

IN THE UNITED STATES DISTRICT COURT  
FOR THE WESTERN DISTRICT OF WISCONSIN

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ALINA BOYDEN and  
SHANNON ANDREWS,

Plaintiffs,

v.

Case No. 17-CV-0264

STATE OF WISCONSIN DEPARTMENT  
OF EMPLOYEE TRUST FUNDS, et al.,

Defendants.

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**DECLARATION OF LAWRENCE MAYER  
IN SUPPORT OF STATE DEFENDANTS' REPLY  
IN SUPPORT OF SUMMARY JUDGMENT**

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I, **LAWRENCE MAYER**, pursuant to 28 U.S.C. § 1746, declare as follows:

1. I have been retained by counsel for the State Defendants as an expert in the above-captioned lawsuit to provide an expert opinion. My qualifications to express an expert opinion on the efficacy, safety, and optimality of hormonal and surgical interventions for the treatment of gender dysphoria are outlined in my opening expert report, dated April 19, 2018.

2. On June 27, 2018, I received from State Defendants' counsel supplemental expert reports authored by Dr. Stephanie Budge and Dr. Loren Schechter.

3. It was not my understanding that Plaintiffs were permitted to submit supplemental expert reports, and so I was not expecting to receive these reports. Nevertheless, I have been able to conduct a preliminary review of the opinions expressed in those supplemental reports and the studies cited therein. Nothing I have seen so far in those opinions or studies changes my own opinion, expressed in my original report dated April 19, 2018, that medical and surgical treatments have not been demonstrated to be safe and effective for treating gender dysphoria.

4. Subject to leave from this Court, I reserve the right to respond to the specific opinions in Plaintiffs' supplemental expert reports, once I have had adequate time to fully review those reports and formulate my responsive opinion.

5. I understand that the Hayes Directory is an organization that performs analysis of available evidence regarding the safety and efficacy of medical treatments for various diagnoses. I understand that it is a reliable authority for this type of analysis.

6. Attached as Exhibit A to this declaration is a true and correct copy of three reports released by the Hayes Directory regarding sex reassignment surgery for the treatment of gender dysphoria, hormone therapy for the treatment of gender dysphoria, and ancillary procedures and services for the treatment of gender dysphoria. The conclusions reached in

these reports are consistent with my own analysis of the state of available evidence regarding the safety and efficacy of various medical treatments for gender dysphoria.

I declare under penalty of perjury that the forgoing is true and correct.

Executed on

7/9/18

  
LAWRENCE MAYER

Paul, 6/27/14  
Promised Material  
Cluster

**Hayes** directory

May 15, 2014

## Sex Reassignment Surgery for the Treatment of Gender Dysphoria

### PURPOSE OF TECHNOLOGY:

Sex reassignment surgery (SRS), which involves genital reconstruction surgery and chest surgery, is part of the treatment approach for persons with gender dysphoria (GD). Individuals with GD have persistent feelings of gender discomfort and inappropriateness of their anatomical sex, strong and ongoing cross-gender identification, and a desire to live and be accepted as a member of the opposite sex. SRS includes the surgical procedures by which the physical appearance and function of a person's existing sexual characteristics are changed to those of the other sex in an effort to resolve or minimize GD and improve quality of life.

### EXECUTIVE SUMMARY:

**Health Problem:** People with gender dysphoria (GD) feel a severe incongruity between anatomical sex and gender identity. The prevalence of GD is 1 in 11,900 to 1 in 45,000 persons for male-to-female (MtF) and 1 in 30,400 to 1 in 200,000 persons for female-to-male (FtM) transgender persons.

The earlier term, *gender identity disorder* (GID), has given way to *gender dysphoria* (GD). This change was intended to reflect a consensus that gender nonconformity is not a psychiatric disorder, as it was previously categorized. However, since the condition may cause clinically significant distress and since a diagnosis is necessary for access to medical treatment, the new term was proposed. The diagnostic criteria for GD outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), as well as the criteria for GID in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), require that the individual believes there is a marked difference between the gender assigned to him or her by others and the gender he or she experiences or wishes to express. Additional criteria must also be met for a diagnosis of GD.

