HEALTH, HEALTH RELATED QUALITY OF LIFE AND EXECUTIVE FUNCTIONING IN YOUNG ADULTS DIAGNOSED WITH FETAL ALCOHOL SPECTRUM DISORDER

by

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Health, Health Related Quality of Life and Executive Functioning in Young Adults Diagnosed With Fetal Alcohol Spectrum Disorder

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Abstract

Fetal Alcohol Spectrum Disorder (FASD) is a disorder caused by prenatal alcohol exposure which leads to neurobehavioral, psychological, and adaptive functioning impairments. It has been well established that executive functioning in this population is significantly impaired. Further, recent research has demonstrated that when compared to the general population, the FASD population has a greater prevalence of chronic health conditions including auto-immune disorders, immune conditions, cardiac disease, and glucose tolerance abnormalities. Executive functioning skills are important in managing chronic health conditions and research has demonstrated that they influence quality of life in multiple clinical populations. However, this relationship has not been examined in the FASD population, where executive functioning deficits are characteristic. Therefore, the purpose of the present study is to understand how executive functioning ability in young adults diagnosed with FASD relates to the presence of their chronic health condition(s) as well as their health related quality of life. To our knowledge, previous research has not investigated these variables in this population before and so this research is considered exploratory. Young adults (between age 15-29) diagnosed with FASD or FAS who were fluent in English were recruited to participate. A total of 12 participants were included in the analysis, with exactly half being diagnosed with at least one chronic health condition, and the majority of participants reporting some impairment in health related quality of life and in executive functioning. Non-parametric statistics (specifically Spearman Rank Correlations and the Mann-Whitney U test) were used to analyze the data. The findings suggest a relationship between the presence of chronic health conditions and health related quality of life, and between executive functioning and health related quality of life. A relationship was not observed between the presence of chronic health conditions and executive function.

Lay Summary

Fetal Alcohol Spectrum Disorder (FASD) is a neurobehavioral disorder caused by alcohol exposure to a fetus before birth. Recent research has demonstrated that individuals with FASD also experience chronic illnesses to a greater degree when compared to the general population, which can impact quality of life. A characteristic of FASD is pronounced difficulties in executive functioning (planning and organization skills), which are important to be able to manage chronic health conditions. Difficulty in the management of chronic illness can negatively impact one's quality of life. The purpose of this study is to understand how executive functioning ability in young adults diagnosed with FASD relates to the presence of chronic health condition(s) as well as their health related quality of life.

Preface

This thesis is the original and unpublished work of the author, Aisha Ghani, under the advisement of her research supervisor, Dr. Rachel Weber. The UBC Ethics Certificate number H19-033 approved the work reported in the methodology and results sections of this thesis. The research design and analysis of research data was done independently by the author, and data collection and entry were completed by the author, Aisha Ghani.

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I. Literature Review

Fetal Alcohol Spectrum Disorder

Fetal Alcohol Spectrum Disorder (FASD) is a neurodevelopmental health condition with a broad spectrum of presentations and disabilities due to alcohol exposure in utero (Cook et al., 2016). Generally, individuals with FASD experience difficulties with mental health as well as physical, behavioural and learning abilities (Chudley et al., 2005; Cook et al., 2016; Khoury, Milligan & Girard, 2015). The estimated prevalence of FASD in Canada is 1 in 100 births, which results in over 300,000 individuals across Canada being affected (Cook et al., 2016), and making it the primary cause of developmental disability in the country (Pei, Tremblay, McNeil, Poole & McFarlane, 2017). Because individuals with FASD include those that have behavioural and cognitive deficits but may experience little to no physical features associated with prenatal alcohol exposure, diagnosis in adulthood can be challenging (Chudley, Kilgour, Cranston & Edwards, 2007). As such, information on the prevalence of FASD in adulthood is minimal. It has also been established that the health conditions that adults with FASD face are largely different from the diagnostic criteria used to diagnose infants and children (Lunde et al 2016).

At birth, defining symptoms of FASD are low birthweight/growth deficiency, dysmorphic facial features, and neurological impairment, among others (Hoyme et al., 2005). As individuals with FASD get older, an association develops with increased obesity (Fuglestad et al., 2014) and endocrine dysfunction (Hellemans, Verma, Yoon, Yu, & Weinberg, 2008) as well as neurobehavioral and mental health concerns. These associated conditions are complex, require a high level of care and are associated with high cost (Lunde et al 2016). FASD has been determined to be a public health priority in Canada; in 2013, the cost associated with FASD in

Canada was estimated to be about 1.8 billion. Therefore, there has been an increase in efforts toward research, prevention and intervention in recent years (Pei et al., 2017).

In 2016, new guidelines for FASD diagnosis were released by Cook and colleagues (2016). After confirmation of alcohol exposure through maternal pregnancy history and/or presence of sentinel features, a diagnosis of FASD requires evidence of pervasive brain dysfunction, which is determined through a neurodevelopmental assessment. Specifically, there must be a severe impairment (i.e. two standard deviations below the mean) in three or more neurodevelopmental domains. These domains include "motor skills; neuroanatomy/ neurophysiology; cognition; language; academic achievement; memory; attention; executive function, including impulse control and hyperactivity; affect regulation; and adaptive behaviour, social skills or social communication" (p. 193). As stated, executive functioning is one of the neurodevelopmental domains that is affected in FASD. Executive functioning can also impact the other neurodevelopmental domains mentioned, including language, affect regulation and adaptive behaviour (Cook et al., 2016; Doyle et al., 2018; Mattson, et al., 2011). This highlights the importance in understanding the nature of executive functioning in individuals with FASD.

The neurobehavioral profile of individuals with FASD or prenatal alcohol exposure is not clearly identified, as the impairments are complex and vary from one person to the next (Kodituwakku, 2009; Mattson, et al., 2011; Rasmussen et al., 2013). Different doses and patterns of prenatal alcohol exposure are associated with different profiles. More specifically, the amount of alcohol to which an individual has been exposed is correlated with the severity of outcome (Mattson, Crocker & Nguyen, 2011; Sood et al. 2001; Streissguth et al., 1989). The pattern of alcohol exposure can also moderate these effects, in that binge exposure leads to greater deficits than chronic exposure. Furthermore, the timing of exposure during pregnancy can differentially

impact function and neural structure (Guerri et al., 2009; Mattson et al., 2011). Prenatal alcohol exposure impacts the structure of the brain in a widespread manner and can lead to variable neurocognitive deficits (Lebel et al. 2011; Norman et al. 2013). Depending on the trimester, amount of alcohol consumed, blood alcohol level, and duration of exposure, different effects on brain structure and function may be observed (Chudley et al., 2007). There does not appear to be a specific region that is solely affected, as abnormalities have been observed in multiple brain areas, including the corpus callosum, cerebellar vermis, basal ganglia, hippocampus, and thalamic nuclei (Fryer et al., 2007; Mattson, et al., 2011; Streissguth et al., 1991). Furthermore, microcephaly is a characteristic feature of FASD, highlighting alcohol exposure's global impact on the brain (Cook et al., 2016). As the impact of prenatal alcohol exposure on the brain is highly variable and includes changes in both specific regions and the brain as a whole, the neurobehavioral deficits observed in this population are also highly variable. Specifically, cognitive and behavioural deficits including executive functioning can vary between individuals. This contributes to the difficulty of identifying a neurobehavioral profile for FASD and understanding the nature of these deficits.

Executive Functioning

A universally accepted definition has not yet emerged (Jurado & Rosselli, 2007), however executive functions are commonly described as higher order cognitive processes that are required to achieve goal-directed behaviour (Khoury & Milligan, 2016; Miller & Cohen, 2001). While some argue conceptualizing executive functioning as a unitary construct (e.g. Baddeley & Hitch, 1974), others believe executive functions to be an umbrella term for multiple cognitive abilities (e.g. Diamond, 2013; Miyake et al., 2000). The list of different executive functioning abilities varies, with 15-plus abilities appearing in current literature; however, the

most commonly reported abilities of executive function are inhibition, working memory, shifting, and planning (Best et al., 2009). Executive functions are integral abilities for daily functioning and include self-regulation, planning and organizing, and problem solving (e.g. Best et al., 2009; Khoury & Milligan, 2016; Miller & Cohen, 2001). Furthermore, executive functioning skills are able to predict one's academic success and learning (e.g. Clark, Pritchard, & Woodward, 2010; Miller & Hinshaw, 2010; Samuels, Tournaki, Blackman, & Zilinski, 2016). Deficits in executive functioning may have detrimental effects on school performance, adherence to treatment, medical management, daily functioning and quality of life in medical populations (Hooper et al., 2015).

