the Reconyx cameras. There was no significant difference between the Reconyx and Spypoint cameras with regards to number of coyote detections (W=-7.00, p=0.31; Figure 4A) or deer detections (W=12.50, p=0.44; Figure 4B). Detection of other species did not take place at enough sites to allow for any statistical analysis (Table 3). Taking all species detections into consideration, there was no significant difference between Reconyx and Spypoint models (W=-0.13, p= 0.90; Figure 4C). It should be noted that at every site the camera height of the Spypoint cameras was significantly higher than that of the Reconyx cameras (W=3.44, p=0.0006; Figure 5).

False positives (blanks) and malfunctions

All of the cameras in this study collected false positives. There was no significant difference between the number of false positives collected by the Reconyx and Spypoint cameras (W=-15.50, p=0.13; Figure 6). There was less variation in the number of false positives collected by each Reconyx camera compared to the Spypoint cameras (Figure 6). Only the Spypoint cameras produced malfunctions. There was a significant difference between the number of malfunctions in the Spypoint cameras and Reconyx cameras (W=27.00, p=0.0039; Figure 7).

False negatives

No significant difference was found between the number of pictures taken by the Reconyx and Spypoint cameras during the walk-by tests at slow (W=3.00, p=0.66), medium (W = 0.00, p = 1.00), or fast speeds (W=-1.00, p=0.89; Figure 8). One Reconyx camera failed to take any pictures during one of the fast walk-by tests. There was less variation in the number of pictures taken at each of the three walk-by speeds by the Reconyx cameras than by the Spypoint cameras (Figure 8).

DISCUSSION

Over the course of the study, the Reconyx cameras had fewer trap nights than did the Spypoint cameras because their batteries failed in the cold weather. Despite this, the Reconyx cameras still detected more species than did the Spypoint cameras. While the

Fig. 3: (A, left) Example of camera placement at 9/10 sites (all except site 62). (B, right) Example of camera placement at 1/10 sites (site 62).

RAI allows for comparison of data from cameras with differing numbers of trap nights, the Spypoint cameras should have a greater probability of detecting wildlife because they were functional for a greater period of time (Rovero *et al.*, 2013). Thus, based on the number of trap nights alone, the Spypoint cameras should detect more species than the Reconyx cameras. The fact that the Reconyx cameras detected more species in fewer trap nights suggests that the model has greater detection ability.

The two species detected only by Reconyx cameras were bobcat (*Lynx rufus*) and deer mouse (*Peromyscus maniculatus*). Although Reconyx cameras have a reputation for being better able to detect smaller mammals (Kelly & Holub, 2008; Wellington *et al.*, 2014) than the game species (e.g., deer) Spypoint cameras were designed to detect, there is little evidence in the literature to suggest that this is actually the case (Driessen *et al.*, 2014). It was suggested that the reason the Spypoint cameras had lower than expected detection rates of bobcat was because bobcats move too quickly to be effectively detected (N. Kahal, pers. comm.). However, the walk-by tests did not find a significant difference in the number of pictures taken between the two camera models. In fact, the only camera that failed to take any photos during a fast walk-by test was a Reconyx camera.

Camera height has been found to account for variation in detection of species (Meek *et al.*, 2016). To avoid blocking the Spypoint cameras' solar panels, the Reconyx cameras were placed below the Spypoint cameras at nine sites. Meek *et al.* (2016) found that cameras placed 300 cm above the ground were less likely to detect species like red foxes and wild dogs (*Canis familiaris*) than those placed 210 cm lower at 90 cm. The greatest camera height in this study was 118 cm and the greatest difference in height between the two cameras at any site was only 31.25 cm. Moreover, there was no significant difference between the Reconyx and Spypoint cameras in the number of detections of coyote, a species comparable in size to wild dogs. The Spypoint cameras were also able to detect other small mammals such as Eastern gray squirrels and snowshoe hares, which are smaller than bobcats. Therefore, there was little indication that height difference was the reason the Reconyx cameras detected more species than did the Spypoint cameras. Camera placement is affected by many variables such as camera angle, distance from wildlife trails, and slope of the ground between the camera and wildlife trail (Meek *et al.*, 2016). In this study, slope and camera angle may have affected species detections, although data for those variables were not collected so they could not be included in the analysis.

Camera settings such as trigger speed can affect the number of blank (false positive) images taken. If the trigger speed is too slow, it is possible for an animal to move through the field of view before a photo is taken (Wellington *et al.*, 2014). In this study, the Reconyx cameras had a slower trigger speed than the Spypoint cameras, so the Reconyx cameras should have produced more false positives, which was not the case.

Only the Spypoint cameras produced malfunctions. This supports Newey *et al.*'s (2015) results showing that recreational quality cameras have performance limitations. Malfunctions negatively impact the quality of data because researchers often cannot identify the species that triggered the camera detection. Thus, susceptibility to malfunction should be considered when selecting a camera model for a study.

It was necessary to consider the variation in the number of trap nights in this study to be able to compare the efficacy of the two camera models. There are a variety of methods that have been used in the literature to standardize camera trap data (e.g. Carbone, Christie, Conforti, Franklin, Ginsberg, Griffiths, ..., Sharuddin, 2001; O'Brien, Kinnaird, & Wibisono, 2003; O'Brien *et al.*, 2010). This study used the method of Kelly & Holub (2008) to calculate RAIs for consistency with the methodology used by the Miistakis Institute (2017). Sollman, Mohamed, Samejima, & Wilting (2013) criticizes the use of RAIs because factors such as encounter rates, home ranges, trap setup, and repeated surveys all affect data quality, so using RAIs to determine wildlife abundance without considering these factors can return biased results. In this study, the RAI values were not used to extrapolate wildlife abundances, but rather were used to compare data collected by wildlife cameras that operated for different numbers of trap nights. Using the RAI values for this purpose precluded much of the biases described by Sollman *et al.* (2013).

CONCLUSIONS

Despite operating for fewer trap nights, the Reconyx cameras detected two species that were not detected by the Spypoint cameras. Because the goal of the Calgary Captured project is to document wildlife occupancy in the city, increased species detection is important. Moreover, the Reconyx cameras did not produce malfunctioned images, whereas the Spypoint cameras did. While the Reconyx cameras performed well, the NiMH batteries used did not. Lithium batteries with a specified operating limit of -40° have been used in other winter camera trap studies in Alberta without issue (L. Gould, pers. comm.; K. Anderson, pers. comm.) and may address this problem. Notwithstanding the battery issues in cold weather, Reconyx appears to be the better model in meeting the goals of Calgary Captured because it did not malfunction and was able to detect more species than did the Spypoint cameras despite operating for fewer trap nights.

The advantages of using wildlife cameras over traditional survey methods include reduced identification errors and false negatives (Vine *et al.*, 2009). Nonetheless, researchers need to be aware of wildlife cameras' limitations and ensure the technology they select is suitable for the goals of their projects (Meek *et al.*, 2015; Newey *et al.*, 2015).

The author would like to thank* Dr Dorothy Hill *"for spending countless hours working on this project with me",* Dr Melanie Rathburn *"for helping me run statistical tests",* Nicole Kahal *"for helping with camera set-up and for being my contact at the Miistakis Institute",* Calgary Captured *"for lending me their sites and equipment and for trusting me to conduct the study", and* Dr Paul Meek (Government of New South Wales), Tyne Baker, and Karen Anderson (Alberta Environment and Parks) *"for sharing their knowledge of wildlife cameras and for their advice".

REFERENCES

[1] Ahumada, J. A., Hurtado, J., & Lizcano, D. (2013). Monitoring the trends and status of tropical forest terrestrial vertebrate communities from camera trap data: a tool for conservation. PLoS One, 8(9). https://doi.org/10.1371/journal.pone.0073707

[2] Carbone, C., Christie, S., Conforti, K., Coulson, T., Franklin, N., Ginsberg, J. R., Griffiths, M., Holden, J., Kawnanishi, K., Kinnaird, M., Laidlaw, R., Lynam, A., Macdonald, D. W., Martyr, D., McDougal, C., Nath, L., O'Brien, T., Seidensticker, J., Smith, D. J. L., Sunquist, M., Tilson, R., & Wan Shahruddin, W. N. (2001). The use of photographic rates to estimate densities of tigers and other cryptic mammals. Animal Conservation, 4, 75-79. https://doi.org/10.1017/S1367943001001081

[3] Driessen, M. M., Jarman, P. J., Troy, S., & Callander, S. (2017). Animal detection vary among commonly used camera trap models. Wildlife Research, 44(4), 291-297. https://doi.org/10.1071/WR16228

[4] Heiniger, J. & Gillespie, G. (2018). High variation in camera trap-model sensitivity for surveying mammal species in Northern Australia. Wildlife Research, 45(7), 578-585. https://doi.org/10.1071/WR18078

[5] Hughson, D. L., Darby, N. W., & Dungan, J. D. (2010). Comparison of motion-activated cameras for wildlife investigation. California fish and game, 92(2), 101-109.

[6] Kelly, M. J. & Holub, E. L. (2008). Camera trapping of carnivores: trap success among camera types and across species, and habitat selection by species, on Salt Pond Mountain, Gile County, Virginia. Northeastern naturalist, 15(2), 249-262. https://doi.org/10.1656/1092-6194(2008)15[249:CTOCTS]2.0. CO;2

[7] MacKenzie, D. I. (2005). What are the issues with presence-absence data for wildlife managers? The Journal of Wildlife Management, 69(3), 849-860. https://doi.org/10.2193/0022-541X(2005)069[0849:WATIWP]2.0.CO2

[8] Meek, P. D., Ballard, G., Claridge, A., Kays, R., Moseby, K., O'Brien, T., O'Connell, A., Sanderson, J., Swann, D. E., Tobler, M., & Townsend, S. (2014). Recommended principles for reporting on camera trapping research. Biodiversity and Conservation, 23(9), 2321-2343. https://doi.org/10.1007/s10531-014-0712-8

[9] Meek, P. D., Ballard, G., & Fleming, P. J. S. (2015). The pitfalls of wildlife camera trapping as a survey tool in Australia. Australian Mammalogy, 37(1), 13-22. https://doi.org/10.1071/AM14023

[10] Meek, P. D., Ballard, G., & Falzon, G. (2016). The higher you go the less you will know: placing camera traps high to avoid theft will affect detection. Remote Sensing in Ecology and Conservation, 2(4), 204-211. https://doi.org/10.1002/rse2.28

[11] Miistakis Institute. (2017). City of Calgary: wildlife camera monitoring: summary statistic May-August 2017. Calgary, Alberta: Kahal, N., Lee, T., & Rondeau, K.

