



Considerations for Transgender People With Diabetes

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This article offers clinicians resources and an overview for supporting gender-diverse individuals with diabetes. Creating a supportive office environment is crucial to providing optimal diabetes care for patients who identify as transgender.

Individuals who identify as transgender have a gender identity that is different from their sex at birth (1). This can lead to gender dysphoria, a condition in which individuals experience feelings of anxiety and distress because of the discrepancy or conflict between their gender identity and physical body (2). In 2016, it was estimated that ~1.4 million adults (390 per 100,000 or ~0.6% of adults) in the United States identify as transgender (3). This is a conservative estimate because not every transgender individual identifies publicly.

As of 2018, the Centers for Disease Control and Prevention reported that 31.4 million (~13%) adult Americans had diabetes, and 88 million had prediabetes (4). There are mixed data on transgender individuals' risk for developing type 2 diabetes compared with the general population. In one study ($n = 352$), the prevalence of diabetes in transgender individuals undergoing sex hormone therapy was 37.3% in transwomen and 14.5% in transmen (5). A retrospective chart review ($n = 82$) found no statistically significant difference in type 2 diabetes rates in transgender individuals compared with the general population (6). The exact rate of diabetes in transgender individuals remains unknown because many studies only ask binary gender (male/female) questions.

The intersection of the transgender and diabetes populations presents unique challenges for clinicians. The lack of existing research about best practices for managing diabetes in transgender individuals adds complexity to already intricate care regimens. The interactions of multiple exogenously administered hormones and hormone analogs are not well studied or well understood,

which introduces uncertainty to diabetes regimens that include insulin in the transgender individuals. In this article, we aim to identify the psychosocial and pharmacological intersections of transgender medicine and diabetes management that may warrant consideration and require additional risk management when simultaneously initiated or monitored by clinicians.

Foundations of Transgender Care

Before discussing how to care for transgender people with diabetes, clinicians should first understand the basics of how to meet the needs of transgender people in a clinical setting generally. Based on the University of California at San Francisco's (UCSF's) Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People (7), all people should be asked about their individual preferences regarding terminology. Table 1 depicts common terminology that can aid in providing gender-affirming care (7). Table 2 lists frequently used pronoun preferences. During office visits, only medical history questions that are relevant to the office visit for diabetes management should be asked (7). Encourage all clinic staff to gain an understanding of pronoun preferences and to approach all people with respect. On forms, consider using a "two-step method" to gather gender identity as well as a person's sex assigned at birth (7).

Maintaining an organ inventory allows providers to follow evidence-based guidelines, especially when providing care for medical concerns beyond diabetes. The diabetes section of the UCSF guidelines (7) for transgender care and treatment recommends that care for transgender people, regardless of hormone status, should not differ from current national guidelines for diabetes care; it notes, however, that the effects of gender-affirming hormone therapy have an unclear impact on diabetes risk and severity. The authors

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TABLE 1 Terms Used to Describe Gender and Sexuality and Their Definitions

Term	Definition
Cis-gender	“Cis” is from the Latin word for same side. This term is used to describe people who are not transgender.
Gender expression	Individual expression or display of gender, including clothing, speech, and mannerisms. Gender expression can differ from gender identity. For example, a woman, whether cis-gender or transgender, can dress in an androgynous style.
Gender dysphoria	Distress or discomfort that may occur if sex designated at birth is not concordant with gender identity.
Gender-nonconforming	Behaviors that are considered outside of the social norms for an assigned sex.
Gender identity	The internal sense of self and how one fits into the world, from the perspective of gender.
Nonbinary	A gender-nonconforming person who identifies as neither male nor female; other common terms include noncisgender, genderqueer, two-spirit, third sex, and gender fluid.
Sex	Assigned at birth, based on chromosomes and gonads.
Sexual orientation	A term that is used to describe sexual attraction and not directly related to gender identity.
Transgender	Used only as an adjective to describe a person whose gender identity defers from the sex assigned at birth. Commonly abbreviated as “trans.” Not to be used as a noun or verb.
Transgender man	A person with a male gender identity and a female sex assigned at birth.
Transgender woman	A person with a female gender identity and a male sex assigned at birth.
Transsexual	An older term that has fallen out of favor but was used to describe transgender individuals who sought gender-affirmative care.
Transvestite	A pejorative term that should not be used.

