Recognizing, Evaluating, and Prioritizing the Fundamental Factors Influencing the Growing Prevalence of Transgender and Non-Binary Gender Identity in the Pediatric Population

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Abstract
This review observes the growing demographic of individuals identifying as transgender or non-binary, which currently represents approximately 1.3% (depending on the source) of the U.S. population. This population is shown to skew younger.

Environmental xenobiotics, particularly those containing endocrine-disrupting chemicals (EDCs), are scrutinized for their role in affecting hormonal regulation crucial for gender identity differentiation. The research also highlights how exposure to pharmaceuticals with endocrine-disrupting properties may induce atypical patterns in gender identity development, suggesting that a variety of exogenous elements could impact neuroendocrine sexual differentiation.

Medical disorders associated with altered androgen levels, such as

More Information


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congenital adrenal hyperplasia (CAH) and androgen insensitivity syndrome (AIS), are considered for their potential influence on gender identity from a biological perspective. Moreover, the role of diet and nutrition, particularly plant-based diets rich in phytoestrogens and conditions linked to obesity and metabolic syndrome, are explored for their effects on hormonal balance and, consequently, gender identity expression. This review acknowledges the significant impact of media representation and societal norms on shaping attitudes concerning gender expression and identity.

The article points to psychological assessments and somatic markers as tools to explore prenatal hormone influences on gender identity, though emphasizing that they are not definitive. Furthermore, genetic and epigenetic findings offer a more in-depth understanding but lack diagnostic application. The identification and recognition of transgender and non-binary individuals continue to be self-determined processes that defy objective measurement by current medical standards.

**Abbreviations**

BDD: Body Dysmorphic Disorder; CAH: Congenital Adrenal Hyperplasia; CAIS: Complete Androgen Insensitivity; DNMTs: DNA Methyltransferases; DSD: Differences of Sex Development; EDCs: Endocrine-Disrupting Chemicals; GD: Gender Dysphoria; PAIS: Partial Androgen Insensitivity; QoL: Quality of Life

**Introduction**

Transgender and non-binary are terms that have evolved to describe experiences of gender that exist beyond the traditional male-female binary. Transgender is an umbrella term that covers a spectrum of gender identities and expressions that differ from societal expectations based on the individual’s sex assigned at birth. A transgender individual may identify as a gender opposite to their birth-assigned sex, or they may identify with a gender that is not exclusively male or female. Generally, non-binary refers to any trans identity that is not always male or female, thereby rejecting the conventional dichotomous model of gender identity [1]. Gender identity—in terms of transgender and non-binary—should be understood as multifaceted and influenced by a range of factors, including biological, psychological, and social elements. Cultural factors also significantly influence how individuals define their gender identity. Moreover, gender identity is shaped by the societal and cultural norms in which an individual is immersed [2].

The genetic basis of gender identity development is complex, with current evidence indicating that genetic components may have a role in gender identification—raising interest in the interrelationship between these genetic factors and environmental stimuli, mainly through epigenetic mechanisms [3,4].

**Discussion**

**Gender Identity Demographics**

The transgender and non-binary populations are growing, with an estimated 0.6% of the United States population identifying as transgender and an additional 0.7% as non-binary [5,6]. However, existing literature on the demographics of these populations is limited.

**Age**

Studies have shown that the transgender population is disproportionately young, with individuals under the age of 35 making up a significant portion of this population. In a survey of over 27,000 transgender adults, 53% were under the age of 35. However, this trend appears to differ for non-binary individuals. According to a survey conducted by the National Center for Transgender Equality, the majority of non-binary participants were over the age of 25 [7,8]. Transgender individuals can identify as strictly male or female, as well as non-binary or genderqueer [9].

**Socioeconomic Status**

Specific groups of transgender individuals may experience poverty, social instability, and decreased quality of life (QoL; Table 1). In a survey of 27,715 transgender adults, 29% were living in poverty. In addition, 30% of respondents reported experiencing homelessness in their lifetime, and 12% reported engaging in sex work for income [10].

