	Ages of patients (years)			Numbers of patients						Interventions			Time: duration and follow-up			Outcomes extracted
Reference	Age at intake range (mean)	Age at start of GnRH range (mean)	Age at start of CSHT range (mean)	*n* referred	*n* TG enrolled	*n* TG HT	*n* TG non-HT	*n* non-TG	*n* TG HT at last FU	GnRH	CSHT	Surgery[b]	GnRH duration range (mean)	CSHT duration range (mean)	Follow-Up time range (mean)	Mental health Bone health Anthropometrics Metabolism
Klaver 2020[32]		12.8–17.2[a] (14.9)	15.3–17.8[a] (16.6)		192	192			192	x	x	x	0.5–2.9 years (1.5)[a]	1.1–3.4 years (2.5[a])	age 22	BMI, SBP, DBP, glucose, insulin, HOMA-IR, cholesterol, triglycerides
Perl 2020[33]		13.4–15.4 (14)	14.2–16.0 (15)		48	15			15	x	x		2–4 months	2–6 months		BMI, BP
Schulmeister 2021[29]		9.0–14.5 (11.5)			92	55	226		55	x			10–14 months		1 year	Height velocity, BMI, z-score
Nokoff 2021[30]		10.2–14.1 (12)			17	17	31		17	x			0.5–5.8 years			Insulin, glucose HbA1c, HOMA-IR, body fat, % lean mass
Tack 2016[34]			NR (15–17)		45	43			43		x			6–18 months (12)	1.5 years	Height, weight, BMI, triglycerides, cholesterol, suicide, side effects
Jarin 2017[35]		103–xx	xx–25 (16–18)		116	116			116	(x)	x				2 years	BMI, BP, haematocrit, Hb, cholesterol
Mullins 2021[13]			13–24 (17)	1406	611	611			611		x			0.8–2.8 years (1.5 years)	3 years	Haematology, thrombosis, BMI

Note: Number of patients:*n* referred = number of patients referred to gender clinic for evaluation of gender dysphoria (not same at number of patients receiving GD diagnosis)*n* TG enrolled = number of patients enrolled in the study at start*n* TG = number of patients with gender dysphoria*n* TG HT = number of patients with gender dysphoria treated with hormones (GnRH alone, GnRH + CSHT, or CSHT only)*n* TG non-HT = number of patients with gender dysphoria treated NOT with hormones*n* TG HT at last FU = number of patients with gender dysphoria treated with hormones (GnRH alone, GnRH + CSHT, or CSHT only) evaluated at last follow-up time*n* non-TG = number of subjects in study without gender dysphoria (reference population).

Abbreviations: BDI, Beck Depression Inventory; BIS, Body Image Scale; BMAD, Bone Mineral Apparent Density; BMD, Bone Mineral Density; BMI, Body Mass Index; BP, Blood pressure; CBCL, Child Behaviour Checklist; CGAS, Global functioning Children's Global Assessment Scale, [higher scores (>80) indicating better global functioning]; CSHT, Cross-Sex Hormone Treatment/ gender-affirming treatment, testosterone, oestradiol, cyproterone acetate (CA), spironolactone, lynestrenol; GAD-7, Generalised Anxiety Disorder-7; GnRH, Gonadotropin Releasing Hormone analogue: triptorelin; HRQoL, Health Related Quality of Life; HT Hormone treatment, either GnRH, CSHT, or both; PHQ-9, Patient Health Questionnaire-9; SF-8, Short Form-8: (<18 years); STAI, Spielberger's Trait Anxiety; TG, Transgender; TPI, Anger Spielberger's Trait Anger; UGDS, Utrecht Gender Dysphoria Scale, score range 12–60 points [high score = high level of GD]; WHR, Waist-hip ratio; YSR, Youth Self Report: YSR (ages 11–18 years); Adult version (ASR, >18 years), [higher scores reflect higher degree of problems]; NR, not reported.

[a] Calculated by SBU.

[b] Surgery = any kind of gender reassignment surgery (gonadectomy, mastectomy, hysterectomy, laryngeal surgery, hair removal, phalloplasty, vaginoplasty).

TABLE 2 Summary of findings on psychosocial outcomes of puberty-blocking treatment (GnRHa) treatment in children with gender dysphoria.[14–19]

Outcome measures	Number of study participants, description of studies	Main result	"Certainty of evidence"	Deduction in GRADE[a]
Global function	*n* on hormones = 254 *n* evaluated = 113 Four observational cohort studies: one prospective and three retrospective studies[14–17]	Improved global function as assessed with the CGAS	Cannot be assessed	−2 risk of overall bias[b] −2 precision[c]
Suicide ideation	*n* on hormones = 42 *n* evaluated = 28 One prospective observational cohort study with mixed treatment (38 subjects with no pharmacological treatment)[18]	No change in suicide ideation	Cannot be assessed	−2 risk of overall bias[b] −2 precision[c]
Gender dysphoria	*n* on hormones = 145 *n* evaluated = 49 Two prospective observational cohort studies[15,16]	No change in gender dysphoria	Cannot be assessed	−2 risk of overall bias[b] −2 precision[c]
Depression	*n* on hormones = 97 *n* evaluated = 60 Two prospective observational cohort studies of which one included mixed treatment[14,18]	No change in depression	Cannot be assessed	−2 risk of overall bias[b] −2 precision[c]
Anxiety	n on hormones = 97 n evaluated = 60 Two prospective observational cohort studies[14,18]	No change in anxiety	Cannot be assessed	−2 risk of overall bias[a] −2 precision[b]
Cognition	*n* on hormones = 20 *n* evaluated = 20 One study[19]	No change in cognition compared with matched controls	Cannot be assessed	−2 risk of overall bias[b] −2 precision[c]
Quality of life	*n* on hormones = 98 *n* evaluated = 46 Two observational cohort studies, whereof one retrospective[16,17]	1. Improvement in quality of life most pronounced in subjects receiving puberty-blocking hormones, followed by gender-affirming hormone treatment[17] 2. Some improvement[16]	Cannot be assessed	−2 risk of overall bias[b] −2 precision[c]

Abbreviation: CGAS, Children's Global Assessment Scale.

[a] Starting at 4 for optimal studies in each study type.

[b] Selection of study participants is difficult to assess, analysis not based on stage in puberty development.

[c] Few study subjects in each study, heterogeneity in outcome and analyses.

could not investigate potential cognitive effects of hormone therapy.

3.5 | Bone health outcomes

Six longitudinal studies used dual-energy X-ray absorptiometry (DXA) scan technology to explore bone health before and again after some time with GnRHa treatment (Table 3). The second DXA scan usually coincided with CSHT initiation leading to different follow-up durations. The third DXA scan was performed after variable time with CSHT, performed with variable dosing and administration. The lumbar spine and hip were most often examined. One study investigated bone geometry.[20] Six studies were retrospective[21–26] and one study was prospective.[20] An additional study was cross-sectional where study participants in early puberty (Tanner stages 2–3) were examined only once, before the start of GnRHa therapy.[27]

Three studies reported a lower bone mineral density (BMD) in patients before or at start of GnRHa treatment compared with the general population of the same biological sex and age.[21,23,27] During GnRHa treatment, BMD estimated through area or volume, and expressed in z-scores increased less compared with general population reference values. However, the mean absolute BMD remained unchanged up to 2–3 years of GnRHa treatment.[20,23] The initiation of CSHT stimulated bone maturation and mineral accrual, increasing BMD.[21,22] After a median CSHT duration of 5.4 years in in female-to-male and 5.8 years in male-to-female, the lumbar spine mean areal BMD z-score was still significantly lower than at the start of GnRH therapy, while the other volume BMD and femoral neck estimates had normalised.[21] In another study, female-to-male receiving testosterone replacement therapy for 1–2 years had not regained their group mean BMD z-score registered at the start of GnRHa therapy.[24]

Bone geometry, estimated as subperiosteal width and endocortical diameter, was studied on DXA scans before start of GnRHa treatment and after at least two years on CSHT and compared with reference values of the general population: the bone geometry resembled the reference curve for the experienced sex only when GnRHa was started during early puberty. Bone geometry estimates in those who started GnRHa treatment during mid and late puberty remained within the reference curve of the biological sex.[26]

3.6 | Body composition and metabolic markers

GnRHa treatment effectively reduced endogenous sex hormone serum levels (Table 4). DXA scans after 1 year of GnRHa treatment revealed increased fat mass and reduced lean body mass.[28] Longitudinal growth depends on bone maturity (bone age) of those in the study group. Ongoing pubertal growth spurt will be arrested when GnRHa therapy is started, reducing the growth velocity to the prepubertal rate.[29]

Nokoff et al studied body composition and insulin sensitivity during 1 year of GnRHa therapy.[30] In addition to body composition, metabolic effects as insulin sensitivity during CSHT, and changes in blood pressure during testosterone therapy were examined.[31–33] Of these studies, three originated from Amsterdam.[29,32,33] The Amsterdam studies included observations during GnRHa therapy,[28] 1 year after starting CSHT,[32] as well as after a group median >5 years with CSHT in a cohort of 22-year-old adolescents.[31,33] The studies from Amsterdam were generally larger than the other studies. CSHT changed body composition towards the affirmed sex.[31,32] Obesity (defined as BMI >30 at age 22 years) was more prevalent in the transgender population[33] (Table 4).

