

CURRENT EVIDENCE ON PUBERTY BLOCKERS



This information sheet summarises current scientific knowledge on the effects of puberty blockers for transgender youth. It is based on a literature review by a researcher in transgender health, with input from clinicians and community experts in transgender health and wellbeing. Its purpose is to assist whānau, families and health professionals supporting transgender* young people.

what are puberty blockers?

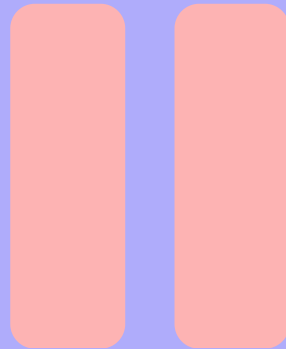


The scientific name for puberty blockers is Gonadotropin-releasing hormone analogues (**GnHa**).

Puberty blockers are used to **pause the physical changes of puberty** that cause or may potentially lead to distress for transgender young people. This gives them time to consider their gender before making decisions about whether to proceed with gender-affirming medical interventions, e.g. hormones, at a later date.

- We use the term transgender to refer to anyone whose gender is different than the gender they were assigned at birth. This is intended to include takatāpui, non-binary, and gender fluid people, alongside anyone who seeks gender-affirming care to express their gender, however they might choose to identify.

Puberty blockers can be used once a transgender young person reaches **Tanner stage 2 of puberty** and would otherwise start to develop secondary sex characteristics. Puberty blockers may also be helpful for adolescents who are further into puberty (Tanner stage 3–5) but are experiencing ongoing changes that are causing distress.



Puberty blockers are **reversible** (Panagiotakopoulos et al 2020, Hembree et al 2017). Young people can stop taking them at any time and puberty will recommence.

how long have puberty blockers been used?

Puberty blockers have been used since the 1980s to treat **precocious puberty** in children and they have been used in clinical care for transgender young people since the 1990s (de Vries et al 2021).

Use of puberty blockers for **transgender young people** has increased in recent years, likely due to social changes meaning these young people feel more able to come forward for help (de Vries et al 2021).




what are the effects of puberty blockers?


While the effects of puberty blockers are reversible, some of the effects of going through puberty are not. Taking puberty blockers allows young people to avoid developing **secondary sex characteristics** such as breasts, facial hair, an Adam's apple, body hair and voice changes, which are hard or sometimes impossible to reverse.

Studies have highlighted that many transgender adults who did not have access to puberty blockers **wish they could have had puberty blockers** in adolescence (Turban et al 2020). Allowing puberty to progress in transgender young people who experience gender dysphoria is not a neutral act and may have **lifelong harmful effects** (de Vries et al 2021).

Puberty blockers can reduce or prevent the need for expensive hair removal procedures and **invasive surgeries** when transgender young people are older, such as facial feminisation and chest masculinising surgeries.



Rigorous observational studies show that puberty blockers **improve the mental health and wellbeing of transgender young people**, lowering depression and suicidal ideation and increasing quality of life (Tordoff et al 2022, Achille et 2020, Turban et al 2020, Ashley, Olsen-Kennedy et al 2023, van der Miesen et al 2020).



Some young people choose to stop taking puberty blockers, as it is the appropriate step for their personal gender development.

Others choose to progress to gender-affirming hormone therapy. Evidence shows that **taking blockers does not influence the choice to subsequently take hormones** (Nos et al 2022).





what are the risks of puberty blockers?

All medicines have risks and benefits. Qualified health professionals explain these risks and benefits to transgender young people and their whānau or family, to ensure **informed consent**. The young person and their whānau or family can then decide, with the support of their clinicians, whether or not to start on puberty blockers.

Side effects of puberty blockers are **very rare** in the short term. One study showed a very small number of young people decided to stop taking puberty blockers due to symptoms including migraine, nausea and hot flushes.

These young people did not stop accessing gender-affirming medical care, but rather went on to take hormones (Brik et al 2020).

Like many other areas of medicine, long-term follow-up studies may help to better understand the impact of puberty blockers across the life course. However, existing data, including from their long-term use for precocious puberty, suggest that **puberty blockers are as safe as other routine medical care** (Ashley, Olsen-Kennedy et al 2023).

