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## **Puberty Blockers and Cross-Sex Hormones for Children and Adolescents with Gender Incongruence/Gender Dysphoria**

*Note: SEGM submitted the original version of this document on September 21, 2026. On further review, we concluded that it would be more useful to cite specific page numbers in lengthy sources such as the Cass Review and the HHS Review, so that the scientific claims are easier to verify. We have also made light edits for clarity and precision. None of the substance has changed.*

Madam President of the Committee on Constitutional Affairs, Rights, Freedoms and Guarantees of the Portuguese Parliament:

The Society for Evidence-Based Gender Medicine (SEGM) is a 501(c)(3) nonprofit organization dedicated to advancing rigorous scientific evaluation of clinical practices affecting children, adolescents, and young adults with gender incongruence/gender dysphoria (GI/GD). Earlier this month, SEGM was contacted by Genspect Portugal and informed that the Portuguese government will be debating several Bills concerning adolescents with GI/GD.<sup>1</sup> Genspect Portugal told us that several Portuguese submissions to the Parliament regarding those bills contained scientific claims about pediatric GI/GD, and asked us to evaluate the accuracy of those claims.

SEGM's position is that public debate affecting young patients should be informed by a rigorous, transparent, and methodologically sound evaluation of the available evidence. In this submission, SEGM is making no statement in support of or against the proposed Bills; rather, it merely wants to assist the Parliament by making sure it has accurate information regarding the evidence for the use of endocrine interventions in gender-dysphoric children and adolescents.<sup>2</sup> We hope that the Portuguese lawmakers will find this information helpful as they deliberate the regulation of these interventions.

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<sup>1</sup> 391/XVII/1<sup>a</sup>, 479/XVII/1<sup>a</sup> and 486/XVII/1<sup>a</sup>

<sup>2</sup> SEGM has relied upon English translations of documents provided by Genspect Portugal.



Below, we respond to the questions in the order that they have been posed to us by Genspect Portugal. We remain available to answer any specific questions.

Respectfully,

William J. Malone, MD on behalf of the SEGM Board

### Abbreviations

|     |                     |
|-----|---------------------|
| CSH | Cross-sex hormones  |
| GD  | Gender dysphoria    |
| GI  | Gender incongruence |
| PB  | Puberty blockers    |

### Claim 1: Puberty blockers are fully reversible.

**SEGM's response to the claim that PB for GD are fully reversible (e.g., submission by the Portuguese Society of Clinical Sexology states that "puberty suppression using GnRH analogues is a fully reversible process").**

### **Response: This claim is incorrect.**

- a) Previously, the field of pediatric gender medicine operated on the assumption that puberty suppression was fully reversible. This assumption was based on the historical context of using PB to stop *abnormally early*, "precocious," puberty affecting very young children (before age 8 in girls, and before age 9 in boys). When such children would reach a normative age for puberty, PB would be stopped, and pubertal physical development would resume.
- b) However, when PB are used for the treatment of GI/GD, they are given to adolescents at a normal pubertal age, and they are used to interrupt *normally timed* puberty already underway. Little is known about the long-term impact of such treatments in this context. In 2020, NHS England removed its prior statement that "The effects of treatment with GnRH analogues are considered to be fully reversible, so treatment can usually be stopped at any time..."—and replaced it with the statement that "Little is known about the long-term side effects of hormone or [PB] in children with gender dysphoria." [1]
- c) While the development of secondary sex characteristics will almost certainly resume when PB are used only for a short time and are stopped—there is now evidence that the impacts of PB on bone health, neurocognitive development, and fertility may have irreversible effects. For example, animal studies suggest that PB have irreversible impacts on neurocognitive function [2]. The findings of recent studies on adolescent natal males treated with PB raise concerns that suppression of male fertility may not be fully reversible [3]; few



Portuguese GI/GD youths take advantage of fertility preservation [4]. Studies on adult bone density in natal males commenced on PB in adolescence followed by CSH show that deficits in bone mineral density do not fully resolve over time, which compromises bone health [5, 6].

