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Gender dysphoria in adolescents with Ehlers–Danlos syndrome

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Abstract

Objectives: Ehlers–Danlos Syndrome represents a family of heritable connective tissue disorders that include joint hypermobility, tissue fragility, and skin hyperextensibility. Ehlers–Danlos Syndrome presents with clinical sequela across multiple body systems that require multidisciplinary care. Little is known about adolescents with Ehlers–Danlos Syndrome who are transgender and gender diverse. To date, there have been no reports of transgender and gender diverse youth in pediatric patients with Ehlers–Danlos Syndrome. The objective of this study was to characterize transgender and gender diverse adolescents with Ehlers–Danlos Syndrome seen in a pediatric multidisciplinary specialty clinic.

Methods: A retrospective chart review was performed and it was found that 28 patients were seen in the Ehlers–Danlos Syndrome multidisciplinary clinic were reported being transgender and gender diverse. Chart review included analysis of all documents in the electronic medical record, including demographic data, gender identity, chosen pronouns, specialty care previously received for Ehlers–Danlos Syndrome, symptoms and conditions related to it, and medications.

Results: Of the 166 total adolescents seen in the pediatric multidisciplinary Ehlers–Danlos Syndrome clinic during the study period, 17% reported gender dysphoria. The average age at Ehlers–Danlos Syndrome diagnosis was 13.5 years (range 8–17 years). Most (61%) reported their gender identity as transgender, followed by nonbinary (14%). Most had preferred male (he/him) pronouns (47%), followed by nonbinary (they/them) pronouns (39%). The vast majority reported fatigue (75%), musculoskeletal issues (96%), psychiatric issues (86%), cardiac issues (71%), gastrointestinal issues (68%), and neurologic issues (79%).

Conclusions: Here we report the first cohort of transgender and gender diverse adolescents in the Ehlers–Danlos syndrome population and show an association between the two. This report increases awareness for providers who care for patients with Ehlers–Danlos Syndrome. As care for those with Ehlers–Danlos Syndrome is often complex and multidisciplinary, providers should adopt practices of gender-affirming medical care that contribute to improved care and outcomes.

Keywords

Ehlers–Danlos syndrome, pediatrics, transgender, gender diverse

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Introduction

Ehlers–Danlos Syndrome (EDS) represents a family of heritable connective tissue disorders with overlapping phenotypic features that commonly include joint hypermobility, tissue fragility, and skin hyperextensibility.[1] Conservative estimates suggest that as a group, EDS occurs in approximately 1 in 2500 to 5000 babies worldwide annually.[2] There are currently 14 recognized distinct clinical subtypes of EDS,[1] each defined by both major and minor criteria. Of those, the most common subtype is hypermobile EDS (hEDS), which represents 80%–90% of all EDS cases and is suspected to have a higher prevalence of up to 20 per 1000 babies.[3] Definitive diagnosis of EDS relies on molecular confirmation with all subtypes except for hEDS, which is a clinical diagnosis based on specific clinical criteria, though a genetic basis is suspected for hEDS.[1] The clinical phenotype

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Table 1. Gender dysphoria in adolescents: DSM-5 criteria.

A: A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least two of the following:
A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
A strong desire for the primary and/or secondary sex characteristics of the other gender
A strong desire to be the other gender (or some alternative gender different from one's assigned gender)
A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender)
A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender)
B: The condition is associated with clinically significant distress or impairment, occupational, or other important areas of functioning

for hEDS commonly include sequelae across multiple body systems with neurological, cardiovascular, gastrointestinal, musculoskeletal, and mental health symptoms.[3] Additionally, some patients are hypermobile and have clinical features consistent with hEDS, but do not fulfill the 2017 hEDS criteria[1] and are subsequently diagnosed with hypermobility spectrum disorder (HSD).