Adapted from refs. 7 and 28.

recommend reviewing UCSF’s guidelines (7) for more information on this topic.

Psychosocial Impacts on Health Management

Psychosocial Impact of Identifying as Transgender

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition (DSM-5), describes gender dysphoria as the associated distress caused by incongruence between sex designated at birth and gender identity (8). According to the DSM-5, a gender dysphoria diagnosis is appropriate when these feelings cause longstanding interference with social activities, school, and other functional areas of life.

TABLE 2 Sample Pronoun Preferences

- She/her/hers
- He/him/his
- Ze/hir/hirs
- They/them/their

Note: neutral pronouns are commonly used and preferred by individuals who have a nonbinary or nonconforming gender identity.

It is important to note that not all transgender individuals experience gender dysphoria (9). Although gender dysphoria is not an appropriate diagnosis for all transgender individuals, the ongoing debate regarding whether gender diversity should be considered a disorder (9,10) is beyond the scope of this article.

The psychosocial impacts of identifying as transgender are well studied. Across the life span, transgender individuals are more likely to experience clinical depression and anxiety and to smoke, attempt suicide, and abuse substances (11). In addition, transgender individuals face widespread discrimination, harassment, and social stigma (12). The higher rate of unemployment within the transgender community may be the result of the discrimination they face in society. Without a stable source of income, they are less likely to be able to afford health insurance, which can restrict their access to medical care (11). Furthermore, transgender individuals with a noticeable nonconforming appearance because of a lack of gender-affirming care are especially vulnerable to marginalization (13).

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Transgender youths with gender dysphoria are at an increased risk for adverse psychosocial outcomes. Olson et al. (14) describe that “finding comprehensive medical and mental health services is extremely difficult for these youths, who are at risk for multiple psychosocial problems, including family and peer rejection, harassment, trauma, abuse, inadequate housing, legal problems, lack of financial support, and educational problems.” Parental or guardian support is pivotal for transgender youths, as is support from their medical care team.

Health care professionals (HCPs) who lack appropriate training and exposure to the transgender community can be a barrier to transgender individuals receiving care (15). This lack of experience hinders HCPs’ ability to provide care that is inclusive of and sensitive to these individuals, further adding to the anxiety and discrimination that causes many transgender people to avoid seeking necessary care. In a National Center for Transgender Equality survey (16), half of respondents reported having to teach their HCPs about transgender health care, and nearly 20% reported being refused care because of their gender. Patients should not have to educate their HCPs about how to provide gender-affirming medical care.

Psychosocial Impact of Diabetes

People with diabetes commonly face a variety of barriers to optimal self-management (17). Compared with those without diabetes, individuals with type 2 diabetes are almost two times as likely, and those with type 1 diabetes are more than three times as likely, to have depression (18). Diabetes distress, a diabetes-specific emotional state often caused by diabetes care demands, is present in 42.1% of adults with type 1 diabetes (19) and 36% of those with type 2 diabetes (20). Consistent with findings in adults, children and adolescents experience similar levels of diabetes distress, which is associated with suboptimal glycemic control (21). Another study determined that comorbid depression had a significantly strong association with poor self-care, likely leading to worsening hyperglycemia and diabetes complications (22).

Individuals with diabetes who are overweight or obese encounter social stigma regarding their bodies that has been shown to negatively affect their self-care habits (e.g., leading to omitting injections and glucose checks in public) and to contribute to their psychological distress around their diabetes (23). This stigma also increases their risk for disordered eating (23). Such

stigma, when detected in the behavior of health care workers, can prevent people with diabetes from attending visits with their diabetes care team and cause a deterioration in their home diabetes care regimen (23).

