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NHS England

Consultation report for the clinical policy on puberty suppressing hormones for children and adolescents who have gender incongruence / gender dysphoria

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Contents

Background

In September 2020, NHS England commissioned an independent and wide-ranging expert review of gender identity services for children and young people. The Independent Review, which will conclude by April 2024, is being led by Dr Hilary Cass, past president of the Royal College of Paediatrics and Child Health. It was established in response to a complex and diverse range of issues including:

1. **A significant and sharp rise in referrals**
   In 2021/22 there were over 5,000 referrals into the Gender Identity Development Service (GIDS) run by the Tavistock and Portman NHS Foundation Trust. This compares to just under 250 referrals in 2011/12.

2. **Marked changes in the types of patients being referred which are not well understood**
   There has been a dramatic change in the case-mix of referrals from predominantly natal males to predominantly natal females presenting with gender incongruence in early teen years. Additionally, a significant number of children are also presenting with neurodiversity and other mental health needs and risky behaviours which requires careful consideration and needs to be better understood.

3. **Scarce and inconclusive international evidence to support clinical decision making**
   This has led to a lack of clinical consensus and polarised opinion on what the best model of care for children and young people experiencing gender incongruence should be; and a lack of evidence to support families in making informed decisions about interventions that may have life-long consequences including Puberty Suppressing Hormones.

In February 2022, the Independent Review published an interim report which set out initial findings and advice. The report emphasised the need to move away from the current model of a sole provider and to establish regional services that work to a new clinical model that can better meet the holistic needs of a vulnerable group of children and young people. The report began to describe the need for these new services to work as networked centres that connected with other local services including children and young people's mental health services and primary care to support all of a patient's clinical needs.

The Independent Review's interim report also came to the following conclusions about the evidence relating to clinical approaches for children and young people with gender incongruence or gender dysphoria:

- The evidence is inconclusive both nationally and internationally
- Aspects of the available literature are open to interpretation in multiple ways, and there is a risk that some authors interpret their data from a particular ideological and/or theoretical standpoint
- Internationally as well as nationally, longer-term follow-up data on children and young people who have been seen by gender identity services is limited, including for those who have received endocrine interventions
- While there has been research on the short-term mental health outcomes and physical side effects of Puberty Suppressing Hormones for children and young people with gender incongruence / dysphoria, there is very limited research on the sexual, cognitive or broader developmental outcomes

In July 2022, the Independent Review offered further advice on the core components of the new clinical model. Dr Cass emphasised the importance of embedding research into the clinical practice of the new services given the substantial gaps that exist in the evidence base. The Review advised NHS England to give rapid consideration as to how it could establish '*the necessary research infrastructure to prospectively enrol young people being considered for hormone treatment into a formal research protocol with adequate follow up into adulthood, with a more immediate focus on the questions regarding puberty blockers'*.

You can read the advice in full here.

In response to this advice, NHS England announced plans to remove the use of Puberty Supressing Hormones as a routine treatment on the NHS pathway of care for gender incongruence / dysphoria due to significant uncertainties around risks, benefits and outcomes.

NHS England also described proposals to put in place a programme of work that would establish a clinical research framework that may provide access to Puberty Suppressing Hormones to some children and young people with gender incongruence / dysphoria, subject to the usual approvals.

How we consulted

The proposed clinical commissioning policy initially went out for two weeks of targeted stakeholder testing between 8 – 25th June 2023, supported by a draft Equality and Health Inequalities Impact Assessment (EHIA) and the report of the review of evidence on gonadotrophin releasing hormone analogues for children and adolescents with gender dysphoria undertaken by the National Institute for Health and Care Excellence (NICE). Comments were received from 23 individuals and organisations. NHS England did not make any changes to the proposed clinical commissioning policy as an outcome of stakeholder engagement but did make some changes to the draft EHIA.

A public consultation on the proposed clinical commissioning policy ran for 90 days on the NHS England consultation website from 3 August to 1 November 2023. The length of the consultation was determined through the recommendation of an independent Patient and Public Voice Assurance Group for Specialised Services. Alongside the proposed policy NHS England published various documents including the amended EHIA, a report on the outcome of the stakeholder testing process, and documents that described the evidence. The process of consultation generated 5,183 responses. NHS England thanks all those individuals and organisations who submitted responses.

NHS England has commissioned TONIC - an independent organisation specialising in public consultation, social research and evaluation - to conduct the analysis on all responses and report back on these findings. Their detailed analysis of the responses can be found here [link].

NHS England's responses to consultation, and consideration of the evidence

NHS England has carefully considered the independent report on the analysis of consultation responses.

The majority of respondents felt that additional evidence needed to be taken into account when developing the proposals (72%) and believed that the EHIA had failed to reflect the potential impact that might arise as a result of adoption of the proposal (82%).

Appendix A - NHS England's responses to the consultation submissions.

Appendix B - a summary of how NHS England sought to identify, and consider, other relevant evidence throughout the process of policy development.

Appendix C - detailed summary review of the evidence that was identified by respondents to consultation.

Appendix D – detailed summary review of the relevant evidence relied upon by the World Professional Association for Transgender Health.

What has NHS England decided?

As an outcome of public consultation NHS England has decided that:

- The NHS in England will not prescribe Puberty Suppressing Hormones to children and young people with gender incongruence / dysphoria, from 1 April 2024
- As a change to the proposed policy, Puberty Suppressing Hormones will not be available through an 'exceptional circumstances' route. Some stakeholders, including the new providers of gender incongruence services for children and young people, were concerned at how such a pathway could operate appropriately, effectively and equitably and NHS England has agreed with that view. Instead, as with all specialised services, a patient's clinician can make an application under NHS England's Individual Funding Request process. Under this process, the clinician making the request would need to explain why the patient's clinical circumstances are exceptional and show all available clinical evidence for why they believe the patient would benefit more from the treatment than other patients with the same condition. They would also need to demonstrate why a treatment that is not routinely commissioned by the NHS is an appropriate treatment option.
- Various amendments should be made to the EHIA (detailed in Appendix A)

How did NHS England make this decision?

NHS England has followed its established method for forming a clinical commissioning policy:

- In January 2024 the NHS England Clinical Panel for Specialised Services considered a report prepared by a public health specialist that explained why respondents to consultation had not identified any new or alternative evidence that would cause NHS England not to adopt the proposed policy
- In March 2024 NHS England's Clinical Priorities Advisory Group, which has an independent chair, considered NHS England's report on the outcome of consultation and the supporting documents, such as the EHIA that had been amended in response to consultation submissions and evidence report, and the views of the National Programme Board for Gender Dysphoria Services about the process that had been followed to form the policy. The Clinical Priorities Advisory

Group agreed for NHS England to recommend that the proposed policy be put to the NHS England National Commissioning Group for Specialised Services for agreement

- In March 2024 NHS England's National Commissioning Group for Specialised Services agreed the recommendations

What happens next?

The Gender Identity Development Service at the Tavistock and Portman NHS Foundation Trust closes on 31 March 2024. The new providers of Children and Young People's Gender Services will work to the new clinical commissioning policy from 1 April 2024.