Due to the complex needs and multisystem involvement, children and adolescents with EDS often seek care from multiple health-care providers.[4,5] Multidisciplinary care is recommended for the treatment of EDS to improve coordination of care, reduce medical visits, and improve outcomes.[6] However, the development of a multidisciplinary care team is predicated on identifying the healthcare needs expressed by patients to inform which specialties are needed for inclusion in these clinics. If multidisciplinary care is not established, patients' expressed health needs can guide specialized referral pathways to meet patient care needs. As such, it is necessary to continually evaluate various medical and psychosocial needs relevant to children and adolescents with EDS. One area of generally unrecognized need is support of transgender and gender diverse (TGD) identity and the need for gender-affirming treatment and gender-affirming clinical practices.[7]

Little is known about children and adolescents with EDS who have gender dysphoria and/or express transgender identity. One recent study found that of adults undergoing gender-affirming surgery, 2.6% had a diagnosis of EDS, which is more than double of what is believed to be the incidence of TGD and 130 times the highest reported prevalence of EDS in the general population.[8] Further, transgender and gender affirming clinics have noted a disproportionate number of patients with EDS[8]; however, these data are limited and more localized to areas and institutions that provide gender-affirming medical care (GAMC). A recent casereport of adults with EDS noted a range of psychological symptoms associated with transvestism, including chronic pain, anxiety, and mood disorders.[9]

Gender dysphoria is defined as an incongruence between one's affirmed gender and the gender assigned at birth[10] and has a prevalence of 0.7% to 1.3% in children and adolescents. Though, the prevalence is higher among self-report[7,11] (Table 1). Several factors have been indicated as affecting the expression of TGD, including psychological factors and biological factors (e.g., identified through brain imaging).[12] In children and adolescents, gender dysphoria is associated with significant psychological distress,[13] including increased prevalence of anxiety, depression, social withdrawal, and suicidal ideation compared to the general population. Additionally, poorer psychological functioning is associated with greater social intolerance of gender dysphoria and gender nonconformity.[14] Conversely numerous studies have shown that GAMC improves mental health outcomes, reduces suicidality, and improves well-being of TGD children and adolescents.[15,16] Reports suggest an increase in number of referrals for GAMC for TGD children and adolescents and the need for resources and enhanced provider education to improve GAMC.[17] In response, clinical practice guidelines have been developed by the Endocrine Society to help guide GAMC.[18] To date, there have been no reports of prevalence of TGD youth in pediatric patients with EDS. The objective of this study was to characterize TGD adolescents with EDS seen in a pediatric multidisciplinary specialty clinic in the Midwest.

Methods and materials

A retrospective chart review was performed between January 2020 and May 2022. Patients were included if they were seen in the multidisciplinary Ehlers–Danlos clinic, had a diagnosis of EDS or HSD, and reported gender dysphoria or transgender identity. They were excluded if they were not seen in the multidisciplinary Ehlers–Danlos clinic, did not have a diagnosis of EDS or HSD, or did not report gender dysphoria. Twenty-eight patients were identified. Chart review included analysis of all documents in the electronic medical record, including demographic data, gender identity, chosen pronouns, specialty care previously received for EDS/HSD, symptoms and conditions related to EDS/HSD, and medications.

Statistical analysis

The results were analyzed, binary and categorical variables were summarized by frequency and percentage. All statistical analysis was completed using IBM Corporation, SPSS statistics for Windows version 24.0 software, Armonk, New York.

Ethical approval and informed consent

This work was conducted in accordance with the Declaration of Helsinki. Institutional review board approval was obtained from Children's Mercy Kansas City (IRB Study ID: 00001628) and it was determined that for this retrospective chart review formal consent was not required.

Results

Of the 166 total adolescents seen in the multidisciplinary EDS clinic during the study period, 28 (17%) reported gender dysphoria and were included in the analysis. There were 25 (89%) patients who were assigned female at birth and 3 (11%) who were assigned male at birth. Most (82%) had a diagnosis of hEDS, while the rest (18%) had a diagnosis of HSD. The average age at diagnosis of EDS/HSD was 13.5 years (range 8–17 years). Most (61%) reported their gender identity as transgender, followed by nonbinary (14%), fluid gender (11%), and agender (7%). Most had preferred male (he/him) pronouns (47%), followed by nonbinary (they/them) pronouns (39%), and female (she/her) pronouns (14%) (Table 2).

