

# Recommendations to Appropriately Dose Medications in Transgender Patients

by Jennifer A. Polenska, PharmD

According to a study completed in 2016 by University of California, Los Angeles's (UCLA) Williams Institute, approximately 0.6% of people identify as transgender, which amounts to 1.4 million Americans.<sup>1</sup> Transgender patients face a considerable number of health disparities, including an increased risk of HIV infection, a lower likelihood of preventative cancer screenings in men, and generally poor access to quality healthcare.<sup>2</sup> In order to provide the best possible care to this specific patient population, it is important to understand and recognize these patients' needs—for example, understanding medication essentials that may require an adjustment based on a changing SCr or weight. Additionally, it is essential that healthcare providers understand the terminology of the transgender community, which helps with communication and documentation. Providers should work to understand the impact that gender transition can have on medication therapy. As laid out in table 1, there are some important terms that providers should understand to help treat this patient population.<sup>3</sup>

When gender transitions occur, hormonal therapy is usually needed to help with the physical transition; this is usually referred to as gender-affirming therapy. Gender-affirming therapy is the primary medical intervention sought out by transgender patients that will allow acquisition of secondary sex characteristics to become more aligned with an individual's gender identity. It is currently unclear how these hormonal therapies can affect the SCr and LBM, and currently only one recommendation exists for how to calculate CrCl and IBW. It is important for healthcare professionals to know how hormonal therapy could potentially affect CrCl and IBW, since medications that are adjusted for renal function or by weight could end up being under- or over-dosed. This article will review the four main studies

## Clinical Question

How does gender-affirming hormonal therapy affect serum creatinine (SCr), body mass index (BMI), and lean body mass (LBM)? How should creatinine clearance (CrCl) and ideal body weight (IBW) be assessed in order to dose medications appropriately?

**TABLE 1. Defining Vocabulary of the Transgender Community**

Term	Definition
Transgender man	A person who identifies as a man and was born with female sex characteristics
Transgender woman	A person who identifies as a woman and was born with male sex characteristics
Cisgender man or woman	A person whose gender identity matches the sex characteristics they were born with

*Adapted from GLAAD Media Reference Guide - Transgender. GLAAD. Published March 28, 2021. Accessed January 26, 2021. <https://www.glaad.org/reference/transgender>*

that exist for this area of study, and will make suggestions on how gender-affirming hormonal therapy can affect SCr, BMI and LBM, and how CrCl and IBW should be assessed to help with medication dosing.

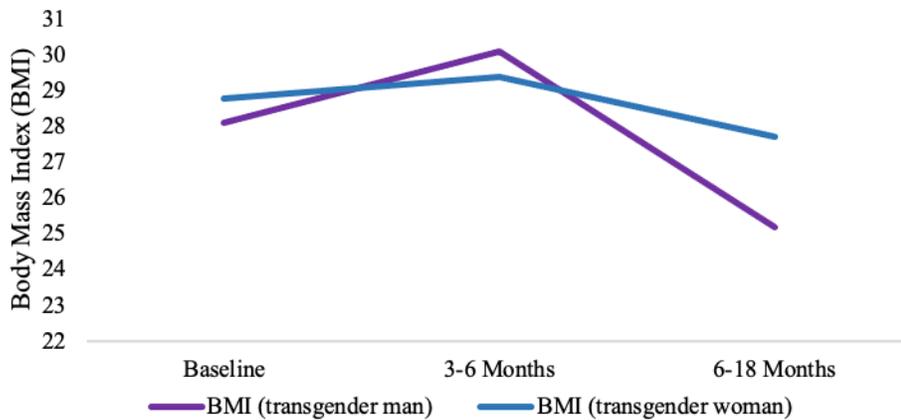
## Literature Review

In 2008, an observational cross-sectional study of 23 transgender women was completed to compare bone composition, LBM, BMI, muscle composition, and laboratory values (including SCr).<sup>4</sup> These 23 transgender women were compared to a control group that included 46 cisgender men. The inclusion criteria for this study included transgender women who had completed gender affirmation surgery (GAS) at least 3 years prior to the enrollment and who had taken estrogen therapy for at least 2 years prior to GAS.<sup>4</sup> When looking at LBM, the median LBM was lower in transgender women than in cisgender men (51.2 kg vs 61.8 kg;  $P < 0.001$ ), and the median SCr was found to be lower in transgender women than in cisgender men (0.78 mg/dL vs 0.94 mg/dL;  $P < 0.001$ ).<sup>4</sup> From this study, it was found that long-term

