

## Appendix A. List of organisations that responded

A total of 57 respondents stated that they were responding on behalf of an organisation, representing 54 different organisations (i.e., some organisations were represented by more than one respondent, noted in brackets).

Alder Hey Children's NHS Foundation Trust  
Authentic Equity Alliance  
Bayswater Support Group  
Bodyswap  
Brighton and Hove LGBT Switchboard  
British Psychological Society  
Christian Concern  
Clinical Advisory Network on Sex and Gender (CAN-SG)  
Elaine Hutton, Lesbian Rights Alliance, Bristol Branch  
EPATH  
Exeter Trans And Non-binary Cafe  
Gender Plus  
General Medical Council  
Genspect (2)  
GIDS Experts by Experience  
Glasgow University's LGBTQ+ Students Association  
Great Ormond Street Hospital NHS Foundation Trust  
Guy's and St. Thomas' NHS trust  
Harem of No One  
Labour Women's Declaration working group  
LGB Alliance  
LGBT Foundation  
Lovewise  
Playground Games  
Proud2Be (2)  
Q:alliance  
Royal Manchester Children's Hospital  
Sex Matters

South London and Maudsley NHS Trust  
South Shropshire Women's Rights Network  
Space Youth Project  
Spectra  
Stonewall  
The Christian Institute  
The Gay Men's Network  
The Gender Identity Research & Education Society  
The Gender Services programme team at Evelina  
The Kite Trust  
The Lesbian Rights Alliance  
The Pharmacists' Defence Association Union's LGBT+ Network  
The Rainbow Project  
The South Hub  
Thoughtful Therapists  
Trans Learning Partnership  
Trans Masculine Birmingham  
TransActual (2)  
Transgender Equality Network Ireland  
Transgender Europe  
Transilience CIC  
Transwidows.com  
University College London Hospitals Endocrine  
University College London Hospitals NHS Foundation Trust  
University of Worcester LGBTQ+ Student Network  
Women's Rights Network

## Appendix B. List of references provided

### Question 1

Many respondents suggested papers, studies, articles, websites, books, blogs, videos and news reports that they felt should have been considered in the evidence review. Some of these were studies included in the NICE review, and some had been listed by NICE as having been considered but ruled out of inclusion in their review. Many suggestions were opinion pieces and other articles which drew on secondary evidence. However, a total of 73 references, papers, analyses and surveys were suggested. These have been listed and summarised in the following table:

Title – Authors - Url	Summary
<p>The Myth of “Reliable Research” in Paediatric Gender Medicine: A critical evaluation of the Dutch Studies—and research that has followed</p> <p>Abbruzzese, E., Levine, S.B., Mason, J.W. (2023)</p> <p><a href="https://www.tandfonline.com/doi/full/10.1080/0092623X.2022.2150346">https://www.tandfonline.com/doi/full/10.1080/0092623X.2022.2150346</a></p>	<p>Commentary on the methodologically biased nature of two Dutch studies (de Vries, et al., 2011 - included in NICE review) and (de Vries, et al. 2014) which have formed the foundation of practice of youth gender transition. Methodological biases include (1) subject selection assured that only the most successful cases were included in the results; (2) the finding that “resolution of gender dysphoria” was due to the reversal of the questionnaire employed; (3) concomitant psychotherapy made it impossible to separate the effects of this intervention from those of hormones and surgery.</p>
<p>“I am afraid for those kids who might find death preferable”: Parental figures’ reactions and coping strategies to bans on gender affirming care for transgender and gender diverse youth.</p> <p>Abreu, R. L., Sostre, J. P., Gonzalez, K. A., Lockett, G. M., Matsuno, E. (2022)</p> <p><a href="https://psycnet.apa.org/record/2021-67997-001?doi=1">https://psycnet.apa.org/record/2021-67997-001?doi=1</a></p>	<p>Survey of 138 parental figures of TGD youth sharing their reactions and coping strategies as a result of current anti-transgender laws and bills. Thematic analysis revealed four themes depicting participants’ cognitive reactions, including: (a) violation of rights, (b) increased stigma, (c) decreased quality of healthcare, and (d) support for the child’s journey. Also, three themes emerged about participants’ emotional reactions, including: (a) fear and anxiety, (b) anger, and (c) relief. Additionally, participants shared narratives about how they are coping with these anti-transgender laws and bills, including: (a) activism and advocacy, (b) educating others, (c) seeking support from communities/groups, and (d) relocation and avoidance. Recommendations for practitioners such as debunking incorrect information about trans healthcare when working with parental figures are discussed.</p>
<p>Longitudinal impact of gender-affirming endocrine intervention on the mental</p>	<p>Examining the associations of endocrine intervention (puberty suppression and/or cross sex hormone therapy) with depression and</p>

<p>health and well-being of transgender youths: preliminary results</p> <p>Achille, C., Taggart, T., Eaton, N.R., et al. (2020)</p> <p><a href="https://doi.org/10.1186/s13633-020-00078-2">https://doi.org/10.1186/s13633-020-00078-2</a></p>	<p>quality of life scores over time in transgender youths. Over a 5-year period, 50 participants completed 3 waves of questionnaires on depression and quality of life. Mean depression scores and suicidal ideation decreased over time while mean quality of life scores improved over time. When controlling for psychiatric medications and engagement in counselling, regression analysis suggested improvement with endocrine intervention. Observed in male-female and female-male but stronger effects in the former.</p>
<p>Animal studies which demonstrate PSH negatively impacts learning, the development of social behaviours and responses to stress</p> <p>Anacker, C., Sydnor, E., Chen, BK., LaGamma, CC., McGowan, JC., Mastrodonato, A., Hunsberger, H.C., Shores, R., Dixon, RS., McEwen, BS., Byne, W., Meyer-Bahlburg, HFL., Bockting, W., Ehrhardt, AA., Denny, C.A. (2020)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/32919399/">https://pubmed.ncbi.nlm.nih.gov/32919399/</a></p>	<p>Study investigating the effects of GnRH on reproductive function, social and affective behaviour, cognition, and brain activity in mice. Six-week-old male and female mice were injected daily with saline or GnRH for 6 weeks and behaviour was tested in various ways. They found that the GnRH increased hyperlocomotion, changed social preference, and increased neuroendocrine stress responses in male mice, while the same treatment increased hyponeophagia (measure of anxiety) and despair-like behaviour in females. The study concluded that GnRH agonist treatment after puberty onset exerts sex-specific effects on social- and affective behaviour, stress regulation, and neural activity in mice.</p>
<p>Association between pre-treatment IQ and educational achievement after gender-affirming treatment including puberty suppression in transgender adolescents</p> <p>Arnoldussen, M., Hooijman, E.C., Kreukels, B.P., de Vries, A.L. (2022)</p> <p><a href="https://doi.org/10.1177/13591045221091652">https://doi.org/10.1177/13591045221091652</a></p>	<p>Study examining the effects of gender affirming treatment (including puberty suppression) on cognitive development. IQ was measured in 72 adolescents (45 trans boys, 27 trans girls) before treatment, educational achievement was evaluated after gender-affirming treatment. Results show a positive association between IQ and educational achievement and appears to be similar to the general population.</p>
<p>Self-Perception of Transgender Adolescents After Gender-Affirming Treatment: A Follow-Up Study into Young Adulthood</p>	<p>Study examining the effect that gender affirming treatment (including puberty suppressors) has on psychological development, including the development of positive self-perception. The total study sample consisted of 70 adolescents. Self-perception was assessed (using a self-</p>

<p>Arnoldussen, M., van der Miesen, A.I.R., Elzinga, W.S., Alberse, A.E., Popma, A., Steensma, T.D., de Vries, A.L.C. (2022)</p> <p><a href="https://doi.org/10.1089/lgbt.2020.0494">https://doi.org/10.1089/lgbt.2020.0494</a></p>	<p>report measure) before the start of gender-affirming hormone treatment and at least 6 months after gender-affirming surgeries. It was found that the domains of physical appearance and global self-worth improved significantly over the course of treatment. No domain worsened significantly over the course of treatment. The domains of scholastic competence, social acceptance, athletic competence, and close friendship remained stable. This suggests that irreversible gender-affirming treatment for adolescents could contribute to the development of a more positive self-perception.</p>
<p>Randomized-controlled trials are methodologically inappropriate in adolescent transgender healthcare</p> <p>Ashley, F., Tordoff, D.M. Olson-Kennedy, J., Restar, A.J. (2023)</p> <p><a href="https://www.tandfonline.com/doi/full/10.1080/26895269.2023.2218357">https://www.tandfonline.com/doi/full/10.1080/26895269.2023.2218357</a></p>	<p>A critical review investigating whether Randomised Control Trials (RCTs) are methodologically appropriate for studying the association between adolescent gender-affirming care and mental health. It was found that RCTs are inappropriate since these interventions have physiologically evident effects and are highly desired by participants, giving rise to concerns over adherence, drop-out, response bias, and generalizability. Complementary and well-designed observational studies can instead be used to ground reliable recommendations for clinical practice and policymaking in adolescent trans healthcare, without the need for RCTs.</p>
<p>The Effect of Puberty Blockers on the Accrual of Bone Mass</p> <p>Biggs, M. (2021)</p> <p><a href="https://www.degruyter.com/document/doi/10.1515/jpem-2021-0180/html">https://www.degruyter.com/document/doi/10.1515/jpem-2021-0180/html</a></p>	<p>Issues with the study by Joseph, et al. (2019) on bone density results from the Tavistock clinic - used in the NICE review. Since the release of data, Biggs' reanalysis concluded that after two years on GnRHa, the bone mass density Z-scores for a significant minority of the children had declined to a level that should trigger clinical concern, such low bone density is found in only 0.13% of the population. He posits that the 2019 study omitted data and comes to a complacent conclusion</p>
<p>The Dutch Protocol for Juvenile Transsexuals: Origins and Evidence.</p> <p>Biggs, M. (2022)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/36120756/">https://pubmed.ncbi.nlm.nih.gov/36120756/</a></p>	<p>A history review of the Dutch Protocol which proposed puberty suppression as an intervention for "juvenile transsexuals," this consequently became the international standard for treating gender dysphoria. The main evidence for this practice came from a longitudinal study of 70 Dutch adolescents who had undergone puberty suppression followed by cross-sex hormones and surgery. Their outcomes shortly after surgery appeared mostly positive: an improved psychological function and reduced gender dysphoria. However, these findings rested on a small number of observations (much fewer than 70) and incomparable measures of gender dysphoria. A replication study found no such improvement in gender</p>

