Timing of Puberty Suppression and Surgical Options for Transgender Youth

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abstract

OBJECTIVES: Puberty suppression (PS) is a cornerstone of treatment in youth experiencing gender dysphoria. In this study, we aim to inform prescribing professionals on the long-term effects of PS treatment on the development of sex characteristics and surgical implications.

METHODS: Participants received PS according to the Endocrine Society guideline at Tanner 2 or higher. Data were collected from adolescents who received PS between 2006 and 2013 and from untreated transgender controls. Data collection pre- and post-PS and before surgery included physical examination and surgical information.

RESULTS: In total, 300 individuals (184 transgender men and 116 transgender women) were included. Of these, 43 individuals started PS treatment at Tanner 2/3, 157 at Tanner 4/5, and 100 used no PS (controls). Breast development was significantly less in transgender men who started PS at Tanner 2/3 compared with those who started at Tanner 4/5 and controls. Mastectomy was more frequently omitted or less invasive after PS. In transgender women, the mean penile length was significantly shorter in the PS groups compared with controls (by 4.8 cm [Tanner 2/3] and 2.1 cm [Tanner 4/5]). As a result, the likelihood of undergoing intestinal vaginoplasty was increased (odds ratio = 84 [Tanner 2/3]; odds ratio = 9.8 [Tanner 4/5]).

CONCLUSIONS: PS reduces the development of sex characteristics in transgender adolescents. As a result, transgender men may not need to undergo mastectomy, whereas transgender women may require an alternative to penile inversion vaginoplasty. These surgical implications should inform decision-making when initiating PS.

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Dr van Gelder collected data, conducted the initial analyses, and reviewed and revised the manuscript; Drs van de Grift, Mullender, and Bouman designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content; Drs Steensma and de Vries designed the study and critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-3653

Accepted for publication Aug 6, 2020

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

WHAT'S KNOWN ON THIS SUBJECT: Puberty suppression (PS) provides transgender adolescents with time to develop their gender identity without unwanted physical developments. The positive psychological effects of PS are well studied.

WHAT THIS STUDY ADDS: PS in transgender adolescents likely results in hypoplastic breast and genital development. Having underdeveloped sex characteristics qualifies individuals for different gender-affirming surgical approaches compared with nonsuppressed adults. This information is important in clinical decision-making and developing surgical facilities.

To cite: van de Grift TC, van Gelder ZJ, Mullender MG, et al. Timing of Puberty Suppression and Surgical Options for Transgender Youth. *Pediatrics.* 2020;146(5):e20193653

Pubertal development in transgender adolescents may be accompanied with a substantial increase in gender dysphoria and subsequent mental health issues.[1] Transgender standards of care[2,3] promote affirming counseling and watchful waiting during childhood, and medical treatments are indicated from approximately the age of 12 (puberty development Tanner 2/3 [breast/testes]). Puberty suppression (PS) aims to provide young adolescents with time to further explore their gender identity without the physical distress of puberty development[3] before irreversible cross-sex hormone (CSH) treatment is initiated. In addition, PS has proven to be safe in treating precocious puberty.[4] The preferred mode of PS treatment is by using long-acting gonadotropin-releasing hormone analogues.[3]

In few studies have researchers followed-up on transgender adolescents receiving PS using patient-reported outcomes.[5,6] de Vries et al[5] assessed 55 transgender adolescents before PS, during CSH treatment, and 1 year after gender-affirming surgery. Their main findings included a steady improvement of psychological function and general well-being bordering normative values. Others observed favorable psychological outcomes of PS compared with counseling only.[6] A qualitative study on the views of transgender adolescents on the possible long-term risks of PS revealed that participants were aware of the limited outcome research and said they weighed possible risks against the increased quality of life they anticipated.[7]