Clinical symptoms

The vast majority reported fatigue (75%); musculoskeletal issues (96%), which included joint and muscle pain; skin issues (78%), such as easy bruising, striae, and atrophic scars; cardiac issues (71%) such as dysautonomia (61%); gastrointestinal issues (68%), and neurologic issues (79%) (Table 2). Most also had prior cardiology evaluation (68%), half (50%) had prior physical therapy evaluation, while less than half had evaluation by clinical departments of rheumatology (43%), orthopedics (32%), neurology (32%), gastrointestinal (25%), endocrine/gender specialty (18%), gynecology (11%), sleep medicine (11%), and sports medicine (4%). In review of medication usage, 36% were on gender-affirming hormone therapy, 57% were on antidepressant, 21% were on anxiolytic, 61% were on an antihistamine, 39% were on a nonsteroidal anti-inflammatory medication, and 25% were on a sleep aid medication (Table 3).

Of the 28 total patients, most reported psychiatric issues (86%) during their EDS visit, including anxiety (75%) and depression (57%). Sixty-four percent reported a prior psychology or psychiatry evaluation, two patients reported self-harm, three reported sexual abuse, and four reported suicidal ideations in the past.

Table 2. EDS characteristics.

Characteristics	*n* (%)
Assigned female at birth	25 (89)
EDS subtype	
hEDS	23 (82)
HSD	5 (18)
Fatigue	21 (75)
Poor sleep	16 (57)
Weakness	10 (35)
Allergies	8 (29)
Gender identity	
Cisgender	1 (4)
Transgender	17 (61)
Nonbinary	4 (14)
Fluid	3 (11)
Agender	2 (7)
Unsure	1 (3)
Chosen pronouns	
Male	13 (47)
Female	4 (14)
Nonbinary	11 (39)
Head, ears, eyes, nose, and throat issues present	17 (61)
Musculoskeletal issues present	27 (96)
Joint pain	22 (79)
Muscle pain	10 (36)
Allodynia	5 (18)
Dermatology issues present	22 (79)
Mast cell activation syndrome	6 (21)
Psychiatric issues present	24 (86)
Depression	16 (57)
Anxiety	21 (75)
Attention deficit/hyperactivity disorder	6 (21)
Post-traumatic stress disorder	5 (18)
Cardiac issues present	20 (71)
Dysautonomia	17 (61)
Postural orthostatic tachycardic syndrome	8 (29)
GI issues present	19 (68)
Abdominal pain	13 (46)
Nausea	10 (36)
Gastroesophageal reflux	6 (21)
Diarrhea	4 (14)
Neurologic issues present	22 (79)
Headaches	21 (75)
Gynecologic issues present	13 (46)
Dysmenorrhea	11 (39)

Discussion

To our knowledge, this is the first report of TGD children and adolescents in the EDS population. Here we report that 17% of the EDS population in our multidisciplinary clinic self-report as TGD, which is dramatically higher than the national average of 1.3%.[7] The cause of the association between TGD and EDS is unclear, but these findings indicate the need for increased awareness of TGD and gender-nonconforming comorbid presentations in pediatric patients with EDS.

Table 3. Medications used by EDS/HSD patients.

Characteristics	*n* (%)
Total	28
Gender-affirming hormone therapy	10 (36)
Anxiolytic	6 (21)
Antidepressant	16 (57)
Other psychiatric medication	2 (7)
Antihistamine	17 (61)
Nonsteroid anti-inflammatory drug	11 (39)
Sleep aid medication	7 (25)

Identification of TGD is especially important as GAMC has the potential to improve mental health outcomes, reduce suicidality, and improve well-being for TGD children and adolescents.[15,16] As care for those with EDS is often complex and multidisciplinary, providers should take consideration to ask relevant screening questions to identify gender identity and to ensure gender-affirming healthcare environments that contribute to improved care and outcomes.[19]