- d) It is also well-acknowledged that the majority (over 90%) of those initiating PB for gender incongruence will proceed to take CSH [7–10]. This high rate of persistence of childhood gender dysphoria contrasts with very low historical rates of persistence observed in the pre-PB era. Thus, it is considered possible that PB may lead to persistence of gender dysphoria, placing children on a pathway toward CSH and surgery [6 (pp. 102-3), 11 (pp. 167-8)].

### Claim 2: Puberty blockers have been proven safe.

**SEGM's response to the claim that the safety profile of PB is well established, including through decades of GnRH use for precocious puberty.**

**Response: This claim is misleading. The safety profile of PB for the indication of precocious puberty cannot be extrapolated to GI/GD.**

- a) The long-term safety of PB when administered in the context of GI/GD is not well established. PB have never been properly tested as a treatment for GI/GD, as such, they represent “off-label” (unlicensed) use. The only approved, licensed use of PB in the pediatric context is in the treatment of precocious puberty—an entirely different condition. While off-label use is common in medicine, it is well-established that such use is associated with a markedly worse safety profile than the use of the same drug according to the licensed indication [12]. As such, the safety profile of PB for precocious puberty cannot be projected to the safety profile of PB for GI/GD.
- b) Precocious puberty (PP) is a fundamentally different condition from GI/GD. There are important differences in the type of diagnosis (PP is confirmed by objective laboratory test results, while GI/GD is based on subjective self-reports); the timing of initiation of treatment (before the age of 8-9 in PP, and usually in the mid-teens for GI/GD); and the duration of treatment. Importantly, in PP, once the PB are stopped, the body's own sex hormones resume functioning to progress a child to normal puberty. In GI/GD, over 90% of the time, natal hormone production continues to be suppressed, and instead CSH are used for the rest of one's life.
- c) Despite the fact that gender clinics have used PB for GI/GD for about 25 years, no systematic study of the health effects of such use has taken place [13 (p. 55)]. The UK is just now initiating the first-ever controlled trial of the use of PB for GI/GD [14], and in



the meantime, has banned their use in standard medical practice [15]. The trial itself has raised controversy over known harms of GnRHa (gonadotropin-releasing hormone agonists, or puberty blockers) use in female adolescents with gynecological problems [16].

- d) As discussed in 1 c), in the domains where the effects of PB have been studied—i.e., fertility, bone health, and brain development—concerning signals of harm have emerged. There are additional concerns regarding the adverse effects of PB on sexual function. A recent Dutch study reported that at an average age of 29, over half of those previously treated with PB had at least one sexual dysfunction [17, 18].
- e) Since sex hormones affect every aspect of developing adolescent bodies, it is possible that other as yet unknown harms of the practice of suppressing normally timed puberty will emerge in the years to come.

**Claim 3: Hormonal treatments for gender dysphoria improve mental health — and treatment restrictions increase the risk of suicide.**

**SEGM’s response to the claim that PB and CSH improve depression, anxiety and suicidality in minors; one submission claims a 73% reduction in suicidal ideation/self-harm and argues that banning blockers would increase suicide risk. (e.g., “The evidence of mental-health benefits for people with gender dysphoria is clear: access to blockers reduces the probability of suicidal ideation by 73%. Prohibiting them is, statistically, to increase the risk of death by suicide among Portuguese young people” (Portuguese Society of Clinical Sexology submission)).**

