

WELL-BEING AND SUICIDALITY AMONG TRANSGENDER YOUTH
AFTER GENDER-AFFIRMING MEDICAL INTERVENTIONS

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DOCTOR OF PHILOSOPHY

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ABSTRACT

Pubertal suppression and gender-affirming hormones have become accepted treatment in the management of gender dysphoria (GD) among transgender adolescents to relieve the distress associated with pubertal development and/or their existing secondary sex characteristics.

This study is a longitudinal evaluation of the effectiveness of these approaches for improving psychological well-being and decreasing suicidality among transgender youth referred to a transgender health specialty clinic at a large children's hospital. A total of 11 adolescents who had received pubertal suppression medication and a total of 47 youth (14 transmen and 33 transwomen; 43 adolescents and 4 young adults) who had received gender-affirming hormones were assessed at least two times: before the start of treatment and at least 3 months after treatment. After pubertal suppression medication, a non-significant increase in general well-being was observed while levels of suicidality remained the same. After gender-affirming hormones, a significant increase in levels of general well-being and a significant decrease in levels of suicidality were observed. These findings suggest that pubertal suppression medication and gender-affirming hormones are valuable medical interventions with promising psychosocial outcomes for transgender youth.

Key words: transgender, pubertal suppression, gender-affirming hormones, suicidality, well-being, adolescence

APPROVAL PAGE

The faculty listed below, appointed by the Dean of the School of Education, have examined a dissertation titled “Well-Being and Suicidality Among Transgender Youth After Gender-Affirming Medical Interventions,” presented by Luke R. Allen, candidate for the Doctor of Philosophy degree, and certify that in their opinion it is worthy of acceptance.

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CHAPTER 1

WELL-BEING AND SUICIDALITY AMONG TRANSGENDER YOUTH AFTER GENDER-AFFIRMING MEDICAL INTERVENTIONS

Statement of Purpose

Clinical practice guidelines recommend the administration of puberty suppression medication (gonadotropin-releasing hormone [GnRH] agonists) and, later, gender-affirming hormones (GAH; estrogen or testosterone) when treating gender dysphoria in adolescents (Coleman et al., 2012; Hembree et al., 2017). To date, however, there is limited evidence for the long-term effectiveness of puberty suppression medication and gender-affirming hormones among transgender adolescents on psychological outcomes (Costa et al., 2015; de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2011; de Vries et al., 2014). In addition, transgender youth experience elevated risks of a wide range of psychosocial problems and other conditions, such as depression, anxiety, autism spectrum disorder, suicidal ideation/attempts, and disordered eating behavior (Bechard, VanderLaan, Wood, Wasserman, & Zucker, 2017; Connolly, Zervos, Barone, Johnson, & Joseph, 2016). Preliminary evidence suggests that gender-affirming interventions may help decrease some of these symptoms, including anxiety and depression (Olson, Durwood, DeMeules, & McLaughlin, 2016). Despite preliminary evidence, as well as the establishment of clinical practice guidelines, gender-affirming care of transgender adolescent minors remains controversial in some outlets of the academic literature (e.g., Marchiano, 2017). Some of this controversy stems from a concern or fear that today's gender-affirming psychotherapeutic practices will lead to a high number of "false positives" (i.e., incorrectly ascribing a transgender identity through immediate affirmation of a youth's gender identity when, in fact, the youth is not "truly

trans;” Marchiano, 2017) and whether these youths transgender identity will stay stable overtime (Chen, Edwards-Leeper, Stancin, & Tishelman, 2018).

More research is needed to further develop and refine existing guidelines for the treatment of gender dysphoria among children and adolescents (Vrouenraets, Fredriks, Hannema, Cohen-Kettenis, & de Vries, 2015). The purpose of this study is to examine the potential effects of pubertal suppression medication and GAH on measures of general well-being and suicidality among youth who experience gender dysphoria.

Literature Review

Over the past few decades, the number of young people presenting to specialty clinics for gender dysphoria (GD) has been increasing world-wide (Chen, Fuqua, & Eugster, 2016; Olson-Kennedy et al., 2016). The term gender dysphoria refers to the distress a person may experience when there exists incongruence between one’s sex assigned at birth and their known, experienced gender identity. By definition, dysphoria means that the person suffers; the root of the word coming from the Greek ‘dysphoros,’ meaning ‘hard to bear’ (Dysphoria, n.d.). Transgender people have varying degrees of dysphoria; some have no gender dysphoria at all. Gender identity is complex and not fully understood (Hembree et al., 2017), but influenced by psychological, hormonal, environmental, genetic, and cultural factors (Hyde, Bigler, Tate, Joel, & van Anders, 2019). To have a transgender identity is to have a gender identity that is incongruent with one’s sex assigned at birth. Or, when used more broadly, a transgender identity may refer to people whose “gender identity and/or gender expression” differs from what is typically associated with their sex assigned at birth (Hembree et al., 2017, p. 3875). The term *gender identity* refers to one’s internal sense of self as contextualized within a specific gender category (or categories) such as male, female,

nonbinary, or agender (Hyde et al., 2019). As a challenge to the “gender binary” (i.e., the idea that only male and female genders exist), the experiences of transgender and nonbinary people demonstrate that one’s sex assigned at birth do not invariably predict how a person might identify with respect to gender. Nonetheless, for most human beings, gender identity is thought to become firmly established during the early childhood years, roughly between the age of four to seven (Ruble, Martin, & Berenbaum, 2006). Though, for some transgender individuals, gender identity may remain fluid for years (Fraser & De Cuypere, 2016), while some may move through a process of exploration or renegotiation of one’s gender throughout childhood or adulthood (Ehrensaft, 2016; Temple NewHook et al., 2018).

It is important for mental health professionals serving transgender and gender diverse youth to remember that the work of gender affirming mental health professionals is situated in a context wherein there is clear historical, and current, pathologizing of transgender individuals (Association of Lesbian, Gay, Bisexual, and Transgender Issues in Counseling, 2009; Winters, 2008). Even today if mental health trainees learn about transgender and gender diverse persons, the topic is likely only covered in a psychopathology course (Singh & dickey, 2016), which is a testament to the need for further affirmative training of mental health professionals as well as the field’s tendency to pathologize gender diverse identities.

Trans youth face much higher rates of societal stressors, discrimination, and interpersonal violence than their cisgender counterparts (Dank, Lachman, Zweig, & Yahner, 2014). Minority stress theory (Meyer, 2003) implies that sexual and gender minorities are at greater risk for mental and physical health problems by way of increased psychological distress resulting from the regular exposure of prejudice, discrimination, and stigma. The bullying of a transgender young person at school, for example, may contribute the

development of anxiety and depressive symptoms. Through the lens of minority stress theory, a psychologist would not necessarily view observed mental health disparities in transgender youth as reflective of inherent pathology inasmuch as the result of persistent stigma and discrimination (Hatzenbuehler & Pachankis, 2016; Meyer, 2003). The American Psychological Association (APA, 2015) reminds us that transgender and gender nonconforming persons tend to have more positive life experiences when they receive social support and trans-affirmative care (Guideline 11)—such affirming care may counteract some of the societal, personal, and environmental discrimination transgender youth can encounter.

From the perspective of gender affirming health care providers, gender diversity is viewed as a natural aspect of human diversity and the human condition. In this model, gender health is defined as the youth's "opportunity to live in the gender that feels most real or comfortable to that child and to express that gender with freedom from restriction, aspersion, or rejection" (Hidalgo et al., 2013, p. 286). Moreover, a child's gender identity is defined as the gender that the child articulates (see also Hidalgo et al., 2013). This model supposes that health providers and parents cannot presume a particular gender identity trajectory and must allow the child to explore and express gender identity for themselves. Correspondingly, a youth whose transgender or gender diverse identity persist into adulthood is not viewed as an unwanted outcome (APA, 2015).

Medicine and Clinical Practice

From the medical perspective, guidelines recommend treating gender dysphoria in peri-pubertal children and adolescents with puberty suppression medication, and later, gender-affirming hormones to help alleviate the distress associated with their dysphoria (Coleman et al., 2012; Hembree et al., 2017). In clinical practice, a young person's reaction

to the changes to their body at the onset of puberty will often offer essential diagnostic information regarding the intensity and persistence of their dysphoria (Coleman et al., 2012; Hembree et al., 2017). The unwanted physical changes that accompany puberty (e.g., facial hair, menses, voice changes, chest growth) often cause or exacerbate dysphoria (McGuire, Doty, Catalpa, & Ola, 2016). The relief provided by pubertal suppression or hormone therapy can be so great such that these interventions are potentially lifesaving (Edwards-Leeper & Spack, 2012; Gridley et al., 2016). Moreover, the timely medical treatment of gender dysphoria in peri-pubertal young persons may contribute to lifelong advantages, such as the avoidance of irreversible secondary sex characteristics (e.g., changes in voice) and promotion of appropriate height (by delaying or extending closure of growth plates; Olson, Forbes, & Belzer, 2011). In addition to treating the dysphoria, GAH can increase the likelihood of others perceiving the individual as their true gender, thereby potentially lessening the likelihood of experiencing hate crime motivated by transphobia or transnegativity.

There can be great risk in the delay of gender-affirming medical interventions for young persons. Feelings common to dysphoria, such as loneliness, hopelessness, and feeling different, may lead to self-harm, impulsivity, or suicide attempts (Skagerberg, Parkinson, & Carmichael, 2013). In the absence of proper medical care, some transgender youth may engage in unhealthy weight management behaviors (e.g., fasting >24 hours, vomiting, diet pill use, laxative use, intentional weight gain to hide the appearance of chest growth, etc.) to help maintain an image congruent with their gender identity (Guss, Williams, Reisner, Austin, & Katz-Wise, 2017). Research consistently demonstrates a much higher rate of suicidal ideation and self-harm or suicide attempts among transgender youth (Aitken, VanderLaan, Wasserman, Stojanovski, & Zucker, 2016).

