

and gynoid (fat percentage), as well as bone mineral content (BMC) (kilograms) and BMC z score. TBF (percentage) z score was calculated on the basis of age-matched birth-assigned sex TBF (percentage), with mean and SD as “logarithm natural (Ln) TBF (%) – (Ln TBF (%) mean/ Ln TBF (%) SD)” for transgender females and Ln “(TBF (%) +10) – (Ln TBF (%) mean/Ln TBF (%) SD)” for transgender males.<sup>23</sup> LBM z score was calculated on the basis of age-matched birth-assigned sex LBM mean and SD.<sup>23</sup>

### Statistical Analysis

Normally distributed data were expressed as mean  $\pm$  SD and compared with the paired sample *t* test. Data that were not normally distributed were expressed as median and interquartile range and the Wilcoxon rank test used for comparison. *P* < .05 was considered statistically significant. However, bond percolation threshold was also used to determine statistical significance, corrected for multiple testing.

### RESULTS

The study included 172 youth with GD; 119 (69.2%) youth self-identified as transgender males (age  $15.2 \pm 1.8$  [SD] years; 90.7% Tanner 4–5), 51 (29.7%) youth as transgender females (age  $15.4 \pm 2.0$  years; 80.3% Tanner 4–5), and 2 (1.1%) youth as nonbinary. Baseline body composition and BMD profiles are summarized in Table 1; transgender females had lower z scores at LS aBMD, LS BMAD, LTH aBMD, and BMC than transgender males.

At baseline, the majority (55.2%) of transgender youth were found to have vitamin D deficiency or insufficiency (Table 2). Baseline vitamin D status was associated with baseline LS aBMD, LS BMAD, and LTH z scores (Fig 1).

Supplementation with 1000 to 2000 IU of vitamin D daily improved the vitamin D status with no case of vitamin D toxicity (Table 2).

A subgroup of the study population, namely, 36 (30.5%) transgender females and 80 (67.8%) transgender males with pre- and post-GnRHa DXA, was analyzed for GnRHa-associated changes. Pre-GnRHa DXA was done  $-51.4 \pm 41.3$  days (range  $-158$  to  $+28$  days) relative to GnRHa initiation; post-GnRHa DXA was done  $355.2 \pm 96.7$  days or median of 352.5 (294.5, 385.8) days (range 188–676 days) after GnRHa initiation. The mean time interval between pre- and post-DXA scans was  $406.7 \pm 98.3$  days (range 210–720 days).

BMD profiles and body composition after GnRHa as well as corresponding changes relative to baseline characteristics are summarized in Table 3. LS, LTH, and TBLH aBMD z scores dropped significantly among both transgender males and transgender females, whereas LS BMAD z scores decreased significantly among transgender males. Considering the limited number of transgender youth at early stages of puberty,<sup>2,3</sup> no statistical comparison of subgroups based on puberty status was done.

Four transgender youth (one birth-assigned girl and 3 birth-assigned males) had a baseline LS aBMD z score below 2 SDs, with 20 transgender youth (all transgender males) having  $>1$ -SD drop ( $1.37 \pm 0.26$ ) in their follow-up LS aBMD z score. Each of these youth had a subsequent lateral spine radiograph, none of which revealed a vertebral fracture.

Transgender males' post-GnRHa body composition analysis revealed significant increases in BMI, LBM (kilograms), TBF (percentage), android (fat percentage), and gynoid

(fat percentage); there was no significant change in BMI z score, LBM z score, or TBF (%) z score. Transgender females showed a significant increase in TBF (percentage), TBF (percentage) z score, and gynoid (fat percentage), as well as a drop in LBM z score. GnRHa-associated changes in body compartment z scores and BMI z score were not different between transgender youth with baseline BMI percentiles above and below the obesity risk (85%) cutoff percentile (Table 4).

### DISCUSSION

With this study, we reviewed BMD and body composition changes in youth with GD after 355.2  $\pm$  96.7 days of GnRHa monotherapy. Youth identifying as transgender males constituted 69.2% of study population in keeping with the current trend of overrepresentation (50%–90%) of birth-assigned female patients in GD clinics.<sup>3,25,26</sup>

Baseline BMD characteristics were remarkable for transgender females' lower LS aBMD and BMAD z scores compared with those of transgender males. Similar baseline differences were previously observed in studies among youth<sup>11,14,15,17</sup> and adult<sup>27</sup> transgender females. Klink et al<sup>15</sup> suggested that lower engagement in physical activities, as is typical for transgender females, is a factor, as well as pubertal stage. Despite lack of consistent records of physical activity among our study population, literature supports reduced involvement of sexual minorities in moderate to vigorous physical activities and team sports.<sup>28</sup> We believe it is prudent to consider evaluating physical activity level as part of baseline and follow-up assessments of youth with GD, although lack of objective scales or specific recommendations from the Endocrine Society or World Professional Association for

**TABLE 1** Baseline Body Composition and BMD Profiles at LS and LTH

	Transgender Males (n = 119)		Transgender Females (n = 51)		P <sup>a</sup>
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
<b>LS</b>					
aBMD, g/cm <sup>2</sup>	1.13 (0.17)	1.16 (1.04 to 1.25)	0.98 (0.18)	0.968 (0.84 to 1.13)	<.001
aBMD z score	0.04 (1.10)	0.1 (-0.70 to 0.70)	-0.84 (1.29)	-0.9 (-1.8 to 0.00)	<.001
BMAD, g/cm <sup>3</sup>	0.37 (0.46)	0.38 (0.33 to 0.41)	0.31 (0.04)	0.31 (0.29 to 0.34)	<.001
BMAD z score	-0.10 (1.00)	0.01 (-0.88 to 0.64)	-0.22 (1.41)	-0.08 (-0.99 to 0.64)	<.001
<b>LTH</b>					
aBMD, g/cm <sup>2</sup>	1.00 (0.15)	1.02 (0.90 to 1.11)	0.95 (0.16)	0.94 (0.813 to 1.10)	NS
aBMD z score	0.10 (1.06)	0.2 (-0.70 to 0.90)	-0.44 (1.39)	-0.5 (-1.60 to 0.30)	<.001
BMC, kg	2.40 (0.54)	2.40 (2.00 to 2.74)	2.39 (0.65)	2.27 (1.96 to 2.83)	NS
BMC z score	0.05 (1.30)	0.05 (-0.86 to 0.93)	-0.66 (1.35)	-0.91 (-1.58 to 0.13)	.001
LBM, kg	36.24 (56.14)	36.46 (32.81 to 39.75)	45.74 (9.98)	44.66 (39.27 to 53.55)	.005
LBM z score	-1.03 (1.22)	-1.15 (-1.86 to -0.34)	-1.19 (1.45)	-1.41 (-2.4 to -0.24)	NS
TBF, %	37.14 (10.46)	37 (29.10 to 45.80)	24.45 (12.48)	24.2 (14.60 to 37)	<.001
TBF z score, %	1.68 (0.96)	1.76 (1.04 to 2.44)	1.42 (1.02)	1.58 (0.62 to 2.38)	NS
BMI	24.04 (5.17)	22.99 (20.04 to 27.66)	23.22 (6.33)	20.38 (18.30 to 26.61)	NS
BMI z score	0.89 (1.25)	0.86 (0.07 to 1.85)	0.62 (1.67)	0.72 (-0.67 to 2.04)	NS

NS, nonsignificant.

<sup>a</sup> t test.

Transgender Health<sup>5,6</sup> are challenges in clinical practice.

Baseline body composition comparison of transgender males and transgender females was remarkable for lower BMC z score among transgender females and no difference in LBM and TBF (percentage) z scores. Of note, both transgender males and transgender females had higher baseline TBF and lower baseline LBM relative to the birth-assigned sex population; however, only transgender females had a lower baseline BMC z score. The latter is likely secondary to factors like physical activity, LBM, and BMI rather than delayed bone accrual, and the noted higher TBF among transgender females may have contributed to it, as some evidence suggests that higher body

fat attenuates bone density in males while supporting bone density in females.<sup>29</sup>

At baseline, the majority (55.2%) of transgender youth had vitamin D deficiency or insufficiency with vitamin D status associated with BMD at LS and LTH. Some evidence suggests potential bone protective effects of physical activity in the presence of very low serum 25OHD.<sup>30</sup> However, the conceivably lower physical activity in transgender youth may heighten vitamin D deficiency effects on BMD. In addition, the combination of low vitamin D and low calcium intake (<600 mg/day) may impair LS mineralization in postmenarchal females.<sup>31</sup> These all suggest that vitamin D and calcium supplementation should be

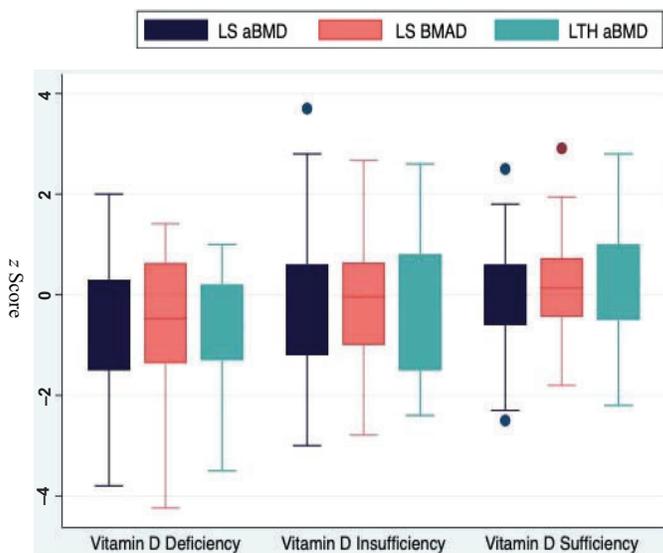
considered for all youth with GD regardless of whether they are considering puberty suppression.