**Table 1. Well-Being in Transgender and Non-Binary vs. Cisgender Individuals**

<table>
<thead>
<tr>
<th>Domains</th>
<th>Transgender and Non-Binary Individuals</th>
<th>Cisgender Individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical health</td>
<td>Gender dysphoria may impact physical health due to stress and stigma. Access to gender-affirming healthcare may vary.</td>
<td>Generally, physical health may not be as directly influenced by gender identity-related stressors. Access to healthcare may still vary based on other factors.</td>
</tr>
</tbody>
</table>
**Mental health** | Higher rates of depression, anxiety, and suicidal ideation are reported due to societal stigma, discrimination, and dysphoria. | Mental health may still be influenced by other factors such as personal health, socioeconomic status, and interpersonal relationships.  

**Personal beliefs** | May experience conflict between internal gender identity and societal norms, impacting personal beliefs and self-acceptance. | Likely to experience congruence between gender identity and societal norms, possibly leading to greater self-acceptance in this domain.  

**Social relationships** | May face challenges in social acceptance, discrimination, and rejection from family, friends, and society. | Social acceptance may be more readily available, potentially leading to more stable social relationships.  

**Environmental factors** | Environmental factors may include access to gender-neutral facilities, legal protections, and community support, which may vary based on location and societal attitudes. | Environmental factors may still impact well-being, but gender-related strains are less likely to be a significant factor.  

**Overall life satisfaction and functioning** | Well-being may be influenced by the interaction of all these domains, with challenges in one area affecting overall satisfaction and functioning. | Well-being may also be influenced by various factors such as personal health, socioeconomic status, and interpersonal relationships. Gender identity-related strains may be less prevalent but not absent.  

*Source: [11,12]*

The transgender and non-binary populations are diverse in terms of age, gender identity, race and ethnicity, socioeconomic status, disability, and mental health. However, research on non-binary individuals is limited.

**Neurobiological Aspects of Gender Identity**

The neurobiological basis of gender identity suggests that prenatal influences, possibly shaped by epigenetic changes, may lead to a gender identity that does not match one’s birth-assigned sex. This perspective proposes that although genetic substrates may establish a baseline for gender identity, environmental factors may modify these genetic expressions throughout an individual’s lifespan [3,13].

**Environmental Xenobiotics and Gender Identity Implications**

Xenobiotic agents in the form of plastics and pesticides have been implicated for their modulatory effects on gender identity, attributed to their capacity to perturb endogenous endocrine signaling. The presence of endocrine-disrupting chemicals (EDCs) in these substances can adversely affect the hormonal regulation associated with gender identity formation. Specific EDC exposure is linked with developmental, reproductive, and neuropsychological anomalies, which might impact neuroendocrine sexual differentiation, with consequences for gender identity. These xenobiotics are believed to exert their influence either through mimicking or antagonizing the physiological actions of intrinsic hormones that are integral during pivotal stages of gender identity differentiation [14–16].

**Pharmacological Disruptors and Gender Identity Discrepancies**

Therapeutically active agents are inadvertently implicated as available modulators of endocrine signaling, affecting the processes integral to gender identity delineation. Current research highlights modifications in endocrine functionality post-exposure to specific pharmaceuticals that may induce atypical patterns in gender identity development. The complex interaction among pharmaceutical-induced effects, hormone regulation, and neurological developmental processes presents challenges in delineating the etiology of gender identity [17,18].

**Impact of Endocrine Interferents on Hormonal Signaling**

Compounds interfering with the endocrine system can disrupt hormonal signaling, leading to developmental, reproductive, and endocrine anomalies. Such agents may disrupt signal transduction via hormonal receptor interaction, modifying the hormonal cues essential for somatic sexual development and the neurobiological processes associated with gender identity. The widespread dispersal of EDCs in the environment and consumer products poses substantive challenges to their impact on sexual development and the modulation of gender identity. Current analytical evaluation of these interactions posits a correlative relationship between EDC exposure and changes in gender identity expression [19,20].