**Response: These claims are incorrect.**

- a) While certain individual studies continue to claim “proven benefits,” such studies suffer from significant methodological limitations. According to the well-established principles of evidence-based medicine, instead of relying on individual studies that suffer from methodological limitations, one must reference high-quality systematic reviews of evidence when such reviews are available [19]. All high-quality systematic evidence reviews conducted to date cohere in concluding that there is no reliable evidence that PB and CSH improve short-, medium- or long-term mental health outcomes or decrease suicide risk [6 (pp. 79-96), 20–25]. A large-scale analysis of psychological outcomes published since the publication of the latest systematic reviews using Finnish registry data indicates psychiatric problems of adolescent patients do not decrease—and may even increase— following hormonal treatments of GI/GD adolescents [26].
- b) Every suicide is a tragic event. GI/GD youth are at increased risk of suicidality, although roughly at the same rate as youth with other mental health conditions. Fortunately,



suicides among GI/GD adolescents remain rare [27]. Unfortunately, there is no indication that either PB or CSH reduce suicide mortality—a finding confirmed by the recent Finnish health registry study [28]. SEGM’s own analysis noted that the highest rates of suicides were reported by gender clinics that transitioned the highest proportion of their presenting patients [29 (tbl. 1)].

- c) A 2022 U.S. study by Tordoff et al. is frequently cited to assert that endocrine interventions in GI/GD minors reduced suicidality by 73% [30]. However, the Tordoff et al. study suffered from profound methodological flaws, and also misrepresented its own results [6 (pp. 106-7)]. The study is highly controversial [31] and its findings cannot be trusted.
- d) Other claims that restrictions on PB and CSH use lead to suicides in the UK and the US have likewise been rebutted by research teams [32, 33] and by the independent UK Appleby Review [34].
- e) In sum, there is no evidence that bans or restrictions on PB or CSH for the pediatric population increase suicide risk.

#### Claim 4: Undergoing endogenous (natal) puberty causes harm.

**SEGM’s response to the claim that allowing a dysphoric adolescent to undergo endogenous puberty itself causes irreversible harm, worsens dysphoria and may necessitate more invasive surgery later. (e.g., “Forcing a minor to undergo endogenous puberty against their identity is to condemn them to irreversible physical changes (voice, bone structure, facial hair or breast development) that will aggravate dysphoria and require far more invasive surgical interventions in the future” (Portuguese Society of Clinical Sexology submission)).**

**Response: This claim is overstated and overly simplistic. It overlooks the developmental role of normally timed puberty, while overstating the benefits and understating the risks of pubertal suppression.**

- a) Normally timed puberty—the development of a child into a sexually and reproductively mature adult—is a crucial life stage and does not constitute a disease or disorder for any child, nor does it constitute a medical treatment harm [6 (pp. 113-5), 35].
- b) Multiple high-quality systematic reviews have found no reliable evidence that PB decrease gender dysphoria or improve mental health outcomes [13 (p. 57)]. Because the benefits of PB have not been demonstrated, it would be illogical to claim that *not* providing PB would cause harm.
- c) A significant number of adolescents presenting to pediatric gender clinics are already well advanced into puberty (at Tanner stages 4 and 5) so physical changes associated with puberty have already occurred [36, 37]. Thus, the use of PB, in this common



situation, will not make any material difference to physical changes that have already occurred.

- d) For natal females the main potential advantage of an earlier use of PB is a reduction in the need to later undergo mastectomy. However, to achieve this, PB must be commenced at the very early stages of puberty, which significantly increases the risk of harm, including loss of fertility (at this phase there are only experimental methods of fertility preservation available) and iatrogenic persistence of GI/GD.
- e) For natal males, PB at early puberty may decrease the desire for some later surgeries (e.g., facial surgeries) and prevent lowering of voice. However, such early intervention also poses greater risks to fertility (with only experimental fertility preservation options available) and sexual function [6 (pp. 119-23)]. PB use in early puberty will also stunt genital growth, necessitating more invasive and complex vaginoplasty surgery with greater risk of complications (one of the patients in the original Dutch studies died from surgical complications for this reason) [6 (p. 62), 38].