GnRHa monotherapy negatively affected transgender youth aBMD z scores at LS, LTH, and TBLH levels and transgender males' LS BMAD z scores. The most pronounced decrease in z score (>0.5) was noted in transgender males' LS aBMD and BMAD. The majority of the youth were late pubertal; this observed decrease is in line with other studies<sup>11,14</sup> and explained by the significant decrease of estrogen on the trabecular rich bone at the spine. Transgender males at early stages of puberty seemed to have less pronounced LS aBMD z score changes. Schagen et al<sup>11</sup> found that transgender youth in both early and late stages of puberty had a drop in aBMD z scores after 24 months of GnRHa regardless of puberty status, but this was more pronounced in transgender males in late puberty, assessing BMD z scores on the basis of sex assigned at birth. Similarly, because we were assessing the effect of GnRHa monotherapy, BMD z scores were based on sex assigned at birth. In future studies, researchers should consider

**TABLE 2** Vitamin D Status Among Youth With GD

	n	Vitamin D Status, n (%)		
		Deficiency <sup>a</sup>	Insufficiency <sup>b</sup>	Sufficiency <sup>c</sup>
Baseline	170	30 (17.6)	64 (37.6)	76 (44.6)
First follow-up	146	5 (3.4)	26 (17.8)	115 (78.8)
Second follow-up	110	4 (3.6)	19 (17.3)	87 (79.1)
Third follow-up	63	1 (1.6)	7 (11.1)	55 (87.3)

<sup>a</sup> 25OHD <30 nmol/L.<sup>b</sup> 25OHD 30 to 50 nmol/L.<sup>c</sup> 25OHD >50 to 250 nmol/L.



**FIGURE 1**  
Pre-GnRHa BMD profiles and baseline vitamin D status.

whether to use sex assigned at birth or identified gender when assessing the effect of gender-affirming hormones on bone health in transgender youth. Given the limited evidence on transgender youth in early puberty, the degree of BMD changes after puberty suppression in early puberty is not known. This

is an important clinical concern for transgender youth in early stages of puberty who are treated with a longer course of GnRHa therapy before gender-affirming hormones are considered.<sup>5,6</sup>

Current evidence on GnRHa effects on body composition of youth with

GD suggests a stable or slightly increased BMI z score, as well as an increase in fat percentage and drop in LBM.<sup>8,15,16,32</sup> In our study, GnRHa was not associated with any significant changes in BMI z score. Among transgender females, GnRHa was associated with a significant increase in TBF (percentage) z score and drop in LBM z score. If transgender females were on GnRHa longer, a significant change in BMI and TBF (percentage) z scores could occur because of loss of testosterone effects on LBM and TBF<sup>33,34</sup> at advanced stages of puberty. The observed fat redistribution (android versus gynoid) is in keeping with youth affirmed gender’s typical fat distribution.<sup>33–35</sup>

**Clinical Implications**

Evidence on GnRHa-associated changes in body composition and BMD will help health care professionals involved in the care of youth with GD to counsel appropriately and optimize their bone health. Given the absence of vertebral fractures detected in those

**TABLE 3** Body Composition Analysis and BMD Profile of Youth With GD After GnRHa

	Transgender Males (n = 80)			Transgender Females (n = 36)		
	Post-GnRHa Mean (SD)	Δ Post-Pre Mean (95% CI)	P, <sup>a</sup> SS <sup>b</sup>	Post-GnRHa Mean (SD)	Δ Post-Pre Mean (95% CI)	P, SS
<b>BMD changes</b>						
LS aBMD z score	-0.72 (0.97)	-0.74 (-0.85 to -0.63)	<.001 S	-1.33 (1.39)	-0.33 (-0.46 to -0.19)	<.001 S
LS BMAD z score	-0.76 (0.93)	-0.59 (-0.74 to -0.45)	<.001 S	-0.76 (1.48)	-0.37 (-0.61 to -0.14)	.003 S
LTH aBMD z score	-0.31 (0.99)	-0.33 (-0.40 to -0.26)	<.001 S	-1.03 (1.64)	-0.46 (-0.60 to -0.31)	<.001 S
TBLH aBMD z score	0.03 (1.05)	-0.34 (-0.43 to -0.25)	<.001 S	-0.48 (1.49)	-0.34 (-0.48 to -0.21)	<.001 S
<b>Body composition changes</b>						
BMI	25.12 (6.04)	1.36 (0.75 to 1.97)	<.001 S	23.18 (6.64)	0.57 (-0.46 to 1.60)	.120
BMI z score	0.99 (1.30)	0.15 (0.01 to 0.29)	.083	0.45 (1.69)	-0.10 (-0.38 to 0.17)	.475
TT-FMR	0.49 (0.04)	0.00 (-0.01 to 0.01)	1.0	0.48 (0.05)	-0.02 (-0.03 to 0.00)	.010 NS
LT-FMR	0.38 (0.04)	0.00 (-0.01 to 0.00)	.209	0.39 (0.04)	0.01 (0.00 to 0.02)	.013 NS
ET-FMR	0.97 (0.17)	0.00 (-0.02 to 0.02)	.813	1.03 (0.19)	0.08 (0.02 to 0.13)	.004 NS
Android, fat %	42.21 (12.36)	2.75 (1.21 to 4.28)	<.001 S	33.41 (13.97)	4.18 (1.09 to 7.28)	.002 NS
Gynoid, fat %	46.76 (7.81)	1.83 (0.77 to 2.88)	<.001 S	38.70 (9.30)	7.17 (4.64 to 9.69)	<.001 S
TBF, kg	25.00 (12.48)	2.19 (0.75 to 3.63)	.001 S	20.44 (13.57)	4.41 (2.22 to 6.60)	<.001 S
TBF, %	39.93 (10.03)	2.21 (0.99 to 3.43)	<.001 S	31.14 (11.62)	5.36 (2.83 to 7.88)	<.001 S
TBF, z score, %	1.78 (0.90)	0.13 (0.00 to 0.25)	.053	2.46 (0.51)	1.05 (0.79 to 1.32)	<.001 S
LBM, kg	37.45 (5.55)	1.05 (0.45 to 1.64)	<.001 S	43.17 (7.86)	-1.58 (-3.0 to -0.15)	.006 NS
LBM z score	-1.01 (1.28)	-0.02 (-0.16 to 0.12)	.891	-1.99 (1.58)	-0.73 (-0.95 to -0.5)	<.001 S
BMC, kg	2.37 (0.43)	0.006 (-0.03 to 0.04)	.998	2.40 (0.46)	0.15 (0.10 to 0.20)	<.001 S
BMC z score	-0.39 (1.12)	-0.39 (-0.51 to -0.28)	<.001 S	-0.99 (1.18)	-0.12 (-0.26 to 0.02)	.059

ET-FMR, extremities/trunk fat mass ratio; LT-FMR, legs/total fat mass ratio; NS, not significant; S, statistically significant; TT-FMR, trunk/total fat mass ratio.

<sup>a</sup> Wilcoxon rank test.

<sup>b</sup> Statistical significance of .0011 to correct for multiple testing.

**TABLE 4** GnRHa-Induced Body Compartment and BMI Changes Among Transgender Youth Subdivided by Baseline BMI Percentile at Cutoff for Obesity Risk

	BMI ≤85 Percentile		BMI >85 Percentile		Difference (95% CI)	P <sup>a</sup> Value, SS <sup>b</sup>
	n	Mean (SD)	n	Mean (SD)		
Δ BMI z score	71	0.11 (0.62)	47	0.00 (0.79)	0.11 (−0.14 to 0.37)	0.867, NS
Δ TBF z score, %	71	0.58 (0.91)	47	0.19 (0.44)	0.39 (0.11 to 0.67)	0.050, NS
Δ LBM z score	71	−0.31 (0.66)	47	−0.15 (0.81)	−0.15 (−0.42 to 0.11)	0.292, NS
Δ BMC z score	71	−0.26 (0.49)	47	−0.37 (0.49)	0.11 (−0.07 to 0.30)	0.326, NS

NS, nonsignificant.

<sup>a</sup> Wilcoxon rank test.<sup>b</sup> Statistical significance of .01 to correct for multiple testing.

with significant decreases in their LS z scores, the significance of BMD effects of GnRHa in transgender youth needs further study, as well as whether future spine radiographs are needed on the basis of BMD trajectory. This study can advance clinical practice guidelines and research in the field.