Schagen et al[8] observed that during PS treatment, development of sex characteristics stopped and in some even regressed (ie, breast and testicular atrophy). For those who progress with gender-affirming surgeries after receiving PS and CSH, surgical approaches strongly depend on physical development of the breasts[9,10] or penis.[11] Severe penoscrotal hypoplasia reduces the feasibility of standard penile inversion vaginoplasty (because of the limited penile skin to create a vaginal cavity and limited prepuce to create labia minora) and can require other types of vaginoplasty, such as intestinal vaginoplasty, with an additional complication risk of colorectal surgery.[11] No data on breast hypoplasia after PS are available, but if feminine breast development is adequately suppressed, transgender men can refrain from undergoing chest surgery. Recognizing the importance of informed decision-making by (parents of) transgender adolescents, accurate information on the long-term effects of PS on the development of sex characteristics, the surgical implications, and psychological gains is of great importance.[12]

In this study, we aim to describe the development of sex characteristics in an adolescent cohort of early (Tanner 2/3) and later-initiated (Tanner 4/5) PS treatment compared with young transgender adults without PS treatments. In transgender boys and men, lesser feminine breast development is expected, whereas in transgender girls and women, less penoscrotal development is expected compared with the groups without PS. Our second study aim is to assess whether breast and genital gender-affirming surgeries were performed, which surgical techniques were used, and how these are associated with PS treatment. With less breast development after PS, no or less invasive mastectomy is expected to be more prevalent in transgender men. On the other hand, more invasive vaginoplasty surgery is expected in transgender women who have insufficient penoscrotal skin to construct a vagina and vulva.

METHODS

Procedure

Clinical

Care was conducted according to the (locally adapted) World Professional Association for Transgender Health Standards of Care[2] and Endocrine Society guidelines.[3] In individuals applying for care, clinical diagnoses and treatment requests were explored in an interdisciplinary setting. Transgender individuals were assessed and supported by a mental health professional before and during somatic treatments. For transgender adolescents, parents were included in these sessions. Following the Endocrine Society guidelines, adolescents diagnosed with gender dysphoria and without substantial interfering psychosocial issues can receive gonadotropin-releasing hormone analogue treatments after the first physical changes of puberty have taken place (minimum Tanner 2) and CSH around the age of 16. At the age of 18, and when having no substantial interfering psychosocial issues, individuals can receive gender-affirming surgeries.

Study

The study was a single-center cohort study using registry and patient record data collected in a retrospective design. Data were reported as part of standardized routine treatment evaluations; they were reported before PS by the pediatrician, before CSH treatment by the endocrinologist, and pre- and postoperatively by the plastic surgeon. Eligible transgender individuals were identified by using local registries. Data were collected standardly on case report forms.

Under Dutch law, retrospective studies using clinical data are exempt from requiring ethical permission.

Participants

All adolescents who applied for gender-affirming medical interventions between 2006 and 2013 were identified by using local registries (n = 386; Fig 1), and outcome data were collected between application and follow-up in 2018. Individuals were included for analyses when (1) a gender dysphoria diagnosis was confirmed, (2) they were at least 18 at the point of data collection, (3) they were <18 when starting PS, (4) they initiated and continued PS treatment, and (5) they were not lost to follow-up. Of the identified individuals, 200 met the inclusion criteria and were included for analyses. A random sample of clinical controls was identified by using hospital records. These 100 controls were approximately the same age as the PS group at follow-up, received no PS treatment, but did receive CSH and applied for gender-affirming surgery in the same years as the PS cohort. Furthermore, the same inclusion criteria (except initiating and continuing PS treatment) applied to controls.

Outcome Measures

Participants were included in the cohort when applying for PS (between 2006 and 2013), and data were registered at fixed points during treatments. For the current study, data were collected at 3 time points; before receiving PS (for the PS group only), post-PS, and around surgical treatments. This outcome database was completed retrospectively at follow-up (after CSH and/or surgery) during a 6-month period in 2018.