Intersectionality of Psychosocial Considerations for Diabetes and Transgender Care

Given the increased risk of mood disorders in both transgender individuals and people with diabetes, clinicians should take special care to screen transgender individuals with diabetes for depression and anxiety. A study in the Netherlands found that the Patient Health Questionnaire-9 is a sensitive and efficient depression screening tool for adults with type 2 diabetes when using 12 as the cutoff score to account for several overlapping symptoms between diabetes and depression (24). The same screening tool was used to successfully detect depression in transgender youth (25). Two versions of a Diabetes Stigma Assessment Scale have been developed to measure experienced stigma in populations with type 2 diabetes or type 1 diabetes (26,27); however, more research is needed to develop a similar tool for the transgender population or a more generally validated tool that is not condition-specific. Although no evidence exists to suggest that the presence of gender dysphoria has a direct impact on diabetes distress, it may be prudent to maintain a frequent screening schedule for diabetes distress in this population given the combined emotional burden of the two conditions.

Clinical Considerations for Primary Care

Providing gender-affirming care does not necessarily involve medications or surgery. Affirmative care can simply mean acknowledging and supporting an individual’s gender identity. Using individuals’ preferred pronouns and terminology is essential, from the clinic front desk to the exam room. Table 3 offers suggestions for establishing a supportive clinical environment for transgender individuals (7,28).

Treatment Guidelines for Transgender People With Diabetes

Although the American Diabetes Association (ADA) has not published specific guidelines for treating transgender individuals with diabetes, several other organizations have created or cosponsored their own guidelines for the care and management of transgender, gender-nonbinary, gender-incongruent, and gender-nonconforming individuals (7,29–31). Despite noting an

TABLE 3 Steps for Establishing Trust and Creating a Gender-Inclusive Clinic

1. Use individuals' preferred pronouns and name. Many patients may not have legally changed their name, so their preferred name may not be reflected on documents such as insurance cards and driver's licenses.
2. Use a two-step system to make intake forms gender-inclusive by allowing individuals to write in both their gender identity and the sex assigned to them at birth.
3. Train the entire clinic staff to use gender-inclusive language.
4. Ensure access to unisex bathrooms.

Adapted from refs. 7 and 28.

increased risk of developing type 2 diabetes while undergoing hormone treatment, these guidelines do not include specific considerations for diabetes care in the transgender population (29,30). The Endocrine Society (29) and the American Academy of Clinical Endocrinologists (AACE) (31) recommend that gender-affirming hormones not be initiated until the age of 16 to ensure the persistence of gender dysphoria, whereas the UCSF Transgender Center of Excellence recommends initiating hormone treatment based on development rather than at a specific age (7). It is also recommended that gender-affirming surgery be performed after the age of 18 years, after a full year of hormone therapy (29,30). The World Professional Association for Transgender Health (WPATH), The Endocrine Society, and the AACE all recommend that gender-affirming treatment not be initiated until preexisting conditions, including diabetes, are well controlled (29–31). In contrast, UCSF's Transgender Center of Excellence (whose guidelines are alone in including diabetes-specific language) warns against requiring adequate control of diabetes before initiating treatment, citing anecdotal evidence that many individuals achieve improved diabetes management after initiating treatment for their gender dysphoria (7). However, in the case of gender-affirming surgery specifically, UCSF does recommend more aggressive glycemic control for trans individuals with diabetes to promote optimal postoperative healing and decrease the risk of infection (7).