Yet, there is limited research on the use of puberty suppression medication in transgender peri-pubertal children (Costa et al., 2015; de Vries et al., 2011; de Vries et al., 2014), and minimal research supporting the use of GAH in transgender adolescents (Hembree et al., 2017). The lack of research regarding gender-affirming care and transgender minors has real-life implications including the prolonged difficulty in securing access to healthcare services as well as insurance coverage (Nahata, Tishelman, Caltabellotta, & Quinn, 2017). Established Standards of Care have been alleged to be more of “expert opinion” rather than evidence-based (e.g., Drescher & Byne, 2012). Those cautious (or critical) of gender-affirming care in minors often cite the possibility of future regret (or “desistance;” i.e., as youth continue to develop socially and physically, they may cease to self-identify as transgender). They worry that regret may occur later in life because young people may lack the cognitive capacity or life experience and inadequate knowledge of self to make such major medical decisions.

The social development of children who go on puberty blockers could be impeded or negatively affected as they will not experience puberty at the same time as their peers. Of course, their social development may suffer if they experience clinically significant gender dysphoria as well. Others voice a concern that early medical intervention may interfere with further gender and/or sexual identity development by restricting “sexual appetite” and thereby the socio-sexual experiences that are potentially useful to the exploration of one’s sexual orientation and gender identity (Giovanardi, 2017; Korte et al., 2008). There may also be loss of fertility as gamete production (i.e., sperm and egg) is prevented when puberty suppression medication is given in the early stages of puberty *and* there is subsequent administration of GAH (e.g., around the age of 16) because the body would not be allowed

the opportunity to produce sperm or mature eggs. Fertility may still be preserved through discontinuing pubertal suppression, or even gender-affirming hormones, long enough to promote gamete maturation for cryopreservation (Hembree et al., 2017); however, this is often not preferred by youth as such maturation is also associated with unwanted secondary sex characteristics.

Understandably, many parents are often uncertain about whether gender-affirming treatments are the “right” choice for their children, given these concerns and the lack of research. Parents play a significant role in the health and well-being of their transgender children, especially as the parents have the medical decision-making power. The American Academy of Pediatrics Committee on Bioethics (1995) argues that social forces tend to give health care decision-making power to parents and physicians, and therefore diminish “the moral status” of youth (see also Vaught, 2008). Consequently, the intersection of being a minor and transgender can be particularly problematic if access to care is denied or unnecessarily delayed, given that pubertal suppression medication and gender-affirming hormone therapy is a potentially lifesaving intervention (Edwards-Leeper & Spack, 2012; Gridley et al., 2016). Simons, Schragar, Clark, Belzer, and Olson (2013) found that parental support was associated with improved quality of life and lower levels of depressive symptoms in transgender adolescents. Conversely, parental rejection seems to be one of the more significant risk factors associated with negative health outcomes among transgender youth (Klein & Golub, 2016; Ryan, Huebner, Diaz, & Sanchez, 2009). In recent qualitative study, having supportive parents and access to (competent) affirming medical care were among the most important things that adult transgender people believed would have helped them during their adolescence (Allen, Watson, & VanMattson, 2019). Notably, some

participants felt that had they been allowed transition earlier, they might have fewer self-esteem problems and less social anxiety.

The limited available research on how to best treat gender dysphoria in youth does not only influence parental decision-making—anecdotally, hospitals and other agencies may also be reluctant to establish gender clinics or provide trans affirmative care due. Despite multi-disciplinary gender clinics becoming more commonplace (see Human Rights Campaign, n.d.), there remains a dearth of trainers and providers, and often lengthy waitlists at specialty clinics (Eyssel, Koehler, Dekker, Sehner, & Nieder, 2017; Vance, Halpern-Felsher, & Rosenthal, 2015). This is a compounding problem given that, simultaneously, the number of referrals to gender clinics are increasing. At Gender Pathway Services (GPS) clinic, some patients come from more than four hours away. Further research on the psychological effects and outcomes of gender-affirming care among transgender children and adolescents may help develop and refine best treatment practices for this underserved and poorly researched population (Vrouenraets, Fredriks, Hannema, Cohen-Kettenis, & de Vries, 2015). By establishing a greater evidence base for treatment, such research has the potential to also aid in dismantling the structural, institutional, and societal barriers that young transgender persons often encounter when seeking care.

Prevalence and Co-Occurring Conditions

The *Diagnostic and Statistical Manual of Mental Disorders–5* offers “modest underestimates” of the prevalence of gender dysphoria occurring in transgender adult men ranging from 0.005% to 0.014%, and for transgender women from 0.002% to 0.003% (American Psychiatric Association, 2013, p. 454), although a credible prevalence estimate of gender dysphoria is hard to ascertain. Studies have rarely used the same or similar

methodology when reporting on prevalence, and there is little standardized or routine collection of data at a population level (Collin, Reisner, Tangpricha, & Goodman, 2016). Many prevalence estimates of gender dysphoria are extrapolated by dividing the number of persons presenting at gender clinics in a given area by the local population (e.g., Judge, O'Donovan, Callaghan, Gaoatswe, & O'Shea, 2014). Some of the obvious problems with prevalence estimates are that not all families or youth have the resources to access care, youth may not have disclosed their identity to the family, or families might be unsupportive of their children's gender identity and refuse care. Thus, those who do not seek care are not included in the estimation. State-level, population-based surveys place estimates of transgender youth at about .7% (Herman, Flores, Brown, Wilson, & Conron, 2017).

There is quite a large body of research documenting that gender dysphoric youth who present at gender clinics are at an increased risk for a wide range of co-occurring psychosocial conditions, including depression, anxiety disorders, disordered eating behavior, and autism spectrum disorder (de Vries et al., 2011; Olson, Schrager, Belzer, Simons, & Clark, 2015; Satterwhite et al., 2013). Bechard and colleagues (2017) reported on suicidality and self-harm across several studies that examined clinic-referred adolescents with gender dysphoria. Approximately 28.8% to 41% engaged in self-harming behaviors, 17.5% to 42.2% reported suicidal ideation, and 11.9% to 15.8% reported suicide attempts. In a different study, Kaltiala-Heino, Sumia, Työläjäarvi, and Lindberg (2015) found a reported rate of 53% for combined "suicidal and self-harming [behaviors]." Another study found a lifetime prevalence of 51% for suicidal ideation and 30% for suicide attempts (Olson et al., 2015). Comparable figures have been reported for transgender adults (e.g., Adams, Hitomi, & Moody, 2017; Marshall, Claes, Bouman, Witcomb, & Arcelus, 2016).

Among various clinics for youth presenting with gender dysphoria, the prevalence of co-occurring depression symptoms of clinical significance ranges between 35% to 58.1% (Bechard et al., 2017; Olson et al., 2015; Spack et al., 2012). In the broader population of youth, 12-month prevalence estimates for depression are about 7.5% (Avenevoli, Swendsen, He, Burstein, & Merikangas, 2015), suggesting that transgender youth experience much higher rates of depression. Anxiety appears to co-occur within about 16.3% to 25% of GD-referred youth (Khatchadourian, Amed, & Metzger, 2014; Spack et al., 2012). In one study, the prevalence of anxiety among adolescent transgender males was 33% (Khatchadourian et al., 2014). For the sake of comparison, the lifetime prevalence of “any anxiety disorder” among the general population of children and adolescents is about 15% to 20% (Beesdo, Knappe, & Pine, 2009).

Around 4% to 5% of GD-referred youth have co-occurring eating disorders (Bechard et al., 2017; Khatchadourian et al., 2014). Guss and colleagues (2017) found that transgender youth had higher odds of using diet pills, taking laxatives, using steroids without prescription, and fasting for greater than 24 hours. The 12-month prevalence of any type of eating disorder among the broader population of youth appears to be around 1.7% (Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011). In addition, up to 20% of referrals to gender clinics report features of autism spectrum disorder (ASD) in the clinical range (Van der Miesen, Hurley, & de Vries, 2016). Prevalence estimates of ASD in the general population are around 1% (Lai, Lombardo, & Baron-Cohen, 2014). In general, the prevalence of psychosocial problems among transgender youth are higher than the general population.

Outcomes After Gender-Affirming Interventions Among Children and Adolescents

There is little research on the mental health or psychological outcomes of transgender youth following gender-affirming medical intervention. Some research has shown parent ratings of children's depression and anxiety improved when the children were supported in their identities and allowed to socially transition (total sample size, $N = 73$) (Olson et al., 2016). *Social transitioning* refers the steps one can take to present (or make others aware of) their gender identity. Such steps might include growing out or cutting one's hair, a name change, or change in type of clothing worn (e.g., traditionally "feminine" or "masculine" appearance). Durwood, McLaughlin, and Olson (2017) examined depression and anxiety among transgender children who had socially transitioned using the National Institutes of Health's Patient Reported Outcomes Measurement Information System (Irwin et al., 2010; Varni et al., 2012). They found that the depression scores of children who had socially transitioned were similar to that of age and gender-matched controls; however, they had also demonstrated marginally higher anxiety. Durwood and colleagues (2017) also measured self-worth among socially transitioned youth; compared to controls, socially transitioned youth did not differ. Although, socially transitioned children scored higher on self-worth compared to other studies of gender-typical children. The authors noted that these findings are striking when compared to the very high rates of depression and anxiety in children who had not socially transitioned. Taken together, these studies suggest that transgender children experience improved mental health outcomes when they are supported in their identities and allowed to socially transition.