**Determinants:** The determinants of GD are poorly understood. Experts believe that gender identity develops as the result of a combination of biological factors, possibly including genetic and/or prenatal and perinatal hormonal influences, and environmental influences that have psychological effects.

**Treatment:** Individuals with GD seeking professional help begin with psychotherapy. An American Psychiatric Association Task Force recommends 2 goals for psychotherapy: (1) to explore issues related to the individual's commitment to living in the cross-gender role; and (2) to fully explore other options for the patient including whether to live as a homosexual person without medical and surgical treatments for gender transition.

The full therapeutic approach to GD consists of 3 elements or phases, typically in the following order: (1) hormones of the desired gender, (2) real-life experience for 12 months in the desired role; and (3) surgery to change the genitalia and other sex characteristics (e.g., breast reconstruction or mastectomy). However, not everyone with GD needs or wants all elements of this triadic approach.

**Technology:** Sex reassignment surgery SRS involves modification of the genitalia and/or breast/chest to resemble that of the opposite sex.

For the FtM patient, surgical procedures may include mastectomy, hysterectomy, salpingo-oophorectomy, vaginectomy, metoidioplasty, scrotoplasty, urethroplasty, placement of testicular prostheses, and phalloplasty.

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## Sex Reassignment Surgery for GD

For the MtF patient, surgical procedures may include breast augmentation, penectomy, orchiectomy, vaginoplasty, clitoroplasty, and labiaplasty.

**Rationale:** The goal of SRS is to feminize or masculinize the body to facilitate an individual's desire to live in the gender role opposite from the biological sex.

**Controversy:** The medical necessity of SRS for the treatment of GD is under debate. The condition does not readily fit traditional concepts of medical necessity since research to date has not established anatomical or physiological anomalies associated with GD. An evidence-based assessment of the effectiveness of SRS procedures for alleviation of symptoms associated with GD and improvement of recipients' well-being can make a helpful contribution to this controversy.

### Relevant Questions:

- Has SRS been shown to be effective in improving patient-important outcomes such as relief of symptoms of GD, quality of life (QOL), satisfaction with sex characteristics, psychological well being, or sexual function?
- Does SRS confer additional benefits to hormone therapy alone?
- Do outcomes vary according to which components of SRS are performed?
- Is SRS safe?
- Have definitive patient selection criteria been established for SRS as treatment for GD?

**Evidence Base:** Nineteen peer-reviewed studies, primarily case series, cross-sectional studies or pretest-posttest studies assessing the effectiveness of SRS were analyzed in this report. In addition, 6 case series evaluating safety outcomes in  $\geq 300$  MtF patients or  $\geq 200$  FtM patients following SRS were analyzed.

**Search Dates:** November 2004 to April 2014.

**Sample Sizes:** 35 to 376 patients for main evidence review, 202-390 patients for safety evidence.

**Patients:** MtF patients (6 studies), FtM patients (6 studies), both MtF and FtM patients (7 studies).

**Interventions:** Chest surgery only (5 studies), genital surgery only (5 studies), both chest and genital surgery (4 studies), unspecified (5 studies).

**Comparisons:** Transgendered patients that had undergone SRS vs. those that had not undergone SRS (5 studies) and outcomes in SRS patients that were MtF vs. FtM (1 study).

**Outcome Measures:** GD, QOL, sexual experience, patient satisfaction, psychological outcomes, and safety outcomes.

**Follow-Up:** 1 month to 7 years.

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**Hayes**

Transforming Healthcare with Evidence

## Sex Reassignment Surgery for GD

**Findings:** Following SRS, patients reported decreased GD, depression and anxiety, and increased QOL. The majority of SRS patients were sexually active, but the ability to orgasm varied across studies. The majority of patients were satisfied with their aesthetic results following SRS.

**Gender Dysphoria:** GD was decreased following SRS relative to baseline (2 studies).

**Quality of Life:** Transgendered patients who underwent SRS had improved QOL relative to patients that had not undergone SRS (1 study), improved QOL relative to before SRS (2 of 3 studies), and had QOL scores similar to those of the general population (2 studies).

**Sexual Function:** The majority of patients were sexually active following SRS (4 studies), and the ability to orgasm varied across studies (5 studies).

