

# Recommendations to Address the Unique Clinical and Psychological Needs of Transgender Persons Living With Multiple Sclerosis

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## CE Information

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**Target Audience:** The target audience for this activity is physicians, advanced practice clinicians, nursing professionals, pharmacists, and other health care providers involved in the management of patients with multiple sclerosis (MS).

### Learning Objectives:

- Identify unique clinical and psychological care needs of transgender (TGD) patients with MS
- Describe best practice recommendations for the care of the TGD person living with MS

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**Background:** People living with multiple sclerosis (MS) face challenges coping with chronic illnesses, and transgender (TGD) persons living with MS may experience additional unique challenges and barriers to care. Medical biases toward TGD people are widely reported, and best practices in TGD MS care have not been identified.

**Methods:** A case report of a TGD person living with MS is reviewed that helped to identify and inform us regarding the unique aspects of their clinical and psychological care needs. We conducted a systematic review of the literature according to the standard methods in PubMed. The literature was reviewed and summarized for relevant topics related to the unique care needs of TGD persons living with MS, and proposed care recommendations were created.

**Results:** We used the aforementioned case to identify and inform the special care needs and subsequently describe proposed recommendations to achieve inclusive comprehensive care of TGD persons with MS. The importance of providing an inclusive environment, comprehensive care, mental health screening, domestic violence screening, and case coordination are highlighted with the goal of providing best practice recommendations for the comprehensive inclusive care of TGD persons living with MS.

**Conclusions:** The lack of published guidance on the care of TGD persons living with MS and our informative case have led to the proposed recommendations for the care of TGD persons living with MS. *Int J MS Care*. 2022;24:35-40. doi:10.7224/1537-2073.2021-066

People with multiple sclerosis (MS) face substantial challenges when coping with a chronic illness. Transgender (TGD) patients with MS experience unique challenges and barriers, and currently there are no TGD MS practice guidelines.<sup>1</sup> The World Professional Association for Transgender Health published standards of care of the health of TGD persons in 1980 and most recently in 2021 (<https://www.wpath.org/publications/soc>), yet the neurologic standards of care of TGD people are limited.<sup>2</sup> Currently, the total number of TGD patients with MS is unknown, although a recent North American Research Committee on Multiple Sclerosis survey of 5604 respondents self-identified 0.45% as TGD.<sup>3</sup> In the United States, studies estimate that approximately 1.0 to 1.4 million people, or 0.3% of adults, identify as TGD, and the numbers are increasing.<sup>4,5</sup> The incidence of pediatric TGD patients is unknown; however, the military health system identified 0.003% TGD youths in their health records.<sup>6</sup>

Disparities in health care and outcomes for TGD persons have been well established in the literature.<sup>4,7,8</sup> Recent nationwide surveys have highlighted TGD persons as a priority population due to these significant disparities.<sup>4</sup> The gaps in quality health care are attributed to many

interrelated factors, including unconscious bias and lack of training.<sup>8</sup> Patients who are TGD and living with MS have reported less comfort in discussing their sexual health with their doctor, and there is lower satisfaction of nonheterosexual patients with their doctor, showing opportunities to improve the patient experience.<sup>3</sup> We propose best practice recommendations related to TGD persons with MS to enhance caregiver education and the care and experience of the patient.

## Methods

We conducted a systematic review of the literature in PubMed (1966-present) according to standard methods.<sup>9</sup> The search terms included *MS and TGD*, *MS and gender identity*, *MS and gender dysphoria*, *MS, gender expression*, *exogenous hormones*, *testosterone*, *estradiol*, *estrogens*, *estriol*, *hypoestrogenic*, *sex hormones*, *transdermal estrogens*, *progesterones*, *antiandrogen*, *hypogonadotropic hypogonadism*, *treatment interactions*, *diagnosis of MS*, and *disease-modifying treatments (DMTs) for MS*. We followed the recent gender dysphoria nomenclature (**Table 1**).

Herein, the case of a TGD person living with MS is reviewed both neurologically and psychologically. We aimed to use this case study to inform our recommendations for the care of a TGD person with MS with the goal of inclusive, competent, and comprehensive care.