Few studies have been conducted examining psychological outcomes after medical interventions among transgender adolescents. Using a repeated-measures analysis of variance (ANOVA) design, a research team from the Netherlands measured behavioral and emotional

problems (i.e., depression, anxiety and anger, general functioning, gender dysphoria, and body satisfaction) before the start of puberty suppression medication and shortly before the administration of gender-affirming hormones ($N = 70$) (de Vries et al., 2011).¹ They found that behavioral and emotional problems and depressive symptoms decreased after these interventions (as measured by the CBCL and the YSR); however, anxiety and anger, gender dysphoria, and body satisfaction scores remained the same.

In a later study of 55 young transgender adults², de Vries and colleagues (2014) examined psychological outcomes (i.e., GD, body image, global functioning, depression, anxiety, emotional and behavioral, social and educational/professional functioning, and quality of life) after puberty suppression and gender confirmation surgery. The authors found psychological functioning had improved over time, gender dysphoria had resolved, and quality of life, satisfaction with life, and subjective happiness were comparable to same-age peers. Costa and colleagues (2015) conducted a study examining the effects of psychological support ($n = 201$) and pubertal suppression ($n = 121$) on global psychosocial functioning among transgender children. They found both psychological support and suppression were associated with improved global psychosocial functioning. Another study has demonstrated that transgender minors who had undergone chest reconstruction showed improvements on a “chest dysphoria” measure (Olson-Kennedy, Warus, Okonta, Belzer, & Clark, 2018).

Body image is another aspect of well-being that is important to consider for transgender youth. Gender-affirming medical interventions such as hormone therapy have

¹ This study had a total sample size of 70. However, not all adolescents received all measures at T0 and T1. Only 41 adolescents were administered measures of depression, trait anger, trait anxiety, global functioning, and gender dysphoria at T0 and T1. For body image, 57 adolescents completed measures at T0 and T1. Only 54 adolescents completed the CBCL and YSR at T0 and T1.

² Some participants reported in this study are the same as those reported on by de Vries et al., (2011).

been related to lower body-related uneasiness (Fisher et al., 2014), improved psychological functioning (Keo-Meier et al., 2015), and quality of life (Ainsworth & Spiegel, 2010). Overall, the evidence suggests that youth who received gender-affirming medical interventions for gender dysphoria experience a corresponding alleviation of the dysphoria and overall improved mental health outcomes may improve differentially, depending on treatment (i.e., GnRH analogues, GAH, and eventually surgery; gender dysphoria appears to decrease most after major interventions such as surgery).

However, medical intervention is not a panacea. Even with affirming medical interventions, transgender youth may experience co-occurring mental health conditions at higher rates when compared to the general population (Dhejne et al., 2011) as outcomes are biased by pre-treatment levels of mental health problems (Jones, Bouman, Haycraft, & Arcelus, 2018). Co-occurring conditions such as anxiety and depression are likely impacted by cultural norms and experienced discrimination (APA, 2015; Testa, Habarth, Peta, Balsam, & Bockting, 2015). Blockers and GAH will not resolve oppression, post-traumatic stress, nor social anxiety. Therefore, comprehensive gender-affirming care should be responsive to oppression and discrimination (Wylie et al., 2016) and examine the potential psychosocial impact of medically transitioning on client's lives, including their mental health, friends and social circles, family, employment, and their role in society (Hembree et al., 2017).

Further research is needed to help develop and refine best practices for serving transgender youth and to alleviate dysphoria and associated co-occurring conditions (e.g., anxiety, depression, suicidality, etc.). Research examining mental health outcomes among transgender youth is a priority (Chew, Anderson, Williams, May, & Pang, 2018; Mahfouda, Moore, Siafarikas, Zepf, & Lin, 2017; Olson-Kennedy et al., 2016), and thus far, no studies

to date have reported on general well-being and suicidality outcomes after gender-affirming medical interventions among transgender children and adolescents.

Gender differences and outcomes. Transgender youth assigned female at birth present to clinics with higher levels of externalizing and internalizing symptoms as measured by the Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1983) and Youth Self-Report (YSR; Achenbach & Edelbrock, 1986) than those assigned male at birth (de Vries et al., 2011). Trans boys and trans girls respond differently to puberty blockers and their respective hormones regimens (Chew et al., 2018; Hembree et al., 2018). There have been some reports of increased health risk (e.g., arterial hypertension) in cisgender girls treated with GnRH analogues for precocious puberty and other conditions (Calcaterra et al., 2013; Hembree et al., 2017; Siomou et al., 2014). Hot flashes tend to be more common among trans boys treated with GnRHa than trans girls (Chew et al., 2018). In response to hormonal treatment, trans men may begin developing a deeper voice, acne, experience menorrhagia, and growing facial hair after about six months of treatment, while trans women on estrogen will not experience any voice change but instead experience chest growth and softening of skin, among other feminizing effects (Chew et al., 2018; Hembree et al., 2017). At the same time, testosterone is known to make one's mood stable and estrogen has the potential make one's mood more labile (Slabbekoorn, Van Goozen, Gooren, & Cohen-Kettenis, 2001). Following pubertal suppression medication and gender-confirmation surgery, de Vries and colleagues (2014) found that transmen reported greater reduction in anger, anxiety and externalizing symptoms (e.g., rule-breaking or aggressive behavior) than transwomen, who demonstrated either stability or a slight increase in these symptoms.

Collectively, the available research suggests that transgender youth respond differently to pubertal suppression and GAH treatment across several domains (e.g., general physical health effects, mood fluctuations, and development of secondary sex characteristics) depending upon sex assigned at birth. General health and mood (in)stability are associated with suicidal ideation (Bowen, Balbuena, Peters, Leuschen-Mewis, & Baetz, 2015; Druss & Pincus, 2000) as well as decreased perceptions of well-being (Houben, Van Den Noortgate, & Kuppens, 2015; Hoyt, Chase-Lansdale, McDade, & Adam, 2012). Moreover, the social aspect of medical transitioning and “passing”³ may be easier for trans boys and men due to clear vocal changes (i.e., voice deepening) and facial hair growth, which are traditionally seen as indicators of one’s gender, compared to transgender girls and women who experience neither of these as a result of GAH. Also, some transgender girls and women wish to publicly transition only after receiving gender-affirming care and may face more social ostracism or rejection due to the societal stigma around birth-assigned boys displaying feminine characteristics or interests (de Vries, Steensma, Cohen-Kettenis, VanderLaan, & Zucker, 2016; Edwards-Leeper et al., 2017), which may result in increased suicidal ideation (Testa et al., 2017). Taken together, these findings suggest there might be differential direct and indirect treatment effects between trans boys and trans girls on each dependent variable (well-being and suicidality). Thus, a secondary objective of this study is to determine if one’s sex assigned at birth does, in fact, interact with time for each treatment (puberty blockers or gender-affirming hormones) to affect clinical outcomes.

³ For some transgender people, ‘passing’ means to be perceived by others as the gender with which they identify or correctly gendered. The concept of ‘passing’ may not be applicable to all transgender people as the goal for some non-binary people is not to be perceived as either “man” or “woman”—rather, society ought to expand its binary conceptualization of gender and allow for a wide range of gender expressions and identities (Flores et al., 2018).

Present Study

Using data collected (throughout the course of standard clinical practice) at a multi-disciplinary gender clinic in a children's hospital, the present study addresses four primary mental health related research questions:

- 1) Is puberty suppression medication related to greater *general well-being* (as measured by the *General Well-Being Scale* [GWBS] of the *Pediatric Quality of Life* [PedsQL] *Inventory*; Varni, Seid, & Kurtin, 1999) among transgender youth?
- 2) Are gender-affirming hormones related to greater *general well-being* (as measured by the GWBS)?
- 3) For transgender youth, is suicidality negatively associated with puberty suppression medication (as measured by the *Ask Suicide-Screening Questions* [ASQ]; Horowitz et al., 2012)?
- 4) For transgender youth, is suicidality negatively associated among gender-affirming hormones (as measured by the ASQ)?

Hypotheses

H1: Pubertal suppression medication will be negatively associated with suicidality between initial intake and final assessment among transgender youth.

H2: Pubertal suppression medication will be positively associated with general well-being between initial intake and final assessment among transgender youth.

H3: Gender-affirming hormones will be negatively associated with suicidality between initial intake and final assessment among transgender youth.

H4: Gender-affirming hormones will be positively associated with general well-being between initial intake and final assessment among transgender youth.

Secondary Objectives

H5: I expect an interaction effect between sex assigned at birth and time such that those assigned female at birth will experience greater improvements in general well-being and larger decreases in suicidality at final assessment for each treatment type (pubertal suppression medication and gender-affirming hormones) than those assigned male at birth.

CHAPTER 2
WELL-BEING AND SUICIDALITY AMONG TRANSGENDER YOUTH
AFTER GENDER-AFFIRMING MEDICAL INTERVENTIONS

Method

Participants

Participants included youth (i.e., adolescents and young adults from roughly ages 13 up to age 20) who have received services for gender dysphoria at Children’s Mercy Hospital’s Gender Pathway Services (GPS) clinic ($N = 310$) since its opening in 2014. In the current study, participants have been included as long as the final assessment was at least three months after administration of the treatment. The final sample size contained a total of 54 participants. Characteristics of participants are described below and can be found in Table 1.

