

# Study on Gender Reassignment Procedures on Minors

*Response to HR 158 of the 2022 Regular Session*

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## Preface

House Resolution (HR) 158 of the 2022 Regular Legislative Session directed the Louisiana Department of Health (LDH) to conduct a study focused on the “risks associated with gender reassignment procedures on minors, including genital and non-genital surgeries, and chemical treatments such as puberty-blockers and cross-sex hormones.” HR 158 specified 10 questions to be answered (hereafter referred to as “Key Questions” [KQs]) but did not limit the study to these questions alone.<sup>1</sup> Study findings presented in this report include Louisiana Medicaid administrative data pertaining to procedures for gender dysphoria in minors (addressing KQ1—KQ4 and KQ8—KQ9) and a review of available published evidence and policy literature on the topic (addressing KQs 5—7 and KQ 10).

## Background on Gender Dysphoria

Gender dysphoria occurs when an individual experiences distress as the result of an incongruence between his or her experienced or expressed gender and his or her assigned gender.<sup>2</sup> The Diagnostic and Statistical Manual of Mental Disorders (DSM-V) provides guidance on terminology and definitions, currently identified as gender dysphoria (GD), and the DSM-V definition for GD is consistent with much of the published literature identified for this report.<sup>2</sup>

An important distinction exists for individuals with GD and those with disorders of sex development (e.g. intersex, ambiguous genitalia).<sup>2,3</sup> Disorders of sex development include chromosome anomaly syndromes (e.g., Klinefelter [XXY], Turner [X]) or where an individual born with XY or XX chromosomes does not develop external genitalia aligned with their chromosomal sex due to endocrine disorders (e.g., congenital adrenal hyperplasia).<sup>2,3</sup>

Youth under the age of 18 are a growing focus in policy, politics, and popular media with implications for parents and transgender youth. Estimates of youth, ages 13 to 17, identifying as transgender in the U.S. increased from 0.7% (2017) to 1.3% (2022).<sup>4,5</sup> Transgender youth and young adults report higher rates of depression, anxiety, and self-injury than their cisgender peers.<sup>6,7</sup> Generally, transgender youth and adults report unmet healthcare needs (e.g., preventive services, mental health) and are less likely to receive cancer screening compared to their cisgender peers.<sup>8–11</sup>

For youth, clinical guidelines recommend a multidisciplinary team to explore the youth’s experiences and feelings of gender incongruence in safe, nonjudgmental, and inclusive environments.<sup>12,13</sup> Medical treatment options include the use of gonadotropin-releasing hormone analogues (GnRHAs) commonly referred to as “puberty blockers” and cross-sex hormones (CSHs; e.g., estrogen, progesterone, testosterone).<sup>14,15</sup> The role of surgery in youth is limited, with professional societies recommending waiting until at least the age of majority to give consent.<sup>15</sup>

The care of youth identifying as transgender or gender diverse is an active area of study that has resulted in evidence-based standards of care for their diagnosis and treatment. All major medical societies in the U. S. endorse health coverage for evidence-based transition-related care for GD, including the American Medical Association, the American Academy of Pediatrics, the American Psychiatric Association, the American College of Obstetrics and Gynecology, and the Endocrine Society.<sup>16</sup>

Across this report we attempt to use consistent language, provided in the following glossary of terms and abbreviations (Box A).

<b>Box A. Glossary of Frequently Used Terms and Abbreviations</b>
<b>AFAB:</b> assigned female at birth
<b>AMAB:</b> assigned male at birth
<b>CSH:</b> cross-sex hormones, also known as gender-affirming hormones (e.g., estrogen, testosterone)
<b>GD:</b> gender dysphoria, or distress an individual can experience when their experienced or expressed gender is incongruent with their assigned gender <sup>a</sup>
<b>GID:</b> gender identity disorder (older definition from DSM-IV <sup>b</sup> , superseded by GD)
<b>GnRHAs:</b> gonadotropin-releasing hormone analogues (i.e., puberty blockers)
<b>TGD:</b> transgender or gender diverse
<sup>a</sup> Coleman et al., 2022
<sup>b</sup> DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4 <sup>th</sup> Edition

## Summary of Findings

Table 1 below provides a succinct summary of the results for each KQ posed in HR 158. Each KQ also has a detailed section in the body of the report dedicated to the data analyses performed and/or literature review that supports and expands on each finding.

<b>Table 1. Summary of Finding for HR 158 Key Questions</b>	
<b>Key Question (KQ)</b>	<b>Summary<sup>a</sup></b>
KQ1: The number and types of procedures performed annually ( <b>Table 4</b> )	<ul style="list-style-type: none"> <li>• Zero surgeries ever performed on minors (2017 to 2021)</li> <li>• Average of 14.6% of minors with GD received a CSH and/or GnRHa each year (2017 to 2021), with total number of minors treated each year as follows: 21, 33, 35, 35, and 57.<sup>b</sup></li> </ul>
KQ2: The historic trends in the number of procedures performed and the number of providers performing the procedures ( <b>Table 5</b> )	<ul style="list-style-type: none"> <li>• Surgeries performed remained at zero (2017 to 2021)</li> <li>• Use of CSHs and/or GnRHAs decreased since 2018</li> <li>• Number of providers decreased from a high of 18 in 2018 to 12 in 2021</li> </ul>
KQ3: The ages of the minors involved ( <b>Table 6</b> )	<ul style="list-style-type: none"> <li>• Among minors receiving CSHs and/or GnRHAs between 2017 to 2021, 24.5% were 10 to 14 years old and 75.5% were 15 to 17 years old</li> </ul>
KQ4: The number of providers performing the procedures and the number of clinics performing the procedures ( <b>Table 5</b> )	<ul style="list-style-type: none"> <li>• In 2021, zero providers performed surgeries on minors and 12 prescribed CSHs and/or GnRHAs</li> <li>• Unable to determine clinic number</li> </ul>
KQ5: An analysis of the psychological and psychiatric outcomes of minors who have undergone gender reassignment procedures	<ul style="list-style-type: none"> <li>• Psychiatric, or mental health outcomes (e.g., depression, suicidal ideation) improved after treatment and when compared to individuals not treated.</li> </ul>
KQ6: An analysis of the physical and medical outcomes of minors who have undergone gender reassignment procedures	<ul style="list-style-type: none"> <li>• Medical or physical health outcomes (e.g., blood pressure, lipids, glucose) varied across studies with some noting small changes (e.g., increased lipids) and others no difference.</li> <li>• The effect of GnRHAs on bone health is complicated by absence of long-term studies on the topic. Bone</li> </ul>

	density differences at baseline or increased frequency of vitamin D deficiency and sedentary lifestyle in transgender youth compared to their peers may bias outcomes.
KQ7: The propensity of minors who have undergone these procedures to regret or request services to return to their previous gender	<ul style="list-style-type: none"> <li>• Regret or retransition in youth is rare (1% or less) in large cohorts with formal diagnostic procedures after diagnosis of GD and start of treatment.</li> <li>• Not all youth expressing gender diverse thoughts or who self-identify as transgender or nonbinary go on to receive formal diagnosis or start medical treatments.</li> </ul>
KQ8: The amount of Medicaid funds used to cover the cost of gender reassignment procedures in this state (Table 7)	<ul style="list-style-type: none"> <li>• Approximately \$3,439.04 per enrollee receiving a chemical procedure in 2021 (\$196,025.50 total for the 57 enrollees who received treatment)</li> </ul>
KQ9: The availability of mental health counseling services for minors experiencing gender dysphoria (Table 9)	<ul style="list-style-type: none"> <li>• Across all nine regions, an average of 37% of all behavioral health providers who treat minors had provided any services to a Medicaid-enrolled minor in 2021, regardless of diagnosis.</li> </ul>
KQ10: A review of a minor's mental and cognitive capacity to consent to gender reassignment procedures	<ul style="list-style-type: none"> <li>• In Louisiana, a minor can consent to medical care in general without the consent of a parent or guardian.</li> <li>• Under the mature minor doctrine, a minor's age, maturity, and cognitive abilities are weighed when making a judicial determination of whether a minor who is otherwise legally incompetent is sufficiently mature to consent to their own medical care.</li> <li>• The American Academy of Pediatrics encourages the involvement of children beginning at age 7, with increasing involvement determined by age, including for those in the transgender population.</li> </ul>
<p><sup>a</sup>Louisiana data is based on Medicaid-enrolled minors.</p> <p><sup>b</sup>The total number of minors diagnosed with gender dysphoria (GD) in 2017 to 2021 was, respectively: 154, 179, 229, 264, and 465.</p> <p>Abbreviations: GD: gender dysphoria; CHS: cross sex hormone; GnRHAs: gonadotropin-releasing hormone analogues</p>	

This report specifically focuses on medical and surgical services for minors with gender dysphoria, however, there are other services available to support youth exploring their gender identity or seeking care. For example, since transgender youth with parental support report reduced depressive symptoms and higher life satisfaction compared to those without parental support, family therapy may be needed.<sup>17,18</sup> Also, because transgender youth report greater rates of unmet healthcare needs (e.g., preventive services, mental health), barriers to accessing the healthcare system that are unique to this population can be reduced, such as stigma.<sup>8-11</sup>

## Section 1 – Overview of Louisiana Data on Gender Dysphoria in Minors (KQ1—KQ4 and KQ8—KQ9)

### Subsection 1.1—Utilization of Medicaid Administrative Data

The number of Louisiana minors who identify as transgender has been estimated through statistical modeling of national and state-level survey data. For example, approximately 4,000 (1.3%) Louisiana adolescents ages 13 to 17 identify as transgender.<sup>4</sup> Exact counts of Louisiana minors who are diagnosed with gender dysphoria, or who receive physical or behavioral health interventions for gender dysphoria, are difficult to track, however, because patients and their providers may use multiple health systems, insurance carriers, and/or self-pay services. **Therefore, for the purposes of this report, estimates of the numbers of minors and providers receiving or providing care related to gender dysphoria were limited to Louisiana Medicaid members, for whom administrative data is available.** Of note, gender affirming surgery is not currently covered in Louisiana fee-for-service Medicaid; however, managed care organizations may pay for this service if deemed medically necessary.

### Subsection 1.2—Parameters for Data Extraction

Business Analytics staff within the Medicaid agency at LDH extracted administrative data – the majority of which was based on Medicaid billing – that was necessary to address the following six key questions (KQs): KQ1—KQ4 and KQ8—KQ9. The results of the data analyses are described and interpreted in each respective subsection below.

Minor’s ages were defined as their age on January 1 of each study year, and they are represented by three general categories in this report: pre-adolescence (less than 10 years of age), early adolescence (approximately 10 to 14 years old), and middle adolescence (approximately 15 to 17 years old). Late adolescence (approximately 18 years old to the early 20s) was not included since HR 158 was only applicable to legal minors (ages younger than 18). The adolescent developmental stages represented by the age categories used in the report represent significant and distinct changes in children’s physical, cognitive, sexual, social, and emotional growth that are part of a normal transition to adulthood.

Utilization trends for the report were obtained by extracting data for 2017 through 2021, allowing five years of complete data. Although the report was compiled in 2022, administrative data for 2022 was not complete until 2023 and therefore unavailable for comparable reporting.

The study population was identified as having of one or more of the following ICD- 10 diagnosis or encounter codes (Table 2):

Administrative Code	Description
F64.2	Gender identity disorder of childhood
F64.8	Other gender identity disorders
F64.9	Gender identity disorder, unspecified
Z87.890	Personal history of sex reassignment

The resulting number and proportion of minors enrolled in Medicaid with a diagnosis related to gender dysphoria or sex reassignment is shown below in Table 3, by year and age group.