**Claim 5: High *quantity* of individual studies claiming benefits overrides low *quality* of the evidence.**

**SEGM's response to the claim that although the evidence is predominantly observational and has methodological limitations, its consistency and convergence are sufficient to establish clinically meaningful benefits and an acceptable safety profile. (e.g., "the absence of such trials [randomized controlled trials] does not invalidate clinically indicated interventions when there is...consistency across studies" (Portuguese Medical Association submission)).**

**Response: This is incorrect.**

- a) This claim shows a fundamental misunderstanding of evidence in medicine. Multiple low-quality studies do not add up to high-quality evidence and common risks of bias and confounding may persist when results are pooled [39 (p. 5)]. Systematic and institutional bias can be consistent across studies, leading to consistent results which are nevertheless erroneous. This is exacerbated when there is publication bias.
- b) Additionally, and importantly, the evidence for the psychological benefits of PB and CSH in adolescents is not consistent. For example, some studies have suggested PB are associated with an improvement in some mental health outcomes whereas other studies have not found any mental health improvements. While the seminal Dutch study [40] that launched the practice of pediatric gender transition showed PB were associated with mild improvements in several measures of mental health, later prospective clinical studies from the U.K and the U.S have not been able to replicate even this modest result [9, 41, 42].



Claim 6: Pediatric gender medicine should be excused from the requirement to generate reliable evidence because randomized controlled trials are challenging.

**SEGM's response to the claims that randomized controlled trials (RCTs) in this area are difficult or ethically problematic, so the lack of high-quality controlled evidence should not be interpreted as evidence against treatment. (e.g., "Research in this area faces limitations inherent in the ethical impossibility of conducting randomized clinical trials in certain contexts" (Portuguese Medical Association submission)).**

**Response: This is misleading. Difficulties in conducting RCTs do not remove the need for reliable evidence of treatment benefits and harms.**

- a) Unfortunately, in the area of pediatric gender medicine, from the very dawn of the practice, when only a single patient had undergone pubertal suppression, gender clinicians already asserted that RCTs in this area of medicine are not possible [43]. RCTs can be difficult—especially in pediatric medicine—but they are done nonetheless, for example in pediatric oncology [44].
- b) In the UK, the PATHWAYS PB randomized delayed-start controlled trial has commenced (participants are randomly assigned to two groups: one starts PB immediately, while the other starts 12 months later) [14]. This at least demonstrates that RCTs are possible in this field, albeit with some methodological limitations.
- c) However the low or very low certainty of the evidence for PB and CSH does not stem from the lack of RCTs: it is primarily due to a lack of high-quality observational studies, inadequate comparison groups and follow-up, and insufficient control of confounding [45, 46].
- d) According to evidence-based medicine principles, the quality of the evidence alone is never sufficient to make a treatment decision. When the evidence is uncertain, "policy making will require substantial debate and involvement of many stakeholders." [47] Besides evidence quality, decision-makers should pay special attention to the benefit-harm balance, as well as other contextual factors including patients' values and preferences and resource considerations [47].

Claim 7: There is international consensus that hormonal interventions for minors are beneficial, with WPATH, the Endocrine Society, and even the Cass Review all objecting to the restrictions.

**SEGM's response to the claim that WPATH and Endocrine Society guidance represents the international clinical consensus, while the Cass Review supports caution and better research but does not justify restricting access.**



**Response: This is incorrect. WPATH and Endocrine Society guidelines are not evidence-based, while the Cass Review has called for both PB and CSH to be used in research-only settings.**