## Case Report of a TGD Person Living With MS

### Medical History

The patient initially presented to the local emergency department as a 16-year-old assigned female at birth with lower-extremity numbness, tingling, and gait difficulty.

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They were admitted to the hospital, underwent diagnostic testing (magnetic resonance imaging and cerebrospinal fluid), and were treated with 5 days of intravenous methylprednisolone sodium succinate. They saw the local pediatric neurologist and were referred to a comprehensive MS center. They met the revised McDonald criteria.<sup>10</sup> They were initially treated with glatiramer acetate, but due to continued clinical and radiographic disease activity, the DMT was changed to dimethyl fumarate, then to fingolimod, and finally to ocrelizumab.

### Psychosocial History

The patient is the only child of divorced parents and was raised primarily by the mother and maternal grandmother. The patient completed 9 years of formal education. Additional online coursework was unsuccessful due to the patient's cognitive difficulties. There is no full-time employment history. Support is limited to a romantic partner, immediate family members, and the online LGBTQIA+ community.

The patient described having non-gender-conforming attitudes beginning in childhood and experimenting with outward expressions of male and female presentations in dress in early adolescence. The patient presented to

our clinic as female initially, then gender fluid at age 18 years, with alternating first names and dress according to their gender presentation. The patient's identity remained gender fluid over time. The patient reported feeling ostracized and verbally criticized by peers and extended family members for their gender fluidity. The patient endorsed significant depression and anxiety symptoms.

### Course of Psychotherapy

The patient worked with the Behavior Medicine team for 25 outpatient psychotherapy appointments. A full psychological assessment, including a neuropsychology evaluation, was completed and confirmed the patient's report of depression, anxiety, and cognitive difficulties.

Psychotherapy focused on improving coping skills for mood symptoms and interpersonal difficulties through use of cognitive-behavioral strategies, as well as exploration of gender identity. The patient was taking citalopram, 10 mg. Two psychotherapy themes emerged: (1) gender identity exploration/affirmation—the experience of coming out to family, transition to live as male, exploring psychological topics associated with gender affirmation treatment, relationship between stress and somatic symptoms; and (2) adjustment to MS—discussion of the relationship between MS exacerbations and psychological stress, needle phobia, coping with functional loss.

**Table 1. Gender-Affirming Nomenclature**

Category	Specific elements
Cisgender	Individuals who identify as their sex assigned at birth
Transgender	Gender identity and/or gender expression that differs from the assigned sex at birth
Transgender male	Male gender identity yet assigned female at birth
Transgender female	Female gender identity yet assigned male at birth
Gender dysphoria	Marked difference between experienced and assigned gender that persists for ≥6 mo and causes significant distress or impaired functioning
Gender identity	One's internal feeling of gender
Sex assigned at birth	Chromosomal and anatomical determinant of sex
Gender expression	The physical and behavioral manifestations of one's gender identity
Gender fluid	Gender identity that varies over time
	Of, relating to, or being a person whose gender identity is opposite the sex the person had or was identified as having at birth
Sexual orientation	Describes the person one finds sexually desirable

### Discussion

Best practice recommendations are proposed to advance culturally sensitive care with a multidisciplinary approach (**Table 2**). Personnel of the MS center contribute to the medical experience of TGD patients with MS. An inclusive environment is paramount to the competent care of TGD patients with MS. The inclusive environment begins with each patient's "touch point," with the first greeting by staff using competent and gender-neutral language until the patient preference is known. In addition, the environment should have visual cues that are easily identifiable, such as gender-neutral bathrooms and public posting of nondiscriminatory policies.<sup>11</sup> Culturally competent language and sensitivity education is lacking in medicine.<sup>8</sup> Establishing training and education about the appropriate ways to ask patients about pronouns or names is essential to providing an inclusive environment. It is important to reflect the recommendations in Table 2 to empower caregivers to use gender-affirming language. Ongoing training of caregivers is warranted to be effective. Qualitative research has shown that insufficient provider training can lead to uneasiness and discomfort for both parties and further perpetuate gender bias stigma.<sup>12</sup> Incomplete and outdated electronic health record

(EHR) platforms can lead to inadequate information and failure to capture important identity information. Limited EHRs can affect cohesive data across different specialties and care clinics, creating a siloed experience for the patient, perpetuating stigma and further limiting care. The adoption of comprehensive, shared EHRs provides a vital opportunity to optimize care for TGD patients with MS by explicitly addressing gender-affirmative care.