<b>Table 3. Medicaid-Enrolled Minors with Gender Dysphoria (GD)<sup>a</sup></b>			
<b>Age (years)</b>	<b>Enrollees with GD (n)</b>	<b>Total Enrollees (n)</b>	<b>Proportion with GD</b>
<b>2017</b>			
<b>Less than 10</b>	11	493,177	0.002%
<b>10—14</b>	67	206,010	0.033%
<b>15—17</b>	76	115,462	0.066%
<b>Total</b>	154	814,649	0.019%
<b>2018</b>			
<b>Less than 10</b>	12	476,210	0.003%
<b>10—14</b>	78	205,325	0.038%
<b>15—17</b>	89	112,574	0.079%
<b>Total</b>	179	794,109	0.023%
<b>2019</b>			
<b>Less than 10</b>	8	470,248	0.002%
<b>10—14</b>	117	206,619	0.057%
<b>15—17</b>	104	110,301	0.094%
<b>Total</b>	229	787,168	0.029%
<b>2020</b>			
<b>Less than 10</b>	9	459,042	0.002%
<b>10—14</b>	134	207,948	0.064%
<b>15—17</b>	121	110,854	0.016%
<b>Total</b>	264	777,844	0.034%
<b>2021</b>			
<b>Less than 10</b>	10	466,067	0.002%
<b>10—14</b>	269	212,981	0.126%
<b>15—17</b>	186	115,731	0.161%
<b>Total</b>	465	794,779	0.059%
<sup>a</sup> Enrollees with gender dysphoria defined as those with any of the following <i>Current Procedural Technology (CPT)</i> <sup>19</sup> Psychotherapy-related Codes: F64.2, F64.8, F64.9, and/or ICD-10 code Z87.890			

## **Section 2 –The Number and Types of Procedures Performed Annually (KQ1)**

“Gender reassignment procedures” were defined in HR 158 to include “genital and non-genital surgeries, and chemical treatments such as puberty-blockers and cross-sex hormones.”<sup>1</sup> The administrative codes and specific medications used to identify these procedures are described in



Appendix A. Total numbers of unique children with Medicaid claims that indicate the receipt of one of these procedures are shown below (Table 4), by year and age group.

Table 4. Number and Types of Procedures Performed Annually on Medicaid-Enrolled Minors with Gender Dysphoria (GD) (KQ1)						
Age (years)	Minors with GD (n)	Minors Treated with Surgical Procedures (n, %)	Minors Treated with Chemical Procedures, by Medication Type			Minors Treated with Any Chemical Procedure (n, %) <sup>a</sup>
			GnRHAs (n)	CSH (n)	Both GnRHAs and CSH	
<b>2017</b>						
Less than 10	11	0 (0.0)	0	0	0	0 (0.0)
10–14	67	0 (0.0)	4	4	1	7 (10.4)
15–17	76	0 (0.0)	1	14	1	14 (18.4)
<b>Total</b>	<b>154</b>	<b>0 (0.0)</b>	<b>5</b>	<b>18</b>	<b>2</b>	<b>21 (13.6)</b>
<b>2018</b>						
Less than 10	12	0 (0.0)	0	0	0	0 (0.0)
10–14	78	0 (0.0)	7	1	1	7 (9.0)
15–17	89	0 (0.0)	1	26	1	26 (29.2)
<b>Total</b>	<b>179</b>	<b>0 (0.0)</b>	<b>8</b>	<b>27</b>	<b>2</b>	<b>33 (18.4)</b>
<b>2019</b>						
Less than 10	8	0 (0.0)	0	0	0	0 (0.0)
10–14	117	0 (0.0)	6	6	3	9 (7.7)
15–17	104	0 (0.0)	3	25	2	26 (25.0)
<b>Total</b>	<b>229</b>	<b>0 (0.0)</b>	<b>9</b>	<b>31</b>	<b>5</b>	<b>35 (15.3)</b>
<b>2020</b>						
Less than 10	9	0 (0.0)	0	0	0	0 (0.0)
10–14	134	0 (0.0)	2	8	2	8 (6.0)
15–17	121	0 (0.0)	4	26	3	27 (22.3)
<b>Total</b>	<b>264</b>	<b>0 (0.0)</b>	<b>6</b>	<b>34</b>	<b>5</b>	<b>35 (13.3)</b>
<b>2021</b>						
Less than 10	10	0 (0.0)	0	0	0	0 (0.0)
10–14	269	0 (0.0)	3	9	1	11 (4.1)
15–17	186	0 (0.0)	3	45	2	46 (24.7)
<b>Total</b>	<b>465</b>	<b>0 (0.0)</b>	<b>6</b>	<b>54</b>	<b>3</b>	<b>57 (12.3)</b>
<sup>a</sup> Minors are counted only once if they were treated with both a puberty blocker and a cross-sex hormone in the same year Abbreviations. GnRHAs: gonadotropin-releasing hormone analogues (i.e., puberty blockers); CSH: cross-sex hormones						

## Section 3 – The Historic Trends in the Number of Procedures Performed and the Number of Providers Performing the Procedures (KQ2)

In the five years represented by this report (2017 through 2021), there were no surgical procedures performed on Medicaid-enrolled children under the age of 18 for the purposes of gender reassignment, and there were also no providers identified who were performing surgical procedures on this population.

The number of providers prescribing chemical treatments for gender dysphoria (e.g., CSHs and/or GnRHAs) showed an overall decrease from 2017 to 2021, as shown below in Table 5:

Table 5. Trends in the Number of Procedures Performed and the Number of Providers Performing the Procedures on Medicaid-Enrolled Minors (under age 18 years) (KQ2)		
Year	Minors Treated with Chemical Procedures (n)	Prescribers of Chemical Treatments to Minors (n)
2017	21	16
2018	33	18
2019	35	17
2020	35	12
2021	57	12

## Section 4 – The Ages of the Minors Involved (KQ3)

The total number of minors diagnosed with GD increased by about 200% between 2017 (n = 154) and 2021 (n = 465), as shown above in Table 4. The number of minors treated with chemical procedures (e.g., CSHs and/or GnRHAs) increased by about 170%, as shown below in Table 6. Also shown in Table 6 is that the proportion of minors in each age group who were treated remained roughly the same over the last four years, with about 20-25% of those treated being between the ages of 10 to 14, and about 75-80% being between the ages of 15 to 17.

Table 6. Ages of Medicaid-Enrolled Minors Treated with Chemical Procedures (KQ3)			
Year (n=total treated)	Age Groups (years)		
	Less than 10 (n, %)	10-14 (n, %)	15-17 (n, %)
2017 (n = 21)	0 (0)	7 (33.3)	14 (66.7)
2018 (n = 33)	0 (0)	7 (21.2)	26 (78.8)
2019 (n = 35)	0 (0)	9 (25.7)	26 (74.3)
2020 (n= 35)	0 (0)	8 (22.9)	27 (77.1)
2021 (n = 57)	0 (0)	11 (19.3)	46 (80.7)

## Section 5 – The Number of Providers Performing the Procedures and the Number of Clinics Performing the Procedures (KQ4)

For years 2017 through 2021, there were no providers identified through Medicaid administrative data who performed surgical procedures on minors, and there was a range of 12 to 18 total providers who prescribed chemical treatments to minors, specifically CSHs and/or GnRHAs (see Table 5 above).

Medicaid administrative data allows identification of billing provider, servicing provider, referring provider, or the prescribing provider associated with a pharmacy claim, however, provider information on a pharmacy claim is not linked to prescriber location or clinic site. Therefore, administrative data was not useful for revealing the number of clinics performing procedures and the total provider number does not necessarily correlate with the number of clinic sites. For example, the 12 individual providers who prescribed chemical treatments to minors in 2021 may have treated those patients from more or fewer than 12 individual sites.

## Section 6 – The Amount of Medicaid Funds Used to Cover the Cost of Gender Reassignment Procedures in this State (KQ8)

<b>Year (n=total treated)</b>	<b>Total Cost</b>	<b>Average Cost Per Enrollee Receiving Chemical Procedures</b>
<b>2017 (n = 21)</b>	\$61,444.96	\$2,925.95
<b>2018 (n = 33)</b>	\$172,998.12	\$5,242.37
<b>2019 (n = 35)</b>	\$193,031.79	\$5,515.19
<b>2020 (n = 35)</b>	\$120,072.98	\$3,430.66
<b>2021 (n = 57)</b>	\$196,025.50	\$3,439.04

<sup>a</sup> There were no known surgical treatments in minors and so none paid for with Medicaid funds.

## Section 7 – The Availability of Mental Health Counseling Services for Minors Experiencing Gender Dysphoria (KQ9)

Based on estimated rates of GD among adolescents (1.3%), roughly 2,000 Medicaid-enrolled adolescents would be expected to have GD in Louisiana.<sup>4,20</sup> However, rates identified through Medicaid administrative data reveal that far fewer adolescents receive a formal diagnosis of GD, as shown in Table 8 below. Additionally, given higher rates of depression and suicidal ideation among adolescents with GD compared to their peers, the number of adolescents with depression and suicidal ideation reported in Table 8 are likely much lower than what is actually experienced due to GD among Medicaid-enrolled adolescents in the state.<sup>6,7</sup>

<b>Age (years)</b>	<b>Enrollees with GD (n)</b>	<b>Enrollee with GD and Depression (n, %)<sup>a</sup></b>	<b>Enrollees with GD and Suicidal Ideation (n, %)<sup>b</sup></b>
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<b>2017</b>			
<b>Less than 10</b>	11	1 (9.1)	0 (0.0)
<b>10—14</b>	67	36 (53.7)	25 (37.3)
<b>15—17</b>	76	32 (42.1)	18 (23.7)
<b>Total</b>	<b>154</b>	<b>69 (44.8)</b>	<b>43 (27.9)</b>
<b>2018</b>			
<b>Less than 10</b>	12	1 (8.3)	1 (8.3)
<b>10—14</b>	78	54 (69.2)	35 (44.9)
<b>15—17</b>	89	42 (47.2)	19 (21.3)
<b>Total</b>	<b>179</b>	<b>97 (54.2)</b>	<b>55 (29.1)</b>
<b>2019</b>			
<b>Less than 10</b>	8	0 (0.0)	0 (0.0)
<b>10—14</b>	117	72 (61.5)	49 (41.9)
<b>15—17</b>	104	53 (51.0)	32 (30.8)
<b>Total</b>	<b>229</b>	<b>125 (54.6)</b>	<b>81 (35.4)</b>
<b>2020</b>			
<b>Less than 10</b>	9	1 (11.1)	1 (11.1)
<b>10—14</b>	134	85 (63.4)	62 (46.3)
<b>15—17</b>	121	67 (55.4)	37 (30.6)
<b>Total</b>	<b>264</b>	<b>153 (58.0)</b>	<b>100 (37.9)</b>
<b>2021</b>			
<b>Less than 10</b>	10	3 (30.0)	1 (10.0)
<b>10—14</b>	269	184 (68.4)	132 (49.1)
<b>15—17</b>	186	99 (53.2)	50 (26.9)
<b>Total</b>	<b>465</b>	<b>286 (61.5)</b>	<b>183 (39.4)</b>
<sup>a</sup> Depression was defined as enrollees with an ICD-10 diagnosis code <sup>21</sup> beginning with F32, representing a depressive episode <sup>b</sup> Suicidal Ideation was defined as enrollees with an ICD-10 diagnosis code <sup>21</sup> of R45.851, defined as having thoughts of committing suicide			

There are no current measures for monitoring the availability of mental health counseling services for youth with gender dysphoria, and any psychiatrist or licensed mental health professional who treats minors may also be a provider for youth with gender dysphoria. However, we were able to assess the number of unique providers who are enrolled with Medicaid managed care organizations and are accepting members under the age of 18. This was compared to the count of unique providers who submitted any administrative claims for their care of minors, regardless of diagnosis, and stratified by Region. There was wide variability in the provision of care to Medicaid-enrolled minors across Regions. However, in 2021 every Region had less than 54% of its Medicaid-enrolled providers submitting claims reflecting the provision of care for a Medicaid-enrolled minor. Across all nine regions, an average of 37% of all Medicaid-enrolled providers who treat minors had provided any services to a Medicaid-enrolled minor in 2021, regardless of diagnosis. Detailed results are shown in Table 9 below.