[12] Miller, D. A., Nichols, J. D., McClintock, B. T., Campbell Grant, E. H., Bailey, L. L., & Weir, L. A. (2011). Improving occupancy estimation when two types of observational error occur: non-detection and species misidentification. Ecology, 92(7), 1422-1428. https://doi.org/10.1890/10-1396.1

[13] Newey, S., Davidson, P., Nazir, S., Fairhurst, G., Verdicchio, F., Irvine, R. J., & van der Wal, R. (2015). Limitations of recreational camera traps for wildlife management and conservation research: a practitioner's perspective. Ambio, 44, 625-635. https://doi.org/10.1007/s13280-015-0713-1

[14] O'Brien, T. G., Kinnaird, M. F., Wibisono, H. T. (2003). Crouching tigers, hidden prey: Sumatran tiger and prey populations in a tropical forest landscape. Animal Conservation, 6, 131-139. https://doi.org/10.1017/S1367943003003172

[15] O'Brien, T. G., Baillie, J. E. M., Krueger, L., Cuke, M. (2010). The wildlife picture index: monitoring top trophic levels. Animal Conservation, 13, 335-343. https://doi.org/doi:10.1111/j.1469-1795.2010.00357.x

[16] Reconyx (2018). Hyperfire 2 Outdoor Series Camera: User Manual. Retrieved January 29, 2019 from http://images.reconyx.com/file/HyperFire2PROUserGuide2018_04_24_v3.pdf

[17] Rovero, F., Zimmerman, F., Berzi, D., & Meek, P. (2013). "Which camera trap type and how many do I need?" A review of camera features and study designs for a range of wildlife applications. The Italian Journal of Mammalogy, 24(2), 148-156. https://doi.org/10.4404/hystrix-24.2-8789

[18] Sollman, R., Mohamed, A., Samejima, H., & Wilting, A. (2013). Risky business or simple solution - relative abundance indices from camera-trapping. Biological Conservation, 159, 405-412. https://doi.org/10.1016/j.biocon.2012.12.025

[19] Spypoint. (n.d.). User Manual: Solar Trail Camera. Retrieved January 29, 2019 from https://www.spypoint.com/manuals/Manual_SOLAR_EN.pdf

[20] Trolliet, F., Huynen, M., Vermeulen, C., & Hambuckers, A. (2014). Use of camera traps for wildlife studies: a review. BASE, 18(3), 446-454.

[21] Vine, S. J., Crowther, M., S., Lapidge, S. J., Dickman, C. R., Mooney, N., Piggott, M. P., & English, A. W. (2009). Comparison of methods to detect rare and cryptic species: a case study using the red fox (Vulpes vulpes). Wildlife Research, 36, 436-446. https://doi.org/10.1071/WR08069

[22] Wellington, K., Bottom, C., Merrill, C., & Litvaitis, J. A. (2014). Identifying performance differences among trail cameras used to monitor forest mammals. Wildlife Society Bulletin, 38(3), 634-638. https://doi.org/10.1002/wsb.425

TABLES

Table 1 Height and number of trap nights for each camera

Site no. (maximum trap nights)	Reconyx trap nights	Spypoint trap nights	Height difference (cm)
39 (39)	15	39	20.04
43 (39)	9	39	18.54
44 (38)	39	39	13.99
45 (39)	15	38	14.73
46 (47)	5	39	20.32
61 (47)	47	47	12.28
62 (47)	16	47	1.01
63 (47)	47	47	21.80
64 (47)	40	37	18.80
66 (47)	47	47	31.25

Table 2 Specifications and settings of each camera model

Specification/setting	Reconyx Hyperfire 2 (2018)	Spypoint Solar Trail
Optical field of view (°)	Not supplied by manufacturer	40°
Detection angle (°)	Not supplied by manufacturer	40°
Detection range (m)	Up to 30.5	1.5-24.4
Trigger speed (s)	0.2	0.07
Delay	RapidFire	Instant
Multi-shot	3 pictures per detection	1 picture per detection
Sensitivity	High	High
Battery type	Nickel metal hyrdide (NiMH)	Lithium (solar-powered), alkaline

Table 3 List of species detected during the study and number of sites where species were detected

Species	Number of sites detecting
White-tailed deer (*Odocoileus virginianus*)	10
Coyote (*Canis latrans*)	10
Snowshoe hare (*Lepus americanus*)	3
Bobcat (*Lynx rufus*)[a]	1
Deer mouse (*Peromyscus maniculatus*)[a]	1
Eastern grey squirrel (*Sciurus carolinensis*)	3
Birds: Black-capped chickadee (*Poecile atricapillus*)	
Birds: Black-billed magpie (*Pica hudsonia*)	5
Birds: American crow (*Corvus brachyrhynchos*)	

[a] Species detected only by Reconyx cameras

FURTHER FIGURES

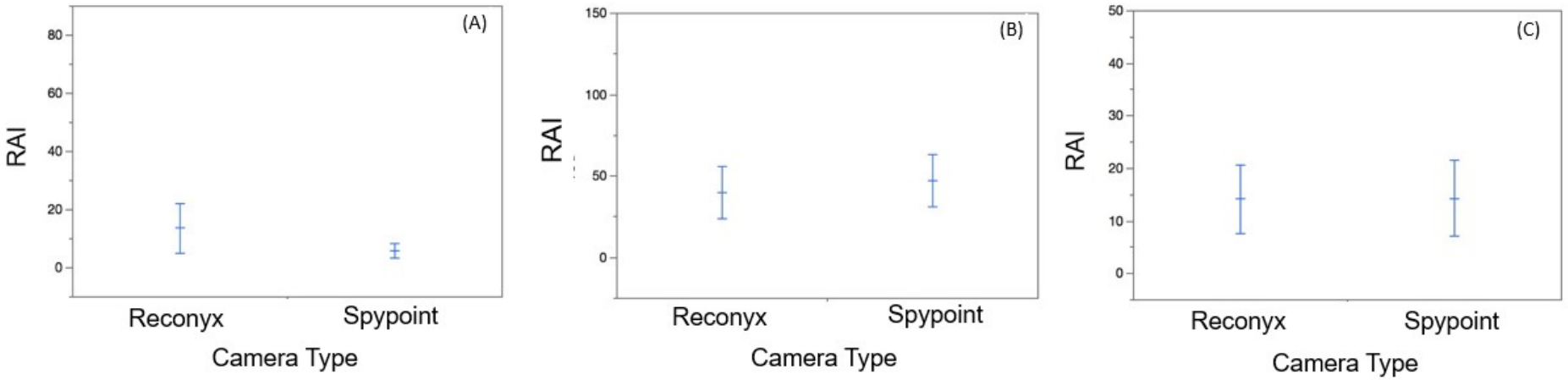

Fig 4 (A, left) Mean relative abundance index (RAI) of coyote (*Canis latrans*) detections by the Reconyx (+/- 8.5 se) and Spypoint cameras (+/- 2.5 se). (B, centre) Mean RAI of white-tailed deer (*Odocoileus virginianus*) detections by the Reconyx (+/- 15.8 se) and Spypoint cameras (+/- 15.9 se). (C, right) Mean RAI of all species detections by the Reconyx (mean=14.2 +/- 6.5 se) and Spypoint (mean=14.4 +/- 7.2 se) cameras

FURTHER FIGURES (CONT'D)

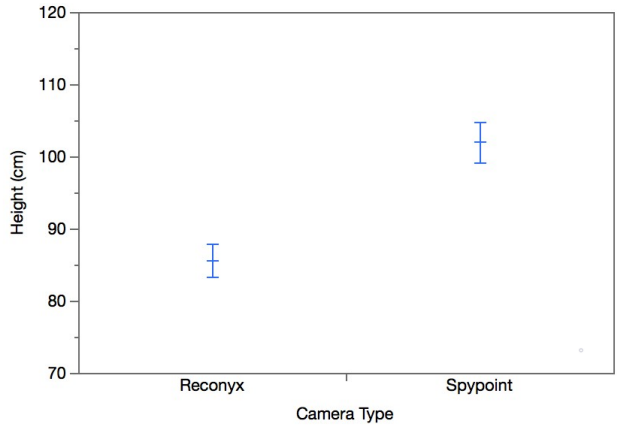

Fig 5 Mean height (+/- standard error) between Reconyx (n=10) and Spypoint (n=10) cameras

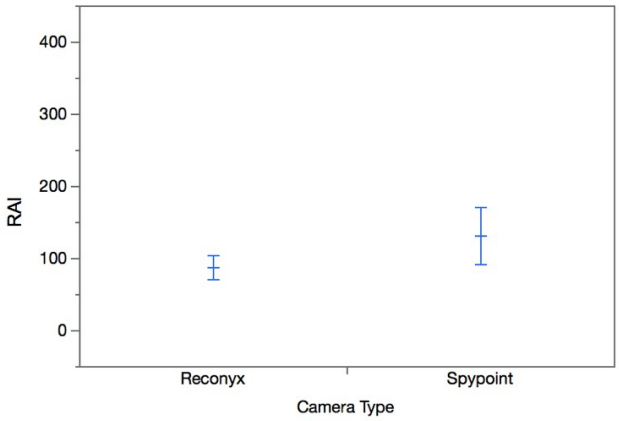

Fig 6 Mean RAI of false positives (blank images) between Reconyx (mean=87.20 +/- 16.1 se, n=10) and Spypoint (mean=130.94 +/- 39.3 se, n=10) cameras

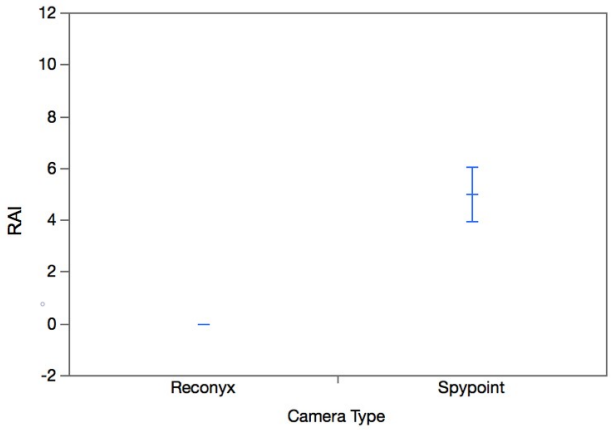

Fig 7 Mean RAI of malfunctions between Reconyx (mean=0.00 +/- 0.0 se, n=10) and Spypoint (mean=5.01 +/- 1.0 se, n=10) cameras

FURTHER FIGURES (CONT'D)