### Strengths and Limitations

The study strengths include the large study population with baseline assessments and pre-post GnRHa subgroup analysis. This is the first study used to examine vitamin D status and provide a comprehensive assessment of body composition after GnRHa monotherapy. Lack of consistent records of physical activity at baseline and follow-up visits limited analysis of physical activity's role as a potential contributing factor to bone health and body composition. The small sample size of youth in early puberty prevented comparison of GnRHa effects in early versus late puberty.

### CONCLUSIONS

BMI z score does not appear to increase significantly in transgender youth on GnRHa monotherapy; however, it is associated with an increase in TBF (percentage) z score and reduction in LBM z score of transgender females. Transgender youth body fat redistribution (android versus gynoid) after GnRHa and transgender females' body composition changes after GnRHa were in keeping with youth affirmed gender. GnRHa monotherapy in transgender youth is associated with a decrease in LS, LTH, and TBLH aBMD z scores. Vitamin D sufficiency was uncommon among transgender youth. Vitamin D and calcium supplementation should be considered for all youth with GD, particularly those who seek pubertal suppression. Given the negative effects of GnRHa monotherapy on BMD, bone density and 25OHD should be considered at baseline and follow-up care of adolescents with GD on GnRHa monotherapy.

### ABBREVIATIONS

aBMD: areal bone mineral density  
 BMAD: bone mineral apparent density  
 BMC: bone mineral content  
 BMD: bone mineral density  
 CHEO: Children's Hospital of Eastern Ontario  
 DXA: dual-energy radiograph absorptiometry  
 GD: gender dysphoria  
 GnRHa: gonadotropin-releasing hormone agonist  
 LBM: lean body mass  
 Ln: logarithm natural  
 LS: lumbar spine  
 LTH: left total hip  
 TBF: total body fat  
 TBLH: total body less head  
 25OHD: 25-hydroxyvitamin D

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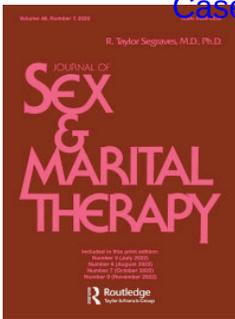
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# Reconsidering Informed Consent for Trans-Identified Children, Adolescents, and Young Adults

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REVIEW

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## Reconsidering Informed Consent for Trans-Identified Children, Adolescents, and Young Adults

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### ABSTRACT

In less than a decade, the western world has witnessed an unprecedented rise in the numbers of children and adolescents seeking gender transition. Despite the precedent of years of gender-affirmative care, the social, medical and surgical interventions are still based on very low-quality evidence. The many risks of these interventions, including medicalizing a temporary adolescent identity, have come into a clearer focus through an awareness of detransitioners. The risks of gender-affirmative care are ethically managed through a properly conducted informed consent process. Its elements—deliberate sharing of the hoped-for benefits, known risks and long-term outcomes, and alternative treatments—must be delivered in a manner that promotes comprehension. The process is limited by: erroneous professional assumptions; poor quality of the initial evaluations; and inaccurate and incomplete information shared with patients and their parents. We discuss data on suicide and present the limitations of the Dutch studies that have been the basis for interventions. Beliefs about gender-affirmative care need to be separated from the established facts. A proper informed consent process can both prepare parents and patients for the difficult choices that they must make and can ease professionals' ethical tensions. Even when properly accomplished, however, some clinical circumstances exist that remain quite uncertain.

### KEYWORDS

Informed consent;  
 ethics;  
 gender dysphoria;  
 gender identity;  
 detransition

### Introduction

Reconsideration of the meanings, purposes, indications, and processes of informed consent for transgender-identified youth is urgently needed. Parents of gender atypical children are considering social transition as early as preschool or grade school. Parents of preteens and teens are considering supporting their children's wishes to present in a new gender, take puberty blockers and cross-sex hormones, and plan for surgical alterations. College-aged youth are declaring new identities for the first time and obtaining hormones and surgery without their parents' knowledge.

When uncertain parents of children and teens consult their primary care providers, they are usually referred to specialty gender services. Parents and referring clinicians assume that specialists with "gender expertise" will undertake a thorough evaluation. However, the evaluations preceding the recommendation for gender transition are often surprisingly brief (Anderson & Edwards-Leeper, 2021) and typically lead to a recommendation for hormones and surgery, known as *gender-affirmative* treatment.

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Despite the widely recognized deficiencies in the evidence supporting gender-affirmative interventions (National Institute for Health & Care Excellence, 2020a; 2020b), the process of obtaining informed consent from patients and their families has no established standard. There is no consensus about the requisite elements of evaluations, nor is there unanimity about how informed consent processes should be conducted (Byne et al., 2012). These two matters are inconsistent from practitioner to practitioner, clinic to clinic, and country to country.

Social transition, hormonal interventions, and surgery have profound implications for the course of the lives of young patients and their families. It is incumbent upon professionals that these consequences be thoroughly, patiently clarified over time prior to undertaking any element of transition. The informed consent process does not preclude transition; it merely educates the family about the state of the science underpinning the decision to transition. Social transition, hormones, and surgeries are unproven in a strict scientific sense, and as such, to be ethical, require a thorough and fully informed consent process.

### **Ethical Concerns About Inadequate Informed Consent**

The concept of informed consent in medicine has roots in both ethical theory and law. The ethical foundation is centered in the principles of beneficence, justice, and respect for autonomy, while the legal issues have to do with questions of malpractice (Katz et al., 2016).

Patients consenting to treatment must meet age-based and decisional capacity requirements (Katz et al., 2016). Minors less than the age of consent participate in decision-making by providing *assent*—an agreement with the intervention. The limited maturational cognitive capacities of minors are the key reason why parents serve as the ethical and legal surrogates for medical decision-making, tasked with signing an informed consent document (Grootens-Wiegers, Hein, van den Broek, & de Vries, 2017).

The informed consent process consists of three main elements: a disclosure of information about the nature of the condition and the proposed treatment and its alternatives; an assessment of patient and caregiver understanding of the information and capacity for medical decision-making; and obtaining the signatures that signify informed consent has been obtained (Katz et al., 2016). The current expectation that clinicians and institutions are required to thoroughly inform their patients about the benefits, risks, and uncertainties of a particular treatment, as well as about alternatives, has a long legal history in the United States (Lynch, Joffe, & Feldman, 2018).

Ethical concerns about inadequate informed consent for trans-identified youth have several potentially problematic sources, including *erroneous assumptions* held by professionals; *poor quality of the evaluation process*; and *incomplete and inaccurate information* that the patients and family members are given.

These concerns are amplified by the *dramatic growth* in demand for youth gender transition witnessed in the last several years that has led to a perfunctory informed consent process. A rushed process does not allow for a proper discussion of not only the benefits, but the profound risks and uncertainties associated with gender transition, especially when gender transition is undertaken before mature adulthood.

#### *a. Dramatic growth in demand for services threatens true informed consent*

Gender identity variations were thought to be extremely rare a generation ago. While the incidence in youth had not been officially estimated, in adults it was 2-14 per 100,000 (American Psychiatric Association, 2013, p. 454). However, around 2006, the incidence among youth began to rise, with a dramatic increase observed in 2015 (Aitken et al., 2015, de Graaf, Giovanardi, Zitz, & Carmichael, 2018). Currently, 2-9% of U.S. high school students identify as transgender, while in colleges, 3% of males and 5% of females identify as gender-diverse (American College Health Association, 2021; Johns et al., 2019; Kidd et al., 2021).

Whereas previously most of the affected individuals identified as the opposite sex, there is now a growing trend toward identifying as *nonbinary*: neither male nor female or both male and female (Chew et al., 2020). A recent study reported that the majority of transgender-identifying youth (63%) now have a non-binary identity (Green, DeChants, Price, & Davis, 2021). Although the incidence of natal males asserting a trans identity in adolescence has significantly increased, the dramatic increase is driven primarily by the natal females requesting services (Zucker, 2017). Many suffer from significant comorbid mental health disorders, have neurocognitive difficulties such as ADHD or autism or have a history of trauma (Becerra-Culqui et al., 2018; Kozłowska, McClure, et al., 2021).

The increase in rates of transgender identification is reflected in the numbers of youth seeking help from medical professionals. For example, according to data reported by the Tavistock gender clinic in the UK, in 2009, there were 51 requests for services (de Graaf et al., 2018); in 2019-2020, 2728 referrals were recorded—a 53-fold increase in just over a decade (Tavistock & Portman NHS Foundation Trust, 2020). The growing number of urban transgender health centers that have arisen in recent years (HRC, n.d.) reflects the increased demand for gender-related medical care among young people in North America, Australia, and Europe.

This unprecedented increase has created pressure on institutions and practitioners to rapidly evaluate these youth and make recommendations about treatment. To respond to growing demand, an innovative *informed consent model of care* has been developed. Under this model, mental health evaluations are not required, and hormones can be provided after just one visit following the collection of a patient's or guardian's consent signature (Schulz, 2018). The provision of transition services under this model of care is available not just to those over 18, but for younger patients as well (Planned Parenthood League of Massachusetts, n.d.).