**Table 9. Availability of Mental Health Services for all Medicaid-Enrolled Minors, by Region (KQ9)**

State Region	Total Medicaid-Enrolled Minors (n)	Medicaid-Enrolled Minors Receiving Common Mental Health Services (n, %) <sup>a</sup>	Providers Accepting Medicaid-Enrolled Minors (<18) <sup>b</sup>	Providers Treating Medicaid-Enrolled Minors (n)	Proportion of Providers who Accept Medicaid who Treat Medicaid Enrolled Minors (%)
<b>2019</b>					
1	152518	11785 (7.7)	1184	305	25.8
2	120260	9192 (7.6)	766	268	35.0
3	68884	6178 (9.0)	364	198	54.4
4	108044	6798 (6.3)	447	207	46.3
5	53244	4114 (7.7)	222	139	62.6
6	55075	5264 (9.6)	277	191	69.0
7	94436	7656 (8.1)	584	177	30.3
8	69262	7524 (10.9)	441	167	37.9
9	93346	9117 (9.8)	580	223	38.4
<b>2020</b>					
1	148663	8927 (6.0)	1314	287	21.8
2	116902	7760 (6.6)	985	245	24.9
3	68307	5632 (8.2)	473	198	41.9
4	108114	6295 (5.8)	579	202	34.9
5	52616	3330 (6.3)	374	139	37.2
6	54173	5209 (9.6)	416	192	46.2
7	92810	7023 (7.6)	692	147	21.2
8	67837	6701 (9.9)	529	142	26.8
9	93664	8001 (8.5)	769	234	30.4
<b>2021</b>					
1	150411	9260 (6.2)	1330	277	20.8
2	122606	7887 (6.4)	945	257	27.2
3	69266	6226 (9.0)	442	222	50.2
4	111393	7007 (6.3)	498	222	44.6
5	53194	3485 (6.6)	307	148	48.2
6	55005	5754 (10.5)	380	205	53.9
7	94592	7232 (7.6)	621	157	25.3
8	68523	6767 (9.9)	487	161	33.1
9	97878	8976 (9.2)	715	235	32.9
<p><sup>a</sup> Behavioral Health Services defined as those with any of the following <i>Current Procedural Technology (CPT)</i><sup>19</sup> Psychotherapy-related Codes: 90785, 90791, 90792, 90845, 90832, 90833, 90834, 90836, 90837, 90838, 90839, 90840, 90846, 90847, 90849, and 90853</p> <p><sup>b</sup> Represents counts of psychiatrists and other Licensed Mental Health Professionals reported by the Managed Care Organizations as accepting members under the age of 18</p>					

## Section 8 – Overview of Available Evidence for Treatment Outcomes (KQ5-7)

Guidance on treatment options for GD in youth are available from international and national sources. Examples of guidelines intended for a global audience of clinicians include the Endocrine Society and the World Professional Association for Transgender Health (WPATH).<sup>14,15</sup> Examples of national guidelines include the Australian Standards of Care from the Royal Children’s hospital in Melbourne and the American Academy of Pediatrics.<sup>12,22</sup>

For youth, clinical guidelines recommend a multidisciplinary team to explore the youth’s experiences and feelings of gender incongruence in safe, nonjudgmental, and inclusive environments.<sup>12,13</sup> Resources should be offered to families and caregivers as well as the youth.<sup>12</sup> Treatment options include social transition, medical treatment, and rarely surgery in certain cases for youth.<sup>12</sup> Social transition includes the use of pronouns, dress, and age-appropriate play that align with the youth’s affirmed gender.<sup>12</sup> Medical treatment options include the use of gonadotropin-releasing hormone analogues (GnRHAs) commonly referred to as “puberty blockers” and cross-sex hormones (CSHs; e.g., estrogen, testosterone).<sup>14,15</sup>

Clinical practice has evolved over time to consider puberty suppression to earlier ages, before puberty to avoid the development of unwelcome secondary sex features (e.g., breasts, voice deepening).<sup>12</sup> The timing of medical treatments is based on puberty development and so is unique to each patient.<sup>12</sup>

The role of surgery in youth is limited, and WPATH recommended waiting until at least the age of majority to give consent with at least 12 months of CSH use and congruent living in gender role.<sup>15</sup> The duration of hormone use is addressed in WPATH without any age specifications.<sup>13</sup>

### Subsection 8.1 – Literature Search Methodology

LDH contracted with the Center for Evidence-Based Policy to assist in a review of the clinical evidence available to address KQs 5–7. Researchers at the Center selected the most robust evidence source(s) available through a search of Ovid MEDLINE for relevant published literature (e.g., systematic reviews [SRs], randomized controlled trials [RCTs], observational studies) published from January 1, 2012, through October 31, 2022. Researchers only reviewed one additional study outside of this search methodology because it was published immediately prior to the release of this report in January 2023.<sup>23</sup> Researchers also searched reference lists of included studies. The search strategy sought longitudinal, comparative studies (e.g., outcomes for youth with GD receiving medical or surgical treatment compared with those not receiving treatment, pre-treatment compared to post-treatment). Noncomparative studies were included only if there were no comparative studies identified for a KQ. Evidence was included if it was published in English from 2012 to present. Researchers excluded studies if they only enrolled individuals over 18 years of age (unless they clearly reported outcomes for individuals starting treatment under age 18), narrative reviews, or individual studies included in an eligible systematic review. A full description of the search strategy and methods is provided in Appendix C.

The majority of participants in the studies were white, of higher socioeconomic backgrounds, and many studies with larger sample sizes or longitudinal data were conducted in European countries with national health care systems.<sup>24–30</sup> The included studies as such are unlikely to represent the transgender and gender-diverse population of youth in the U.S.

## Subsection 8.2 – Limitations of Clinical Evidence

Limitations across SRs and individual studies include the small number of individuals enrolled in each study, variation in outcome assessment tools used, inconsistent follow-up durations, and selection bias.<sup>24–26</sup> While meta-analysis could synthesize and account for the large number of small studies, the use of different outcome measures prevents authors from using this technique in SRs.<sup>24–26</sup> Long-term studies (e.g., over 12 months) are rare, especially physical or medical health studies. Rarely is a contemporaneous comparison group used. Studies also represent outcomes from a predominantly white, higher socioeconomic, and nationalized health care perspective, which limits the generalizability of these findings to the U.S.<sup>24–26</sup>

Additionally, studies approached enrollment differently, with many requiring a formal diagnosis of GD through a centralized clinic while others included youth reporting gender-diverse tendencies (via electronic health record) or self-identification as TGD.<sup>28,30–32</sup> These different definitions may capture disparate populations, making comparisons difficult. Studies from centralized clinics report long wait times to receive services, and this may select for a more motivated, more supported, or more affected (i.e., more dysphoric) individuals.

Across the SRs, search strategies appeared limited based on the number of citations identified compared to this review.<sup>24–26</sup> An additional limitation to search strategies may be insufficient indexing for articles in this field. Finally, there are several long-term cohort studies underway which may address many of the shortcomings of the current literature.<sup>33–35</sup>

## Section 9 – Psychological and Psychiatric Outcomes of Minors who have Undergone Gender Reassignment Procedures (KQ5)

All three SRs and an additional eight individual studies reported psychological or psychiatric outcomes.<sup>23–26,36–43</sup> Interventions from the eight individual studies were CSHs alone (two studies),<sup>40,42</sup> any hormone treatment (four studies),<sup>36,38,41</sup> {NEJM 2023} or surgery (two studies).<sup>39,43</sup>

Relevant outcomes included suicidality, body image, anxiety, and depression. Tools to assess anxiety, depression, or suicidality outcomes included the Center for Epidemiological Studies Depression Scale (CES-D),<sup>38</sup> General Anxiety Disorder-7 (GAD-7),<sup>36,40</sup> the Patient Health Questionnaire (PHQ9) which includes questions on self-harm and suicidal thoughts, the Beck Depression Inventory–II, the Revised Children’s Manifest Anxiety Scale (Second Edition).<sup>23</sup> Studies also reported engagement in treatment (e.g., medications, counseling, visits) for these conditions.<sup>41,42</sup> Quality of life or self-worth assessments included the Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q-SF)<sup>38</sup> and the Positive Affect and Life Satisfaction measures from the NIH (National Institutes of Health) Toolbox Emotion Battery.<sup>23</sup> Other studies assessed chest dysphoria, transgender congruence, and body image satisfaction.<sup>23,39,43</sup>

Appendix D contains further details on the individual studies reporting psychological or psychiatric outcomes used to respond to KQ5.

### Subsection 9.1—Medical Treatments

#### Any Hormone Treatment (GnRHAs or CSHs)

In an SR of studies published through 2021, D’hoore and T’Sjoen identified six studies reporting mental health outcomes in adolescents on any form of hormone treatment (e.g., GNRHAs, CSHs).<sup>26</sup> Overall,

studies reported improved psychological function compared to cisgender controls (one study), global function (one study), body satisfaction (three studies), depression (one study), and anxiety (one study).<sup>26</sup>

Three individual studies not included in SRs reported psychological outcomes after any hormone treatment (GNRHAs or CSHs).<sup>3,36,41</sup> Compared to a group of transgender or gender-diverse (TGD) youth not receiving treatment, levels of depression (adjusted odds ratio [aOR], 0.40; 95% confidence interval [CI], 0.17 to 0.95;  $P = .04$ ) and self-harm or suicidal thoughts (aOR, 0.27; 95% CI, 0.11 to 0.65;  $P = .003$ ) improved while severe anxiety did not.<sup>36</sup> The cohort of individuals untreated also experienced increased likelihood of severe depression or self-harm over time compared to their baseline.<sup>36</sup> In a separate study comparing pre- and post-treatment, depression symptoms and suicidal ideation improved.<sup>3,8</sup> In a cohort of TGD youth receiving care through the U.S. Military system, no significant difference was observed in the number of health visits before compared to after the initiation of treatment.<sup>41</sup> However, the number of medication days (based on prescription data) improved after treatment across many different classes of medication (e.g., anxiety, depression, attention disorders). The study does not have data on whether symptoms or conditions improved with higher number of medication days.<sup>41</sup>

#### GNRHAs

In an SR of 13 studies published through 2017, Chew and colleagues reported improvement in global functioning (three studies), depression (two studies), and behavioral problems (two studies) with GnRHAtreatment.<sup>25</sup> The authors also noted the limited number of small observational studies in this field. The authors highlighted that although hormonal treatment is associated with greater physical alignment of appearance, the effect on psychosocial or cognitive outcomes is uncertain.<sup>25</sup>

#### Cross-sex Hormones

One SR searched for studies on CSH and reported GD improvements (one study) and body dissatisfaction (one study).<sup>25</sup> The authors highlighted the high risk of selection bias and small sample sizes.<sup>24</sup>

One cohort study reported a significant reduction in the number of individuals needing treatment for depression, anxiety, and suicidality or self-harm after CSHs compared to before.<sup>42</sup> A second study did not observe significant improvements in depression, anxiety, or suicidal thoughts four months after CSH initiation.<sup>40</sup> However, a newly released US-based prospective, two-year longitudinal study with a large sample size ( $n = 315$ ) reported decreased anxiety and depression with use of CSH.<sup>23</sup>

### **Subsection 9.2. Surgical Treatments**

In both studies reporting psychological outcomes following chest reconstruction (e.g., mastectomy), symptoms of chest dysphoria, transgender congruence, and body image improved overall.<sup>39,43</sup> However, only one of the two studies reported statistically significant improvement for chest dysphoria (higher mean score is worse dysphoria; control, 29.6 vs. post-surgery, 3.3;  $P < .001$ ).<sup>43</sup> In a separate study of adolescents assessed prior to any treatment and then followed up after hormone therapy and surgery (all surgeries occurred after age 18) measures of self-worth and physical appearance improved, but no statistical analysis was performed.<sup>37</sup>

## **Section 10 – Physical and Medical Outcomes of Minors who have Undergone Gender Reassignment Procedures (KQ6)**

There were three SRs and four individual studies identified that reported on medical or physical health outcomes for individuals with GD seeking services.<sup>24–26,44–47</sup> Only one individual study followed youth (12 years of age and older) post-chest surgery (i.e., mastectomy),<sup>46</sup> with the rest of the included studies



comparing outcomes, generally pre- versus post-hormone treatment (e.g., GNRHAs alone, CSHs alone, both GNRHAs and CSHs).<sup>24–26,44,45,47</sup> No studies reported comparative data for all-cause mortality or costs.