Due to the heterogeneity of executive function definitions, measuring said abilities can be a challenge. There are often multiple assessments available to researchers for a single ability. This can make it a challenge to directly compare studies as the assessments may differ in key areas (e.g. visual versus verbal presentation of stimuli; Khoury & Milligan, 2016). Because of the complexities associated with measuring executive functions, Miyake and colleagues (2000) introduced an integrative framework for executive function that consists of three key abilities. These three abilities are lower level executive functions (Miyake et al., 2000). They are most likely involved in the performance of other more complex executive functioning tasks and therefore are thought to serve as a proxy for one's ability on more complex executive functioning abilities (Miyake et al., 2000). The first executive function in the model is shifting between tasks, operations, or mental sets (i.e. shifting; Monsell, 1996). The second executive function is updating and monitoring working memory representations (Miyake et al., 2000; i.e., working memory). This requires one's ability to manipulate information in immediate memory and then use that information for a given task. The third executive function is the inhibition of dominant

or proponent responses (Miyake et al., 2000). One's ability to inhibit automatic responses when required is a controlled and deliberate process. Confirmatory factor analysis has supported Miyake and colleagues' model. The three different executive functioning abilities were moderately correlated with each other; however, they were also separable and independent. In addition, research on typically developing individuals shows that there is a different pattern of brain activation during tasks of working memory, set shifting and inhibition, providing further support for this model (Bissonette et al., 2013; Kamigaki et al., 2012; Kawashima et al., 1996; Khoury, Milligan & Girard, 2015; Levy & Goldman-Rakic, 2000; Nakahara et al., 2002).

Fetal Alcohol Spectrum Disorder and Executive Functioning

Multiple studies demonstrate that executive functions are impacted for individuals with FASD (e.g. Cook et al., 2016; Kodituwakku, 2009; Rasmussen et al., 2013). In a meta-analysis of 15 studies (Khoury & Milligan, 2016), it was concluded that children and adolescents prenatally exposed to alcohol do have executive functioning difficulties when compared to children not exposed to alcohol, with the effect size being in the upper limit of the medium range. Another meta-analysis on FASD and executive functioning was completed using Miyake et al.'s model of executive function as a framework and included 46 studies with 3735 participants (Khoury et al., 2015). After controlling for publication bias, their analysis revealed a medium effect size for the overall difference in executive function performance between FASD and non-FASD controls, with individuals with FASD performing worse. Specifically, a medium effect size was found with 23 studies for working memory and inhibitory control.

Regarding working memory, there was a difference between groups based on the type of working memory task used, with the Wechsler Scale of Intelligence for Children (WISC) and Working Memory Index (WMI) showing the greatest difference (Khoury et al., 2015). Regarding

both working memory and inhibitory control, the results differed significantly based on the Intelligence Quotient (IQ) of the participants, in that studies in which there was a large IQ discrepancy between the groups also tended to show a greater difference in executive function performance (Khoury et al., 2015). Lastly, the effect size for set shifting was large, with a total of 16 studies being included in the analysis (Khoury et al., 2015); the authors proposed that the reason set-shifting demonstrated the largest effect could be due to the complexity of the task used to assess set shifting (e.g. Wisconsin Card Sorting Task). This task may also rely on other cognitive processes, including inhibition and working memory (Best and Miller 2010; Mattson et al. 2011; Miyake et al. 2000). Alternatively, they suggest that set shifting may be more highly affected by prenatal alcohol exposure.

To measure executive functioning, studies have used behavioural ratings and neuropsychological tests, and both have demonstrated executive functioning deficits in the FASD population (Mohamed, Carlisle, Livesey & Mukherjee, 2019; Rai et al., 2017). Specifically, studies investigating executive functioning in children with FASD through parental reports on the Behaviour Rating Inventory of Executive Function (BRIEF) have found that considerable difficulties with executive functioning exist in this population, supporting the results of meta-analyses (Mohamed et al., 2019; Rai et al., 2017; Rasmussen et al., 2010; Rasmussen, Horne, & Witol, 2006). This is reflected through high scores on the general scales, as well as individual scales, with the working memory scale showing the greatest deficits (Rai et al., 2017). However, Rai et al. (2017) noted that multiple studies have not considered potential moderators such as gender, or the presence of other conditions such as ADHD and depression, which are also associated with executive functioning difficulties. Mohamed et al. (2019) examined the relationship between the BRIEF and the Delis–Kaplan Executive Function System

(DKEFS) for children diagnosed with FASD, finding clinical elevations on all BRIEF indices except for organization of materials and indicating executive function deficits, which is consistent with other literature. Regarding the DKEFS, 15 out of 18 subtests were significantly below the normative mean, reflecting difficulty in inhibiting thoughts, generating abstract thoughts, and flexibility of thinking. This is consistent with the results obtained by Rai et al. (2017). While there was a high degree of comorbidity in their sample, no comorbidity effect was observed in this particular study (Mohamed et al., 2019). Additionally, they did not find any gender differences, which is consistent with the findings of a large meta-analysis (Mohamed et al., 2019).

Furthermore, studies using Functional Magnetic Resonance Imaging (fMRI) of the brain have also found differences in executive functioning ability in the FASD population. These studies have shown that individuals with FASD display differences in the activation of the prefrontal cortex and caudate nucleus during tasks of executive functioning when compared to controls (Khoury & Milligan, 2016). Some of the pronounced executive functioning difficulties in FASD can be attributed to alterations in the parietal and temporal lobes (Archibald et al., 2001; Sowell, Thompson, Tessner, & Toga, 2001) and the corpus callosum (Riley et al., 1995) displaying a more diffuse pattern of altered or atypical structure (Khoury & Milligan, 2016).

Adults with FASD also have demonstrated deficits in their executive functioning (e.g. Chudley et al., 2007; Kerns et al 1997), however, less is known about their typical executive function profile. Additionally, when conducting research on FASD and executive functions, there are multiple factors to consider that may influence the association between FASD and executive functions as well as our ability to clearly understand this association. As discussed previously, there is heterogeneity in the impact of prenatal alcohol exposure on the developing

brain and there is heterogeneity in previous and current diagnostic classifications (Flak et al., 2014; Khoury et al., 2015; Mattson, et al., 2011). The nature of prenatal alcohol exposure, as well as the criteria used to diagnose FASD, can be difficult to obtain in studies, and studies often differ in their criteria for how much alcohol exposure is considered low, moderate or severe (Mattson, et al., 2011). Furthermore, the extent to which variability in IQ, age and sex account for differences in executive function is unclear. Khoury et al. (2015) found IQ to moderate executive functioning ability suggesting that executive functioning differences may be most prominent when IQ is average or lower, as there is likely more variability in performance and less reliability on other cognitive processes to help with executive functioning tasks. Furthermore, the reporting of other psychiatric diagnoses in studies is inconsistent, which confounds findings, as there is a high degree of comorbidity in this population (e.g. Chudley et al., 2007; Mattson, et al., 2011; Khoury et al., 2015). More research on executive function and FASD is needed to understand the executive functioning profile in adults with FASD and to understand how these abilities evolve with development and age. It is also important to investigate which variables may moderate this relationship when conducting future research.