treated transgender women with estrogen therapy ended up presenting with a different body composition, smaller bone size, and a lower bone turnover compared to the control group of cisgender men.<sup>4</sup> While this study is one of the first to report volumetric and geometric bone parameters in long-term treated transgender women, it also has some limitations. This study used a cross-sectional design, which did not allow the researchers to draw any causative conclusions from the results.<sup>4</sup> A second limitation is the lack of baseline measurements for the participants, meaning that the differences in body composition, bone metabolism, and size could be attributed to lifestyle factors that might have been present before gender-affirming therapy was started.<sup>4</sup>

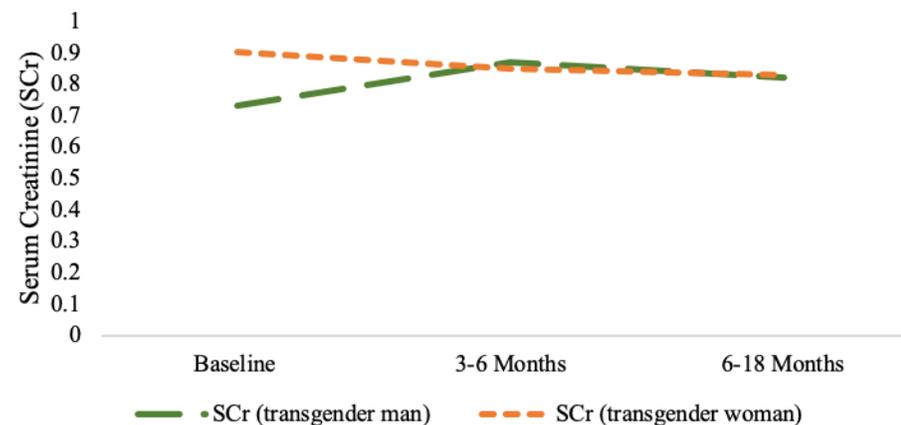
Additionally, in 2016, a retrospective cohort study of transgender women and transgender men who were using gender-affirming hormone therapy was completed to compare their BMIs, blood pressures, and laboratory values (including SCr) at baseline, 3 to 6 months after starting hormone therapy, and 6 to 12 months after starting hormone therapy.<sup>5</sup> This study

**FIGURE 1. Effect of Hormonal Therapy on Body Mass Index**



Adapted figure 1 from Fernandez JD, Tannock LR. Metabolic effects of hormone therapy in transgender patients. *Endocr Pract.* 2016;22(4): 383-8. doi: 10.4158/EP15950.OR

**FIGURE 2. Effect of Hormonal Therapy on Serum Creatinine (SCr)**



Adapted figure 2 from Fernandez JD, Tannock LR. Metabolic effects of hormone therapy in transgender patients. *Endocr Pract.* 2016;22(4): 383-8. doi: 10.4158/EP15950.OR

included only patients with a baseline and at least one follow-up visit in the study window, which included 33 transgender women and 19 transgender men. These patients were analyzed separately and grouped into two study arms. One study arm was transgender women, and on average they did not experience a significant change in BMI, and their SCr did decrease from a mean baseline of 0.9 mg/dL to a

mean of 0.85 mg/dL.<sup>5</sup> The second study arm included transgender men, and on average their BMI did increase from a baseline of 28.1 to 30.1 at follow-up, and their SCr did increase from 0.73 mg/dL at baseline to 0.87 mg/dL at follow-up.<sup>5</sup> Figures 1 and 2 display the data from this study, and the figures represent the effects of hormonal therapy on BMI and SCr in transgender women and men. These

figures illustrate how the long-term use of gender-affirming therapy can affect BMI and SCr the longer the hormonal therapy is being used. There are limitations to this study as well. Since this was a retrospective chart review, the data that was available for review was limited.<sup>5</sup> Also, this study experienced a significant drop-out rate that affected the power of the study.<sup>5</sup> Lastly, the timing of follow-up visits after hormone initiation varied among patients, where some had sooner follow-ups, while others had longer intervals between visits.<sup>5</sup> Despite these limitations, it was found that both transgender women and transgender men experienced changes in biomarkers that are used to calculate creatinine clearance and ideal body weight as early as 3 months after starting hormone therapy.