**Associations Between Gender Identity and Psychiatric Disorders**

Individuals with variations in gender identity may experience an increased prevalence of psychiatric
conditions compared to the cisgender population. Research demonstrates heightened risks of mood disorders, anxiety disorders, and suicide among trans and gender-diverse individuals. These findings suggest a psychiatric vulnerability that may arise from societal stigma, discrimination, and difficulties concerning gender identity that deviates from societal norms. The gender dysphoric condition, characterized by a marked incongruence between one’s experienced or expressed gender and assigned sex, has been associated with greater psychiatric comorbidity, particularly with disorders such as depression and anxiety [21].

Table 2. Overview of Gender Dysphoria Symptoms and Characteristics

<table>
<thead>
<tr>
<th>Gender dysphoria symptoms</th>
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</thead>
<tbody>
<tr>
<td>- Strong desire to be treated as experienced gender</td>
</tr>
<tr>
<td>- Profound sense of inappropriateness in assigned gender role</td>
</tr>
<tr>
<td>- Strong conviction of typical feelings and reactions of experienced gender</td>
</tr>
<tr>
<td>- Strong dislike of sexual anatomy</td>
</tr>
<tr>
<td>Duration and intensity of gender dysphoria</td>
</tr>
<tr>
<td>- Varies among individuals</td>
</tr>
<tr>
<td>- Some experience intensification over time</td>
</tr>
<tr>
<td>- Others experience fluctuations in intensity</td>
</tr>
</tbody>
</table>

Source: [23]

Studies on the Correlation Between Gender Dysphoria (GD) and Psychiatric Conditions
GD manifests through profound psychological distress stemming from the discord between an individual’s experienced gender and their biological sex (Table 2). This distress is frequently correlated with adverse mental health outcomes, including major depressive disorder and generalized anxiety disorder. Evidence suggests that these associations may be mediated by factors such as minority stress and victimization. Multiple empirical studies support the notion that the experience of GD can elevate the risk for psychiatric sequelae, with depression and anxiety being the most commonly reported co-occurring conditions [22].
on the atypical nature of the arousal pattern and any resultant distress or impairment [30].

**Self-Amputation**
Self-amputation, or autotomy, is often associated with severe psychiatric issues such as psychosis or certain paraphilic disorders. This extreme behavior is not related to transgender healthcare, where surgical interventions are conducted in controlled, clinical environments to align an individual’s physical body with their gender identity [31].

**Schizophrenia**
Schizophrenia is a chronic brain disorder characterized by delusions, hallucinations, and other cognitive difficulties. It is a condition encompassing psychotic symptoms and is not intrinsically linked to gender identity or sexuality [32].

**Transvestitism**
Transvestitism, now more commonly referred to as cross-dressing, is the practice of wearing clothes typically associated with the opposite gender. Unlike being transgender, which relates to an individual’s gender identity, cross-dressing is usually considered a form of gender expression. It may or may not have any implications for an individual’s identity or sexual orientation [33]. When diagnosing an individual who may identify as transgender or non-binary, it is critical to distinguish their identity from conditions such as autogynephilia, body dysmorphic disorder, or various psychiatric disorders. While there may be some superficial similarities or misunderstandings about the presentation of these conditions, each has distinctive and separate diagnostic criteria and implications for treatment. The differential diagnosis of GD necessitates a nuanced approach. Consequently, precise evaluation of the diagnostic criteria outlined in the DSM-5 is imperative (Table 3).