There are multiple neurodevelopmental disabilities that demonstrate marked difficulty in executive functions and that are often compared to executive function skills in FASD. Research on Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) show a different pattern of executive functioning deficits when compared to the deficits observed in FASD, therefore there is evidence for some distinction between the three groups. However, to confirm these findings, a study that directly compares executive functioning differences between individuals with ASD, ADHD and FASD should be conducted (Khoury et al., 2015). This can be challenging to investigate as some samples see comorbidity rates exceeding 60% for ADHD and

FASD (Khoury & Milligan, 2016; Rasmussen et al., 2010) and children with FASD often exhibit inattentive and hyperactive behaviours (Infante et al., 2015). Children with ADHD also experience deficits in all three executive functions of Miyake et al's (2000) model. However, FASD is associated with greater social, cognitive, emotional and behavioural problems than ADHD (Khoury et al., 2016). In their meta-analysis investigating studies of executive functioning in FASD and ADHD, Khoury & Milligan (2016) found large effect sizes when comparing FASD with typically developing controls, medium effect sizes when comparing ADHD with typically developing controls, and small effect sizes when comparing FASD and ADHD. This indicates that individuals with FASD likely have more pronounced deficits in executive functioning when compared to those with ADHD. In addition, socioeconomic background and IQ emerged as significant moderators, with greater differences between the groups observed when IQ and SES were lower. Overall, while individuals with FASD and ADHD can both have deficits in executive functioning, the characteristics of their deficits, as well as the magnitude, are different, with the FASD population experiencing relatively larger and more pronounced difficulties for a variety of reasons.

Fetal Alcohol Spectrum Disorder and Chronic Health Conditions

Prenatal alcohol exposure may produce deleterious effects on multiple areas of functioning outside of neural functioning and cognitive ability (Lunde et al., 2016). This includes one's cardiac (Burd et al., 2007), vascular (Ramadoss & Magness, 2012), endocrine (Zhang, Sliwowska, & Weinberg, 2005) and uteroplacental (Gundogan et al., 2008) health and functioning, indicating that alcohol has the ability to influence most fetal organ systems (Lunde et al., 2016). Similar to the neurobehavioral deficits described above, the severity and nature of alcohol's impact on fetal organ systems depends on the volume and timing of alcohol

consumption (Lunde et al., 2016; May et al., 2013). This leads to variable profiles in the health of individuals with FASD. In 2004, Barker proposed the Developmental Origins of Adult Health and Disease hypothesis, which states that the patterns of fetal growth program one's blood pressure, metabolism, insulin responsiveness, and cardiovascular functioning for later on in life. Barker stated that adverse events, such as alcohol consumption, can affect a fetus's development by changing the utero environment. Since the proposal of this hypothesis, there has been a growing body of evidence to support the role of early environmental triggers in causing adulthood chronic disease (Lunde et al 2016). While this is true for multiple environmental triggers, there is a limited amount of literature available on one's vulnerability for adult-onset diseases following prenatal alcohol exposure.

While it is difficult to draw causal links between prenatal alcohol exposure and health conditions in humans, animal models have contributed to this evidence, demonstrating direct effects of alcohol on multiple health conditions. Specifically, animal models have demonstrated that prenatal alcohol exposure leads to adult hypothyroidism (Wilcoxon & Redei, 2004), cardiac problems (Nguyen et al., 2014) and delayed growth (Probyn et al., 2012), changes in insulin response (Probyn et al., 2013) and adult-onset metabolic syndrome (Dobson et al., 2012). For instance, one study assessed whether prenatal alcohol exposure causes an alteration in the hypothalamic–pituitary–adrenal (HPA) axis, that may be related to an increased vulnerability to adult onset metabolic diseases (Xia et al., 2014). They demonstrated physiological changes (e.g. lipid droplet accumulation) in the HPA axis that promotes the occurrence of metabolic diseases. Additionally, prenatal alcohol exposure could suppress the functional development of the HPA axis, leading to increased blood glucose and decreased blood lipids. These results indicate that prenatal alcohol exposure can create vulnerability for metabolic conditions through glucose and

lipid metabolic disorder (Xia et al., 2014). Another study demonstrated in animal models that prenatal alcohol exposure resulted in alterations in the mRNA expression of multiple insulin and Insulin Like Growth Factor-related genes in the liver and in the prefrontal cortex (integral for executive functioning). This suggests that prenatal alcohol exposure can induce metabolic dysregulation in adulthood (Dobson et al., 2014). On the other hand, there is some evidence to suggest that these metabolic and organ system impairments may be linked to cognitive decline. For instance, one study links hypothyroidism in rats with fetal alcohol exposure to cognitive dysfunction (Wilcoxon, Kuo, Disterhoft, & Redei, 2005). Mothers consuming alcohol suppress their own and the babies' hypothalamic-pituitary-thyroid function, which has a snowball effect on their offspring's cognitive impairments. This was due to a decrease in a protein needed in the hippocampus and amygdala which is linked to learning and memory. Moreover, experts of epigenetic mechanisms suspect that alcohol exposure in utero has the capacity to alter chromatin structure during development, which increases vulnerability to adult-onset diseases (Ungerer, Knezovich, & Ramsay, 2013). However, evidence remains limited in this field, with the underlying mechanisms remaining unknown, and therefore more research needs to be conducted to draw conclusions (Lunde et al., 2016).

One study to date has investigated the prevalence of health conditions in young adults prenatally exposed to alcohol, with the majority being diagnosed with Fetal Alcohol Syndrome (Himmelreich, Lutke, & Travis, 2017). They reported on the health of 514 individuals (mean age 27.5 years) who completed surveys of over 260 questions. All participants included in the analysis had a primary health care physician or nurse practitioner. They found that the prevalence of auto-immune disorders (e.g. celiac disease, rheumatoid arthritis, fibromyalgia) was four to six times higher in the FAS population than in the general population (29.5% vs. 5-8%,

respectively). The prevalence of rheumatoid arthritis specifically was found to be 12 times higher in the FASD population. The authors note that these diseases can be very difficult to manage with impaired executive functioning, chronic stress and memory impairment, which are diagnostic characteristics of FASD. Immune conditions were significantly more prevalent in this population as well. For instance, the prevalence of chronic ear infections in adults was 147 times higher in individuals with FASD than in the general population. Additionally, regarding cardiac disease, the prevalence of congenital heart defects was seven times higher in their sample when compared to the general population and the prevalence of supraventricular tachycardia was 27 times higher. Furthermore, they described a significantly higher prevalence of glucose tolerance abnormalities or metabolic dysfunction and hypothyroidism, among multiple other health conditions. While this research is preliminary, it suggests that individuals diagnosed with FASD are diagnosed with chronic health conditions at a higher rate than the general population.

Animal models alone don't provide strong evidence for mechanisms in humans, and direct cause and effect is difficult to establish when investigating substance use and a specific adult pathology. However, strong epidemiological data as well as research investigating epigenetic mechanisms of inheritance and their impact on adulthood disease combined would strengthen our knowledge of the relationship between prenatal alcohol exposure and adult-onset metabolic diseases (Lunde et al., 2016). Overall, the literature presented clearly demonstrates that alcohol exposure in-utero has detrimental effects across the entire body, resulting in neurological, behavioral, and organ system impairments. This results in neurobehavioral and chronic health conditions in the adult FASD population that are complex, costly, and require high levels of medical attention (Lunde et al 2016).

Executive Functioning and Chronic health

Executive functioning abilities play an important role in the lives of individuals with chronic health conditions, in that they support their adherence to treatment plans and day to day tasks associated with having a chronic illness. When executive functioning skills are weak in these populations, studies have found evidence of poorer adherence and self-management (Duke et al., 2014; Gutierrez-Colina et al., 2019; Hopkins & Jackson, 2006). For example, weak executive functioning abilities may lead a person to experience difficulty in remembering to attend or schedule medical appointments, following doctor's recommendations, and consistently taking medications (Alosco, et al., 2012; Gleb, Shapiro, & Thorton, 2010; Hooper et al., 2015; Stilley et al., 2010).