- a) The World Professional Association for Transgender Health's standards of care (WPATH SOC 8) and the Endocrine Society Guidelines do not represent international consensus; rather they represent the viewpoint of those clinicians and professionals who support the use of PB and CSH (and surgeries) in minors, while excluding the views of those who do not. Several independent guideline analyses of WPATH SOC 8 and the Endocrine Society Guidelines, using an internationally accepted and validated guideline appraisal tool (AGREE-II), have found that these guidelines do not meet international standards for trustworthy guidelines, and concluded that they are not recommended for implementation [48–51]. Recently, the Past President of the Endocrine Society wrote about the problematic conflicts of interest that undermined the trustworthiness of those guidelines [52].
- b) Revelations about the development of WPATH SOC 8 demonstrated that the organization's leadership suppressed systematic reviews of evidence from publication because the organization was concerned the findings would not support the planned treatment recommendations [6 (pp. 171-7), 53]. Of the 13 registered questions, only three resulted in publications; the remaining 10, including the long-term effects of PB in adolescents, cardiovascular and thrombotic risks of estrogen, and effects on fertility, were evaluated but never published [54].
- c) There is no international professional consensus regarding treatments of GI/GD youth. The health policies of several international jurisdictions now heavily restrict or ban the use of PB and/or CSH in minors – e.g., the UK, Sweden and Finland, as well as multiple states/ provinces/ territories in the US, Australia and Canada [6 (pp. 59-66)]. These changes were made not only because of the very low to low certainty of evidence of benefit, but also for several other reasons. These include an unexplained sharp increase in referral numbers and changed demographics and clinical presentations of those referred—the increase has been driven primarily by adolescent natal females, often with no history of early childhood GI/GD and many reporting a non-binary identity—all of which have raised concerns about the role of social media and peer influence contributing to gender incongruence in young people [55]. Furthermore, little is known about the natural course (i.e., stability of GI/GD) in this new population. There have also been increasing concerns about the harms of these treatments, including increasing reports of detransition and regret [6 (pp. 67-99)]. The untrustworthy nature of international guidelines has also become more recognized:
- d) The U.K.'s Cass Review has been subject to considerable misrepresentation and inaccurate criticism in the peer-reviewed and gray literature. Various peer-reviewed articles are now available rebutting these erroneous criticisms [44, 56–58].



Claim 8: Detransition and regret are rare and usually stem from external pressures and unsupportive environments.

**SEGM's response to the claim that detransition and regret are rare; cited figures include 1.6–9.8% treatment discontinuation and approximately 4% regret, with discontinuation often attributed to social or financial factors rather than regret. ("Requests to reverse gender transition are rare ... recent studies show that, when they occur, they generally result from external factors - such as stigma, lack of social support, violence or interpersonal conflicts - and not from a change in gender identity" (Submission by a group of health professionals and academics specializing in gender identity)).**

**Response: This statement is misleading. Studies already report up to 30% of medical detransition rates among teens within a relatively short timeframe, painting a more complex picture.**

- a) The literature on rates of detransition/regret suffers from serious methodological limitations, including—crucially—high loss to follow-up [59, 60]. Thus, it is quite possible that the studies are substantially underestimating rates of discontinuation, detransition and regret. Current studies report rates ranging from 1.9% to 29.8% [6 (pp. 131-2), 61]; the upper range of the estimates indicates that treatment discontinuation is not rare among recent adolescent cohorts. Treatment discontinuation of this magnitude, before any restrictions were imposed, sends a troubling signal that youth discontinuing what is meant to be life-long treatment will be left with a number of irreversible changes to their bodies, since many of the effects of CSH are permanent.
- b) Other studies support the notion that the stability of gender incongruence diagnoses from adolescence through to adulthood is low. For example, a large German study of individuals aged 5–24 at baseline found that persistence of a recorded diagnosis of gender dysphoria (F64, the diagnostic code for gender identity disorders in the ICD-10) was below 50% in every age group, and that among females aged 15–19—the most rapidly rising subpopulation in the field— only 27.3% persisted after five years [62, 63].
- c) Not all people who detransition do so because their gender identity changes and/or they are dissatisfied with or regret the hormones and surgery that they have received, but many do. The studies that have claimed most people who detransition do not regret their transition but rather they do so due to stigma or financial reasons have substantial methodological limitations; i.e., they are either non-representative online surveys which have been promoted on LGBTQ advocacy sites (which will cause a selection bias toward people whose gender identity has not shifted), or they depend on patients returning to clinicians to tell them about detransition—which many do not. For example, one study found only 25% of patients who had detransitioned had informed their clinicians [64]. See also [6 (pp. 131-2)].