**Patient Satisfaction:** The majority of patients were satisfied with aesthetic results following SRS (10 studies).

**Psychological Outcomes:** Depression (3 studies) and anxiety (2 studies) decreased following SRS.

**Other Outcomes:** Following SRS, almost all FtM patients were able to micturate while standing (1 study), and rates of employment were high (3 studies).

**Comparative Effectiveness of Hormone Therapy Alone and SRS:** The evidence was too sparse to allow any conclusion regarding the comparative benefits of SRS and hormone therapy alone.

**Comparative Effectiveness of Different Types of SRS:** The evidence was too sparse to allow any conclusion regarding the comparative benefits of different SRS procedures.

**Safety:** Following SRS, there were very low rates of regret of surgery (0% to 6%) (5 studies) and suicide (2 to 3%) (3 studies). Only 6 of the 19 studies reported on complications following SRS, and the most common complications were urinary tract complications (4% to 33%) (3 studies), necrosis of tissue (1% to 10%) (6 studies), vaginal stenosis or prolapse (2% to 14%) (3 studies), and need for revision surgery (4% to 29%) (3 studies). The most common complications reported in the 6 safety studies were need for revision surgery (22% to 40%) (5 studies), urinary tract complications (40% to 41%) (2 studies), and wound healing difficulties (11% to 33%) (2 studies). The majority of studies reported a length of follow-up of at least 1 year following surgery (12 studies).

**Patient Selection Criteria:** There is insufficient evidence to establish patient selection criteria for SRS to treat GD. Professional groups recommend that SRS be restricted to individuals who are referred for sex reassignment services by a qualified mental health professional, and that while 1 referral is sufficient for breast or chest surgery, 2 independent referrals should be required for genital SRS. Individuals who have medical contraindications to surgery should not undergo SRS.

**Quality of Evidence:** Very low.

Overall, the quality of the evidence was very low due to limitations of individual studies, including small sample sizes, few studies evaluating any 1 outcome, retrospective data, lack of randomization of patients to treatment groups, failure to blind outcome assessors to group assignment, lack of a control or comparator group or

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## Sex Reassignment Surgery for GD

minimal adjustment for confounders, lack of baseline assessments to assess change over time, a possible procedural learning curve, and a lack of objective and validated outcome measures.

**Conclusions:** The evidence suggests positive benefits but because of serious limitations permit only weak conclusions regarding sex reassignment surgery (SRS) for gender dysphoria (GD). No conclusions can be made about the comparative benefits of hormone therapy alone and SRS, or about different components of SRS.

- Patients who underwent chest/breast or genital surgery were generally pleased with the aesthetic results.
- Following SRS, patients reported decreased GD, depression and anxiety, and increased quality of life.
- The majority of SRS patients were sexually active, but the ability to orgasm varied across studies.
- Complications of surgery following SRS were common and could be serious.
- Rates of regret of surgery and suicide were very low following SRS.
- Data were too sparse to draw conclusions regarding whether SRS conferred additional benefits to hormone therapy alone.
- Data were too sparse to draw conclusions regarding whether outcomes vary according to which surgeries were performed.

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### Hayes Rating:

- C - For sex reassignment surgery (SRS) to treat gender dysphoria (GD) in adults for whom a qualified mental health professional has made a formal diagnosis of GD, have undergone hormone therapy and psychotherapy, and have undergone a "real-life" test (i.e., in which they lived as the desired gender role). This Rating reflects the reporting of some positive evidence but serious limitations in the evidence of both effectiveness and safety.
- D2 - For SRS to treat GD in adolescents. This rating reflects the paucity of data of SRS in adolescents.

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### INSIGHTS:

- Since part of the reason for the psychopathology experienced by transgender persons has to do with the reactions or expected reactions of family and society, evolving social norms theoretically could diminish the perceived need to undergo physical changes in order to live in the desired gender role.
- The majority of the studies selected for this report reflect the diagnostic criteria of *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, rather than the somewhat expanded criteria published in 2013 in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*.

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Transforming Healthcare with Evidence

May 19, 2014

**Hormone Therapy for the Treatment of Gender Dysphoria****PURPOSE OF TECHNOLOGY:**

Continuous feminizing or masculinizing hormone therapy is administered to some adolescents and adults who have a diagnosis of gender identity disorder (GID) or gender dysphoria (GD). The purpose of this therapy is to facilitate a transgender individual's desire to transition to a sexual identity other than his or her biological (natal) sex. Some individuals undergo hormone therapy as a prelude to sex reassignment surgery; other individuals seeking gender transition undergo hormone therapy without ever undergoing any type of surgery.