**Table 3. DSM-5 Criteria for Gender Dysphoria**

<table>
<thead>
<tr>
<th>DSM-5 criteria for gender dysphoria</th>
<th>Definition</th>
<th>Diagnostic criteria (adults and adolescents)</th>
<th>Additional criteria (adolescents)</th>
<th>Clarification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marked incongruence between experienced/expressed gender and assigned gender at birth, persisting for at least six months, with associated distress/impairment.</td>
<td>- Strong desire to be of a different gender or insistence of being another gender.</td>
<td>- Anticipated trajectory for secondary sex characteristics incongruent with experienced gender, with a desire to prevent their development.</td>
<td>Not merely a desire for perceived cultural advantages of being the other gender.</td>
<td></td>
</tr>
<tr>
<td>Diagnostic criteria (adults and adolescents)</td>
<td>- Strong preference for wearing clothes typical of the opposite gender.</td>
<td>- Powerful rejection of primary or secondary sex characteristics, with a desire for those of the other gender.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarification</td>
<td>- Deep conviction of having feelings/reactions aligning with the experienced gender.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Associations Between Gender Identity and Personality Traits**
Personality traits, including neuroticism—a dimension characterized by emotional instability and a propensity towards psychological distress—have been examined concerning gender identity. While the breadth of research precisely defining these associations remains limited, preliminary studies indicate a possible higher incidence of neuroticism in transgender and non-binary populations when compared with cisgender cohorts [34]. The relationships among gender identity, personality traits, and psychosocial functioning could clarify the complexities inherent in the lived experiences of individuals navigating gender identity concerns.

**Medical Disorders Possibly Contributing to Gender Identity**
Human sexuality is influenced by various factors such as environment, genes, and hormones.

**Congenital Adrenal Hyperplasia (CAH)**
CAH is a genetic condition that affects the production of cortisol and aldosterone hormones in the adrenal glands. It results from a deficiency in an enzyme called 21-hydroxylase, which leads to an overproduction of androgens. CAH is classified into different forms based on the severity of the enzyme deficiency. The most common form of CAH is the classic type, which affects about 1 in 10,000 to 1 in 20,000 births [35]. Studies have suggested that exposure to high levels of androgens in the fetal stage can impact the development of the brain, including the areas related to sexual behavior and identity. Individuals with CAH, especially those with the classic form, may be more likely to identify as homosexual or transgender. One study found that women with CAH were more likely to have a non-heterosexual sexual orientation compared to women without the condition. The study also found that women with CAH reported feeling more masculine in childhood than women without the condition.
Androgen Insensitivity Syndrome (AIS)
AIS is a condition where an individual with XY chromosomes is born with external female genitalia due to a partial or complete insensitivity to androgens. Androgens are male hormones responsible for the development of male genitalia and secondary sex characteristics. In individuals with AIS, the body cells are unable to respond to androgens, resulting in the development of female genitalia [38].

Individuals with AIS may experience challenges in their gender identity, as they may identify as female despite having XY chromosomes. Studies have suggested that the degree of androgen insensitivity may impact the gender identity of individuals with AIS. Individuals with complete androgen insensitivity (CAIS) may have a more unambiguous female gender identity as they exhibit typical female physical characteristics. In contrast, individuals with partial androgen insensitivity (PAIS) may have a more ambiguous gender identity due to variations in their physical characteristics [38].

Trans and Non-Binary Sexuality
Both CAH and AIS have been linked to the development of trans and non-binary sexuality. Studies have suggested that exposure to high levels of androgens in the fetal stage can impact the sexual behavior and gender identity of individuals. Individuals with CAH, especially those with the classic form, have been found to have a higher likelihood of identifying as non-heterosexual. Similarly, the degree of androgen insensitivity in individuals with AIS has been found to impact their gender identity [39].

The impact of medical conditions such as CAH and AIS on the development of sexuality has been a subject of research for many years. Studies have suggested that exposure to high levels of androgens in the fetal stage can impact the development of sexual behavior and gender identity in individuals with these conditions.