A total of 11 participants had pre-test (i.e., initial intake) and final assessment data for puberty suppression medication. Participants largely were assigned female at birth (8 [72.7%]) and 3 assigned male at birth (27.3%). At pre-test (T_0 ; i.e., administration of blockers), the age of participants ranged from 12.10 to 16.40 years ($M = 14.29$, $SD = 1.43$). The range of treatment length was 116 to 743 days, with a mean of 297 days ($SD = 193$). For most of the sample (90.9%), duration of treatment was at, or under, 435 days. Among those treated with puberty blockers, 9 (81.8%) identified as White; 1 (9.1%) identified as Hispanic/Latinx; 1 (9.1%) as Asian. Due to the small sample size and to lessen the likelihood of potential re-identification of study participants (see El Emam, Jonker, Arbuckle, & Malin, 2011), only overall median income is reported. The median overall ZIP-code based household income was \$63,163. Eight participants (72.7%) paid with private insurance and three (26.3%) participants paid with Medicaid.

A total of 47 eligible participants had pre-test and final assessment data for gender-affirming hormones. Of the 47 participants, eight were administered GnRH analogs in our clinic prior to beginning GAH. However, only four of those eight participants were included in the GnRH analogs treatment group (as the other four did not have pre-test data available). Participants who had received GAH were largely assigned female at birth (33 [70.2%]) and 14 assigned male at birth (29.8%). At pre-test (T_0 ; i.e., before administration of GAH), the age of participants ranged from 13.73 to 19.04 years ($M = 16.59$, $SD = 1.19$). Most participants (90%), were at, or below, the age of 18.01 years at the administration of GAH. Of the pre-test and final assessment data utilized for this study, the range of treatment length was 113 to 1016 days, with a mean of 349 days ($SD = 193$). For most of the sample (90%), duration of treatment was at, or under, 600 days. Of the sample treated with GAH, 39 (83%) identified as White; 3 (6.4%) as Hispanic/Latinx; 2 (4.3%) as Multiracial; 1 (2.1%) identified as American Indian or Alaskan Native; 1 (2.1%) as Black or African American.

Similar to other chart review studies (e.g., Gilbert, Savage, Whitesell, Conklin, & Fineberg, 2015), the median household income for each participants' zip code was obtained to use as a proxy for socio-economic status (SES) from publicly available information derived from the United States Census Bureau (Income by Zip Code, n.d.). Median income was chosen as a metric because it is less likely to be influenced by outliers. The ZIP-code based household income varied, with 13 participants (27.7%) living in ZIP codes with a median income equal to or less than \$47,165, 12 participants (25.5%) with incomes from \$48,043 to \$58,818, 13 participants (27.7%) with incomes from \$61,168 to \$69,370, and 9 participants (19.1%) with incomes over \$75,900. For the GAH treatment group, the median overall ZIP-code based household income was \$57,355. Also similar to other chart review

studies (e.g., Gilbert et al., 2015), insurance coverage was reported as either private insurance, Medicaid, or self-pay. Forty-one participants (75.9%) paid with private insurance, 12 participants (22.2%) paid with Medicaid, and one participant (1.9%) used self-pay.

Table 1

Demographic Characteristics for Participants who received Blockers (N = 11), GAH (N = 47), and the Groups Combined (N = 54).

Demographic characteristics	Blockers <i>n</i> (%)	GAH <i>n</i> (%)	Combined Groups <i>n</i> (%) ^a
Mean age at administration	14.29 years	16.50 years	-
Mean duration of treatment	297 days	349 days	-
Birth assignment			
Assigned female at birth	8 (72.7)	33 (70.2)	38 (70.7)
Assigned male at birth	3 (27.3)	14 (29.8)	16 (29.3)
Race/Ethnicity			
White	9 (81.8)	39 (83)	45 (83.3)
Biracial or multiracial	0 (0)	2 (4.3)	2 (3.7)
Latinx or Hispanic	1 (9.1)	3 (6.4)	4 (7.4)
Black or African American	0 (0)	1 (2.1)	1 (1.9)
American Indian or Alaskan Native	0 (0)	1 (2.1)	1 (1.9)
Asian	1 (9.1)	1 (2.1)	1 (1.9)
Medium Income (Based on ZIP code)	\$63,163	\$57,355	\$60,937
Insurance Type			
Self-Pay	0 (0)	1 (2.1)	1 (1.9)
Private	8 (72.7)	36 (76.6)	41 (75.9)
Medicaid	3 (27.3)	10 (21.3)	12 (22.2)

^a The combined treatment group column does not equal the sum of each treatment group as some participants were in each treatment group and not counted twice.

Services provided at Gender Pathway Services (GPS). The services provided in GPS clinic are similar to other specialty gender clinics (e.g., Edwards-Leeper & Spack, 2012) and gender-affirming models of care (Chen, Hidalgo, et al., 2016). Patients and their families are self-referred or referred by professionals in the community who are familiar with the services provided at GPS clinic. An administrative assistant obtains information related to the referrals. The GPS social worker then schedules a telephone psychosocial assessment. If there is an outside mental health referral with a diagnosis of gender dysphoria, then the

patient may be sent directly to multidisciplinary team where they may be seen by nurses, an endocrinologist, psychologists, chaplain, and social workers to be assessed for the appropriateness of pubertal suppression medication (or “blockers”) and/or GAH. The multidisciplinary team meets once a week for a half-day clinic, during which they see up to four patients. Individual appointments may last two to three hours, whereby patients are seen by each team member. The multiple disciplinary team sees patients once a year, and during the interim patients may see GPS endocrinologists, nurses, and psychologists individually for follow-up care. Assent or informed consent (depending upon age and legal status) is obtained from the youth and informed permission obtained from their legal guardian(s). Discussion occurs around fertility preservation, length of care, current mental and physical health, and social support.

If patients do not have an outside mental health referral with a diagnosis of GD, then the youth and their family are seen for a more comprehensive diagnostic evaluation to determine eligibility for treatment. Provided youth meet eligibility criteria for gender-affirming interventions, they are referred to the multidisciplinary treatment team or directly to endocrinology. Patients are “aged out” of the children’s hospital by age 22. GPS clinic broadly conforms to World Professional Association for Transgender Health (WPATH) Standards of Care, version 7 (Coleman et al., 2012)⁴ and the Endocrine Society’s Clinical Practice Guidelines for the treatment of gender-dysphoric/gender-incongruent people (Hembree et al., 2017). Consistent with existing standards of care, youth are considered eligible if: i) there is a history of gender nonconformity or gender dysphoria, ii) emergence or worsening of GD at the onset of puberty, iii) any coexisting medical, or psychosocial

⁴ The WPATH Standards of Care, version 8, is currently being developed.

problems that may interfere with assessment or treatment (e.g., treatment adherence) have been addressed, and iv) there is parental permission and support, informed consent and adequate comprehension of the impact of medical interventions.

Procedure

The Institutional Review Board (IRB) of the University of Missouri-Kansas City ceded IRB review and continuing oversight duties to the Children's Mercy Hospital (CMH) IRB. Study approval was received from the CMH IRB. Data collection has been, and is, an on-going part of standard clinical care at Children's Mercy Hospital Gender Pathway Services ("GPS Clinic").

In clinical practice at GPS Clinic, patients are administered questionnaires at intake and then once again during their (roughly) 1-year multidisciplinary follow-up appointment. The patient's Medical Record Number is input manually into a REDCap server in order to create a record for the patient. REDCap is a secure HIPAA-compliant web application for building and managing online surveys and databases. When the patient has a REDCap record, the mental health provider on the team opens a survey in the patient's record for the patient to complete (so that their responses may be linked to their existing REDCap record). The REDCap survey is then administered to the patient. Responses are reviewed on REDCap by the treatment team prior to meeting with the patient. On the measure for suicidality, the treatment team considers patients to screen "positive" if they answered yes to any item of the four items (and the mental health providers have a better sense of areas to focus on when meeting with the patient). Patient responses to a general well-being measure provides the mental health professionals insight into the patient's psycho-social functioning (e.g., friends and familial support, general health, depression, hope for the future), which help guide the

interaction with the patient. The times between multidisciplinary follow-up appointments sometimes vary, with some patients being seen roughly at 5 to 6 months.

A list of potential participants were obtained by screening REDCap data for records that indicate a GPS Clinic patient has been administered the general well-being measure and suicide screener on at least two occasions (i.e., possible pre-test and final assessment data points); patients with at least two data points were considered potential participants. Cerner medical records of these potential participants were reviewed in order to determine if these patients were, in fact, administered a treatment during their visit (i.e., puberty blocking medication or GAH). Patients with pretest and final assessment data for the dependent variables, and with a treatment duration of at least three months for at least one treatment type, comprised the final sample.

Perhaps due to already limited sample sizes and the utilization of real-world data, previous studies examining the effect of blockers and hormones have not often statistically (or by design) controlled for duration of treatment (i.e., time between pre-test and final assessment; de Vries et al., 2011; de Vries et al., 2014). However, effects of pubertal suppression medication have been reported as soon as three months after administration (Chew et al., 2018; Klink, Caris, Heijboer, van Trotsenburg, & Rotteveel, 2015). In existing studies, the physical effects of GAH in transgender youth are reported as soon as three months after administration (Burke et al., 2016; Tack et al., 2017) and most effects of the medication are seen by this time—though, maximum effects may take longer (e.g., up to 2 to 3 years to see the full effect on estrogen chest development). Most studies have provided only the mean duration and range of treatment (e.g., Chew et al., 2018; de Vries et al., 2011; de Vries et al., 2014; Klink et al., 2015).

Measures

Dependent variables. The outcome variables for these analyses include two measures: suicidality and well-being.