**EXECUTIVE SUMMARY:**

**Health Problem:** Individuals with gender dysphoria (GD) experience a severe incongruity between their biological sex and gender identity.

The prevalence of transsexualism is estimated to be 1 in 11,900 to 1 in 45,000 persons for male-to-female (MtF) prevalence and 1 in 30,400 to 1 in 200,000 for female-to-male (FtM) prevalence. The prevalence of gender dysphoria within the transsexual population is unknown. The earlier term, *gender identity disorder* (GID), has given way to *gender dysphoria* (GD). This change was intended to reflect a consensus that gender nonconformity is not a psychiatric disorder, as it was previously categorized. However, since the condition may cause clinically significant distress and since a diagnosis is necessary for access to medical treatment, the new term was proposed. The diagnostic criteria for GD outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), as well as the criteria for GID in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), require that the individual believes there is a marked difference between the gender assigned to him or her by others and the gender he or she experiences or wishes to express. Additional criteria must also be met for a diagnosis of GD.

**Determinants:** The determinants of gender dysphoria are poorly understood. Experts believe that gender identity develops as the result of a combination of biological factors, possibly including genetic and/or prenatal and perinatal hormonal influences, and environmental influences that have psychological effects.

**Treatment:** Individuals with GD seeking professional help begin with psychotherapy. An American Psychiatric Association Task Force recommends 2 goals for psychotherapy: (1) to explore issues related to the individual's commitment to living in the cross-gender role; and (2) to fully explore other options for the patient, including whether to live as a homosexual person without medical and surgical treatments for gender transition. The full therapeutic approach to GD consists of 3 elements or phases, typically in the following order: (1) hormones of the desired gender; (2) real-life experience for 12 months in the desired role; and (3) surgery to change the genitalia and other sex characteristics (e.g., breast reconstruction or mastectomy). However, not everyone with GD needs or wants all elements of this triadic approach.

**Technology:** The goal of cross-sex hormone therapy for GD is to alter secondary sex characteristics, including such features as fat distribution, hair growth, voice pitch, and muscle strength.

Cross-sex hormone therapy includes estrogens and testosterone-blocking agents administered to natal (biologic) males and androgens (usually testosterone) administered to natal females. Adolescents with a

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## Hormone-GD

diagnosis of GD may be eligible for puberty-delaying hormones as soon as pubertal changes begin; the effects of this treatment are fully reversible.

**Rationale:** Hormone therapy serves to feminize or masculinize the body to facilitate an individual's desire to live in the gender role opposite from biological sex.

**Controversy:** Numerous professional groups have advocated for third-party payers to cover all medically necessary treatments to alleviate GD. However, the condition does not readily fit traditional concepts of medical necessity since research to date has not established anatomical or physiological anomalies associated with GD.

An evidence-based assessment of the effectiveness of hormone therapy for alleviation of symptoms associated with GD and improvement of recipients' well being can make a helpful contribution to this controversy.

### Relevant Questions:

- Has feminizing or masculinizing hormone therapy in adolescents and adults been shown to be effective in improving patient-important outcomes such as relief of symptoms of GD, psychological well-being, sex-specific function, quality of life (QOL), functional status, or employment status?
- How does hormone therapy alone as a treatment for GD compare with sex reassignment surgery (SRS)?
- Is feminizing or masculinizing hormone therapy safe?
- Have definitive patient selection criteria been established for feminizing or masculinizing hormone therapy as a treatment for GD?

**Evidence Base:** Ten peer-reviewed studies, primarily of a cross-sectional or pretest-posttest design, assessing the effectiveness of hormone therapy plus 11 other studies with safety data for  $\geq 100$  adult patients or any safety data for adolescent patients.

**Search Dates:** Inception of databases to April 2014.

**Sample Sizes:** 50 to 376 pts (effectiveness); 1 to 2307 (safety).

**Patients:** Adult or adolescent patients with a diagnosis of GD. Mean age in effectiveness studies of adults, 29 to 45 years. Mean age in safety studies of adults, 41 to 52 years. Typical patients had not undergone either chest or genital SRS.