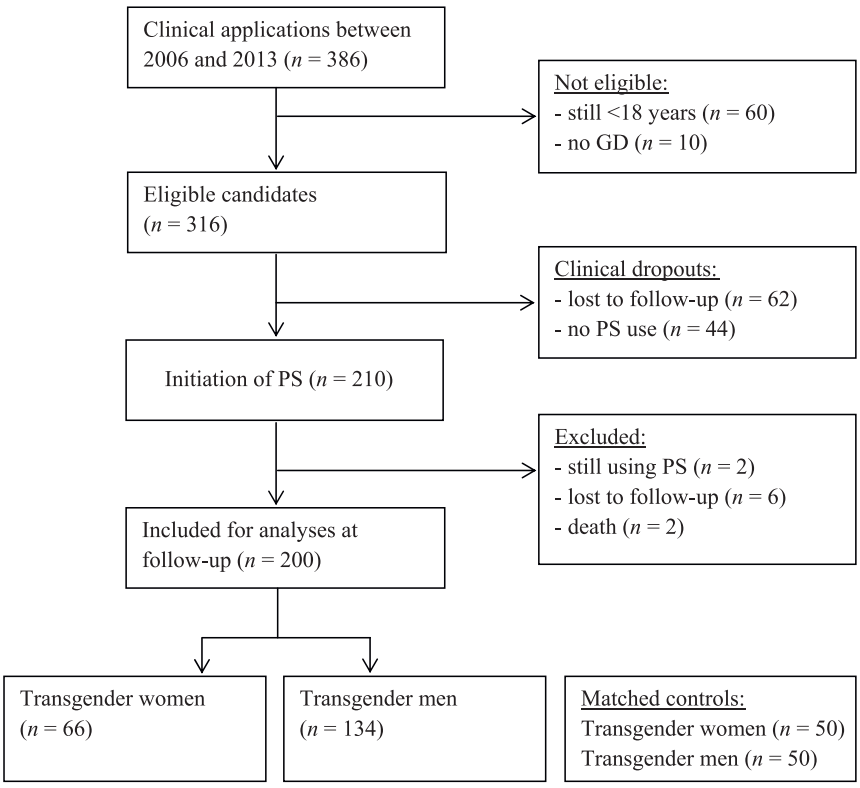

FIGURE 1
Participant flowchart of participants included in June 2018. GD, gender dysphoria.

A full overview of the points of data collection and the data collected is displayed in Fig 2.

Data on demographic characteristics were collected through history taking and patient records (eg, gender, age, sexual activity screening question). Standardized information on the onset and type of PS and CSH treatment was collected. Standardized routine physical examinations were conducted by trained pediatric endocrinologists according to clinical guidelines. These included height and weight measurement and Tanner staging of breasts and genitals. Preoperative physical examination by trained specialists included the examination of breasts in transgender men and genitals in transgender women (penile length and testes descended) by using standardized classification and report forms.[9–11] Physical examination of the breasts was conducted according to conventional principles and included visual assessment of the breast cup and combined visual `and manual assessment of breast ptosis (level of breast sagging and nipple position relative to inframammary fold [IMF]) and elasticity (elastic ability of the skin). Lastly, surgical reports were reviewed for the surgical techniques applied by using predefined standardized case report forms.

Statistical Analyses

The sample background characteristics were calculated as means, medians, and frequencies for the Tanner 2/3, Tanner 4/5, and clinical control groups. Physical (sex) characteristics before PS and CSH were presented as descriptive data for the Tanner 2/3 and Tanner 4/5 groups for each gender separately. Data on the sex characteristics before gender-affirming surgery and the surgical