Children and young people who are already receiving Puberty Suppressing Hormones through the NHS pathway, or who have been referred into an endocrine team commissioned by NHS England by 31 March 2024, will not be subject to the new policy. In these cases the relevant NHS paediatric endocrine team (at Leeds Teaching Hospital NHS Trust or University College London Hospitals NHS Foundation Trust) will continue to hold clinical responsibility for these patients. The intervention will continue to be administered / be initiated for these patients because there is an expectation of continued treatment, if that is the informed choice of the young person / parents of a child under 16 years, subject to the outcome of usual clinical review of the individual's existing individual care plan jointly between the individual's Lead Clinician and the young person / parents of a child under 16 years.

Clinical Study

NHS England's adoption of the new clinical commissioning policy is not contingent on the establishment of a clinical study but work is well underway to develop the framework for study design. A National Research Oversight Board for Children and Young People's Gender Services was established in 2023, chaired by Professor Sir Simon Wessely, a Past President of the Royal College of Psychiatrists, and Royal Society of Medicine. The National Research Oversight board includes representation from the Royal College of Paediatrics and Child Health, the National Institute for Health and Care Research, the Medical Research Council, other academic and clinical experts, and Dr Hilary Cass. In November 2023, Professor Emily Simonoff (Kings College London) was confirmed as the Chief Investigator who will lead on study design.

In order for the clinical study to become operational, it will need to pass the usual ethics and approvals process. The current planning assumption is that, should the approvals be granted, the study will begin to recruit eligible individuals in late 2024.

NHS England explained as part of the public consultation that unless and until a clinical study is established, no child or young person will have access to Puberty Suppressing Hormones for gender incongruence / dysphoria. The study design process will define access criteria into the study, which NHS England has said will initially be focused on children with early onset gender incongruence / dysphoria.

Appendix A: Responses to consultation submissions

Question 1: Has all the relevant evidence been taken into account?

Group A Respondents said…	NHS England response …
The experiences, views and outcomes of transgender people, patients, and their families had not been considered as evidence, as well as the views of experts in the field.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. The policy proposition has been formed following NHS England's established method for forming clinical commissioning policies. This method takes account of relevant, peer-reviewed, quality academic and clinical research – it does not take account of lived experiences.
The evidential review had not included enough studies and had strict inclusion criteria, which may have excluded other relevant, good quality studies.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).

Studies that rated PSH treatment positively had been ignored, possibly due to unfair bias.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).
There has not been an evidential review of the outcomes of transgender children and young people who had been denied PSH.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).
Guidance and advice from leading international bodies, such as World Professional Association for Transgender Health (WPATH), had been ignored.	NHS England has undertaken a detailed summary review of the relevant evidence relied upon by the WPATH in support of its position about prescribing Puberty Suppressing Hormones, as set out in its Standards of Care v8 (2023). The report on the outcome of the evidence review is in Appendix D. The conclusion of the evidence review is that the WPATH standards of care do not identify evidence about the risks, benefits and

	outcomes of Puberty Suppressing Hormones, including safety outcomes, contrary to the findings of the NICE evidence review. Although not a factor in NHS England's decision-making process, many international health systems and medical bodies are now moving to restrict the use of Puberty Suppressing Hormones as a response to gender incongruence / dysphoria because of the limited evidence base, including Canada, Sweden, Finland and France. Reflecting this trend, in January 2024 the World Health Organisation concluded that it was unable to advance any recommendations or guidance about gender affirming interventions for children and young people because '*the evidence base for children and adolescents is limited and variable regarding the longer-term outcomes of gender affirming care for children and adolescents*".
Evidence that PSH are used safely for other conditions (such as precocious puberty and prostate cancer) was not included.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B). The EHIA that supported the process of public consultation identified children receiving PSH as a response to Central Precocious Puberty (CPP) as an

	appropriate comparator group, and it described that the aetiology and epidemiology of CPP and treatment aims are quite different to that of gender incongruence. The EHIA describes how the evidence base to support use of PSH as a response to CPP is well formed.
The statement that children and young people treated with PSH do not show a statistically significant difference in mental health and psychosocial functioning misunderstands the intended results of PSH treatment.	The difficulties about describing the aims and intended results of Puberty Suppressing Hormones were addressed by Dr Cass in her letter to NHS England of 19 July 2022, in which she advised that urgent consideration be given to the establishment of the necessary research infrastructure for children and young people considering hormone treatment. In responding to the point made during consultation, it is helpful to set out the advice in some detail: "*As already highlighted in my interim report, the most significant knowledge gaps are in relation to treatment with puberty blockers, and the lack of clarity about whether the rationale for prescription is as an initial part of a transition pathway or as a 'pause' to allow more time for decision making.* *For those who will go on to have a stable binary trans identity, the ability to pass in later life is paramount, and many will decide that the trade-offs of medical treatment are a price that is fully justified by the ability to live confidently and comfortably in their identified gender.* *The widely understood challenge is in determining when a point of certainty about gender identity is reached in an adolescent who is in a state of developmental maturation, identity development and flux. It is the latter option*

	regarding a 'pause' for decision making about which we have the least information. The rationale for use of puberty blockers at Tanner Stage 2 of development was based on data that demonstrated that children, particularly birth registered boys who had early gender incongruence, were unlikely to desist once they reached early puberty; this rationale does not necessarily apply to later presenting young people, including the predominant referral group of birth-registered girls. *We do not fully understand the role of adolescent sex hormones in driving the development of both sexuality and gender identity through the early teen years, so by extension we cannot be sure about the impact of stopping these hormone surges on psychosexual and gender maturation. We therefore have no way of knowing whether, rather than buying time to make a decision, puberty blockers may disrupt that decision-making process*".

Group B Respondents said…	**NHS England response …**
The review does not highlight harm caused by PSH or the importance of going through puberty.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant

	evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).
It omits animal studies that have concluded that PSH cause harm.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).
The review omits experiential evidence from de-transitioners.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. The policy proposition has been formed following NHS England's established method for forming clinical commissioning policies. This method takes account of relevant, peer-reviewed, quality academic and clinical research – it does not take account of lived experiences.
The review fails to use evidence that studies the causes of gender dysphoria.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has

	considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).
There was no review of evidence addressing psychological treatments of gender dysphoria.	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).

Respondents from both groups said…	**NHS England response …**
Respondents from both groups suggested that the evidence included in the review was unfit for purpose due to small sample sizes, a lack of randomised control trials, and poor quality or inconclusive results. Many respondents from both groups also submitted details of a number of articles, references, papers and studies they	The evidence review by the National Institute for Health and Care Excellence (NICE) follows the NHS England Specialised Commissioning process and template and is based on the outcomes and search criteria agreed by an expert working group that had an independent chair. NHS England has considered all of the additional evidence that has been proposed during the public consultation and has concluded that, while some new, relevant

felt should have been included in the evidence review.	evidence was identified by stakeholders, it did not materially affect the conclusions of the existing evidence review (see Appendix B).

Question 2 – Does the equality and health inequality impact assessment (EHIA) reflect the potential impact that may arise as a result of the proposed changes?