A review of several recent studies shows **no significant change in bone density** among young people on blockers (Joseph et al 2019). Some studies suggest transgender young people may already have lower bone density prior to taking blockers, due to lifestyle factors such as reduced physical activity compared to their peers (Ceolin et al 2023).

Bone density is likely to increase when a young person **ceases blockers or starts hormones** (Hembree et al 2017, Schagen et al 2020).

To reduce any potential impact on bone health, young people should not stay on puberty blockers for **prolonged periods**, unless they go on to take hormones alongside puberty blockers.



To **optimise bone health**, it is important to ensure adequate calcium intake and encourage physical activity (Hembree et al 2017). Vitamin D supplements should be given if a young person has risk factors for vitamin D deficiency, especially in winter.

what is the quality of the evidence about puberty blockers?

The use of puberty blockers has become the **most widely accepted clinical approach** to supporting transgender young people in specialised transgender clinics around the world and is accepted best practice amongst specialist clinicians.

It forms part of the two main international guidelines in the field (Coleman et al 2022, Hembree et al 2017). It is also reflected in the guidelines of many countries, including Canada (Canadian Pediatric Society 2023), Australia (Telfer et al 2020) and New Zealand (Oliphant et al 2018).

Randomised-controlled trials (RCTs) would provide high quality evidence of the full risks and benefits of blockers in the short and long term. But RCTs cannot be used for this purpose because it would be **unethical to withhold puberty blockers** from transgender young people for the purpose of research, when they are the current best treatment and withholding them poses a risk of serious harm (Ashley, Olsen-Kennedy et al 2023).

The lack of RCTs means that evidence on the effects of blockers is scientifically classified as 'low quality'.
'Low quality' evidence is

common for many paediatric conditions

where it would be unethical to withhold treatment, e.g. medications to treat fever, so this is not specific to puberty blockers.

On this basis, a recent analysis concludes that clinicians can **confidently prescribe puberty blockers** where appropriate, based on the current scientific evidence (Ashley, Olsen-Kennedy et al 2023).

The lack of RCTs does not mean that the use of puberty blockers is based on insufficient evidence (Ashley, Olsen-Kennedy et al 2023). **Well-designed observational studies** can and have been used to ground reliable recommendations for clinical practice and policymaking in healthcare for transgender young people, without the need for RCTs (Ashley, Olsen-Kennedy et al 2023).

where can I get more information?

This is one of a series of three information sheets about puberty blockers, compiled in Aotearoa New Zealand in August 2023 by a researcher in transgender health, with input from clinicians and community experts in transgender health and wellbeing.

These information sheets can be downloaded at www.projectvillageaotearoa.com/pubertyblockers

Text: Julia de Bres

Graphic design: Ia Morrison-Young

Illustrations: Julia de Bres





references

Achille C, Taggart T, Eaton NR, Osipoff J, Tafuri K, Lane A, & Wilson TA 2020. Longitudinal impact of gender-affirming endocrine intervention on the mental health and well-being of transgender youths: preliminary results. *International Journal of Pediatric Endocrinology* 8, <https://doi.org/10.1186/s13633-020-00078-2>


Ashley F, Tordoff DM, Olson-Kennedy J, & Restar AJ 2023. Randomized-controlled trials are methodologically inappropriate in adolescent transgender healthcare, *International Journal of Transgender Health*, <https://doi.org/10.1080/26895269.2023.2218357>

Brik T, Vrouenraets L J J J, de Vries MC, & Hannema SE 2020. Trajectories of Adolescents Treated with Gonadotropin-Releasing Hormone Analogues for Gender Dysphoria. *Archives of Sexual Behavior*, <https://doi.org/10.1007/s10508-020-01660-8>.