	dysphoria or psychological functioning. The paper also evaluates the side effects of puberty suppression, including negative effects on cognitive and emotional development and on sexual functioning.
“Deconstructing the Feminine Essence Narrative”	Commentary and analysis of the feminine essence theory, and comparison with other theories of male-to-female transsexualism.
Blanchard, R. (2008)	
<a href="https://www.researchgate.net/publication/5420507_Deconstructing_the_Feminine_Essence_Narrative">https://www.researchgate.net/publication/5420507_Deconstructing_the_Feminine_Essence_Narrative</a>	
Transgender Girls Grow Tall: Adult Height Is Unaffected by GnRH Analogue and Estradiol Treatment	Retrospective cohort study of 161 transgender girls (biological males) treated with GnRHa and estradiol, high growth-reductive doses of estradiol, or ethinyl estradiol. Growth velocity and bone maturation was found to decelerate while receiving gonadotropin-releasing hormone analogues (GnRH) but to accelerate during gender-affirming hormone therapy (GAHT). Adult height was found to be lower than predicted at the start of GnRHa treatment (-1.5cm) and lower still after high-dose ethinyl estradiol treatment (-3.0cm).
Boogers, L.J., Wiepjes, C.M., Klink, D.T., Hellinga, I., van Trotsenburg, A.S.P., den Heijer, M., Hannema, S.E. (2022)	
<a href="https://academic.oup.com/jcem/article/107/9/e3805/6603101">https://academic.oup.com/jcem/article/107/9/e3805/6603101</a>	
Trajectories of Adolescents Treated with Gonadotropin-Releasing Hormone Analogues for Gender Dysphoria	Retrospective study documenting trajectories after the initiation of GnRHa in 143 adolescents, as well as exploring the reasons for extended use and discontinuation of GnRHa. After a median duration of 0.8 years on GnRHa, 125 (87%) started gender-affirming hormones (GAH) and 9 (6%) discontinued GnRHa, 5 (3.5%) of whom no longer wished gender-affirming treatment. Due to the observational character of the study, however, it was stated that it was not possible to say if GnRHa treatment itself influenced the outcome.
Brik, T., Vrouwenraets, L., de Vries, M., Hannema, S. (2020)	
<a href="https://link.springer.com/article/10.1007/s10508-020-01660-8">https://link.springer.com/article/10.1007/s10508-020-01660-8</a>	
Puberty suppression in a gender-dysphoric adolescent: a 22-year follow-up.	A case report on a 22-year follow-up of a female-to-male transsexual, treated with GnRH analogs at 13 years of age and considered eligible for androgen treatment at age 17, and who had gender reassignment surgery at 20 and 22 years of age. At follow-up, he indicated no regrets about his treatment. He was functioning well psychologically, intellectually, and socially; however, he experienced some feelings of sadness about choices he had made in a long-lasting intimate
Cohen-Kettenis, P., Schagen, S., Steensma, T., de Vries, A., de Waal, H.D.-v. (2011)	

<p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3114100/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3114100/</a></p>	<p>relationship. There were no clinical signs of a negative impact on brain development. He was physically in good health, and metabolic and endocrine parameters were within reference ranges. Bone mineral density was within the normal range for both sexes. His final height was short as compared to Dutch males; however, his body proportions were within normal range. This first report on long-term effects of puberty suppression suggests that negative side effects are limited and that it can be a useful additional tool in the diagnosis and treatment of gender dysphoric adolescents.</p>
<p>Cognitive, Emotional, and Psychosocial Functioning of Girls Treated with Pharmacological Puberty Blockage for Idiopathic Central Precocious Puberty</p> <p>Hayes, P. (2017)</p> <p><a href="https://doi.org/10.3389/fpsyg.2017.00044">https://doi.org/10.3389/fpsyg.2017.00044</a></p> <p>4</p>	<p>A commentary on Wojniusz, S., et al.'s (2016) study exploring differences in cognitive function, behaviour, emotional reactivity, and psychosocial problems between 15 GnRHa treated precocious puberty girls and 15 age-matched controls. They reported that both groups showed very similar scores with regard to cognitive performance,</p> <p>However, Hayes believes this may be overly optimistic. These statements minimise the fairly substantial difference found in IQ scores and may also overemphasise its lack of statistical significance, as given the small number of participants in the study statistical significance has a high threshold. The statements should be qualified to indicate that the research has, in fact, reinforced concerns over the impact of GnRHAs on cognitive performance in children.</p>
<p>Conclusions Not So NICE: A Critical Analysis of the NICE Evidence review of puberty blockers for children and adolescents with gender dysphoria</p> <p>Eckert, A.J. (2021)</p> <p><a href="https://sciencebasedmedicine.org/a-critical-look-at-the-nice-review/">https://sciencebasedmedicine.org/a-critical-look-at-the-nice-review/</a></p>	<p>A critical review of the studies included in the NICE Evidence review and the omitted studies. Eckert concludes that the totality of evidence shows that gender-affirming treatment with puberty blockers significantly decreases distress, depression, emotional and behavioural problems and suicidality, while improving global functioning, psychological and psychosocial functioning, quality of life, satisfaction and happiness. There are expected decreases in Z-scores, but bone mineral density remains stable on puberty blockers, as does executive function. Adrenal androgen levels change but yield no negative effects at follow-up. Body changes that occur are aligned with the blocked youth's affirmed gender. Obesity is more common in trans youth, but treatment with blockers does not increase cardiovascular risk factors. More studies are needed on the neurodevelopmental impact of blockers, though the effect of blockers on mental health improvement can be neuroprotective. Research studies continue to confirm that</p>

	puberty blockers are safe and effective with minimal complications, and that youth do not discontinue blockers due to side effects.
Effects of Medical Interventions on Gender Dysphoria and Body Image: A Follow-Up Study van de Grift, T.C., Elaut, E., Cerwenka, S.C., Cohen-Kettenis, P.T., De Cuypere, G., Richter-Appelt, H., Kreukels, B.P.C. (2017) <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5580378/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5580378/</a>	A follow-up survey of 201 participants, investigating medical intervention (hormone therapy and surgery) on gender dysphoria (GD). They found that medical care effectively reduced feelings of GD and improved body satisfaction. Hormone therapy decreased overall body dissatisfaction, whereas surgery contributed mostly to genital satisfaction. Analysis of predictors of persisting body dissatisfaction indicated that psychological mechanisms, next to medical interventions, contributed to body satisfaction. The concept of body image may assist clinicians and individuals with GD to develop treatment plans, which optimally improve psychological well-being. Especially, people with more profound and more overall body dissatisfaction could benefit from receiving additional counselling on this subject. Because current data suggest that a complete medical transition cannot dissolve all body dissatisfaction in some, psychotherapy may additionally offer guidance to accept the less than perfect body.
Autism Spectrum Disorder and Gender Dysphoria/Incongruence. A systematic Literature Review and Meta-Analysis Kallitsounaki, A., Williams, D.M. (2022) <a href="https://pubmed.ncbi.nlm.nih.gov/35596023/">https://pubmed.ncbi.nlm.nih.gov/35596023/</a>	A literature review and meta-analysis on autism and gender dysphoria. The findings suggest that there is (a) a positive relationship between ASD traits and GD/GI feelings among people from the general population, (b) an increased prevalence of GD/GI in the autistic population, and (c) an increased prevalence of ASD diagnoses and ASD traits in the GD/GI population. Overall, these findings suggest the existence of a link between ASD and GD/GI that warrants the investigation of mechanisms that could explain that link and the intensification of clinical attention to autistic GD/GI individuals.
A reduction in long-term spatial memory persists after discontinuation of peripubertal GnRH agonist treatment in sheep Hough, D., Bellingham, M., Haraldsen, I.R., McLaughlin, M., Robinson, J.E., Solbakk, A.K., Evans, N.P. (2016) <a href="https://pubmed.ncbi.nlm.nih.gov/279874">https://pubmed.ncbi.nlm.nih.gov/279874</a>	A previous ovine study demonstrated that long-term spatial memory is reduced in adult rams following GnRHa treatment. The current study investigated whether this effect is reversed after discontinuation of GnRHa-treatment. A total of 25 rams that were previously given the puberty suppressing hormone were compared with 30 control subjects. The long-term spatial memory performance of the recovery rams remained reduced after discontinuation of GnRHa (at 83 and 99 weeks of age), compared to Controls. This result suggests that the time at which puberty normally occurs may represent a critical period of hippocampal plasticity. Perturbing normal hippocampal formation in