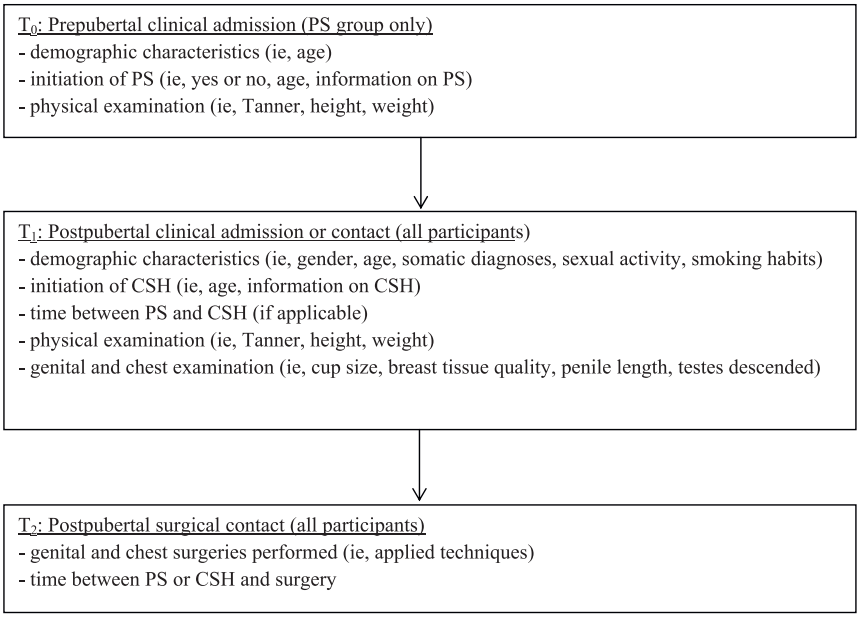

FIGURE 2
Overview of data collection; T_0, time 0; T_1, time 1; T_2, time 2.

techniques performed were calculated as means, medians, and frequencies for the Tanner 2/3, Tanner 4/5, and clinical control groups. Subgroup differences were assessed through analysis of variance and Kruskal-Wallis testing. Effect sizes were calculated via Cohen's *d* and likelihood ratios. Outcomes were corrected for multiple testing. All analyses were conducted in SPSS 22 (IBM SPSS Statistics, IBM Corporation).

TABLE 1 Clinical Characteristics of the Study Sample

	Total (*N* = 300)	Tanner 2/3, *n* = 43 (14.3%)	Tanner 4/5, *n* = 157 (52.3%)	Controls, *n* = 100 (33.3%)	Test Statistics, *P*
Gender, *n* (%)					<.001
Transgender man	184 (61.3)	17 (39.5)	117 (63.6)	50 (50.0)	—
Transgender woman	116 (38.7)	26 (60.5)	40 (34.5)	50 (50.0)	—
Age, y					
At study follow-up, mean (SD)	23 (2.9)	20 (0.3)	22 (0.2)	25 (0.2)	<.001
At initial assessment, median (IQR)	16 (12–18)	10 (9–11)	15 (12.5–16)	19 (18–21)	<.001
At start of PS, mean (SD)	15 (2.0)	12 (0.1)	15 (0.1)	N/A	<.001
At start of CSH, mean (SD)	18 (2.9)	15 (0.5)	17 (1.0)	21 (2.4)	<.001
At first surgery (transgender man), median (IQR)	19 (18–21)	18 (18–18)	18 (18–19)	23 (21–25)	<.001
At first surgery (transgender woman), mean (SD)	21 (2.5)	18 (0.8)	19 (1.3)	23 (2.2)	<.001
Educational level, *n* (%)					<.001
Lower	25 (10.3)	6 (15.4)	3 (2.4)	16 (20.5)	—
Intermediate	196 (81.0)	25 (64.1)	112 (89.6)	59 (75.6)	—
Higher	21 (8.7)	8 (20.5)	10 (8.0)	3 (3.8)	—
Sexually active, *n* (%)[a]	76 (70.4)	6 (28.6)	20 (64.5)	50 (89.3)	<.001
Smoking, *n* (%)	57 (19.1)	5 (11.6)	29 (18.6)	23 (23.0)	.28

Data presented for subgroups starting PS at Tanner 2/3, at Tanner 4/5, and controls with CSH treatment only. IQR, interquartile range; N/A, not available; —, not applicable.
[a] Data collected at onset of CSHs.

RESULTS

The total sample included 184 (61.3%) transgender men and 116 (38.7%) transgender women, having an average age of 23 years (SD = 2.9) at follow-up. Clinical characteristics of the study sample are displayed in Table 1. Forty-three (14.3%) participants started with PS at Tanner 2/3 and 157 (52.3%) at Tanner 4/5, whereas the 100 controls (33.3%) received no PS. The Tanner 2/3 group included more transgender women, whereas the Tanner 4/5 group included more transgender men compared with the other groups. The Tanner 2/3 and 4/5 groups were, on average, younger at initial clinical assessment, onset of CSH treatments, and first gender-affirming surgery. When compared with transgender individuals without PS, a lower share reported to be sexually active at the start of CSH (but also being younger when asked).