Canadian Pediatric Society 2023. Position statement: An affirming approach to caring for transgender and gender-diverse youth. <https://cps.ca/en/documents/position/an-affirming-approach-to-caring-for-transgender-and-gender-diverse-youth>

Ceolin C, Scala A, Dall'Agnol M, Ziliotto, Delbarba A, Facondo P, Citron A, Vescovi B, Pasqualini S, Giannini S, Camozzi V, Cappelli C, Bertocco A, De Rui M, Coin A, Sergi G, Ferlin A, & Garolla A, on behalf of the Gender Incongruence Interdisciplinary Group (GIIG) 2023. Bone health and body composition in transgender adults before gender-affirming hormonal therapy: data from the COMET study. *Journal of Endocrinological Investigation*, <https://doi.org/10.1007/s40618-023-02156-7>

Coleman, E., Radix, A. E., Bouman, W.P., Brown, G.R., de Vries, A. L. C., Deutsch, M. B., Ettner, R., Fraser, L., Goodman, M., Green, J., Hancock, A. B., Johnson, T. W., Karasic, D. H., Knudson, G. A., Leibowitz, S. F., Meyer-Bahlburg, H. F.L., Monstrey, S. J., Motmans, J., Nahata, L., ... Arcelus, J. 2022. Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. *International Journal of Transgender Health*, 23(S1), S1-S260, <https://doi.org/10.1080/26895269.2022.2100644>



references




de Vries, ALC, Richards C, Tishelman AC, Motmans J, Hannema SE, Green J, & Rosenthal SM 2021. Bell v Tavistock and Portman NHS Foundation Trust [2020] EWHC 3274: Weighing current knowledge and uncertainties in decisions about gender-related treatment for transgender adolescents. *International Journal of Transgender Health* 22:3, 217–224, <https://doi.org/10.1080/26895269.2021.1904330>

Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, & T'Sjoen GG 2017. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an endocrine society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism* 102(11): 3869–903, <https://doi.org/10.4158/1934-2403-23.12.1437>

Joseph T, Ting J, & Butler G 2019. The effect of GnRH analogue treatment on bone mineral density in young adolescents with gender dysphoria: findings from a large national cohort. *Journal of Pediatric Endocrinology and Metabolism* Oct 25;32(10):1077–1081, <https://doi.org/10.1515/jpem-2019-0046>

Nos AL, Klein DA, Adirim TA, Schvey NA, Hisle-Gorman E, Susi A, & Roberts CM 2022. Association of Gonadotropin-Releasing Hormone Analogue Use With Subsequent Use of Gender-Affirming Hormones Among Transgender Adolescents. *JAMA Network Open* 5(11):e2239758, <http://doi:10.1001/jamanetworkopen.2022.39758>

Oliphant J, Veale J, Macdonald J, Carroll R, Johnson R, Harte M, Stephenson C, Bullock J, Cole D, & Manning P 2018. Guidelines for gender affirming healthcare for gender diverse and transgender children, young people and adults in Aotearoa, New Zealand. *NZMJ*, 14 December 2018, vol 131, no 1487.



references

Panagiotakopoulos L, Chulani V, Koyama A, Childress K, Forcier M, Grimsby G, & Greenberg K 2020. The effect of early puberty suppression on treatment options and outcomes in transgender patients. *Nature Reviews. Urology*, 17(11), 626–636, <https://doi.org/10.1038/s41585-020-0372-2>

Schagen, SEE, Wouters FM, Cohen-Kettenis PT, Gooren LJ, & Hannema SE 2020. Bone Development in Transgender Adolescents Treated With GnRH Analogues and Subsequent Gender-Affirming Hormones. *Journal of Clinical Endocrinology and Metabolism* Dec 1;105(12):e4252–63, <https://doi.org/10.1210/clinem/dgaa604>

Telfer MM, Tollit MA, Pace CC, & Pang KC 2020. Australian Standards of Care and Treatment Guidelines for Trans and Gender Diverse Children and Adolescents Version 1.3. Melbourne: The Royal Children's Hospital.

Tordoff DM, Wanta JW, Collin A, Stepney C, Inwards-Breland DJ & Ahrens K. Mental Health Outcomes in Transgender and Nonbinary Youths Receiving Gender-Affirming Care 2022. *JAMA Netw Open* 5(2):e220978, doi:10.1001/jamanetworkopen.2022.0978

Turban JL, King D, Carswell JM, & Keuroghlian AS 2020. Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation. *Pediatrics*. 2020;145(2), <https://doi.org/10.1542/peds.2019-1725>

Van der Miesen AIR, Steesma TD, & de Vries ALC 2020. Psychological Functioning in Transgender Adolescents Before and After Gender-Affirmative Care Compared With Cisgender General Population Peers. *Journal of Adolescent Health* 66, 6: 699–704, <https://doi.org/10.1016/j.jadohealth.2019.12.01>