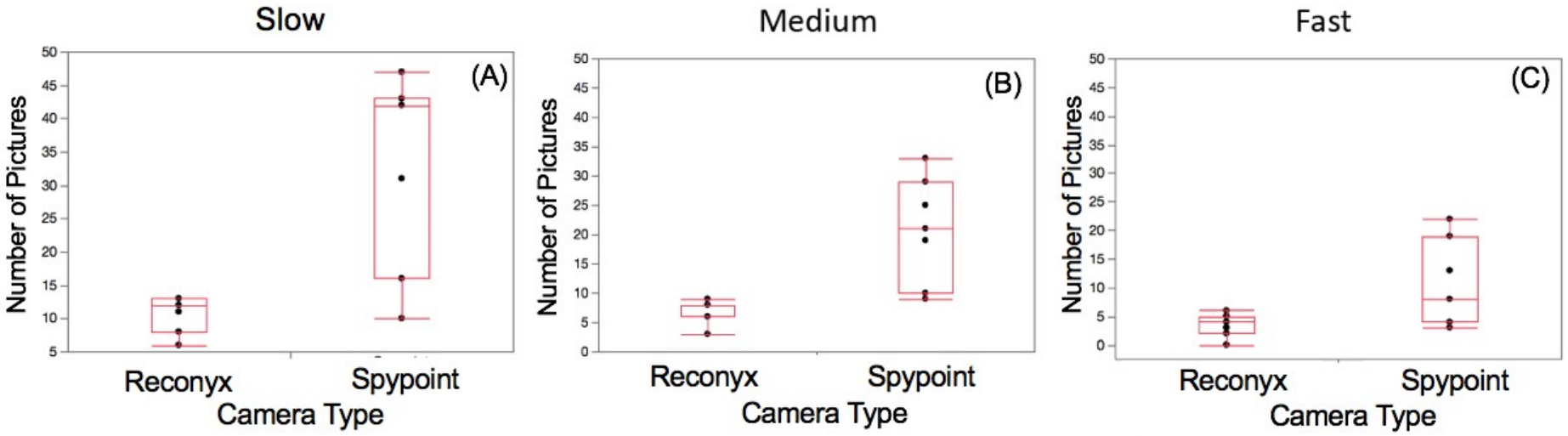

Fig 8 Comparison of number of pictures taken by Reconyx (n=7, min=6, Q1=8, median=12, Q3=13, max=13) and Spypoint (n=7, min=10, Q1=16, median=42, Q3=47, max=47) at a slow (0.5m/s-0.6m/s) speed. (B): Comparison of number of pictures taken by Reconyx (n=7, min=3, Q1=6, median=8, Q3=8, max=9) and Spypoint (n=7, min=9, Q1=10, median=21, Q3=29, max=33) at a medium (0.9m/s-1.3m/s) speed. (C): Comparison of number of pictures taken by Reconyx (n=7, min=0, Q1=2, median=4, Q3=5, max=6) and Spypoint (n=7, min=3, Q1=4, median=8, Q3=19, max=22) at a fast (1.5m/s-3.1m/s) speed

Nanomedicine: the use of nanoparticles to treat acute traumatic spinal cord injuries

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Abstract Spinal cord injuries (SCIs) are difficult to treat without using traditional invasive methods that are not always precise or efficient. Traditional methods used to treat SCIs often involve targeting a broad area in close proximity to the specific locality of the injury as opposed to direct targeting. Recent studies suggest the use of nanoparticles can be a viable way to treat SCIs. Nanoparticles are nanotechnological devices that operate on a nanometre (1x 10-9m) scale, varying in dimension from 1-100nm. They can be designed to target an assigned area with a high degree of specificity, thus ensuring that the affected area is treated with maximum proficiency. This article will explore the properties of silica nanoparticles, polymer nanoparticles, and chondroitinase ABC-(chABC)-releasing nanoparticles to determine whether they present a non-invasive alternative treatment for acute traumatic spinal cord injuries (tSCIs). A review of the literature suggests that the use of multifunctional silica-polymer nanoparticles can plausibly treat SCIs by maximizing the beneficial characteristics of both materials. Silica nanoparticles have a zero-order drug-releasing property which provides efficacious targeting, and when combined with polyethylene glycol (PEG) this polymer increases aqueous stability and retention of the nanoparticle, which protects the loaded drug when it crosses the blood-brain barrier to target the SCI. In addition, chABC-releasing nanoparticles show promising results in treating SCIs due to their ability to remove glycosaminoglycans (GAGs) and promote nerve regeneration, potentially decreasing the healing time of SCIs. Overall, the application of nanoparticles provides a potential non-invasive treatment method for SCIs in mice models. However, further research needs to be done to explore the potential medical applications of nanoparticles regarding human SCIs.

Published online
23 December 2020

Citation
Ellis, P. (2020). Nanomedicine: the use of nanoparticles to treat acute traumatic spinal cord injuries. *CJUR*, 5(2), 20-25.

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INTRODUCTION

The spinal cord is the bundle of nerves connected to the brain that extends down the spinal canal (Noonan, 2012). A temporary or permanent impairment of the spinal cord is termed a spinal cord injury (SCI) (Noonan, 2012). There are two general classes of SCIs: (i) traumatic spinal cord injuries (tSCIs), which occur due to external physical impact; and (ii) non-traumatic spinal cord injuries (ntSCIs), which occur when damage is done to the spinal cord by means other than physical impact (Noonan, 2012).

In order to implement an appropriate treatment plan for an SCI, it is important to distinguish the type of SCI and its severity. The severity of SCIs can vary from acute to chronic (Beaulieu, 2018). Acute SCIs result from sudden trauma that is potentially repairable depending on the circumstances of the injury; chronic SCIs result from trauma that has happened over time (Beaulieu, 2018). SCIs often have debilitating effects on patients and can severely impact their quality of life (Infante, 2018). Damage to the spinal cord can result in tetraplegia, which indicates damage to the cervical cord, or paraplegia, which indicates damage to the thoracic, lumbar, or sacral spinal cord (Noonan, 2012).This article will solely discuss acute tSCIs to delineate the mechanism of action of each treatment regarding the site of inflicted physical injury.

Research indicates that tSCIs affected approximately 43,974 Canadians in the year 2010 (Noonan, 2012). These injuries often have extensive recovery times, and traditional methods of treatment are invasive to the human body, prolonging recovery times (Ho et al., 2018). Traditional methods of treating SCIs such as electrical stimulation often entail stimulation of a broad area in close proximity to the specific area of treatment (Ho et al., 2018). However, this does not target the affected area with specificity. Nanoparticles have the potential to treat SCIs more effectively due to their ability to perform immaculate targeting specificity to their assigned locality without being invasive (White-Schenk et al. 2015; Ellis, 2017). Nanoparticles are nanotechnological devices that operate at 1x 10-9m, or one nanometre (nm) (Ellis, 2017). Nanoparticles offer a potential method of treatment for acute tSCIs by selectively degrading damaged nerve tissue in the spinal cord to promote axonal regeneration, potentially reducing patient recovery time (Prabhakar et al., 2005).

METHODS

A scoping review was performed to outline the advantageous properties of silica, polymer, and chABC-releasing nanoparticles and this review explored the characteristics of these devices as potential treatments for acute tSCIs. The articles retrieved were all written in English. Secondary research was conducted at the University of Ottawa using the PubMed database: a narrow keyword search using combinations of the search terms ‘tSCIs’, ‘nanoparticles’, and ‘proteoglycans’ was performed. A full description of the search strategy is presented in Table 1. The search was last updated October 13, 2020. No additional databases were used.

However, additional lecture material from Physical Activity, Work and Health Ergonomy presented at the University of Ottawa was included.

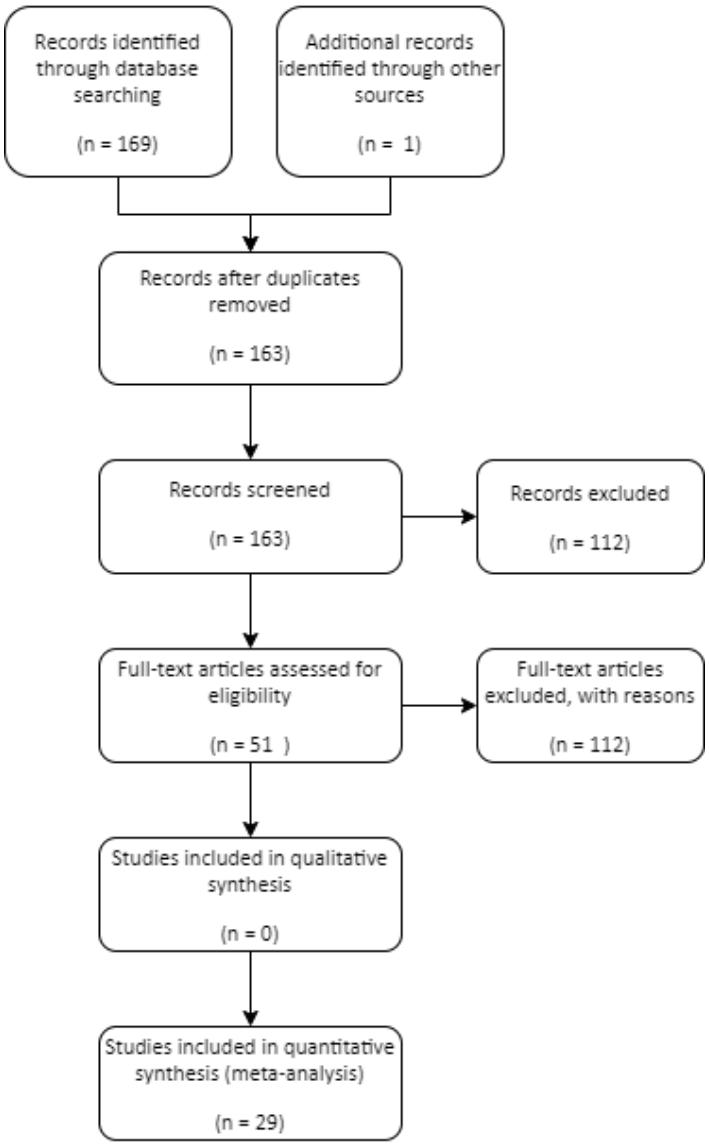

Fig. 1: PRISMA flow diagram: a total of 169 original articles were retrieved of which 29 articles were considered relevant.

Study selection

After eliminating duplicate results, title and abstract screening was performed by the author. Then, full-text screening was performed dating back to the last 15 years to retrieve relevant articles according to the inclusion criteria. Articles that explored the characteristics of silica, polymer, and chABC-releasing nanoparticles as potential treatment methods for acute tSCIs were eligible under these criteria. The characteristics of the nanoparticles were explored and the intent of this review was to explain their potential applications as a non-invasive alternative method to treat acute tSCIs. Studies that did not report on these criteria were excluded. The search sensitivity was confirmed by reviewing the articles cited in each study. The search results and selection process using the PRISMA protocol are summarized in Figure 1.

Quality assessment

The quality of the selected articles was assessed based on their study characteristics and methodological approach. The two selection criteria narrowed the search to those that explored the properties of silica, polymer, and chABC-releasing nanoparticles; these nanoparticles were further described in terms of their potential as treatments for tSCIs. In terms of the methodological approach, articles that outlined the characteristics of the nanoparticles with regards to treating tSCIs were considered high-quality studies. Only moderate- to high-quality studies were considered in this review.

Data extraction

The author extracted data from eligible studies from their original publications and lecture material from Physical Activity, Work and Health Ergonomy which included information about the type of SCI, study design, intervention used, country of origin, and primary and secondary research. If the data did not comprehensively explore the characteristics of nanoparticles or did not explore SCIs it was excluded from the review.