Clinical Considerations for Female-to-Male Transitioning Individuals With Diabetes

Gender-affirming hormone therapy is associated with changes that place transgender individuals at greater risk for developing certain comorbidities. For those undergoing a female-to-male (FtM) transition, the most frequently observed changes are increases in LDL cholesterol and triglyceride levels and a decrease in HDL cholesterol, potentially putting them at a greater risk for developing complications associated with diabetes (32). Although no correlation between masculinization hormones and cardiovascular morbidity or mortality

has been shown in this population (33), atherosclerotic cardiovascular disease (ASCVD) is the leading cause of death in people with diabetes, likely because of the common comorbidity of dyslipidemia (34).

Given the preexisting increased cardiovascular risk from diabetes (34), the additional risk of testosterone treatment should prompt an emphasis on regular lipid screening in transgender individuals with diabetes. Clinicians may consider annual lipid screening in these patients regardless of their age or whether they are on statin therapy (34,35). Maintaining adequate surveillance will enable clinicians to initiate lipid management, such as the widely used approach of high-intensity statin therapy, at the appropriate time, if necessary.

Another unique consideration is for individuals with a history of polycystic ovarian syndrome (PCOS) before initiating hormone therapy. Although PCOS in cis-gender females is a known risk factor for insulin resistance and development of type 2 diabetes, the risk is unclear for transgender males when taking testosterone. The UCSF guidelines suggest this patient population may need continued close screening for diabetes because outcome studies in this area have not been conducted to date (7).

Masculinization therapy leads to increased insulin sensitivity and incretin response, perhaps explained by the decrease in fat mass and increase in lean muscle observed after initiating testosterone therapy (36). Especially for individuals taking exogenous insulin to treat their diabetes, initiation of testosterone should prompt increased blood glucose monitoring to prevent hypoglycemic episodes as a result of increased insulin sensitivity. Insulin requirements may decrease in the presence of testosterone, which would be detected by an increase in hypoglycemia frequency and through review of glucose data at follow-up visits. HCPs should discuss this potential increased risk and review the self-care protocol for hypoglycemia with patients before initiating testosterone treatment.

Clinical Considerations for Male-to-Female Transitioning Individuals With Diabetes

Individuals undergoing male-to-female (MtF) transitioning seem to experience different, seemingly opposite, effects of their hormone treatment. One such observation is that ethinyl estradiol and cyproterone acetate, two commonly prescribed medications for MtF gender transitions, have been noted to increase insulin resistance and subsequent development of diabetes (37). One review reported an increase in fat mass, decrease in lean muscle mass, and increase in fasting insulin levels after initiation of feminizing hormones (36), potentially providing further explanation of increased insulin resistance. For MtF individuals with insulin-dependent diabetes, these changes call for additional glucose monitoring after initiation of hormone therapy to identify the need for increasing insulin doses.

Antiandrogens can be used to suppress testosterone production, which will contribute to phenotypic characteristics targeted for MtF transition (7). The addition of spironolactone, a potassium-sparing diuretic with androgen blockers, is often used for treatment of hirsutism. Spironolactone is also associated with causing breast tissue enlargement. This medication may cause hyperglycemia in <5% of people, so close monitoring of blood glucose is recommended (38). Other medications such as 5- α reductase inhibitors do not induce hyperglycemia or worsen diabetes management. They are often used if there is a contraindication to the use of spironolactone (7).

Although the aforementioned review (35) noted an overall lowering effect of estrogens on LDL cholesterol, HDL cholesterol, and triglyceride levels, another study showed a trend (although not statistically significant because of insufficient sample size) of more frequent cardiovascular events in individuals taking feminizing hormones than in those taking masculinizing hormones (33). Given the higher risk of ASCVD-related death in individuals with diabetes (33), monitoring of lipid levels remains important for this population.

One of the more recent reviews on the relationship between diabetes and venous thromboembolism (VTE) suggests at most a modest positive association between the two (39). For this reason, it may be additionally important to adhere to the WPATH guidelines of using transdermal estrogen patches when treating transgender individuals with additional risk factors for

developing VTE, including diabetes, especially if those individuals are >40 years of age (30). Table 4 summarizes recommendations for managing diabetes in individuals receiving gender-affirming hormone therapy.