**Interventions:** Cross-sex hormone therapy or pubertal suppression therapy.

**Comparisons:** No medical treatment, SRS (chest and/or genital).

**Outcome Measures:** QOL, functional status, or employment status; psychological well-being (e.g., depression, self-esteem, reduced incidence of suicide); sexual function and satisfaction; and complications of hormone therapy, regret, or any other adverse event attributable to treatment.

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Hormone-GD

**Follow-Up:** 3 months to 1 year (effectiveness studies, usually not reported); 2 to 23 years (safety studies).

**Findings:** Studies that evaluated hormone therapy in adults suggested the possibility of a small effect on QOL and function, specific psychological symptoms, social support, and alcoholism. The findings were inconsistent with respect to a relationship between hormone therapy and general psychological health, substance abuse, suicide attempts, and sexual function and satisfaction (9 studies).

**QOL/Functional Status (Adults):** 5 studies ( $\geq 812$  participants;  $\geq 796$  FtM) reported positive findings on  $\geq 1$  scale, but usually not on all scales used in the study. Differences between treated and untreated study participants were very small or of unknown magnitude in cross-sectional analyses that adjusted for potential confounders but were substantial in 1 pretest-posttest study.

**Psychological Symptoms (Adults):** In 6 studies, the results for a variety of specific psychological states (e.g., depression, anxiety) were positive, but overall measures of change in psychological symptomatology were mixed. In the studies that provided information on the magnitude of scales and/or cutoff points for normal ranges, the differences, if observed, were generally very small and scores for patients representing the control condition were typically already in the normal or mild range.

**Other Outcomes (Adults):** Improved social support and reduced alcoholism were suggested but the results regarding substance abuse were conflicting (2 studies). The prevalence of suicide attempts was not affected by hormone therapy (2 studies). Findings regarding the association of hormone therapy with sexual function and satisfaction were mixed (3 studies).

**Comparative Effectiveness of Hormone Therapy Alone Versus Surgery (Adults):** The evidence was too sparse to allow any conclusion regarding the comparative benefits of SRS and hormone therapy alone.

**Adolescents (Pubertal Suppression):** Evidence from a single small study was insufficient to suggest conclusions regarding the value of pubertal suppression therapy.

**Safety (Adults):** Hormone therapy has the potential to alter patients' risk of cardiovascular disease, cerebrovascular and thromboembolic events, osteoporosis, and cancer. The risk of no benefit must also be considered. There was an increased risk of cerebrovascular and thromboembolic events in MtF patients. There was *no* elevated risk of cancer in FtM patients. Hormone therapy and subsequent SRS failed to bring overall mortality, suicide rates, or death from illicit drug use in MtF patients close to rates observed in the general male population. It is possible that mortality is nevertheless reduced by these treatments, but that cannot be determined from the available evidence. Mortality data for FtM patients is less clear than for MtF patients. For safety issues other than the specific findings described here, the evidence was insufficient to suggest conclusions. There was no evidence concerning the prevalence of regret after hormone therapy.

**Safety (Adolescents):** The chief risks cited for pubertal suppression therapy are related to the possibility the GD could worsen because of the delay in definitive treatment. No serious side effects during pubertal suppression were reported. Older adolescents may begin cross-sex hormone therapy, but only a single case report provided long-term data for individuals who began therapy as adolescents. The body of evidence

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Transforming Healthcare with Evidence

## Hormone-GD

concerning the safety of pubertal suppression and cross-sex hormone therapy in adolescents was too sparse and the studies too limited to suggest conclusions.

**Patient Selection Criteria:** The evidence is insufficient to support patient selection criteria for hormone therapy to treat GD. Professional associations recommend that hormone therapy be restricted to patients who have been referred for such treatment by a health professional who is qualified to assess GD. In adults, medical conditions that can be exacerbated by endocrine treatment must be evaluated and addressed prior to initiation of treatment. Practice guidelines advise that pubertal suppression therapy should not be initiated until adolescents have at least reached Tanner stage 2.