RESULTS

The reviewed secondary literature indicates that nanoparticle-based strategies for the delivery of neurotrophic factors to promote functional axon regeneration in the spinal cord can occur in an effective and safe manner (Infante, 2018). Thus, nanoparticle delivery methods may be a promising alternative treatment for SCIs due to their non-invasiveness, precision, and specificity (Infante, 2018).

Research has explored the combination of polymer and silica nanoparticles as a potential treatment for SCIs by maximizing their individual chemical properties to create multifunctional silica-polymer nanoparticles with a maximized therapeutic effect.

Materials such as long-chain polymers have been used to treat SCIs in the past due to their ability to first plug the damaged membrane; then close the holes to prevent the entry of unwanted ions and molecules (White-Schenk et al. 2015). One polymer material of interest in SCI therapy is hydrophilic polyethylene glycol (PEG) , a stealth polymer that is used to extend the half-life of therapeutics and prevent protein adsorption on the surface of nanoparticles during opsonization (White-Schenk et al. 2015). This reduces the likelihood of an immune response against the nanoparticle, which makes PEGs very successful in crossing the blood-brain barrier and targeting an assigned locality in the spinal cord (Rollerova et al., 2011). Silica nanoparticles are characterized as being mesoporous with a zero-order drug release, which enables efficacious drug-loading and accurate targeting of an assigned locality (White-Schenk et al. 2015). Silica nanoparticles have cytotoxic properties, however they can be used in conjunction with PEG to maximize their beneficial properties while simultaneously reducing their cytotoxic effects, improving their aqueous stability and retention to reduce toxicity in vivo and in vitro (White-Schenk et al. 2015). One study explored the chemical properties of PEG-decorated silica nanoparticles and their effect on the restoration of membrane integrity, axonal conductivity, and functional recovery in model animals (Cho, 2010). This study analyzed the in-vitro crush/contusion model of a SCI in a guinea pig, which was injected with PEG-decorated silica nanoparticles; the model showed signs of conduction recovery through the cord lesion (Cho, 2010). This suggests that the use of multifunctional nanoparticles such as silica and polymer nanoparticles may present a novel approach to

treating SCIs (Rollerova et al., 2011).

Chondroitin sulfate proteoglycans (CSPGs) are inhibitors of neural stem/progenitor cells (NSPC) whose regeneration is essential to the healing process of an SCI (Ikegami, 2005; Massey, 2006). However, the bacterial enzyme chABC has been shown to digest CSPGs and promote the migration of transplanted cells and neurite outgrowth (Ikegami, 2005). An in vitro study revealed that the migration of NSPC-derived cells was inhibited by CSPG, and that chABC treatment combined with NSPC transplantation into an injured spinal cord significantly induced the axonal outgrowth due to an increase of growth-associated protein-43 positive fibres at the lesion epicentre, which is important to new neuronal growth (Ikegami, 2005)This suggests that chABC-based treatment may encourage regeneration of injured spinal cords (Ikegami, 2005). Another study indicated that using chABC to degrade CSPGs in the cuneate nucleus of rats reduced the number of CSPGs present in the injured spinal cord (Massey, 2006). Another study explored the effects of increasing the rate of delivery of chABC using nanoparticles to promote axonal regeneration following injury and to protect the enzyme from rapid degradation in a rodent contusion model (Zuidema et al., 2016). Although there is limited data presented in this area of research it is plausible that chABC-releasing nanoparticles are a potential treatment method for tSCIs due to their ability to remove CSPGs and promote NSPCs which are essential to reducing the healing time of an SCI (Zuidema et al., 2016).

DISCUSSION

A novel potential treatment

An injured spinal cord does not regenerate; it undergoes expansion and demyelination, resulting in macrophage activation, which increases axon growth and motor function (Gensel & Zhang, 2015). A macrophage is a type of white blood cell that travels to sites of inflammation to remove damaged material, which is essential to axon growth because this helps to degrade the damaged axons and encourage new axonal sprouting (Gensel & Zhang, 2015). Therefore, in order to treat these areas of inflammation with a high degree of specificity, it is imperative that the treatment be very precise (Infante, 2018).

Because nanotechnology operates at nanometre scale, it operates at the molecular and atomic level (Abou et al. 2015). Nanotechnology includes a variety of technological devices such as nano-assemblers, nano-shells, and nanoparticles, which may play a role in treating SCIs (Ellis, 2017). Nanoparticles offer both precision and target specificity with regards to treating SCI-affected tissues. Nanoparticles are designed through layer-by-layer synthesis, each layer changing the characteristics of the nanoparticle, which adds functionality; this makes nanoparticles programmable (White-Schenk et al. 2015). Nanoparticles are popularly used as a drug-delivery system because they are capable of crossing the cell membrane due to their small size (Amezcua et al., 2017). Nanoparticles are molecular units that behave as a whole unit during their mobile phase in the human body, and they can be modified with organic and inorganic substances, such as silica or polymer (Gupta, 2010).

Material format of multifunctional silica–polymer nanoparticles

Silica and polymers are used to create nanoparticles because of their unique properties, and they have been extensively tested as potential platforms for drug-delivery to the spinal cord (R.N., 2017). Silica is an inorganic compound that is used to create nanoparticles because of its porous structure (White-Schenk et al. 2015). Polymer nanoparticles are spherical and are a potentially beneficial treatment for SCIs because they have low toxicity (Rollerova et al., 2011; Kreuter, 2014). Silica and polymeric nanoparticles are notably capable of absorbing and encapsulating drugs (White-Schenk et al. 2015).

Polymer nanoparticles release their drug load to the target area in the form of a burst, resulting in a controlled release (White-Schenk et al. 2015). Polymer nanoparticles are notably much larger than silica particles because of their extensive bonding properties, which is useful in increasing the bioavailability of an otherwise scarce substance (White-Schenk et al. 2015). This is because polymer nanoparticles can directly interact with the desired substance and release it in large quantities in an assigned locality (White-Schenk et al. 2015). Polymeric nanoparticles are usually encapsulated via self-assembly, and as they disassemble their loaded drugs are released in large amounts at a time, potentially causing adverse side effects (White-Schenk et al. 2015). However, polymer nanoparticles can cross the blood-brain barrier, which is advantageous to SCI treatment due to the local nature of such injuries (Kreuter, 2014).

Silica nanoparticles on the other hand are very porous, giving them advantageous qualities such as zero-order drug release (i.e. a constant rate of release), enabling it to minimize interaction with the tissues surrounding an assigned area of treatment ; this is very beneficial because most of the loaded drug will be released in the affected area at a constant rate necessary for effective delivery (Ukmar and Planinsek, 2010; White-Schenk et al. 2015). Depending on the material format of silica nanoparticles conjugated with an appropriate polymer nanoparticle such as PEG, this multifunctional type of nanoparticle could potentially be used to treat acute spinal cord injuries through silica encapsulation, enabling the programmed nanoparticle to reach its target area and deliver the appropriate substance (Kreuter, 2014).

It is important that the successful treatment of an SCI entails stimulated and guided axon regrowth along a specific path (Zuidema et al., 2016). This ensures that the axons grow in the appropriate direction so that the healing process occurs properly (Zuidema et al., 2016). Multifunctional silica nanoparticles show promise in treating SCIs because of their ability to increase axonal sprouting through target specificity due to their zero-order drug release capability and their ability to cross the blood-brain barrier (Kreuter, 2014).

Based on the reviewed literature multifunctional silica particles are a more feasible treatment for tSCIs because controlled amounts of silica simultaneously minimize potential toxicity and ensure precise drug release in the targeted locality, while the polymer nanoparticles will ensure a safe crossing through the blood-brain barrier (Kreuter, 2014). Due to the lack of clinical research regarding the use of silica and polymer nanoparticles, it is difficult to draw conclusions on whether they can be used to effectively treat SCIs based on the minimal assessments that have been made using theoretical reasoning. Thus, the results obtained in these controlled studies cannot be directly translated to the treatment of acute tSCIs.

Potential of chABC-releasing nanoparticles

Glycosaminoglycans (GAGs) are linear acidic polysaccharides; these biomacromolecules are believed to be responsible for the inhibition of nerve regeneration following injury to the central nervous system and they constitute the side chains of CSPGSs (Prabhakar et al., 2005). CSPGs are major components of the extracellular matrix responsible for nerve regeneration failure (Prabhakar et al., 2005). Research has shown that one effective strategy to promote nerve regeneration is the removal of GAG side chains from the proteoglycan core protein in CSPGs using chABC (Massey et al., 2006).

ChABC is an enzyme that is purified from the bacterium Proteus vulgaris (Chondroitinase ABC for Neuroscience Research, 2016). This bacterium produces two related enzymes with broad substrate specificity; this includes chondroitinase ABC I (cABC I) and chondroitinase ABC II (cABC II) (Prabhakar et al., 2005). These two enzymes depolymerize a variety of GAG substrates including chondroitin 4-sulphate, dermatan sulphate, chondroitin 6-sulphate, and hyaluronic acid (Prabhakar et al., 2005). The principle of this depolymerization methodology is to remove GAGs which inhibit nerve regeneration in the spinal cord and promote functional recovery through axon regeneration and reactivation of plasticity through chABC treatment (Massey et al., 2006). Research suggests that there is a mobile functional change directly linked to anatomical evidence of sprouting by spinal cord primary afferents after chABC treatment, potentially decreasing the healing time of an SCI (Massey et al., 2006). Thus, the application of chABC in combination with precise nanoparticles increases their efficiency in treating SCIs (Massey et al., 2006). The application of chABC-releasing nanoparticles differs from that of silica and polymer nanoparticles: although silica and polymer nanoparticles would be effective in targeting and degrading the damaged nerve tissue of the spinal cord they do not promote nerve regeneration (White-Schenk et al. 2015). chABC-releasing nanoparticles remove GAGs from the damaged nerve tissue while still promoting rapid nerve regeneration (Prabhakar et al., 2005). Theoretically, this makes chABC-releasing nanoparticles a more effective method to treat SCIs

Currently, research in North America regarding the use of nanoparticles in SCI treatment is limited to model organisms, such as mice, to test the effectiveness of chABC releasing nanoparticles (Zuidema et al. 2016; Ikegami et al. 2005). chABC-releasing nanoparticles target CSPGs which are known to inhibit axon regeneration by creating glial scars on the spinal cord (Justin et al., 2014). Glial scars inhibit repairs to brain and spinal cord damage (Justin et al., 2014).

By targeting CSPGs to promote axon growth, chABC-releasing nanoparticles present an opportunity to improve the outcome of SCI treatment (Mahajan, 2018). Ikegami et al. (2005) performed chABC treatment combined with neural stem cell (NSC) transplantation to the injured spinal cord of rats and found that this enhanced growth associated with protein-43 axons. Protein-43 is also known as neuromodulin and is associated with axonal growth (Denny, 2006). The results of this study potentially imply that the use of neural stem cell transplantation in combination with chABC-releasing treatment may encourage axon growth and potentially speed up the healing process of a SCI (Ikegami et al. (2005).