Physical (Sex) Characteristics Before PS

The physical characteristics of transgender men and women before PS are displayed in Table 2. Transgender men who started PS at Tanner 4/5 showed more advanced breast development, were taller, and had a higher weight, BMI, and hip circumference compared with those who started at Tanner 2/3. Transgender women who started at Tanner 4/5 were also taller and heavier compared with those who started at Tanner 2/3.

TABLE 2 Physical Characteristics of the Study Sample Before PS

	Tanner 2/3	Tanner 4/5
Transgender men (n = 134), n	17	117
Height, m, mean (SD)	1.55 (0.08)	1.66 (0.08)
Wt, kg, median (IQR)	42 (38–49.5)	58 (51–65)
BMI, median (IQR)	17.4 (16.3–19.1)	21.0 (19.3–23.1)
Tanner stage (breasts), n (%)		
1	0 (0)	0 (0)
2	6 (35.3)	0 (0)
3	11 (64.7)	0 (0)
4	0 (0)	24 (20.5)
5	0 (0)	93 (79.5)
Waist circumference, cm, mean (SD)[a]	72 (4.9)	72 (7.9)
Hip circumference, cm, mean (SD)[a]	89 (5.7)	96 (7.9)
Transgender women (n = 66), n	26	40
Height, m, mean (SD)	1.60 (0.06)	1.75 (0.08)
Wt, kg, mean (SD)	49 (9.3)	64 (13.4)
BMI, median (IQR)	19.0 (16.6–20.8)	19.8 (18.3–22.9)
Tanner stage (genitalia), n (%)		
1	0 (0)	0 (0)
2	10 (40)	0 (0)
3	15 (60)	0 (0)
4	0 (0)	9 (22.5)
5	0 (0)	31 (77.5)
Waist circumference, cm, mean (SD)[a]	73 (7.4)	77 (8.8)
Hip circumference, cm, mean (SD)[a]	91 (7.9)	97 (7.6)

Data presented for subgroups starting PS at Tanner 2/3 and at Tanner 4/5. IQR, interquartile range.
[a] Data collected after PS.

Transgender Men: Physical (Sex) Characteristic After PS and Surgical Procedures Performed

At the visit just before initial (breast) surgery, no statistically significant differences were observed n height, weight, and BMI between the Tanner 2/3, 4/5, and no PS control groups (Table 3). Yet, breast development was significantly less in the Tanner 2/3 group compared with the Tanner 4/5 and control groups. Also, breast development was less in the Tanner 4/5 group compared with controls. No statistically significant group differences in breast elasticity, ptosis grade, and chest circumference were observed. As a result of differences in breast development, mastectomy surgery was frequently omitted in the Tanner 2/3 group (in contrast with the other groups; Table 3), and if performed, it was conducted via periareolar approaches with low resection weight. In general, a periareolar approach is used for small-size breasts without ptosis, whereas a more invasive approach via the IMF is used for larger-size breasts. The Tanner 4/5 group was an intermediate group with more frequent IMF mastectomy compared with the Tanner 2/3 group but less frequent than the controls. Phallic reconstructive surgeries were infrequently performed (yet) in all subgroups. No data on future treatment wishes were collected.

Transgender Women: Physical (Sex) Characteristics After PS and Surgical Procedures Performed

Analogous to transgender men, no statistically significant differences in length, weight, and BMI were observed between the Tanner 2/3, 4/5, and control groups (Table 3). Penile length was assessed before genital-affirming surgery and revealed that the onset of PS significantly influences penile development. As a result, the conventional technique used for vaginoplasty (penile inversion) was used less frequently in the PS groups (Tanner 2/3: 21.1%; Tanner 4/5: 73.3%; and controls: 85%; significant for Tanner 2/3 versus controls), whereas vaginoplasty using the intestine was most frequently performed in the Tanner 2/3 group (68.4%). No differences between groups were observed in the frequency of performed penile inversion vaginoplasty with additional full-thickness graft (FTG). All participants applied for vaginoplasty surgery, yet some were still waiting at the time of data collection.