3.7 | CSHT in children without prior GnRHa treatment

We were able to identify three studies of low-to-moderate bias examining CSHT in children without prior GnRHa treatment.[13,34,35] All were retrospective longitudinal studies. Because the number of study participants was small, studies were deemed to have low external validity, and because the studies examined different outcomes (e.g., lipid serum levels, Hb, blood pressure, metrorrhagia), it was not possible to draw any overall conclusions from these studies. Although the Mullins et al. paper[13] included several individuals at elevated risk of arterial or venous thrombosis, no cases of thrombosis were reported.

4 | DISCUSSION

We performed an extensive literature search to examine psychosocial and cognitive outcomes as well as metabolic and bone health in children with gender dysphoria taking hormone therapy. No randomised controlled trials were found, but we could identify 24 relevant observational studies. However, these were limited by

TABLE 3 Summary of effects on bone development by puberty-blocking treatment (GnRHa) followed by CSHT in children with gender dysphoria.[20–25]

Outcome measures	Number of study participants, description of studies	Main Result	"Certainty of Evidence"	Deduction in GRADE[a]
Bone density during puberty-blocking hormonal treatment (g/cm², g/cm³)	*n* on hormones = 363 *n* evaluated = 297 Five observational cohort studies (four retrospective and one prospective)[20–24]	Unchanged bone density (DXA measurement)	⊕⊕○○ Low certainty	−1 risk of overall bias[b] −1 precision
Bone density during puberty blocking hormonal treatment in relation to reference data in the literature (z-score)	*n* on hormones = 408 *n* evaluated = 292 Five observational cohort studies (four retrospective, and one prospective)[21–25]	Decreased increase in bone density over time	⊕⊕○○ Low certainty	−1 risk of overall bias[b] −1 precision
Bone density after 1–3 years (up to 22 years of age) of CSHT, which had been preceded by puberty-blocking hormonal treatment in relation to reference data in the literature	*n* on hormones = 268 *n* evaluated = 165 Three observational cohort studies (two retrospective and one prospective)[21,24,25]	After group median five years with CSHT, bone density recovered in hip but not in lumbar spine compared to data at start of treatment (z-score)	⊕⊕○○ Low certainty	−1 risk of overall bias[b] −1 precision

Abbreviations: CSHT, Cross-sex hormone treatment; DXA, Dual-Energy X-ray Absorptiometry.

[a] Starting at 4 for optimal studies in each study type.

[b] Analysis not based on stage in puberty development.

TABLE 4 Summary of findings of puberty-blocking (GnRHa) hormone treatment on anthropometric measures, body composition, and metabolism in children with gender dysphoria.[28–33]

Outcome measures	Number of study participants, description of studies	Main result	"Certainty of Evidence"	Deduction in GRADE[a]
Anthropometric measures	*n* on hormones = 192 *n* evaluated = 192 One retrospective observational cohort study[31]	Increased weight and body mass index	Cannot be assessed	−2 risk for overall bias[b] −1 precision[c] −1 indirectness[d]
Body composition	*n* on hormones = 325 *n* evaluated = 286 Two prospective observational cohort studies and one controlled cross-sectional study[28,30,31]	Decreased lean body mass	Cannot be assessed	−2 risk for overall bias[b] −1 precision[c] −1 indirectness[d]
Metabolic measures	*n* on hormones = 209 *n* evaluated = 209 One retrospective observational cohort study and one controlled cross-sectional study[30,32]	No change in serum lipids or blood pressure Increased insulin level in MtF Decreased insulin sensitivity	Cannot be assessed	−2 risk for overall bias[b] −1 precision[c] −1 indirectness[d]
Blood pressure	*n* on hormones = 15 *n* evaluated = 15 One retrospective observational cohort study[33]	Change in blood pressure	Cannot be assessed	−2 risk for overall bias[b] −1 precision[c] −1 indirectness[d]
Growth (cm/year)	*n* on hormones = 55 *n* evaluated = 55 One prospective multicentre observational GnRHa treatment cohort study[29]	Reduced growth velocity	Cannot be assessed	−2 risk for overall bias[b] −1 precision[c] −1 indirectness[d]

[a] Starting at 4 for optimal studies in each study type.

[b] Selection of study participants is difficult to assess. Analysis not based on stage in puberty development.

[c] Few study subjects in each study, hence there is heterogeneity in outcome and analyses.

[d] Single study. In this context, 'indirectness' is similar to 'external validity'.

methodological weaknesses, for instance lack of or inappropriate control group, lack of intra-individual analyses, high attrition rates that precluded conclusion to be drawn. The exception being that children with gender dysphoria often had lower group mean values for BMD already prior to GnRHa treatment, and that GnRHa treatment delays the physiologically occurring BMD gain during pubertal sex hormone stimulation. However, this GnRHa-induced delay in BMD gain is almost fully compensated for by later ensuing CSHT. Although study participants were followed up to 22 years of age, the observed remaining deficit may depend on the limited study group size or on too short observation time.[21]

Our review highlights several specific knowledge gaps in gender dysphoria that are important to bridge not least given the recent increased incidence in many countries.[6,7] First, randomised controlled trials are lacking in gender dysphoria research. We call for such studies, which may be the only way to address biases that we have noted in the field. Given the current lack of evidence for hormonal therapy improving gender dysphoria, another ethically feasible option would be to randomise individuals to hormone therapy with all study participants, independent of intervention status, receiving psychological and psychosocial support. However, controlled trials do not necessarily require placebo treatment, but could for example build on the date or time of starting hormonal therapy to generate comparison groups. However, it should also be noted that this is a highly vulnerable population.

A second limitation concerns the statistical management of data. In the reviewed studies, observational data have frequently been analysed at a group level where intra-individual changes would have been more appropriate. Intra-individual analyses would allow for a better understanding of how subgroups of individuals respond (both positively and negatively) to hormone therapy. Group-level analyses are sensitive to selection bias because of high drop-out rates: The group studied at the end of the study is a selection of the group studied at baseline, which increases indirectness (reduces external validity). Moreover, it is important to analyse the distribution of individual data to be able to identify outliers who may be at risk for severe consequences of treatment.

Third, many studies only present data on chronological age but fail to account for puberty stage and biological age. This is a concern because the main purpose of GnRHa treatment is to suppress puberty and, with that, biological ageing.

Fourth, long-term studies are lacking. The duration of GnRHa treatment and CSHT was rarely >4 years. The absence of long-term studies is worrying because many individuals start treatment as minors (<18 years) and CSHT is lifelong. Fifth, individuals who stop GnRHa treatment before the start of CSHT need to be described and followed up. Sixth, some of the findings underlying this review are old, and studies reflecting the changing demographics of individuals seeking care for gender dysphoria are warranted.

TABLE 5 The GEnder Dysphoria HORmone treatment (GENDHOR) checklist.

	Recommendations
Aim	Describe the aim of the study
Study participants:	
Cases/exposed	Define gender dysphoria in your study, including the assessment tools used. Define eligibility criteria for your study (including chronological age, bone age or puberty stage, according to Tanner or Prader (when study concerns adolescents), biological sex, perceived gender identity, psychiatric and somatic comorbidities, medications at baseline). List exclusion criteria (diagnoses). List ages of participants at the start of each treatment (including absolute age ranges).
Comparators/ unexposed	Clarify how controls were selected (were controls recruited from the general population?) or whether national/ regional reference data (for instance, Z-scores) were used instead of individual controls.
Study design	Describe the study design: Cross-sectional, retrospective, prospective; case–control (and if nested), cohort study, randomised clinical trial.
Setting	Describe the setting of the study. Were study participants included at a tertiary centre or from the general population? Describe the catchment area/population of participating centres.
Intervention	Hormone treatment Describe whether GnRHa, anti-androgens, CSHT, or a combination was used. List generic names, mode of administration, and dosages of all treatments. Specify the treatment duration of each treatment. If hormone serum concentrations are studied, include the standard procedure for the timing of blood samples to hormone intake. If patients undergo surgery, clarify the type of surgery and number of participants undergoing each surgical procedure (gonadectomy, mastectomy, laryngeal surgery, vaginoplasty/phalloplasty, etc.). Clarify if any participant received psychiatric counselling before, or during the study, including total duration and frequency of counselling.
Variables	Define each variable (including co-variates) and its source. If possible, mention any effort to validate the variables.
Data measurement	Clarify who collected the data on study participants. Present time between first and second measurements if your study is longitudinal and includes "before-after" measurements in relation to the intervention. Mention if study participants had previously been included in other studies with a different aim or examining other outcomes.
Blinding	Describe if the data collectors were blinded to participant status/treatment or not.
Loss to follow-up	Indicate the number of participants discontinuing GnRHa/ CSHT and the reason(s) for discontinuation, including no longer wish to pursue gender reassignment treatment. Describe loss to follow-up/missing data
Statistical methods	Describe statistics according to a relevant checklist. Consider when applicable: Intra-individual changes (mean, SD, median, range) vs. between-group differences.
Descriptive data	In addition to usual demographic, clinical, social/socioeconomic information, report body mass index (BMI), smoking, use of oral contraceptives (type) or other hormonal treatment, puberty stage. Report any psychiatric illness at baseline, as well as the use of psychotropic medication. Describe other comorbidities, including disorders that could be considered contraindications for either hormone treatment or surgery. Specify follow-up time (median, mean) since the start of the intervention and since start of hormone treatment (define intervention start).
Outcome data	Specify main outcome of the study. Indicate all secondary outcomes, including adverse events.
Adverse events/ complications	Describe all adverse events.
Main results	Present absolute numbers. Calculate absolute and relative risks/Intraindividual effects/change and group mean/ median. Present incidence data. Describe any adjustment for potential confounders.
Limitations	Discuss limitations of your study, including limitations of the measurements used (e.g., DXA) and sources of potential bias or imprecision.
Generalisability/ external validity	Can data be generalised to individuals with gender dysphoria outside your study centre and the study country?
Conflict of interest	Report any conflict of interest.