A second study carried out by Zuidema et al. (2016) inflicted external physical force on mice to induce an acute tSCI. This study involved two experiments, where: (i) controlled nanoparticles were used to treat the tSCIs of one group of mice; and (ii) chABC-releasing nanoparticles were used to treat the tSCIs in a second group of mice (Zuidema et al., 2016). Upon comparing outcomes between groups, it was observed that the treatment with chABC-releasing nanoparticles resulted in rapid and enhanced axonal sprouting in the spinal cord in comparison to the controlled nanoparticles (Zuidema et al., 2016). This study could also be used to draw the conclusion that although nanoparticles are effective in targeting their assigned tissue localities, it is possible that chABC-releasing nanoparticles are more effective in encouraging axon growth due to their CSPG-targeting properties (Zuidema et al., 2016).

It is important to keep in mind that although chABC-releasing nanoparticles seem to encourage axonal growth, their instability as a compound makes it difficult to use them in an effective SCI treatment (Raspa et al. (2019) . To overcome this, Sasaki et al. (2015) proposed modifying them through site-directed mutagenesis or viral-mediated chABC gene delivery to host cells. These modifications seem theoretically reasonable, but changes to an enzyme such as chABC could have adverse health effects on the human body, and the enzyme itself could denature if the conditions in the body are unfavorable (Mahajan, 2018; Raspa et al. 2019). chABC-releasing nanoparticles have great potential, and their applications in the human spinal cord needs to be further studied.

CONCLUSIONS

Based on the evidence available in various studies, multifunctional silica-polymer nanoparticles are a more appropriate method of treatment for SCIs because of their ability to target specific regions with a zero-order drug release while safely crossing the blood-brain barrier (Kreuter, 2014) (White-Schenk et al. 2015). Although these nanoparticles can be made porous to avoid provoking the immune system (Zuidema et al., 2016) (Ukmar and Planinsek, 2010). More research is necessary to explore these characteristics in depth and to evaluate the potential use of silica and polymer nanoparticles and their application to SCI treatments.

Similarly, the limited research on chABC-releasing nanoparticles indicates that they can ensure maximum substrate specificity to lesion sites in encouraging nerve regeneration and may reduce the time of the healing process (Prabhakar et al., 2005). However, there are many factors to take into consideration when using nanoparticles to release chondroitinase ABC such as enzyme stability, bioavailability, and material used for encapsulation. It is important to further understand the various functions of the enzyme and its effect on the human body by performing additional research that explores its characteristics and functions.

Due to the limited research with regards to nanoparticles and their applications in SCI treatments, it is imperative that extensive research is done in order to further understand the potential function of each nanoparticle. Further steps would entail the testing of safety precautions of nanoparticle release in humans, potentially testing for allergenicity. Then, clinical trials could be carried out to give a better understanding as to whether designed nanoparticles are compatible with the human body in treating SCIs.

***The author would like to acknowledge the help of* Dr Francois Beaulieau.**

REFERENCES

[1] Amezcua, R., Vimbela, G., & Stout, D. A. (2017). Nanomaterials for Spinal Cord Injury Recovery. *Spine Research*, **03**(01), 1–4. https://doi.org/10.21767/2471-8173.10003

[2] Abou Neel, E. A., Bozec, L., Perez, R. A., Kim, H.-W., & Knowles, J. C. (2015). Nanotechnology in dentistry: prevention, diagnosis, and therapy. International Journal of Nanomedicine, 10, 6371–6394. http://doi.org/10.2147/IJN.S86033

[3] Beaulieu, F (2018). Physical Activity, Work and Health Ergonomy. Lecture. University of Ottawa

[4] Cho, Y., R. Shi, A. Ivanisevic, R.B. Borgens (2010) Functional silica nanoparticle-mediated neuronal membrane sealing following traumatic spinal cord injury. J Neurosci Res 88: 1433– 1444.

[5] Chondroitinase ABC for Neuroscience Research. (2016, October). Retrieved from http://www.amsbio.com/brochures/ChondroitinaseABC_flyer.pdf

[6] Denny, J. B. (2006, October). Molecular mechanisms, biological actions, and neuropharmacology of the growth-associated protein GAP-43. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2475799/

[7] Ellis, P. J. (2017). Nanodentistry: The benefits of nanotechnology in dentistry and its impact on oral health. Journal of Student Science and Technology, 10(2), 45–50. https://doi.org/10.13034/jsst.v10i2.218

[8] Gensel, J. C., & Zhang, B. (2015). Macrophage activation and its role in repair and pathology after spinal cord injury. Brain Research, 1619, 1–11. https://doi.org/10.1016/j.brainres.2014.12.045

[9] Gupta, J. Nanotechnology applications in medicine and dentistry. University of Toronto Libraries [online] 2010, 1, 1-16.

[10] Gupta, S., Rakesh, K., Gupta, O. P., Khanna, S., Purwar, A., & Verma, Y. (2013). Role of Nanotechnology and Nanoparticles in Dentistry: A Review. Int. J. Res. Dev, 1, 95-102.

[11] Gwinn, M. R., & Vallyathan, V. (2006). Nanoparticles: Health effects – Pros and cons. Environmental Health Perspectives, 114(12), 1818–1825. https://doi.org/10.1289/ehp.8871

[12] Ho, C. H., Triolo, R. J., Elias, A. L., Kilgore, K. L., DiMarco, A. F., Bogie, K., Vette, A. H., Audu, M. L., Kobetic, R., Chang, S. R., Chan, K. M., Dukelow, S., Bourbeau, D. J., Brose, S. W., Gustafson, K. J., Kiss, Z. H., & Mushahwar, V. K. (2014). Functional electrical stimulation and spinal cord injury. Physical medicine and rehabilitation clinics of North America, 25(3), 631–ix. https://doi.org/10.1016/j.pmr.2014.05.001

[13] Ikegami, T. , Nakamura, M. , Yamane, J. , Katoh, H. , Okada, S. , Iwanami, A. , Watanabe, K. , Ishii, K. , Kato, F. , Fujita, H. , Takahashi, T. , Okano, H. J., Toyama, Y. and Okano, H. (2005), Chondroitinase ABC combined with neural stem/progenitor cell transplantation enhances graft cell migration and outgrowth of growth-associated protein-43-positive fibers after rat spinal cord injury. European Journal of Neuroscience, 22 : 3036-3046. Doi :10.1111/j.1460-9568.2005.04492.x

[14] Infante, J. C. (2018). Nanoparticle-Based Systems for Delivery of Protein Therapeutics to the Spinal Cord. Frontiers in Neuroscience, 12, 484. http://doi.org/10.3389/fnins.2018.00484

[15] Justin R. Siebert, Amanda Conta Steencken, and Donna J. Osterhout, "Chondroitin Sulfate Proteoglycans in the Nervous System: Inhibitors to Repair," BioMed Research International, vol. 2014, Article ID 845323, 15 pages, 2014. https://doi.org/10.1155/2014/845323.

[16] Kazem Nejati-Koshki, Yousef Mortazavi, Younes Pilehvar-Soltanahmadi, Sumit Sheoran, Nosratollah Zarghami Biomed Pharmacother. 2017 Mar 23; 90: 85–92. Published online 2017 Mar 23. Doi: 10.1016/j.biopha.2017.03.035

[17] Kreuter, J. (2014) Drug delivery to the central nervous system by polymeric nanoparticles: what do we know? Adv Drug Deliv Rev 71: 2–14.

[18] LI, S., SUN, Y., & GAO, D. (2013). Role of the nervous system in cancer metastasis. Oncology Letters, 5(4), 1101–1111. http://doi.org/10.3892/ol.2013.1168

[19] Mahajan R. (2018). Chondroitinase ABC Enzyme: A Potential Treatment Option for Spinal Cord Injury. International journal of applied & basic medical research, 8(4), 203.

[20] Mantri, S. S., & Mantri, S. P. (2013). The nano era in dentistry. Journal of Natural Science, Biology, and Medicine, 4(1), 39–44. http://doi.org/10.4103/0976-9668.107258

[21] Massey, J. M., Hubscher, C. H., Wagoner, M. R., Decker, J. A., Amps, J., Silver, J., & Onifer, S. M. (2006, April 19). Chondroitinase ABC Digestion of the Perineuronal Net Promotes Functional Collateral Sprouting in the Cuneate Nucleus after Cervical Spinal Cord Injury. Retrieved from http://www.jneurosci.org/content/26/16/4406.long

[22] Noonan V, K, Fingas M, Farry A, Baxter D, Singh A, Fehlings M, G, Dvorak M, F: Incidence and Prevalence of Spinal Cord Injury in Canada: A National Perspective. Neuroepidemiology 2012;38:219-226. doi: 10.1159/000336014

[23] Prabhakar, V., Capila, I., Bosques, C. J., Pojasek, K., & Sasisekharan, R. (2005, February 15). Chondroitinase ABC I from Proteus vulgaris: Cloning, recombinant expression and active site identification. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1134771/

[24] Raspa, A., Bolla, E., Cuscona, C., & Gelain, F. (2019). Feasible stabilization of chondroitinase abc enables reduced astrogliosis in a chronic model of spinal cord injury. CNS neuroscience & therapeutics, 25(1), 86–100. https://doi.org/10.1111/cns.12984

[25] Rollerova, E., S. Scsukova, J. Jurcovicova, A. Mlynarcikova, E. Szabova, J. Kovriznych, D. Zeljenkova (2011) Polymeric nanoparticles – targeted drug delivery systems for treatment of CNS disorders and their possible endocrine disrupting activities. Endocr Regul 45: 49–60.

[26] Siebert, J.R., A. Conta Steencken, D.J. Osterhout (2014) Chondroitin sulfate proteoglycans in the nervous system: inhibitors to repair. Biomed Res Int 2014: 845323.

[27] Ukmar, T., O. Planinsek (2010) Ordered mesoporous silicates as matrices for controlled release of drugs. Acta Pharm 60: 373–385.