Effect Sizes of PS Treatment

The use of PS had substantial effects on body development and technical approaches to gender-affirming surgeries. Transgender men who initiated PS treatment at Tanner 2/3 developed less breast tissue. For those who underwent mastectomy, on average, 540 g less breast tissue was removed compared with those who did not have PS treatment (d = −2.12). For this reason, they were less likely to undergo an IMF mastectomy. Furthermore, the likelihood of not undergoing mastectomy at all was higher. If PS was initiated at Tanner 4/5, the effects were less pronounced. The majority of this group still applied for a mastectomy. Compared with controls, resected breast tissue was on average 209 g less (d = −0.46), and the surgical technique was less frequently an IMF mastectomy (Table 4).

Penile length was measured before transwomen underwent vaginoplasty. In transwomen who started with PS at Tanner 2/3, this was on average 4.8 cm less compared with controls without PS (d = −1.73). In this group, the likelihood of receiving an intestinal vaginoplasty was 84 times increased. If individuals started with PS at Tanner 4/5, penile length was 2.1 cm shorter than controls (d = −0.83) and the

TABLE 3 Physical Characteristics of the Study Sample Before Surgery or Surgical Procedures Performed

	Tanner 2/3	Tanner 4/5	Controls	Test Statistics, *P*
Transgender men (*n* = 184)	*n* = 17	*n* = 117	*n* = 50	—
Height, m, mean (SD)	1.73 (0.08)	1.68 (0.07)	1.68 (0.07)	.05
Wt, kg, mean (SD)	67 (7.6)	66 (11.5)	71 (13.6)	.12
BMI, mean (SD)	22.4 (2.1)	23.5 (3.6)	24.8 (4.5)	.04
Breasts cup, *n* (%)				<.001
AA, A	7 (87.5)	35 (41.2)	3 (9.1)	
Greater than or equal to B	1 (12.5)	50 (58.8)	30 (90.9)	
Elasticity, *n* (%)				.04
Poor, moderate	0 (0)	18 (30)	13 (46.4)	
Good	8 (100)	42 (70)	15 (53.6)	
Ptosis, *n* (%)				.18
Grade 1, 2	6 (100)	44 (74.6)	20 (64.5)	
Grade 3, 4	0 (0)	15 (25.4)	11 (35.5)	
Chest circumference, cm, mean (SD)	84 (1.5)	81 (1.4)	83 (1.5)	.48
Mastectomy, *n* (%)				<.001
None required	9 (52.9)	1 (1.0)	0 (0)	
Periareolar, semicircular resection	8 (47.1)	76 (72.4)	18 (48.6)	
IMF resection	0 (0)	28 (26.7)	19 (51.4)	
Total wt resected, g, mean (SD)	144 (33)	474 (43)	684 (91)	.006
Genital surgery, *n* (%)				
Metoidioplasty	0 (0)	1 (0.9)	2 (4.0)	.59
Phalloplasty	1 (5.9)	13 (11.1)	8 (16.0)	—
Surgical removal of uterus and ovaries	11 (64.7)	91 (77.8)	37 (74.0)	.45
Colpectomy	6 (35.3)	29 (24.8)	16 (32.0)	.47
Transgender women (*n* = 116)	*n* = 26	*n* = 40	*n* = 50	
Height, m, mean (SD)	1.81 (0.01)	1.80 (0.00)	1.79 (0.01)	.42
Wt, kg, mean (SD)	68 (1.8)	70 (2.2)	74 (1.9)	.13
BMI, mean (SD)	20.7 (0.6)	21.9 (0.6)	22.9 (0.5)	.03
Genitalia				
Penile length, cm, mean (SD)[a]	7.9 (0.6)	10.7 (0.5)	12.8 (0.3)	<.001
Circumcised	5 (20.8)	7 (24.1)	4 (9.3)	.20
Testes descended	21 (91.3)	31 (100)	42 (100)	.06
Vaginoplasty[b]				<.001
Intestinal vaginoplasty, *n* (%)	13 (68.4)	6 (20)	1 (2.5)	
Penis inversion with FTG, *n* (%)	2 (10.5)	2 (6.7)	5 (12.5)	
Penis inversion, *n* (%)	4 (21.1)	22 (73.3)	34 (85)	
Not executed yet, *n*	7	10	8	

—, not applicable.