Suicidality. The *Ask Suicide-Screening Questions* (ASQ) is a four-item dichotomous (*yes, no*) response measure with high sensitivity (i.e., ability to identify patients who are at risk of attempting suicide or “true positives”), released by the National Institute of Mental Health designed to identify risk of suicide (Horowitz et al., 2012). Questions include: In the past few weeks have you... “...wished you were dead?”, “...felt that you or your family would be better off if you were dead?”, “...been having thoughts about harming or killing yourself?”, or “...done anything to hurt yourself or to end your life?” For the purposes of this study, a response of “no” was scored as 0 and a response of “yes” was scored as 1; each item was summed generating an overall score for suicidality on scale ranging from 0 to 4, with higher scores indicating greater levels of suicidal ideation. The ASQ has a sensitivity of 97.6%, a specificity (i.e., ability to identify patients who are not at risk of attempting suicide or “true negatives”) of 65.6%. When compared to the Suicidal Ideation Questionnaire (SIQ; Reynolds, 1987), the ASQ had a negative predictive value of 96.9% (Horowitz et al., 2012). The Cronbach’s alpha for the current study was .81 at pre-test and at final assessment.

Well-being. The *PedsQL General Well-Being Scale* (GWBS; Varni et al., 1999) utilizes a 5-point response scale, contains 7 items, and measures two dimensions (“general well-being” and “general health”). The general well-being subscale includes six items. Example items include “I feel happy” and “I think my health will be good in the future.” Participants are asked to consider each item over the past month and rate responses from 0 (*never*) to 4 (*almost always*). The general health subscale contains one item, “In general, how

is your health?" ranging from 0 (*Bad*) to 4 (*Excellent*). All items are scored and linearly transformed to a 0 to 100 scale (initial score of 0 = 0, 1 = 25, 2 = 50, 3 = 75, and 4 = 100) for standardized interpretation. High scores indicate perceptions of minimal problems, high well-being. The measure has demonstrated adequate to good internal consistency (ranging from .70 to .92). Clinical validity has been established by demonstrating that PedsQL scores are able to distinguish between pediatric cancer patients on- and off-treatment (Varni et al., 1999). The Cronbach's alpha for the current study was .81 at pre-test and .82 at final assessment.

Independent Variables

Independent variables. The key independent variables for these analyses include pubertal suppression medication and gender-affirming hormones.

Pubertal suppression medication. The preferred method of pubertal suppression in the treatment of transgender children and adolescents is through the administration of GnRH agonists, which work by greatly reducing or stopping gonadal hormone production, thus preventing the start of puberty or halting puberty (Chen et al., 2016; Shumer, Nokoff, & Spack, 2016). Transgender youth who are administered blockers are temporarily spared future distress and dysphoria via the prevention of unwanted secondary sex characteristics, often providing great relief. The effects of blockers occur relatively immediately: Menses stop, although a single period may occur two weeks after therapy has been started. Breast, pubic hair, testicular, and phallus growth stop and often regress. Skeletal growth and maturation slow to age-appropriate rates. Serum testosterone or estradiol concentrations fall to prepubertal levels. (Muir, 2006, p. 380)

Guidelines suggest that transgender children begin pubertal suppression at Tanner stages 2 or 3 (Hembree et al., 2017). Tanner stages are stages of puberty and not necessarily reflective of chronological age (Edwards-Leeper, Feldman, Lash, Shumer, & Tishelman, 2017). Stages 2 and 3 indicate puberty has just begun (de Vries & Cohen-Kettenis, 2012). In terms of breast development, Tanner stage 2 is defined by budding nipples and slightly more breast volume (Hembree et al., 2017). In terms of male external genitalia, Tanner stage 2 is defined by a slight enlargement of penis, enlarged scrotum and reddening of the scrotal skin, and greater testicular volume (Hembree et al., 2017). It is common to begin pubertal suppression in later Tanner stages because of time of presentation to the clinic (e.g., youth presenting to clinic after puberty has already begun). At GPS clinic, a pediatric endocrinologist confirms that puberty has started prior to the administration of blockers. Pubertal suppression medication alone is not typically offered at stage 5 (Coleman et al., 2012), which indicates full adult growth has been reached. However, pubertal suppression medication might still be administered at later stages to stop menses in trans males and prevent future facial hair growth in trans women (Hembree et al., 2017).

Pubertal suppression medication has been used since the 1960s for children with precocious puberty (Collipp, Kaplan, Boyle, Plachte, & Kogut, 1964; Schoen, 1966). Precocious puberty is defined as the onset of puberty occurring before age nine for those assigned male at birth and before age eight for those assigned female at birth (Fuqua, 2013). Potential side effects of GnRH analogs (or agonists) include lower bone mineral density (BMD); however, lower BMD may be mitigated with calcium supplements and regular exercise or physical activity (Hembree et al., 2017). BMD levels may also return to near normal levels after GAH treatment (Cohen-Kettenis, Delemarre-van de Waal, & Gooren,

2008). Other side effects may include arterial hypertension, hot flashes, fatigue, and mood alternation.

In the treatment of gender dysphoria among children and adolescents, other alternatives to GnRH analogs exist, such as progestin or antiandrogens, which directly suppresses androgen synthesis or action (Hembree et al., 2017). These alternatives are acceptable when persons may not have access to GnRH analogs because of insurance denial, high cost, or other reasons. Blockers are considered a fully reversible intervention (Hembree et al., 2017), with puberty usually resuming and progressing at a normal rate following discontinuance of treatment (Muir, 2006). In testing the effect of puberty blockers, time 0 (T_0) was the most recent score of general well-being and suicidality available prior to administration of blockers. Time 1 (T_1) was the last available assessment point. However, if a participant has continued on to be administered GAH after having been on blockers *only*, then T_1 was operationalized as the last available assessment point prior to the patient having started GAH.

Gender-affirming hormones. Current practice guidelines by WPATH (Coleman et al., 2012) and the Endocrine Society (Hembree et al., 2017) recommend the administration of sex hormone treatment roughly around the age of 16. This age is also when adolescents have sufficient mental capacity or “competence,” to provide informed consent (Coleman & Rosoff, 2013; Mann, Harmoni, & Power, 1989; Vaught, 2008). In many countries, 16-year-olds are considered legal adults, possessing medical-decision making autonomy (Coleman et al., 2012; Milrod, 2014). The Endocrine Society recognizes there may be compelling reasons to initiate sex hormone treatment before the age of 16, although there is limited research on the use of sex hormones in transgender youth prior to the age of 13.5 to 14 years old. When

hormone treatment is administered before the age of 16, it is recommended that, “an expert multidisciplinary team of medical and [mental health professionals] manage this treatment” (Hembree et al., 2017, p. 3,871).

Hormone regimens for transgender girls and women include estrogen as well as anti-androgens or GnRH agonist to suppress endogenous masculinizing sex hormones (Hembree et al., 2017). The feminizing effects of hormone treatment for transgender girls and women include: redistribution of body fat, decrease in muscle mass and strength, softening of skin or/decreased oiliness, decreased sexual desire, decreased spontaneous erections, breast growth, decreased testicular volume (Hembree et al., 2017). All of these effects may be seen by six months after treatment, with onset of these effects occurring between one to six months (Hembree et al., 2017).

Hormone regimens for transgender males consist of testosterone. The masculinizing effects of hormone treatment for transgender males include: skin oiliness/acne, facial/body hair growth, increased muscle mass/strength, fat redistribution, cessation of menses, clitoral enlargement, vaginal atrophy, and deepening of voice (Hembree et al., 2017). Most of these effects occur by at least six months, with onset most often occurring between one to six months (Hembree et al., 2017).

Like most medical procedures, there are also risks associated with sex hormone therapy. Transgender girls and women on estrogen are at a very high risk of thromboembolic disease and at a moderate risk for macroprolactinoma, breast cancer, coronary artery disease, cerebrovascular disease, cholelithiasis, and hypertriglyceridemia (Hembree et al., 2017). Transgender males on testosterone are at a very high risk of erythrocytosis and a moderate risk of severe liver dysfunction, coronary artery disease, cerebrovascular disease,

hypertension, and breast or uterine cancer (Hembree et al., 2017). At GPS clinic, endocrinologists monitor for these adverse outcomes through regularly scheduled follow-up appointments. When conducting the analysis for the effect of gender-affirming hormones, T_0 represents the most recent score available prior to start of GAH. The final assessment (T_1) represents the last data point available for the participant, as long as the data point is at least roughly three months after administration of GAH. Participants who did not have a second data point at least roughly three months after having started either treatment were not included in the analyses.

Results

Data Cleaning Procedures

Prior to March 2017, only three items of the ASQ were administered (i.e., the item “...felt that you or your family would be better off if you were dead?” was not included). No additional data were missing. As opposed to data that may be missing in nonrandom patterns for unknown reasons possibly related to bias in the variable being measured or sampling bias, the reason for the missing data in this study is known (i.e., the item was not asked by providers prior to March 2017). Thus, for purposes of statistical analyses, the data for the ASQ item that was missing are considered *missing at random* (MAR), as they likely do not introduce unknown bias (McKnight, McKnight, Sidani, & Figuerdo, 2007). As an additional measure to demonstrate the data are MAR (i.e., to assess whether there might be systematic differences between the two groups related to the DVs), two *t*-tests were conducted on the final assessment ASQ and GWBS scores between people who had and did not have missing data at T_0 . There were no significant differences at final ASQ assessment between participants with and without missing data, $t(56) = -.38, p = .71$. Likewise, there were no significant differences at final GWBS assessment for participants with and without missing

data, $t(56) = -.38, p = .70$. Thus, the missing values were truly considered MAR and were imputed with expectation maximization (EM; Graham, 2009). The assumption-testing procedures described below for the pubertal suppression and GAH treatment groups were conducted prior to the EM being performed.