[28] White-Schenk, D., Shi, R., & Leary, J. F. (2015). Nanomedicine strategies for treatment of secondary spinal cord injury. International Journal of Nanomedicine, 10, 923–938. http://doi.org/10.2147/IJN.S75686

[29] Zuidema J, M, Gilbert R, J, Osterhout D, J, Nanoparticle Technologies in the Spinal Cord. Cells Tissues Organs 2015/2016;202:102-115

TABLES

Table 1 Summary of search strategy and results as of February 2019

No.	Search terms	PubMed results
1	SCI OR tSCI OR Acute OR Canada OR Nanoparticles OR Silica OR Polymer OR ChondroitinaseABC OR Proteoglycans	169

Adolescent cancer patient referral patterns in British Columbia

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Abstract Recent studies have suggested that adolescent cancer may have better survival outcomes when treated at paediatric centres, which better emphasize enrolment in clinical trials and have more capacity to support the social and emotional needs of adolescents. This study investigated 616 cancer cases in adolescents aged 15-18 from 1995 to 2010 in British Columbia, Canada with data from the Childhood, Adolescent, and Young Adult Cancer Survivors Research (CAYACS) Program of the BC Cancer Research Agency (BCCA). This study examined whether referrals to the adult centres BC Children's Hospital (BCCH) or BCCA were influenced by age, socioeconomic status, rurality, seasonality, radiotherapy treatment, different diagnoses based on the International Classification of Childhood Cancer (ICCC), and driving time to each centre. Between 1995 and 2010, only 27% of adolescent cancer patients in BC were referred to the BCCH, the only paediatric oncology centre in BC. Rural patients might have limited accessibility to BCCH, despite referral, due to travel restrictions and costs. As a result, patients are less likely to be referred to their closest cancer treatment centre as driving time increases (OR 0.995, P= 1.9e-10). Odds ratios of each modifier to BCCA or BCCH were calculated using univariate and multivariate logistic regression models in R Studio 3.5.1. Overall, 80% of younger adolescent (age 15-16) were referred to BCCH and only 14% of older adolescents (age 17-18) were referred to BCCH, which suggested that older adolescents were less likely than younger adolescents to be referred to BCCH (P= <2e-16). Additionally, leukaemia and Central Nervous System (CNS) cancer patients were more likely than all other patients to be referred to BCCH (P= 0.0014). The study of referral patterns is an essential factor when determining adolescent cancer survival rate.

Published online
30 December 2020

Citation
Li, A. (2020). Adolescent cancer patient referral patterns in British Columbia. *CJUR*, 5(2), 26-34.

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INTRODUCTION

On average, 412 adolescents in Canada aged 15-19 are diagnosed with cancer every year, and 73 die as a result (Canadian Cancer Registry, 2011). Over the past 50 years, the 5-year survival rate for childhood cancer (ages 0-14) has significantly increased by 40% in the United States due to improved therapy and supportive care. Nevertheless, the same progress is not seen for adolescent patients (ages 15-19). This is the "Adolescent and Young Adult Cancer Survival Gap", which is observed in the US and Canada and can be attributed to a combination of adolescent cancer biology, varying responses to treatment, and a lack of enrolment in clinical trials (Bleyer, 2005; Pollock, 2007). The site of adolescent cancer treatment matters because paediatric centres often place greater emphasis on clinical trial participation and provide greater psychosocial support for adolescents, which can ultimately lead to better survival outcomes (Pollock, 2007; Brand et al., 2016). In British Columbia, the BC Children's Hospital (BCCH) is the only children's oncology treatment centre; therefore, the first aim of this study investigates where adolescents with cancer are receiving their treatment and what factors influence those referral patterns that ensure best treatment practices.

More specifically to BC, adolescent patients living in the northern and southern interior may experience greater constraints in accessing care due to longer travel times to BCCH and the scarcity of care providers. Travel impedance has been known to be a controlling factor in the utilization of health care systems (Kanaroglou et al., 2016). Thus, the second aim of this study investigates whether driving time influences referral decisions for adolescent cancer patients in BC. Such an approach encompasses the perspective of health geography, where patients' locations can impede access to cancer treatment centres. Currently, there is no specialized adolescent cancer treatment unit nor universal guidelines for adolescent treatment at either paediatric or adult cancer centres in Canada or the US (Albritton & Bleyer, 2003).

This study analyzed data from 1995 to 2010 because the patient data up to 2010 was the most complete, comprehensive, and readily available. Despite the data being more than a decade old, the study on adolescent cancer patients' accessibility is one of the first in British Columbia. Moreover, the "Adolescent and Young Adult Cancer Survival Gap" still occurs across Canada and there still lacks systematic guidelines on how adolescent cancer patients should be referred and medical subspecialties that specifically treat adolescent cancer patients

METHODS

Data source

The patient data was collected from the Childhood, Adolescent, and Young Adult Cancer Survivors Research Program (CAYACS) by the BC Cancer Research Agency. The CAYACS program is a longitudinal cohort study that follows children and adolescent cancer patients from their initial diagnoses (McBride et al., 2010). Consent for personal data was given by the BC Cancer Research

Agency via a confidentiality agreement. This dataset included all individuals diagnosed with cancer (excluding non-melanoma skin cancer) between ages 15-18 inclusive (n= 616) from 1995 to 2010, who are BC residents at the time of diagnosis and survived at least one month from the diagnosis.

For this study, all BCCA centres were defined as adult centres (Vancouver Centre, Vancouver Island Centre, Fraser Valley Centre, Southern Interior Centre, Abbotsford Centre) while BCCH was the paediatric treatment centre. Between 1995 and 2010, the Southern Interior Centre was opened 3 April 1998 and the Abbotsford Centre was opened 25 August 2008. The Northern Centre was excluded from this study because it was opened in 2012. Therefore, the patient dataset was categorized as 1 January 1995 to 2 April 1998; 3 April 1998 to 24 August 2008; and 25 August 2008 to 31 December 2010.

Geocoding
The hospital locations were geocoded using the "Geocode Addresses Tool" in ArcGIS and the address locator was provided by the DMTI Route Logistic package. The DMTI Postal Code Suite contained polygon files of local delivery units (LDU) in BC that consist of 6-digit postal codes. Patient data was geocoded to the corresponding LDU.

Road network dataset
The road network dataset was created using the Network Analyst extension in ArcGIS from the DMTI Route Logistics package as a necessary procedure to produce driving times.

Driving time
Driving time of each patient to the closest cancer treatment centres was calculated using the OD cost matrix from the ArcGIS Network Analyst extension. In the driving time output, every patient had driving times to every centre calculated and ranked from shortest to longest. The shortest driving time to any centre indicated the closest facility for that patient.

Driving map
To visualize the driving times to the closest cancer treatment centre for patients in BC, aggregated dissemination areas (ADA) from Statistics Canada were used as the patient data was too small to represent the driving time for the entire province and spatial interpolation would not be accurate. After driving times were calculated for each ADA; driving time was categorized as falling within 1 hour, 1-2 hours, 2-5 hours, 5-10 hours, or 10+ hours (Figs. 1, 2, 3).

Statistical analysis
Univariate and multivariate logistic regressions between each modifier such as age, socioeconomic status (SES), ICCC categories, radiotherapy treatment, seasonality, rurality. Patients farther from paediatric centers were tested for whether they were referred to BCCH or BCCA on R Studio version 3.5.1., where odds ratios were calculated.

RESULTS

Population referral characteristics
Between 1995 and 2010, a total of 616 adolescents between ages 15-18 were diagnosed with cancer in BC. Table 1 highlights the distribution of referral to every cancer treatment centre in BC based on age, income, rurality, regional health authority catchment, seasonality, and diagnosis groups. Overall, 59% of patients were referred to BCCA and 27% were referred to BCCH. Among BCCA referrals, 30% of patients were referred to the Vancouver centre and only 6% were referred to the Southern Interior centre.

The univariate logistics regression models (Table 2) showed that only age and diagnosis groups including leukaemia, CNS, germ cell, and thyroid carcinoma had a statistically significant impact on referral. 63% of older adolescents were referred to BCCA while 80% of younger adolescents were referred to BCCH. This showed that patients between ages 17-18 were less likely than patients between ages 15-16 to be referred to paediatric centres (OR 0.14, P= <2e-16) which is the most expected result similar to previous studies (Table 2).

Although referrals to BCCA and BCCH seem to be evenly distributed between ICCC diagnosis, leukaemia and CNS patients were more likely than all other patients to be referred to BCCH (OR 2.23, P=0.0013; OR 2.42, P= 0.0014). Germ cell and thyroid carcinoma are both less likely than all other diagnoses to be referred to BCCH (OR 0.39, P= 0.0029; OR 0.27, P= 0.0348). Sarcoma patients were more likely to be referred to BCCH but not with statistical significance whereas lymphoma patients were less likely to be referred to BCCH based on the odds ratio (Table 2).

Patients of higher SES, urban locality, and who were closer to BCCH were more likely to be referred to BCCH but not with statistical significance. The overall referral characteristics showed that referral based on neighbourhood income quintile was evenly distributed across all centres. Referral to the Southern Interior centre consisted of 54% urban and 46% non-urban patients whereas referral to all other centres consisted of mostly urban patients. Additionally, whether a patient received radiotherapy treatment did not affect whether a patient was treated at BCCH.

The multivariate logistic regression model tested for the combined effect of all the modifiers on referral to BCCA or BCCH (Table 3). The model showed that age was the only factor that impacted referral to BCCA or BCCH after all the factors were accounted for (OR 0.13, P < 2e-16).

Driving time and referral
Fig. 1, 2, 3 visualized the overall distribution of driving time to the closest cancer centre across BC. From 1995 to 1998, the driving time was shortest for patients living the Vancouver lower mainland where which was within 1 hour of their closest treatment centre, gradually increasing as one moves away to other parts of BC. This is expected as there were three treatment centres (Vancouver centre, Fraser Valley centre and BC Children's) in the area, easing access to those three facilities for patients living there, translating to shorter driving times. Since the opening of the Southern Interior centre in 1998, driving time for patients in that area significantly decreased as indicated by the dark green cluster in Fig. 2. Nonetheless, driving time for patients in all the other parts of BC remained relatively the same. After the Abbotsford centre opened in 2008, the dark green region expanded further north and east from the Vancouver lower mainland, which shows that more patients had access to a cancer centre within 1 hour of driving time (Fig. 3). However, minimal change was observed in other parts of BC since the Abbotsford centre is still within the Fraser Valley, and often acts as an overflow centre to complement the Fraser Valley Centre in Surrey. The opening of the Southern Interior and Abbotsford