In addition, many chronic health conditions are associated with difficulties in executive functioning and related struggles in health management (e.g., Duke & Harris, 2014; Berkelhammer et al., 2007; Gerson et al., 2006). For instance, adolescent patients with Type 1 diabetes, have demonstrated difficulty in managing their condition (Hagger, Hendrieckx, Sturt, Skinner, & Speight, 2016). They commonly do not follow their medical team's recommendations, which can lead to complications due to inadequate metabolic control (Anderzen, Samuelsson, Gudbjornsdottir, Hanberger, & Kesson, 2016). Managing this condition can be an onerous task as it can require one to constantly monitor their blood glucose levels, calculate and self-administer insulin doses, engage in physical activity, and estimate the amount of carbohydrates in meals (Duke & Harris, 2014). Studies have found a higher rate of executive functioning difficulties in adolescents diagnosed with type 1 diabetes than in their peers without the condition (see Duke & Harris, 2014 for review). In addition, poorer executive functioning is associated with less adherence to their disease management. Similarly, for individuals diagnosed

with the chronic kidney disease, the inability to adhere to medical recommendations and treatment can lead to complications and hospitalization (Hooper et al., 2015). It has been found that individuals with chronic kidney disease have poor executive functioning ability (Hooper et al., 2015; Lee, et al., 2011). Furthermore, in heart failure management, adequate self-care is essential (Lovell, Pham, Noaman, Davis, Johnson, & Ibrahim, 2019) and individuals with heart failure who have impaired executive functioning have been found to have difficulties with functional independence (Alosco et al., 2014). Self-care includes adhering to complex medications, meeting dietary fluid and sodium restrictions, proper exercise, and identifying, managing and visiting a health care professional for advice when there are changes in their medical symptoms (Cameron et al, 2015; White, Kirschner, & Hamilton, 2014). By investigating the relationship between cognitive impairment, self-management, and identifying any variables that may moderate the relationship, clinicians may be able to better tailor their disease management planning to the specific individual's ability (Lovell, 2019).

While research is limited, a relationship between executive functioning and the experiences of individuals with chronic health conditions does exist. The extent to which chronic conditions themselves impact executive functioning, however, is unclear. Existing evidence suggests that executive functioning is required to manage many chronic illnesses, as these conditions are complex and demanding on individuals. In self-management, executive functioning skills are integral as it includes tasks such as calculations, consistent exercise, meeting requirements in their diet, adhering to medication schedules and attending appointments. Additionally, it has been demonstrated by the research summarized above that deficits in executive functioning are associated with poorer management of one's health conditions. As executive functions are important to adherence and self-management of chronic health

conditions, understanding the relationship between chronic health conditions and executive functioning ability will help make interventions for abilities such as adherence more targeted towards specific executive functions. In addition, practitioners who better understand this relationship can use it to plan treatment and self-management that may be tailored for their patient's strengths and weaknesses. In the future, this may help reduce the cost of health care.

Health Related Quality of Life, Executive Functioning and Fetal Alcohol Spectrum Disorder

Health related quality of life (HRQOL) is defined by the Centre for Disease Control and Prevention (2000) as the way an individual perceives their own health over time, which can include both physical and mental health. It has also been defined as "aspects of self-perceived well-being that are related to or affected by the presence of disease or treatment" (Ebrahim, 1995). Health related quality of life and its relationship to executive functioning has been investigated in multiple medical populations. The majority of studies find that worse executive functioning ability is associated with poorer HRQOL. This includes those with pediatric acute liver failure, epilepsy, sickle cell disease and survivors of pediatric brain tumors (Allen et al., 2016; Netson et al., 2016; Schraegle & Titus, 2016; Sorensen et al., 2015; Ventura et al., 2017). In fact, some argue that individuals with any childhood disorder that is known to have difficulties with executive functioning, by default, are likely at risk for low HRQOL (Sherman, Slick & Eyrl, 2006). In addition, this relationship has been observed in a typically developing population (Cohrdes Mensink & Holling, 2018). One study wanted to determine factors that may support HRQOL and investigate age-related differences (Cohrdes et al., 2018). They found that executive functioning may potentially promote HRQOL in individuals at various ages outside of individual or social factors. Furthermore, one study examined this relationship in individuals

with ADHD, which is known for significant executive functioning difficulties. Specifically, Brown & Langraf (2015) sought to determine whether an increase in executive functioning ability correlated with greater HRQOL in those diagnosed with ADHD. They found that, in two independent clinical trials, improvement in executive functioning was correlated with self-reported improvement in health related quality of life.

Multiple studies have taken moderators and other variables into consideration. Factors such as psychiatric functioning and adaptive ability have an impact on HRQOL, and they both are likely to be influenced by executive functioning ability (Schraegle & Titus 2016). Schraegle and Titus (2016) found, in the pediatric epilepsy population, that low executive functioning (as rated by their parents) was found to correlate with certain portions of HRQOL, specifically with the well-being, cognitive and behavioral components of HRQOL and less so with the social activities and physical activities components of HRQOL. Another study of the epilepsy population found executive functioning to be an important predictor of HRQOL when taking other factors, such as adaptive ability and number of anti-epileptic drugs, into account (Sherman et al., 2006). In the sickle cell disease population, where executive functioning ability predicted HRQOL, socioeconomic status was not found to be a significant moderator of the relationship. However, Cohrdes et al. (2018) found that executive functioning skills may buffer the impact of one's socioeconomic status has on HRQOL in the lower socioeconomic population.

The relationship between executive functioning and HRQOL has not been examined in those with FASD despite their having demonstrated a significant impairment in executive functioning. However, studies have documented that FASD is associated with other risk factors for a lower HRQOL. For example, individuals with FASD experience greater adverse life outcomes, difficulties in adaptive functioning, and a high degree of psychiatric conditions (Doyle

et al., 2018; Mattson, et al., 2011). In addition, research suggests that individuals with FASD have an increase in suicide attempts throughout their lifetime when compared to the general population (Mattson, et al., 2011). Often, children with FASD continue to experience adverse life outcomes as they age, such as substance abuse problems (Alati et al. 2006; Alati et al. 2008; Baer et al. 1998; Baer et al. 2003) as well as difficulty with the law (Mattson, et al., 2011) which can impact their health and quality of life. Moreover, individuals with FASD who have not been diagnosed early and/or have not received appropriate interventions are at an increased risk of adverse outcomes, which include involvement in criminal activity, as well as mental health concerns (Streissguth et al. 2004). However, access to multidisciplinary teams to obtain a diagnosis can be a challenge for multiple reasons (Pei et al., 2017). Overall, health related quality of life in individuals with FASD can be impacted by their chronic health and executive functioning ability, as well as other factors, such and their social and psychological functioning.

Summary, Rationale and Purpose of Present Study

There is a strong body of research demonstrating the impairment of executive functioning skills in the pediatric FASD population. However, it is unclear the extent to which the same profile of executive functioning deficits exists in the adult FASD population. Therefore, more research is needed to identify executive functioning deficits in adults with FASD. In addition to the neurobehavioral, psychological, and adaptive functioning difficulties the FASD population faces, there may also be a greater prevalence of chronic health conditions when this population is compared to the general population. Executive functioning skills are utilized in managing chronic diseases like, diabetes, and auto-immune disorders such as arthritis, which are seen frequently in those diagnosed with FASD. The underlying mechanisms and epidemiology of this phenomenon remains understudied. What remains evident is that alcohol exposure in-utero has

detrimental effects across the entire body, resulting in neurological, behavioral, and organ system impairments. In addition, research has indicated a relationship between HRQOL and executive functioning in multiple clinical populations as well as typically developing populations. However, this relationship has not been examined in the FASD population, where there is a known deficit in executive functioning ability. Therefore, the purpose of the study is to understand how executive functioning ability in young adults diagnosed with FASD relates to the presence of chronic health condition(s) in this population, as well as their health related quality of life. As research in this field is minimal, and this is (to our knowledge) the only study analyzing these variables together, this research is considered exploratory. It is hypothesized that firstly, the prevalence of chronic health disorders will be greater in this population when compared to the general population; secondly, a greater number of chronic illnesses will be associated with poorer health related quality of life and more executive functioning deficits; thirdly, that greater executive functioning deficits are associated with poorer health related quality of life.