Clinical Considerations for Transgender Youths

Hormonal interventions to suppress puberty may be beneficial for transgender youths in conjunction with multidisciplinary care, including psychosocial support (29). Suppression of puberty for these youths may decrease the risk of developing body dysphoria, which is associated with comorbid psychosocial issues. The effect on diabetes management of gonadotropin-releasing hormone (GnRH) therapy to suppress puberty is largely unknown. Commonly used medications include histrelin acetate subcutaneous implants or intramuscular injections of leuprolide acetate or triptorelin pamoate. In individuals receiving androgen deprivation therapy for prostate cancer, hyperglycemia has been reported (40). Thus, monitoring blood glucose and A1C may be warranted in youths using these medications at baseline and periodically thereafter.

Conclusion

Caring for people with diabetes can present numerous challenges ranging from titration of medications to monitoring for emotional well-being and managing the risks of complications. Incorporating the additional complexity of clinical care for transgender individuals can be especially challenging for both patients and providers, especially without research-based and accessible guidelines for navigating this intersectionality.

Validated screening tools for psychosocial issues, including depression, anxiety, diabetes distress, and the harmful effects of stigma, should be used for all individuals with diabetes. Because transgender people with diabetes are a high-risk group for psychosocial complications and should be regularly monitored, new tools should be created and validated for this population.

HCPs should attempt to reduce diabetes and cardiovascular risk factors among all people, with a particular attention to transgender patients taking hormone therapies or GnRH analogs.

There are disparities in research on the intersectionality of many areas of transgender medicine and diabetes management. Although the literature provides some insight for care recommendations, more research,

TABLE 4 Recommendations for Diabetes Management in People Receiving Gender-Affirming Hormone Therapy

Patient Scenario	Metabolic Effects	Treatment Considerations
MtF gender-affirming hormone therapy (estrogen predominance)	Increased insulin resistance	Increased risk of hyperglycemia; consider monitoring glucose for hyperglycemia. Titrate medications accordingly and consider increasing insulin doses as needed.
	Decreased LDL cholesterol, HDL cholesterol, and triglycerides and increased risk of VTE	Maintain lipid screening schedule per ADA guidelines. Consider using transdermal estrogen patch, especially in patients >40 years of age.
FtM gender-affirming hormone therapy (testosterone predominance)	Increased insulin sensitivity	Increased risk of hypoglycemia; consider monitoring glucose for hypoglycemia and decreasing insulin doses accordingly.
	Increased LDL cholesterol and triglycerides and decreased HDL cholesterol	Adhere closely to ADA screening recommendations for dyslipidemia and cardiovascular complications given the additive risk of both treatments/conditions.
Adolescents using GnRH therapy to suppress puberty	Possible hyperglycemia	Monitor for diabetes at baseline and periodically thereafter.

including both case studies and clinical trials, is necessary to develop well-informed best practices guidelines for clinicians who treat transgender people with diabetes. Many of the studies cited in this article had very small sample sizes. Further research is needed to understand the co-treatment of gender dysphoria and diabetes, as well as the long-term impact of a history of PCOS on transgender male individuals.

All HCPs should practice cultural humility in providing care to all people (41). Cultural humility is a lifelong process of learning, self-reflection, self-evaluation, and collaboration with people who belong to different cultures. To reduce transgender health disparities and provide optimal diabetes care, HCPs, health care organizations, and health care policymakers should strive for the provision of culturally humble care and services.

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DUALITY OF INTEREST

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AUTHOR CONTRIBUTIONS

S.L., B.C, and D.V. researched data and wrote the manuscript. J.M. researched data, wrote the manuscript, and reviewed and edited the manuscript. J.M. is the guarantor

of this work and, as such, had full access to all the data reported and takes responsibility for the integrity of review.

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