There have been many reports that impairments are present in the psychosocial and emotional functioning in children and adolescents with TGD,[13] including higher rates of depression, suicidality, self-harm, and eating disorders.[11] Additionally, there are similar reports in individuals with EDS that show increased rates of anxiety, depression,[20] and suicide attempts[21] suggesting that both groups have a significant mental health burden. Our study was consistent with previous findings that a high percentage of mental health issues are present in those with EDS with 86% reporting psychiatric and mental health issues. Anxiety was the most reported mental health condition (75%), which is similar to previous reports of anxiety in EDS (70%),[22] and depression was the second most reported mental health condition (57%), which is higher than previous reports of depression in EDS (25%).[23] Suicidal ideation (14%) and self-harm (7%) were also reported in our cohort of TGD adolescents with EDS and is similar to national averages for adolescents in the United States.[24,25] Though this study is unable to determine whether the psychosocial difficulties associated with TGD are additive to the impairments already experienced by children and adolescents with EDS, it suggests that there are distinct needs associated with a self-reported TGD status.

In this study the majority (89%) identified as transmasculine as they were assigned female at birth, but do not identify as female presently. This finding is higher than previous reports that suggest 55%–61% of TGD adolescents identify as transmasculine.[16,26] Prior to 2005, the sex ratio of individuals with TGD was around 1:1. However, there has been a noted shift in referrals for TGD since 2006 with increase in female referrals versus male referrals, especially in the adolescent population.[27] The reason for shift is unclear and some have proposed sociological and sociocultural explanations. In this study, most adolescents seen in the multidisciplinary EDS clinic are assigned female at birth (>90%), which likely introduces a sex bias for our EDS population.

Most of the individuals in this study reported previous subspecialty care with evaluation by psychology or psychiatry, cardiology, and physical therapy. There were also many other visits across several other specialties, which can be common as healthcare utilization is high for patients with EDS.[5] Of the subspecialty care, 18% were seen in the endocrine gender specialty clinic, which provides GAMC. Subspecialty care and multidisciplinary care teams[28] are integral to the diagnosis and care of patients with EDS and are well positioned to be a referral source for gender-affirming care clinics, to help connect patients with needed clinical care. This study suggests that multidisciplinary EDS clinics should be mindful of their own clinical screenings and practices and adopt GAMC practices when possible (e.g., chosen pronoun usage, use of multiple gender labels when collecting demographic information); this may necessitate the development of clinical screening measures to identify this need in patients. Additionally, primary and subspecialty care providers who manage patients with EDS must be knowledgeable about the specific needs and local resources related to EDS so that patients can be properly and expeditiously triaged to the appropriate subspecialty or multidisciplinary teams.[29] A listing of gender specialty pediatric clinics nationwide can be found at https://www.hrc.org/resources/interactive-map-clinical-care-programs-for-gender-nonconforming-childr.

Our study has several limitations. This study included a small number of individuals that self-reported TGD or gender-nonconforming status, which precludes more sophisticated data analysis including structural equation modeling and subgroup analysis of individuals. However, this study consists of a large cohort of children and adolescents with EDS, and the number of TGD individuals in this population substantiate previously reported issues that are seen in individuals with TGD. Additionally, this study utilized a retrospective chart review design and may underestimate the number of children and adolescents with TGD and EDS who are not seen in our clinic or did not self-report TGD as clinic visits are conducted jointly with adolescent patients and with parents, a caregiver, or legal guardian, and adolescents who identify as TGD, but have not disclosed this information to their family, may not disclose their identity status to the medical team. In this article we have not tested causal relationships and therefore cannot answer the question of why children with EDS have higher risk for gender dysphoria. Speculation may suggest that minority stress related factors common to TGD children, such as increased depression, anxiety, social isolation, and lack of access to exercise could exacerbate EDS symptoms. Nonetheless, our goal is to encourage a gender-affirming healthcare environment to improve care and outcomes of EDS and to assist with