### Quality of Evidence: Very low.

Most studies were considered to be of very poor quality due to the nature of the study designs, failure to control for confounders, possible recall bias and selection bias, lack of blinded outcomes assessment, and/or unknown or short follow-up intervals. Not all positive results were statistically significant. For other outcomes, the findings were conflicting. For QOL and function, almost all of the available data were collected from FtM individuals for whom a diagnosis of GD could not be verified. For outcomes other than QOL and function, the quantity of evidence was very small. In safety studies, the relatively young age of study participants at the time of outcomes assessment and the lack of adjustment for risk factors in comparisons of study participants with age-matched general populations seriously diminishes the reliability of the available adverse event rates. No studies analyzed safety outcomes according to whether patients had undergone SRS, which is significant since hormone doses are lowered after SRS. The safety evidence described for adults in the **EXECUTIVE SUMMARY** is considered to be of low quality, but all other adult safety evidence was considered to be of very low quality.

**Conclusions:** A substantial number of studies of cross-sex hormone therapy each show some positive findings suggesting improvement in well-being after cross-sex hormone therapy. However, there are several serious limitations to the evidence.

Statistically significant improvements have not been consistently demonstrated by multiple studies for most outcomes. Five studies representing primarily female-to-male (FtM) adults reported modestly positive findings on  $\geq 1$  of the multiple quality of life (QOL) or functional scales for individuals who had undergone cross-sex hormone therapy, but for most of these individuals, a diagnosis of gender dysphoria (GD) was not confirmed. Evidence regarding QOL and function in male-to-female (MtF) adults was very sparse. Evidence for less comprehensive measures of well-being in adult recipients of cross-sex hormone therapy was directly applicable to GD patients but was sparse and/or conflicting. The study designs do not permit conclusions of causality and studies generally had weaknesses associated with study execution as well. There are potentially long-term safety risks associated with hormone therapy but none have been proven or conclusively ruled out. The evidence for adolescent populations was too sparse to suggest any conclusions.

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Hayes Rating:

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## Hormone-GD

- C - For hormone therapy to treat GD in adults for whom a qualified mental health professional has made a formal diagnosis of GD and a recommendation for hormone therapy and who do not have any medical contraindications to endocrine therapy.  
This Rating reflects the reporting of some positive evidence but serious limitations in the evidence of both effectiveness and safety. Also of concern is the fact that the magnitude of suggested benefit was typically small, which diminishes confidence in a true treatment effect.
- D2 - For pubertal suppression therapy or cross-sex hormone therapy in adolescents.  
This Rating is based on a paucity of data.
- 

## INSIGHTS:

- Since part of the reason for the psychopathology experienced by transgender persons has to do with the reactions or expected reactions of family and society, evolving social norms theoretically could diminish the perceived need to undergo physical changes in order to live in the desired gender role.
- The benefits of hormone therapy appear to be of very small magnitude in the studies published to date. The literature does not provide guidance for assessing the clinical relevance of improvements in this population. One factor that may prevent the observation of large improvements is that individuals with a better social support and a better baseline psychological profile are probably seen to be better candidates by the mental health professionals who make recommendations for treatment.
- As the population of recipients of hormone therapy ages, better data concerning long-term safety risks should become available.
- Most studies have been performed in Europe. The results may not be generalizable to the United States.
- The studies selected for this report reflect the diagnostic criteria of DSM-IV, rather than the somewhat expanded criteria published in 2013 in the DSM-5.

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May 9, 2014

## Ancillary Procedures and Services for the Treatment of Gender Dysphoria

### PURPOSE OF TECHNOLOGY:

Some persons with gender dysphoria (GD) may seek hormone therapy and /or sex reassignment surgery (SRS) to resolve their incongruity between biological sex and gender identity. Additional ancillary surgeries or services, such as facial modifications, vocal cord surgery, or voice training, may be desired by transgender persons to further feminize or masculinize the body and/or perception of gender. In some cases, ancillary procedures are performed without SRS.

### EXECUTIVE SUMMARY:

**Health Problem:** Individuals with gender dysphoria (GD) feel a severe incongruity between their biological sex and their gender identity. The prevalence of GD is 1 in 11,900 to 1 in 45,000 persons for male-to-female (MtF) and 1 in 30,400 to 1 in 200,000 persons for female-to-male (FtM) transgender persons.