Group A Respondents

Respondents said…	**NHS England response …**
The EHIA fails to address the impact on transgender children denied PSH treatment. It was noted by some that the equality and health inequality impact assessment had recognised the potential for harm by acknowledging that potential distress may be experienced and that there may be an increase in risk taking behaviour, however the level of acknowledgement was seen as insufficient, understating the seriousness of the issues, and	The EHIA reads: "*Potential consequences of the proposal may be an increase in the number of children and young people who seek GnRHa from unregulated sources; and some stakeholder groups have previously suggested that withholding GnRHa will lead to an increase in emotional and psychological distress, leading to risk-taking behaviour particularly amongst adolescents. Conversely, some stakeholder groups have suggested that GnRHa should be removed from the NHS pathway of care completely in the best interests of children and young people in view of the limited evidence around treatment aims, benefits, risks and outcomes*". NHS England has had to weigh a consideration of potential harms with potential benefits to individuals who may be impacted by the decision. It has made the proposal to remove PSH from the NHS pathway of care because of

appearing to mitigate that the risks of such harm was acceptable.	a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. It is therefore proposed that adoption of the policy would in itself be a risk mitigation measure. The EHIA describes that other forms of specialist clinical support will remain available through the NHS for this patient cohort; the proposed NHS England interim service specification for gender incongruence (June 2023) describes a multi-disciplinary approach to care that focuses on psychosocial and psychological approaches, and psychoeducation. NHS England strongly discourages the sourcing of any medication from unregulated providers and unregulated sources such as the internet – but the risk that some individuals may seek PSH from unregulated sources regardless, cannot be used to compel the NHS to continue to prescribe PSH, for which there is very limited evidence of safety.
Group A respondents also objected to the repeated statement that the potential impact on transgender children and young people would be alleviated by other modes of specialist clinical support being made available. They argued that the assessment should explicitly address the potential negative impact of withdrawing access to PSH treatment, regardless of alternative treatments, and felt that	The policy position has been proposed because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. It is therefore proposed that adoption of the policy would in itself be a risk mitigation measure. NHS England plans to establish around eight new providers of CYP Gender Services by 2026, thereby increasing the clinical workforce and clinical capacity to address the long waiting times. **The EHIA has been amended to**

the reference to other treatments ignored ongoing issues in being able to access healthcare in a timely fashion. Wait lists for such services were predicted to be inordinately lengthy, with backlogs meaning that some young patients would be unable to receive treatment for several years, and beyond the period that they needed it most.	**read that**: *As a risk mitigation measure, in April 2024 NHS England will have commissioned a rapid assessment service for every child or young person on the waiting list for CYP Gender Services, through local NHS children and young people's mental health services. This will be a directly commissioned service for this cohort over-and-above existing mental health provision.*
Respondents also noted that there was no mention of the potential impact on those who were currently receiving PSH treatment but who may be forced to stop treatment due to the proposed changes in the clinical policy. Respondents also wondered whether endocrinologists and other supervising clinicians would receive training in preparation for such scenarios.	The EHIA did address this, but for clarity the EHIA has **been amended** to read: "*For children and young people who, at the point the clinical commissioning policy takes effect on 1 April 2024:* • *have been referred into an endocrine clinic by the former NHS Gender Identity Development Service but have not yet been assessed by a consultant endocrinologist for suitability of PSH; or* • *are under the clinical care of an endocrine team at University College of London Hospitals NHS Foundation Trust or Leeds Teaching Hospitals NHS Trust following a referral by the former NHS Gender Identity Development Service* *there is an expectation that GnRHa will continue to be administered / be initiated, if that is the informed choice of the young person / parents of a child*

	under 16 years, subject to the outcome of usual clinical review of the individual's existing individual care plan jointly between the individual's Lead Clinician and the young person / parents of a child under 16 years". NHS England's adoption of the proposal would not be intended to compel young people / parents of children under 16 years to choose to continue with GnRHa if, after a consideration of the issues raised by the adoption of the policy, they make a decision to cease the intervention. As part of the programme of work to oversee the decommissioning of the GIDS at Tavistock and the establishment of new services, NHS England has asked a Paediatric Endocrinology Working Group to develop a framework for obtaining informed consent from relevant young people / parents of children under 16 years, to ensure rigour and consistency of approach.
The requirement for taking part in a research trial is discriminatory. The terms 'early onset' and 'late onset' have not been defined.	The policy position has been proposed because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. The development of a research protocol is well underway and will be subject to the usual approvals through the National Institute for Health and Care Research, but NHS England's proposal to remove PSH from routine NHS prescribing protocols is not contingent upon the establishment of a clinical

	study. **The wording of the proposed policy has been amended** to provide greater clarity on this point. The consequence of a decision by NHS England, should it be made, that PSH are no longer routinely commissioned by the NHS as a response to gender incongruence / dysphoria will be that the PSH pathway will be closed, regardless of the outcome of a separate programme of work through the National Research Oversight Board to determine the feasibility of a clinical study. It will also be for the National Research Oversight Board to define access criteria into the study.
Protected characteristic: Gender Reassignment Group A respondents felt that the EHIA misinterpreted the breadth of the characteristic and discriminated against those who had socially transitioned but not medically transitioned. Respondents referenced the Equality Act 2010, which states that "a person has the protected characteristic of gender reassignment if the person is proposing to undergo, is undergoing, or has undergone a process (or part of a process) for the purpose of reassigning the person's sex by changing physiological or other attributes of sex". There	In response to submissions on this point, NHS England has correctly applied the law. In considering the application of Equality Act 2010, section 7, to this service, the High Court in R (AA) v NHS Commissioning Board (2023). found that not every child or young person referred to a specialised gender incongruence service will have the protected characteristic of gender reassignment. The Court held that children and young people who are referred to such a service do not – at the point of referral or while they remain on the waiting list - share the protected characteristic of 'gender reassignment' as a class or cohort of patients. The whole cohort of patients cannot be treated as "proposing to undergo" a process (or part of a process) for the "purpose of reassigning" their sex "by changing physiological or other attributes of sex" as a class. However, as the Court found and as NHS England accepts, many children and young people in this position will, individually, have the protected

is, therefore, no requirement for medical treatment to have taken place in order to be covered by the protected characteristic gender reassignment.	characteristic of gender re-assignment at this stage although determining that will involve a case-specific factual assessment. It is for this reason that NHS England has determined to treat <u>all</u> of the children and young people who will be impacted by the proposals as likely to share the protected characteristic of gender reassignment, and it has proceeded on that basis throughout the whole process of policy formation.
Protected characteristic: Disability Group A respondents felt that the EHIA had failed to recognise the potential for the interim clinical policy to discriminate against neurodivergent children and young people by unfairly excluding them from research and PSH treatment. There was no case, it was stated, to conclude that those with diagnoses and conditions such as autism, ADHD, learning difficulties, or low IQ would be unable to recognise their own gender identity and make their own decisions, or that they should be denied PSH treatment and steered into purely psychological treatments on the basis that they experienced psychological conditions in	The basis for this submission is not clear. Firstly, the policy position has been proposed because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. A policy *not* to prescribe PSH would apply to all individuals, regardless of disability or any other protected characteristic. Secondly, the consequence of a decision by NHS England, should it be made, that PSH are no longer routinely commissioned by the NHS as a response to gender incongruence / dysphoria will be that the PSH pathway will be closed, regardless of the outcome of a separate programme of work through the National Research Oversight Board to determine the feasibility of a clinical study. It will be for the National Research Oversight Board to define access criteria into any study in due course, but NHS England is unable to identify from the policy proposition or the EHIA why respondents to consultation would