This research will help us better understand the severity of EF deficits in FASD, add to the knowledge of the prevalence of chronic health conditions in FASD population and help us understand the relationship between chronic illness and executive functioning ability. In addition, this research may inform future health management planning in this population and inform services and interventions for FASD. The inability to adhere to a treatment plan can increase financial burden for patients, their families, insurance companies and public organizations (Stilley et al., 2010). With better management, the cost of health care for this population may decrease. With the variable obstacles that individuals with FASD can face,

having a better understanding of the challenges they experience in maintaining good health may lead to better health outcomes and quality of life.

II. Methods

Participants

Young adults, ages 15-29 (Ballantine, 2018; Geiger, & Castellino, 2011) diagnosed with FASD or FAS (with or without sentinel features), who speak English as their primary language were recruited. A total of 14 participants completed the questionnaire. One participant was removed from the study as they were not formally diagnosed with FASD or FAS; another participant was removed as they did not meet the age criteria. Therefore, a total of 12 participants were included in the analysis, with 3 identifying as male and 10 as female. The mean age of participants was 22.8 years (*Mdn* = 22.5, range: 18-29).

Procedures

The consent form and questionnaire (see Appendix A) was uploaded to Qualtrics, an online survey platform provided by UBC. Participants completed the questionnaire at their convenience. Recruitment occurred via online websites and postings. Firstly, a study description and virtual flyer was posted on the Asante Centre's website. The Asante Centre is a clinic in metro Vancouver specializing in the diagnosis of FASD and other neurodevelopmental disorders. Secondly, The Canada Fetal Alcohol Spectrum Disorder Research Network (CanFASD) was contacted, and a blog post was written about the study on their website. Lastly, multiple FASD groups on Facebook were contacted, requesting they post about the study on their pages.

Ethical considerations and Consent

Consent was obtained online through Qualtrics. When a participant navigated to the survey website, they were initially presented with the consent form. They were asked to answer 4 questions about the consent form before continuing, to ensure they read and understood the consent form. If they agreed to participate, participants entered their name in place of a signature.

They were also asked to provide their email address if they wanted to receive results of the study or enter a draw to win a gift card. Identifying information, including participant's names, were kept separate to the questionnaire data, and all documents were password protected and stored on local hard drives. Approval for this research was granted through the UBC Research Ethics Board.

Measures

Demographic Information. The demographic survey included questions regarding the participants' identified gender, age, ethnicity, and socioeconomic status. It also included questions regarding any diagnosed psychological disorders and substance use.

Chronic Health Conditions. Participants identified any current chronic health conditions and their date of diagnosis, per the methodology used by Himmelreich and colleagues (2017). Chronic health conditions included auto-immune disorders, general immune difficulties, and cardiovascular conditions. In the analysis, the number of chronic health conditions was used for correlation and the group was split based on the presence of a chronic health condition for other analyses.

Health Related Quality of Life. The Centre for Disease Control's Health Related Quality of Life Measure (CDC HRQOL–14) was used to measure health related quality of life (HRQOL; Hennessey, 1994; CDC, 2000; http://www.cdc.gov/hrqol/methods.htm). The 14-item self-report scale includes 4 core items with 10 supplemental items and measures one's perceived physical and mental health status in the last 30 days. The core scale provides an Unhealthy Days Score between 0 to 30, on which a higher score indicates worse perceived health. The days can be broken down into physical unhealthy days and mental unhealthy days. The additional 10 questions provide more specific information on the impact of health on daily life, including

recent pain, vitality, and activity limitation. The instrument has demonstrated good validity and reliability (Albert, 2000; Andresen, Catlin, Wyrwich, & Jackson-Thompson, 2003; Zullig, Valois, Huebner, & Drane, 2004; Andresen, Fitch, McLendon, & Meyers, 2000; Keller, Ostbye, & Goy, 2004). In addition, it has been shown to have adequate psychometric properties when utilized with medical populations diagnosed with chronic health conditions, such as those with rheumatoid arthritis and fibromyalgia (Andreson Fouts, Romeis, & Brownson, 1999; Mielenz, Jackson, Currey, DeVellis, & Callahan, 2006). The unhealthy physical days score, which ranges from 0-30, was used as the measure of overall health related quality of life.

Executive Functioning. The Barkley Deficits in Executive Functioning Scale (BDEFS; Barkley, 2011) was used as a measure of executive functioning in daily life; it is a 20-item self-report scale. It uses a 4-point Likert scale as a response for all items ranging from "never/rarely" to "very often". This scale was normed on a large, nationally representative sample of adults in the United States with equal representation of males and females, with a total sample of 1,249 individuals. The scale has strong convergent and discriminant validity and test-retest reliability properties. The form provides a single score for executive functioning ability called the Total EF Summary Score. The EF total raw score was used in the analysis. For some analyses, EF was used as the independent variable; the group was split by median to create two independent levels.

Research Questions

The purpose of the study is to understand how executive functioning ability in young adults diagnosed with FASD relates to the presence of their chronic health condition(s) as well as their health related quality of life. Specific research questions are as follows:

1) What is the nature of chronic health, health related quality of life, executive function and other health related characteristics among young adults diagnosed with FASD or FAS?

2) What is the relationship between chronic health, health related quality of life and executive functioning among young adults diagnosed with FASD or FAS?
    a. What is the relationship between chronic health and health related quality of life in this group?
    b. What is the relationship between chronic health and executive function in this group?
    c. What is the relationship between executive function and health related quality of life in this group?

Analysis

Correlation. Multiple Spearman's Rank Order correlations were conducted to assess the strength and direction of the relationship between chronic health conditions, health related quality of life and executive functions. For executive functioning, the total EF Summary raw score was used; for chronic health conditions, the number of chronic health conditions was used; lastly, for health related quality of life, the unhealthy physical days score was used. The correlations are based on the ranks of the data and the correlation coefficient, r_s, ranges from -1 (indicating a perfect negative correlation between two variables) to 1 (indicating a perfect positive correlation between two variables). A value of zero indicates that there is no relationship between the two variables of interest.

Mann-Whitney U Test. The Mann-Whitney U test is the nonparametric equivalent to a t-test. It tests for the location of the medians of two groups and uses the ranks of the observations instead of the observation values. It requires a categorical independent variable and an ordinal or continuous dependent variable. This test was applied to each component of research question 2. For research questions 2a and 2b, the sample was split into 2 groups by the presence or absence

of a chronic health condition and the unhealthy days score was used for HRQOL and the EF total raw score was used for executive functioning. For question 2c, to create 2 independent variable levels, the sample was split into 2 groups by median of the EF total score (i.e. one level consisted of participants equal to or below the median, and the other level consisted of participants above the median).

III. Results

Preparation of Data

The sample was checked for assumptions of parametric tests, specifically a t-test. Regarding normality, the data was checked for skewness, kurtosis, the Shapiro-Wilk's test was conducted, and histograms were examined for research questions 2a, 2b and 2c. For research question 2a, the kurtosis and skewness were within normal limits, however the Shapiro-Wilk test indicated that one group was not normally distributed, and one group was approximately normal. The histogram did not support normality, as the data appeared positively skewed. For research question 2b, the kurtosis and skewness were within normal limits, and the Shapiro-Wilk test was not significant, supporting normality of data. However, examination of the histogram did not support normality as one group was more positively skewed. For research question 2c, the kurtosis, skewness and Shapiro-Wilk test indicated normality, however, examination of the histogram did not support normality. Overall, the data did not meet the assumption of approximate normality required to conduct a t-test. Additionally, the sample collected did not meet the sample size assumption of a t-test. Therefore, non-parametric methods were chosen for the analysis.

The assumptions of a Spearman's rank order correlation are, first, that the data are at least ordinal, and, second, that the two variables represent paired observations. The sample met these assumptions. The last assumption is that the data appear monotonic (i.e. that they both simultaneously increase, or that as one variable increases, the other decreases). Examining scatterplots of the data, it appears that for research question 2a and 2b, the data only appears slightly monotonic. Because the Spearman's correlation determines the level of monotonicity,

the analyses were still conducted, however this was considered in the interpretation of the results. For research 2c, the data did appear monotonic.