29/	this peripubertal period may also have long lasting effects on other brain areas and aspects of cognitive function.
<p>Psychological assessments before and after treatment of early puberty in adopted children</p> <p>Mul, D., Versluis-den Bieman, H.J., Slijper, F.M., Oostdijk, W., Waelkens, J.J., Drop, S.L. (2001)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/11683207/">https://pubmed.ncbi.nlm.nih.gov/11683207/</a></p>	<p>A randomised trial of 30 adopted children with early puberty treated with GnRHa and psychologically evaluated. Treatment with GnRHa with or without GH did not increase emotional and behavioural problems in adopted children, nor was their self-perception decreased, however IQ levels dropped (this was not deemed to be clinically relevant).</p>
<p>Bone Health in the Transgender Population</p> <p>Rothman, M.S., Iwamoto, S.J. (2019)</p> <p><a href="http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6709704/">http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6709704/</a></p>	<p>A review of studies investigating bone health in transgender conclude that studies to date show that when oestrogen is initiated in trans women, there are positive changes in BMD and some measures of bone quality, when testosterone is initiated in trans men, the changes in BMD are not as robust, but body composition changes and direct effects of testosterone on the bone likely protect BMD. Low levels of estradiol likely still offer bone protection in trans men as in cis men. They also point out that this is not a straightforward result; variables such as ethnicity, BMI and lifestyle habits play a crucial role. It is worth remembering that trans individuals may not have optimal healthy lifestyles to achieve peak bone mass (baseline BMD is found to be below average in transgender before treatment begins). Fracture risk is still unknown.</p>
<p>Puberty blockers for transgender and gender diverse youth—a critical review of the literature</p> <p>Rew, L., Young, C.C. (2021)</p> <p><a href="https://doi.org/10.1111/camh.12437">https://doi.org/10.1111/camh.12437</a></p>	<p>A review of the literature on puberty blockers for transgender youth. From an initial sample of 211 articles, 9 research studies that met inclusion/exclusion criteria were systematically reviewed. Positive outcomes were decreased suicidality in adulthood, improved affect and psychological functioning, and improved social life. Adverse factors associated with use were changes in body composition, slow growth, decreased height velocity, decreased bone turnover, cost of drugs, and lack of insurance coverage. The authors advise that given the potentially life-saving benefits of these medications for TGD youth, it is critical that rigorous longitudinal and mixed methods research be conducted that includes stakeholders and members of the gender diverse community with representative samples.</p>

<p>Access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults</p> <p>Turban, J.L., King, D., Kobe, J., Reisner, S.L., Keuroghlian, A.S. (2022)</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8754307/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8754307/</a></p>	<p>A secondary analysis of the 2015 U.S. Transgender Survey with a sample of 27,715. Using multivariable logistic regression adjusting for potential confounders, they examined associations between access to GAH during early adolescence (age 14–15), late adolescence (age 16–17), or adulthood (age ≥18) and adult mental health outcomes, with participants who desired but never accessed GAH as the reference group. 21,598 participants (77.9%) reported ever desiring GAH. Of these, 8,860 (41.0%) never accessed GAH, 119 (0.6%) accessed GAH in early adolescence, 362 (1.7%) accessed GAH in late adolescence, and 12,257 (56.8%) accessed GAH in adulthood. Access to GAH during adolescence and adulthood was associated with favourable mental health outcomes compared to desiring but not accessing GAH.</p>
<p>Psychosexual outcome of gender-dysphoric children</p> <p>Wallien, M.S., Cohen-Kettenis, P.T. (2008)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/18981931/">https://pubmed.ncbi.nlm.nih.gov/18981931/</a></p>	<p>A study looking into the psychosexual outcomes of 77 gender dysphoric children used questionnaires and found that most will not remain gender dysphoric after puberty. Children with persistent GID are characterised by more extreme gender dysphoria in childhood than children with desisting gender dysphoria. With regard to sexual orientation, the most likely outcome of childhood GID is homosexuality or bisexuality.</p>
<p>A systematic review of hormone treatment for children with gender dysphoria and recommendations for research</p> <p>Ludvigsson, J.F., Adolfsson, J., Höistad, M., Rydelius, P-A., Kriström, B., Landén, M. (2023)</p> <p><a href="https://doi.org/10.1111/apa.16791">https://doi.org/10.1111/apa.16791</a></p>	<p>Systematic review assessing hormone treatment effects on psychosocial and mental health, cognition, body composition, and metabolic markers in youths with gender dysphoria. 24 studies were deemed relevant: in 21 studies adolescents were given GnRHa treatment; in three studies cross-sex hormone treatment (CSHT) was given without previous GnRHa treatment. No randomised controlled trials were identified. The few longitudinal observational studies were hampered by methodological weaknesses, such as small numbers and high attrition rates. Hence, the long-term effects of hormone therapy on psychosocial health could not be evaluated. The exception being that children with gender dysphoria often had lower group mean values for Bone Mineral Density already prior to GnRHa treatment, and that GnRHa treatment delays the physiologically occurring BMD gain during pubertal sex hormone stimulation. However, this GnRHa-induced delay in BMD gain is almost fully compensated for by later ensuing Cross Sex Hormone Therapy. Evidence was concluded to be insufficient in this area.</p>
<p>Endocrine Treatment of Gender-</p>	<p>A team from the Endocrine Society carried out two systematic reviews</p>

<p>Dysphoric/Gender-Incongruent Persons: and a literature review, which contributed to an evidence-based guideline using the GRADE approach. They concluded that Hormone treatment is not recommended for prepubertal gender-dysphoric/gender-incongruent persons. They recommend treating gender-dysphoric adolescents who have entered puberty at Tanner Stage G2/B2 by suppression with gonadotropin-releasing hormone agonists. For the care of peripubertal youths and older adolescents, they recommend that an expert multidisciplinary team comprised of medical professionals and mental health professionals manage this treatment.</p> <p>An Endocrine Society Clinical Practice Guideline</p> <p>Hembree, W.C., Cohen-Kettenis, P.T., Gooren, L., Hannema, S.E., Meyer, W.J., Murad, M.H., Rosenthal, S.M., Safer, J.D., Tangpricha, V., T'Sjoen, G.G. (2017)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/28945902/">https://pubmed.ncbi.nlm.nih.gov/28945902/</a></p>	<p>and a literature review, which contributed to an evidence-based guideline using the GRADE approach. They concluded that Hormone treatment is not recommended for prepubertal gender-dysphoric/gender-incongruent persons. They recommend treating gender-dysphoric adolescents who have entered puberty at Tanner Stage G2/B2 by suppression with gonadotropin-releasing hormone agonists. For the care of peripubertal youths and older adolescents, they recommend that an expert multidisciplinary team comprised of medical professionals and mental health professionals manage this treatment.</p>
<p>2015 U.S. Transgender Survey</p> <p><a href="https://www.ustranssurvey.org/reports/#2015report">https://www.ustranssurvey.org/reports/#2015report</a></p>	<p>Anonymous online survey of 27,715 transgender people in the United States.</p>
<p>Toward Trans Reproductive Justice: A Qualitative Analysis of Views on Fertility Preservation for Australian Transgender and Non-binary People</p> <p>Riggs, D. W., Bartholomaeus, C. (2020)</p> <p><a href="https://spssi.onlinelibrary.wiley.com/doi/abs/10.1111/josi.12364">https://spssi.onlinelibrary.wiley.com/doi/abs/10.1111/josi.12364</a></p>	<p>Article drawing on three Australian studies focused on views about fertility preservation among (1) parents of transgender and non-binary children, (2) transgender and non-binary adults, and (3) healthcare professionals working with transgender and non-binary people.</p>
<p>'Taking the lid off the box': The value of extended clinical assessment for adolescents presenting with gender identity difficulties.</p> <p>Churcher Clarke, A., Spiliadis, A. (2019)</p> <p><a href="https://journals.sagepub.com/doi/abs/10.1177/1359104518825288">https://journals.sagepub.com/doi/abs/10.1177/1359104518825288</a></p>	<p>Article presenting a joint case review of the authors' caseloads over an 18-month period, to identify and describe those young people who presented to the Gender Identity Development Service (GIDS) with gender dysphoria (GD) emerging in adolescence, and who, during the course of assessment, ceased wishing to pursue medical (hormonal) interventions and/or came to understand their distress and its alleviation (at that particular point in time) differently and eventually chose to identify their gender identity as broadly aligned with their biological sex.</p>
<p>Transgender Adolescent Suicide Behavior</p> <p>Toomey, R., Syvertsen, A., Shramko, M. (2018)</p>	<p>Examination of prevalence rates of attempted suicide among 120,617 adolescents over a 36-month period between June 2012 and May 2015. Disparities by gender identity were found, with female to male adolescents reporting the highest rate (50.8%), followed by</p>