conjunction with their sense of gender dysphoria.	conclude that individuals with this protected characteristic would be at risk of exclusion from such a study.
Protected characteristic: Age Some respondents felt that the EHIA had not sufficiently reflected on how the interim clinical policy could potentially discriminate against young people by negating their individual autonomy and making the assumption that they aren't capable of knowing themselves or their own minds.	The policy position has been proposed because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. NHS England is content that the EHIA accurately describes that the proposal is a reasonable, rational and clinically necessary response to the findings of NICE and the Cass Review that a key limitation to identifying the effectiveness and safety of PSH in regard to children and young people with gender incongruence / dysphoria is the lack of reliable comparative studies. In other words, the age of the individuals for whom risk and benefits cannot be defined because of the lack of evidence is in itself a contributory reason for taking steps to mitigate clinical risk and safety issues.
Protected characteristic: Age Issues of age were also linked to questions regarding the definitions of 'early onset' and 'late onset' gender dysphoria, and how some transgender youth may be discriminated against because their ages would be unreasonably linked to these so-called "arbitrary definitions"	The policy position has been proposed because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. The consequence of a decision by NHS England, should it be made, that PSH are no longer routinely commissioned by the NHS as a response to gender incongruence / dysphoria will be that the PSH pathway will be closed,

and that they would therefore be impacted by missing out on potentially beneficial treatment.	regardless of the outcome of a separate programme of work through the National Research Oversight Board to determine the feasibility of a clinical study. It will also be for the National Research Oversight Board to define access criteria into such a study.
Protected characteristic: Age Some respondents also felt that the EHIA should have mentioned Gillick competency, and how this is viewed and applied by NHS England with regard to transgender children and young people.	The policy position has been proposed because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. The consequence of a decision by NHS England, should it be made, that PSH are no longer routinely commissioned by the NHS as a response to gender incongruence / dysphoria will be that PSH are no longer routinely commissioned by the NHS, and this policy would apply to all children and young people on the gender incongruence pathway irrespective of whether they would be deemed Gillick competent.
Protected characteristic: Race Respondents pointed out that there were no mentions of how the protected characteristic of race would be impacted by the interim clinical policy, nor any mentions of plans for how these groups would be recognised and supported.	In response to this submission, NHS England has assured itself that the impact to individuals who share the protected characteristic of race and ethnicity is indeed addressed by the EHIA.
Protected characteristic: Pregnancy	In response to this submission, NHS England has assured itself that the EHIA states that NHS England is in receipt of no evidence to suggest otherwise and

Respondents pointed out that there were no mentions of how the protected characteristic of pregnancy would be impacted by the interim clinical policy, nor any mentions of plans for how these groups would be recognised and supported.	therefore is of the view that the proposed interim service specification does not have any significant impact on individuals who may share this protected characteristic.
Protected characteristic: Religion Respondents pointed out that there were no mentions of how the protected characteristic of religion would be impacted by the interim clinical policy, nor any mentions of plans for how these groups would be recognised and supported.	In response to this submission, NHS England has assured itself that the EHIA states that it has concluded that the proposal does not significantly impact individuals who share this protected characteristic.
Protected characteristic: Sex It was pointed out that the EHIA had not sufficiently reflected on how the denial of PSH treatment would differently and negatively impact biological males going through undesired puberty (for example, in the development of an Adam's apple, or the deepening of the voice).	**The EHIA has been amended to read that: "***Some respondents to public consultation pointed out that the EHIA had not sufficiently reflected on how the withdrawal of PSH from the NHS pathway of care would differently and negatively impact natal males going through undesired puberty, for example, in the development of an Adam's apple or the deepening of the voice. The policy position has been proposed because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes".*

	Other forms of specialist clinical support will remain available through the NHS for this patient cohort; the NHS England interim service specification for gender incongruence (June 2023) describes a multi-disciplinary approach to care that focuses on psychosocial and psychological approaches, and psychoeducation".
Other Groups Children and young people from low-income homes who would be discriminated against because they would not be able to utilise treatments from private clinics available to those from more affluent families.	Some respondents to consultation invited NHS England to accept that inequity may arise as a consequence of adoption of the policy in that lower-income families will be disadvantaged by not being able to afford to source Puberty Suppressing Hormones from private clinics. NHS England cannot share that view because it is not able to support the sourcing of PSH from any source outside of the NHS because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. Moreover, NHS England is not aware of any **regulated** source of Puberty Suppressing Hormones for children and young people with gender incongruence outside of the NHS, hence NHS England's position being the following, regardless of the socio-economic status of the individual child or young person (source: NHS England's Interim Service Specification for CYP Gender Services, 2023). *NHS England strongly discourages the sourcing of any medication from unregulated providers and unregulated sources such as the internet.*

	The EHIA has been amended to reflect the wording above.
Other Groups Children and young people who, having been denied PSH treatment through NHS England (or being unwilling to enrol in a research trial), would choose to access treatments from unregulated sources, with potentially negative consequences.	NHS England strongly discourages the sourcing of any medication from unregulated providers and unregulated sources such as the internet – but the risk that some individuals may seek PSH from unregulated sources regardless, cannot be used to compel the NHS to continue to prescribe PSH, for which there is not sufficient evidence relating to safety and clinical effectiveness.
Other Groups Those who either lived with unsupportive families or who lived outside the family home, who would find it more difficult to access services than those who had the support and encouragement of their adult carers.	It is not clear how this submission directly relates to the proposal that PSH will not be routinely commissioned by the NHS as a response to gender incongruence.
Other Groups Those who, for a variety of reasons, could be considered to have low health literacy	**The EHIA has been amended to read that: "***There is evidence that there are lower levels of health literacy in communities that are socially and economically disadvantaged. NHS England is of the view that the proposals do not discriminate against this group; and that the proposals will have a neutral impact on reducing health inequalities in accessing services or achieving outcomes for this group*".