- d) We also do not know how many people, had they not received treatment as minors (e.g., delaying such treatment to adulthood in the event their GI/GD persisted), would feel about delays in initiation of treatment which enabled them to be at an age where they had the maturity to make the decision for themselves. For example, the study cited by the group of gender identity health professionals and academics to support the statement that regret is rare [65] drew its participants from the US-based Trans Youth Project, whose average age of social transition was 6.49 years, with some children as young as two years old [66 (p. 39)].

**Claim 9: The high burden of psychiatric problems found in gender dysphoric youth is due to 'minority stress' and should not present a barrier to medically transitioning a minor.**

**SEGM's response to the claim that psychiatric comorbidities are largely attributed to minority stress and are not, in themselves, a reason to withhold medical transition.**

**Response: This claim is overly simplistic. The relationship between gender dysphoria and psychiatric comorbidities is much more complex.**

- a) Young people presenting to gender clinics with GI/GD have high rates of psychiatric comorbidities [26, 27, 67]. High rates of psychiatric comorbidity were also a key finding reported in a Portuguese clinical cohort [4].
- b) Claims that this is solely due to minority stress are not supported by the evidence. Studies and reports of clinicians and people who have detransitioned demonstrate that psychiatric and neurodevelopmental conditions, as well as adverse childhood experiences (ACE) and peer group and social media influences, often predate the emergence of GI/GD [64, 68–70]. This suggests a complex causal pathway in which various conditions/events—i.e., psychiatric, neurodevelopmental, ACEs, homophobia—may causally contribute to GI/GD rather than a simplistic pathway in which GI/GD leads to minority stress which leads to psychiatric comorbidities [11 (pp. 121-2), 71–73].
- c) Such potential complex causal pathways are very important to understand and may in themselves be reasons to withhold medical transition. For example, a young person whose GI/GD has developed in the aftermath of homophobic bullying or sexual abuse or whose GI/GD represents part of a psychotic illness ought not to be assessed for PB and CSH for treatment of their GI/GD until their underlying issues have been suitably resolved.

**Claim 10: When gender dysphoria intensifies during puberty, it is likely to become a lifelong, permanent condition.**

**SEGM's response to the claim that persistence of gender dysphoria is substantially higher after puberty begins, and remission is said to be rare when dysphoria intensifies**



with puberty. (e.g., “when dysphoria is exacerbated by puberty, remission rarely occurs” (Portuguese Society of Clinical Sexology submission)).

**Response: This claim is not supported by the data.**

- a) This claim has commonly been made by the proponents of pediatric gender transition, but it remains a mere assertion. No data exist to track the natural trajectory of adolescent GI/GD absent medical intervention, since the youth in the studies were all already referred to gender clinics and were on a path to receiving such interventions, and received them in short order after consultation [74]. The paper cited by the Portuguese Society of Clinical Sexology in support of their claim that adolescent gender dysphoria rarely remits [75] in fact immediately qualifies the quoted statement by adding: “However, little empirical evidence exists to support this association”.
- b) It is, however, possible that in today’s climate of trans-advocacy groups and gender clinics promoting medical interventions, young people may be subject to nocebo effects, intensifying their distress: children are exposed to catastrophic and non-evidence based claims, such as that “puberty will be torture” and “children will be at high risk of suicide” [76]. Thus, increasing distress with puberty cannot by itself be considered a reliable indicator of GI/GD that will inherently persist throughout life.
- c) The most typical referrals to pediatric gender clinics in recent years are of adolescents who have no history of childhood GI/GD [55, 77–79]. The natural trajectory of their condition without treatment—either persistence or resolution—is unknown. As discussed in Claim 8, emerging evidence suggests persistence may be especially low for the currently presenting cohorts of adolescents [62].

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