Tidsskriftet Tidsskrift for Den norske legeforening

Puberty suppression

OPINIONS

ATLE FRETHEIM

atle.fretheim@fhi.no
Atle Fretheim, professor II at OsloMet – Oslo Metropolitan University and head of the Centre for Epidemic Interventions Research, Norwegian Institute of Public Health
The author has completed the ICMJE form and declares no conflicts of interest.

ANNE KVEIM LIE

Anne Kveim Lie, professor in medical history at the Institute of Health and Society, University of Oslo
The author has completed the ICMJE form and declares no conflicts of interest.

KETIL SLAGSTAD

Ketil Slagstad, postdoctoral research fellow at the Institute for the History of Medicine and Ethics in Medicine, Charité – Universitätsmedizin Berlin, Germany
The author has completed the ICMJE form and declares no conflicts of interest.

Political and medical decisions to restrict access to puberty blockers for transgender adolescents ignore the most important primary outcome measure.

Edgar Degas: Youth with Arms Upraised (ca. 1860). Robert Lehman Collection / In public ownership

Health authorities in Norway and several other countries have recently tightened access to puberty blockers for transgender adolescents (1). This is a direct result of the work of a group established by NHS (National Health Service) England, headed by Hilary Cass. In her report, Cass concluded that there is insufficient documentation on the effect of puberty blockers for adolescents diagnosed with gender incongruence (2).

The conclusions of the report led to apparent broad consensus that the evidence base for the use of puberty blockers in transgender adolescents is weak. An editorial in the BMJ described the evidence base for gender medicine interventions as 'threadbare' (3).

> ***«The most important aspect for adolescents was, unsurprisingly, puberty suppression, with a view to preventing the development of secondary sex characteristics»***

Selecting outcome measures

Systematic reviews are the cornerstone of evidence-based practice, and it is essential to involve patients in their design – particularly in the selection of outcome measures (4). Authors of systematic reviews should therefore gather information on how affected

groups value different outcome measures, even if this is challenging to achieve in practice (4).

The Cass group's approach started well. They held focus groups to gain insight into the outcome measures that transgender adolescents care about. In relation to puberty blockers, the responses were quite clear. The most important aspect for adolescents was, unsurprisingly, puberty suppression, with a view to preventing the development of secondary sex characteristics. The Cass group heard transgender girls express anxiety about developing facial hair and a deeper voice, fearing these changes would make it harder for them to present as a woman later in life. Transgender boys talked about the painful and potentially harmful practice of binding their breasts to conceal them (5).

Identified and ignored

As a decision-making basis for the Cass group, several systematic reviews were carried out, including on the effects of puberty blockers (6, 7). In line with core principles of evidence-based practice, the expectation would be for puberty suppression to be chosen as the primary outcome measure. However, this was not the case. Puberty suppression was not even mentioned as a relevant outcome in the first version of the systematic review (6). Instead, the authors of the review chose gender dysphoria, mental health and quality of life as outcome measures. It is unclear how and why they settled on these outcomes.

> ***«In line with core principles of evidence-based practice, the expectation would be for puberty suppression to be chosen as the primary outcome measure. However, this was not the case»***

It is also unclear why the outcome measures were changed in the updated version of the systematic review (7). Puberty suppression was now added to a long list of outcome measures, and the authors stated that the documentation on its effectiveness in slowing puberty was clear (7). In other words, the systematic review found strong evidence that puberty blockers have a positive effect on the outcome measure that is most important to patients. Despite this, the authors concluded that there was insufficient evidence to support the use of puberty blockers in young people with gender dysphoria (7).

Consequences of disregarding important outcome measures

Cass and her colleagues also chose to disregard the fact that puberty blockers have been shown to effectively delay pubertal development – the primary outcome measure for patients – with the justification that 'this has never been at issue' (2). Given the poor evidence base for other outcome measures, the Cass group could therefore conclude that the documentation for the clinical effectiveness of puberty blockers is insufficient.

It could be argued, to protests from the patient group, that puberty suppression should be viewed as a surrogate outcome measure, since what truly matters is whether the treatment is effective for gender dysphoria. It has been correctly pointed out that there is evidence, albeit weak, that puberty blockers lead to little or no improvement in the experience of gender dysphoria. Some interpret this as an indication of the treatment's inefficacy (2), but as the authors of the systematic reviews explain, the absence of a reported reduction in gender dysphoria could also be viewed as a positive treatment effect: when puberty progresses and secondary sex characteristics develop, an increase could be expected in gender dysphoria (6).

Difficult balancing act

There is no doubt that puberty blockers raise complex medical and ethical questions, particularly when parents and young people have differing views. However, the debate about puberty blockers seems to have lost sight of a fundamental principle of evidence-based practice, namely to prioritise the outcome measures that are most important to the users (8): in this case, the outcome measures that matter most to young transgender people.

REFERENCES

1. Galvin G. The UK is the latest country to ban puberty blockers for trans kids. Why is Europe restricting them? Euronews 13.12.2024. https://www.euronews.com/health/2024/12/13/the-uk-is-the-latest-country-to-ban-puberty-blockers-for-trans-kids-why-is-europe-restrict Accessed 24.2.2025.

2. Cass H. Independent review of gender identity services for children and young people final report. https://cass.independent-review.uk/home/publications/final-report/ Accessed 24.2.2025.

3. Abbasi K. The Cass review: an opportunity to unite behind evidence informed care in gender medicine. BMJ 2024; 385: q837. [CrossRef]

4. Thomas J, Kneale D, McKenzie JE et al. Determining the scope of the review and the questions it will address. I: Higgins J, Chandler J, Cumpston M et al, red. Cochrane Handbok for Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd, 2019: 13– 31.

5. Cass H. Independent review of gender identity services for children and young people: Interim report. https://cass.independent-review.uk/home/publications/interim-report/ Accessed 24.2.2025.

6. National Institute for Health and Care Excellence (NICE). Evidence review: Gonadotrophin releasing hormone analogues for children and adolescents with gender dysphoria. https://cass.independent-review.uk/wp-content/uploads/2022/09/20220726_Evidence-review_GnRH-analogues_For-upload_Final.pdf Accessed 24.2.2025.

7. Taylor J, Mitchell A, Hall R et al. Interventions to suppress puberty in adolescents experiencing gender dysphoria or incongruence: a systematic review. Arch Dis Child 2024; 109 (Suppl 2): s33–47. [PubMed][CrossRef]

8. Wright D, Pang KC, Giordano S et al. Evaluating the benefits and risks of puberty blockers and gender-affirming hormones for transgender adolescents. J Paediatr Child Health 2025; 61: 7–11. [PubMed][CrossRef]

Publisert: 14 March 2025. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.25.0079
Received 3.2.2025, first revision submitted 14.2.2025, accepted 24.2.2025.