Analyses for Pubertal Suppression Medication

A power analysis was conducted to determine the number of participants needed in this study. The α for the mixed Analysis of Covariance (ANCOVA) was set at .05. To achieve power of .80 and a medium effect size ($f^2 = .25$), a total sample size of 34 was required for each ANCOVA (i.e., puberty suppression medication and gender-affirming hormones) to detect a significant model ($F[1, 33] = 4.15$) where sex assigned at birth is a between-subjects factor and time is the within-subjects factor. Due to an insufficient sample size for the pubertal suppression treatment group to conduct mixed ANCOVA(s), two paired-samples t -tests were conducted instead (see Figure 1). A paired-samples t -test is an appropriate statistical test when the purpose of research is to assess if there is a difference of means between two related groups (e.g., a “before” and “after” group) on the same continuous dependent variable (Field, 2013). We combined participants regardless of sex assigned at birth for the paired-samples t -test. Therefore, H5 could not be fully tested and results do not capture any potential sex-based differences.

Suicidality. A paired-samples t -test was used to determine whether there was a statistically significant change in mean suicidality scores between pre-test and final assessment, after receiving pubertal suppression medication. One outlier was detected that was more than 1.5 box-lengths from the edge of the box in a boxplot. Transformation of the scores did not have meaningful effect on the level of statistical significance. Therefore, the

analysis was conducted on non-transformed data. The change scores between pre-test and final assessment were normally distributed, as assessed by Shapiro-Wilk's test ($p = .06$). Participants' suicidality pre-test scores were roughly equivalent before receiving blockers ($M = 1.29, SD = 1.49$) and when measured at final assessment ($M = 1.29, SD = 1.54$); the mean increase of .002, 95% CI [-1.36, 1.37], $t(10) = .004, p = .99, d = -.001$, was not statistically significant. Thus, Hypothesis 1 was not supported.

General well-being. A paired-samples t -test was used to determine whether there was a statistically significance change in general well-being mean scores between pre-test and final assessment, after receiving pubertal suppression medication. One outlier was detected that was more than 1.5 box-lengths from the edge of the box in a boxplot. Inspection of the value did not reveal it to be extreme. Transformation of the scores did not have meaningful effect on the level of statistical significance. Therefore, the analysis was conducted on non-transformed data. The change scores between pre-test and final assessment were normally distributed, as assessed by Shapiro-Wilk's test ($p = .76$). Although participants' general well-being pre-test scores were lower before receiving blockers ($M = 69.22, SD = 17.67$) than when measured at final assessment ($M = 74.68, SD = 10.77$), the mean increase of 5.45, 95% CI [-2.75, 13.66], $t(10) = 1.48, p = .17, d = .37$, was not statistically significant. Thus, Hypothesis 2 was not supported.

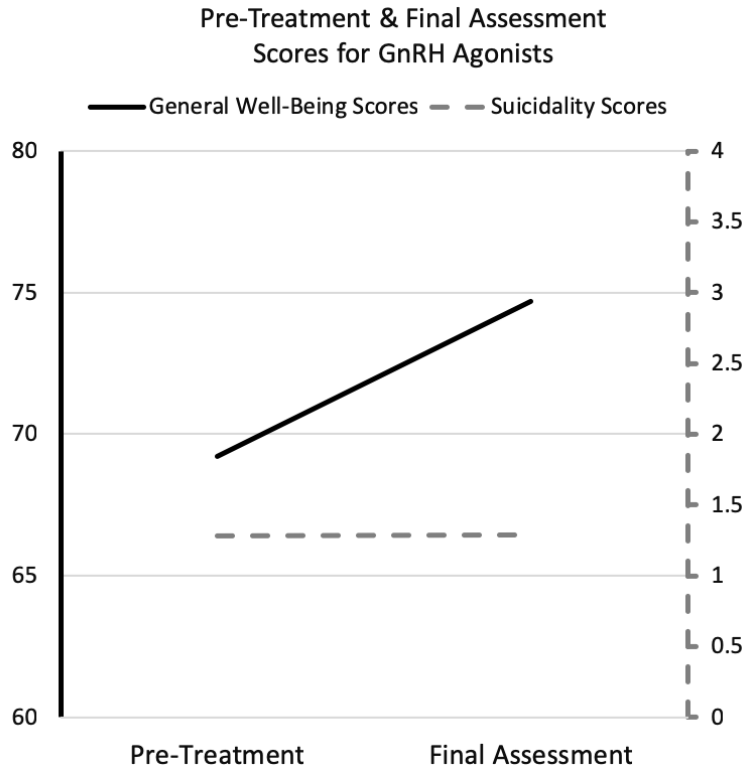


Figure 1. General Well-Being Scores (GWBS) and Suicidality (ASQ) scores at pre-treatment (T_0) and final assessment (T_1). ASQ = Ask Suicide-Screening Questions. GWBS = General Well-Being Scale.

Analyses for Gender-Affirming Hormones

To examine hypotheses 3 and 4 (i.e., GAH will be negatively associated with suicidality scores and positively associated with general well-being scores), two mixed repeated-measures analyses of covariance (ANCOVAs) were conducted with time (i.e., T_0 and T_1) as the within-subject variable and sex assigned at birth as the between-subject variable. Because there is variability between duration of treatment among participants, the period of time (i.e., duration of treatment) between T_0 and T_1 functioned as a covariate. Mixed ANCOVAs are an appropriate way to compare two or more discrete groups (i.e., sex assigned at birth) on a continuous dependent variable that is measured at more than one point

in time (Tabachnick & Fidell, 2013). A mixed ANCOVA uses the F test, which provides an overall comparison of group means to determine whether or not the means differ. Partial eta squared (partial η^2) was used to assess effect size. Partial η^2 values of approximately .01, .06, and .14 indicate small, medium, and large effects, respectively (Cohen, 1988; see also Richardson, 2011).

Suicidality. Data were screened for outliers using boxplots for each level of the within-subject factor. There were no outliers at T_0 or T_1 in the ASQ data, as assessed by inspection of a boxplot for values greater than 1.5 box-lengths from the edge of the box. Schneider, Avivi-Reich, and Mozuraitis (2015) point out that when the between-groups are not randomly assigned in an ANCOVA, then the assumption that the covariate is the same for all participants is not valid (as it is for experimental designs). Thus, the covariate should be centered to account for differences. Accordingly, scores on the covariate were centered by subtracting the sample mean (see also Murrar & Brauer, 2018). Skewness and kurtosis (skew ≥ 3 , kurtosis ≥ 10) statistics and histograms were examined to assess univariate normality (Weston & Gore, 2006). Despite being severely positively skewed, the absolute values of skewness and kurtosis were within acceptable limits and thus considered normally distributed. Test comparisons were conducted between transformed and non-transformed data to determine if there were any meaning changes in the statistical conclusions. Both tests lead to similar conclusions, therefore non-transformed scores were used for the final analyses for ease of interpretation. There was homogeneity of variance, as assessed by Levene's test of homogeneity of variance ($p > .05$). There was a linear relationship between pre-test and final assessment ASQ data for each level of the between-subjects variable, as assessed by visual inspection of a scatterplot. To test the ANCOVA-specific assumption of homogeneity of

regression slopes, a customized model including the interaction between the covariate, duration of treatment, and sex assigned at birth was used (Field, 2013). The interaction term was not statistically significant, $F(1, 14) = .01, p = .92$, indicating the assumption of homogeneity of regression slopes was met.

The first mixed analyses of covariance (ANCOVA) was conducted to ascertain within-subject differences between baseline suicidality scores (T_0) and suicidality after GAH (T_1), with sex-assigned at birth as the between-subjects factor, duration of treatment as the covariate. Duration of treatment was not significantly related to participant's ASQ scores, $F(1, 44) = .09, p = .77$, partial $\eta^2 = .002$. The predicted interaction effect of sex assigned at birth on suicidality scores after controlling for duration of treatment was not significant, $F(1, 44) = .08, p = .79$, partial $\eta^2 = .002$ (see Figure 1 and Table 2). Thus, hypothesis 5 (i.e., an interaction effect between sex assigned at birth time for both general well-being and suicidality scores) was not supported. Inclusion of the (nonsignificant) predicted interaction effect of sex assigned at birth on suicidality did not change the pattern of results and, thus, was kept in the model. After adjusting for duration of treatment, the main effect of time showed a statistically significant difference in mean suicidality scores at pre-test and final assessment, $F(1, 44) = 15.09, p < .001$, partial $\eta^2 = .26$, demonstrating a large effect size. The estimated adjusted mean for suicidality scores decreased by .84 from 1.11 at T_0 to .24 at T_1 . Thus, hypothesis 3 was supported (i.e., GAH will be negatively associated with suicidality between initial intake and final assessment).

General well-being. The dependent variable was screened for missing data and no data were missing. Next, data were screened for outliers using boxplots for each level of the within-subject factor. There was one outlier in the general well-being pre-test data, as

assessed by inspection of a boxplot for values greater than 1.5 box-lengths from the edge of the box. There were no outliers in the general well-being final assessment data, as assessed by inspection of a boxplot for values greater than 1.5 box-lengths from the edge of the box. Transformation nor removal of the outlier at T_0 had a meaningful effect on the level of statistical significance. Therefore, the outlier was kept in the data set. General well-being scores were normally distributed across each level of the within-factor variable, as evidenced by skewness and kurtosis statistics being within acceptable limits (skew ≥ 3 , kurtosis ≥ 10) and examination of histograms (Weston & Gore, 2006). There was homogeneity of variance, as assessed by Levene's test of homogeneity of variance ($p > .05$). There was a linear relationship between pre-test and final assessment general well-being data for each level of the between-subjects variable, as assessed by visual inspection of scatterplots. The interaction term between the covariate, duration of treatment, and sex assigned at birth was not statistically significant, $F(1, 43) = .80, p = .38$, indicating the assumption of homogeneity of regression slopes was met. Scores on the covariate were centered by subtracting the sample mean (Murrar & Brauer, 2018; Schneider et al., 2015).