Regarding adverse events, studies reported on bone density alterations (but not fractures).<sup>45</sup> Bone mineral density is traditionally assessed by a radiograph of the spine and hips. The density levels are then compared to standardized age and or sex-matched peers creating a z-score, reflecting the distance from normal range.<sup>48</sup>

One study reported on thrombotic events after CSHs.<sup>44</sup> The three SRs included studies reviewing metabolic changes after treatment (e.g., lipids, blood pressure). One study reported on the role of age at GNRHA initiation on need for surgery (e.g., mastectomy) or surgical approach (i.e., vaginoplasty).<sup>47</sup> Included studies are detailed in Appendix E.

## Subsection 10.1—Medical Treatments

### **Any Hormone Treatment (GnRHAs or CSHs)**

#### ***Bone Health***

Across three SRs, the authors narratively described all studies. The included studies reported on changes in bone health during GNRHA therapy and following CSH use.<sup>24–26</sup> There was a high degree of overlap of included studies across the three SRs with seven individual studies ultimately reviewed. The number of included participants ranged from 21 to 322. Although bone density remained stable during GNRHA treatment, z-scores decreased and were statistically significant in two of the three studies. Chew and colleagues reported that this represents a failure to gain expected density during this time in puberty.

The SRs note mixed effects on bone density for individuals receiving GNRHAs followed by CSHs.<sup>25,26</sup> In one study on bone density after GNRHA followed by years of CSH use, youth assigned male at birth (AMAB) and assigned female at birth (AFAB) gained bone density, however, their z-scores still remained lower than those of their peers.<sup>25</sup> Another study noted stable or small density decreases with decreased z-scores that did not catch up to peers after three years of CSH for AMAB, but did normalize for AFAB.<sup>26</sup> The largest study (n = 322) on GNRHAs followed by CSHs for at least two years observed similar bone characteristics for transgender youth to their aligned gender (as opposed to sex assigned at birth) when started in early puberty (age not specified) while those starting later aligned with the sex assigned at birth.<sup>26</sup>

The authors noted the findings are limited by small sample sizes, limited follow-up, and different measures across studies.<sup>25,26</sup> Additionally, the authors highlighted that even prior to initiation of CSHs, TGD individuals in the study all started with lower z-scores and significant differences in physical activity and vitamin D levels (i.e., lower) than their peers.

A single study reported outcomes after 12 months of GNRHA use, with no significant difference in height velocity for those receiving treatment compared to prepubertal controls.<sup>45</sup> The authors reported that for those initiating at later Tanner stages (4/5), their height velocity decreased compared to prepuberty controls (1.6 cm per year vs. 6.1 cm;  $P = .006$ ).<sup>45</sup> For studies on bone health, important covariates (e.g., baseline bone density compared to peers, vitamin D levels, physical activity) are not consistently included in analyses. No studies reported on fractures.



## **GnRHs**

### ***Metabolic Parameters***

Across two SRs, the metabolic profiles (e.g., cholesterol, insulin, glucose, blood pressure) of transgender youth after six to 12 months of treatment generally matched those of their cisgender peers (three studies).<sup>25,26</sup> The SR authors noted longitudinal studies are needed.<sup>25,26</sup>

### ***Surgical Considerations***

One study reported on timing of GNRHA by Tanner stage and implications for surgical approaches for gender-affirming surgery later in life.<sup>47</sup> All surgeries (e.g., mastectomies, vaginoplasties) occurred at 18 years or older. For AFAB individuals receiving GNRHAs at Tanner 2/3, mastectomy could be avoided in half of individuals (52.9% vs. 0 in TGD individuals never receiving GNRHAs; no statistical analysis). For individuals AMAB, initiating GNRHAs at an earlier Tanner stage (2/3) was associated with increased odds of needing a more complicated vaginoplasty procedure (odds ratio [OR], 84; 95% CI, 9.29 to 768.82) compared to transgender individuals AMAB never receiving GNRHAs.<sup>67</sup> The authors noted that providers should counsel patients and caregivers of these implications when discussing GNRHA initiation.<sup>47</sup>

## **CSHs**

### ***Metabolic Parameters***

The potential effect of CSHs on metabolic parameters includes an array of laboratory markers (e.g., lipid levels, insulin, and glucose) or vital signs (e.g., weight, body mass index, and blood pressure). D’Hoore and T’Sjoen identified two studies on CSHs and blood pressure, with no increases after estrogen use (2 studies).<sup>26</sup> Chew and colleagues noted that in one study weight and body mass index initially increased but returned to baseline at 12 months.<sup>25</sup> Progestins negatively affected some metabolic parameters (e.g., lipid profiles) but had no influence on others (e.g., glucose, insulin).<sup>25,26</sup> Neither metabolic parameters (three studies), nor blood pressure (one study) worsened with use of estrogen.<sup>25</sup> The majority of studies followed individuals for six to 12 months, and the SR authors noted that longitudinal studies are needed.<sup>25</sup>

In their SR, Mahfouda and colleagues identified one study reporting statistically significant decreases in high density lipoprotein levels with testosterone, with increases in blood pressure after two years (not reported if significant).<sup>24</sup> One individual study of individuals AFAB on testosterone observed no difference in body mass index after 12 months of use.<sup>45</sup>

## **Subsection 10.2—Surgical Treatments**

We did not identify any studies comparing physical or medical outcomes for youth with GD who did or did not undergo surgical treatments. However, we did identify a single study summarizing medical outcomes after chest surgery.<sup>46</sup>

A cohort study of youth (ages 12 to 18) with GD receiving care at Kaiser Permanente of Northern California from 2013 to 2020 reported outcomes following mastectomy (i.e., chest reconstruction).<sup>46</sup> In line with WPATH guidelines, eligibility for chest surgery included at least one year of hormone treatment and evaluation by a multidisciplinary team including licensed gender therapist. A total of 209 individuals, 87% identifying as male (10% as nonbinary, 3% as other), underwent mastectomy at a median age of 16 years.<sup>65</sup> Nearly all (88%) received testosterone treatment pre- and post-surgery. Overall, two individuals later reported regret, but neither underwent revision. Surgical complications included hematomas,

hypertrophic scars, infections, and seromas. Complications occurred in 3.5% or fewer of individuals. Of patients with at least one year of follow-up (n = 137), 7% (n = 15) underwent revisions due to complications.<sup>46</sup> These are lower complication rates compared to complication rates for patients undergoing mastectomy for breast cancer treatment which can range from 5% to 10%.<sup>49,50</sup>

## Section 11 – Propensity of Minors to who have Undergone These Procedures to “Detransition” to the Gender Aligned with their Biological Sex (KQ7)

This KQ reviews the evidence related to the propensity of minors to regret receiving services or request services to return to the gender assigned at birth.<sup>1</sup> Language and approach across studies varied regarding this concept. Studies reported GD diagnoses in a cohort of gender-diverse youth, receipt and continuation of medications, regret after surgery, and retransitions or detransition.

There were 13 publications identified (from eight cohorts) in youth or individuals starting treatment in their youth who were followed-up as adults.<sup>27–30,32,46,51–57</sup> Three publications are from a single center in the Netherlands using different subgroups.<sup>29,32,53</sup> The Amsterdam site originated the medical treatment approaches for youth with GD used in nearly all included studies.<sup>58</sup> Two publications are from the Gender Identity Development Service serving England and Wales.<sup>27,56</sup> Four publications are from the U.S, with two studies identifying youth by health system or insurance coverage by the U.S. Military Healthcare system (one study),<sup>28</sup> or Kaiser Permanente of Georgia, northern California, and southern California (one study).<sup>30</sup> The remaining two cohorts from the U.S. include a cohort of self-identified TGD youth from the ongoing, multisite Trans Youth Project<sup>28</sup> and individuals undergoing mastectomy (e.g., chest reconstruction) at a single Center.<sup>43</sup> The included studies are summarized in Appendix F.

Populations across studies differed in important ways. In eight cohorts, all participants obtained a formal diagnosis of GD from medical centers with standardized protocols.<sup>27,29,32,53–57</sup> In contrast, two studies included cohorts of young children who either fully socially transitioned before age 12 without a formal diagnosis<sup>28</sup> or expressed gender dysphoric behaviors without a formal diagnosis before age 18, based on medical record review.<sup>30</sup> One study used chart diagnoses of gender dysphoria to identify individuals without clear diagnostic criteria.<sup>52</sup> Detailed outcomes from larger cohort studies are described below.