[a] *n* = 103.

[b] Percentages and statistics calculated over those who underwent surgery.

likelihood of requiring an intestinal vaginoplasty was increased as well (9.8 times, all compared with controls; Table 4).

DISCUSSION

Although PS has become an increasingly important treatment modality in young adolescents experiencing gender dysphoria, little evidence has been produced on the physical development of sex characteristics after PS and the implications for gender-affirming surgeries. Our findings suggest a dependency on the onset or duration of PS treatment; the earlier the onset of PS, the greater the effects on the development of breasts (in transgender men) and penis (in transgender women). Because technical feasibility of various gender-affirming surgical techniques depends on physical characteristics (eg, tissue availability), individuals who used PS may select for different types of surgery.

No statistically significant effects of PS on height, weight, and BMI were observed before surgery in both transgender men and women. In the transgender men, the most significant difference in physical development was observed in breast development, being least in the Tanner 2/3 group, intermediate in the Tanner 4/5 group, and most in the control group. Decrease or even regression of breast tissue development when using PS has previously been reported,[3,8] yet no data on the effect of the onset of PS have been described. As a consequence of the effects on breast development, less mastectomies were performed after PS (Tanner 2/3) and those performed were less invasive mastectomies (Tanner 2/3 and 4/5) compared with controls. This finding is in line with surgical guidelines suggesting which mastectomy technique to perform on the basis of breast size, elasticity, and ptosis grade.[10] Earlier studies revealed that individuals having gone through puberty without PS nearly always require a mastectomy to obtain a more masculine chest.[10] Although PS increases the chance of not requiring mastectomy for chest, this is no guaranteed outcome.

In transgender women, PS was found to have significant effect on penile development. Penile development was less in the Tanner 2/3 group when compared with the other 2 groups, and it was also less in the Tanner 4/5 group compared with controls. The penile length is of importance for vaginoplasty surgery because the penile skin is typically used to create the vaginal lining. In individuals with a small penis size, the penoscrotal skin is not sufficient to reconstruct both a vulva (requiring sufficient prepuce and scrotal skin) and sufficient neovaginal length (requiring sufficient penile skin).[11] In these individuals, an alternative vaginoplasty technique is required (eg, by using intestinal tissue or FTG). The effects of PS on the type of vaginoplasty performed are reflected

TABLE 4 Effects of PS Treatments on Physical Characteristics and Surgical Procedures Performed

	Values
Transgender men	
Tanner 2/3 versus controls	
Total breast volume resected	540 g less
Cohen's *d* (95% CI)	−2.12 (−3.09 to −1.15)
Likelihood of no mastectomy required, % vs %	52.9 vs 0.0
Likelihood of IMF mastectomy required, % vs %	0 vs 51.4
Tanner 4/5 versus controls	
Total breast volume resected	209 g less
Cohen's *d* (95% CI)	−0.46 (−0.89 to −0.02)
Increased likelihood of no mastectomy required, % vs %	1.0 vs 0.0
Increased likelihood of IMF mastectomy required, % vs %	26.7 vs 51.4
Transgender women	
Tanner 2/3 versus controls	
Penile length	4.8 cm shorter
Cohen's *d* (95% CI)	−1.73 (−2.30 to −1.15)
Increased likelihood of intestinal vaginoplasty, OR (95% CI)	84 (9.29 to 768.82)
Tanner 4/5 versus controls	
Penile length	2.1 cm shorter
Cohen's *d* (95% CI)	−0.83 (−1.29 to −0.37)
Increased likelihood of intestinal vaginoplasty increasing, OR (95% CI)	9.8 (1.11 to 86.01)

CI, confidence interval; OR, odds ratio.

by data from an earlier study[11] as well as the data in the current study. We observed a dependency on the onset of PS; standard penile inversion vaginoplasty was generally possible in the control group, whereas this was less frequently possible in Tanner 4/5 and infrequently in Tanner 2/3. Intestinal vaginoplasty was performed as an alternative method in most transgender women who started PS in Tanner 2/3.