Note: Based on our literature review, we created a *GEnder Dysphoria HORmone treatment checklist* (GENDHOR).

This list consists of recommendations that researchers may consider when planning a study of gender dysphoria, whether observational or interventional.

Abbreviations: CSHT, Cross-sex hormone treatment; DXA, Dual-Energy X-ray Absorptiometry; GnRHa, Gonadotropin-releasing hormone agonist (analogues).

Finally, we could not evaluate the frequency of individuals who drop out from GnRHa treatment and no longer wish to continue with gender transition. However, a follow up study was published after our literature search.[36] Of 720 children (31% born male and 69% born female) who started GnRHa treatment in adolescence, 98% continued to use hormone treatment into adulthood, which suggests that children generally continue with gender transition once they have started GnRHa treatment. We know from internet-based surveys that detransitioning exists,[37] but such studies cannot provide reliable estimates of detransitioning frequency because of selection bias. Studies that closely follow individuals who start GnRHa therapy and/or CSHT until at least age 30 are urgently needed. We also acknowledge there are other potential side effects from GnRHa therapy or CSHT that were not included in our review such as alopecia and abscesses from injections.[38]

Due to limitations in reporting of data, previous published studies in this field repeatedly contain insufficient details on drug administration and dosages, treatment duration, and the type of surgery performed. Some of these limitations will be partly remedied by the introduction of the new ICD version 11, and the Utrecht criteria,[39] but the field also urgently needs high quality longitudinal studies that not only assess medical outcomes but also those outcomes that matter most for affected individuals. Building on the identified limitations in previous research, we compiled a checklist to improve gender dysphoria research ("GENDHOR", Table 5). The aim of this checklist is not to replace existing research guidelines, but using it together with existing guidelines might support researchers and peer reviewers, and ultimately benefit patients and their families.

Last, there have been studies in this field published after the date of our literature search (9 November 2021). These have not been added to this study in order to not depart from the systematic approach. We nevertheless wish to comment on some of the publications. First, the National Institute for Health and Care Excellence in England (NICE) conducted evidence reviews of GnRHa[40] as well as CSHT[41] for children with gender dysphoria, which were independent from our work. The conclusions generally align with our findings. Second, Chien et al.[42] recently published a prospective study of psychosocial functioning during 2 years after initiation of CSHT in youths (12–20 years of age) with gender dysphoria. Of 315 participants, 162 completed that study. Life satisfaction increased, and depression and anxiety scores decreased, among biological females but not biological males. The strongest finding was a moderately improved appearance congruence. No information on concomitant psychological or psychopharmacological therapy was provided.

5 | CONCLUSION

This systematic review of almost 10 000 screened abstracts suggests that long-term effects of hormone therapy on psychosocial and somatic health are unknown, except that GnRHa treatment seems to delay bone maturation and gain in bone mineral density.

AUTHOR CONTRIBUTIONS

Study concept and design: All authors. Acquisition of data: Malin Höistad, Jan Adolfsson. Drafting of the manuscript: All authors. Interpretation of data and critical revision of the manuscript for important intellectual content: All authors. Administrative, technical, or material support: Jan Adolfsson, Malin Höistad. Funding acquisition: the Swedish agency for technology assessment and assessment for social services.

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CONFLICT OF INTEREST STATEMENT

JFL coordinated an unrelated study on behalf of the Swedish inflammatory bowel disease quality register (SWIBREG) that received funding from the Janssen Corporation. JFL has also received financial support from Merck Sharp & Dohme developing a paper reviewing national healthcare registers in China. JFL is currently discussing potential research collaboration with Takeda. ML has received lecture honoraria for Lundbeck pharmaceuticals and served as consultant for AstraZeneca. The other authors report no conflict of interest.

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Age Is Just a Number: WPATH-Affiliated Surgeons' Experiences and Attitudes Toward Vaginoplasty in Transgender Females Under 18 Years of Age in the United States

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ABSTRACT

Background: A rising number of female-affirmed transgender adolescents are being treated with gonadotropin-releasing hormone analogues and subsequently cross-sex hormones at early or mid-puberty, with vaginoplasty as the presumed final step in their physical transition. But, despite the minimum age of 18 years defining eligibility to undergo this irreversible procedure, anecdotal reports have shown that vaginoplasties are being performed on minors by surgeons in the United States, thereby contravening the World Professional Association for Transgender Health (WPATH) standards of care (SOC).

Aim: To explore surgeons' attitudes toward ethical guidelines in the SOC; any professional experiences of performing vaginoplasty on transgender minors; views of surgical risks, benefits, and harm reduction measures; and perceptions of future challenges and concerns in this area of surgical practice.

Methods: A qualitative semistructured interview approach was used to collect data from 13 male and 7 female surgeons who perform transgender vaginoplasty in the United States.

Outcomes: Professional experiences and attitudes toward vaginoplasty in transgender minors were analyzed using the constant comparative method applied to 20 individual interview transcripts.

Results: While there was close agreement concerning surgical techniques, proper patient selection, and predictive elements of postoperative success, attitudes toward the SOC and the reliance on the guidelines varied. The sole practitioner model is gradually giving way to a more holistic team approach, with patient responsibility dispersed among different professionals. Different approaches to surgical training, professional standards, and fellowship programs were suggested. Several participants expressed a need for centralized data collection, patient tracking, and increased involvement of the WPATH as a sponsor of studies in this emergent population.

Clinical Implications: Drawing on surgeons' attitudes and experiences is essential for the development of standards and practices. A more precise and transparent view of this surgical procedure will be essential in contributing to the updated version 8 of the WPATH SOC.

Strengths and Limitations: The abundant data elicited from the interviews address several meaningful research questions, most importantly patient selection criteria, surgical methods, and issues critical to the future of the profession. Nevertheless, the limited sample might not be representative of the surgical cadre at large, particularly when exploring experiences and attitudes toward vaginoplasty in minors. A larger participant pool representing WPATH-affiliated surgeons outside the United States would improve the generalizability of the study.

Conclusion: Taken together, the study and its findings make a significant contribution to the planned revision of the WPATH SOC. **Milrod C, Karasic DH. Age Is Just a Number: WPATH-Affiliated Surgeons' Experiences and Attitudes Toward Vaginoplasty in Transgender Females Under 18 Years of Age in the United States. J Sex Med 2017;14:624–634.**

Key Words: Adolescent; Gender Confirming Surgery; Surgeon; Transgender; Vaginoplasty; World Professional Association for Transgender Health

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INTRODUCTION

During the past 5 years, treatment of gender dysphoric adolescents presenting for medical interventions in the United States has received increased attention and visibility in the clinical literature and the mainstream media.[1–5] Supported by parents and referred by psychiatrists, psychologists, and other mental health professionals, transgender youths are seeking gender-affirmative treatment in private practice settings, public health centers, and hospitals with specialized services dedicated to transgender health care.[6–8] Major American insurance exchanges and health maintenance organization networks also are beginning to cover medical care designed to alleviate gender dysphoria in teens, ranging from fully reversible interventions such as puberty-suppressing gonadotropin-releasing hormone analogues and partly reversible gonadal steroid treatment to irreversible procedures such as bilateral mastectomy with chest reconstruction for male-affirmed late teens and genital surgeries such as orchiectomy and/or vulvovaginoplasty in female-affirmed older adolescents.[9] Medical providers of transgender care generally adhere to the most recent (version 7) World Professional Association for Transgender Health (WPATH) Standards of Care (SOC), in which eligibility and readiness criteria for irreversible interventions can be applied when the adolescent has reached the legal age of majority in a given country.[10] The document specifies that the age criterion should not be seen as an indication for "active intervention," only as an age threshold, with the understanding that the legal age of majority varies from nation to nation. The current SOC provide some flexibility in the minimum age requirement for chest reconstruction in male-affirmed adolescents, although it could be argued that this procedure is practically irreversible. Conversely, female-affirmed teenagers must defer orchiectomy and/or vaginoplasty until 18 years of age to stay compliant with the SOC and the legal age of majority in the United States. This position also is supported by the Endocrine Society, a worldwide organization dedicated to the education and practice advancement of endocrinology.[11] The society has issued recommendations concerning the treatment of trans youth, in which it is suggested that genital surgery be deferred until the individual has reached 18 years of age. The Endocrine Society does acknowledge that 16-year-olds are legal adults in many countries and are mature enough to make medical decisions of some cognitive complexity; nevertheless, because data are not available on outcome studies concerning genital surgery in minors, the shared recommendation by the two organizations still stands.