<p><a href="https://publications.aap.org/pediatrics/article-abstract/142/4/e20174218/76767/Transgender-Adolescent-Suicide-Behavior?redirectedFrom=fulltext">https://publications.aap.org/pediatrics/article-abstract/142/4/e20174218/76767/Transgender-Adolescent-Suicide-Behavior?redirectedFrom=fulltext</a></p>	<p>adolescents who identified as not exclusively male or female (41.8%), male to female adolescents (29.9%), questioning adolescents (27.9%), female adolescents (17.6%), and male adolescents (9.8%).</p>
<p>Perceptions of Sex, Gender, and Puberty Suppression: A Qualitative Analysis of Transgender Youth        Vrouenraets, L.J., Fredriks, A.M., Hannema, S.E., Cohen-Kettenis, P.T., de Vries, M.C. (2016)  <a href="https://pubmed.ncbi.nlm.nih.gov/27251640/">https://pubmed.ncbi.nlm.nih.gov/27251640/</a></p>	<p>Interviews with 13 transgender adolescents (12 receiving puberty suppressing hormones) explicating the considerations of gender dysphoric adolescents in the Netherlands concerning the use of puberty suppression and exploring whether the considerations of gender dysphoric adolescents differ from those of professionals working in treatment teams. From the interviews four themes emerged: (1) the difficulty of determining what is an appropriate lower age limit for starting puberty suppression; (2) the lack of data on the long-term effects of puberty suppression; (3) the role of the social context, for which there were two subthemes: (a) increased media attention, on television and on the Internet; and (b) an imposed stereotype; and (4) compared to clinicians, adolescents were often more cautious in their treatment views.</p>
<p>Puberty and puberty blockers        Healthtalk (2022)  <a href="https://healthtalk.org/Experiences-of-trans-and-gender-diverse-young-people/Trans-and-gender-diverse-young-peoples-experiences-of-puberty-and-puberty-blockers">https://healthtalk.org/Experiences-of-trans-and-gender-diverse-young-people/Trans-and-gender-diverse-young-peoples-experiences-of-puberty-and-puberty-blockers</a></p>	<p>Interviews with 50 trans and gender diverse young people in England, Wales and Scotland describing their experience of puberty blockers, or the impact puberty blockers would have had on their lives if they had been able to access them at puberty.</p>
<p>Chronic psychosocial stress and experimental pubertal delay affect socioemotional behavior and amygdala functional connectivity in adolescent female rhesus macaques        Pincus, M., Godfrey, J.R., Feczko, E., Earl, E., Miranda-Dominguez, O., Fair, D.,</p>	<p>Investigating how the timing of puberty interacts with stress in the female adolescent brain. The study used female monkeys: comparing those that experienced puberty spontaneously (n=34) with a pubertal delay (n=36). They examined the effects of stress and experimental pubertal delay on socioemotional behaviour and amygdala connectivity at 43–46 months, after all animals had begun puberty. Social status and pubertal delay did not interact - late onset of puberty did not exacerbate subordination stress. In the brain, however,</p>

<p>Wilson, M.E., Sanchez, M.M., Kelly, C. (2021)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/33647571/">https://pubmed.ncbi.nlm.nih.gov/33647571/</a></p>	<p>delayed puberty and subordination stress had separable effects, suggesting that the overlapping socioemotional outcomes may be mediated by distinct neuroplastic mechanisms. To gain further insights, additional longitudinal studies are required.</p>
<p>Treatment of Central Precocious Puberty</p> <p>Eugster, E. (2019)</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6486823/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6486823/</a></p>	<p>Literature review discussing issues pertaining to treating children with central precocious puberty (CPP) with long-acting analogs of GnRH (GnRHAs). GnRHAs are described as having “an enviable track record of safety and efficacy” and that while “bone mineral density typically [...] progressively decreases during GnRHa treatment, follow-up of patients several years after cessation of therapy reveals bone mineral accrual to be within the normal range compared with population norms.” It is also noted that there is less safety information for newer extended-release GnRHa formulations than for historically used preparations, though “the efficacy and safety of longer-acting and sustained-release forms of GnRHAs is not expected to [change]”.</p>
<p>Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer.</p> <p>Keating, N.L., O’Malley, A.J., Smith, M.R. (2006)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/16983113/">https://pubmed.ncbi.nlm.nih.gov/16983113/</a></p>	<p>Observational study of 73,196 people aged 66 years or older who were diagnosed with prostate cancer assessing whether treatment with GnRH agonists or orchiectomy was associated with diabetes, coronary heart disease, myocardial infarction, and sudden cardiac death. More than one third of men received a GnRH agonist during follow-up. GnRH agonist use was associated with increased risk of incident diabetes, coronary heart disease, myocardial infarction and sudden cardiac death.</p>
<p>Puberty-blocking hormonal therapy for adolescents with gender identity disorder: A descriptive clinical study</p> <p>Zucker, K. J., Bradley, S. J., Owen-Anderson, A., Singh, D., Blanchard, R., Bain, J. (2010)</p> <p><a href="https://www.tandfonline.com/doi/abs/10.1080/19359705.2011.530574">https://www.tandfonline.com/doi/abs/10.1080/19359705.2011.530574</a></p>	<p>Study of 109 adolescents with GID examining whether demographic, behaviour problem, and psychosexual measures correlated with the clinical decision to recommend, or not recommend, puberty-blocking hormonal therapy.</p>
<p>Treatment with a luteinizing hormone-releasing hormone agonist in adolescents</p>	<p>Study of fifty short adolescents with low predicted adult height who received either a luteinising hormone-releasing hormone (LHRH)</p>

<p>with short stature</p> <p>Yanovski, J.A., Rose, S.R., Municchi, G., Pescovitz, O.H., Hill, S.C., Cassorla, F.G., Cutler Jr, G.B. (2003)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/12621135/">https://pubmed.ncbi.nlm.nih.gov/12621135/</a></p>	<p>agonist (26 subjects) or placebo (24 subjects). Forty-seven of the fifty were followed until they attained adult height and those who were treated with an LHRH agonist were found to attain significantly greater adult height than those who received a placebo, but also to experience substantially decreased bone mineral density. Treatment with an LHRH agonist was therefore not recommended to augment height in adolescents with normally timed puberty.</p>
<p>Perceptions on the function of puberty suppression of transgender adolescents who continued or discontinued treatment, their parents, and clinicians</p> <p>Vrouenraets, L.J., de Vries, M.C., Hein, I.M., Arnoldussen, M., Hannema, S.E., de Vries, A.L. (2022)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/36324881/">https://pubmed.ncbi.nlm.nih.gov/36324881/</a></p>	<p>Study using interviews with eight transgender adolescents who proceeded with gender affirming medical treatment (GAMT) after puberty suppression (PS), six adolescents who discontinued PS, 12 parents, and focus groups with ten clinicians.</p>
<p>Efficacy and Safety of Gonadotropin-Releasing Hormone Agonist Treatment to Suppress Puberty in Gender Dysphoric Adolescents</p> <p>Schagen, S.E., Cohen-Kettenis, P.T., Delemarre-van de Waal, H.A., Hannema, S.E. (2016)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/27318023/">https://pubmed.ncbi.nlm.nih.gov/27318023/</a></p>	<p>Studying the efficacy and safety of puberty blocking hormones. 49 male-to-female and 67 female-to-male gender dysphoric adolescents treated with Triptorelin (a type of GnRH) were included in the analysis. A physical examination took place every 3 months and blood samples were drawn at 0, 3, and 6 months and then every 6 months. No sustained abnormalities of liver enzymes or creatinine were encountered. Alkaline phosphatase decreased, probably related to a slower growth velocity, because height standard deviation (SD) score decreased in boys and girls. Lean body mass percentage significantly decreased during the first year of treatment in girls and boys, whereas fat percentage significantly increased. Conclusion: Triptorelin effectively suppresses puberty in gender dysphoric adolescents. These data suggest routine monitoring of gonadotropins, sex steroids, creatinine, and liver function is not necessary during treatment with triptorelin. Further studies should evaluate the extent to which changes in height SD score and body composition that occur during GnRHa treatment can be reversed during subsequent cross-sex hormone treatment.</p>