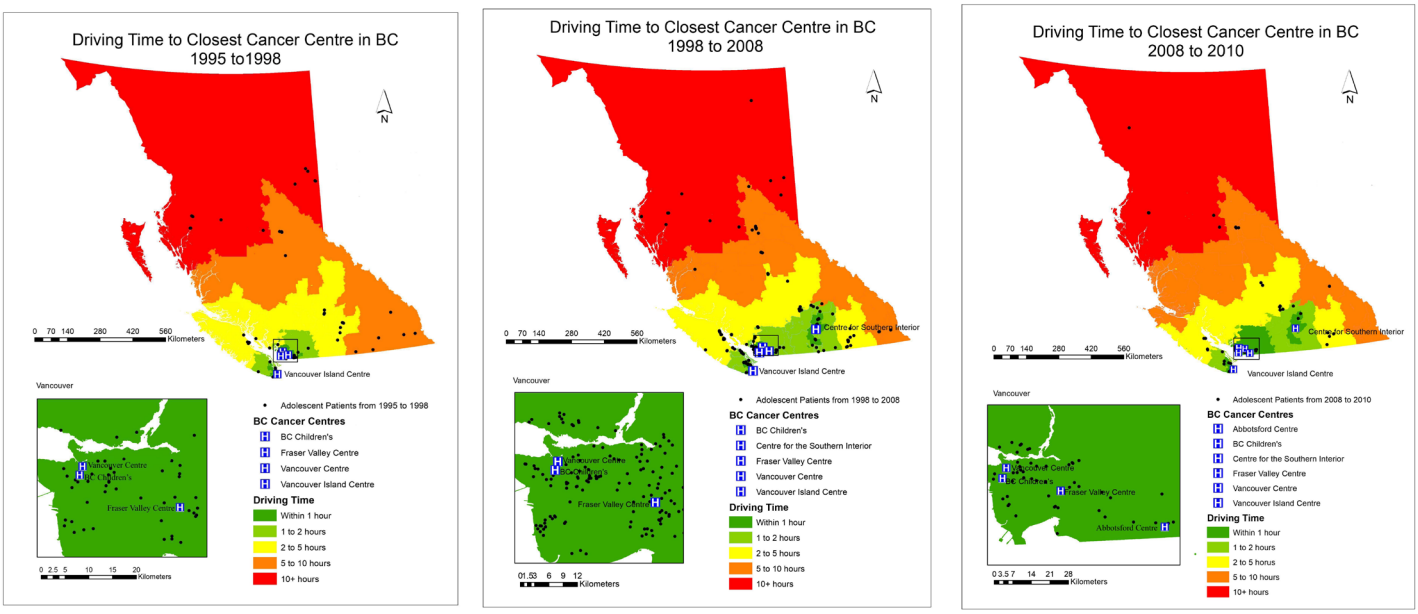

Fig. 1: (left) Driving time to the closest cancer centre for adolescents in BC between 1995 to 1998. Only cancer patients in the Lower Fraser Valley region and Southern Vancouver Island have within one hour driving time to their closest centre. Driving time increases radially from the clusters of short driving time to other parts of the province.

Fig. 2: (centre) Driving time to the closest cancer centre for adolescents in BC between 1998 to 2008. The opening of the Southern Interior centre benefited cancer population living in those regions where another cluster of population are within one hour to their closest centre in addition to the Lower Fraser Valley and Southern Vancouver Island cluster. Other areas remain the same.

Fig. 1: (right) Driving time to the closest cancer centre for adolescents in BC between 2008 to 2010. The opening of the Abbotsford centre largely benefited population within the Lower Fraser Valley extending eastward. The area where cancer population is within one hour of their closest cancer centre dramatically increased with the opening of this centre. Northern BC remain the least accessible to cancer centres.

centre shows that access to cancer treatment centre improved only locally. Between 1995 and 2010, 61% of patients were not referred to their closest treatment centre and only 35% were. As driving time increased, the patient's referred centre was less likely to be their closest treatment centre (OR 0.995, P= 1.9e-10).

DISCUSSION

Since older adolescents were less likely than younger adolescents to be referred to BCCH, age was one of the most important factors influencing referral which showed that older adolescents still had limited access to BCCH. This result is consistent with the lower referral rate to paediatric centres for patients aged 18-19 compared to those aged 15-17 according to a 2004 study by the Canadian Childhood Cancer Surveillance and Control Program (Klein-Geltink et al., 2004). To illustrate the effect of age on referral, the multivariate logistic regression also demonstrated that age was the only factor that had a statistically significant impact on referral when all the tested factors were combined.

Similarly, studies in North Carolina, Washington State, Georgia and Ohio found that referral to paediatric centres significantly decreased as adolescent age increases from 15 to 19 (Gordon et al., 2018; Howell et al., 2007; Yeager, et al., 2006). The contributing factor could be the physician conducting the referral: for example, although there is no defined age limit for adolescents to be treated at BCCH, there might still be a "perceived age limit" by the physician even though it might be beneficial for patients in their early 20s to be referred to paediatric centres (Gordon et al., 2018). Moreover, paediatric primary care physicians (PCP) were more likely to refer their patients to paediatric centres if they had colleagues that they personally knew working in these centres (Gordon et al., 2018).

Older adolescents living in rural areas of BC might prefer a BCCA centre because it is geographically closer and they can drive themselves to the treatment sessions despite the more specialized care provided in BCCH (Albritton et al., 2007). Older adolescent patients might also be reluctant to receive treatment at BCCH because they do not want to be perceived as children and want to be more connected to their peers who are also entering adulthood (Albritton et al., 2007; Howell et al., 2017; Klein-Geltink et al., 2005). The result showed that as driving time increased, adolescent patients were less likely to be referred to their closest centre, which can benefit rural patients. Since the driving time to their closest BCCA might be just as far as BCCH, families might choose BCCH instead due to better treatment options. In general, improved survival outcomes were seen at the paediatric centre because they provided supportive care more tailored towards the emotional needs of adolescents and inpatient care which improves survival outcomes in cases of adverse complications (Howell et al., 2007). More importantly, lack of access to BCCH for these older adolescents might suggest lack of enrolment in clinical trials, which may significantly impact their survival outcome (Parsons et al., 2015).

Referral was also influenced by diagnosis. Leukaemia (all subgroups) and CNS tumour patients were more likely than patients with other cancers to be referred to BCCH. According to the Surveillance, Epidemiology, and End Results (SEER) Program, 68.2% of average annual incidence per million of leukaemia from 1975-2000 occurred in children less than 5 years old (Bleyer et al., 2006). Similarly, higher incidence of CNS tumours was seen in children under 5 (33.7%) compared to adolescents between ages 15-19 (19.2%). This suggests that adolescent patients with cancer more commonly seen in younger children are more likely to be referred to BCCH. This is important when considering the survival

outcome of referrals because the 5-year survival rate for leukaemia is often lower when it is not treated at paediatric centres (Howell et al., 2007).

Patients diagnosed with germ cell and thyroid carcinoma were less likely to be referred to BCCH and both cancers were more common in the older teens than in younger children according to the SEER Program (Bleyer et al., 2006). Those patients diagnosed with germ cell and thyroid carcinoma may also be seen by physicians with surgical specialties, which decreases their chances of being referred to BCCH (Albritton et al., 2007; Parsons et al., 2015).

Other ICCC diagnoses also affect referral but not with statistical significance. Bone tumours and soft tissue sarcomas are more likely to be treated at a paediatric centre where survival for patients with those cancers is usually favored (Howell et al., 2007). Lymphoma patients are less likely to be referred to BCCH, which is surprising because lymphoma is usually considered a more "paediatric-specific cancer" (Bleyer et al., 2006). This suggests a potentially unfavourable survival outcome for those lymphoma patients treated at BCCA, since survival may improve when they are treated at BCCH instead (Parsons et al., 2015). Furthermore, SES, rurality, seasonality, and distance to BCCH, which are internally correlated factors, did not influence referral with statistical significance. Since lower SES and rural patients are expected to have less accessibility to BCCH, the logistic regression showed that referral patterns were in fact not as affected by those factors than by age and diagnosis. This reflects health care access equality in British Columbia under the premise of this study.

Of greater implication for referral location is the patient's potential survival rate. Each category of adolescent cancer has biologically distinct characteristics and thus requires careful consideration of whether an adult or paediatric center will be better suited for a particular patient (Wolfson et al., 2014). There are major benefits when treated is received at a paediatric centre, such as participation in clinical trials, peer support, and better follow-up care (De et al., 2011). Given the uniqueness of adolescent cancer, referral decisions are often complex and there is no "one size fits all" solution.

CONCLUSIONS

This study suggests that patients who were younger, of higher SES, urban, suffered from lymphoma, sarcoma, without radiotherapy, not traveling in the winter, and located farther from an adult centre would be more likely to be referred to BCCH. More specifically, age and diagnosis were the two major factors affecting adolescent cancer patient referrals in British Columbia. From a physician's perspective, the awareness that older adolescents might be better treated at paediatric centres is critical (Yeager et al., 2006). Additional systematic efforts should also be implemented such as developing hospital policies that facilitate the appropriate referral based on each adolescent's age and diagnosis, and improving access to these appropriately referred treatment centres to further reduce the AYA cancer gap (Gordon et al., 2018; Parsons et al., 2015). Currently, the Adolescent and Young Adult Committee has prioritized the identification of new treatment protocols tailored towards treating adolescent cancer, improving psychosocial support during therapy, and increasing the participation in clinical trials (Pollock, 2007).

It should be noted that referral location may differ from where patients actually receive treatment, because such data is not available through the CAYACS program. Nonetheless, this study contributed insights on access to adolescent cancer care in BC, with the additional dimension of driving time. This can also be considered in the planning of another paediatric hospital or cancer centre in other parts of BC, while further informing paediatric and adult oncologists about referral and survival patterns. Since the Northern BC Centre was omitted in this study due to the limited dataset timeline, this project should be repeated when data after 2012 becomes available. Furthermore, the two studies could be compared to analyze whether the Northern centre increased accessibility to care and survival for adolescents living in Northern BC. As a critical next step to this study, the 5-year survival outcome for this cohort and enrolment in clinical trials based on referral difference should also be examined.

The author would like to thank **Dr Martin Putterman** ***"for introducing me to Mary McBride, the program leader of CAYACS, who made this entire project possible",*** **Mary McBride** ***and*** **Dr Meera Rayar** ***who "came up with the research topic and objectives which I was able to investigate",*** **Dr Brian Klingenberg** ***"for supervising this directed study",*** **Dr. Trevor Dummer** ***"for helping with the study design and consultation", and*** **Yang Zhang** ***and*** **Terry Tang** ***who "have offered tremendous help in the CAYAC data organization".***

REFERENCES

[1] Albritton, K., & Bleyer, W. A. (2003, December). The management of cancer in the older adolescent. Retrieved April 3, 2019, from https://www.ncbi.nlm.nih.gov/pubmed/14642921

[2] Albritton, K. H., Wiggins, C. H., Nelson, H. E., & Weeks, J. C. (2007). Site of oncologic specialty care for older adolescents in utah. Journal of Clinical Oncology, 25(29), 4616-4621. doi:10.1200/JCO.2006.08.4103

[3] Bleyer, A. (2005). The adolescent and young adult gap in cancer care and outcome. Current Problems in Paediatric and Adolescent Health Care, 35(5), 182-217. doi:10.1016/j.cppeds.2005.02.001

[4] Bleyer, A, O'Leary, M, Barr, R, Ries, L.A.G. (2006). Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000. National Cancer Institute, NIH Pub. No. 06-5767. Bethesda, MD 2006.