In the Netherlands, where adolescents from 16 years of age are legally competent to make treatment choices independent of parental consent,[12] the policy of Dutch clinics treating transgender teens is that genital surgery should not be performed before 18 years of age. A review of the available literature concerning the Dutch protocol shows that although clinicians agree that emotional maturity represents a better criterion than minimum age, there is acknowledgment that objective criteria do not exist in assessing readiness for genital surgery in adolescents.[13] In addition, although puberty suppressants are available to gender dysphoric adolescents at 12 years of age and cross-sex hormones are permitted at the minimum age of 16 years,[14–16] a recommended candidate for genital surgery is at least 18 years old and has been living in the affirmed gender for a minimum of 2 years after initiating hormone treatment. Dutch outcome studies of late adolescents and young adults who have undergone irreversible procedures 1 to 4 years before follow-up have reported psychologically normative functioning and a high satisfaction rate with no regrets by transsexuals after surgery.[17–19] Moreover, anecdotal reports and at least one news media release have reported that vaginoplasties in patients younger than 18 years have been performed by surgeons in the United States, who thereby contravene or sidestep the SOC.[20,21] Contrary to the concise criteria guiding decisions for postadolescent surgical treatment [p. 54], there are no guidelines in the WPATH SOC that support the surgeon in the decision to perform vaginoplasty on transgender women younger than 18 years. The surgeon must rely on evaluations by other professionals, careful patient selection, and the personal conviction that proceeding with surgery is the right decision, with the added legal burden of obtaining consent from parents in lieu of the minor and assuming principal responsibility for the physical risk to the young patient who might not always be compliant with or fully understand postoperative care. The surgeons who perform the procedure on transgender minors have, without exception, refrained from publishing any peer-reviewed outcome data or technical articles on this small but increasingly important population. In addition, although only a few teaching programs offer endocrinology fellowships that include transgender health care,[22] no American educational institutions currently provide fellowships or standardized training in genital surgery for female-affirmed transgender adolescents. These factors have contributed to a dearth of specific medical information, a lack of shared surgical expertise, and inadequate guidance that would otherwise be widely available to all practitioners of transgender medicine and to the general public. To go beyond anecdotal evidence and explore the collective experiential knowledge of surgeons who specialize in performing vaginoplasty as part of gender-confirming surgery (GCS), the authors report the findings of their qualitative research study investigating WPATH-affiliated surgeons' views, experiences, and attitudes toward performing vaginoplasty on transgender minors in the United States.

AIMS

The aim of the study was to explore any professional experiences of performing vaginoplasty on transgender minors in the United States; views of surgical risks, benefits, harm reduction measures, beliefs, and attitudes related to the ethical guidelines on adolescents in the SOC; and perceptions of future challenges and concerns in this area of surgical specialty. The proximate goals of the study were to elucidate experiences and attitudes toward the growing surgical practice of vaginoplasty in transgender minors and to provide foundational knowledge in an under-researched area, with the long-term objective of using the study findings in the future development of criteria for irreversible surgical procedures in the eighth version of the WPATH SOC.

METHODS

Because of the anticipated small number of potential participants active in a highly specialized surgical field, a qualitative study format was preferred. A modified analytic induction approach was chosen because of the specifically targeted research questions.[23] Purposive sampling was initiated; a search under the *Medicine: Surgery* and *Medicine: Gynecology/Urology* tabs inside the optional provider directory located on the WPATH website[24] yielded the names of 21 affiliated plastic surgeons and 20 gynecology or urology specialists practicing in the United States. Additional names of member surgeons whose names were not in the directory were found after performing multiple Google searches using key words pertaining to vaginoplasty or GCS. After verifying that the procedure was offered by telephoning each surgical practice and by viewing proprietary websites when available, 22 surgeons nationwide were identified as providers of vaginoplasty to the transgender female patient population. An invitation e-mail was sent to each surgeon, followed by telephone calls to the corresponding surgical practice, in which potential participants were informed in detail about the study objectives and its parameters. Twenty surgeons chose to participate, and two declined. A semistructured interview sheet consisting of 30 items related to the study goals and supplemented by additional prompt questions, when applicable, were used to elicit responses in the following main areas:

1. Demographic information and professional GCS experience of participant
2. Any concerns regarding performing vaginoplasty in minors
3. Negotiating consent or assent and risk management
4. Training, professionalism, and the WPATH SOC

All interviews were conducted by the first author, a licensed psychotherapist, during a 45-day period by telephone, with exception of one face-to-face interview. Average interviewing time was 25 minutes. All interviews were audio-recorded with the participant providing verbal consent at the beginning of each recording. Interviews were transcribed by the first author, de-identified, and checked multiple times against the master recording files to ensure accuracy. Transcripts were saved in rich text format (.rtf) files and processed using HyperRESEARCH qualitative data analysis software (Researchware Inc, Randolph, MA, USA). Analysis was implemented using line-by-line coding of the transcribed material and by performing the constant comparison procedure to identify repeated patterns in the available data. Codes were refined into categories that were used to structure the analysis further into major thematic areas according to standard grounded theory.[25] Coding checks were performed by the 2 authors to ensure intercoder reliability.[26] Data gathering procedures were reviewed and approved to ensure their consistency with the ethical principles required by the institutional review board of the second author's affiliated institution.

RESULTS

Demographic and general participant data are presented in Table 1. The vast majority of participants operated at in-patient hospitals; however, one surgeon reported performing the procedure at an out-patient surgery center, with multiple visitations at the patient's home or hotel after surgery. The preferred method of vaginoplasty was a one-stage penile inversion, most often augmented by a full-thickness scrotal skin graft. Nine surgeons had never performed vaginoplasty on a transgender female minor, and the remaining 11 participants reported 1 to 20 cases per surgeon. Of the 11 surgeons who had performed vaginoplasty on a transgender female minor, 10 were in private practice. Reported ages of minors undergoing surgery ranged from 15 to "a day before 18" years (surgeon 7). Most participants had noticed a definite increase in the number of minors requesting information about the procedure on their own or being referred for vaginoplasty by their mental health providers.

Table 1. Basic participant demographics (N = 20)

Participants	n
Sex	
Men	13
Women	7
Surgical specialty or board certification	
General plastic surgery	13
Urology	4
OBG	2
Plastic surgery + urology (double board certification)	1
Primary practice setting	
Private practice	16
University hospital or teaching institution	4
Insurance network contracted provider	
Yes	14
No	6
Years in practice	
Minimum—maximum	4–43
Average	19
Years performing GCS	
Minimum—maximum	< 1–26
Average	10
Performed vaginoplasty on transgender minor	
Yes	11
No	9

GCS = gender-confirming surgery; OBG = obstetrics and gynecology.

Surgeon 16 quantified a shift in the general age group of patients: "When I first started my practice, I would estimate that 85% of patients were older than 25. Now, I would say that only 40% of my patients are older than 25 in the last nine years." In addition, although there was no unanimous recall of the youngest patient ever reported in the media to undergo the procedure, a few participants believed that they were responsible for having operated on "the youngest," with surgeon 16 stating that "… the patient was a 15-year-old who was just on the cusp of turning 16."

Anatomic and Physiologic Issues

There was little concern over the younger adolescent and her ability to physically withstand the invasive procedure compared with a middle-age or elderly patient; however, almost all surgeons remarked on the penoscrotal hypoplasia or limited penile shaft size that would ensue after the use of puberty-suppressing gonadotropin-releasing hormone analogues, sometimes for as long as 3 years. Two surgeons who reported operating on minors commented, "… they are coming in after being put on blockers, so they have 11-year-old genitalia" (surgeon 9) and "… you are really doing vaginoplasty on a micropenis" (surgeon 16). Most participants emphasized that the surgical techniques were the same for all patients no matter the age; of those who had performed the procedure on several minors, the use of flank skin grafts most commonly resolved the problem of inadequate tissue availability. In other reported measures, surgeon 2 implanted a scrotal tissue expander that required periodic infusion during 2 months, and surgeon 14 used donor tissue matrix (LifeCell, Branchburg, NJ, USA), deeming it "nicely successful" and thereby avoiding patient exposure to external flank scarring. The alternative procedure of using sigmoid- or ileum-derived grafts to create the neovagina was seen as a last resort by a few participants who stated diversion colitis, excessive secretion, persistent odors, and potential leakage of stool into the peritoneum as some of the concomitant morbidities.