<p>Trans YP evidence and resources - looking into the effects of puberty blockers</p> <p>Summary of evidence and resources relating to the effects of puberty blockers on transgender youth.</p> <p>Scottish government document (2017)</p> <p><a href="https://www.gov.scot/binaries/content/documents/govscot/publications/foi-eir-release/2020/01/foi-201900010673/documents/foi-201900010673---document-3---puberty-blockers-and-trans-yp---april-2017/foi-201900010673---document-3---puberty-blockers-and-trans-yp---april-2017/govscot%3Adocument/FOI-201900010673%2B-%2BDocument%2B3%2B-%2B%2B%2Bpuberty%2Bblockers%2B%2B-%2B%2B%2BApril%2B2017.pdf">https://www.gov.scot/binaries/content/documents/govscot/publications/foi-eir-release/2020/01/foi-201900010673/documents/foi-201900010673---document-3---puberty-blockers-and-trans-yp---april-2017/foi-201900010673---document-3---puberty-blockers-and-trans-yp---april-2017/govscot%3Adocument/FOI-201900010673%2B-%2BDocument%2B3%2B-%2B%2B%2Bpuberty%2Bblockers%2B%2B-%2B%2B%2BApril%2B2017.pdf</a></p>	<p>Summary of evidence and resources relating to the effects of puberty blockers on transgender youth.</p>
<p>Reddit 2023 detransition survey</p> <p>DeTransIS (2023)</p> <p><a href="https://www.reddit.com/r/detrans/comments/11sfyvu/the_rdetrans_2023_screened_demographic_summary/">https://www.reddit.com/r/detrans/comments/11sfyvu/the_rdetrans_2023_screened_demographic_summary/</a></p>	<p>Survey of 207 'detransitioners' answering questions about their experience of gender dysphoria and their subsequent decision to cease social transition and/or cross-sex HRT and/or surgery and returned to living as their birth sex.</p>
<p>Trans Mental Health Study 2012</p> <p>McNeil, J., Bailey, L., Ellis, S., Morton, J., Regan, M. (2012)</p> <p><a href="https://www.scottishtrans.org/wp-content/uploads/2013/03/trans_mh_study.pdf">https://www.scottishtrans.org/wp-content/uploads/2013/03/trans_mh_study.pdf</a></p>	<p>Survey of 889 participants by the Scottish Transgender Alliance. Key related findings were: 70% of participants were more satisfied with their lives since transitioning and 2% were less satisfied; 85% were more satisfied with their body since undertaking hormone therapy and 2% were less satisfied; 74% felt that their mental health had improved as a result of transitioning, while the 5% who reported a decline in their mental health since transitioning felt that their issues were unrelated or 'not directly related' to the transition; 63% thought about or attempted suicide more before they transitioned and 3% thought about or attempted suicide more post-transition; and with regard to physical changes which they had undergone in relation to being trans, 86% had no regrets, 10% had minor regrets and 2% had major regrets.</p>

<p>'If they didn't support me, I most likely wouldn't be here': Transgender young people and their parents negotiating medical treatment in Australia</p> <p>Riggs, D. W., Bartholomaeus, C., Sansfaçon, A. P. (2019)</p> <p><a href="https://doi.org/10.1080/15532739.2019.1692751">https://doi.org/10.1080/15532739.2019.1692751</a></p>	<p>Ten qualitative interviews with Australian transgender young people (aged 11–17) and their parents with regard to medical treatment in two Australian states. Themes developed focused on the importance of strong supportive parent-child relationships, the meaning of and access to hormone blockers, and the meaning of and access to hormones. The paper concludes by discussing the implications of the findings for clinical services, particularly in relation to supporting parents to be affirming of a transgender child, the need to prepare transgender young people and their parents for the passage of time in regard to medical treatment, and the need to focus on expectations in regard to sense of self in relation to medical treatment.</p>
<p>Risk of pseudotumor cerebri added to labelling for gonadotropin-releasing hormone agonists</p> <p>US Food and Drug Administration (2022)</p> <p><a href="https://www.fda.gov/media/159663/download">https://www.fda.gov/media/159663/download</a></p>	<p>The Food and Drug Administration has added a warning about the risk of pseudotumour cerebri (occurs when too much cerebrospinal fluid accumulates in your skull and creates pressure, causing symptoms such as headaches and blurred vision) to the labelling for GnRHa. Six cases were identified that supported a plausible association between GnRH agonist use and pseudotumour cerebri.</p>
<p>Is puberty delaying treatment 'experimental treatment'?</p> <p>Giordano, S., Holm, S. (2020)</p> <p><a href="https://www.tandfonline.com/doi/full/10.1080/26895269.2020.1747768">https://www.tandfonline.com/doi/full/10.1080/26895269.2020.1747768</a></p>	<p>Study investigating whether puberty delaying treatment is experimental. It reviews published evidence and concludes that the international clinical community has found a sensible point of balance: GnRHa can be prescribed to adolescents who experience strong and distressing dysphoria. GnRHa is not usually recommended for prepubertal children, when there is still significant uncertainty around the future gender identity development trajectory. The reaction to pubertal development will be part of the clinical assessment. In this way, most likely GnRHa will only be given to those who most likely will choose to continue to transition, but should the patient change their mind, then no permanent changes will have been affected (whereas, should an untreated person transition, permanent changes of pubertal development will only be partially reversible surgically). Parents, clinicians and significant others should continue to be open to the idea that the gender identity development of an adolescent might fluctuate even after puberty and therefore that the provision of gender affirming medical treatment is a separate decision from the earlier provision of puberty delaying treatment.</p>



<p>Impact of gender-affirming care bans on transgender and gender diverse youth: Parental figures' perspective.</p> <p>Matsuno, E. (2022)</p> <p><a href="https://psycnet.apa.org/record/2022-47098-001">https://psycnet.apa.org/record/2022-47098-001</a></p>	<p>Qualitative study exploring parents' perceptions of how bans on gender affirming care affect their TGD child and advice for legislators/policymakers regarding the impact on the well-being of TGD youth. Responses to an online survey with 134 participants were analysed. Thematic analysis revealed five themes regarding the impact that these anti-transgender laws and bills have on TGD youth, including (a) depression and suicidal ideation/risk of suicide, (b) anxiety, (c) increased gender dysphoria, (d) decreased safety and increased stigma, and (e) lack of access to medical care. Parental figures also provided direct feedback to legislators/policy makers regarding the impact of these laws and bills on the well-being of TGD youth, including (a) transgender youth health is not a political issue, (b) decriminalise gender affirming medical care, (c) decrease discrimination and violence against transgender people, and (d) become educated on transgender health-care issues.</p>
<p>Experiences of Puberty and Puberty Blockers: Insights From Trans Children, Trans Adolescents, and Their Parents</p> <p>Horton, C. (2022)</p> <p><a href="https://doi.org/10.1177/07435584221100591">https://doi.org/10.1177/07435584221100591</a></p>	<p>Study exploring experiences of transgender children and their families, understanding experiences relating to puberty and puberty blocking medication. Data were drawn from 30 parents of 40 trans children and adolescents. Qualitative interviews covered aspects of family life, healthcare, and education, as well as experiences of puberty, and of accessing, or trying to access, puberty blockers. Three major themes emerged, relating to pre-pubertal anxiety; difficulties accessing blockers; and, for a minority who were on blockers, experiences of relief and frustration. These accounts from adolescents and parents align with the perspectives of a number of clinicians who have written on the potential harms of inflexible protocols that inhibit options for gender-congruent peer-concordant puberty</p>
<p>The Amsterdam Cohort of Gender Dysphoria Study (1972–2015): Trends in Prevalence, Treatment, and Regrets</p> <p>Wiepjes, C.M., Nota, N.M., de Blok, C.J.M., Klaver, M., de Vries, A.L.C., Wensing-Kruger, S.A., de Jongh, R.T., Bouman, M.B., Steensma, T.D., Cohen-Kettenis, P., Gooren, L.J.G., Kreukels, B.P.C., den Heijer, M. (2018)</p>	<p>Study examining the current prevalence of gender dysphoria, how frequently gender-affirming treatments are performed, and the number of people experiencing regret of this treatment. The records of 6,793 people who visited a Dutch gender identity clinic from 1972 through 2015 were assessed. The number of people assessed per year increased 20-fold from 34 in 1980 to 686 in 2015. The percentage of people who started HT within 5 years after the 1st visit decreased over time, with almost 90% in 1980 to 65% in 2010. The percentage of people who underwent gonadectomy within 5 years after starting HT remained stable over time . Only 0.6% of trans women and 0.3% of</p>