Other Groups Homeless transgender youth, who were seen as particularly vulnerable, but who weren't addressed in the impact assessment.	**The EHIA has been amended to read that:** *The charity akt reports that 24% of homeless people identify as "LGBT" but we do not have specific data on the prevalence of children 16 years and under who are homeless and who present with gender incongruence. A decision that PSH will not be routinely commissioned by the NHS will not have any specific impact on this group. Separately, if a clinical study is determined to be feasible, it will be for the National Research Oversight Board to define access criteria into such a study and to consider the equalities implications of the access criteria.*

Group B Respondents

Respondents said…	**NHS England response …**
The EHIA does not assess the negative impact of using PSH.	That is not the purpose of the EHIA, which has considered the implications and potential consequences of adoption of the proposal that PSH is *not* routinely available to children and young people. Separately, the NICE evidence review examined the evidence about outcomes, safety and effectiveness of GnRHa and the EHIA has referred to, and is informed by, NICE's conclusions about the limited evidence base.
The language used in the EHIA shows signs of pro-transgender ideology. Some Group B respondents also highlighted what they	NHS England is aware of the disagreements that inevitably manifest about the language used in literature relating to children and young people who present with issues of gender incongruence. NHS England will not be changing the

considered unscientific and ideological terms such as “sex assigned at birth”.	language used in the EHIA. In any event, the term “sex assigned at birth” was not used in the EHIA.
There is no assessment of how others are impacted by gender affirming treatments.	That is not the purpose of the EHIA, which has correctly considered the implications and potential consequences of adoption of the proposal that PSH is *not* routinely available to children and young people with gender incongruence / dysphoria.
Protected characteristic: Sexual Orientation Most Group B respondents who provided an answer to this question believed that the EHIA had inadequately addressed the impact on the protected characteristic of sexual orientation, considering it a troubling and unusual oversight that NHS England had declared that it did not hold sexual orientation data for transgender children and young people. For many Group B respondents some of the primary causes of gender dysphoria among young people were likely to be internalised homophobic impulses and/or mistaken ideas regarding the expression of human sexuality and gender. Group B respondents tended to believe that a large proportion of gender dysphoric young people	NHS England, as a commissioning body, does not routinely collect any personal data on individuals who use NHS services; any consolidated data relating to patients that is held by NHS England is collected by the providers of healthcare services. Data on the sexual orientation of children and young people who have accessed the GIDS has not been provided to NHS England by the Tavistock and Portman NHS Foundation Trust. The Trust’s website explains the challenges of collecting this data from children and **the EHIA has been amended to read:** *In our [Tavistock] most recent statistics (2015), of the young people seen in our service who were assigned male at birth and for whom we have data, around 30% were attracted to males, 30% to females, and 30% to both males and females (or other genders). The remaining approximately 10% of those for whom we have data described themselves as not being attracted to either males or females, or as asexual. For young people assigned female at birth for whom we have data: over half were attracted to females, a quarter were attracted to males, just under 20% were to*

would become healthy homosexual or bisexual adults if allowed to develop and evolve naturally, and that there was a significant body of evidence that supported this.	*both males and females (or other genders), and a small percentage described themselves as asexual or as not being attracted to either males or females".* The EHIA explains that The Cass Review has said that in forming further advice to NHS England it is considering further the complex interaction between sexuality and gender identity, and societal responses to both – the Review's Interim Report (2022) cited the example of "young lesbians who felt pressured to identify as transgender male, and conversely transgender males who felt pressured to come out as lesbian rather than transgender".
Protected Characteristic: Age In opposition to Group A respondents who promoted the application of Gillick competency and individual autonomy, Group B respondents tended to feel that children under the age of 16 were too young to be able to make such important decisions, and that decisions around PSH treatment and gender transition should be made by parents, carers, and experienced clinicians. If PSH were made available to children under 16, therefore, it was believed that the protected characteristic of age would be	The EHIA has correctly considered the implications and potential consequences of adoption of the proposal that PSH is *not* routinely available to children and young people with gender incongruence / dysphoria.

negatively impacted and that this should have been more directly addressed in the EHIA.	
Protected Characteristic: Gender Reassignment Some Group B respondents believed that the EHIA had inaccurately described the protected characteristic of gender reassignment, stating that, in terms of statute law, expressing a wish to change sex did not qualify a child under 16 for the protected characteristic. Some Group B respondents also stated that the Equality Act 2010 does not define gender reassignment in relation to children in its main body, but rather only in explanatory notes, and that the Gender Recognition Act 2005 requires those who undergo gender reassignment to be 18 at minimum, and to have lived as the desired gender for two years.	In response to submissions on this point, NHS England has correctly applied the law. In considering the application of Equality Act 2010, section 7, to this service, the High Court in R (AA) v NHS Commissioning Board (2023). found that not every child or young person referred to a specialised gender incongruence service will have the protected characteristic of gender reassignment. The Court held that children and young people who are referred to such a service do not – at the point of referral or while they remain on the waiting list - share the protected characteristic of 'gender reassignment' as a class or cohort of patients. The whole cohort of patients cannot be treated as "proposing to undergo" a process (or part of a process) for the "purpose of reassigning" their sex "by changing physiological or other attributes of sex" as a class. However, as the Court found and as NHS England accepts, many children and young people in this position will, individually, have the protected characteristic of gender re-assignment at this stage although determining that will involve a case-specific factual assessment. It is for this reason that NHS England has determined to treat all of the children and young people who will be impacted by the proposals as likely to share the protected characteristic of gender reassignment, and it has proceeded on that basis throughout the whole process of policy formation.

Some respondents highlighted the claim made in the EHIA that “the majority of individuals who will be impacted by the proposals are likely to have the protected characteristic of gender reassignment” as incompatible with statute law, as outlined above, and as unsupported and unevidenced by objective data.	
Protected Characteristic: Gender Reassignment Some also stated that even if the protected characteristic of gender reassignment was correctly applied this should only ensure that such individuals weren’t unfairly discriminated against, and not that they should be guaranteed treatment.	The EHIA has correctly considered the implications and potential consequences of adoption of the proposal that PSH is not routinely available to children and young people.
Protected Characteristic: Disability Some Group B respondents believed that the protected characteristic of disability had not been fully reflected, particularly with regard to autistic children and young people who, it was felt, were more susceptible than non-autistic children to arrive at the mistaken conclusion that	This is outside the scope of the consultation. The approach for assessment and diagnosis of gender incongruence is set out in NHS England’s published interim service specification for CYP Gender Services, which was agreed following a process of public consultation. The current EHIA has correctly considered the implications and potential consequences of adoption of the proposal that PSH is not routinely available to children and young people.

they were transgender and to fix their intentions on transition. According to Group B respondents, such comorbidities and the increased difficulties and risks faced by neurodivergent children and young people should have been more adequately addressed. Some respondents believed that it is impossible for an autistic person to have a gender identity and, therefore, that they could not experience gender dysphoria. That the EHIA and, apparently, the medical profession has ignored this was seen as discriminatory and in urgent need of review.	
Protected Characteristic: Sex Some respondents felt that the negative impact on young females had not been adequately addressed, and that though the EHIA recognised that more females than males are presenting with gender dysphoria there was not enough acknowledgement of the disparity and potential inequality.	The EHIA has explained that the terms of reference for the Cass Review include "*exploration of the reasons for the increase in referrals and why the increase has disproportionately been of natal females, and the implications of these matters*". The EHIA also explains that further engagement is also planned by the National Research Oversight Board to identify the key evidence gaps for children and young people with later-onset gender dysphoria – recognising that there is even greater uncertainty in terms of the supporting clinical evidence base, less established clinical practice and less known about the natural history of gender dysphoria in this group. The