The Mann Whitney U test has 4 assumptions. It requires the dependent variable to be ordinal, the independent variable to consist of two categorical groups, and that the observations are independent. The data was examined, and it met those assumptions. The last assumption is that the two levels of the independent variable are similarly distributed. This was evaluated for each analysis in research question 2 by examining histograms. For research question 2a, and 2c, data appeared similarly distributed (positively skewed). For research question 2b, data appeared slightly dissimilar in terms of distribution. While 2 of the analyses meet the criteria for a Mann Whitney U test, p values will not be reported due to the small sample size making inferences not meaningful. Therefore, the Mann-Whitney U test will not be used to compare the medians of each group and instead will be used to determine whether the distributions themselves are different; the p-value will not be reported and instead the focus will be on the trend of the data for the group comparisons.

Research Question 1

The first research question examined the nature of chronic health, health related quality of life, executive function and other health related characteristics among young adults diagnosed with FASD or FAS. This question was addressed by examining the demographic information collected.

Demographic Information. Table 1 (see Appendix B) summarizes demographic information for the sample including gender, ethnicity and parental education level. SES was measured by parental education level. The sample was fairly evenly distributed across parental (maternal and paternal, respectively) education level, with approximately 1/3 (n = 4 and 5,

respectively) of the sample not knowing or reporting this level, approximately 1/3 having completed partial high school (*n* = 4 and 3, respectively), and 1/3 having completed high school or attended a post-secondary institution (*n* = 4 and 4, respectively).

Health Related Information. Table 2 (see Appendix B) summarizes health related information. Regarding diagnosed mental health conditions (see Table 3, Appendix B), 9 of the 12 participants reported at least one diagnosis, with all 9 diagnosed with an Anxiety disorder. Depression was the second most prevalent diagnosis (*n* = 7), with PTSD being the third most prevalent diagnosis (*n* = 4). The highest number of mental health diagnoses in a single participant was 7. The majority of participants were also diagnosed with a neurodevelopmental disorder (*n* = 10), with both ADHD and Intellectual Disability being the most prevalent conditions (*n* = 6 respectively) and Specific Learning Disorder being the next most prevalent condition (*n* = 5). A language disorder or impairment was also reported (*n* = 3); 2 participants reported some substance use. The only substance that participants reported using daily was tobacco. One participant reported the use of cocaine in social situations. The remainder of reported substance use involved alcohol and marijuana. No binge drinking was reported.

Research Variables. This information is summarized in Table 4 (see Appendix B).

***Chronic Health Conditions*.** The participants were asked to report and list any chronic health conditions that they had been diagnosed with (see Table 5, Appendix B). Out of 12 participants, 6 had at least one diagnosis, with each participant reporting between 1 and 5 total conditions. Chronic ear infections and Asthma were the most common diagnoses (*n* = 4). Participants also reported Rheumatoid Arthritis, and Scoliosis (*n* = 2). Congenital Heart Defect, Chiari Malformation Type 2, Gout and Severe Anemia were each reported once. Chronic UTI

infections were also reported, however this was determined not to be a chronic health condition following consultation with a medical professional.

Health Related Quality of Life. Out of all 12 participants, 10 reported at least 1 day where they felt physically unhealthy. Of the participants that reported a diagnosis of a chronic health condition (n = 6), all 6 reported at least 1 day where they felt physically unhealthy (Mdn = 10, range: 7-26). Out of participants that did not report a chronic health condition (n = 6), 4 reported at least 1 physically unhealthy day (Mdn = 5, range: 0-30).

Executive Functioning. All 12 participants reported some level of executive functioning difficulties on the BDEFS. Almost every participant's score was at least 1 standard deviation above the mean, when compared to the normative group (n = 11); 9 participants' scores were above the 95th percentile for executive functioning difficulties compared to the normative group, indicating severe executive functioning difficulties.

Research Question 2.

The second research question examined the relationship between chronic health, health related quality of life and executive functioning among young adults diagnosed with FASD or FAS. This was assessed via 3 independent analyses stated in research questions 2a, 2b and 2c.

Research Question 2a: What is the relationship between chronic health and health related quality of life in this group?

Correlation. A spearman's rank order correlation between the number of chronic health condition diagnoses and the HRQOL score was conducted. The results indicated a small positive correlation between these two variables ($r_s(10) = .292$). The trend observed here indicated that, as an individual experienced more chronic health diagnoses, they tended to also report a higher number of physically unhealthy days.

Mann-Whitney U Test. For this analysis, the sample was split into 2 independent groups by the presence (n = 6) or absence (n = 6) of a chronic health condition. The number of physically unhealthy days was used as the dependent variable to represent HRQOL, Consistent with the correlation, the Mann-Whitney U test indicated that those who reported having at least one chronic health condition tended to report more physically unhealthy days than those who did not report any chronic health conditions (U = 10.5).

Research Question 2b: What is the relationship between chronic health and executive function in this group?

Correlation. A spearman's rank order correlation between the number of chronic health condition diagnoses and the EF total raw score identified no clear trend in the relationship between these variables.

Mann-Whitney U Test. The sample was again split into 2 independent groups by the presence (n = 6) or absence (n = 6) of a chronic health condition. The total EF raw score was used as the dependent variable to represent executive functioning difficulties. Similar to the correlation findings, the Mann-Whitney U test indicated that no trend in terms of group differences in executive functioning difficulties (U = 16).

Research Question 2c: What is the relationship between executive function and health related quality of life in this group?

Correlation. A spearman's rank order correlation between the EF total raw score and the number of physically unhealthy days indicated a strong positive correlation between executive functioning and health related quality of life ($r_s(10) = .729$). This analysis demonstrated a trend for participants to report more days feeling physically unhealthy as their executive functioning difficulties increased.

Mann-Whitney U Test. For this analysis, the sample was split into 2 independent groups by their total EF raw score median. Therefore, one group consisted of participants equal to or below the EF median (n = 6), and the other group consisted of participants above the median (n = 6). The number of physically unhealthy days was used as the dependent variable to represent HRQOL. Consistent with the correlation results, the Mann-Whitney U test indicated a trend for the participants with higher reported EF difficulties to experience more physically unhealthy days, with a medium effect size (U = 4.5). In other words, those with more executive functioning difficulties also indicated worse HRQOL.

IV. Discussion

The overall purpose of this study was to understand how executive functioning ability in young adults diagnosed with FASD or FAS relates to the presence of their chronic health condition(s) as well as their health-related quality of life.

Research Question 1

The first objective of this study explored the nature of chronic health conditions, HRQOL, executive function and other health related characteristics among young adults diagnosed with FASD or FAS. The majority of participants (n = 9) had at least one mental health disorder, with the most prevalent being Anxiety. This is consistent with the literature as Anxiety is included in the diagnostic guidelines for FASD as being impaired in the affect regulation domain (Cook et al, 2016). Neurodevelopmental disorders were also present in the majority of participants (n = 10) with intellectual disability and ADHD being the most common. Again, this is consistent with the diagnostic guidelines and common impairments found in this population (Cook et al., 2016). ADHD is also associated with significant difficulties in executive functioning and attention is a characteristic impairment in the FASD neurocognitive profile of FASD (Cook et al., 2016).