[5] Brand, S. R., Pickard, L., Mack, J. W., & Berry, L. L. (2016). What Adult Cancer Care Can Learn From Paediatrics. Journal of oncology practice, 12(9), 765–767. doi:10.1200/JOP.2016.015057

[6] De, P., Ellison, L. F., Barr, R. D., Semenciw, R., Marrett, L. D., Weir, H. K., . . . for the Steering Committee for Canadian Cancer Statistics. (2011). Canadian adolescents and young adults with cancer: Opportunity to improve coordination and level of care. Canadian Medical Association Journal (CMAJ), 183(3), E187-E194. doi:10.1503/cmaj.100800

[7] Gordon, L. M., Johnson, R. H., Au, M. A., Langer, S. L., & Albritton, K. H. (2018). Primary care physicians' decision making regarding initial oncology referral for adolescents and young adults with cancer. Journal of Adolescent Health, 62(2), 176-183. doi:10.1016/j.jadohealth.2017.09.006

[8] Howell, D. L., Ward, K. C., Austin, H. D., Young, J. L., & Woods, W. G. (2007). Access to paediatric cancer care by age, race, and diagnosis, and outcomes of cancer treatment in paediatric and adolescent patients in the state of georgia. Journal of Clinical Oncology, 25(29), 4610-4615. doi:10.1200/JCO.2006.07.6992

[9] Kanaroglou, P., Delmelle, E., Páez, A., & Taylor & Francis eBooks A-Z. (2015;2016;). Spatial analysis in health geography (New ed.). Farnham, Surrey, UK, England;Burlington, VT, USA;: Ashgate. doi:10.4324/9781315610252

[10] Klein-Geltink, J., Shaw, A. K., Morrison, H. I., Barr, R. D., & Greenberg, M. L. (2005). Use of paediatric versus adult oncology treatment centres by adolescents 15–19 years old: The canadian childhood cancer surveillance and control program. European Journal of Cancer, 41(3), 404-410. doi:10.1016/j.ejca.2004.10.023

[11] McBride, M. L., Rogers, P. C., Sheps, S. B., Glickman, V., Broemeling, A., Goddard, K., . . . Xie, L. (2010). Childhood, adolescent, and young adult cancer survivors research program of british columbia: Objectives, study design, and cohort characteristics. Paediatric Blood & Cancer, 55(2), 324-330. doi:10.1002/pbc.22476

[12] Parsons, H. M., Harlan, L. C., Schmidt, S., Keegan, T. H. M., Lynch, C. F., Kent, E. E., . . . the AYA

[13] Pollock, B. H. (2007). Where adolescents and young adults with cancer receive their care: Does it matter? Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 25(29), 4522-4523. doi:10.1200/JCO.2007.12.1715

[14] Statistics Canada. (2018, March 12). 2010 Census Boundary files. Retrieved February 3, 2019, from https://www12.statcan.gc.ca/census-recensement/2011/geo/bound-limit/bound-limit-2016-eng.cfm

[15] Statistics Canada. (2019, January 28). Canadian Cancer Registry (CCR). Retrieved February 2, 2019, from http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3207

[16] Wolfson, J., Sun, C., Kang, T., Wyatt, L., D'Appuzzo, M., & Bhatia, S. (2014). Impact of treatment site in adolescents and young adults with central nervous system tumors. JNCI : Journal of the National Cancer Institute, 106(8), dju166-dju166. doi:10.1093/jnci/dju166

[17] Yeager, N. D., Hoshaw-Woodard, S., Ruymann, F. B., & Termuhlen, A. (2006). Patterns of care among adolescents with malignancy in ohio. Journal of Paediatric hematology/oncology, 28(1), 17.

TABLES

Table 1 Characteristics of the study population overall and by referral centre

Characteristic	Overall	Any BCCA	No referral	Centre for the Southern Interior
Number of patients	616 (100%)	364 (59%)	84 (13%)	37 (6%)
Average age at diagnosis				
Younger	288 (47%)	134 (37%)	19 (23%)	9 (24%)
Older	328 (53%)	230 (63%)	65 (77%)	28 (76%)
Neighbourhood income quintile				
1	101 (16%)	63 (17%)	12 (14%)	11 (30%)
2	120 (19%)	63 (17%)	15 (18%)	6 (16%)
3	110 (18%)	73 (20%)	14 (17%)	9 (24%)
4	121 (20%)	67 (18%)	25 (30%)	5 (14%)
5	130 (21%)	71 (20%)	14 (17%)	5 (14%)
9	34 (6%)	27 (7%)	< 6 (5%)	< 6 (3%)
Residence				
Urban	510 (83%)	301 (83%)	62 (74%)	20 (54%)
Non-urban	95 (15%)	57 (16%)	18 (21%)	17 (46%)
Unknown	11 (2%)	6 (2%)	< 6 (5%)	0 (0%)
Regional health authority				
Interior	102 (17%)	60 (16%)	18 (21%)	37 (100%)
Fraser Valley	215 (35%)	131 (36%)	24 (29%)	0 (0%)
Vancouver Coastal	126 (20%)	74 (20%)	13 (15%)	0 (0%)
Vancouver Inland	106 (17%)	63 (17%)	13 (15%)	0 (0%)
Northern	56 (19%)	30 (8%)	12 (14%)	0 (0%)
Unknown	11 (2%)	6 (2%)	< 6 (5%)	0 (0%)
Seasonality				
Winter	230 (37%)	117 (32%)	15 (18%)	15 (41%)
Other	386 (63%)	247 (68%)	69 (82%)	22 (59%)
Diagnosis group				
Leukaemia	83 (13%)	41 (11%)	5 (6%)	3 (8%)
Lymphoma	155 (25%)	100 (27%)	13 (15%)	12 (32%)
CNS	78 (3%)	30 (8%)	18 (21%)	1 (3%)
Bone tumour and soft tissue carcinoma	91 (15%)	53 (15%)	6 (7%)	5 (14%)
Germ cell	88 (14%)	65 (18%)	10 (12%)	7 (20%)
Thyroid carcinoma	34 (6%)	23 (6%)	8 (10%)	2 (5%)
All other	82 (13%)	52 (14%)	19 (23%)	7 (19%)
Unknown	< 6 (1%)	0 (0%)	< 6 (6%)	0 (0%)

TABLES (CONT'D)

Table 1 (cont'd) Characteristics of the study population overall and by referral centre

Characteristic	Fraser Valley Centre	Vancouver Centre	Vancouver Island Centre	BCCH
Number of patients	85 (14%)	186 (30%)	56 (9%)	168 (27%)
Average age at diagnosis				
Younger	23 (27%)	78 (42%)	24 (43%)	135 (80%)
Older	62 (73%)	108 (58%)	32 (57%)	23 (14%)
Neighbourhood income quintile				
1	13 (15%)	31 (17%)	9 (16%)	26 (15%)
2	15 (18%)	34 (18%)	8 (14%)	42 (25%)
3	37 (44%)	37 (20%)	14 (25%)	23 (14%)
4	10 (12%)	30 (16%)	10 (18%)	29 (17%)
5	0 (0%)	39 (21%)	12 (21%)	45 (27%)
9	7 (8%)	15 (8%)	< 6 (5%)	< 6 (2%)
Residence				
Urban	81 (95%)	149 (80%)	52 (93%)	147 (87%)
Non-urban	< 6 (5%)	35 (1%)	3 (5%)	20 (12%)
Unknown	0 (0%)	2 (1%)	1 (2%)	< 6 (1%)
Regional health authority				
Interior	0 (0%)	25 (13%)	0 (0%)	24 (14%)
Fraser Valley	83 (98%)	48 (26%)	0 (0%)	60 (36%)
Vancouver Coastal	1 (1%)	73 (39%)	0 (0%)	39 (23%)
Vancouver Inland	0 (0%)	9 (5%)	55 (98%)	30 (18%)
Northern	1 (1%)	29 (16%)	0 (0%)	14 (8%)
Unknown	0 (0%)	2 (1%)	1 (2%)	< 6 (1%)
Seasonality				
Winter	25 (29%)	62 (33%)	15 (27%)	55 (33%)
Other	60 (71%)	124 (67%)	41 (73%)	113 (67%)
Diagnosis group				
Leukaemia	6 (7%)	27 (15%)	5 (9%)	37 (22%)
Lymphoma	18 (21%)	58 (31%)	13 (23%)	42 (25%)
CNS	9 (11%)	16 (9%)	5 (9%)	30 (18%)
Bone tumour and soft tissue carcinoma	12 (14%)	30 (16%)	6 (11%)	32 (19%)
Germ cell	19 (22%)	26 (14%)	13 (23%)	13 (8%)
Thyroid carcinoma	9 (11%)	8 (4%)	< 6 (5%)	< 6 (2%)
All other	12 (14%)	2 (11%)	11 (20%)	11 (7%)
Unknown	0 (0%)	0 (0%)	0 (0%)	0 (0%)

TABLES (CONT'D)

Table 2 Odds ratio comparing factors that affect likelihood of referral to BCCA or BCCH

Factor	Odds ratio (CI 95%)	P value
Age		
Younger	Reference	-
Older (17-18)	0.14 (0.091- 0.22)	<2e-16
SES		
Lower	Reference	-
Higher (categories 1-2)	1.17 (0.80-1.71)	0.406
Radiotherapy		
Yes	0.91 (0.61-1.35)	0.65
No	Reference	-
Residence		
Non-urban	Reference	-
Urban	1.39 (0.82-2.45)	0.235
Seasonality		
Winter	Reference	-
Non-winter	0.844 (0.58-1.23)	0.372
BCCH is closest treatment centre		
Yes	1.55 (0.88-2.69)	0.121
No	Reference	-
Diagnosis group		
Leukaemia	2.23 (1.36-3.63)	0.0013
Lymphoma	0.88 (0.58-1.33)	0.549
CNS	2.42 (1.40-4.18)	0.0014
Bone tumours & soft tissue sarcomas	1.38 (0.85-2.23)	0.19
Germ cell	0.39 (0.20-0.70)	0.0029
Thyroid carcinoma	0.27 (0.063-0.79)	0.0348
All other	0.42 (0.20-0.80)	0.0123

TABLES (CONT'D)

Table 3 Multivariate logistic regression model affecting likelihood of referral to BCCA or BCCH

Factor	Odds ratio (CI 95%)	P value
Age		
Younger	Reference	-
Older (17-18)	0.13 (0.08- 0.21)	<2e-16
SES		
Lower	Reference	-
Higher (categories 1-2)	1.23 (0.80-1.88)	0.34
Radiotherapy		
Yes	1.01 (0.67-1.68)	0.78
No	Reference	-
Residence		
Non-urban	Reference	-
Urban	1.35 (0.70-2.69)	0.235
Seasonality		
Winter	Reference	-
Non-winter	0.91 (0.59-1.41)	0.684
BCCH is closest treatment centre		
Yes	1.57 (0.86-2.38)	0.085
No	Reference	-
Diagnosis group		
Leukaemia	0.82 (0.26-1.90)	0.65
Lymphoma	0.73 (0.34-1.57)	0.421
CNS	0.91 (0.37-2.20)	0.834
Bone tumours & soft tissue sarcomas	0.37 (0.32-1.68)	0.19
Germ cell	1.22 (0.54-2.79)	0.618
Thyroid carcinoma	0.91 (0.25-2.99)	0.882
All other	1.21 (0.52-2.79)	0.65