Although following the informed consent model of care for hormones and surgeries for youth may diminish clinicians' ethical or moral unease (Vrouenraets et al., 2020), we believe this model is the antithesis of true informed consent, as it jeopardizes the ethical foundation of patient autonomy. Autonomy is not respected when patients consenting to the treatment do not have an accurate understanding of the risks, benefits, and alternatives.

b. *Assumptions held by professionals influence the integrity of the informed consent process*

Gender-dysphoric children and teens can intensely occupy the belief that their lives will be immensely improved by transition. Clinicians who have embraced the gender-affirmative model of care operate on the assumption that children and teens know best what they need to be happy and productive (Ehrensaft, 2017). These professionals, responding to the youths' passionate pleas, see their role as validating the young person's fervent wishes for hormones and surgery and clearing the path for gender transition. In doing so, they privilege the ethical principle of respect for patient autonomy (Clark & Virani, 2021) over their obligations for beneficence and non-maleficence.

Many of the gender-affirmative clinicians subscribe to the theory of *minority stress* – the supposition that the frequently co-occurring psychiatric symptoms of gender-dysphoric individuals are a result of prejudice and discrimination brought about by gender non-conformity (Rood et al., 2016; Zucker, 2019), and that gender transition will ameliorate these symptoms. Some even claim that gender-affirmative care will successfully treat not only depression and anxiety but will also resolve neurocognitive deficits frequently present in gender-dysphoric individuals (Turban, 2018; Turban, King, Carswell, & Keuroghlian, 2020; Turban & van Schalkwyk, 2018). These latter assertions have proven controversial even among the proponents of gender-affirmative interventions (Strang et al., 2018; van der Miesen, Cohen-Kettenis, & de Vries, 2018). The minority stress theory as the sole explanatory mechanism for co-occurring mental health illness has also been questioned in light of the evidence that psychiatric symptoms frequently predate the onset of gender dysphoria (Bechard, VanderLaan, Wood, Wasserman, & Zucker, 2017; Kaltiala-Heino, Sumia, Työlajärvi, & Lindberg, 2015; Kozłowska, Chudleigh, McClure, Maguire,

& Ambler, 2021). Other clinicians recognize the limits of gender-affirmative care and are aware that youth with underlying psychiatric issues are likely to continue to struggle post-transition (Kaltiala, Heino, Työläjäarvi, & Suomalainen, 2020), but, unaware of alternative approaches such as gender-exploratory psychotherapy or watchful waiting (Bonfatto & Crasnow, 2018; Churcher Clarke & Spiliadis, 2019; Spiliadis, 2019), these well-meaning professionals continue to treat youth with gender-affirmative interventions despite lingering doubts.

It is common for gender-affirmative specialists to erroneously believe that gender-affirmative interventions are a *standard of care* (Malone, D'Angelo, Beck, Mason, & Evans, 2021; Malone, Hruz, Mason, Beck, et al., 2021). Despite the increasingly widespread professional beliefs in the safety and efficacy of pediatric gender transition, and the endorsement of this treatment pathway by a number of professional medical societies, the best available evidence suggests that the benefits of gender-affirmative interventions are of very low certainty (Clayton et al., 2021; National Institute for Health & Care Excellence, 2020a; 2020b) and must be carefully weighed against the health risks to fertility, bone, and cardiovascular health (Alzahrani et al., 2019; Biggs, 2021; Getahun et al., 2018; Hembree et al., 2017; Nota et al., 2019). Recently, emphasis has also been placed on psychosocial risks and as yet unknown medical risks (Malone, D'Angelo, et al., 2021).

Five scientific observations question and refute the assumption that an individual's experience of incongruence of sex and gender identity is best addressed by supporting the newly assumed gender identity with psychosocial and medical interventions.

1. The most foundational aspect of the diagnoses of "gender dysphoria" (DSM-5) and "gender incongruence" (ICD-11), requisite for the provision of medical treatment, is in flux, as professionals disagree on whether the presence of distress is a key diagnostic criterion, as stated in the DSM-5, or is irrelevant, as is the case according to the latest ICD-11 criteria (American Psychiatric Association, 2013; World Health Organization, 2019). Further, these diagnoses have never been properly field-tested (de Vries et al., 2021).
2. There are no randomized controlled studies demonstrating the superiority of various affirmative interventions compared to alternatives. There isn't even agreement about which outcome measures would be ideal in such studies.
3. There are few long-term follow-up studies of various interventions using predetermined outcome measures at designated intervals. Studies that have been conducted are, at best, inconsistent. Higher quality studies with longer-follow-up fail to demonstrate durable positive impacts on mental health (Bränström & Pachankis, 2020a; 2020b).
4. Rates of post-transition desistance, increased mental suffering, increased incidence of physical illness, educational failure, vocational inconstancy, and social isolation have not been established.
5. Numerous cross-sectional and prospective studies of transgender adults consistently demonstrate a high prevalence of serious mental health and social problems as well as suicide (Asscheman et al., 2011; Dhejne et al., 2011). Controversies about how to deal with trans-identified youth must consider the well described vulnerabilities of transgender adults.

It is equally important to realize that to date, research about alternative approaches, such as psychotherapy or watchful waiting, shares the scientific limitations of the research of more invasive interventions: there are no control groups, nor is there systematic follow-up at predetermined intervals with predetermined means of measurement (Bonfatto & Crasnow, 2018; Churcher Clarke & Spiliadis, 2019; Spiliadis, 2019). Parents and patients need to be informed of this as well.

Perhaps the single most problematic assumption held by some gender clinicians is that the young patients have simply been "born in the wrong body." This assumption seemingly frees clinicians from having to contend with the ethical dilemmas of recommending body-altering

interventions that are based on very low-quality evidence. Despite the principle of development that biology, psychosocial factors, and culture generate behavior, these clinicians may believe that atypical genders are created by biology. This reductionistic approach has been criticized repeatedly (Kendler, 2019).

While the origins of childhood or adolescent onset of gender incongruence have not yet been fully elucidated, brain studies of increasing technical sophistication have yet to demonstrate a distinct structure or pattern that accounts for an atypical gender identity, after statistically controlling for sexual orientation and exposure to exogenous hormones (Frigerio, Ballerini, & Valdés Hernández, 2021). Twin studies also demonstrate that while biology plays a role in one's experience of "gender incongruence," it is far from deterministic (Diamond, 2013).

A growing number of clinicians and researchers are noting that the dramatic rise of teens declaring a trans identity appears to be, at least in part, a result of peer influence (Anderson, 2022; Hutchinson, Midge, & Spiliadis, 2020; Littman 2018; Littman, 2020; Zucker, 2019). Some have noted yet another influx of trans-identified youth emerging during the COVID lockdowns, and have hypothesized that increased isolation coupled with heavy internet exposure may be responsible (Anderson, 2022). While the research into the phenomenon of social influence as a contributor to trans identification of youth is still in its infancy, the possibility that clinicians are providing treatments with permanent consequences to address what may be transient identities in youth poses a serious ethical dilemma.

### c. *Poor evaluations*

There is a growing recognition that rapid evaluations which disregard factors contributing to the development of gender dysphoria in youth are problematic. In November 2021, two-leaders of the World Professional Organization for Transgender Health (WPATH) warned the medical community that the "The mental health establishment is failing trans kids" (Anderson & Edwards-Leeper, 2021). Frequently, evaluations provided by gender clinicians may only ascertain the diagnosis of *gender dysphoria* (DSM-5) or its ICD-11 counterpart *gender incongruence*, and screen for conspicuous mental illness prior to recommending hormones and surgeries. These limited, abbreviated evaluations overlook, and as a result fail to address, the relevant issue of the forces that may have influenced the young person's current gender identity.

Confirming the young person's self-diagnosis of gender dysphoria or gender incongruence is easy. Clarifying the developmental forces that have influenced it and determining an appropriate intervention are not. Contextualizing these forces involves an understanding of child and adolescent developmental processes, childhood adversity, co-existing physical and cognitive disadvantages, unfortunate parental or family circumstances (Levine, 2021), as well as the role of social influence (Anderson, 2022; Anderson & Edwards-Leeper, 2021; Littman, 2018; 2021).

The poor quality of mental health evaluations has been a point of significant discontent for a growing number of parents of gender-dysphoric youth. Increasingly, parents have formed dozens of support groups in North America, Europe, Australia and New Zealand, united in their objections to the idea that the best or the only treatment for their gender-dysphoric children is affirmation (Genspect, 2021). These distressed parents, recognizing that their son or daughter may eventually decide to present to others as a trans person, want a psychotherapeutic investigation to understand what contributed to the development of this identity and an exploration of noninvasive treatment options. Frequently, they cannot find anyone in their community who does not recommend immediate affirmation.