In terms of our research variables of interest, we found that the sample was evenly split between those that had a chronic health condition and those that did not. This is similar to the general adult population, as approximately 44% of individuals over the age of 20 have at least one chronic health condition in Canada (Public Health Agency of Canada, December 2019). However, this includes all adults above 20 and therefore includes the older adults and the geriatric population which has a higher prevalence of chronic health concerns. To our knowledge, there is only one other study that examined the prevalence of chronic health

conditions in young adults prenatally exposed to alcohol; Himmelreich, Lutke, and Travis (2017) reported similar types of chronic health illnesses as in the present study, including a high prevalence of chronic ear infections, Asthma, and Rheumatoid Arthritis. However, they found prevalence rates much higher when compared to the general population than our study. For instance, they found that auto-immune conditions were 4-6 times higher in the young adult FASD population when compared to the general population. This difference may be due to sample size as they had included 514 participants in their analysis. Regarding HRQOL, 10 out of 12 participants reported physically unhealthy days, including those that did not report a chronic illness. Specifically, all participants reported experiencing at least 5 physically unhealthy days in the last 30 days, with the median of the sample being 10 days. The CDC reported an average of 5.3 unhealthy days in the general population, however this includes both physically and mentally unhealthy days (Centers for Disease Control and Prevention [CDC], 2000). Therefore, we a found higher number of unhealthy days in our sample than the general population. While some of this may be attributed to chronic illness, future research could investigate what participants may consider the cause of these physically unhealthy days. In addition to their chronic illnesses, it is also possible that the sample's mental health conditions could be impacting their physical well-being. For example, research has identified an association between having Separation Anxiety and having poorer physical health in the long term (Battaglia et al., 2017) and Major Depressive Disorder has been associated with physical symptoms such as significant weight loss or weight gain, insomnia or hypersomnia, and fatigue (American Psychiatric Association, 2013). Lastly, the executive functioning difficulties of the sample overall were significantly elevated, consistent with research demonstrating impairments in this population (Khoury et al., 2015; Khoury & Milligan, 2016). The majority of participant's results indicated some level of

difficulty with executive functioning, with most indicating severe difficulty. Studies measuring executive functioning using questionnaires have also found impairments in the FASD population however, typically this research has involved parental report (Mohamed et al., 2019; Rai et al., 2017; Rasmussen et al., 2010; Rasmussen, Horne, & Witol, 2006). Due to small sample size, we were unable to control for specific mental health and neurodevelopmental disorders that are also associated with executive functioning difficulties such as ADHD and Depression (Rai et al 2017). Therefore, we may not be able to assume that the difficulties in executive functioning observed are due to the diagnosis of FASD, as other conditions may contribute as well.

Overall, the sample reported a high number of physically unhealthy days compared to the general population. Additionally, half of the sample reported at least 1 chronic health condition, which may or may not be more than what is seen in the general young adult population but is similar to the general adult population (over 20 years). And lastly, consistent with previous literature, the sample reported very high levels of executive functioning difficulties.

Research Question 2

The second objective of this study was to examine the relationship between chronic health, HRQOL and executive functioning among young adults diagnosed with FASD or FAS. When examining the relationship between chronic health and HRQOL, it was hypothesized that as the number of chronic health conditions increased, HRQOL would decrease. The analyses supported this hypothesis. Previous literature has demonstrated a similar association between general quality of life and chronic health (Bai, G., Herten, M. H., Landgraf, J. M., Korfage, I. J., & Raat, H., 2017 Else et al., 2008), with this study's contribution being that this relationship is still present when using measures specifically for HRQOL. Still, the association found in our study was more modest than hypothesized. The number of chronic health condition diagnoses

that an individual has, may not fully capture severity of chronic health. For instance, chronic health conditions differ in the way that they are managed and impact health. For example, asthma's main symptoms include coughing, difficulty breathing and shortness of breath (CDC, May 2020) and rheumatoid arthritis's main symptoms are joint pain and aching, stiffness and tenderness in joints, weight loss and fatigue (CDC, July 2020). Further, individuals can have mild to severe versions of a given chronic health condition. Therefore, future research measuring chronic health by the severity of chronic health symptoms for example, may find a stronger relationship between these variables. Additionally, the small sample size must be taken into consideration, as it may have limited the ability of this study to identify a relationship between these variables, should one exist.

When examining the relationship between the presence of chronic health conditions and executive functioning, the analysis did not find a relationship between these two variables. It was hypothesized individuals with more chronic health conditions would experience greater impairment in their executive functioning. This finding was unexpected as multiple studies have found that many chronic health conditions are related to executive functioning difficulties (e.g., Duke & Harris, 2014; Berkelhammer et al., 2007; Gerson et al., 2006). However, it may just be that the number of chronic health conditions a person experiences, or the mere presence of at least one chronic condition, is not associated with additional executive functioning difficulties in a population that requires these difficulties in the diagnostic process. Alternatively, as previously mentioned, using a different indicator of chronic health severity may reveal an association between chronic health and executive functioning.

When examining the relationship between executive function and HRQOL, a strong association was found between these two variables. Our data shows an inverse relationship

between executive functioning and HRQOL, which is supported by previous research in multiple health populations; however, no previous studies seemedx to have examined this in the FASD/FAS populations. In patients with pediatric acute liver failure, epilepsy, sickle cell disease and survivors of pediatric brain tumors, it has been demonstrated that a lower executive functioning ability is related to worse HRQOL (Allen et al., 2016; Netson et al., 2016; Schraegle & Titus, 2016; Sorensen et al., 2015; Ventura et al., 2017). Further, research has also demonstrated that in the ADHD population, executive function improvements were correlated with better HRQOL. Another study found that executive functioning abilities may diminish the impact of SES on HRQOL (Cohrdes et al., 2018). Further, in other populations it has been reported that weak executive functioning skills are associated with worse treatment adherence and difficulties in self-management management (Duke et al., 2014; Gutierrez-Colina et al., 2019; Hopkins & Jackson, 2006). Therefore, further investigation into this relationship may help with future interventions that have goals such as treatment adherence and improvements in quality of life.

General Conclusions

The present findings indicate that executive functioning, HRQOL and the presence of chronic health conditions do relate to one another in the FASD/FAS young adult population. We found that the presence or absence of one or more chronic health conditions is related to one's HRQOL – in that those with a chronic health condition report more physically unhealthy days than those with no chronic health condition. We also found that those with no reported chronic health conditions still report some physically unhealthy days (however, on average fewer than those who have a diagnosis). Exactly half of the sample was diagnosed with 1 or more chronic health condition, with the range being 1-5. While this is not dissimilar to the general adult

population, this may be greater than what is seen in the general young adult population. We also found a relationship between HRQOL and executive functioning. Specifically, as executive functioning difficulties increased (as indicated by a self-report scale) HRQOL worsened (as indicated by more physically unhealthy days). The sample reported a high level of mental health and neurodevelopmental disorders which may have potentially confounded our results. These findings highlight the importance of considering physical health and health outcomes such as HRQOL in this population. We have also found an association between executive functioning and reported physical health. In a population with high levels of EF difficulties, monitoring physical health may be beneficial as this population may be at risk for lower HRQOL.

Limitations and Strengths of the Study

The greatest limitation of the present study is the small sample size. This did not allow for the ability to control for potentially confounding variables. For example, ADHD and Depression were reported by participants in the study, and these conditions are associated with executive functioning deficits (Rai et al., 2017). Additionally, the small sample size did not allow for the use of inferential statistics due to low statistical power. Secondly, the method used to measure the severity of chronic health condition could be improved. The number of chronic health diagnoses may not be the best indicator of severity as each diagnosis is different in the way it affects your physical health. Another limitation is the way that executive function is measured, as one overall score was obtained. Ideally a more comprehensive measure that included subscales would have been used to learn more about the executive functioning profile of young adults with FASD or FAS. Lastly, the way socioeconomic status was measured may not have provided a complete representation of this variable as parental education level was used. Parental income and the socioeconomic status of the participants themselves was not taken

into consideration. Additionally, the socioeconomic status of multiple participants was missing as some participants (approximately a third) indicated that they did not know their parental education level.

One of the main strengths of this present study is that – to our knowledge – this is the first time these variables have been investigated together in this population and that we have learned about how they relate to each other. Additionally, there is minimal research on young adults, as well as older adults with FASD/FAS when compared to the research on infants and youth. Further, this study highlights the physical difficulties associated with FASD, which can be overlooked, as the focus tends to be on mental health and cognitive ability. Lastly, HRQOL was measured with a tool specifically designed for this purpose, instead of a more generic quality of life measure.

Future considerations

Future mental health practitioners and health care providers should consider the complex profile that these patients present with, especially the increased physical health difficulties in this population. This may not be as commonly known by mental health practitioners and can aid in coming up with the best interventions and can increase empathy and the client practitioner relationship. When planning for chronic health management, executive functioning difficulties should be considered and accounted for in the intervention plan to increase adherence. Further, targeting both EF and their health difficulties simultaneously may yield more improvements in both than if only one of these areas was targeted at a time. When conducting any psychological assessment, consulting with their health care providers on whether the individual has physical health difficulties and what their management plan is would beneficial so that it can be considered and reflected in the recommendations.