A prospective cohort trial was completed in 1998 that compared LBM, BMI, and laboratory values (including SCr) in 17 transgender women and 17 transgender men, before and after they were on gender-affirming hormone therapy for at least 4 months.<sup>6</sup> The mean SCr baseline values decreased in the transgender women from 0.97 mg/dL to 0.89 mg/dL, but increased in the transgender men from 0.87 mg/dL to 0.96 mg/dL.<sup>6</sup> These findings suggest that after 4 months of hormone therapy, SCr was more closely related to the affirmed gender identity than the patients' sex at birth.

Lastly, a cross-sectional study was completed in 2014 that included 55 transgender women and compared laboratory values (including SCr) to those of 20 cisgender men and 20 cisgender women, to help characterize normal laboratory value ranges in transgender women.<sup>7</sup> For inclusion criteria, the transgender women had to have been receiving estrogen therapy for a least 6 months.<sup>7</sup> The percentile range for SCr values that were reported in transgender women (0.55-1.2 mg/dL) was found to be more like SCr in cisgender men (0.73-1.3

**TABLE 2. Recommendations for Pharmacists to Assess Creatinine Clearance and Ideal Body Weight**

<i>Duration of Hormonal Therapy</i>	<i>Recommendation for IBW Dosing</i>	<i>Recommendation for Estimating CrCl</i>
Not taking hormonal therapy or has started taking for less than 1 month prior to admission	Calculate IBW based on sex at birth	Calculate CrCl based on sex at birth
Initiation of hormonal therapy is less than 6 months prior to admission	Consider calculating IBW based on sex at birth	Consider calculating CrCl based on sex at birth
Initiation of hormonal therapy is greater than or equal to 6 months prior to admission	Consider calculating IBW based on gender identity	Consider calculating CrCl based on gender identity

CrCl = Creatinine Clearance; IBW = Ideal Body Weight  
Adapted table 2 from Webb AJ, McManus D, Rouse GE, Vonderheyde R, Topal JE. Implications for medication dosing for transgender patients: A review of the literature and recommendations for pharmacists. *American Journal of Health-System Pharmacy.* 2020; 77(6): 427-433. doi:10.1093/ajhp/zxz355

mg/dL) than in cisgender women (0.65-1.0 mg/dL).<sup>7</sup> The findings of this study suggest that the possible range of SCr values for transgender women is more similar to cisgender men, but since cisgender men's and women's SCr ranges already overlap, it is difficult to interpret these results accurately.

### Evidence-Based Answer

The literature review above indicates that after transgender patients have taken gender-affirming hormone therapy, their physiology more closely reflects their affirmed gender identity than their sex at birth. Based on the literature review, table 2 demonstrates existing recommendations to help pharmacists assess CrCl and IBW when transgender patients are being seen in the outpatient setting or while they are hospitalized and taking hormonal therapy.<sup>8</sup> While table 2 gives recommendations for assessing CrCl and IBW, there are currently no recommendations for which weight metric to use when calculating CrCl. We believe it would be appropriate to calculate CrCl using the Cockcroft-Gault equation,

in which IBW is routinely used, actual body weight is used if a patient's weight is less than their IBW, and adjusted body weight is used when a patient's actual body weight is greater than 130% of their IBW. In addition, we agree that these 4 studies are a good starting point for this specific topic, but that more studies should be conducted to help make these recommendations stronger. Additionally, this review would be beneficial for healthcare providers to help ensure that transgender patients are being treated effectively and safely with their medications, no matter the healthcare setting where they are being seen.

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