The Role of Diet and Nutrient Availability in Sexual Differentiation
Sexual differentiation—the process by which individuals develop phenotypic sex characteristics—is guided by complex interactions between genetics, hormones, and environment. Nutritional status can directly influence hormonal environments responsible for sexual differentiation, with animal models suggesting that maternal nutrition can impact fetal hormonal milieu, implicating consequential effects on the development of the offspring’s sex characteristics. Environmental endocrine disruptors, including those present in various foods and diets, have been observed to affect sex hormone levels, which could, in turn, interfere with normal sexual differentiation [19,40].

Impact of Vegan and Vegetarian Diets on Hormones
Studies have investigated the influence of dietary choices, mainly vegetarian and vegan diets, on endocrine function. Hormonal variations, such as changes in sex hormone-binding globulin, cortisol, and adrenal androgens, have been documented following adopting a vegetarian diet. These dietary interventions, often characterized by higher intakes of phytoestrogens and lower intakes of animal-derived products, may alter hormone levels due to decreased ingestion of exogenous hormones from animal products and altered lipid intake affecting steroid hormone metabolism. While these findings provide valuable insights, further research is needed to explicate the full effects of plant-based diets on endocrine function and hormone-driven processes [17,41,42].

Role of Obesity and Metabolic Disease in Gender Identity
The interrelation between obesity, metabolic syndrome, and gender identity remains a subject of emerging inquiry. Obesity and metabolic disorders can create hormonal imbalances that influence sex hormone levels and metabolic cytokines, which may play a role in the expression of gender identity. Transgender individuals undergoing hormone treatment provide a distinctive context for examining the interaction between sex hormones and metabolic changes, where treatment with exogenous hormones can lead to variations in body composition and metabolic parameters [43,44]. Furthermore, conditions such as polycystic ovary syndrome, which is closely linked to obesity and metabolic aberrations, have been studied for contributions to variations in gender identity [45].

Influence of Media and Society on Gender Identity
Media and society play a vital role in shaping attitudes, expectations, and norms surrounding gender expression and identity. These influences vary based on cultural traditions, geographic location, and socio-political environments [46]. Non-binary and transgender individuals, in particular, may face marginalization and reduced access to healthcare services [47].

Impact of Social Factors on Gender Identity
Research has found that bullying and discrimination based on gender identity can have detrimental effects on mental and physical health. These effects may persist into adulthood and can present as lower self-esteem, anxiety, depression, and chronic disease risk factors such as obesity [48].

Medical Tests, Biomarkers, or Psychological Profiles for Identifying Transgender and Non-Binary Sexuality
The identification of transgender and non-binary individuals is a complex process that primarily involves personal understanding and self-identification rather than a set of medical tests or psychological profiles. While biomarkers and psychological assessments are used in various medical contexts, their applicability and
ethics in determining gender identity are contentious and nuanced.

**Biomarkers and Hormonal Influences**
Research into the neurobiology of gender identity has investigated the possible role of prenatal hormone exposure in shaping gender identity and sexual orientation. Findings suggest that prenatal exposure to testosterone may masculinize gender identity and sexual orientation. Contrarily, its absence may not, with transgender identities possibly emerging from the complexity of these hormonal factors. However, such biomarkers are not definitive indicators of transgender or non-binary identity, and it remains unclear how such biological differences translate into the lived experience of gender [3].

**Psychological Profiles**
Psychological assessments are generally used to support individuals in understanding their gender identity rather than to categorize or diagnose gender variation. While there are no psychological tests that can “identify” transgender or non-binary individuals, mental health professionals may utilize assessments to better understand an individual’s experiences with gender dysphoria [49].

**Somatic Markers and Cognitive Tests**
The prenatal androgen theory also points toward cognitive tests and somatic markers as possible indicators of prenatal hormone influences on gender identity and sexual orientation. However, these are not diagnostic tools but research instruments that explore the complex associations between biological development and gender identity [50,51]. The relationship between somatic features and transgender identity is still poorly understood, and these features cannot be used to confirm or determine gender identity.