Psychological and Contextual Concerns

An overwhelming majority of surgeons cited psychological maturity as the main criterion for adolescent patient selection, stating "Age is arbitrary. The true measures of how well a patient will do are based on maturity, discipline and support" (surgeon 11). Most participants emphasized that mental maturity was related to the ability to understand the stressors of undergoing surgery and expectations of postoperative self-care, particularly the commitment to a consistent dilatation schedule to maintain patency of the neovagina:

> The biggest concern is, will they be mature enough to be able to take care of themselves after surgery. Not just having the surgery done. Will they do what they need to do after surgery maintain the vaginal depth involved? In actuality, I don't think it is age dependent, it is the maturity of the patient. An 18-year-old goes off to college and leaves the parents. They leave that protective environment and everything becomes less important to them in terms of the dilatation and care. Some of my biggest struggles have not been with the 16-year-old group because they are still at the parents' house—it is the 18-year-olds who disappear and go to college within a few months after their surgery. Those are the patients who are most likely to lapse in their aftercare. (Surgeon 9)

The confluence of undergoing vaginoplasty and leaving home to become a college student in the same year was seen by many as problematic:

> Oftentimes, a child in the United States comes in after or during their senior year in high school; they want surgery over the summer and they want to go off to a dormitory in September, in their first year of college, which is a disaster. And that is a more important situation than just the age of the patient. What is going on socially with the patient is more important than the age. (Surgeon 16)

> I have found that it is very difficult when the patients have to transition once they are in college. … Plus with their busy schedules and their busy lifestyles, it is very difficult for them to adhere to their dilation schedule. So the reason why I decided to operate on people younger than 18, is that I would prefer that they have their gender reassignment surgery done while they are still at home and their parents can help them adhere to their schedule until a significant period of time has passed so they will not compromise their results. I base it on very strong family support, very strong letters from their psychologist and their behavioral health therapist and that is really how I make the decision. You also need to take into account the maturity of the individual and whether they are at a point where they are mature enough to understand the seriousness of the surgery and the seriousness of adhering to all of the post-op instructions so that they maximize their results. (Surgeon 15)

Some surgeons viewed timing the procedure before college attendance as a harm reduction measure:

> Younger patients who have the support of their families, support of their parents, and can have the operation while they are still at home, as opposed to being alone at school or at work, anecdotally tend to do much better than someone who is alone and doesn't have appropriate support. (Surgeon 5)

> There could be benefits that could outweigh the risks when you look at the demographics of women who are in their late teens wanting to have GCS prior to going to college, or prior to entering into very sensitive social roles. (Surgeon 17)

Participants also pointed to the importance of a safe and affirmative environment in which to recuperate (ie, being cared for by supportive parents at home who monitor the recovery process):

> The added issue with the under 18 patient is parental involvement, and I personally would want to have the parents on board. Particularly if the child is still living at home with the parents. The place people go back to after surgery is critically important for the result. And that's not just for GCS—if someone is going back to a hostile place and the place is not supportive of the surgery, it is often likely that the person has a less than optimal result. (Surgeon 18)

Opinions were sometimes divided as to the adolescent undergoing the procedure for mainly social or sexual purposes:

> The benefit is not because they want to have sex, but because they can fully socially transition with their peers before they go off to college—assuming they want to go to college. (Surgeon 14)

> I personally know of two young women who are trying to transition. They are seeing mental health providers and endocrinologists. They are 16 and there is a real struggle there because there is a sense of urgency on their part and they are being held back. I get that, they need to go through some steps. But I know that they do not want to do a full transition later in their life; they want to do this so that they can be intimate in college. (Surgeon 17)

In addition, a few participants urged caution, suggesting that some adolescents engage in gender exploration as part of a developmental phase and as part of the current zeitgeist:

> I think it goes along the lines of a young person's mind still being in the developmental stage. Things may happen and they may reorient their thinking, not just whether they are trans or not, but they may reorient their thinking about which surgery will serve their transgender needs. It is not a binary or tertiary model where they are just gay, straight, bisexual, or trans; there are a whole host of colors in-between. Many trans patients do not want GCS—it could be that at 15 they do, and at 25 they do not. (Surgeon 18)

> Depending on how old they are, there are a lot of classes that adolescents, even preadolescents in elementary schools, are getting these days. And they are trying to figure out if they are doing it because it is a new norm, versus what they really want. I have seen some of my patients' children go through phases of in and out, of thinking transgender. So that would be my concern—is it because it is popular now? (Surgeon 19)

Consent and Risk Management

While participants had a clear understanding of the legal constraints in obtaining informed consent specifically from the adolescent, there were a few different approaches to securing consent from the family unit. Parents or legal guardians were invariably signators; however, Surgeon 2 also added the requirement of the young patient writing an essay about the reasons for wanting to undergo the procedure and "describe what her feelings are in her identity as a person." Surgeon 16 explicitly required the parents to become active participants in the post-operative dilatation process, or else the patient would not be deemed "a good candidate for surgery." Other participants requested multiple or longer office visits when going over the various written consent forms, ranging from 5 to 40 pages, and always in the presence of parents or legal guardians. The parents' marital status was often a concern, because most surgeons were aware of divorce creating a change in guardianship or custody of the minor. Comparatively few participants addressed the issue of postsurgical infertility in the interviews; among those who reported having discussions with the patient and her family, there was the recognition that the topic had been explored beforehand with other practitioners or "not often something that is at the forefront of people" (Surgeon 4).

All participants adhered strictly to the SOC by requiring separate evaluation letters from two mental health professionals clearing the minor for surgery. Many emphasized that a recommendation from an unfamiliar psychotherapist was not acceptable; in addition, a third letter from an independent psychiatrist or the patient's pediatric endocrinologist was occasionally required to bolster the surgeon's confidence that the minor had been thoroughly vetted. The professional quality of each letter also was very important and should demonstrate the writer's qualifications as an expert in transgender issues. Surgeon 12 clarified:

> We ask for two letters. One of them has to be from someone who has an established relationship with the patient. I don't remember exactly what the wording is, but they can't just go to one session and say, "Hey, I'm transgender, I want surgery." We do read the letters and we also do confirm that the letters are real. You can imagine (laughs). We call the therapist's office and make sure that our patient is a patient of theirs. We just get confirmation that the letters are real and that it's not something they just typed up on their own, you know. The letter has a certain verbiage and anybody who is experienced with treating gender issues should know the language of the final letter of recommendation. Not just, "there were three monthly sessions." No!

Nearly all participants reported an overwhelming reliance on mental health practitioners to assess the minor's psychological readiness for surgery. Statements including "completely" (Surgeon 9) or "extremely" (Surgeon 10) were used to emphasize trust in the diagnostic expertise of mental health providers. Surgeon 3 concurred:

> I rely on them entirely. I need to make sure that the patients have realistic expectations, that they are not … I need to judge their maturity level and that they can handle pretty significant stress of any surgical procedure. But I don't pretend to be a psychologist or have any expertise in the diagnosis of gender dysphoria, that's a decision that needs experts.

However, a few pointed out that they were sometimes just as attuned to potential concerns as mental health professionals and would assume some responsibility for evaluating the patient's psychological condition:

> I scrutinize the letters that the mental health providers forward to me. If they are negative, I rely a lot on them because that has a lot of value. But since they are almost never negative, I may rely a lot less on them! Then I rely on my own experience. I cover everything that I believe should have been covered in the letter, and then I go through that list of capacity, development, all those issues in my check-off list. I do this because any other way is a disservice to the patient; I'm responsible for all that. (Surgeon 20)

Despite the legal impossibility to obtain informed consent from the underage patient, the vast majority of participants were not concerned with malpractice lawsuits from parents or even from the patients as adults in the future. Engaging in best practices, maintaining open communication with the patient and her parents, and above all providing good results were seen as protective measures against any legal action. Nevertheless, opinions were evenly split as to the surgeon's assumption of physical risk to the adolescent patient. Some asserted that this was uniquely the surgeon's domain:

> It should be the surgeon, not the hormone prescriber. There is a lot of misinformation that the hormone prescribers give, in my opinion. They have no business talking about surgical issues, unless they have training. We could train the hormone providers, but too often they have never set foot in an operating room, and say things from a surgical standpoint that in my opinion simply is not true. And I don't think that the hormone providers understand that when there is a micropenis, it's a different surgery. When you all you have is a hammer, everything looks like a nail! (Surgeon 16)

Others advocated for a dispersion of responsibility:

> I think it should be everybody. And I think it should be me, the endocrinologist, the mental health provider. It has to be multidisciplinary to make sure they are sexually mature in terms of development, and that from an endocrine standpoint they are able to be on the hormones successfully and manage them appropriately. One of the concerns for me would be if they haven't been on the hormones long enough or they haven't had adequate endocrine care—how will that change the tissue postoperatively? I know it's a concern for top surgery and it would also be for bottom surgery. It has to be both. (Surgeon 17)

Training, Professionalism, and the WPATH SOC

When asked about the lack of published data on surgery in minors, most participants asserted that GCS in all age groups had been a very small part of surgical medicine until very recently and that data on large volumes of procedures were not yet available. Some also cited the perceived "taboo" or outright stigma in performing the surgery and therefore a certain reluctance to share results or specific techniques. One surgeon pointed to the closure of US-based academic gender services programs in the 1970s, resulting in fewer publications, no tracking data, and privatization of the procedure. But while, none of the participants reported currently tracking patients, a multidisciplinary team approach with elaborate data collection was unanimously favored by those who practiced in academic settings. A vision of close collaboration with non-surgical professionals also emerged among the private practitioners, particularly when there were added concerns of operating on pediatric patients:

> My thought is that with patients like this, there should be a group formed. It should have regularly scheduled meetings. The meetings should include a surgeon, mental health professionals, and endocrinologist and/or interested parties and they should all sit at the same table to specifically assess the patient's case. So someone comes into the TG clinic and they are age 11. By the time they are 14 or 15, they may have had multiple discussions about this, they've been tracked for three or four years, there is a history there and the question becomes much clearer than someone just showing up at your office with two letters. In younger patients, it's much more important to be tracked for a few years and to not just get a snapshot of what they are at any given point in time on the temporal graph. (Surgeon 18)

A few participants described attempts to contribute their surgical expertise to the creation of post-residency programs or accredited GCS fellowships in various academic settings. For those in private practice, the complexity in shaping a transgender surgical excellence center appeared daunting and the difficulties and frustrations in coordinating private practice with teaching responsibilities were echoed by several solo practitioners. Anger and resentment at the perceived lack of established training centers in teaching hospitals sometimes spilled over in complaints that indicated a polarization of long-term practitioners against newcomers to the field who were seen as motivated by profit, often at the expense of the transgender population:

> I believe that anyone who is performing vulvoplasty should have a fellowship training that is at least one year. It is going to be a rough period figuring that out, but I think we will get there eventually. I have seen horrific unethical practices by surgeons who lie about their experience and horrific results surgically as a result of that. We are using transgender people as guinea pigs and the medical profession allows this to happen. WPATH has the ability to have some teeth and regulate this more. But we don't. And while there is a concern that there are not enough surgeons and there is a 41% suicide attempt rate thrown around a lot, I don't feel that there is any emergency regarding the provision of substandard care. There have been no major changes in surgery since the 1970s or 1980s. And there has been plenty of time to establish a fellowship. And now all of a sudden because it's in the media, and really, the biggest reason for why everyone is doing it now, is the money is flowing. Because now insurance is paying. And now all these institutions have to have a program yesterday. And they are not doing it correctly, in my opinion. Seeing a week's worth of surgery—maybe for a mastectomy, or maybe for an orchiectomy, or some of these other surgeries that are closely related, but this surgery is very advanced. The complications have severe consequences on patients' lives and you can't learn it in a week. And that is what's happening; someone is going to see someone with a reputable name; they learn for a week, and they start doing them. And that is completely unethical! (Surgeon 14)

The term *Wild West* also was used by a few highly experienced surgeons who were alarmed at the absence of surgical standards and the ease of entering the subspecialty without any documented training. To remedy the potential influx of "a bunch of solo practitioners, basically cowboys or cowgirls who kind of build their little house, advertise, and suck people in" (surgeon 13), several participants called on the WPATH to assume a larger role in demanding more stringent professional requirements and contribute toward sponsoring fellowships and surgical trainings across the country. However, despite the desire for the WPATH to create mechanisms for data tracking and providing greater oversight, a plurality of participants perceived the SOC as purposely "vague" and more as "inherently flexible guidelines" when the question of lowering or keeping the minimum age requirement was brought to the forefront. In fact, approximately one third of participants agreed that the SOC were appropriate in maintaining 18 years as the minimum age criterion for vaginoplasty; the remaining surgeons favored a case-by-case approach or endorsed a shift toward accepting patients younger than 18, although none were certain when any such changes would officially occur. Surgeon 17, a urologist, encapsulated the major points of concern:

> I believe in time they will probably lower it. But I don't know if it should be a number or a developmental stage. Physiologically, it would make more sense if it were a multi-disciplinary guideline in terms of sexual maturity and emotional maturity. The problem is that it is up to interpretation, and that's where the dangers lie. But it's needed. Just because someone has reached the age of 18 doesn't mean that they are a better candidate than someone who is 16. That's the complexity and the difficulty in having a stringent age number guideline. I think it will change in time. My experience of these women is that no one just wakes up and says, "oh yeah, I think I'm a woman" at 17. This is a lifelong realization and a process of transition that's gradual. And I think that they need to consider care for the younger female patient. Mostly just because of the social implications, her happiness and her mental health—and let's not forget about the intimacy and the sexual health. To me, it would make sense to lower it and assess each patient individually. I don't know if it can be a number. To me, there might be a minimum age but I don't know what that should be. I will see a 16- or 17-year-old that I will agree to do surgery on, and then there could be another one I won't agree to, based on sexual and physical maturity.

DISCUSSION

The present study of 20 US-based, WPATH-affiliated surgeons provides novel information on how surgeons interpret the current SOC and thus shape their subjective criteria when deciding to perform vaginoplasty on female transgender minors and their overall attitudes toward best surgical practices in transgender medicine. The vast majority of surgeons agreed on a variety of methodologic and treatment issues, including patient selection and surgical techniques. In particular, plastic surgeons were biased toward penile inversion augmented by scrotal grafts, sometimes adding flank grafts, tissue expanders, or donor matrix tissue,[27–29] and decisively rejecting intestinal vaginoplasty that would require no such additional measures and eliminate the need for lifelong dilatation. However, although diversion colitis, excess mucus, or malodor were cited by the American surgeons as negative sequelae, a meta-review of 21 studies using data on cisgender women with vaginal agenesis and transgender women reported no occurrence of diversion colitis; in addition, odor occurrence in the ileal neovagina was not observed and transient excessive discharge decreased to acceptable levels within 6 months in sigmoid-derived and ileal vaginoplasty.[30] Bowel vaginoplasty in transgender women is performed to a greater extent in Europe, where genitourinary surgery maintains a presence in public health-funded transgender care and acceptable patient satisfaction rates have been documented on a relatively consistent basis, most recently in a sample of postadolescent transgender women.[31,32] The authors surmise that as rates of GCS in adolescent minors treated with gonadal steroids begin to increase, colon vaginoplasty in the

United States could become a more commonly available alternative to penile inversion, particularly as more urologic surgeons obtain training in the procedure and additional outcome studies are published in the future.

Among nearly all surgeons, the term *maturity* rather than specific chronological age defined the desired mental readiness criterion for undergoing vaginoplasty and participating in crucial postsurgical dilatation. Oberman[33] remarked that "maturity operates as a code word, invoked to permit minors access to treatments that society deems desirable, and to limit their access to treatments that carry the possibility of long-term negative consequences" [p. 127]. If the dedication to consistent dilatation represented a positive marker of mental maturity to the participants, the most significant psychological detractor was not being underage; rather, it was the looming problem of turning 18 and leaving home for college, becoming distracted by new experiences, and losing parental supervision of the long-term aftercare necessary for a final successful outcome. In fact, the penultimate senior high school year was considered the most ideal to undergo surgery, largely seen as a measure of harm reduction by the surgeons who had performed vaginoplasty on minors. Decreasing harm as a justification for transgender adolescent treatment has been previously acknowledged among different practitioners, with the vast majority endorsing earlier medical intervention to prevent psychological suffering and potentially more invasive treatments in later adulthood.[1,34,35] Moreover, the American College of Obstetricians and Gynecologists issued a position paper noting that cisgender female teenagers seeking corrective plastic surgery procedures in the United States were motivated by a desire to "fit in" rather than stand out.[36] This is in sharp contrast to a recent Dutch qualitative study of gender dysphoric adolescents who unexpectedly found it difficult to define an appropriate minimum age concerning the initiation of gonadotropin-releasing hormone analogues.[16] The surgeons in the present sample might be pursuing a conventional harm-decreasing strategy in balancing the putative suffering of the adolescent with the necessary elements of maturity and universally developmental milestones to secure a good surgical outcome.