The earlier term, *gender identity disorder* (GID), has given way to *gender dysphoria* (GD). This change was intended to reflect a consensus that gender nonconformity is not a psychiatric disorder, as it had been previously categorized. However, since the condition may cause clinically significant distress and since a diagnosis is necessary for access to medical treatment, the new term was proposed. The diagnostic criteria for GD outlined in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), Fifth Edition (DSM-V), as well as the criteria for GID in the DSM, Fourth Edition (DSM-IV), require that the individual believes there is a marked difference between the gender assigned to him or her by others and the gender he or she experiences or wishes to express. Additional criteria must also be met for a diagnosis of GD.

**Determinants:** The determinants of GD are poorly understood. Experts believe that gender identity develops as the result of a combination of biological factors, possibly including genetic and/or prenatal and perinatal hormonal influences, and environmental influences that have psychological effects.

**Treatment:** The treatment of GD is multifaceted. Psychotherapy helps the individual explore roles and expression and adopt various coping mechanisms to deal with societal and internal conflicts. Some transgender persons may seek hormone therapy to change their secondary sex characteristics and/or apply for sex reassignment surgery (SRS), which may include mastectomy/chest reconstruction or genital reconstruction. Additional ancillary surgeries or services, such as facial modifications, vocal cord surgery, or voice training, may be desired by transgender persons to further feminize or masculinize the body and/or perception of gender.

**Technology:** Ancillary procedures and services other than cross-sex hormone therapy or SRS for GD.

Some transgender persons desire procedures to feminize or masculinize their body and/or face. Also, some MtF transgender persons may desire voice therapy or vocal cord surgery to feminize their voice. Ancillary procedures include facial modifications, voice modification, reduction of the Adam's apple, enhancement of the buttocks, and permanent hair removal.

**Rationale:** Additional procedures may enhance the benefits of hormone therapy or SRS for GD, and for some individuals with GD, less comprehensive treatments may be sufficient for assuming the desired gender identity.

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**Hayes**

Transforming Healthcare with Evidence

**Short (Abbreviated) Title**

A transgender person who is readily accepted as their chosen gender may have a better quality of life and a reduction in the symptoms of GD.

**Controversy:** The medical necessity of treatments for GD is under debate. However, the condition does not readily fit traditional concepts of medical necessity since research to date has not established anatomical or physiological anomalies associated with GD. An evidence-based assessment of the effectiveness of ancillary procedures for alleviation of symptoms associated with GD and improvement of recipients' well-being can be a helpful contribution to this issue.

**Relevant Questions:**

- Have ancillary procedures and services been shown to be effective in improving patient-important outcomes such as relief of symptoms of GD or quality of life?
- Are ancillary procedures and services safe?
- Have definitive patient selection criteria been established for ancillary procedures and services as treatments for GD?

**Evidence Base:** Thirteen case series studies and chart reviews.

**Search Dates:** Inception of database to April 2014.

**Sample Sizes:** 10 to 76 patients; 1 study had 247 patients.

**Patients:** MtF (n=533) or FtM (n=3) adult transgender patients. It was not specified whether or not patients had a formal diagnosis of GD. The status of cross-sex hormone therapy or SRS among the study population was not reported by 4 of the studies. The remaining studies had variability regarding other GD treatments; however, none had inclusion criteria that specified these characteristics.

**Interventions:** Vocal cord surgery (5 studies), voice training (3 studies), rhinoplasty (2 studies), facial feminization surgery (2 studies), hair removal (1 study).

**Comparisons:** Twelve of the studies had no comparison group. One study of facial feminization surgery compared surgery recipients with patients who had not had facial surgery.

**Outcome Measures:** Patient satisfaction; voice characteristics; Voice Handicap Index; SF-36 Health Survey (QualityMetric Inc.) (1 study); grade, roughness, breathiness, asthenia, strain (GRBAS) Hirano scale.

**Follow-Up:** Mean of 6 to 30 months (5 studies did not report follow-up).

**Findings:** Patients were satisfied with the results of facial feminization and rhinoplasty; however, the results of vocal cord procedures and voice training were mixed.

**Vocal Cord Procedures:** Of the 5 reviewed studies of vocal cord surgery, 2 evaluated cricothyroid approximation, 2 evaluated laser vaporization, and 1 evaluated laryngoplasty. Cricothyroid approximation significantly raised the fundamental frequency of MtF transgender patients by a mean of 74 hertz (Hz). Laser vaporization significantly raised the fundamental frequency of MtF transgender patients by a mean of 48 Hz.