### Subsection 11.1—Diagnosis of Gender Dysphoria

The Study of Transition, Outcomes, and Gender (STRONG) identified youth under 18 receiving healthcare across three sites within Kaiser Permanente (Georgia, northern California, and southern California) from 2006 to 2014.<sup>30,50</sup> Review of chart notes identified eligible individuals without a GD diagnosis through a search for terms and keywords (e.g., transgender, gender identity).<sup>30,33</sup> The cohort included 958 individuals, 431 AMAB (45%), 527 AFAB (55%), with 205 between the ages of 3 and 9 (21%), 300 between the ages of 10 and 14 (31%), and 453 were at least 15 years old(47%).<sup>30</sup> At an average of three years of follow-up (maximum nine years), 281 individuals (29%) received a diagnosis of GD and 236 (25%) initiated hormone treatment. Individuals who were older at their index visit had a significantly increased likelihood of receiving a GD diagnosis (adjusted hazard ratio [aHR], 2.7; 95% CI, 1.8 to 3.9 for ≥ 15 years; aHR, 2.0; 95% CI, 1.3 to 3.0 for 10 to 14 years, compared to 3 to 9 years of age at index visit). Initiation of hormone

treatment was more likely for AFABs compared to AMABs, (aHR, 2.5; 95% CI, 1.8 to 3.3). Compared to non-Hispanic white children, individuals from other racial or ethnic groups were marginally less likely to receive a diagnosis of GD (aHR, 0.8; 95% CI, 0.6 to 1.0) and significantly less likely to initiate hormone treatment (aHR, 0.6, 95% CI, 0.5 to 0.8).<sup>30</sup>

### Subsection 11.2—Continuation of Medical Treatments

Two large cohort studies (more than 500 individuals) reported on continuation of hormone treatment at follow-up for youth with GD diagnoses using different definitions to define their population.<sup>27,29,32,52,56</sup> Both cohorts were from single or national centers with protocols for diagnosis of GD and were located in countries with national health registries.<sup>27,29,32,56</sup> One additional study used data from the U.S. Military Healthcare System including transgender youth and adults receiving treatment hormone treatment.<sup>27</sup>

In a study from the Netherlands, of youth starting GNRHAs and continuing for at least three months (median age, 14.1 years for individuals AMAB and 16.0 years for individuals AFAB), 704 of 720 individuals (98%) continued to receive prescriptions for hormone treatment (GNRHAs or CSH based on age) at a median of six years follow-up for youth AMABs and three years for youth AFABs. In a separate study of the larger Amsterdam cohort (n = 1,360), only 1.9% of youth discontinued GNRHA treatment.<sup>29</sup>

In a study from England and Wales, the authors assessed outcomes for 1,089 of the 1,151 youth referred for assessment (the missing 66 either moved out of the country or self-discharged from the clinic).<sup>27</sup> Most of these youth (999 individuals, or 91.7%), continued to identify as transgender or gender variant. Ninety individuals (8.3%) no longer identified as transgender, and for 32 of this group (2.9% of original cohort), that decision arose after their initial consultation. After initiating either GNRHAs or CSHs, 58 (5.3% of original cohort) returned to cisgender identity, with a greater proportion of those under 16 stopping hormone treatment (GNRHA or CSH; 20 of 217, 9.2%) compared to those over 16 years of age (38 of 872, 4.4%). Masic and colleagues described outcomes for a smaller subset of individuals receiving care from 2018 to 2019, with only 6.9% of those initiating GNRHAs stopping (most often for reasons unknown).<sup>56</sup>

A cohort study from the U.S. Military healthcare system identified children and spouses (but not active duty members) with a transgender-related diagnosis code on at least two encounters between 2009 and 2018 who received two or more prescriptions for CSHs.<sup>52</sup> Of individuals receiving two prescriptions, 668 of 952 (70.2%) went on to continue to receive prescriptions for at least four years. Discontinuing treatment was significantly more common for those older than 18 at time of CSH initiation (hazard ratio [HR], 1.69; 95% CI, 1.14 to 2.52) compared to those under 18.

### Subsection 11.3—Regret after Surgery

Wiepjes and colleagues reported on the frequency of regret in the cohort of 6,793 individuals with diagnosis of gender identity disorder (GID) and at least one visit to a national center in Amsterdam.<sup>32</sup> Individuals 18 and under constituted 1,360 (20.0%) of the cohort. Regret after gonadectomy (only eligible to individuals over 18 and after one and a half years of CSHs) was rare (0.6% in AMAB, 0.3% in AFAB). All individuals who later expressed regret started CSHs after the age of 25.

In a cohort of 209 youth (median age 16) post-mastectomy for GD, two later reported regret

(0.95%), and none underwent reversal.<sup>46</sup> In a cohort of 136 AFAB in the U.S., comparing post-mastectomy to pre-surgical patients, all 68 individuals undergoing mastectomy reported it was a good decision, and nearly all (67 of the 68) denied any regret about the procedure.<sup>43</sup>

#### Subsection 11.4—Retransitions in Socially Transitioned Children

An ongoing cohort study in the U.S. enrolled socially transitioned children at ages 3 to 12, notably without a requirement for formal GD diagnosis but based on self-reported transgender or gender-diverse identity.<sup>28</sup> At an average of five years since their social transition, 7.3% (23 of 317) reported they re-transitioned their gender identity. In the 23 individuals, the majority reported being cisgender (eight) or nonbinary (11). The remainder (four individuals) transitioned to cisgender, then back to transgender within the five years. Just under a third of the cohort initiated puberty suppression (29%) or hormone treatment (30.9%), with more than 95% of each group continuing to report transgender identities. This cohort will continue to be followed through adolescence and adulthood.<sup>28</sup>

## Section 12 – Review of Minor’s Mental and Cognitive Capacity to Consent to Gender Reassignment Procedures (KQ10)

The Center reviewed relevant policy sources (e.g., state laws and regulations) to address KQ10. The information provided in this discussion of a minor’s capacity to consent to treatment does not, and is not intended to, constitute legal advice; instead, information, content, and materials discussed in this KQ are for background purposes only.

### Subsection 12.1—Capacity under the Law

Decision-making authority for medical treatment is determined by decisional capacity and legal authority.<sup>59</sup> Laws that govern a minor’s capacity to consent to medical treatment are state-specific.<sup>60</sup> In most states, the age of majority is 18, and treatment of patients under the age of 18 requires consent from the parent or legal guardian.<sup>61</sup> However, many states recognize exceptions for treatment related to abortion, mental health, and substance use.<sup>59,61–63</sup> The reasons for these exceptions involve the intersection of constitutional, policy, and practical factors.<sup>63</sup>

A minor in Louisiana, a person under the age of 18, is able to consent to medical care in general without the consent of a parent or guardian.<sup>60,64</sup> Although the Louisiana statute is broadly written permitting extensive consent by minors to medical treatment, exceptions exist for abortion, blood donation, drug misuse, and sterilization.<sup>60,65–68</sup> Minors must have reached the age of 16 and have the written consent of their parent(s) or legal guardian to donate blood,<sup>65</sup> and minors are unable to consent to an abortion or sterilization.<sup>60,66,67</sup>

### Subsection 12.2—Considerations and Guidelines Regarding Minor’s Capacity to Consent

A minor’s capacity to consent varies depending on the specific medical treatment or procedure, and necessitates a nuanced approach to decision making.<sup>62</sup> There are a variety of opinions regarding the role a minor can and should play in decisions related to their medical care.<sup>12,59,62</sup> Regarding assent to medical treatment, the 2016 American Academy of Pediatrics (AAP)’s statement on informed consent encourages the involvement of children beginning at age 7, with increasing involvement determined by age, including for those in the transgender population.<sup>12,59,62</sup> The AAP does not consider a diagnosis of GD to interfere with an adolescent’s capacity to make decisions regarding their medical treatment.<sup>12,62</sup>

Another consideration is the mature minor doctrine which acknowledges that there is a “subset of adolescents who have adequate maturity and capacity to understand and appreciate an intervention’s benefits, risks, likelihood of success, and alternatives.”<sup>59</sup> Under this doctrine, a minor’s age, maturity, and cognitive abilities are weighed when making a judicial determination of whether a minor who is otherwise legally incompetent is sufficiently mature to consent to their own medical care.<sup>59</sup>

This doctrine is consistent with the WPATH which states that in “adolescence, consent and decision-making require assessment of the individual’s emotional, cognitive, and psychosocial development” and recommend that an “adolescent demonstrates the emotional and cognitive maturity required to provide informed consent/assent for the treatment.”<sup>22</sup> WPATH guidelines developed specific questions to help

assess an adolescent’s emotional and cognitive capacity to consent to gender-affirming care, as shown in Box B below.<sup>15</sup>

<b>Box B. WPATH Questions to Assess an Adolescent’s Capacity to Consent</b>
• Can the young person think carefully into the future and consider the implications of a partially or fully irreversible intervention?
• Does the young person have sufficient self-reflective capacity to consider the possibility that gender-related needs and priorities can develop over time, and gender-related priorities at a certain point in time might change?
• Has the young person, to some extent, thought through the implications of what they might do if their priorities around gender do change in the future?
• Is the young person able to understand and manage the day-to-day short- and long-term aspects of a specific medical treatment (e.g., medication adherence, administration, and necessary medical follow-ups)?

Considerations for capacity to consent may also need to be given for the range and severity of treatments that fall under gender-affirming care.<sup>13,69</sup> For example, a minor’s capacity to consent to a temporary treatment may need to be considered differently than their ability to consent to the “surgical removal of reproductive organs with life-changing, fertility-affecting, gender-transitioning consequences.”<sup>69</sup>

The WPATH also recommends that additional consideration and care be given in instances where an adolescent minor is consenting to care without the permission of their parent or legal guardian.<sup>13</sup> In Statement 6.11, WPATH recommends involving the parent, caregiver, or legal guardian in all situations except when “an adolescent is in foster care, child protective services, or both, and custody and parent involvement would be impossible, inappropriate, or harmful.”<sup>13</sup> In instances where an adolescent is consenting for their own medical treatment in the absence of parental or guardian consent, WPATH notes that higher levels of engagement of and collaboration with clinicians working with the adolescent will be necessary “to provide the young person appropriate cognitive and emotional support to consider options, weigh benefits and potential challenges/costs, and develop a plan for any needed (and potentially ongoing) supports associated with the treatment.”<sup>13</sup>



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## Appendix A – Identifying Procedures

<b>Appendix A. Administrative Codes for Identifying Procedures</b>	
<b>Surgical CPT Codes<sup>a</sup></b>	<b>Description</b>
19303	Mastectomy, simple, complete
19325	Breast augmentation with implant
53420	Urethroplasty, two-stage reconstruction or repair of prostatic or membranous urethra; first stage
53425	Urethroplasty, two-stage reconstruction or repair of prostatic or membranous urethra; second stage
53430	Urethroplasty, reconstruction of female urethra
54125	Amputation of penis; complete
54520	Orchiectomy, simple (including subcapsular), with or without testicular prosthesis, scrotal or inguinal approach
54660	Insertion of testicular prosthesis (separate procedure)
54690	Laparoscopy, surgical; orchiectomy
55175	Scrotoplasty; simple
55180	Scrotoplasty; complicated
55866	Laparoscopy, surgical prostatectomy, retropubic radical, including nerve sparing, includes robotic assistance, when performed
55970	Intersex surgery; male to female
55980	Intersex surgery; female to male
56625	Vulvectomy simple; complete
56800	Plastic repair of introitus
56805	Clitoroplasty for intersex state
57106	Vaginectomy, partial removal of vaginal wall;
57110	Vaginectomy, complete removal of vaginal wall;
57291	Construction of artificial vagina; without graft
57292	Construction of artificial vagina; with graft
57295	Revision (including removal) of prosthetic vaginal graft; vaginal approach
57296	Revision (including removal) of prosthetic vaginal graft; open abdominal approach
57335	Vaginoplasty for intersex state
57426	Revision (including removal) of prosthetic vaginal graft, laparoscopic approach
58150	Total abdominal hysterectomy (corpus and cervix), with or without removal of tube(s), with or without removal of ovary(s);
58180	Supracervical abdominal hysterectomy (subtotal hysterectomy), with or without removal of tube(s), with or without removal of ovary(s)
58260	Vaginal hysterectomy, for uterus 250 g or less

58262	Vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s), and/or ovary(s)
58275	Vaginal hysterectomy, with total or partial vaginectomy;
58290	Vaginal hysterectomy, for uterus greater than 250 g;
58291	Vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58541	Laparoscopy, surgical, supracervical hysterectomy, for uterus 250 g or less;
58542	Laparoscopy, surgical, supracervical hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)
58543	Laparoscopy, surgical, supracervical hysterectomy, for uterus greater than 250 g;
58544	Laparoscopy, surgical, supracervical hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58550	Laparoscopy, surgical, with vaginal hysterectomy, for uterus 250 g or less;
58552	Laparoscopy, surgical, with vaginal hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)
58553	Laparoscopy, surgical, with vaginal hysterectomy, for uterus greater than 250 g;
58554	Laparoscopy, surgical, with vaginal hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58570	Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less;
58571	Laparoscopy, surgical, with total hysterectomy, for uterus 250 g or less; with removal of tube(s) and/or ovary(s)
58572	Laparoscopy, surgical, with total hysterectomy, for uterus greater than 250 g;
58573	Laparoscopy, surgical, with total hysterectomy, for uterus greater than 250 g; with removal of tube(s) and/or ovary(s)
58720	Salpingo-oophorectomy, complete or partial, unilateral or bilateral (separate procedure)
<b>Medications<sup>b</sup></b>	
<b>“Puberty Blockers”</b>	
Histrelin (implant)	Gonadotropin releasing hormone analogue
Leuprolide (injection)	Gonadotropin releasing hormone analogue
Triptorelin (injection)	Gonadotropin releasing hormone analogue
<b>“Cross Sex Hormones”</b>	
Estradiol (injection, oral, sublingual, intradermal, or topical)	Feminizing hormone
Spironolactone	Feminizing hormone
Bicalutamide	Feminizing hormone
Finasteride	Feminizing hormone
Testosterone (injection or topical)	Masculinizing hormone
<sup>a</sup> Surgical Current Procedural Terminology (CPT) <sup>19</sup> codes that were selected for extraction were based on the Centers for Medicare & Medicaid Services Article “Billing and Coding: Gender Reassignment	



Services for Gender Dysphoria”, revised January 1,2021, and available at:  
<https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=53793&ver=22&bc=CAAAAAAAAAA>  
<sup>b</sup>Pharmacy claim/encounter codes used for extraction were specific to claim type, location of administration, and route of administration.