Participants were almost in lockstep reliance on mental health professionals to provide two separate, detailed patient recommendation letters for surgery in accordance with the WPATH SOC. The surgeons had a clear understanding that the burden of differentiating between gender-variant children who grow up to request gender transition and those who retain their assigned gender identity falls first and foremost on behavioral clinicians, although a few participants were willing to share the ultimate responsibility for assessing the minor's mental readiness. Milrod[35] described "a genuine expression of fear among clinicians in making the wrong diagnosis, based on the fact that young people often experiment with gender role behavior as a consequence of normative identity development, and perhaps more so when the adolescent is gender variant" [p. 341]. Any such trepidation was not present among the participants who mostly denied concerns about lawsuits or fears of postsurgical regret among their adolescent patients. It appears that the preference for a team approach and dispersion of responsibility among several professionals were expressed partly as added safeguards before preoperative consultations, among them the discussion of fertility preservation. From an ethics perspective this presents a dilemma, because surgical castration is often the last link in a chain of transitioning related medical interventions. Even if the surgeon deems the teenager to be mature and expressing a definite intent to undergo the procedure, there simply might not be sufficient recognition of its finality. Recommendations in this area are to create a fertility preservation team in which the surgeon's and hormone prescriber's roles overlap when communicating facts, and that obtaining assent from the minor should be viewed as a continuing process rather than a singular event.[37-39]

Two areas of considerable divergence, if not contention, were training and professionalism in the field. Long-time private practitioners pitted their expertise against more newly practicing surgeons who allegedly operate without sufficient training and are motivated by insurance payments plus a rapidly increasing patient flow. Hafferty and Light[40] normalized these professional skirmishes as "turf battles," indicative of an emerging area of medicine in which the "exclusive right" to perform certain procedures gradually erodes as provider organizations and hospitals begin to establish their own centers dedicated to comprehensive care for a specific population. Insurance companies also have begun to create their own standards, presumably to control costs, and have become the new gatekeepers, particularly vis-à-vis lower- and middle-income patients who benefit from procedures performed by surgeons employed in public and non-profit health care settings.[41] In addition, plastic surgery residents from more than 20 accredited plastic surgery programs across North America recently expressed a critical need for more education related to transgender surgery[42]; whether nascent fellowships and residency programs will devote a portion of their instruction to vaginoplasty in minors will probably depend on any changes to the minimum age requirement in future versions of the WPATH SOC.

Participants espoused conflicting opinions of the WPATH. On one hand, there were complaints that the organization lacked interest in promoting surgical standards or deeper engagement in sponsoring educational activities or fellowships; on the other, there was often a neutral stance toward the current age requirement and favoring the SOC as sufficiently vague, thereby not interfering with the surgeon's selection of the appropriate surgical candidate. Paradoxical attitudes to the WPATH and its standards are not unique to this particular group of affiliated members; a study including 36 psychologists, psychiatrists, and endocrinologists in 10 countries showed that the WPATH SOC were considered "too liberal and too conservative."[43] The WPATH has recently taken action in a number of educational areas, primarily in its Global Education Initiative, to provide certification of mental health professionals and to offer surgical courses encompassing didactic sessions and cadaver laboratories.[24] As the field matures, it is certain that the WPATH will play a more prominent role in contributing to, if not setting, the surgical standards, particularly for genital surgeries in adolescents. The current absence of directives does not appear to stop vaginoplasties in female-affirmed minors; in fact, the rate of such procedures will likely continue to increase as surgeons refine their techniques and expand their patient population in tandem with earlier social transition and gonadal treatment of gender dysphoric adolescents in the United States.

LIMITATIONS

There are several limitations to the study. Despite attempts to include every surgeon performing transgender vaginoplasty in the United States, it was not always possible to locate surgeons who were not listed in the WPATH directory or on proprietary websites. The limited sample might not be representative of the surgical cadre at large, particularly when exploring experiences and attitudes toward vaginoplasty in minors. A larger participant pool representing WPATH-affiliated surgeons outside the United States would improve the generalizability of the study. An international surgeon study also would address the cultural differences between the United States and other regions, in which adolescent life transitions such as college attendance might be negotiated differently and potentially influence the results. The authors also are aware of age, gender, and generational cohort of participants potentially influencing the responses; for this study, however, these variables were not the focus and therefore are not presented in the results. Another consideration is the collegial relationship between the study authors and some of the participants; the surgeons might not have been entirely forthcoming in their responses because of impression management or concerns of losing anonymity in a professional community limited to a few hundred members. Future studies dealing with genital surgery in minors would benefit from the added participation of gender professionals from other disciplines in a more inclusive approach.

CONCLUSIONS

The available research literature contains no data on vaginoplasty in transgender minors. The findings of this study represent the experiences and attitudes of surgeons who until now have declined open discussion and disclosure of results that could further advance surgical treatment in transgender adolescents. The abundant data elicited from the interviews address several meaningful research questions, most importantly patient selection criteria, surgical methods, and issues critical to the future of the profession. Taken together, the study and its findings make a significant contribution to the planned revision of the WPATH SOC.

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LETTER TO THE EDITOR

Suicide by Clinic-Referred Transgender Adolescents in the United Kingdom

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Introduction

Surveys show that adolescents who identify as transgender are vulnerable to suicidal thoughts and self-harming behaviors (dickey & Budge, 2020; Hatchel et al., 2021; Mann et al., 2019). Little is known about death by suicide. This Letter presents data from the Gender Identity Development Service (GIDS), the publicly funded clinic for children and adolescents aged under 18 from England, Wales, and Northern Ireland. From 2010 to 2020, four patients were known or suspected to have died by suicide, out of about 15,000 patients (including those on the waiting list). To calculate the annual suicide rate, the total number of years spent by patients under the clinic's care is estimated at about 30,000. This yields an annual suicide rate of 13 per 100,000 (95% confidence interval: 4–34). Compared to the United Kingdom population of similar age and sexual composition, the suicide rate for patients at the GIDS was 5.5 times higher. The proportion of patients dying by suicide was far lower than in the only pediatric gender clinic which has published data, in Belgium (Van Cauwenberg et al., 2021).

Suicidality in Transgender Adolescents

"About half of young trans people…attempt suicide," declared the United Kingdom Parliament's Women and Equalities Committee (2015). Similar figures are cited by news media and campaigning organizations. The *Guardian* reported Stonewall's statistic that "almost half" of transgender young people "have attempted to kill themselves" (Weale, 2017). "Fifty percent of transgender youth attempt suicide before they are at age 21" stated the mother of the most famous transgender youth in the English-speaking world (Jennings & Jennings, 2016). As a transgender theologian has observed, "the statistic about suicide attempts has, in essence, developed a life of its own" (Tanis, 2016).

Representative surveys of students in high schools provide one source of evidence for this statistic. In New Zealand, 20% of transgender students reported attempting suicide in the past 12 months, compared to 4% of all students (Clark et al., 2014). In the United States, 15% of transgender students reported a suicide attempt requiring medical treatment in the last 12 months, compared to 3% of all students (Centers for Disease Control & Prevention, 2018; Jackman et al., 2021; Johns et al., 2019). In another American survey, 41% of transgender students reported having attempted suicide during their lifetime, compared to 14% of all students (Toomey et al., 2018).

To what extent are self-reported suicide attempts reflected in fatalities? The connection is not straightforward. Respondents who report suicide attempts are not necessarily indicating an intent to die. One survey of the American population found that almost half the respondents who reported attempting suicide subsequently stated that their action was a cry for help and not intended to be fatal (Nock & Kessler, 2006). In two small samples of non-heterosexual youth, half the respondents who initially reported attempting suicide subsequently clarified that they went no further than imagining or planning it; for the remainder who did actually attempt suicide, their actions were usually not life-threatening. To an extent, then, "the reports were attempts to communicate the hardships of lives or to identify with a gay community" (Savin-Williams, 2001). Although such elaborate survey methods have not been used to study transgender populations, there is anecdotal evidence for a similar disjuncture. The pediatric endocrinologist who established the first clinic for transgender children in the United States stated that "the majority of self-harmful actions that I see in my clinic are not real suicide attempts and are not usually life threatening" (Spack, 2009).

Suicide mortality has been studied in the transgender population using registry data. The annual suicide rate is calculated by dividing the number of suicides by the total number of years each person was at risk. An individual who was observed for 20 years, for instance, contributes 20 person-years to the denominator. The

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largest study covers over 8,000 patients who visited the gender clinic in Amsterdam from 1972 to 2017 (Wiepjes et al., 2020). The annual suicide rate was 29 per 100,000 for transmen, quadruple the rate for the female population, and 64 for transwomen, quadruple the rate for the male population. A Swedish study of 324 individuals who had undergone genital surgery between 1973 and 2003 found much higher annual suicide rates: 250 per 100,000 for transmen, 43 times the rate for matched female controls, and 285 for transwomen, 16 times the rate for matched male controls (M. Boman, personal communication, 12 April 2021; Dhejne et al., 2011). Only one published study has reported suicide fatalities among transgender adolescents. Belgium's pediatric gender clinic provided counseling to 177 youth aged from 12 to 18 years, who had been referred between 2007 and 2016: five of them (2.8%) committed suicide (Van Cauwenberg et al., 2021). The mean age of referral was 15, implying a mean duration of 3 years before transition to an adult clinic, which translates to an annual suicide rate of 942 per 100,000. This is the highest suicide mortality recorded for any transgender population.