Some respondents also believed that further research into discovering why more females than males currently presented as gender dysphoric was urgently required in order to ensure that young females weren't advanced into treatment for the wrong reasons.	engagement will include an analysis of the impacts to individuals who may share this protected characteristic.
Other Groups: Young People in Care Some Group B respondents believed that the EHIA had not sufficiently addressed the evidence and research regarding gender dysphoric children and young people who had lived in care, which could lead to a disproportionately negative impact for this group. Respondents believed that the numbers of transgender youth who lived in care situations was unusually high, and that this therefore suggested that the causes of their gender dysphoria and desire to transition was more likely to be linked to issues such as trauma, unhealthy parental influences, unstable home situations, and other psychological and mental health conditions. More research and study for	The EHIA has recorded that there is an over-representation percentage wise of looked after children seen by services for children and young people with gender incongruence. This was noted by the Cass Review, which is due to deliver final advice early 2024. The EHIA has correctly considered the implications and potential consequences of adoption of the proposal that PSH is not routinely available to children and young people. Further "research and study" is not needed on this group in order for NHS England to make a decision on the proposal.

this group was therefore urged before final decisions are reached.	

Summary of themes raised by all respondents

Respondents said…	**NHS England response …**
The potential impact cannot be reflected because the evidence used is inadequate. A significant number of respondents from both groups believed that it was not possible to accurately comment on the EHIA due to the assessment itself based on inadequate evidence and research. Respondents argued that the current state of research, particularly regarding the long-term effects of gender-affirming care (including PSH treatment) was insufficient and scientifically questionable. While some respondents asserted that it was unethical to subject children to drugs without a clear understanding of their safety and long-term	The EHIA has described the very limited evidence about PSH**,** including about the risks, benefits and long-term outcomes. Specifically, under the heading "*What key sources of evidence have informed your impact assessment and are there key gaps in the evidence*" the EHIA refers to the evidence review on GnRHa as a response to gender dysphoria by the National Institute for Health and Care Excellence in 2020 and says: "*The evidence review confirms that there is limited evidence. Criteria for enrolment in the clinical study alongside the first study to which children and young people with early on-set gender dysphoria may enrol, further engagement is also planned by the Research Oversight Board to identify the key evidence gaps for children and young people with later-onset gender dysphoria – recognising that there is even greater uncertainty in terms of the supporting clinical evidence base, less established clinical practice and less known about the natural history of gender dysphoria in this group*". The EHIA has therefore correctly considered the implications and potential consequences of adoption of the proposal that PSH is *not* routinely available to children and young people, using evidence where

effects, others argued that it was unethical to withdraw potentially life-saving treatment without conclusive proof that it causes harm. Likewise, in some cases the same studies were used by both groups to support their points of view (the Dutch Protocol, for example), highlighting that the evidence is inconclusive on which both the interim clinical policy and the equality and health inequality impact assessment were based. Both groups raised concerns regarding the limitations of existing research, selectivity issues, and short follow-up duration.	it exists, noting where there are gaps in evidence and describing plans to increase the evidence base.
The document and question are unclear	The EHIA is, necessarily, a detailed technical document that seeks to support decision makers, with reference to the Equality Act, by examining the implications and potential consequences of adoption of the proposal on individuals who may share a protected characteristic, and / or for whom otherwise adoption of the proposal may cause or exacerbate inequalities. NHS England will give consideration to how future EHIAs may be written in a form that is more accessible to a lay-person, and how questions about the content of EHIAs are worded.

Question 3 – Are there any changes or additions you think need to be made to this policy?

Group A Respondents

Respondents said…	**NHS England response …**
The requirement to participate in a research trial is unethical	The development of a research protocol is well underway and will be subject to the usual approvals through the National Institute for Health and Care Research, but NHS England's proposal to remove PSH from routine NHS prescribing protocols is not contingent upon the establishment of a clinical study. **The wording of the proposed policy has been amended** to provide greater clarity on this point. The consequence of a decision by NHS England, should it be made, that PSH are no longer routinely commissioned by the NHS as a response to gender incongruence will be that the PSH pathway will be closed, regardless of the outcome of a separate programme of work through the National Research Oversight Board to determine the feasibility of a clinical study. The EHIA explained that, were the study to gain the usual approvals, some young people would likely not be eligible for the study. Should the study not gain the usual approvals, no child or young person would be eligible for the study.
The terms 'early onset' and 'late onset' are not defined for the purpose of the clinical study.	This falls outside the scope of the consultation. The development of a research protocol is well underway and will be subject to the usual approvals through the National Institute for Health and Care Research, but NHS England's proposal to remove PSH from routine NHS prescribing protocols is not contingent upon the establishment of a clinical study. **The wording of the proposed policy has**

The research trial is poorly designed and will not provide the desired results.	**been amended** to provide greater clarity on this point. The feasibility of a clinical study, including definition of access into a clinical study, is being led by a National Research Oversight Board following usual design principles.
The policy does not address certain risks of harm it may cause to transgender youth. The risks of not using PSH should be addressed in the policy.	NHS England has had to weigh a consideration of potential harms with potential benefits to individuals who may be impacted by the decision. It has made the proposal to remove PSH from the NHS pathway of care because of a lack of sufficient evidence relating to the safety and clinical effectiveness of PSH for children and young people with gender incongruence / dysphoria, including about the benefits, risks and long-term outcomes. It is therefore proposed that adoption of the policy would in itself be a risk mitigation measure. The EHIA describes that other forms of specialist clinical support will remain available through the NHS for this patient cohort; the proposed NHS England interim service specification for gender incongruence (June 2023) describes a multi-disciplinary approach to care that focuses on psychosocial and psychological approaches, and psychoeducation.
The policy should be informed by the lived experiences of transgender people and experts.	The policy proposition has been formed following NHS England's established method for forming clinical commissioning policies. This method takes account of relevant, peer-reviewed, quality academic and clinical research – it does not take account of lived experiences. The report on the analysis of consultation responses records that respondents have referred to the process of stakeholder testing that NHS England undertook prior to public consultation. That process of stakeholder testing was open to all

	individuals and organisations who had previously registered as stakeholders. The stakeholder testing asked the same questions as those put to respondents to the subsequent public consultation – it did not seek to use lived experience to inform the development of the policy itself.
Transgender healthcare should be available everywhere, not only in specialist clinics	This falls outside the scope of the consultation.
The policy should remove harmful terminology that pathologises transgender people. Some respondents felt that the policy conspicuously avoided the use of terms such as 'transgender' and 'gender dysphoria' in favour of the clinical term 'gender incongruence.'	The clinical commissioning policy has to refer to a recognised diagnostic tool in order to describe those individuals who would fall within the scope of the clinical commissioning policy. The search criteria agreed by the Policy Working Group for the purpose of the NICE evidence review was: "*children and adolescents aged 18 years or less who have gender dysphoria, gender identity disorder or gender incongruence of childhood".* The NICE evidence review reported that all of the studies that reported diagnostic criteria for gender dysphoria used the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria that was in use at the time (6/9 studies) and the other 3 studies did not report how gender dysphoria / gender incongruence / gender identity disorder was defined. The proposed policy published by NHS England for the purpose of public consultation used 'gender incongruence' as defined by the International Classification of Diseases v11, which is consistent with the diagnostic framework that is referenced in NHS England's interim service specification for the new