Clinical Considerations

We are aware that PS treatment includes many other aspects that need consideration besides its effect on physical development and the implications for surgery. We included no data on the development of other physical characteristics (eg, hair and voice) nor on the adolescents' well-being. Nevertheless, transgender youth, parents, and prescribing professionals should be aware of the long-term (surgical) consequences of PS treatments when individuals wish to continue medical transition to gender-affirming surgery. For transgender men, less breast development corresponds with an increased likelihood of not requiring mastectomy (52.9% of the Tanner 2/3 group). Noticeably, the favorable effects of PS on breast growth were not only observed for the Tanner 2/3 group but also for adolescents starting at Tanner 4/5. For transgender women, reduced genital development after PS treatment may result in penoscrotal hypoplasia and an increased likelihood of requiring more invasive vaginoplasty approaches (84 times increased in Tanner 2/3 and 9.8 times in Tanner 4/5). If transgender women with penoscrotal hypoplasia wish to have satisfactory vaginal depth, a vaginal cavity may be created by using intestine, adding an extra risk of a colorectal surgery to the procedure. Also, an intestinal vaginoplasty can result in a more moist vagina, which requires more self-care and extensive clinical follow-up.[11]

Clinicians should counsel transgender youth and their parents in making informed decisions when starting PS. Counseling consists of informing about the possible surgical consequences when puberty is suppressed and that these techniques may not be available in general transgender care facilities. Long-term (surgical) risks can be considered along with anticipated psychological gains, other pubertal developments, and so forth.

Regarding health care facilities, service providers should be aware that when pediatricians prescribe PS to transgender youth, this will have "downstream" consequences on the demand for technically complex gender-affirming surgery. For example, plastic surgeons will have to be skilled in minimally invasive mastectomy techniques and more extensive vaginoplasty approaches. Sufficient infrastructure to collaborate with colorectal surgeons and mental health professionals is inevitable to provide this care. Generally, referring physicians should be aware that early referrals to specialized pediatric care can positively impact pubertal development and surgical treatments (along with mental health).

Limitations and Future Directions

Some limitations can be defined for the current study, including the sample size of some subgroups, reducing statistical power. Secondly, the included sample consisted of approximately two-thirds of the eligible candidates. Because no follow-up data of the remaining third were collected, a selection bias cannot be ruled out. Resulting from the retrospective design, some outcome variables suffered from missing data, leaving some information unreported (eg, breast development in those who did not apply for breast surgery) and creating possible selection

bias (eg, control transgender men applying for mastectomy specifically were compared with all transgender men receiving PS, leaving control transgender men with little breast growth out of scope). Lastly, some possibly influential data were not reported (eg, scrotal development). Hence, future research ideally should include multicenter standardized prospective data collection, including patient-reported outcomes, to put the clinical findings into perspective.

CONCLUSIONS

Our findings indicate that PS effectively reduces the physical development of sex characteristics. As a result, transgender adolescents who received PS often qualify for different gender-affirming surgical techniques. In transgender men, early PS treatment is associated with no or less invasive chest surgery, whereas in transgender women, it is associated with more invasive genital surgery. Transgender youth and their parents should be aware of these long-term consequences when initiating PS. This asks for a multidisciplinary approach at an early stage. Transgender girls and women, especially, should be informed that they might require more extensive, centralized surgical care with long-term aftercare.

ABBREVIATIONS

CSH: cross-sex hormone
FTG: full-thickness graft
IMF: inframammary fold
PS: puberty suppression

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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DOI: 10.1542/peds.2019-3653 originally published online October 26, 2020;

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