## Appendix B – Identifying Behavioral Health Services

<b>Appendix B. Administrative Codes for Identifying Behavioral Health Services</b>	
<b>Behavioral Health Current Procedural Terminology (CPT)<sup>19</sup> Code</b>	<b>Short Description</b>
90785	Add-on code for interactive complexity reported in conjunction with codes for diagnostic psychiatric evaluation, psychotherapy, and group psychotherapy
90791	Psychiatric diagnostic evaluation
90792	Psychiatric diagnostic evaluation with medical services
90832	Psychotherapy, 30 minutes with patient
90833	Psychotherapy, 30 minutes with patient when performed with an evaluation and management service
90834	Psychotherapy, 45 minutes with patient
90836	Psychotherapy, 45 minutes with patient when performed with an evaluation and management service
90837	Psychotherapy, 60 minutes with patient
90838	Psychotherapy, 60 minutes with patient when performed with an evaluation and management service
90839	Psychotherapy for crisis; first 60 minutes
90840	Psychotherapy for crisis; each additional 30 minutes
90845	Psychoanalysis
90846	Family psychotherapy (without the patient present), 50 minutes
90847	Family psychotherapy (conjoint psychotherapy) (with patient present), 50 minutes
90849	Multiple-family group psychotherapy
90853	Group psychotherapy (other than of a multiple-family group)

## Appendix C – Detailed Search Methods

### A. Search Strategy

Center policy sources were searched to identify relevant documents related to Key Question (KQ) 10 using the terms minor capacity to consent to gender reassignment Louisiana. Ovid MEDLINE was searched for systematic reviews (with and without meta-analysis), randomized controlled trials, cohort studies, and case-control studies using the approach below. Searches were limited to sources with citations published after 2012.

### B. Ovid MEDLINE Search Strategy

The original Ovid MEDLINE search was run on October 10, 2022, and updated it for interval articles on

November 7, 2022:

1. ((trans or transgender\* or trans-identi\* or transexual\* or genderqueer or gender-varian\* or nonbinary or transfem\* or transmasculine or transmale\* or genderfluid\* or gender fluid\* or bi-gender\* or pan-gender\* or agender\*) adj2 (child\* or adolescent\* or juvenile\* or youth\* or teen\* or minor\$1)).mp.
2. Gender Dysphoria/ or transgender persons/ or exp gender identity/ or transsexualism/
3. (gender\* adj2 (dysphor\* or varian\* or incongru\* or identit\* or nonconform\* or non-conform\* or atypical or minorit\* or divers\* or questioning or fluid\* or expansi\*)).ti,ab,kw.
4. (male-to-female or female-to-male).ti,ab,kw.
5. or/2-4
6. Adolescent/ or Child/ or Child, Preschool/ or Minors/
7. (child\* or youth or pre-pubesc\* or prepubesc\* or pre-puber\* or prepuber\* or teen or pre-teen\* or tween or school-age\* or school age\* or young person\* or young people or juvenile\* or adolescen\* or p?ediatric or minor or minors or post-pube\* or postpube\* or p?ediatric or p?ediatric-aged).ti,ab,kw.
8. or/6-7
9. 1 or (5 and 6)
10. limit 9 to english language
11. Health Services for Transgender Persons/
12. 11 and 10
13. (social\* transition\* or non-medical intervention\*).ti,ab,kw.
14. ((change or changed or changing or "use") adj3 pronoun\$1).ti,ab,kw.
15. or/13-14
16. 15 and 10
17. Gonadotropin-Releasing Hormone/
18. (gonadotropin\* or GnRH\*).ti,ab,kw.
19. Gonadal Hormones/ or exp Gonadal Steroid Hormones/
20. ((hypothalamic-pituitary gonad\* or gonad\* sex\*) adj3 sup?res\*).ti,ab,kw.
21. ((cross-sex or gender-affirm\*) adj3 (hormon\* or testosterone\* or ?estrogen\* or estradiol or steroid\* or medication\* or medicin\* or pharmatherap\* or pharmacotherap\* or pharmaceutical\* or drug\*)).ti,ab,kw.
22. ((treatment\* or therap\* or medication\* or medicin\* or pharmatherap\* or pharmacotherap\* or pharmaceutical\* or drug\*) adj3 (hormon\* or testosterone\* or ?estrogen\* or estradiol or steroid\*)).ti,ab,kw.
23. sex hormon\*.ti,ab,kw.
24. (puberty-block\* or puberty-suppres\* or (pubert\* adj3 (block\* or sup?res\*))).ti,ab,kw.
25. ((gender-affirm\* or gender affirm\* or gender-confirm\* or gender confirm\*) adj3 (hormon\* or testosterone\* or ?estrogen\* or estradiol or steroid\* or medication\* or medicin\* or pharmatherap\* or pharmacotherap\* or pharmaceutical\* or drug\*)).ti,ab,kw.
26. ((delay\* or disrupt\*) adj3 puber\*).ti,ab,kw.
27. or/17-26
28. 27 and 10
29. (Non-hormon\* adj2 (treatment\* or intervention\* or care or healthcare or procedure\* or service\*)).ti,ab,kw.
30. exp Sex Reassignment Procedures/
31. ((sex reassignment or gender-affirm\* or gender affirm\* or gender-confirm\* or gender confirm\* or reconstructive or esthetic or aesthetic or cosmetic) adj5 (procedure\* or surg\* or service\* or operation\* or care or healthcare or intervention\*)).ti,ab,kw.

32. ((transgender or trans?exual or sex-change or sex change or masculini\* or femini\*) adj5 (procedure\* or surg\* or service\* or operation\* or care or healthcare or intervention\*)).ti,ab,kw.
33. ((breast or chest) adj1 (reconstruction\* or augment\* or reduc\* or implant\*)).ti,ab,kw.
34. exp mammoplasty/ or Breast Implantation/ or exp mastectomy/ or (mamm?plast\* or mastectom\*).ti,ab,kw.
35. (vaginoplast\* or phalloplast\* or (top adj2 (surger\* or surgical)) or (bottom adj2 (surger\* or surgical))).ti,ab,kw.
36. or/29-35
37. 36 and 10
38. Suicide/ or \*Suicide, Attempted/ or \*Suicide, Completed/ or \*Resilience, Psychological/ or \*Depression/ or \*Self-Injurious Behavior/ or \*Self Mutilation/ or \*Stress, Psychological/ or \*Anxiety Disorders/ or \*Mood Disorders/ or \*Depressive Disorder/
39. (suicide\* or suicidal ideation or suicidal thought\* or suicidal think\* or self-harm\* or self harm\* or self-injur\* or cutting or self-mutilat\* or self mutilat\*).ti,ab,kw.
40. (((depress\* or mood\* or anxi\* or stress\*) adj3 disorder\*) or mental health outcome\* or functional status).ti,ab,kw.
41. Functional Status/ or Psychosocial Functioning/ or "Quality of Life"/ or Patient Reported Outcome Measures/
42. (psycho\* adj2 (function\* or outcome\*)).ti,ab,kw.
43. (outcome\* adj3 importan\* adj2 patient\*).ti,ab,kw.
44. ("quality of life" or QOL).ti,ab,kw.
45. ((patient-reported or patient report\* or patient-importan\* or patient importan\* or patientcent\* or patient cent\*) adj3 outcome\*).ti,ab,kw.
46. (harm\* or adverse event\* or adverse effect\$1 or unwanted outcome\*).ti,ab,kw.
47. 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48. 47 and (12 or 16 or 28 or 37)
49. (regret\$3 or detransition\* or desist or desist?r\* or desistance or desistence or persistence or persist?r\*).ti,ab,tw. or ((discontinu\* or revers\*) adj3 treatment\*).ti.
50. 49 and 10
51. 12 or 16 or 28 or 37 or 48 or 50
52. limit 51 to yr="2012 -Current"

### C. Inclusion Criteria

1. Populations: Minors (< 18 years of age) experiencing and seeking care for gender dysphoria (GD)
2. Interventions
  - a. Nonsurgical or medical treatments (e.g., gonadotropin-releasing hormone analogues, cross-sex hormone treatments, social transition),
  - b. Surgical procedures (e.g., augmentation mammoplasty, clitoroplasty, hysterectomy, mastectomy, oophorectomy, orchiectomy, penectomy, phalloplasty, vaginoplasty, vulvoplasty),
  - c. Interventions delivered in combination, including with psychosocial counseling
3. Comparators: No treatment, including wait list or deferred treatment, social transitioning, or psychosocial counseling alone
4. Outcomes
  - a. Psychological and psychiatric outcomes using standardized assessment instruments (e.g., instruments that assess anxiety, depression, GD, suicidal ideation)
  - b. Physical or medical outcomes (e.g., adverse events, all-cause mortality)

- c. Health care utilization (e.g., hospitalizations, emergency room encounters, outpatient visits)
- d. Patient-centered outcomes (e.g., body image, quality of life, satisfaction)
- e. Total cost of care

Studies enrolling youth and adults were included if they reported outcomes for those under 18 separately.

#### D. Exclusion Criteria

Studies were excluded if they were not published in English, did not provide comparative outcomes (unless no other studies identified), or a newer systematic review (SR) included the same studies.

#### E. Participant Characteristics and Association With Outcomes

When discussing risk and protective factors or variables in statistical models in Center research products, in almost all cases, we are referring to associations of participant characteristics with outcomes, and not causation of outcomes. This is important because participant characteristics, such as race and ethnicity, serve as proxy or surrogate measures for underlying etiological factors not measured or evaluated in analyses. Etiological factors that might cause differences in outcomes for subgroups of participants could include systemic racism or other forms of systemic discrimination, stress, poverty, housing instability, or epigenetics. For example, by describing any differences in outcomes by race and ethnic groups, we are noting observed associations; these associations are not caused by biological determinants of being Black, White, or Hispanic.