Complete medical, family, and surgical histories, including pronouns, assigned birth sex history, organ inventory, reproductive history, hormone therapy, and contraceptive use, are important in the care of cisgender and TGD persons with MS. A complete review of systems is needed for comprehensive care because common MS symptoms, such as urinary hesitation and frequent urinary tract infections, were also seen at a rate of 35% as a result of TGD surgical procedures, such as vaginal colpectomy (ie, removal of the vaginal epithelium), which may be performed in TGD men.<sup>13</sup> A primary care provider needs to be confirmed, and the common risks of exogenous hormones need to be known. Because MS can start in the pediatric population, they may experience gender dysphoria, and the caregiver needs to recognize and direct care to the appropriate gender management specialist.<sup>14</sup> Youths who are TGD have high rates of mental health needs, including depression, anxiety, suicidality, and substance abuse; therefore, identifying, supporting, and directing to interdisciplinary care is warranted. A preliminary study of pediatric gender

dysphoria management shows improvement in mental health with pubertal suppression.<sup>15</sup> Other pediatric TGD studies have shown improvement in relationships and academic performance; therefore, connecting the patients to the comprehensive team can have long-lasting effects on quality of life.<sup>16</sup>

Gender-affirming exogenous hormone use history must be taken because it may affect laboratory values, psychological state, risk of autoimmunity, and neurologic states in both the general population and those living with MS.<sup>17</sup> The long-term effect of exogenous hormones on brain structure, function, and cognition are not known. In cisgender adults, declines in testosterone and estradiol are associated with mood and cognitive changes.<sup>17-19</sup> The main pattern of treatment for TGD female to male (TrM) is lifelong testosterone; for TGD male to female (TrW), it is oral or transdermal estrogens, progesterone, and an antiandrogen (cyproterone acetate).<sup>20</sup> The effects of long-term use of antiandrogen therapy is not clear yet; its use in prostate cancer has been associated with a decrease in age-matched autoimmune diseases, including MS.<sup>20</sup> Estrogen use in the general population has been theorized to be neuroprotective and has shown improvement in a controlled study of verbal memory in TrW without MS. The long-term effects of estrogen use in TrW patients with MS are not known.<sup>21,22</sup> Exogenous hormone can also cause changes in laboratory values, so knowledge of these common adverse effects is needed to enhance the care of TGD persons with MS.<sup>5</sup> Exogenous hormones may also

**Table 2. Checklist for Inclusive Care of the TGD Person Living With MS**

Staff	Policies	Check if present in your MS center
Support staff	Gender-neutral patient intake forms Physical center: gender-neutral language and facilities Educational material gender neutral and diverse in representation	
All staff	Greet with gender-neutral terms Ongoing diversity training Resources to refer to TGD support groups	
Medical and psychological staff	Gender-neutral language until pronoun and names established Clarify current gender identity and sex at birth Inclusive medical and surgical history (including an organ inventory as indicated) OCP and exogenous hormone history, current and past Collaborate with gender management teams and refer as indicated Routine mental health screens Connect with primary care provider Screen living arrangements, personal safety, domestic violence; refer as needed Screen for substance abuse, refer as needed	

MS, multiple sclerosis; OCP, oral contraceptive; TGD, transgender.

increase the risk of autoimmune disorders such as lupus, although their link to MS is not well understood.<sup>23</sup> A pattern of an association with TGD people and gender dysphoria and subsequent MS in TrW has been reported, suggesting a possible supporting role for low testosterone and exogenous estrogens on MS risk in males.<sup>17,23,24</sup> Exogenous hormone use has a possible effect on brain structure, function, and regional connectivity, which may influence cognition and other cerebral functioning. One small study showed an improvement in cognition on the Paced Auditory Serial Addition Test correlated to preserved gray matter volume after estradiol use in the TGD person living with MS.<sup>25</sup> For a TrM, taking high-dose testosterone and being left in a hypoestrogenic state may influence the cognitive functional level as well; however, more needs to be seen in this area and other areas related to exogenous hormone use.<sup>26</sup>