	Children and Young People's Gender Services (2023); and 'gender dysphoria' as defined by the DSM.
The policy should give evidence that psychological therapies alone are an effective treatment.	The EHIA described that other forms of specialist clinical support will remain available through the NHS for this patient cohort; the proposed NHS England interim service specification for gender incongruence (June 2023) describes a multi-disciplinary approach to care that focuses on psychoeducation, psychosocial and psychological approaches, and aims to reduce distress and promote wellbeing and functioning. However, both the interim advice from the Cass Review and NHS England's previous public consultation on the interim service specification have acknowledged the scarce and inconclusive evidence to support clinical decision making in regard to children and young people who present with gender incongruence or gender variance, including approaches for social transition and psychological therapies. The Cass Review will deliver final advice to NHS England, including on the evidence base to support clinical decision making, by March 2024 and this advice will inform the development of a substantive service specification for the new CYP Gender Services by NHS England in 2024.
The requirement for those currently using PSH to desist is misguided.	This is not what NHS England has proposed. The policy proposition and the EHIA **have been amended to make clearer that:** "*For children and young people who, at the point the clinical commissioning policy takes effect on 1 April 2024:*

	• *have been referred into an endocrine clinic by the former NHS Gender Identity Development Service but have not yet been assessed by a consultant endocrinologist for suitability of PSH; or* • *are under the clinical care of an endocrine team at University College of London Hospitals NHS Foundation Trust or Leeds Teaching Hospitals NHS Trust following a referrals by the former NHS Gender Identity Development Service* *there is an expectation that GnRHa will continue to be administered / be initiated, if that is the informed choice of the young person / parents of a child under 16 years[1], subject to the outcome of usual clinical review of the individual's existing individual care plan jointly between the individual's Lead Clinician and the young person / parents of a child under 16 years".* NHS England's adoption of the proposal would not be intended to compel young people / parents of children under 16 years to choose to continue with GnRHa if, after a consideration of the issues raised by the adoption of the policy, they make a decision to cease the intervention. As part of the programme of work to oversee the decommissioning of the GIDS at Tavistock and the establishment of

[1] NHS England's adoption of the proposal would not be intended to compel young people / parents of children under 16 years to choose to continue with GnRHa if, after a consideration of the issues raised by the adoption of the policy, they make a decision to cease the intervention.

	new services, NHS England has asked a Paediatric Endocrinology Working Group to develop a framework for obtaining informed consent from relevant young people / parents of children under 16 years, to ensure rigour and consistency of approach.

Group B Respondents

Respondents said…	**NHS England response …**
Need for consistency and clarity in the definition of 'gender incongruence' within the interim clinical policy, suggesting that the definition should align with the diagnostic framework of the interim service specification and adopt the ICD-11 definition. Current version refers to "gender incongruence / dysphoria".	The proposed policy refers to 'gender incongruence' as defined by the International Classification of Diseases v11, which is consistent with the diagnostic framework that is referenced in NHS England's interim service specification for the new Children and Young People's Gender Services; and 'gender dysphoria' as defined by DSM V.
The proposed research trial is unethical.	The development of a research protocol is well underway and will be subject to the usual approvals through the National Institute for Health and Care Research, but NHS England's proposal to remove PSH from routine NHS prescribing protocols is not contingent upon the establishment of a clinical study. **The wording of the proposed policy has been amended** to provide greater clarity on this point. The consequence of a decision by NHS England, should it be

	made, that PSH are no longer routinely commissioned by the NHS as a response to gender incongruence will be that the PSH pathway will be closed, regardless of the outcome of a separate programme of work through the National Research Oversight Board to determine the feasibility of a clinical study.
There should be no exceptional cases outside of the research trial.	**As a change to the proposed policy:** Puberty Suppressing Hormones will not be available through an 'exceptional circumstances' route; the providers of gender incongruence services for children and young people were concerned at how such a pathway could operate appropriately, effectively and equitably; instead, as with all specialised services, a patient's clinician can make an application under NHS England's Individual Funding Request process, if the clinician can demonstrate that there are no other patients with similar clinical circumstances who might benefit from the treatment in a similar way.
Safeguarding policies should be clearly set out and described in full.	Since 2020 NHS England has commissioned a Multi-Professional Review Group (MPRG) to review all proposed referrals made by the Tavistock GIDS of children under 16 years to an endocrine clinic. The purpose of the review is to ensure that proper process has been followed, including compliance with safeguarding approaches and consent requirements. From April 2024 the role of the MPRG will be subsumed by a new national Multi-Disciplinary Team, with an independent chair.
The policy should address how modern culture has influenced the rise of gender dysphoria.	This is outside the scope of the consultation. The approach for assessment and diagnosis of gender incongruence is set out in NHS England's published interim service specification for CYP Gender Services, which was agreed following a process of public consultation.

The policy should make support available for de-transitioners and those harmed by PSH	NHS England will await the final report from the Cass Review to determine how to take this forward; any such work would be undertaken outside of the work to agree the final version of the clinical commissioning policy.
The research trial should be a clinical trial of an Investigational Medicinal Product.	This falls outside the scope of the consultation. The feasibility of a clinical study, including definition of access into a clinical study, is being led by a National Research Oversight Board following usual design principles. The development of a research protocol is well underway and will be subject to the usual approvals through the National Institute for Health and Care Research, but NHS England's proposal to remove PSH from routine NHS prescribing protocols is not contingent upon the establishment of a clinical study. **The wording of the proposed policy has been amended** to provide greater clarity on this point.
Patients and their families should be educated on the risks of using PSH	The feasibility of a clinical study, including definition of access into a clinical study, is being led by a National Research Oversight Board following usual design principles. Should a clinical study be feasible and were the study to gain the usual approvals, children and young people taking part in the study, and their families, would be fully appraised of the available evidence around the risks, benefits and outcomes of PSH, including where the evidence is uncertain.
The language used in the policy should be scientifically and medically accurate.	The language that is used needs to be accessible to a lay-person. NHS England has reviewed the language used in the policy and has concluded that the content is accurate.

The policy should address private or overseas prescribers.	This is outside the scope of the consultation. The scope of the proposed clinical commissioning policy is the use of PSH by the NHS in England.
Research participants must be carefully screened.	The development of a research protocol is well underway and will be subject to the usual approvals through the National Institute for Health and Care Research. The feasibility of a clinical study, including definition of access into a clinical study, is being led by a National Research Oversight Board following usual design principles.