Method

This Letter estimates the suicide rate at the world's largest pediatric gender clinic. Based in London, the GIDS is part of the Tavistock and Portman NHS Foundation Trust, and serves youth under 18 from England, Wales, and Northern Ireland who are "experiencing difficulties with their gender identity development" (Carmichael & Davidson, 2009). Like all such services throughout Western Europe and North America, it has experienced enormous growth; referrals increased from 100 in 2009 to a peak of 2700 in 2019. The waiting list in April 2021 exceeded 5300.

The GIDS patients manifest typically high rates of self-harming behavior. In a sample of 900 adolescents (aged from 13 to 17) admitted to the clinic from 2009 to 2017 and given the Youth Self-Report questionnaire, 44% answered that they sometimes or very often "deliberately try to hurt or kill myself" (de Graaf et al., 2020). Unfortunately, both behaviors are combined in this question. In a different sample of over 700 children and adolescents (aged from 4 to 17) assessed by the GIDS in 2012 and 2015, 10% were flagged by clinicians as having attempted suicide (Morandini et al., 2021).

Suicides

Since the early 2000s, the National Health Service has implemented mandatory reporting of "serious incidents" (Department of Health, 2001, 2010). The death of any patient—including those on the waiting list—suspected to be suicide is reported to the Tavistock's Board of Directors. The Tavistock cooperates with a comprehensive surveillance system for every death classified as suicide or (after an open verdict by the coroner) probable suicide in the United Kingdom (National Confidential Inquiry into Suicide & Homicide by People with Mental Illness, 1999; National Confidential Inquiry into Suicide and Safety in Mental Health, 2019). Papers for the Tavistock's Board meetings are available from April 2007 onwards; those not on the Trust's website were acquired by a Freedom of Information request. The pdf files of the *Agenda and Papers* (through September 2021) were searched for the keyword "suicid"; all 442 instances were inspected. From 2007 to 2020, four patients of the GIDS died by suspected suicide: two on the waiting list, in 2016 and 2017; and two after having been seen, in 2017 and 2020. The last case was described as "likely" to be suicide, because the inquest has not yet been held. These figures were confirmed by Freedom of Information requests to the Tavistock.

Triangulation is possible from two sources. Comprehensive mortality data on all adolescents aged from 10 to 19 who committed suicide in the United Kingdom from 2014 to 2016 include five transgender individuals (Rodway et al., 2020). Due to confidentiality restrictions, it is not possible to disaggregate these further by age or by country. Presumably, one of these is the patient of GIDS who died in 2016. The remaining four might have been 18 or 19—the risk of suicide increases significantly in the late teens—or might have lived in Scotland. Alternatively, they might have been eligible for the GIDS but had not sought a clinical referral (made by the local Child and Adolescent Mental Health Service, the child's general practitioner, social worker, or teacher) or had not obtained it.

Another source is the Transgender Day of Remembrance website, which aims to record all deaths by suicide or violence (Metcalfe, 2021). For the United Kingdom between 2007 and 2020, the website names 3 adolescents under the age of 18 who committed suicide. One was one of the GIDS patients (the match is certain because they were named in the *Agenda and Papers*). The other two had no involvement with the GIDS (or any other gender clinician), as was evident from their inquests, though one was under the psychiatric care of another NHS Trust (BBC News, 2021; Bunyan, 2008). In addition, the website lists suicides by two "young" transgender people, sourced from Twitter, without information on their name or age. In one case, it is not clear whether the person lived in the United Kingdom.

Patients

With suicides as numerator, two denominators are relevant. Because comprehensive data on patient numbers became available from 2010, the period will be the 11 years from 2010 to 2020. (These are financial years; thus, 2020 runs from April 2020 to March 2021.) The first denominator is the total number of individual patients, estimated by summing the annual number of referrals to the GIDS from 2010 to 2020—excluding those aged 18 or over, as they are not accepted. The total number is 15,032. This sum omits patients at the clinic who had been referred before

2010, and so is a slight underestimate. (The Online Supplement provides full details.)

The second denominator is the total number of patient-years: the sum of the number of years spent by each individual as a patient of the GIDS. The number of patients seen by the GIDS each year was available from 2014 to 2020. Before 2014 only the number of patients first seen was available. From 2014 to 2016, the number of patients seen was consistently double the number first seen, and so the former number for 2010 to 2013 was estimated by doubling the latter. All these numbers exclude patients on the waiting list. The number waiting at the beginning of each year from 2016 to 2020 was obtained by Freedom of Information request. Before then the number was not available, and so must be treated as zero. This leads to an underestimate, of course, but the waiting list became appreciable only from 2015. The total number of patient-years over this period is estimated as 30,080. In other words, patients spent on average 2 years at the GIDS (including time on the waiting list). Time on the waiting list contributed 41% of the total patient-years.

Results

From 2010 to 2020, the four suicide deaths equate to 0.03% of the 15,032 patients. Taking the denominator as 30,080 patient-years, the annual suicide rate is calculated as 13 per 100,000 (95% confidence interval: 4 to 34 per 100,000). For comparison, the annual suicide rate in England and Wales between 2010 and 2020 for adolescents aged from 15 to 19 years averaged 4.7 (Office for National Statistics, 2021). This does not quite correspond to the age range of the GIDS patients, however. At referral, the patients ranged in age from 3 to 17 years; only 7% were younger than 10. The mean was 14 years and the median 15. Most patients stay with the GIDS until transitioning to an adult service. Therefore, the average age of patients at any point in time will lie somewhere between 14 and 17. A better comparison is therefore the overall suicide rate for adolescents aged from 14 to 17 (available only for the entire United Kingdom for 2015–2017), which was 2.7 per 100,000 (Office for National Statistics, 2018; Rodway et al., 2020). Comparison should also account for the difference between the sexes, because males are more likely to commit suicide than females. Of the GIDS patients, 69% were female. Adjusting for sex, the GIDS patients were 5.5 times more likely to commit suicide than the overall population of adolescents aged 14 to 17.

Discussion

How reliable are these estimates? The chief uncertainty about the numerator is whether the fourth death will be ruled as suicide when the inquest is eventually held. It could be speculated that there were further suicides unknown to the Tavistock and to the National Confidential Inquiry into Suicide and Safety in Mental Health. All that can be said is that the single suicide by a GIDS patient from 2014 to 2016 is not out of line with comprehensive mortality data on suicides by transgender adolescents in the United Kingdom which counted five suicides in a longer age range and wider geographical area. The denominator for the annual suicide rate, however, is pieced together from various series and so is inevitably approximate. Statistics from the early 2010s are less reliable, though they make only a small contribution to the grand total; the last three years contribute more than half of the total number of patient-years. The most significant limitation is the lack of information on the age and sex of all the patients who committed suicide.

Direct comparison can be made with the Belgian pediatric gender clinic (Van Cauwenberg et al., 2021). Its annual suicide rate was about 70 times greater than the rate at the GIDS. This is especially puzzling because patients at the Belgian clinic scored better, on average, than those at the GIDS on tests of psychological functioning (de Graaf et al., 2018). The explanation for the huge disparity in suicide is not clear. The Amsterdam's clinic annual suicide rate was four times greater than the rate at the GIDS. The higher rate is not surprising, however, because the Dutch clinical population was dominated by older adults: the median age at first visit was 25 (Wiepjes et al., 2020). Suicide rates peak in middle age, and so a population of older adults would be at higher risk than a population of adolescents.

The suicide rate of the GIDS patients is not necessarily indicative of the rate among all adolescents who identify as transgender. On the one hand, individuals with more serious problems (and their families) would be particularly motivated to seek referral and more likely to obtain it, and so the clinical subset would be more prone to suicide. One study suggests that a child who frequently attempted suicide was more readily referred to the GIDS (Carlile et al., 2021). On the other hand, young people facing hostility from their families would be less able to seek referral, and this hostility could make them especially vulnerable to suicide.

Taking into account these limitations, the estimated suicide rate at the GIDS provides the strongest evidence yet published that transgender adolescents are more likely to commit suicide than the overall adolescent population. The higher risk could have various causes: gender dysphoria, accompanying psychological conditions, and ensuing social disadvantages such as bullying. Studies of young people referred to the GIDS in 2012 and 2015 found a high prevalence of eating disorders, depression, and autism spectrum conditions (ASC) (Holt et al., 2016; Morandini et al., 2021)—all known to increase the probability of suicide (Simon & VonKorff, 1998; Smith et al., 2018). Eating disorders and depression could be consequences of transgender identity and its ensuing social repercussions, but this is implausible for ASC insofar as it originates in genes or the prenatal environment. From a sample of over 700 referrals to the GIDS in 2012 and 2015, 14–15% were diagnosed with ASC (Morandini