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### Short (Abbreviated) Title

Feminization laryngoplasty significantly increased the fundamental frequency by 57 Hz. Patient satisfaction with the vocal cord surgery was variable, but the results suggest that patients were more satisfied following cricothyroid approximation than laser vaporization.

**Voice Training:** Three studies evaluated voice training as a method to increase the fundamental frequency of MtF transgender patients. The fundamental frequency increased by 14 to 28 Hz after voice training sessions and approximately half of the patients were satisfied with the outcome. One study evaluated voice training to decrease the fundamental frequency of 3 FtM patients; however, results of only 1 patient were available and his fundamental frequency decreased by 35 Hz after vocal training.

**Rhinoplasty:** Two studies evaluated feminization rhinoplasty on MtF transgender patients. All but 1 of the patients felt that their face had become more feminine in appearance and were satisfied with the results.

**Facial Feminization Surgery:** Two studies of facial feminization surgery were reviewed. In a retrospective case series study, MtF transgender patients who had various facial modification procedures felt that their faces had become more feminine in appearance. In a large retrospective cross-sectional study, quality of life was measured in MtF transgender patients who did or did not have facial feminization surgery. Patients who had facial feminization surgery were significantly more satisfied with their appearance than those who did not have facial surgery.

**Permanent Hair Removal:** One study of intense pulsed light epilation for permanent hair removal on MtF transgender patients was reviewed. After a mean of 9 epilation sessions, 90% of the patients achieved treatment success.

**Safety:** Most of the studies did not report complications; however, complications that were reported included bone nonunion following facial surgery (2% of patients); and dysphagia (34% of patients) or throat pain (29% of patients) following cricothyroid approximation.

**Patient Selection Criteria:** There is insufficient evidence to establish definitive patient selection criteria for ancillary procedures and services for the treatment of GD.

### Quality of Evidence: Very low.

The individual study quality was generally very poor. The quality of the evidence was low because of study limitations, including small sample size and few studies evaluating each procedure category, lack of a control or comparator group, variable follow-up duration, inconsistent availability of results for all outcome measures, lack of baseline data for self-rated outcome measures, and lack of statistical analysis of results. Outcome measures were focused on technical success and patient satisfaction; only 1 study evaluated an overall measure of well-being using a validated instrument.

**Conclusions:** There is some evidence that transgender patients are satisfied with the results of rhinoplasty and facial feminization surgery, but patient satisfaction with vocal cord surgery and voice training was mixed. The evidence has serious limitations, and the effect of these procedures on overall individual well-being is unknown.

- Patients who had rhinoplasty or facial feminization surgery were generally pleased with the results.

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**Short (Abbreviated) Title**

- Vocal cord procedures and voice training had variable outcomes. Although the fundamental frequency was reduced by all treatment methods, patient satisfaction with the outcome was mixed.
- Most of the studies did not report complications; however, there was a low rate of bone nonunion following facial surgery, and moderate rates of dysphagia or throat pain following cricothyroid approximation.

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**Hayes Rating:**

- D2 - For vocal cord surgery for voice feminization in patients with GD.  
This Rating reflects the positive but limited evidence of this technology for transgender patients.
- D2 - For voice training for voice feminization in patients with GD.  
This Rating reflects the limited evidence of this technology for transgender patients, and conflicting results.
- D2 - For feminization rhinoplasty for patients with GD.  
This Rating reflects the limited evidence of this technology for transgender patients, and conflicting results.
- D2 - For facial feminization surgery in patients with GD.  
This Rating reflects the positive but limited evidence of this technology for transgender patients.
- D2 - For permanent hair removal technologies for patients with GD.  
This Rating reflects the positive but limited evidence of this technology for transgender patients.

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**INSIGHTS:**

- Since part of the reason for the psychopathology experienced by transgender persons has to do with the reactions or expected reactions of family and society, evolving social norms theoretically could diminish the perceived need to undergo physical changes in order to live in the desired gender role.
- As the population of recipients of ancillary procedures ages, better understanding concerning long-term safety risks should become available.

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