Future research should consider measuring chronic health difficulties as a part of their demographic profile, so that we learn more about the prevalence and nature of physical health conditions in this population. Additionally, conducting executive functioning research in this population with a comprehensive questionnaire containing subscales for different components of executive function and performance-based measures may provide a more comprehensive profile of these skills. Further, it would be interesting to investigate why people rated physically unhealthy days without a formal diagnosis; and whether the presence or absence of certain psych conditions moderates this relationship. It would also be informative to examine what types of executive functioning skills are specifically impacted in this population and how they relate to HRQOL and physical health. Lastly, it would be interesting to research how these different abilities affect adherence to medications and medical treatment plans. This type of research could inform future practice in in patient management and intervention. The hope is that future research continues in this population as there is much to learn about young adults and older adults with FASD and how their cognitive, behaviour and health profile changes over time.

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Appendix A: Questionnaires

Demographics

Age: ___

Gender:
- Male
- Female
- Other, please specify: ___

Ethnicity (which ethnic group(s) do they most identify with):
- Aboriginal (Inuit, Métis, North American Indian)
- Black (e.g., African, Haitian, Jamaican, Somali)
- Chinese
- Filipino
- Japanese
- Korean
- Latin American
- Arab/West Asian (e.g., Armenian, Egyptian, Iranian, Lebanese, Moroccan)
- South Asian
- South East Asian
- White (Caucasian)
- Other, please specify: ___

Your mother's highest education level:
- High school (incomplete)
- High school degree
- Diploma
- Bachelor's degree
- Graduate School/Professional degree (e.g. Law, Medicine)
- Other, please specify: ___
- Unknown

Your father's highest education level:
- High school (incomplete)
- High school degree
- Diploma
- Bachelor's degree
- Graduate School/Professional degree (e.g. Law, Medicine)
- Other, please specify: ___
- Unknown

Your highest education level:
- High school (incomplete)

- High school degree
- Diploma
- Bachelor's degree
- Graduate School/Professional degree (e.g. Law, Medicine)
- Other, please specify: ___
- Unknown

Current Employment Status
- Employed
- Unemployed
- Student
- Other

At what age were you diagnosed with Fetal Alcohol Spectrum Disorder? __

Do you have any psychological diagnoses/mental health conditions?
- No
- Yes
    - Please specify:
        - Depression
        - Anxiety
        - Bipolar disorder
        - ADHD/ADD
        - Conduct Disorder
        - Schizophrenia
        - Personality Disorder
        - Obsessive Compulsive Disorder
        - Substance use disorder (including any addictions)
        - Other: Please Specify:__

Do you have any language, learning or intellectual disabilities?
- No
- Yes
    - Please specify:
        - Learning disorder (e.g. dyslexia, dyscalculia)
        - Language disorder/impairment
        - Intellectual disability
            - Mild
            - Moderate
            - Severe
            - Severity unknown

Do you currently use any of the following substances?
- Alcohol
- Tobacco

- Marijuana
- Other: please specify __

If they respond yes to any, the following question will be asked: Approximately how many times per month do you use this substance? __

Chronic Health Questionnaire

Please indicate whether you have been diagnosed with the following health conditions:

- Lupus
- Sarcoidosis
- Angioedema
- Celiac Disease
- Rheumatoid Arthritis
- Psoriasis
- Chron's Disease
- Ulcerative Colitis
- Fibromyalgia
- Kawasaki's Disease
- Asthma
- Chronic Ear Infections
- Genital Heart Defect
- Supraventricular Tachycardia
- Scoliosis
- Osteoarthritis
- Osteopenia
- Osteoporosis
- Other: Please Specify: __

Healthy Days Core Module (CDC HRQOL– 4)

1. Would you say that in general your health is

Please Read
a. Excellent
b. Very good
c. Good
d. Fair

or

e. Poor

Don't know/Not sure

Refused

2. Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was your physical health not good?

a. Number of Days _ _

b. None

Don't know/Not sure

Refused

3. Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?

a. Number of Days _ _

b. None If both Q2 AND Q3 = "None," skip next question

Don't know/Not sure

Refused

4. During the past 30 days, for about how many days did poor physical or mental health keep you from doing your usual activities, such as self-care, work, or recreation?

a. Number of Days _ _

b. None

Don’t know/Not sure	
Refused	

Activity Limitations Module

These next questions are about physical, mental, or emotional problems or limitations you may have in your daily life.

1. Are you LIMITED in any way in any activities because of any impairment or health problem?

a. Yes	
b. No	Go to Q1 of Healthy Days Symptoms Module

Don’t know/Not sure	Go to Q1 of Healthy Days Symptoms Module
Refused	Go to Q1 of Healthy Days Symptoms Module

2. What is the MAJOR impairment or health problem that limits your activities?

3. For HOW LONG have your activities been limited because of your major impairment or health problem?

Don’t know/Not sure
Refused

4. Because of any impairment or health problem, do you need the help of other persons with your PERSONAL CARE needs, such as eating, bathing, dressing, or getting around the house?

a. Yes
b. No

Don’t know/Not sure
Refused

5. Because of any impairment or health problem, do you need the help of other persons in handling your ROUTINE needs, such as everyday household chores, doing necessary business, shopping, or getting around for other purposes?

a. Yes

b. No

Don’t know/Not sure

Refused

Healthy Days Symptoms Module

1. During the past 30 days, for about how many days did PAIN make it hard for you to do your usual activities, such as self-care, work, or recreation?

a. Number of Days _ _

b. None

Don’t know/Not sure

Refused

2. During the past 30 days, for about how many days have you felt SAD, BLUE, or DEPRESSED?

a. Number of Days _ _

b. None

Don’t know/Not sure

Refused

3. During the past 30 days, for about how many days have you felt WORRIED, TENSE, or ANXIOUS?

a. Number of Days _ _

b. None

Don’t know/Not sure

Refused

4. During the past 30 days, for about how many days have you felt you did NOT get ENOUGH REST or SLEEP?

a. Number of Days _ _

b. None

Don’t know/Not sure

Refused

5. During the past 30 days, for about how many days have you felt VERY HEALTHY AND FULL OF ENERGY?

a. Number of Days _ _

b. None

Don’t know/Not sure

Refused

Appendix B: Tables

Table 1: Demographic Information.

Category	Frequency
Gender	
Male	2
Female	10
Ethnicity	
Caucasian	8
First Nations	2
Caucasian and First Nations	2
Maternal Education Level	
Incomplete High School	4
High School Diploma	3
Post-Secondary Degree	1
Unknown	4
Paternal Education Level	
Incomplete High School	3
High School Diploma	3
Post-Secondary Degree	1
Unknown	5

Table 2: Health Related Information

Median and range is provided for the number of diagnoses or number of substances used per participant.

Category	Frequency	*Mdn*, Range
Mental Health Diagnosis		
Yes	9	2, 1-7
No	3	
Neurodevelopmental Diagnosis		
Yes	10	2, 1-4
No	2	
Substance Use		
Yes	8	1.5, 1-3
No	4	

Table 3: Frequencies of Mental Health Conditions

Diagnosis	Frequency
Anxiety	9
Depression	7
PTSD	4
Bipolar Disorder	3
Personality Disorder	2
Substance Use Disorder	2
Schizophrenia, Bulimia, Tourette's Syndrome, or Conduct Disorder	1

Table 4: Research Variables

Frequencies, and central tendencies of research variables.

Variable	*Mdn*, Range	Frequency
Executive Functioning		
Total EF Raw Score	52, 34-79	12
EF Percentile	98, 63-99	12
HRQOL (Physically Unhealthy Days)		
No unhealthy days	0	2
1 or more unhealthy days	10, 5-30	10
Chronic Health Conditions		
No chronic health conditions	0	6
1 or more chronic health conditions	2.5, 1-5	6

Table 5: Frequencies of Chronic Health Condition Diagnoses

Condition	Frequency
Chronic Ear Infection	4
Asthma	4
Rheumatoid Arthritis	2
Scoliosis	2
Congenital Heart Defect, Chiari Malformation Type 2, Gout, or Severe Anemia	1