referrals to GAMC as appropriate. Also, documentation of co-occurring psychiatric diagnoses may not be reliable, as not all patients have a history of engaged psychiatric or psychological care. Additional work is needed to better characterize psychological co-diagnoses in patients with EDS and TGD versus those with either EDS or TGD alone. This cohort represents a convenience sample identified in the EDS clinic, which may introduce sample bias of increased clinical severity and need. Given that this was not a population-based study, the percentage of TGD seen in this clinic could be underestimated. Additionally, hEDS was the only EDS subtype represented in this study and it likely reflects the prevalence of hEDS compared to other EDS subtypes. However, these findings may be unique to hEDS and the conclusions may not be generalizable for other EDS subtypes. Future studies in a larger population with other EDS subtypes will allow for more detailed exploration of this cohort and these findings. Sample size calculations were not completed as this was a retrospective chart review and exploratory. Also, while clinical charts were reviewed for notes of deficits associated with psychological functioning, formal measures were not obtained from patients. Subsequently, this study cannot compare patients with TGD and EDS to patients with EDS only; future work in this area would clarify whether individuals with TGD are at an increased risk for psychological comorbidity compared to those with EDS and without TGD who are seen in clinic. Lastly, this study may not reflect a higher incidence of TGD in EDS patients compared to the normative population, but rather the data here may capture overall increasing rates of TGD seen in youth in the United States.[30]

Conclusion

Here we report the first cohort of TGD children and adolescents in the EDS population. There is an association between TGD and EDS, however, the cause is currently unclear. This report indicates that clinicians and multidisciplinary clinics that care for patients with EDS should be aware of TGD presentations. Identification of TGD and provision of GAMC have the potential to improve mental health outcomes, reduce suicidality, and improve well-being for TGD children and adolescents. Additionally, improvements in mental health and well-being for those with TGD and EDS may improve patient adherence to other medical recommendations. As care for those with EDS is often complex and multidisciplinary, providers should consider to ask relevant screening questions and adopt practices of GAMC that contribute to improved care and outcomes.

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Author contributions

JJ, WB, CM, ER, LMW equally contributed to the conception, drafting, and final version of the whole article. All authors read and approved the final article.

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References

1. Malfait F, Castori M, Francomano CA, et al. The Ehlers-Danlos syndromes. *Nat Rev Dis Primers* 2020; 6(1): 64.
2. Joseph AW, Joseph SS, Francomano CA, et al. Characteristics, diagnosis, and management of Ehlers-Danlos syndromes: a review. *JAMA Facial Plast Surg* 2018; 20(1): 70–75.
3. Tinkle B, Castori M, Berglund B, et al. Hypermobile Ehlers-Danlos syndrome (a.k.a. Ehlers-Danlos syndrome Type III and Ehlers-Danlos syndrome hypermobility type): clinical description and natural history. *Am J Med Genet C Semin Med Genet* 2017; 175(1): 48–69.
4. Williams SE, Tran ST, Lynch-Jordan A, et al. Healthcare utilization among youth with Ehlers-Danlos syndrome hypermobile type. *Am J Med Genet Part A* 2022; 188(4): 1109–1117.
5. Jones JT, Black WR, Cogan W, et al. Resource utilization and multidisciplinary care needs for patients with Ehlers-Danlos syndrome. *Mol Genet Genomic Med* 2022; 10(11): e2057.
6. Kalisch L, Hamonet C, Bourdon C, et al. Predictors of pain and mobility disability in the hypermobile Ehlers-Danlos syndrome. *Disabil Rehabil* 2020; 42(25): 3679–3686.
7. Zucker KJ. Epidemiology of gender dysphoria and transgender identity. *Sex Health* 2017; 14(5): 404–411.
8. Najafian A, Cylinder I, Jedrzejewski B, et al. Ehlers-Danlos syndrome: prevalence and outcomes in gender affirming surgery-a single institution experience. *Plastic Aesthetic Res* 2022; 9(5): 35.
9. Ishiguro H, Honobe N, Suzuki T, et al. Transvestism recognized in Ehlers-Danlos syndrome: report of two cases. *Case Rep Psychiatry* 2019; 2019: 7472301.
10. Beek TF, Cohen-Kettenis PT and Kreukels BP. Gender incongruence/gender dysphoria and its classification history. *Int Rev Psychiatry* 2016; 28(1): 5–12.
11. Connolly MD, Zervos MJ, Barone CJ, et al. The mental health of transgender youth: advances in understanding. *J Adolesc Health* 2016; 59(5): 489–495.
12. Leibowitz S and de Vries AL. Gender dysphoria in adolescence. *Int Rev Psychiatry* 2016; 28(1): 21–35.
13. Ristori J and Steensma TD. Gender dysphoria in childhood. *Int Rev Psychiatry* 2016; 28(1): 13–20.
14. Steensma TD, Zucker KJ, Kreukels BP, et al. Behavioral and emotional problems on the Teacher's report form: a cross-