The American Academy of Pediatrics' Committee of Bioethics recognizes that "parents...are better situated than others to understand the unique needs of their children and to make appropriate, caring decisions regarding their children's health care" (Katz et al., 2016). The plight of the families unable to find specialists capable of conducting thorough evaluations draws attention to the widespread acceptance of medical interventions for gender-dysphoric youth as the first line of treatment. The problem is that such care has been established through precedent rather

than through scientific demonstrations of its efficacy. We contend that parents and patients have a right to know this, and that it is the professionals' responsibility and obligation to inform them of the state of knowledge in this arena of care.

d. *Incorrect information shared*

In sharing the information with patients and families, two key areas of uncertainty must be emphasized. The first one is the uncertain permanence of a child's or an adolescent's gender identity (Littman, 2021; Ristori & Steensma, 2016; Singh, Bradley, & Zucker, 2021; Vandebussche, 2021; Zucker, 2017). The second is the uncertain long-term physical and psychological health outcomes of gender transition (National Institute for Health & Care Excellence, 2020a; 2020b). Unfortunately, gender specialists are frequently unfamiliar with, or discount the significance of, the research in support of these two concepts. As a result, the informed consent process rarely adequately discloses this information to patients and their families.

Problematically, it is common for gender clinicians to emphasize the risk of suicide if a young person's wish to transition gender is not immediately fulfilled. There is a significant amount of misinformation surrounding the question of suicidality of trans-identified youth (Biggs, 2022). Providers of gender-affirmative care should be careful not to unwittingly propagate misinformation regarding suicide to parents and youths. They should also be reminded that any conversations about suicide should be handled with great care, due to its socially contagious nature (Bridge et al., 2020; HHS, 2021).

i. High rate of desistance/natural resolution of gender dysphoria in children is not disclosed

There have been eleven research studies to date indicating a high rate of resolution of gender incongruence in children by late adolescence or young adulthood without medical interventions (Cantor, 2020; Ristori & Steensma, 2016; Singh et al., 2021). An attempt has been made to discount the applicability of this research, suggesting that the studies were based on merely gender non-conforming, rather than truly gender-dysphoric, children (Temple Newhook et al., 2018). However, a reanalysis of the data prompted by this critique confirmed the initial finding: Among children meeting the diagnostic criteria for "Gender Identity Disorder" in DSM-IV (currently "Gender Dysphoria in DSM-5), 67% were no longer gender-dysphoric as adults; the rate of natural resolution for gender dysphoria was 93% for children whose gender dysphoria was significant but subthreshold for the DSM diagnosis (Zucker, et al., 2018). It should be noted that high resolution of childhood-onset gender dysphoria had been recorded before the practice of social transition of young children was endorsed by the American Academy of Pediatrics (Rafferty et al., 2018). It is possible that social transition will predispose a young person to persistence of transgender identity long-term (Zucker, 2020).

The information regarding the resolution of gender dysphoria among those with adolescent-onset gender dysphoria, which is currently the predominant presentation, is less clear. A growing body of evidence suggests that for many teens and young adults, a post-pubertal onset of transgender identification can be a transient phase of identity exploration, rather than a permanent identity, as evidenced by a growing number of young detransitioners (Entwistle, 2020; Littman, 2021; Vandebussche, 2021). Previously, the rate of detransition and regret was reported to be very low, although these estimates suffered from significant limitations and were likely undercounting true regret (D'Angelo, 2018). However, in the last several years since gender-affirmative care has become popularized, the rate of detransition appears to be accelerating.

According to a recent study from a UK adult gender clinic, 6.9% of those treated with gender-affirmative interventions detransitioned within only 16 months of starting treatment, and another 3.4% had a pattern of care suggestive of detransition, yielding a rate of probable detransition in excess of 10%. Another 21.7% of patients disengaged from the clinic without completing

their treatment plan (Hall, Mitchell, & Sachdeva, 2021). While some of these individuals later reengaged with the gender service, the authors concluded, “detransitioning might be more frequent than previously reported.” Another study from a UK primary care practice found that 12.2% of those who had started hormonal treatments either detransitioned or documented regret, while the total of 20% stopped the treatments for a wider range of reasons. The mean age of their presentation with gender dysphoria was 20, and the patients had been taking gender-affirming hormones for the average 5 years (17 months-10 years) prior to discontinuing.

Comparing these much higher rates of treatment discontinuation and detransition to the significantly lower rates reported by the older studies, the researchers noted: “Thus, the detransition rate found in this population is novel and questions may be raised about the phenomenon of overdiagnosis, overtreatment, or iatrogenic harm as found in other medical fields” (Boyd, Hackett, & Bewley, 2022 p.15). Indeed, given that regret may take up to 8-11 years to materialize (Dhejne, Öberg, Arver, & Landén, 2014; Wiepjes et al., 2018), many more detransitioners are likely to emerge in the coming years. Detransitioner research is still in its infancy, but two recently published studies examining detransitioner experiences report that detransitioners from the recently-transitioning cohorts feel they had been rushed to medical gender-affirmative interventions with irreversible effects, often without the benefit of appropriate, or in some instances any, psychologic exploration (Littman, 2021; Vandenbussche, 2021).

Clinicians should also disclose to patients and parents that there is no test which can accurately predict who will persist in their transgender identification upon reaching mature adulthood (Ristori & Steensma, 2016). Families should be made aware that a period of strong cross-sex identification in childhood is commonly associated with future homosexuality (Korte et al., 2008). Research in desistance confirms that the majority of youth whose gender dysphoria resolves naturally do indeed grow up to be gay, lesbian, or bisexual adults (Cantor, 2020, Appendix; Singh et al., 2021).

- ii. Implications of very low-quality evidence that underlies the practice of pediatric gender transition are not explained

The evidence underlying the practice of pediatric gender transition is widely recognized to be of very low quality (Hembree et al., 2017). In 2020, the most comprehensive systematic review of evidence to date, commissioned by the UK National Health System (NHS) and conducted by the National Institute for Health and Care Excellence (NICE), concluded that the evidence for both puberty blocking and cross-sex hormones is of very low certainty (National Institute for Health & Care Excellence, 2020a; 2020b).

According to the NICE review of evidence for puberty blockers, the studies “are all small, uncontrolled observational studies, which are subject to bias and confounding, and are of very low certainty as assessed using modified GRADE [Grading of Recommendations, Assessment, Development and Evaluations]. All the included studies reported physical and mental health comorbidities and concomitant treatments very poorly” (National Institute for Health & Care Excellence, 2020a, p.13). NICE reached similar conclusions regarding the quality of the evidence for cross-sex hormones (National Institute for Health & Care Excellence, 2020b).

Problematically, the implications of administering a treatment with irreversible, life-changing consequences based on evidence that has an official designation of “very low certainty” according to modified GRADE is rarely discussed with the patients and the families. GRADE is the most widely adopted tool for grading the quality of evidence and for making treatment recommendations worldwide. GRADE has four levels of evidence, also known as certainty in evidence or quality of evidence: very low, low, moderate, and high (BMJ Best Practice, 2021). When evidence is assessed to be “very low certainty,” there is a high likelihood that the patients will not experience the effects of the proposed interventions (Balshem et al., 2011).

In the context of providing puberty blockers and cross-sex hormones, the designation of “very low certainty” signals that the body of evidence asserting the benefits of these interventions is

highly unreliable. In contrast, several negative effects are quite certain. For example, puberty blockade followed by cross-sex hormones leads to infertility and sterility (Laidlaw, Van Meter, Hruz, Van Mol, & Malone, 2019). Surgeries to remove breasts or sex organs are irreversible. Other health risks, including risks to bone and cardiovascular health, are not fully understood and are uncertain, but the emerging evidence is alarming (Alzahrani et al., 2019; Biggs, 2021).

iii. The question of suicide is inappropriately handled

Suicide among trans-identified youth is significantly elevated compared to the general population of youth (Biggs, 2022; de Graaf et al., 2020). However, the “transition or die” narrative, whereby parents are told that their only choice is between a “live trans daughter or a dead son” (or vice-versa), is both factually inaccurate and ethically fraught. Disseminating such alarmist messages hurts the majority of trans-identified youth who are not at risk for suicide. It also hurts the minority who are at risk, and who, as a result of such misinformation, may forgo evidence-based suicide prevention interventions in the false hopes that transition will prevent suicide.

The notion that trans-identified youth are at alarmingly high risk of suicide usually stems from biased online samples that rely on self-report (D’Angelo et al., 2020; James et al., 2016; The Trevor Project, 2021), and frequently conflates suicidal thoughts and non-suicidal self-harm with serious suicide attempts and completed suicides. Until recently, little was known about the actual rate of suicide of trans-identified youth. However, a recent analysis of data from the biggest pediatric gender clinic in the world, the UK’s Tavistock, found the rate of completed youth suicides to be 0.03% over a 10-year period, which translates into the annual rate of 13 per 100,000 (Biggs, 2022). While this rate is significantly elevated compared to the general population of teens, it is far from the epidemic of trans suicides portrayed by the media.

The “transition or die” narrative regards suicidal risk in trans-identified youth as a different phenomenon than suicidal risk among other youth. Making them an exception falsely promises the parents that immediate transition will remove the risk of suicidal self-harm. Trans patients themselves complain about the so-called “trans broken arm syndrome” – a frustrating pattern whereby physicians “blame” all the problems the patients are experiencing on their trans status, and a result, fail to perceive and respond to other sources of distress (Paine, 2021). Clinicians caring for trans-identified youth should be reminded that suicide risk in all patients is a multi-factorial phenomenon (Mars et al., 2019). To treat trans youths’ suicidality as an exception is to deny them evidence-based care.