#### F. Search Summary

In total, the original search identified 1,362 articles, with 294 undergoing full text review. Ultimately, we included seven SRs without meta-analysis,<sup>24–26,70–74</sup> cohort, case-control, or cross-sectional studies.<sup>38–41,74–77,78–80,82,83,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000</sup>

We did not identify any RCTs or SRs with meta-analysis. Generally, studies used a pre-treatment versus post-treatment approach to follow a cohort of individuals over months or years. In a few studies, comparison groups included a cohort of cisgender peers,<sup>45</sup> siblings, untreated individuals,<sup>39,43</sup> or a convenience sample of youth from a separate study.<sup>85</sup>

However, for the outcome of regret or request to re-transition (KQ7), studies only reported overall frequency within a cohort of individuals who all received treatment (e.g., medical or surgical), and did not compare them to another group. Given the specific request to address this outcome, we included noncomparative studies for this KQ only.

Across the seven identified SRs, there was high overlap of included studies.<sup>24–26,70–73</sup> We therefore focused on more recently published and more robust SRs and reviews with clearly described methods, leaving three SRs.<sup>24–26</sup> When performed by the authors of the SRs, we included their risk of bias assessments from the studies included in their review. Interventions, comparators, and outcomes varied across studies identified in the SRs, preventing the authors from performing meta-analysis. All SRs narratively described outcomes.<sup>24–26,70–73</sup>

Reflecting the growing literature base of this topic, we identified 14 individual studies published in 2022.<sup>27,28,77,79,85,29,36,37,39,45,46,56,75</sup> This is notable when compared to the SRs, which all searched a minimum of five prior years or more and identified 13 to 22 studies at most.<sup>24–26</sup>

## Appendix D – Individual Studies Reporting Psychological or Psychiatric Outcomes (KQ5)

Author Setting Enrollment Period or First Visit	Population Treatment	Outcomes
Medical Treatments		
Achille et al., 2020 <sup>38</sup> Single center, U.S. 2013 to 2018	Ages 9 to 25, endocrine naïve at baseline, with at least 18 months of data  n = 50 (33 AFAB, 17 AMAB)  Treatment initiated: n = 47 (94%) GNRHAs: n = 23 (46%) CSHs: n = 35 (70%) Both: n = 11 (22%) None: n = 3 (6%)	Pre- vs. post-treatment: mean change (SD) CES-D (score < 16, no clinical depression): 21.4 vs. 13.9; $P < 0.01$ Suicidal ideation: 10% (five individuals) vs. 6% (three individuals); no statistical testing  Data not extractable. The authors reported: Statistical improvements in PHQ9 QOL improved, but not statistically
Cantu, et al., 2020 <sup>40</sup> Single center, U.S. 2017 to 2019	Ages 11 to 18, seeking care for GD, with at least one follow-up visit  n = 80  Average follow-up 4.7 months (80% within two to seven months)  CSH Treatment initiated: n = 28 (35%) Feminizing hormones: 6 Masculinizing hormones: 22	Pre- vs. post-CSHs: mean (SD) PHQ-9: 10.5 (6.5) vs. 10.0 (6.4); $P = .39$ GAD-7: 9.1 (6.1) vs. 8.8 (5.7); $P = .56$  Of 27 individuals with suicidality at a baseline, 22 continued to endorse at follow- up  No difference with adjusting for distance from clinic or initiation of hormone treatment
Chen, et al., <sup>23</sup> 4 centers, U.S. 2016 to 2019	Ages 12 to 20, prospective observational, initiating CSH and followed at 6, 12, 18, and 24 months  n = 315 (190 AFAB, 125 AMAB)  Followed at 6, 12, 18, and 24 months after initiation of CSH	Higher appearance congruence at baseline was associated with lower baseline scores for depression ( $r = -0.60$ ) and T scores for anxiety ( $r = -0.40$ ), and increases in appearance congruence were associated with decreases in scores for depression ( $r = -0.68$ ) and T scores for anxiety ( $r = -0.52$ ) over time.  Higher appearance congruence at baseline was associated with higher

		baseline T scores for positive affect (r=0.46) and life satisfaction (r=0.72), and increases in appearance congruence were associated with increases in T scores for positive affect (r=0.74) and life satisfaction (r=0.84) over time.
Hisle-Gorman et al., 2021 <sup>41</sup> U.S. military healthcare data repository 2010 to 2018	Youth < 18 with at least one visit to identify TG status (inpatient or outpatient) using diagnosis codes  n = 3,754  Treatment (GNRHAs or CSHs) initiated n = 963 (25.6%)	Pre- vs. post-treatment: Median number health visits: aIRR, 1.09; 95% CI, 0.95 to 1.25; P = .6  No statistical difference by type of mental health condition (e.g., anxiety, ADHD, mood) Mental health medication days: aIRR 1.67; 95% CI, 1.46 to 1.91; P < .001 More days of use for all classes of medications (e.g., SSRI, SNRI, Wellbutrin, anti-psychotics) except for stimulants, migraine meds, and lithium  Average follow-up: 1.7 years after initiation of HT
Surgical Treatments		
Ascha et al., 2022 <sup>39</sup> Multiple sites, U.S. 2019 to 2021	13 to 24 years, AFAB, TG, or NB Not required to be on hormone treatment (any kind)  Mastectomy patients matched to two control patients (by age and duration of T therapy)  n = 36 in surgery, 34 in control  11 patients lost to follow up (six surgery, five control)  Mean age 18.6 (SD 2.7) years Testosterone use (96%) for average of 20.1 months (SD 9.3)	At three months, control (n = 25) vs. surgery (n = 65): mean (SD)  <i>Excluded individuals with low chest dysphoria from analysis</i>  Chest dysphoria (higher score is worse): 30.5 (8.37) vs. 3.80 (3.47) <sup>a</sup>  Transgender Congruence Scale (higher score is better): 36.90 (4.25) vs. 44.4 (3.59) <sup>a</sup>  Body Image Scale: (higher score is worse): 91.90 (15.8) vs. 77.00 (13.00) <sup>a</sup>
Olson-Kennedy, et al., 2018 <sup>43</sup> Single site, U.S. 2016	Ages 13 to 25, AFAB, identify as other than female	Control vs. post-surgery: mean (SD)  Chest dysphoria (higher is more distress):

	n = 136 (68 control, 68 post-mastectomy/chest reconstruction)  Average age: 16.9 (SD 2.5) vs. 18.9 (2.5)	29.6 (10.0) vs. 3.3 (3.80); $P < .001$
<p><sup>a</sup> No analysis performed.</p> <p>Abbreviations. AFAB: assigned female at birth; aIRR: adjusted incidence rate ratio; AMAB: assigned male at birth; aOR: adjusted odds ratio; CES-D: Center for Epidemiological Studies Depression Scale; CI: confidence interval; CSH: cross-sex hormones; GAD-7: Generalized Anxiety Disorder-7; GD: gender dysphoria; GNRHA: gonadotropin-releasing hormone analogues; NB: nonbinary; PB: puberty blocker; QOL: quality of life; SD: standard deviation; TG: transgender.</p>		

## Appendix E – Individual Studies Reporting Medical or Physical Outcomes (KQ6)

Author Setting	Population Treatment	Outcomes
GNRHAs		
Schulmeister et al., 2022 <sup>45</sup> Trans Youth Care Multisite, U.S. 2016 to 2018	Age under 18 GNRHA naïve at enrollment ≥ 10 months of GNRHA use  n = 55 (26 AMAB, 29 AFAB) Mean age initiation: 11.5 (SD, 1.2) Compared to a cohort of prepubertal children N = 226 (118 DMAB, 108 DFAB) Mean age 11.0 years (SD, 2.8)	Median height velocity over first 12 months of GNRHA use: TGD: 5.1 cm/year (IQR, 3.7 to 5.6) vs. prepubertal control (not reported); $P = .8$  By Tanner stage at GNRHA start vs. prepubertal control: II: 5.3 vs. 6.1 cm/year; $P = .7$ III: 4.4 vs. 6.1 cm/year; $P = .9$ IV: 1.6 vs. 6.1 cm/year; $P = .006$
	Tanner stage at initiation of GNRHAs II: n = 55 III: n = 19 IV: n = 7	Authors noted most of this effect was mediated by age in multivariate analyses ( $R^2 = .3$ ; $P = .02$ )

<p>Van de Grift et al., 2020<sup>47</sup> Single center, the Netherlands 2006 to 2013</p>	<p>GD diagnosis Initiated GNRHAs &lt; 18 and now &gt; 18 years</p> <p>n = 200 For AMAB (n = 66) Tanner 2/3: n = 26 Tanner 4/5: n = 40</p> <p>For AFAB (n = 134) Tanner 2/3: n = 17 Tanner 4/5: n = 117</p> <p>Matched to 100 individuals (50 AMAB, 50 AFAB) randomly selected, never receiving PS but now on CSHs and seeking gender-affirming surgery</p>	<p>AFAB outcomes: Tanner 2/3 vs. controls Mastectomy (%):</p> <ul style="list-style-type: none"> <li>No mastectomy: 52.9 vs. 0</li> <li>IMF mastectomy: 0 vs. 51.4</li> </ul> <p>Tanner 4/5 vs. controls:</p> <ul style="list-style-type: none"> <li>No mastectomy (%): 1.0 vs. 0</li> <li>IMF mastectomy (%): 26.7 vs. 51.4</li> </ul> <p>No analyses reported</p> <p>AMAB outcomes Tanner 2/3 at PS initiation vs. controls</p> <ul style="list-style-type: none"> <li>Need for intestinal vaginoplasty: OR, 84; 95% CI, 9.29 to 768.82; <i>P</i> not reported</li> </ul> <p>Tanner 4/5</p> <ul style="list-style-type: none"> <li>Need for intestinal vaginoplasty: OR, 9.8; 95% CI, 1.11 to 86.01; <i>P</i> not reported</li> </ul>
<p>CSHs (any)</p>		
<p>Mullins et al., 2021<sup>44</sup> Single center, U.S. 2013 to 2019</p>	<p>Age 13 to 24 Seeking TG services N = 611 (428 AFAB, 183 AMAB)</p> <p>176 identify as female 416 identify as male 19 identify as non-binary</p> <p>CSHs initiation</p> <ul style="list-style-type: none"> <li>Median age 17; IQR 16 to 19)</li> <li>Estradiol: n = 182</li> </ul> <p>Testosterone: n = 429</p>	<p>Median duration of CSHs use: 574 days (IQR: 283 to 962)</p> <p>Venous thromboembolism: no events</p> <p>Arterial thrombosis (including stroke): no events</p>
<p>Valentine et al., 2022<sup>85</sup> Multiple sites, U.S. 2009 to 2019</p>	<p>Age &gt; 2 at last visit GD diagnosis in EHR Compared to random sample</p> <p>n = 4,172 TGD youth n = 16,648 controls</p>	<p>AFAB Overweight/obesity: aOR, 1.8; 95% CI, 1.7 to 2.0; <i>P</i> &lt; .0001</p> <p>AMAB Dysglycemia: aOR, .6; 95% CI, 0.4 to 0.9; <i>P</i> = .01</p> <p>Adjusted for depression, antipsychotic medication use</p>
<p>Testosterone</p>		



Sequeira et al., 2019 <sup>83</sup> Single center, U.S. 2014 to 2017	Age 13 to 19 GD  n = 46 AFAB	Pre- vs. 12 months after initiation of testosterone <ul style="list-style-type: none"> <li>BMI (kg/m<sup>2</sup>): 26.2 vs. 25.6 (no analysis)</li> </ul> BMI z-score: .9 vs. .7; P = .52
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*Abbreviations. AFAB: assigned female at birth; AMAB: assigned male at birth; aOR: adjusted odds ratio; CI: confidence interval; CSH: cross-sex hormones; dL: deciliter; EHR: electronic health record; GD: gender dysphoria; GNRHA: gonadotropin-releasing hormone analogues; IMF: inframammary fold; IQR: interquartile range; NB: non-binary; OR: odds ratio; PS: puberty suppression; SD: standard deviation; TG: transgender; TGD: transgender or gender diverse.*