<p><a href="https://doi.org/10.1016/j.jsxm.2018.01.016">https://doi.org/10.1016/j.jsxm.2018.01.016</a></p>	<p>trans men who underwent gonadectomy were identified as experiencing regret.</p>
<p>Body Dissatisfaction and Mental Health Outcomes of Youth on Gender-Affirming Hormone Therapy</p> <p>Kuper, L.E., Stewart, S., Preston, S., Lau, M., Lopez, X. (2020)</p> <p><a href="https://doi.org/10.1542/peds.2019-3006">https://doi.org/10.1542/peds.2019-3006</a></p>	<p>Study examining body dissatisfaction and mental health of youth taking gender-affirming hormones (including puberty suppression). 148 participants (n=25 puberty suppression only; n=123 feminising or masculinising hormone therapy) completed surveys assessing body dissatisfaction, depression and anxiety. Info on suicidal ideation, suicide attempt, and NSSI was collected at initial presentation to the clinic and at follow-up. One year of receiving gender-affirming hormone therapy resulted in large reductions in youth body dissatisfaction and modest improvements in mental health. No demographic or treatment-related factors were associated with change over time.</p>
<p>Bone Development in Transgender Adolescents Treated With GnRH Analogues and Subsequent Gender-Affirming Hormones</p> <p>Sebastian, E.E., Schagen, F.M., Wouters, P.T., Cohen-Kettenis, P.T., Gooren, L.J., Hannema, S.E. (2020)</p> <p><a href="https://academic.oup.com/jcem/article/105/12/e4252/5903559?login=false">https://academic.oup.com/jcem/article/105/12/e4252/5903559?login=false</a></p>	<p>Study investigating bone mass development in adolescents with gender dysphoria treated with gonadotropin-releasing hormone analogues (GnRHa), subsequently combined with gender-affirming hormones. It enlisted 51 transgirls and 70 transboys receiving GnRHa and 36 transgirls and 42 transboys receiving GnRHa and gender-affirming hormones, subdivided into early- and late-pubertal groups. Bone Mass Apparent Density z-scores decreased during GnRHa treatment and increased during gender-affirming hormone treatment. Transboys had normal z-scores at baseline and at the end of the study. However, transgirls had relatively low z-scores, both at baseline and after 3 years of oestrogen treatment, but as z-scores were already lower at baseline, this may be due to other factors than the endocrine treatment, such as lifestyle factors. It is currently unclear whether this results in adverse outcomes, such as increased fracture risk, in transgirls as they grow older.</p>
<p>Association of Gonadotropin-Releasing Hormone Analogue Use With Subsequent Use of Gender-Affirming Hormones Among Transgender Adolescents</p> <p>Nos, A.L., Klein, D.A., Adirim, T.A., et al. (2022)</p>	<p>Study investigating the association between GnRH analogue and the increased subsequent use of gender affirming hormones. Using a sample of 434 adolescents, and a retrospective cohort study design they found no significant association. These findings suggest that clinicians can offer gonadotropin-releasing hormone analogues to transgender and gender-diverse adolescents during pubertal development for mental health and cosmetic benefits without an increased likelihood of subsequent use of gender-affirming hormones.</p>

<p><a href="https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2798002">https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2798002</a></p>	
<p>Association of Gender-Affirming Hormone Therapy With Depression, Thoughts of Suicide, and Attempted Suicide Among Transgender and Nonbinary Youth.</p> <p>Green, A.E., DeChants, J.P., Price, M.N., Davis, C.K. (2021)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/34920935/">https://pubmed.ncbi.nlm.nih.gov/34920935/</a></p>	<p>Study examining associations among access to Gender Affirming Hormone Therapy with depression, thoughts of suicide, and attempted suicide among transgender and non-binary youth. Data were collected as part of a survey of 34,759 lesbian, gay, bisexual, transgender, queer, and questioning youth aged 13-24, including 11,914 transgender or non-binary youth. Adjusted logistic regression assessed whether receipt of Gender Affirming Hormone Therapy (GAHT) was associated with lower levels of depression, thoughts of suicide, and attempted suicide among those who wanted to receive GAHT.</p> <p>Half of transgender and non-binary youth said they were not using GAHT but would like to, 36% were not interested in receiving GAHT, and 14% were receiving GAHT. Parent support for their child's gender identity had a strong relationship with receipt of GAHT, with nearly 80% of those who received GAHT reporting they had at least one parent who supported their gender identity. Use of GAHT was associated with lower odds of recent depression and seriously considering suicide compared to those who wanted GAHT but did not receive it. Findings support a relationship between access to GAHT and lower rates of depression and suicidality among transgender and non-binary youth.</p>
<p>Psychological Support, Puberty Suppression, and Psychosocial Functioning in Adolescents with Gender Dysphoria</p> <p>Costa, R., Dunsford, M., Skagerberg, E., Holt, V., Carmichael, P., Colizzi, M. (2015)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/26556015/">https://pubmed.ncbi.nlm.nih.gov/26556015/</a></p>	<p>Study assessing 201 GD adolescents' global functioning after 6 months and 12 months of psychological support and puberty suppression. Results from this study indicate that psychological support is associated with a better psychosocial functioning in GD adolescents, especially if presenting psychological/psychiatric problems. Moreover, puberty suppression was associated with a further improvement in global functioning. Finally, global functioning improved steadily over time in GD adolescents receiving both psychological support and GnRHa.</p>
<p>Effect of Concurrent Gonadotropin-Releasing Hormone Agonist Treatment on Dose and Side Effects of Gender-Affirming Hormone Therapy in</p>	<p>Study assessing data from 83 patients to establish whether the use of GnRHa effects the dose and side effects of gender affirming hormones; GnRHa use was correlated with lower doses of gender-affirming hormones at the final point of data collection, suggesting that</p>

<p>Adolescent Transgender Patients</p> <p>Jensen, R. K., Jensen, J. K., Simons, L. K., Chen, D., Rosoklija, I., Finlayson, C. A. (2019)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/31663037/">https://pubmed.ncbi.nlm.nih.gov/31663037/</a></p>	<p>concurrent GnRHa may decrease doses of hormones needed to achieve desired physiological changes. This is significant in relation to findings from other studies around the concerning side effects of gender affirming hormones such as elevated liver enzymes (which if left unaddressed can lead to organ damage). The current study suggests that the less hormone dose is required, the less severe the side effects, therefore showing a potential benefit of puberty suppressing hormones. It should be noted that though these data support the use of GnRHa in adjunct to gender-affirming hormones, GnRHa are not without their own side effects, (hot flashes, mood swings, and weight gain). Though not inherently dangerous to the patient, such side effects can cause substantial discomfort and should be included in risk-benefit discussions with patients.</p>
<p>Psychological Functioning in Transgender Adolescents Before and After Gender-Affirmative Care Compared With Cisgender General Population Peers</p> <p>van der Miesen, A.I.R., Steensma, T.D., de Vries, A.L.C., Bos, H., Popma, A. (2020)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/32273193/">https://pubmed.ncbi.nlm.nih.gov/32273193/</a></p>	<p>Study comparing transgender adolescents before and after gender-affirmative care with a sample of cisgender adolescents on psychological well-being and aimed to investigate the possible effect of transgender care involving puberty suppression. Emotional and behavioural problems were assessed by the Youth Self-Report in a sample of 272 adolescents who did not yet receive any affirmative medical treatment and compared with 178 transgender adolescents receiving affirmative care consisting of puberty suppression and compared with 651 high school cisgender adolescents from the general population. Transgender adolescents showed poorer psychological well-being before treatment but show similar or better psychological functioning compared with cisgender peers from the general population after the start of specialised transgender care involving puberty suppression.</p>
<p>Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study</p> <p>de Vries ALC. (2020)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/20646177/">https://pubmed.ncbi.nlm.nih.gov/20646177/</a></p>	<p>This study compares psychological functioning and gender dysphoria before and after puberty suppression in 70 gender dysphoric adolescents. Behavioural and emotional problems (Child Behaviour Checklist and the Youth-Self Report), depressive symptoms (Beck Depression Inventory), anxiety and anger (the Spielberger Trait Anxiety and Anger Scales), general functioning (the clinician's rated Children's Global Assessment Scale), gender dysphoria (the Utrecht Gender Dysphoria Scale), and body satisfaction (the Body Image Scale) were assessed.</p>