A recent study of three major youth clinics concluded that suicidality of trans-identifying teens is only somewhat elevated compared to that of youth referred for mental health issues unrelated to gender identity struggles (de Graaf et al., 2020). Another study found that transgender-identifying teens have relatively similar rates of suicidality compared to teens who are gay, lesbian and bisexual (Toomey, Syvertsen, & Shramko, 2018). Depression, eating disorders, autism spectrum conditions, and other mental health conditions commonly found in transgender-identifying youth (Kaltiala-Heino, Bergman, Työlajärvi, & Frisen, 2018; Kozłowska, McClure, et al., 2021; Morandini, Kelly, de Graaf, Carmichael, & Dar-Nimrod, 2021) are all known to independently contribute to the probability of suicide (Biggs, 2022; Simon & VonKorff, 1998; Smith, Zuromski, & Dodd, 2018).

The “transition or suicide” narrative falsely implies that transition will prevent suicides. Clinicians working with trans-identified youth should be aware that although in the short-term, gender-affirmative interventions can lead to improvements in some measures of suicidality (Kaltiala et al., 2020), neither hormones nor surgeries have been shown to reduce suicidality in the long-term (Bränström & Pachankis, 2020a; 2020b). Alarmingly, a longitudinal study from Sweden that covered more than a 30-year span found that adults who underwent surgical transition were 19 times more likely than their age-matched peers to die by suicide overall, with female-to-male participants’ risk 40 times the expected rate (Dhejne et al., 2011, Table S1).

Another key longitudinal study from the Netherlands concluded that suicides occur at a similar rate at all stages of transition, from pretreatment assessment to post-transition follow-up (Wiepjes et al., 2020). The data from the Tavistock clinic also did not show a statistically significant difference between completed suicides in the “waitlist” vs. the “treated” groups (Biggs, 2022). Luckily, in both groups, completed suicides were rare events (which may have been responsible for the lack of statistical significance). Thus, we consider the “transition or die” narrative to be misinformed and ethically wrong.

In our experience working with trans-identified youth, an adolescent’s suicidality can sometimes arise as a response to parental distress, resistance, skepticism, or wish to investigate the forces shaping the new gender identity before social transition and hormone therapy. When mental health professionals or other healthcare providers fail to recognize the legitimacy of parental concerns, or label the parents as transphobic, this only tends to intensify intrafamilial tension. Clinicians would be well-advised that gender transition is not an appropriate response to suicidal intent or threat, as it ignores the larger mental health and social context of the young patient’s life—the entire family is often in crisis. Trans-identified adolescents should be screened for self-harm and suicidality, and if suicidal behaviors are present, an appropriate evidence-based suicide prevention plan should be put in place (de Graaf et al., 2020).

### **The Dutch Study: the questionable basis for the gender affirmative model of care for youth**

Few practitioners of gender-affirmative interventions, and even fewer patients and families, realize that the foundation of the practice of medically transitioning minors stems from a single Dutch proof of concept study, the outcomes of which were documented in two publications (de Vries, Steensma, Doreleijers, Cohen, & Kettenis, 2011; de Vries et al., 2014). The former (de Vries et al., 2011) reported on cases who underwent puberty blockade, while the latter (de Vries et al., 2014) reported on a subset of the cases who completed surgeries.

The Dutch study subjects’ high level of psychological functioning at 1.5 years after surgery, which was the study end point, was an impressive feat. However, both of the studies suffer from a high risk of bias due to their study design, which is effectively a non-randomized case series—one of the lowest levels of evidence (Mathes & Pieper, 2017; National Institute for Health & Care Excellence, 2020a). In addition, the studies suffer from limited applicability to the populations of adolescents presenting today (de Vries, 2020). The interventions described in the study are currently being applied to adolescents who were not cross-gender identified prior to puberty, who have significant mental health problems, as well as those who have non-binary identities—all of these presentations were explicitly disqualified from the Dutch protocol. Despite these limitations, the Dutch clinical experiment has become the basis for the practice of medical transition of minors worldwide and serves as the basis for the recommendations outlined in the 2017 Endocrine Society guidelines (Hembree et al., 2017).

We contend that the Dutch studies have been misunderstood and misrepresented as providing evidence of the safety and efficacy of these interventions for all youth. It is important that both the strengths and the weaknesses of these two studies are understood, as to date, the Dutch experience presents the best available evidence behind the practice of pediatric gender transition.

### ***Rationale for pediatric transition***

Prior to the 1990s, gender transitions were typically initiated in mature adults (Dhejne et al., 2011). However, it was noted that particularly for natal male patients, hormonal and surgical interventions failed to achieve satisfactory results, and patients had a “never disappearing masculine appearance” (Delemarre-van de Waal & Cohen-Kettenis, 2006). The lack of adequate cosmetic outcomes was thought to contribute to the frequently disappointing outcomes of medical

gender transition, with persistently high rates of mental illness and suicidality post-transition (Delemarre-van de Waal & Cohen-Kettenis, 2006; Dhejne et al., 2011; Ross & Need, 1989).

In the mid 1990s, a team of Dutch researchers hypothesized that by carefully selecting a subset of gender-dysphoric children who would likely be transgender-identified for the rest of their lives, and by medically intervening before puberty left an irreversible mark on their bodies, the cosmetic outcomes would be improved—and as a result, mental health outcomes might be improved (Gooren & Delemarre-van de Waal, 1996).

### ***Mixed study findings***

In 2014, the Dutch research team published a key longitudinal study of mental health outcomes of 55 youths who completed medical and surgical transition (de Vries et al., 2014). The 2014 paper (sometimes referred to as the “Dutch study”) reported that for youth with severe gender dysphoria that started in early childhood and persisted into mid-adolescence, a sequence of puberty blockers, cross-sex hormones, and breast and genital surgeries (including a mandatory removal of the ovaries, uterus and testes), with ongoing extensive psychological support, was associated with positive mental health and overall function 1.5 years post-surgery.

While the Dutch reported resolution of gender dysphoria post-surgery in study subjects, the reported psychological improvements were quite modest (de Vries et al., 2014). Of the 30 psychological measurements reported, nearly half showed no statistically significant improvements, while the changes in the other half were marginally clinically significant at best (Malone, D’Angelo, et al., 2021). The scores in anxiety, depression, and anger did not improve. The change in the Children’s Global Assessment Scale, which measures overall function, was one of the most impressive changes—however it too remained in the same range before and after treatment (de Vries et al., 2014).

### ***Problematic discordance between reduced gender dysphoria and lack of meaningful improvements in psychological measures***

The discordance between the marked reduction in gender dysphoria, as measured by the UGDS (Utrecht Gender Dysphoria Scale), and the lack of meaningful changes in psychological function using standard measures, warrants further examination. There are three plausible explanations for this lack of agreement. Any one of these three explanations calls into question the widely assumed notion that the medical interventions significantly improve mental health or lessen or eradicate gender dysphoria.

One possible explanation is that gender dysphoria as measured by UGDS, and psychological function as measured by most standard instruments, are not correlated. This contradicts the primary rationale for providing gender-affirmative treatments for youth (which is to improve psychological health and functioning), and if true, ethically threatens these medical interventions. The other plausible explanation stems from the high psychological function of all the subjects at baseline; the subjects were selected because they were free from significant mental health problems (de Vries et al., 2014). As a result, there was little opportunity to meaningfully improve. This explanation highlights a key limitation in applying the study’s results to the majority of today’s gender-dysphoric youth, who often present with a high burden of mental illness (Becerra-Culqui et al., 2018; Kozłowska, McClure, et al., 2021). The study cannot be used as evidence that these procedures have been proven to improve depression, anxiety, and suicidality.

A third possible explanation for the discordance between only minor changes in psychological outcomes but a significant drop in gender dysphoria comes from a close examination of the UGDS scale itself and how it was used by the Dutch researchers. This 12-item scale, designed by the Dutch to assess the severity of gender dysphoria and to identify candidates for hormones

and surgeries, consists of “male” (UGDS-aM) and “female” (UGDS-aF) versions (Iliadis et al., 2020). At baseline and after puberty suppression, biological females were given the “female” scale, while males were given the “male” scale. However, post-surgery, the scales were flipped: biological females were assessed using the “male” scale, while biological males were assessed on the “female” scale (de Vries et al., 2014). We maintain that this handling of the scales may have at best obscured, and at worst, severely compromised the ability to meaningfully track how gender dysphoria was affected throughout the treatment.

Consider this example. At baseline, a gender-dysphoric biological female would rate items from the “female” scale such as: “I prefer to behave like a boy” (item 1); “I feel unhappy because I have to behave like a girl” (item 6) and “I wish I had been born a boy” (item 12). Positive answers to these questions would have contributed to a high baseline gender dysphoria score. After the final surgery, however, this same patient would be asked to rate items from the “male” scale, including the following: “My life would be meaningless if I had to live as a boy” (item 1); “I hate myself because I am a boy” (item 6) and “It would be better not to live than to live as a boy” (item 12). A gender-dysphoric female would not endorse these statements (at any stage of the intervention), which would lead to a lower gender dysphoria score.