national, cross-clinic comparative analysis of gender dysphoric children and adolescents. *J Abnorm Child Psychol* 2014; 42(4): 635–647.
15. Olson KR, Durwood L, DeMeules M, et al. Mental health of transgender children who are supported in their identities. *Pediatrics* 2016; 137(3): e20153223.
16. Tordoff DM, Wanta JW, Collin A, et al. Mental health outcomes in transgender and nonbinary youths receiving gender-affirming care. *JAMA Netw Open* 2022; 5(2): e220978.
17. Chen M, Fuqua J and Eugster EA. Characteristics of referrals for gender dysphoria over a 13-year period. *J Adolesc Health* 2016; 58(3): 369–371.
18. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an endocrine society clinical practice guideline. *Endocr Pract* 2017; 23(12): 1437.
19. The Joint Commission. *Advancing effective communication, cultural competence, and patient- and family-centered care for the lesbian, gay, bisexual, and transgender (LGBT) community: A Field Guide*. Oak Brook, IL: The Joint Commission, October 2011. LGBTFieldGuide.pdf.
20. Kennedy M, Loomba K, Ghani H, et al. The psychological burden associated with Ehlers-Danlos syndromes: a systematic review. *J Osteopath Med* 2022; 122(8): 381–392.
21. Bulbena-Cabre A, Baeza-Velasco C, Rosado-Figuerola S, et al. Updates on the psychological and psychiatric aspects of the Ehlers-Danlos syndromes and hypermobility spectrum disorders. *Am J Med Genet C Semin Med Genet* 2021; 187(4): 482–490.
22. Bulbena A, Baeza-Velasco C, Bulbena-Cabre A, et al. Psychiatric and psychological aspects in the Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet* 2017; 175(1): 237–245.
23. Hershenfeld SA, Wasim S, McNiven V, et al. Psychiatric disorders in Ehlers-Danlos syndrome are frequent, diverse and strongly associated with pain. *Rheumatol Int* 2016; 36(3): 341–348.
24. Xiao Y, Cerel J and Mann JJ. Temporal trends in suicidal ideation and attempts among US adolescents by sex and race/ethnicity, 1991–2019. *JAMA Netw Open* 2021; 4(6): e2113513.
25. Monto MA, McRee N and Deryck FS. Nonsuicidal self-injury among a representative sample of US adolescents, 2015. *Am J Public Health* 2018; 108(8): 1042–1048.
26. Becerra-Culqui TA, Liu Y, Nash R, et al. Mental health of transgender and gender nonconforming youth compared with their peers. *Pediatrics* 2018; 141(5): e20173845.
27. Aitken M, Steensma TD, Blanchard R, et al. Evidence for an altered sex ratio in clinic-referred adolescents with gender dysphoria. *J Sex Med* 2015; 12(3): 756–763.
28. Bathen T, Hangmann AB, Hoff M, et al. Multidisciplinary treatment of disability in Ehlers-Danlos syndrome hypermobility type/hypermobility syndrome: a pilot study using a combination of physical and cognitive-behavioral therapy on 12 women. *Am J Med Genet Part A* 2013; 161A(12): 3005–3011.
29. Jones JT and Black WR. Provider knowledge and experience in care, management, and education of pediatric Ehlers-Danlos syndrome. *Glob Pediatr Health*. Epub ahead of print 19 July 2022. DOI: 10.1177/2333794X221112841.
30. Herman JL, Flores AR and O'Neill KK. *How many adults and youth identify as transgender in the United States?*. Los Angeles, CA: The Williams Institute, UCLA School of Law. 2022.