	<p>Behavioural and emotional problems and depressive symptoms decreased, while general functioning improved significantly during puberty suppression. Feelings of anxiety and anger did not change. Gender dysphoria and body satisfaction did not change. No adolescent withdrew from puberty suppression, and all started cross-sex hormone treatment, the first step of actual gender reassignment.</p>
<p>Sexual Experiences of Young Transgender Persons During and After Gender-Affirmative Treatment</p> <p>Bungener, S.L., de Vries, A.L.C., Popma, A., Steensma, T.D. (2020)</p> <p><a href="https://doi.org/10.1542/peds.2019-1411">https://doi.org/10.1542/peds.2019-1411</a></p>	<p>Study describing sexual and romantic development during and after gender affirming treatment. The participants were 113 transgender adolescents treated with puberty suppression, affirmative hormones, and affirmative surgery. A questionnaire on sexual experiences, romantic experiences, and subjective sexual experiences was administered and compared to the experiences of a same-aged sample. One year post surgery, young transgender adults reported a significant increase in experiences with all types of sexual activities. In comparison with the general population, young transgender adults were less experienced with all types of sexual activities. Therefore, treatment may provide young transgender adults with the opportunity to increase their romantic and sexual experiences.</p>
<p>Psychosocial Characteristics of Transgender Youth Seeking Gender-Affirming Medical Treatment: Baseline Findings From the Trans Youth Care Study - Journal of Adolescent Health</p> <p>Chen, D., Abrams, M., Clark, L., Ehrensaft, D., Tishelman, A.C., Chan, Y.M., Garofalo, R., Olson-Kennedy, J., Rosenthal, S.M., Hidalgo, M.A. (2021)</p> <p><a href="https://doi.org/10.1016/j.jadohealth.2020.07.033">https://doi.org/10.1016/j.jadohealth.2020.07.033</a></p>	<p>Study examining baseline mental health and well-being among GD youth taking GnRHa treatment (n=95) and GAH treatment (n=316). Elevated depression symptoms were endorsed by 28.6% of GnRHa vs 51.3% of GAH cohort, and 22.1% vs 57.3% endorsed clinically significant anxiety. 23.6% vs 66.6% endorsed lifetime suicidal ideation, with 7.9% vs 24.6% reporting a past suicide attempt. GnRHa cohort youth recognised their gender as different from their designated sex at birth, on average, at an age approximately four years younger than GAH cohort youth and were able to access gender-affirming medical treatment earlier in development. It is possible that early access to medical treatment, which prevents an unwanted puberty in the GnRHa cohort, alleviates psychological distress and accounts for the better picture of mental health and well-being in the GnRHa cohort compared to the GAH cohort.</p>
<p>Pubertal Suppression for Transgender Youth and Risk of Suicidal Ideation</p> <p>Turban, J.L., King, D., Kobe, J., Carswell, J.M., Keuroghlian, A.S. (2022)</p>	<p>Study examining associations between access to pubertal suppression during adolescence and adult mental health outcomes. A sample of 20 619 transgender adults were enlisted; multivariable logistic regression was the method used to examine associations between access to pubertal suppression and adult mental health outcomes, including</p>

<p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7073269/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7073269/</a></p>	<p>multiple measures of suicidality. Of the sample, 16.9% reported that they ever wanted pubertal suppression as part of their gender-related care. Of them, 2.5% received pubertal suppression. After adjustment for demographic variables and level of family support for gender identity, those who received treatment with pubertal suppression, when compared with those who wanted pubertal suppression but did not receive it, had lower odds of lifetime suicidal ideation</p>
<p>Australian children and adolescents with gender dysphoria: Clinical presentations and challenges experienced by a multidisciplinary team and gender service</p> <p>Kozłowska, K., McClure, G., Chudleigh, C., Maguire, A.M., Gessler, D., Scher, S., Ambler, G.R. (2021)</p> <p><a href="https://journals.sagepub.com/doi/full/10.1177/26344041211010777">https://journals.sagepub.com/doi/full/10.1177/26344041211010777</a></p>	<p>Study examining the clinical characteristics of 79 children with gender dysphoria at a gender service in Australia, and the challenges faced by the clinicians. The clinical characteristics included a slightly higher number of biological females to males, high levels of distress, suicidal ideation, self-harm and suicide attempts and high rates of comorbid mental health disorders: anxiety, depression behavioural disorders and autism. Key challenges faced by the clinicians included the following: the effects of increasingly dominant, polarised discourses on daily clinical practice; issues pertaining to patient and clinician safety (including pressures to abandon the holistic [biopsychosocial] model); the difficulties of untangling gender dysphoria from comorbid factors such as anxiety, depression, and sexual abuse; and the factual uncertainties present in the currently available literature on longitudinal outcomes. Results suggest the need to bring into play a biopsychosocial, trauma-informed model of mental health care for children presenting with gender dysphoria. Ongoing therapeutic work needs to address unresolved trauma and loss, the maintenance of subjective well-being, and the development of the self.</p>
<p>Continuation of gender-affirming hormones in transgender people starting puberty suppression in adolescence: a cohort study in the Netherlands</p> <p>van der Loos, M.A.T.C., Hannema, S.E., Klink, D.T., den Heijer, M., Wiepjes, C.M. (2022)</p> <p><a href="https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00254-1/fulltext">https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00254-1/fulltext</a></p>	<p>Study examining the proportion of people who continued gender-affirming hormone treatment at follow-up after having started puberty suppression and gender-affirming hormone treatment in adolescence. 720 people were included, of whom, 31% were assigned male at birth and 69% were assigned female at birth. Most participants who started gender-affirming hormones in adolescence continued this treatment into adulthood. The continuation of treatment is considered reassuring by the authors considering the worries that people who started treatment in adolescence might discontinue gender-affirming treatment.</p>

<p>Cognitive, Emotional, and Psychosocial Functioning of Girls Treated with Pharmacological Puberty Blockage for Idiopathic Central Precocious Puberty</p> <p>Wojniusz, S., Callens, N., †, Sütterlin, S., Andersson, S., De Schepper, J., Gies, I., Vanbesien, J., De Waele, K., Van Aken, S., Craen, M., Vögele, C., Cools, M., Haraldsen, I. R. (2016)</p> <p><a href="https://doi.org/https://dx.doi.org/10.3389/fpsyg.2016.01053">https://doi.org/https://dx.doi.org/10.3389/fpsyg.2016.01053</a></p>	<p>Study exploring differences in cognitive function, behaviour, emotional reactivity, and psychosocial problems between GnRHa treated CPP girls and age-matched controls. Fifteen girls with precocious puberty treated with GnRHa and 15 age-matched controls were assessed, both groups showed very similar scores with regard to cognitive performance, behavioural and psychosocial problems. Compared to controls, treated girls displayed significantly higher emotional reactivity.</p>
<p>“I Didn’t Want Him to Disappear” Parental Decision-Making on Access to Puberty Blockers for Trans Early Adolescents.</p> <p>Horton, C. (2022)</p> <p><a href="https://journals.sagepub.com/doi/10.1177/02724316221107076">https://journals.sagepub.com/doi/10.1177/02724316221107076</a></p>	<p>Study exploring parental views on puberty blockers, aiming to understand how supportive parents of socially transitioned trans children view puberty blockers, how they consider risks and benefits, and how they approach decision-making. Semi structured interviews were conducted with 30 parents, thematic analysis produced three key themes relating to the purpose of puberty blockers, parental perspectives on consent, and parental approaches to decision making without certainty. Parents viewed puberty blockers as critical to protection of their children’s mental health and quality of life.</p>
<p>Peri-pubertal gonadotropin-releasing hormone analog treatment affects hippocampus gene expression without changing spatial orientation in young sheep</p> <p>Nuruddin, S., Wojniusz, S., Ropstad, E., Krogenæs, A., Evans, N.P., Robinson, J.E., Solbakk, A.K., Amiry-Moghaddam, M., Haraldsen, I.R. (2013)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/23266521/">https://pubmed.ncbi.nlm.nih.gov/23266521/</a></p>	<p>Study exploring the effects of GnRHa on hippocampal gene expression and spatial orientation in sheep. The study was conducted with 30 same-sex twin lambs, half of which were treated with GnRHa every 4th week, beginning before puberty, until 50 weeks of age. Animals were tested in their spatial orientation ability at 48 weeks of age. A quantitative analysis was conducted to examine the effects of treatment on the expression of genes associated with synaptic plasticity and endocrine signalling. They found significant changes, within the hippocampus, of levels of expression of mRNA transcripts known to be involved in endocrine signalling and synaptic plasticity. The treatment had no significant effect on spatial orientation. These results have to be taken into consideration when long-term peripubertal GnRHa treatment is used in children.</p>
<p>Impact of Hormone Treatment on Psychosocial Functioning in Gender-</p>	<p>Study of a cohort of 38 young people before treatment, 1 year into GnRHa, and 1 year into GAH treatment to understand psychological</p>