Thus, the detected drop in the gender dysphoria scores for biological males and females may have had less to do with the success of the interventions, and more to do with switching the scale from the “female” to the “male” version (and vice-versa) between the baseline and post-surgical period. This, too, may explain why no changes in gender dysphoria were noted between baseline and the puberty blockade phase, and were only recorded after the final surgery, when the scale was switched.

It must be considered that had the researchers administered the “flipped” scale earlier, at the completion of the puberty blocker stage, UGDS scale could have registered a reduction in gender dysphoria. Likewise, however, one must consider the possibility that had *both sets of scales* been administered to the same individual at baseline, a “reduction” in gender dysphoria could have been registered upon switching of the scale, *well before any interventions began*. The question here is whether the diminishment of quantitative measures of gender dysphoria is largely an artifact of what scale was used.

It must be noted that the UGDS measure has been demonstrated only to effectively differentiate between clinically referred gender-dysphoric individuals, non-clinically referred controls, and participants with disorders of sexual development, and was not designed to detect changes in gender dysphoria during treatment (Steensma, McGuire, Kreukels, et al. 2013). The presence of items such as “I dislike having erections” (item 11, UGDS-aM), which would have to be rated by birth-females, and “I hate menstruating because it makes me feel like a girl (item 10, UGDS-aF), which would be presented to birth-males, neither of which could be meaningfully rated by either at any stage of the interventions, further illustrates that UGDS has questionable validity for the purpose of detecting meaningful changes in gender dysphoria as a result of medical and surgical treatment.

The updated UGDS scale (UGDS-GS), developed by the Dutch after the publication of their seminal study, has eliminated the two-sex version of the scale in favor of a single battery of questions applicable to both sexes (McGuire et al., 2020). This change may lead to a more reliable measurement of treatment-associated changes in future research. Other gender dysphoria scales also exist (Hakeem, Črnčec, Asghari-Fard, Harte, & Eapen, 2016; Iliadis et al., 2020) and may or may not be better suited for the purposes of measuring the impact of medical interventions on underlying gender distress. Gender dysphoria, of course, may also prove to be a more complex concept than can be measured by any scale.

### **Other limitations**

The two Dutch studies were conducted without a control group (de Vries et al., 2011; de Vries et al., 2014). Nor could the researchers control for mental health interventions, which all the

subjects received in addition to hormones and surgery. The Dutch only evaluated mental health outcomes and did not assess physical health effects of hormones and surgery. The sample size was small: the final study reported the outcomes of only 55 children, and as few as 32 were evaluated on key measures of psychological outcomes.

It is important to realize that the Dutch sample was carefully selected, which introduced a source of bias, and also challenges the study's applicability. From the 196 adolescents initially referred, 111 were considered eligible to start puberty blockers, and of this group, only the 70 most mature and mentally stable who proceeded to cross-sex hormones were included in the study (de Vries et al., 2011). Of note, 97% of the selected cases were attracted to members of their natal sex at baseline. All were cross-sex identified, with no cases of nonbinary identities. The final study only followed 55, rather than the original 70 cases, further excluding from reporting the outcomes of subjects who had experienced adverse events, including: one death from surgery-related complications and three cases of obesity and diabetes that rendered subjects ineligible for surgery. Three more subjects refused to be contacted or dropped out of care, which may mask adverse outcomes (de Vries et al., 2014).

There is no knowledge of the fate of 126 patients who did not participate in the Dutch study. Longer term outcomes of the subjects who did participate are lacking. We are aware of only one case of long-term follow-up for a female-to-male patient treated by the Dutch team in the 1990s. The case study describing the subject's functioning at the age of 33 found that the patient did not regret gender transition. However, he reported struggling with significant shame related to the appearance of his genitals and to his inability to sexually function; had problems maintaining long-term relationships; and experienced depressive symptoms (Cohen-Kettenis, Schagen, Steensma, de Vries, & Delemarre-van de Waal, 2011). Notably, these problems had not yet emerged when the same patient was assessed at the age of 20, when he reported high levels of satisfaction in general, and was "very satisfied with the results [of the metoidioplasty]" in particular (Cohen-Kettenis & van Goozen, 1998, p.248). Since the last round of psychological outcomes of the individuals in the Dutch study was obtained when the subjects were around 21 years of age (de Vries et al., 2014), it raises questions how they will fare during the decade when new developmental tasks, such as career development, forming long-term intimate relationships and friendships, or starting families come into focus.

As to the unknown outcomes of the patients rejected by the Dutch protocol, one study did report on 14 adolescents who sought gender reassignment in the same clinic, but were disqualified from treatment due to "psychological or environmental problems" (Smith, Van Goozen, & Cohen-Kettenis, 2001, p. 473). The study found that at follow-up 1-7 years after the original application, 11 of the 14 no longer wished to transition, and 2 others only slightly regretted not transitioning (Malone, D'Angelo, et al., 2021; Smith et al., 2001). This further underscores the importance of conducting research utilizing control groups and following the subjects for an extended period.

A recent attempt to replicate the results of the first Dutch study (de Vries et al., 2011) found no demonstrable psychological benefit from puberty blockade, but did find that the treatment adversely affected bone development (Carmichael et al., 2021). The final Dutch study (de Vries et al., 2014) has never been attempted to be replicated with or without a control group.

### ***The scaling of the Dutch Protocol beyond original indications***

The medical and surgical sequence of Dutch protocol has been aggressively scaled worldwide without the careful evaluations and vetting practiced by the Dutch. The protocol's original investigators have recently expressed concern that the interventions they described have been widely adopted on four continents without several of the protocol's essential discriminatory features (de Vries, 2020).

The extensive multi-year multidisciplinary evaluations of the children have been abbreviated or simply bypassed. The medical sequence is routinely used for children with post-pubertal onset of transgender identities complicated by mental health comorbidities (Kaltiala-Heino et al., 2018), and not just for those high-functioning adolescents with persistent early life cross-identifications, as was required by the Dutch protocol (de Vries & Cohen-Kettenis, 2012). Further, it has become increasingly common to socially transition children before puberty (Olson, Durwood, DeMeules, & McLaughlin, 2016), even though this was explicitly discouraged by the Dutch protocol at the time (de Vries & Cohen-Kettenis, 2012).

In addition, medical transition is frequently initiated much earlier than recommended by the original protocol (de Vries & Cohen-Kettenis, 2012). The authors of the protocol were aware that most children would have a spontaneous realignment of their gender identity with sex by going through early- to mid-stages of puberty (Cohen-Kettenis, Delemarre-van de Waal, & Gooren, 2008). The average age of initiating puberty blockade in the Dutch study was around 15. In contrast, currently the age limit has been lowered to the age of Tanner stage II, which can occur as early as 8-9 years (Hembree et al., 2017). Irreversible cross-sex hormones, initiated in the Dutch study at the average age of nearly 17, are currently commonly prescribed to 14-year-olds, and this lower age threshold has been recommended by WPATH Standard of Care 8 draft, the final version of which is due to be released in early 2022. The fact that children are transitioned before their identity is tested against the biological reality and before natural resolution of gender dysphoria has had a chance to occur is a major deviation from the original Dutch protocol. Systematic follow-up, reassessments, and tracking and publishing of outcomes are not performed.

As the lead Dutch researchers have begun to call for more research into the novel presentation of gender dysphoria in youth (de Vries, 2020; Voorzij, 2021) and question the wisdom of applying the hormonal and surgical treatment protocols to the newly presenting cases, many recently educated gender specialists mistakenly believe that the Dutch protocol proved the concept that its sequence helps all gender-dysphoric youth. Although aware of the Dutch study's importance, they seem to be unaware of its agreed upon limitations, and the Dutch clinicians' own discomfort that most new trans-identified adolescents presenting for care today significantly differ from the population the Dutch had originally studied. These facts, of course, underscore the need for a robust informed consent process.

## **The recommendations for informed consent process for children, adolescents, and young adults**

### ***Consent for all stages of gender transition should be explicit, not implied***

Noninvasive medical care or care that carries little risk of harm does not require a signed informed consent document; rather, consent is implied through the act of a patient presenting for care. For example, when a parent brings in a child for a skin laceration or abscess, consent for sutures or simple incision and drainage is implied. Similarly, when a child presents with pneumonia and is hospitalized, consent for chest x-ray, IV fluids, and antibiotics is also implied. It is assumed that patients or their guardians agree to the interventions and understand the benefits and risks. When risks are greater, such as prior to surgery, chemotherapy, or another invasive procedure, an informed consent document is signed. Such situations require an explicit, or express informed consent.

In the context of interventions for gender dysphoria or gender incongruence, the uncertainties associated with puberty blocking, cross-sex hormones, and gender-affirmative surgeries are well-recognized (Manrique et al., 2018; National Institute for Health & Care Excellence, 2020a; 2020b; Wilson et al., 2018). In these cases, consent should be explicit rather than implied because of the complexity, uncertainty, and risks involved.