A second mixed ANCOVA was conducted to ascertain within-subject differences between baseline general well-being scores (T_0) and general well-being after administration of GAH (T_1), with sex-assigned at birth as the between-subjects factor, duration of treatment as the covariate. Duration of treatment was not significantly related to participants' general well-being scores, $F(1, 44) = .37, p = .54$, partial $\eta^2 = .01$, showing a small effect size. The predicted interaction effect of sex assigned at birth was not significant, $F(1, 44) = 1.00, p = .32$, partial $\eta^2 = .02$, demonstrating a small effect size. Inclusion of the (nonsignificant) predicted interaction effect of sex assigned at birth on general well-being did not change the

pattern of results and, thus, was kept in the model. The main effect of time showed a statistically significant change in mean general well-being scores at pre-test and final assessment, $F(1, 44) = 11.39, p < .002$, partial $\eta^2 = .21$, demonstrating a large effect size (see Figure 1 and Table 2). The estimated adjusted mean for general well-being scores increased by 8.53 from 61.7 at T_0 to 70.23 at T_1 . Thus, hypothesis 4 was supported (i.e., GAH is positively associated with general well-being between initial intake and final assessment).

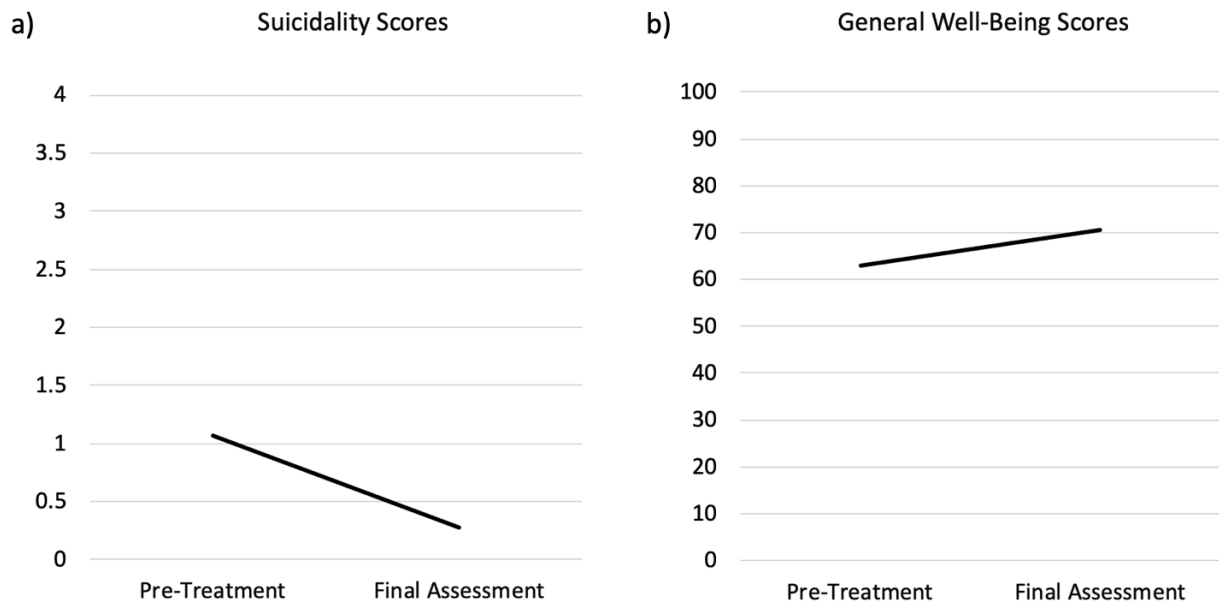


Figure 2. a) Estimated marginal means of general well-being scores (GWBS) adjusted for the covariate, duration of treatment, at pre-test and final assessment; b) Estimated marginal means of suicidality (ASQ) scores adjusted for the covariate, duration of treatment, at pre-test and final assessment. ASQ = Ask Suicide-Screening Questions. GWBS = General Well-Being Scale.

Table 2

Estimated Marginal Means and Standard Errors of the Analysis of Covariance for each DV.

Scale	T ₀			T ₁		
	All <i>M</i> (<i>SE</i>)	AFAB <i>M</i> (<i>SE</i>)	AMAB <i>M (SE)</i>	All <i>M</i> (<i>SE</i>)	AFAB <i>M</i> (<i>SE</i>)	AMAB <i>M (SE)</i>
ASQ	1.11 (.22)	1.01 (.23)	1.21 (.36)	.27 (.12)	.29 (.13)	.24 (.19)
GWBS	61.7 (2.43)	64.95 (2.66)	58.44 (4.09)	70.23 (2.15)	70.94 (2.35)	69.52 (3.62)

Note. Results from each ANCOVA adjusted for duration of treatment. The assessment point is the repeated measure, covarying duration of treatment. $N = 47$. GWBS = General Well-Being Scale; ASQ = Ask Suicide-Screening Questions; AFAB = Assigned Female at Birth; AMAB = Assigned Male at Birth.

Discussion

Blockers (Hypotheses 1 and 2)

In our study, contrary to prediction, a paired-samples *t*-test of suicidality scores suggested no significant decrease in suicidality among transgender youth before and after pubertal suppression medication (Hypothesis 1). In fact, when rounded at the hundredths decimal place, the pre-post scores had same mean score at pre-test and final assessment ($M = 1.29$). In addition, there was no significant change in general well-being scores between pre-test and final assessment after receiving blockers. Despite a slight mean increase in general well-being scores (5.75) between initial and final assessment, this increase was not statistically meaningful. Thus, Hypothesis 2 was also not supported.

There are multiple interpretations for these findings. As noted by others (Costa et al., 2015), it may be the case that by virtue of scheduling an appointment with a gender-affirming

multidisciplinary treatment team, adolescents' level of distress decreased because they knew steps were being taken to receive care. Thus, the initial assessment scores would not have captured any immediate relief resulting from the knowledge that an initial appointment was scheduled. At the same time, blockers are intended to prevent future bodily changes but not to resolve current dysphoria. Therefore, depending upon relevant contextual factors (e.g., age, youths' eagerness for treatment, degree of dysphoria), clinicians should make parents aware that the relief provided by blockers for the youth may not be as great as the relief provided by other interventions (e.g., GAH or gender-confirmation surgeries).

Similarly, de Vries and colleagues (2011) found that transgender adolescents assigned female at birth became more dissatisfied with their secondary and neutral sex characteristics (i.e., those characteristics unresponsive to hormones, such as face and height) over time while on pubertal suppression medication alone. However, our current data are too limited to provide solid support for any one interpretation beyond the finding that suggests that adolescents do not meaningfully improve or worsen on measures of suicidality or well-being after receiving puberty blockers. Personal clinical experience may offer some additional insight into these findings. In clinical practice, many transgender youth desire affirming hormones and the delay in access appears to perpetuate distress (Healy & Allen, 2019). Thus, it may be that the administration of *only* pubertal suppression medication over an extended period of time, without access to GAH, does not substantially improve well-being or decrease suicidality for some trans youth. There are multiple reasons that access to hormones may be postponed (e.g., parental uncertainty, lack of insurance coverage, precluding medical conditions). When parental uncertainty is largely the cause of the delay, it is particularly

important to adequately acknowledge parental concerns as failure to do so may contribute to shame parents have about offering their child support and understanding (Rafferty, 2018).

Gender-Affirming Hormones (Hypotheses 3 and 4)

Results of the analyses confirmed each of our two primary hypotheses regarding GAH. We found that at final assessment, participants' suicidality scores had significantly decreased following administration of GAH, confirming Hypothesis 3. In other words, prior to receiving GAH patients, on average, were endorsing at least one item of suicidality (estimated marginal mean ASQ score of 1.11). At final assessment after receiving GAH, however, participants endorsed almost no symptoms of suicidality (estimated marginal mean ASQ score of .27). In addition, we found that at final assessment, participants' general well-being scores had significantly increased, supporting Hypothesis 4. Clinical experience and the literature have previously suggested that securing access to gender-affirming hormones is a potentially lifesaving intervention for transgender youth (Edwards-Leeper & Spack, 2012; Gridley et al., 2016). These findings demonstrate that levels of suicidality decrease, while general well-being increases, among adolescents diagnosed with gender dysphoria after receiving gender-affirming hormones. The findings contribute to a growing literature that transgender adolescents and adults benefit from gender-affirming hormones in terms of quality of life and psychological functioning (de Vries et al., 2014; Keo-Meier et al., 2015).

Concordant with existing guidelines (APA, 2015, Guideline 11), our findings support the notion that transgender people tend to have more positive life experiences when they receive trans-affirming care. Affirmative care may help to counteract the wide range of societal, personal, and environmental discrimination transgender youth often encounter. However, the pathway through which beneficial outcomes arise following affirming care is

not entirely clear. It is plausible that affirming hormones influence bodily changes, which in turn reduces gender dysphoria and lowers body-related uneasiness (Fisher et al., 2014), resulting in increased well-being and decreased suicidality. It may also be that the sense of affirmation that comes with receiving care by affirming professionals and a potential increase in parental acceptance lessens distal minority stress factors (i.e., non-affirmation; see Testa et al., 2015), thereby resulting in improved mental health.