Multiple sclerosis is more common in women than in men, possibly due to the disease being linked to low testosterone or estrogen levels; therefore, sex hormones likely play a role in the risk and progression of MS.<sup>27,28</sup> Case reports have raised concerns for an increase in risk of MS due to hypogonadotropic hypogonadism.<sup>29</sup> The use of exogenous hormones in TrW, such as estrogen, may have an increased risk of MS, and 1 survey found that TGD persons with MS reported higher levels of disability and more frequent relapses than their cisgender counterparts.<sup>3</sup> The TrM not taking testosterone should be aware of a possible increased risk of autoimmunity due to estrogen remaining prevalent in their bodies. Estrogens may serve multiple roles in MS, such as shifting the inflammatory pattern from Th1 and Th2 autoimmunity, and a positive effect on myelin repair that wanes as natural estrogens decline.<sup>30</sup> Exogenous hormone and DMT use has not seemed to alter the timing of menopause in patients with MS, yet the long-term use of exogenous hormones in TGD patients in relation to the activity of their MS disease course is unknown.<sup>28</sup> Testosterone may have effects on the immune system and cell death; it may lessen the autoimmune shift seen with estrogens and may trigger greater central nervous system cell death, leading to atrophy.<sup>31</sup> Knowledge of whether a patient is taking any form of exogenous hormone is crucial in ensuring proper comprehensive care, and yet long-term consequences related to the risk, progression, and treatment of MS is not conclusively known.

Magnetic resonance imaging patterns in TGD people with MS may not be unique, yet concern about additional changes to the cortex related to exogenous hormones may be relevant because MS is a neurodegenerative disease and brain atrophy is a known consequence of MS and a common treatment outcome.<sup>32</sup> There are preliminary small studies suggesting that the cortical thickness of the TGD population alters according to exogenous hormone use.

Short- and long-term effects of testosterone replacement therapy are unknown. Small studies demonstrate an increase in the cortical thickness as seen on imaging. Diffusion-weighted imaging studies demonstrate a change in the neural structure of the hypothalamic microstructure after exogenous hormone use, suggesting that exogenous hormone changes structure toward cisgender male proportions.<sup>33</sup> The cortical thickness and subcortical volumetric measures of TrW decreased after estrogen and antiandrogen treatment, again approaching cisgender comparisons, yet these studies are small and not conclusive.<sup>34</sup>

Research has not addressed DMT effectiveness in the setting of TGD MS care. There is little empirical evidence surrounding the intersection of exogenous hormones, neuro-immunologic processes, and DMTs. There is 1 study suggesting a concern for a higher risk of MS in males with gender dysphoria undergoing gender affirmation due to exogenous hormones; this may increase the risk of MS in TGD patients and make recommendations even more relevant.<sup>24</sup> There is much work to be done in this area to clarify DMT use and choice in TGD persons living with MS.

Although it is not inherent that TGD persons will experience psychological distress, rates of mental health disorders are higher in this population. The current literature cites psychological distress rates in this population as high as 39%, compared with 5% in the general population. In addition, TGD persons have a 40% lifetime suicide attempt rate, 9 times that of the general US population.<sup>35</sup> Depression and anxiety are common comorbidities in patients with MS, with a lifetime prevalence of depression of 50%, which is often associated with poor quality of life.<sup>36</sup> Therefore, regular screening for mood symptoms is essential to competent care. In addition, a recent study found that TGD persons who reported a TGD-inclusive vs TGD-noninclusive provider were less likely to report mood symptoms and suicidality, suggesting that TGD persons may experience a reduction in psychological distress by having a provider who is educated and competent in gender dysphoria-inclusive care.<sup>37</sup>

## PRACTICE POINTS

- The clinical and psychological care of transgender (TGD) people living with multiple sclerosis (MS) has additional complexities compared with that of cisgender patients with MS.
- There are currently no recommendations for the comprehensive care of TGD persons living with MS. Following an informative patient experience, we have proposed a set of TGD MS care recommendations to share globally as a start to consistently optimize the care of this unique marginalized population.

## Conclusions

This case highlights the unique challenges and opportunities of providing comprehensive, competent care for the underserved TGD MS population. The proposed recommendations are a start to educate and guide caregivers and to improve the patient experience and outcomes. □

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