## Appendix F – Gender Identity or Hormone Treatment Continuation (KQ7)

Study Setting Time Frame	Population	Outcomes
Social Transition		
Olson, 2022 <sup>28</sup> Trans Youth Project Multisite, U.S. Enrolled 2013 to 2017	317 socially transitioned children aged 3 to 12 years at enrollment <ul style="list-style-type: none"> <li>Not required to have formal GD diagnosis</li> <li>280 (88%) not on GNRHAs at enrollment</li> </ul> None on CSHS given age	Retransitions, as of 2021 <ul style="list-style-type: none"> <li>23 of 317 re-transitioned (7.3%) <ul style="list-style-type: none"> <li>four transitioned to cisgender then back to TG</li> <li>eight to cisgender</li> <li>11 to nonbinary</li> </ul> </li> </ul>
		GNRHA initiation by 2021 <ul style="list-style-type: none"> <li>92 individuals (29.0%)</li> <li>88 of 92 (95.7%) continue to report TG <ul style="list-style-type: none"> <li>one reports cisgender, three nonbinary</li> </ul> </li> </ul> CSHS initiation by 2021 <ul style="list-style-type: none"> <li>98 (30.9%)</li> </ul> 97 of 98 (99.0%) continue to report TG
Medical treatments		
Wiepjes et al., 2018 <sup>32</sup> Single center Amsterdam, the Netherlands 1972 to 2015	At least one visit, diagnosis of transsexualism or GID <ul style="list-style-type: none"> <li>n = 6,793 (4,432 AMAB, 2,361 AFAB)</li> </ul> 812 (11.9%) age 12 to 18	1.9% of 12 to 18-year-olds discontinued GNRHA  Regret after gonadectomy, entire cohort <ul style="list-style-type: none"> <li>11 (0.6 %) AMAB</li> </ul>

	<p>548 (8.1%) age &lt; 12</p> <p>Eligibility for treatments:</p> <ul style="list-style-type: none"> <li>• GNRHA: usually only ≥ 12 years</li> <li>• CSHs ≥ 16 years</li> <li>• Gonadectomy &gt; 18 years and ≥ 1.5 years of CSHs</li> </ul>	<ul style="list-style-type: none"> <li>• 3 (0.3 %) AFAB</li> </ul> <p>All of this group started CSHs after age 25</p> <p>Reasons included social regret, true regret, or non-binary</p>
<p>Steensma et al., 2013<sup>53</sup></p> <p>Single center</p> <p>Amsterdam, the Netherlands</p> <p>Consecutive referrals 2000 to 2008</p>	<p>Diagnosis of GD, &gt; 15 years of age between 2008 to 2012</p> <ul style="list-style-type: none"> <li>• n = 127</li> </ul> <p>47 reapplied for medical treatment, considered persisters</p> <p>80 did not reapply, 46 provided follow-up data</p> <p>This is a subset of individuals also included in Wiepjes et al., 2018<sup>57</sup></p>	<p>Predictors of persistence:</p> <ul style="list-style-type: none"> <li>• Age at intake: OR, 1.65 (95% CI, 1.12 to 2.44) <i>P</i> &lt; .01</li> <li>• Childhood role transition: OR, 5.06 (95% CI, 1.61 to 15.87) <i>P</i> &lt; .01</li> </ul> <p>Also report higher rates of GD and body dissatisfaction</p>
<p>van der Loos et al., 2022<sup>29</sup></p> <p>Single center</p> <p>Amsterdam, the Netherlands 1972 to 2018</p>	<p>&lt; 18 years of age</p> <p>GD diagnosis</p> <p>GNRHAs for ≥ 3 months</p> <p>n = 720 (222 AMAB, 500 AFAB)</p> <p>This is a subset of individuals also included in Wiepjes et al., 2018<sup>57</sup></p>	<ul style="list-style-type: none"> <li>• 16 individuals (2%) without prescription for CSHS</li> <li>9 AMAB, 7 AFAB</li> <li>12 of 16 with history of gonadectomy</li> </ul> <p>Age at first visit, start of GNRHA, start of CSHs, puberty stage at start of GNRHA treatment, or gonadectomy associated with no prescription at follow-up</p>
<p>Butler, et al., 2022<sup>31</sup></p> <p>Single center, U.K. 2008 to 2021</p>	<p>All youth referrals to center</p> <p>n = 1,089 with known outcomes (of 1,151 referrals)</p>	<ul style="list-style-type: none"> <li>• 999 (91.7%) TG or gender-diverse</li> <li>• 90 (8.3%) no longer identify as TG</li> <li>32 at first visit to clinic</li> <li>• 5.3% of entire cohort stopped GNRHAs or CSHs</li> </ul> <p>More common in those starting under age 16 (9.2%) vs. after age 16 (4.4%)</p>
<p>Masic et al., 2022<sup>56</sup></p> <p>National data</p> <p>England</p> <p>2017 to 2018 cohort</p>	<p>GD diagnosis, referred to pediatric endocrinology, ≤ 18 years of age, seeking and evaluated for GNRHAs or CSHs</p> <ul style="list-style-type: none"> <li>• n = 439 (154 AMAB, 285 AFAB)</li> <li>• 431 consented to GNRHA, 8 to CSHs only</li> </ul> <p>This is a subset of individuals in Butler et al., 2022<sup>4</sup></p>	<p>GNRHA continuation</p> <ul style="list-style-type: none"> <li>• 30 (6.9%) stopped or never started</li> <li>Reason unknown (13)</li> <li>Physical health problems (five)</li> <li>Pause for fertility preservation (four)</li> <li>Transfer of care to private provider (four)</li> <li>Feeling unsure (three)</li> <li>Mental health concerns (one)</li> </ul> <ul style="list-style-type: none"> <li>• 121 initiated and continued</li> </ul>

		17 of the 30 left service line entirely or were only receiving psychological services
Roberts et al., 2022 <sup>52</sup> U.S. Military Healthcare 2009 to 2018	Adults or children, non-active duty, with two encounters for GD diagnoses, and at least two prescriptions for CSHs <ul style="list-style-type: none"> <li>n = 952 (34.1% AMAB, 65.9% AFAB)</li> <li>39.1% initiated CSHS &lt; 18</li> </ul> No information on patient reason for discontinuing	≥ 4-year continuation rate: <ul style="list-style-type: none"> <li>Overall 70.2%; 95% CI, 63.9 to 76.5</li> <li>AMAB: 81.0%; 95% CI, 72.0 to 90.0</li> <li>AFAB: 64.4%; 95% CI, 56.0 to 72.8</li> <li>HR, 2.40; 95% CI, 1.50 to 3.86</li> </ul> < 18 years at initiation: 74.4% (95% CI, 66.0 to 82.8) ≥ 18 years at initiation: 64.4% (95% CI, 56.0 to 72.8)  HR, 1.69 (95% CI, 1.14 to 2.52)
Wagner et al., 2021 <sup>30</sup> STRONG cohort Multisite, U.S. 2006 to 2014	Youth < 18 at index date with ≥ 1 follow-up visit, without GD diagnosis but with potential GD behaviors, no receipt of CSHs <ul style="list-style-type: none"> <li>n = 958 (431 AMAB, 527 AFAB)</li> </ul> 21% < 10 years of age	At average follow-up of three years (maximum nine years): <ul style="list-style-type: none"> <li>281 (29%) with GD diagnosis</li> <li>162 (58%) initiated CSHST</li> <li>677 (71%) without GD diagnosis</li> <li>74 (11%) went on to receive CSHs</li> </ul> Of original cohort, 236 (25%) received CSHs GD diagnosis by age, compared to 3 to 9 years of age: <ul style="list-style-type: none"> <li>10 to 14 years: HR, 2.0; 95% CI, 1.3 to 3.0</li> <li>&gt; 15 years: HR, 2.7; 95% CI, 1.8 to 2.9</li> </ul>
McCallion et al., 2021 <sup>57</sup> Glasgow, Scotland 2011 to 2019	Youth with GD or GID referred to pediatric endocrinology clinic <ul style="list-style-type: none"> <li>n = 91 (59 AFAB, 32 AMAB);</li> <li>79 eligible for GNRHA</li> <li>four decided against puberty suppression</li> <li>two pre-pubertal</li> <li>three medical comorbidities</li> <li>three unable to complete assessments)</li> </ul> 41 eligible for CSHS (include some from the GNRHA group)	GNRHA discontinuation: <ul style="list-style-type: none"> <li>six of 79 (7.6%)</li> <li>three for resolved GD</li> <li>three for nonadherence</li> </ul> CSHs discontinuation: <ul style="list-style-type: none"> <li>one of 41 for resolved GD</li> </ul> No discontinuations due to side effects
Brik et al., 2020 <sup>54</sup> Single Center Leiden, The Netherlands 2010 to 2018	Initiated GNRHAs with a GD diagnosis, ≤ 18 years of age <ul style="list-style-type: none"> <li>n = 143 (38 AMAB, 105 AFAB)</li> </ul> Of 214 presenting for evaluation not included in study:	Continuation to CSHs <ul style="list-style-type: none"> <li>125 (93%)</li> </ul> No longer seeking care for GD <ul style="list-style-type: none"> <li>5 (3.49%)</li> <li>2 exploring non-binary</li> <li>3 no longer with GD</li> </ul>

	<p>No GD diagnosis: 39  Coexisting complications: 9  Hormone treatment not wanted: 4  Ongoing evaluation: 10  Lost to follow-up: 9</p>	<p>Restarted GNRHA or CSHs  4 (2.8%)</p>
<p>Olson-Kennedy, et al., 2018<sup>43</sup>  Single site, U.S. 2016</p>	<p>Ages 13 to 25, AFAB, identified as gender other than female</p> <p>Pre-surgical compared to post chest-reconstruction (e.g., mastectomy)</p> <p>n = 136 (68 control, 68 post-surgical)</p>	<p>No regret reported by individuals under 18 at time of surgery</p>
<p>Hewitt et al., 2012<sup>55</sup>  Single center Victoria, Australia 2003 to 2011</p>	<p>Diagnosis of GID, referred to pediatric endocrinology for hormone treatment</p> <ul style="list-style-type: none"> <li>n = 21 (13 AMAB, 8 AFAB)</li> </ul> <p>In Australia at this time CSHs required court approval after confirmation of GID diagnosis until over 18 years of age</p>	<p>Continuation to CSHs</p> <ul style="list-style-type: none"> <li>17 (81%) eligible <ul style="list-style-type: none"> <li>11 applied to court for CSHs <ul style="list-style-type: none"> <li>three without parental or financial support</li> <li>one purchased CSHs privately</li> <li>two deferred till over 18 (court approval not needed)</li> </ul> </li> </ul> </li> </ul> <p>GD symptoms resolved</p> <ul style="list-style-type: none"> <li>Four (19%) resolved or accepted gender variance without treatment</li> <li>Seven individuals started treatment, all continued hormone treatment</li> </ul>
<p><i>Abbreviations. AFAB: assigned female at birth; AMAB: assigned male at birth; CI: confidence interval; CSH: cross-sex hormones; GD: gender dysphoria; GID: gender identity disorder; GNRHA: gonadotropin-releasing hormone analogues; HR: hazard ratio; OR: odds ratio; STRONG: Study of Transition, Outcomes, and Gender; TG: transgender.</i></p>		

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