Sex Assigned at Birth and Time Interaction (Hypothesis 5)

We lacked sufficient sample size in the blockers treatment group to examine an interaction effect between sex assigned at birth and time. Thus, we were not able to fully examine hypothesis 5. However, within the GAH treatment group, H5 (i.e., those assigned female at birth will experience greater improvements in general well-being and larger decreases in suicidality) was not supported. Research has shown transgender girls and boys differ on measures of behavioral and emotional symptoms upon presentation to a gender clinic (de Vries et al., 2014) with transgender girls showing lower levels of externalizing (e.g., rule-breaking or aggressive behavior) and internalizing (e.g., depression) symptoms compared to transgender boys. There are also differential physiological outcomes in response to treatment (e.g., development of acne, or chest growth; Hembree et al., 2017). Nonetheless, our study did not find significant differences between sex assigned at birth and general well-being or suicidality outcomes. In other words, we may only infer from our findings that youth assigned male and female at birth benefit from gender-affirming hormones. Although there were not significant between-group differences found in the present study, this may have been due to insufficient power as we did observe a small effect size for general well-being scores (partial $\eta^2 = .02$).

Practice and Counseling Implications

Despite the statistically non-significant results in this study for those treated with pubertal suppression medication, blockers may be one of many helpful steps in the progression toward improved mental health (de Vries et al., 2014) with future medical steps possibly including other gender-affirming interventions (e.g., hormones or surgeries). Pubertal suppression medication is an intervention considered fully reversible and allows the family more time to make a thoughtful decision about next steps. Parents often have fears or are uncertain about the appropriateness of social transitioning, the use of blockers or hormones, and using appropriate names and pronouns. Recent, controversial research has suggested many parents of trans youth might feel as if mental health professionals inadequately screen for co-occurring conditions and fail to assess the history of GD (Littman, 2018). Moreover, parents may be generally distrustful of clinicians (Littman, 2018). Given the beneficial outcomes observed among the participants in this study after GAH, it is important for clinicians to earn the trust caregivers in order to facilitate appropriate care for the youth, so the child does not suffer harm by delayed access to care (nonmaleficence).

However, tension may arise between respecting the autonomy of the child and advocating that the parents use appropriate pronouns, name, provide permission for affirming medical interventions—such an affirming stance, may scare away some caregivers, potentially resulting in the youth receiving no services (ultimately causing harm). One way to guide parents through the process of affirming their child may be to help them think of each affirmative step (e.g., allowing the child to explore gender, using appropriate names, and pronouns, providing permission for blockers or hormones) as just one *step in time*. It can be suggested that if, after each affirmative step, the parents notice improvements in the child's

mood or overall well-being, then such information may be used by them to inform future decisions.

For many youth in this study, the parents and child will have spent many hours with a psychologist or other mental health professional completing a comprehensive psychodiagnostic interview. The psychodiagnostic process may have played a beneficial role in promoting desired health outcomes. For instance, during the process, a “gender history” is typically elicited from the youth’s perspective in the presence of the parents. The clinical value of this is that parents who may have thought their child’s transgender identity “came out of the blue” are able to hear the unfolding of gender, over time, from the youth's perspective. Subsequently, the caregivers may develop greater awareness and understanding of their children’s gender diversity. This could then be a pathway toward greater acceptance. Improved parental acceptance alone has positive impact on beneficial outcomes for the youth (Klein & Golub, 2016; Ryan, Russell, Huebner, Diaz, & Sanchez, 2010). It may also be that the psychoeducational aspect of the diagnostic interviews allays some parental concerns. Therefore, clinicians should be able to explain the state of the science with regard to psychosocial outcome research following gender affirming interventions for transgender youth in an easy to understand way for parents—which may allow caregivers to more comfortably provide permission for affirming medical interventions.

However, only focusing on the youth’s medical needs may function to minimize a wide range of painful social challenges (Lev & Wolf-Gould, 2018). We live in a cisnormative world and the mental health professional working with trans youth must support the needs of parents and assist the family to develop protective strategies when they exist in hostile or disaffirming environments (dickey, Singh, Chang, & Rehrig, 2017; Lev & Wolf-

Gould, 2018). For instance, parents may benefit being connected to parent support groups and gaining guidance on how to approach school administrators. Discussions about how, when, and if to disclose a transgender identity to family and friends (if not already disclosed) may be important to individual and family functioning (Galupo, Krum, Hagen, Gonzalez, & Bauerband, 2014; Katz-Wise, Ehrensaft, Vettters, Forcier, & Austin, 2018). Transgender adolescents may be uncertain about when is an appropriate time to disclose their transgender identity to a romantic interest, potential partner, and their partner's parents (Allen, In Press). Developing a plan with the youth and family on how to handle such disclosure can be important in avoiding potentially hostile situations.

Strengths, Limitations, and Directions for Future Research

A strength of the study is having adjusted for duration of treatment by introducing duration as a covariate and removing the associated variance, thus making participants statistically equal on this variable. Additionally, real-world data was used and the sample is representative of the actual treatment-seeking population. However, youth served in our clinic receive comprehensive care by an experienced multi-disciplinary team. Thus, these findings may not generalize to all transgender youth (nor do all transgender youth desire medical treatment). Though, our findings have a high level of ecological validity and likely generalize well to other clinics with similar treatment models. There have been multiple calls in the literature to investigate mental health outcomes among transgender youth (Chen et al., 2018; Chew et al., 2018; Mahfouda et al., 2017; Olson-Kennedy et al., 2016). Few studies have examined well-being before and after gender affirming medical interventions among transgender youth and none have specifically examined suicidality.

Some confounding variables of this study may include level of familial support, whether a patient is actively receiving therapy, or differences in the specifics of gender-affirming medications (e.g., dosage). Given the role parental support has on health and well-being outcomes (Simons et al., 2013), such support could be argued to affect the dependent variables in this study. However, at baseline, a relatively high level of parental support is required among all participants (compared to youth, for example, who may never have visited the clinic due to lack of parental support), as the parents must agree for their child to receive gender affirming medical interventions. That is, most participants in this study had some degree of parental support. It may be that these treatments, combined with parental support, are “active ingredients” in producing beneficial outcomes, but our study did not access this. Future research may wish to examine the concomitant roles of parental support and gender-affirming medications on psychological outcomes among transgender youth.

It also is unclear whether the beneficial outcomes associated with GAH take effect immediately after administration, come about after physical changes begin to manifest, or vary over-time. In addition to tracking changes over longer periods of time, future studies might consider incorporating more follow-up observations over shorter periods of time (e.g., after two weeks of treatment, using a time-series design) to assess for how long it takes for beneficial changes to occur while also accounting for level of parental support and outward physical appearance, as these factors may explain or alter the intervention’s effect on suicidality and well-being. Relatedly, Olson-Kennedy and colleagues (2018) found that chest dysphoria among transmasculine youth increased over time while taking testosterone, reflecting “a common clinical phenomenon: a honeymoon period after testosterone initiation that quickly becomes eclipsed by the greater disparity between a more masculine

presentation and a female chest contour” (p. 435). Therefore, clinicians should advise caregivers and transmasculine youth that chest dysphoria may increase after beginning testosterone.

It should be noted that the endocrinologists in our clinic sometimes begin patients at hormone levels lower than the recommended protocol (Hembree et al., 2017). Starting patients out at low doses might allow patients to feel comfortable enough to provide permission for further increase in dosage at a later time. And typically, patients’ doses are gradually increased every three to six months so that the dosage levels recommended by suggested protocols are reached by the end of treatment (Hembree et al., 2017). Nonetheless, it might be the case that if there had been higher starting doses, then the observed benefits in this study may have been of a larger magnitude. In addition, the blockers treatment group was likely underpowered due to the small sample size. With a larger sample size, the mean increase of 5.75 in general well-being scores may have been statistically significant.

The sample was primarily White (83.3%), and thus not likely to capture the diversity inherent in, or be representative of, the overall population of transgender youth. For instance, in recent non-clinical, national sample of transgender youth only 62.7% identified as White, non-Latino (Toomey, Syvertsen, & Shramko, 2018). For transgender youth of color, due to additional discrimination and societal barriers transgender people of color experience (James et al., 2016), it could be the case that such discrimination functions to lessen the beneficial outcomes observed after administration of gender-affirming medical interventions. Research from other regions of the United States with more racially diverse clinical populations can help answer such a research question. Participation in community outreach events by clinic staff members may also help to recruit more representative clinic populations while at the

same time better serving the traditionally underserved. Unfortunately, our study did not make any distinction among participants for non-binary gender identities and classified participants based upon sex assigned at birth. To date, no studies have outlined GAH regimens for non-binary individuals (Chen et al., 2018). Future studies should explore the trajectory of nonbinary and genderqueer identities overtime and describe outcomes associated with affirming medical interventions. Because our data comes from a clinic within a children's hospital, we are unable to provide follow-up data beyond young adulthood. The strengths and limitations outlined here should be taken into consideration when interpreting the results.

Conclusion

Our study found an increase in general well-being (albeit statistically non-significant), while levels of suicidality remained comparable, following administration of blockers. This is consistent with what has been indicated the literature (Costa et al., 2015; de Vries et al., 2011; de Vries et al., 2014); namely, blockers may be a helpful medical intervention for transgender youth as they prevent future bodily changes and allow families more time to make medical decisions. Gender-affirming hormones appear to be associated with improvements in general well-being and decreasing suicidality among transgender youth. To the author's knowledge, this is the first study to demonstrate that levels of suicidality decrease, and general well-being increases, among adolescents diagnosed with gender dysphoria after receiving gender-affirming hormones. The findings also contribute to a growing literature that transgender adolescents and adults benefit from gender-affirming hormones in terms of quality of life and psychological functioning (de Vries et al., 2014; Keo-Meier et al., 2015).

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VITA

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