Informed consent for social transition represents a gray area. Evidence suggests that social transition is associated with the persistence of gender dysphoria (Hembree et al.,

2017; Steensma, McGuire, Kreukels, Beekman, & Cohen-Kettenis, 2013). This suggests that social gender transition is a form of a psychological intervention with potential lasting effects (Zucker, 2020). While the causality has not been proven, the possibility of iatrogenesis and the resulting exposure to the risks of future medical and surgical gender dysphoria treatments, qualifies social gender transition for explicit, rather than implied, consent.

### ***Full unbiased disclosure of benefits, risks and alternatives is requisite***

When mental health professionals are involved in evaluations and recommendations, the informed consent process begins either as part of an extended evaluation or is integrated in a psychotherapeutic process, separately or together, with the parents and patient. When pediatricians, nurse practitioners, or primary care physicians perform the initial evaluation, the informed consent process is more likely to be labeled as such in a briefer series of meetings.

In all settings, the informed consent discussions for gender-affirmative care should include three central ideas:

1. The decision to initiate gender transition may predispose the child to persist in their transgender identity long-term.
2. Many of the physical changes contemplated and undertaken are irreversible.
3. Careful long-term studies have not been done to verify that these interventions enable better physical and mental health or improved social functioning, or that they do not cause harm.

The informed consent process, culminating with a signed document, signifies that parents and patient have been educated about the short- and long-term risks, benefits and uncertainties associated with all relevant stages of the gender-affirmative interventions. The process must also inform the patients and families about the full range of alternative treatments, including the choice of not socially or medically treating the child's or adolescent's current state of gender/body incongruence.

### ***Decisional capacity to consent needs to be assessed and family should be involved***

Trans-identified youth typically present themselves as strongly desiring hormones and ultimately, surgery. It should not be assumed that their eagerness is matched with the capacity to carefully consider the consequences of their realized desires. Trans-identified youth younger than the age of consent should be part of the informed consent process, but they may not be mature enough to recognize or admit their concerns about the proposed intervention. For this reason, it is the parents who, after careful consideration, are responsible for signing an informed consent document.

The issue of the exact age at which adolescents are mature enough to consent to gender transition has proven contentious: courts have been asked to decide about competence to consent to gender-affirmative hormones for youth in the United Kingdom and Australia (Ouliaris, 2021). In the United States, the legal age for medical consent for gender-affirmative interventions varies by state.

When patients are age 18 and older, and in some jurisdictions as young as age 15 (Right to medical or dental treatment without parental consent, 2010), they do not legally require parental approval for medical procedures. But because an individual's change of gender has profound implications for parents, siblings, and other family members, it is usually prudent for clinicians to seek their input directly or indirectly during the informed consent process. This is done by requesting a meeting with the parents.

A recent study by a Dutch research team attempted to evaluate the decisional capacity of adolescents embarking on gender transition (Vrouenraets, de Vries, de Vries, van der Miesen, & Hein, 2021). The researchers administered the MacCAT-T tool, comprised of the *understanding*, *appreciating*, *reasoning*, and *expressing a choice* domains, to 74 adolescents who were 14.7 years old on average (with the minimum age of 10). They concluded that the adolescents were competent to consent to starting pubertal suppression, calling for similar research for the <12 group, particularly because “birth-assigned girls ... may benefit from puberty suppression as early as 9 years of age” (Vrouenraets et al., 2021 p.7).

This study suffers from two significant limitations involving the MacCAT-T tool. It was never designed for children. Rather, it was designed to assess medical consent capacities of adults suffering from conditions such as dementia, schizophrenia, and other psychiatric disorders. There is a fundamental lack of equivalency between consenting to treatment by adults with cognitive impairments and obtaining consent from healthy children whose age-appropriate cognitive capacities are intact, but who lack the requisite life experiences to consent to profound life-changing medical interventions. We doubt, for example, whether even highly intelligent children who have not had sexual experiences can meaningfully comprehend the loss of future sexual function and reproductive abilities.

In addition, even for adults, the MacCAT-T tool has been criticized for its exclusive focus on cognitive aspects of capacity, failing to account for the non-cognitive aspects such as values, emotions and other biographic and context specific aspects inherent in the complexity of the decision process in real life (Breden & Vollmann, 2004). Children’s values and emotions undergo tremendous change during the process of maturation.

The authors’ conclusion about their young patients’ competence to consent should be compared with what a panel of judges wrote in the challenge to the Tavistock treatment protocol (Bell v Tavistock, 2020):

...the clinical intervention we are concerned with here is different in kind to other treatments or clinical interventions. In other cases, medical treatment is used to remedy, or alleviate the symptoms of, a diagnosed physical or mental condition, and the effects of that treatment are direct and usually apparent. The position in relation to puberty blockers would not seem to reflect that description. [para 135]

...we consider the treatment in this case to be in entirely different territory from the type of medical treatment which is normally being considered. [para 140]

... the combination here of lifelong and life changing treatment being given to children, with very limited knowledge of the degree to which it will or will not benefit them, is one that gives significant grounds for concern. [para 143]

It seems clear that perceptions of children as young as 10 years of age as medically competent vary by country, state, and the institution where the doctor works, and, by clinicians’ beliefs about the long-term benefits of these interventions. We maintain that the claim that children can consent to extremely life-altering intervention is fundamentally a philosophical claim (Clark & Virani, 2021). Our view in this matter is that consent is primarily a parental function.

### ***Informed consent should be viewed as a process rather than an event***

Most institutions that care for transgender-identified individuals have devised obligatory consent forms that outline the risks and uncertainties of hormonal and surgical gender-affirmative interventions. However, the requisite signatures are frequently collected in a perfunctory manner (Schulz, 2018), akin to signatures collected ahead of a common surgical procedure. The purpose of such informed consent documents appears to be to protect practitioners from lawsuits, rather than attend to the primary ethical foundation of the process.

Although obtaining the signatures is important, the signed document should signify that the process of informed consent has been undertaken over an extended time period and is not simply quickly completed (Vrouenraets et al., 2021). We believe the latter approach poses an ethical concern (Levine, 2019).

The internal dynamics of the trans-identified young person and their families vary considerably. Parental capacities, their private marital and intrafamilial relationships, their cultural awareness, religious and political sensibilities all influence the amount of time necessary to undertake a thorough informed consent process. It is not prudent to suggest a specific duration for the process of informed consent, other than to emphasize that it requires a slow, patient, thoughtful question and answer period as the parents and patient contemplate the meaning of what is known and unknown and whether to embark on alternative approaches to the management of gender dysphoria before the age of full neurological maturity has been reached, mental health comorbidities have been addressed, and a true informed consent by the patient is more likely.

### **Final thoughts**

Sixty years of experience providing medical and surgical assistance to transgender-identified persons have seen many changes in who is treated, when they are treated, and how they are treated. Today, the emphasis has shifted to the treatment of the unprecedented numbers of youth declaring a trans identity. As adolescents pursue social, medical, and surgical interventions, health care providers may experience unease about patients' cognitive and emotional capacities to make decisions with life-changing and enduring consequences. An unrushed informed consent process helps the provider, the parents, and the patient.

Three issues tend to obscure the salience of informed consent: conspicuous mental health problems, uncertainty about the minor's personal capacity to understand the irreversible nature of the interventions, and parental disagreement. Physical and psychiatric comorbidities can contribute to the formation of a new identity, develop as its consequence, or bear no connection to it. Assessing mental health and the minor's functionality is one of the reasons why rapid affirmative care may be dangerous for patients and their families. For example, when situations involve autism, learning disorders, sexual abuse, attachment problems, trauma, separation anxiety, previous depressed or anxious states, neglect, low IQ, past psychotic illness, eating disorders or parental mental illness, clinicians must choose between ignoring these potentially causative conditions and comorbidities and providing appropriate treatment before affirmative care (D'Angelo et al., 2020).

For youth less than the age of majority, informed consent via parents provides a legal route for treatment but it does not make the decision to socially transition, provide hormones, or surgically remove breasts or testes less fraught with uncertainty. The best that health professionals can do is to ensure that the consent process informs the patient and parents of the current state of science, which is sorely lacking in quality research. It is the professionals' responsibility to ensure that the benefits patients and parents seek, and the risks they are assuming, are clearly appreciated as they prepare to make this often-excruciating decision.

Young people who have reached the age of majority, but who have not reached full maturation of the brain represent a unique challenge. It is well-recognized that brain remodeling proceeds through the third decade of life, with the prefrontal cortex responsible for executive function and impulse control the last to mature (Katz et al., 2016). The growing number of detransitioners who had been old enough to legally consent to transition, but who no longer felt they were transgender upon reaching their mid-20's, raises additional concerns about this vulnerable age group (Littman, 2021; Vandebussche, 2021).

When the clinician is uncertain whether a young person is competent to comprehend the implications of the desired treatment—that is, when informed consent cannot inform the patient—the clinician may need more time with the patient. When parents or guardians do

not agree about whether to use puberty blockers or cross-sex hormones, clinicians are in an uneasy spot (Levine, 2021). This occurs in both intact and divorced families. Australia has given legal instructions to clinicians facing these uncertainties: the court is to be asked to decide (Ouliaris, 2021). The court system in the UK has been grappling with similar issues in recent years. While it is a rare case that ends up in a courtroom, clinicians devoted to a deliberate informed consent process are still likely to encounter ethical dilemmas that they cannot resolve.

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