<p>Diverse Young People</p> <p>Lavender, R., Shaw, S., Maninger, J.K., Butler, G., Carruthers, P., Carmichael, P., Masic, U. (2023)</p> <p><a href="https://doi.org/10.1089/lgbt.2022.0201">https://doi.org/10.1089/lgbt.2022.0201</a></p>	<p>and behavioural impacts over time. Young people completed the Youth Self Report (YSR), the Body Image Scale, and the Utrecht Gender Dysphoria Scale, while caregivers completed the Child Behaviour Checklist (CBCL) and the Social Responsiveness Scale-2 at all time points. They found that Dissatisfaction with primary sexual characteristics, gender dysphoria, and social motivation improved significantly over time. Self-harm and suicidality also showed a general decrease. Caregivers reported a significant reduction in internalising behaviours on the CBCL after GnRHa.</p>
<p>Short-term outcomes of pubertal suppression in a selected cohort of 12 to 15 year old young people with persistent gender dysphoria in the UK</p> <p>Carmichael, P., Butler, G., Masic, U., Cole, T.J., De Stavola, B.L., Davidson, S., Skageberg, E.M., Khadr, S., Viner, R.M. (2021)</p> <p><a href="https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243894">https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243894</a></p>	<p>Study investigating the short-term outcomes of puberty suppression. It was an uncontrolled prospective observational study of GnRHa as monotherapy in 44 youths with persistent and severe GD. Pre-specified analyses were limited to key outcomes: bone mineral content/density and psychological functioning (measured using scans, scales questionnaires, parent/self-reports and interviews) BMD increased with treatment in the lumbar spine and was stable at the hip, and BMD z-score fell consistent with delay of puberty. There were no psychological function changes, Most participants reported positive or a mixture of positive and negative life changes on GnRHa. Anticipated adverse events (e.g. side effects) were common. At the end of the study one ceased GnRHa and 43 elected to start cross-sex hormones. Overall patient experience of changes on GnRHa treatment was concluded as positive. but larger and longer-term prospective studies using a range of designs are needed to more fully quantify the benefits and harms of pubertal suppression in GD.</p>
<p>Retraction Note: Rapid Onset Gender Dysphoria: Parent Reports on 1655 Possible Cases.</p> <p>Diaz, S., Bailey, J.M. (2023)</p> <p><a href="https://link.springer.com/article/10.1007/s10508-023-02576-9">https://link.springer.com/article/10.1007/s10508-023-02576-9</a></p>	<p>Study investigating the explanation for the increase in GD as being a socially contagious syndrome: Rapid Onset Gender Dysphoria (ROGD). It uses results from a survey of parents who contacted the website ParentsofROGDKids.com because they believed their child had ROGD. Results focused on 1655 children whose gender dysphoria reportedly began between ages 11 and 21 years. Pre-existing mental health issues were common, and youths with these issues were more likely than those without them to have socially and medically transitioned. Parents reported that they had often felt pressured by clinicians to affirm their child's new gender and support their transition. According to the parents, mental health deteriorated considerably after social transition.</p>



<p>Regret after Gender-affirmation Surgery: A Systematic Review and Meta-analysis of Prevalence</p> <p>Bustos, V.P., Bustos, S.S., Mascaro, A., et.al (2021)</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8099405/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8099405/</a></p>	<p>Study looking into regret rate of those having had gender affirming surgery. A systematic review and meta-analysis which included 27 studies / 7928 patients concluded that there is an extremely low prevalence of regret in transgender patients after GAS (less than 1%).</p> <p>The authors acknowledge that there is high subjectivity in the assessment of regret and lack of standardised questionnaires, which highlight the importance of developing validated questionnaires in this population.</p>
<p>Children and adolescents in the Amsterdam Cohort of Gender Dysphoria: trends in diagnostic- and treatment trajectories during the first 20 years of the Dutch Protocol</p> <p>van der Loos, M.A.T.C., Klink, D.T., Hannema, S.E., Bruinsma, S., Steensma, T.D., Kreukels, B.P.C., Cohen-Kettenis, P.T., de Vries, A.L.C., den Heijer, M., Wiepjes, C.M. (2023)</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/36763938/">https://pubmed.ncbi.nlm.nih.gov/36763938/</a></p>	<p>Study looking into trends in diagnosis treatment paths in children and adolescents who were referred for evaluation of gender dysphoria and/or treated following the Dutch Protocol. It is based on a retrospective cohort of 1766 children and adolescents in the Amsterdam Cohort of Gender Dysphoria. They found that a substantial number of adolescents did not start medical treatment. In the ones who did, risk for retransitioning was very low, providing ongoing support for medical interventions in comprehensively assessed gender diverse adolescents. The authors concluded that trajectories in diagnostic evaluation and medical treatment in children and adolescents referred for gender dysphoria are diverse. Initiating medical treatment and need for surgical procedures depends not only on personal characteristics but societal and legal factors as well.</p>
<p>Mental Health Outcomes in Transgender and Nonbinary Youths Receiving Gender-Affirming Care</p> <p>Tordoff, D.M., Wanta, J.W., Collin, A., Stepney, C., Inwards-Breland, D.J., Ahrens, K. (2022)</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8881768/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8881768/</a></p>	<p>Study of 104 trans and non-binary youths: 69 received PBs or GAHs or both, 35 received no treatment. The treatment route was associated with 60% lower odds of moderate or severe depression and 73% lower odds of suicidality but no significant change in anxiety over a 12-month follow-up. The study used a health questionnaire and an anxiety scale to assess changes.</p>
<p>Systematic Review: Puberty suppression with GnRH analogues in adolescents with gender incongruity</p>	<p>Study reviewing the treatment of gender incongruity with GnRHa analogues. 11 articles published between 2009 and 2019 which studied transgender adolescents treated with GnRHa were selected. It assessed psychosocial effects, bone health, body composition and</p>

<p>Ramos, G. G. F., Mengai, A. C. S., Daltro, C. A. T., Cutrim, P. T., Zlotnik, E., Beck, A. P. A. (2020)</p> <p><a href="https://link.springer.com/article/10.1007/s40618-020-01449-5">https://link.springer.com/article/10.1007/s40618-020-01449-5</a></p>	<p>metabolism, and therapy persistence. The use of GnRHa seems to be well tolerated by the studied population. When started in pubertal transition, it was associated with a more distinct resemblance to body shape than to the affirmed sex. In addition to preventing the irreversible phenotypic changes that occur in cross-hormonal therapy, the use of GnRHa can equally contribute to the mental health of these adolescents. However, the authors also point out that long-term effects of hormone therapy on psychosocial health are unknown. GnRHa treatment delays bone maturation and gain in bone mineral density. GnRHa treatment in children with gender dysphoria should be considered experimental treatment of individual cases rather than standard procedure.</p>
<p>Low Bone Mineral Density in Early Pubertal Transgender/Gender Diverse Youth: Findings From the Trans Youth Care Study</p> <p>Janet Y. Lee, Courtney Finlayson, Johanna Olson-Kennedy, Robert Garofalo, Yee-Ming Chan, David V. Glidden, Stephen M. Rosenthal (2020)</p> <p><a href="https://doi.org/10.1210/jendso/bvaa065">https://doi.org/10.1210/jendso/bvaa065</a></p>	<p>To examine Bone Mineral Density (BMD) in early-pubertal transgender youth. 63 participants were studied, and BMD was found to be lower than reference standards This lower BMD may be explained, in part, by suboptimal calcium intake and decreased physical activity.</p>
<p>Factors Associated With Desistence and Persistence of Childhood Gender Dysphoria: A Quantitative Follow-Up Study</p> <p>Steensma, T.D., McGuire, J.K., Kreukels, B.P., Beekman, A.J., Cohen-Kettenis, P.T. (2013)</p> <p><a href="https://www.transgendertrend.com/wp-content/uploads/2017/10/Steensma-2013_desistance-rates.pdf">https://www.transgendertrend.com/wp-content/uploads/2017/10/Steensma-2013_desistance-rates.pdf</a></p>	<p>Study examining the factors associated with the persistence of childhood gender dysphoria (GD), and to assess the feelings of GD, body image, and sexual orientation in adolescence. The sample consisted of 127 adolescents (79 boys, 48 girls), who were referred for GD in childhood and followed up in adolescence. They examined childhood differences among persisters and desisters in demographics, psychological functioning, quality of peer relations and childhood GD, and adolescent reports of GD, body image, and sexual orientation. They examined contributions of childhood factors on the probability of persistence of GD into adolescence. They found a link between the intensity of GD in childhood and persistence of GD, as well as a higher probability of persistence among natal girls. Psychological functioning and the quality of peer relations did not predict the persistence of childhood GD. The support of children with GD may need to be</p>

	developed independently for natal boys and for girls.
Brain Maturation, Cognition and Voice Pattern in a Gender Dysphoria Case under Pubertal Suppression  Schneider, M. A., Spritzer, P. M., Soll, B. M. B., Fontanari, A. M. V., Carneiro, M., Tovar-Moll, F., Costa, A. B., da Silva, D. C., Schwarz, K., Anes, M., Tramontina, S., Lobato, M. I. R. (2017)  <a href="https://doi.org/10.3389/fnhum.2017.00528">https://doi.org/10.3389/fnhum.2017.00528</a>	Study of the effects of puberty suppression on the brain white matter (WM) during adolescence. WM Fractional anisotropy, voice and cognitive functions were assessed before and during the treatment. MRI scans of a pubertal transgender girl were acquired before, and after 22 and 28 months of hormonal suppression. Brain white matter fractional anisotropy remained unchanged in the GD girl during pubertal suppression with GnRHα for 28 months, which may be related to the reduced serum testosterone levels and/or to the patient's baseline low average cognitive performance. Global performance was slightly lower during pubertal suppression compared to baseline, predominantly due to a reduction in operational memory. Either a baseline of low average cognition or the hormonal status could play a role in cognitive performance during pubertal suppression. The voice pattern during the follow-up seemed to reflect testosterone levels under suppression by GnRHα treatment.

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[https://explore.bps.org.uk/binary/bpsworks/bf9d9fead1dfec7c/3acfadeebe810a324dde720ea7b34b6e87a80cad1de5471be0810935dac0415b/inf94\\_2021.pdf](https://explore.bps.org.uk/binary/bpsworks/bf9d9fead1dfec7c/3acfadeebe810a324dde720ea7b34b6e87a80cad1de5471be0810935dac0415b/inf94_2021.pdf)

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