**Genetic and Epigenetic Factors**
Genetic studies have explored associations between gender dysphoria and polymorphisms in genes related to sex hormone signaling, which may contribute to the development of a transgender identity. Identified genetic links may offer insight into the biological underpinnings of gender dysphoria, but they are not used as diagnostic tests for being transgender or non-binary [52].

While the science examining the biological components of gender identity is evolving, its application in the clinical or diagnostic setting is highly limited and ethically complex. The process of identifying as transgender or non-binary remains a deeply personal and subjective experience that current medical tests cannot objectively measure.

**Limitations of Research**
The area of study concerning the sexuality of transgender and non-binary individuals is evolving, with a growing number of publications addressing this subject. Yet, the field still contends with significant research gaps [53].

Research into epigenetics as it pertains to gender identity has shown there are differing patterns of DNA methylation [54] among transgender people. However, quantitative prevalence data and in-depth comparative analysis with cisgender individuals are not thoroughly available in the current literature [4]. (“DNA methylation is a heritable epigenetic mark involving the covalent transfer of a methyl group to the C-5 position of the cytosine ring of DNA by DNA methyltransferases (DNMTs)” [54]).

Moreover, there is a range of opinions among experts regarding the optimal support for individuals who identify as transgender or are experiencing gender dysphoria, particularly regarding mental health care and the long-term psychosocial outcomes of gender transition [55,56]. This debate indicates an ongoing need for a consensus and well-founded evidence base to guide policy and healthcare practices.

**Conclusion**
Transgender and non-binary demographics suggest these gender identity groups are younger on average, diverse in socio-economic status, and face unique challenges, including higher poverty and homelessness rates.

Critical to understanding gender identity is recognizing the interplay between genetic, psychological, social, and cultural factors.

Environmental factors, including exposure to endocrine-disrupting chemicals (EDCs) found in xenobiotics such as plastics and pesticides, are also under scrutiny for shaping gender identity by mimicking or inhibiting endogenous hormones during crucial developmental periods. Moreover, pharmaceuticals acting as endocrine disruptors possibly alter endocrine functions, influencing gender identity development.

Medical conditions like congenital adrenal hyperplasia (CAH) and androgen insensitivity syndrome (AIS) have spawned discussions about their potential to influence gender identity through biological mechanisms.

Nutritional influences on hormones add further complication and considerations. Vegan and vegetarian diets potentially affect endocrine function due to higher levels of phytoestrogens and less exogenous hormone intake from animal products. Obesity and metabolic disorders affect hormonal imbalances that may also contribute to the expression of gender identity.

The influential roles of media and societal norms in forming gender identity norms and biases are evident. While research points towards biomarkers, hormonal influences, and psychological profiles that could correlate with gender identity variations, identification largely remains personal and self-reported, with no definitive medical tests to determine transgender or
non-binary identities. Genetics and epigenetics offer insights but are not used diagnostically. The composite factors that shape and impact gender, extending beyond the traditional male-female binary, represent an emerging field of research. An equitable examination of the initial data, albeit limited, on likely factors influencing transgender and non-binary gender identification suggests that while epigenetics may play a role, its significance appears slight compared to neurobiological, environmental, pharmacological, hormonal, and social factors.

**Conflict of Interest Statement**

The authors declare that this paper was written without any commercial or financial relationship that could be construed as a potential conflict of interest.

**References**


[20] Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, Hauser R, Prins GS, Soto AM, Zoeller RT,
Possible Gender Influence in the Mechanisms Underlying the Oxidative Stress, Inflammatory Response, and the Metabolic Alterations in Patients with Obesity and/or Type 2 Diabetes. Antioxidants (Basel). 2021 Oct 29;10(11):1729. doi: 10.3390/antiox10111729