Summary of themes raised by all respondents

Respondents said…	**NHS England response …**
The policy should be closely reviewed and updated following the new research outcomes.	All NHS England clinical commissioning policies for specialised services are subject to regular planned review, and a review can take place before the planned review date if new evidence emerges. It is the intention that the future review of the PSH policy will be informed by the evidence that emerges from the proposed clinical study over time.
The general public should not be consulted on medical matters.	NHS England has a statutory duty to make arrangements to involve the public in commissioning services under section 13Q of the National Health Service Act 2006 (as amended by the Health and Social Care Act 2012). The section 13Q

	duty is aimed at ensuring that NHS England acts fairly in making plans, proposals and decisions in relation to the health services it commissions.
Concerns were raised about the lack of explicit details on whether psychological treatment would be inherently gender affirming. A lack of elucidation on how decisions will be made concerning individuals already undergoing treatment through alternative providers or routes.	This is outside the scope of consultation. The approach for delivery of services as a response to gender incongruence, including psychological approaches, is set out in NHS England's published interim service specification for CYP Gender Services, which was agreed following a process of public consultation. As part of the programme of work to oversee the decommissioning of the GIDS at Tavistock and the establishment of new services, NHS England has asked a Paediatric Endocrinology Working Group to establish a framework for obtaining informed consent from relevant young people / parents of children under 16 years, to ensure rigour and consistency of approach.
Ambiguity surrounding the criteria for determining "exceptional circumstances" within the context of the research trial was also flagged as an issue.	**As a change to the proposed policy:** Puberty Suppressing Hormones will <u>not</u> be available through an 'exceptional circumstances' route; the providers of gender incongruence services for children and young people were concerned at how such a pathway could operate appropriately, effectively and equitably; instead, as with all specialised services, a patient's clinician can make an application under NHS England's Individual Funding Request process, <u>if</u> the clinician can demonstrate that there are no other patients with similar clinical circumstances who might benefit from the treatment in a similar way. NHS England **has amended the EHIA accordingly.**

Need for a more transparent policy that avoids ambiguity and ensures that individuals, including those already in the treatment process, clearly understand what the policy means for them, how it will affect them, and where they stand.	NHS England will consider the broader communication approach around implementation of the clinical commissioning policy.

Appendix B

Summary of NHS England's Approach for Review of the Evidence

In 2020 NHS England commissioned a systematic evidence review from the National Institute for Health and Care Excellence (NICE)[2]. The search criteria that were used by NICE[3] were based on the PICO table agreed by an independent working group[4] of expert clinicians and academics chaired by Dr Hilary Cass. Nine observational studies were identified in the evidence review (date range 2011 to 2020): five studies were retrospective observational studies; three studies were prospective longitudinal observational studies; and one study was a cross-sectional study. Two studies provided comparative evidence and the remaining seven studies used within-person, before and after comparisons. NICE concluded that overall: there was no statistically significant difference in gender dysphoria, mental health, body image and psychosocial functioning in children and adolescents treated with GnRHa; the quality of evidence for all these outcomes was assessed as very low certainty using modified GRADE; there remains limited short-term and long-term safety data for GnRHa; and GnRHa may reduce the expected increase in lumbar or femoral bone density during puberty.

In April 2023 experts in public health and evidence review methods at NHS England re-ran the search (using the same bibliographic search strategies that were used by NICE) to determine if any new evidence had been published subsequent to the NICE search. In total, an initial 358 references were identified across all databases, and following a process of de-duplication, 256 unique references remained which were screened against the details in the PICO table used for the NICE evidence review using their titles and abstracts. The outcome was that 54 references[5] were identified for the purpose of full text assessment against the details in the PICO table.

Of the 54 full texts:

- 45 studies were not relevant
    - 3 studies are unobtainable in full text
    - 5 studies were already identified in the NICE evidence review
    - 37 studies were not relevant according to the PICO details
- 9 studies were relevant according to the PICO details:

Of the 9 studies that were relevant:

- 7 studies were unlikely to materially affect the conclusions of the NICE evidence review (date range of this evidence was 2020 to 2022)

[2] The NICE report on the review of the evidence was published in March 2021.
[3] The search criteria were published and made available to respondents to consultation: literature-surveillace-report-on-gnrh-analogues-for-children-and-adolescents-with-gender-dysphoria-may-2023.pdf (england.nhs.uk)
[4] The PICO table was published and made available to respondents to consultation: literature-surveillace-report-on-gnrh-analogues-for-children-and-adolescents-with-gender-dysphoria-may-2023.pdf (england.nhs.uk)
[5]The list of studies was published and made available to respondents to consultation: literature-surveillace-report-on-gnrh-analogues-for-children-and-adolescents-with-gender-dysphoria-may-2023.pdf (england.nhs.uk)

- 2 studies may materially have affected the conclusions of the NICE evidence review (the dates of these evidence were 2020 and 2023)

In May 2023 NHS England's Specialised Services Clinical Panel considered the refreshed review of the evidence, and it concluded that the new evidence did not materially affect the conclusions of the NICE review.

In June 2023 NHS England ran a process of stakeholder testing on the policy proposition and asked stakeholders if they could identify other material evidence that had not been identified by the 2020 NICE evidence review or the subsequent literature review in April 2023, which was shared with them. No relevant evidence was identified through the process of stakeholder testing.

In August 2023 NHS England ran a 12-week public consultation on the policy proposition. The consultation asked respondents if they could identify other material evidence that had not been identified by the 2020 NICE evidence review or the subsequent literature review in April 2023, which was published as part of the consultation material. The process of consultation generated 246 proposed search references, which were subsequently reviewed by a team of experts in public health and evidence review methods in NHS England for relevance against the search strategy and PICO used for the NICE evidence review and the 2023 literature review. Where necessary, references were obtained in full text. NHS England's consideration of this evidence in January 2024 is set out in Appendix C below.

❖ In summary, of these 246 references:

- 3 were general website pages from which specific information could not be determined
- 34 were evidence already identified as part of the NICE evidence review or literature surveillance report (the date range of this evidence was 2008 to 2023)
- 206 were new evidence identified by respondents that did not fall within the PICO and search methodology (the date range of this evidence was 1989 to 2023)
- 3 were new evidence identified by respondents that fell within PICO and search methodology but did not materially affect the conclusions of the existing evidence review (the date range of these papers was 2020 to 2023)

No new evidence was identified by respondents that fell within the PICO and search methodology, and that would materially affect the conclusions of the existing evidence review.

Appendix C

Public Health Evidence Report Following Engagement Activity

This form is to be completed by the Policy Working Group's Public Health Lead if stakeholders identify potential new evidence during policy development engagement activities. The Public Health Lead will assess the evidence raised to against the Population, Intervention, Comparator and Outcome (PICO) criteria and will record the studies in the appropriate boxes in the '*Outcome for studies suggested during engagement activities*' section of this form. In cases where newly identified evidence has a material impact, please return the completed form to the Clinical Effectiveness Team (CET).

URN	1927
Policy title:	Draft Interim Clinical Policy: Puberty Suppressing Hormones
CRG:	Gender Dysphoria Clinical Programme
NPOC:	National Programme Board for Gender Dysphoria Services
Engagement activity	Public consultation
Date	5th January 2024

Description of comments during engagement (If studies have been suggested please provide a list of references)	251 URLs related to the public consultation questions: • Has all of the relevant evidence been taken into account? • Are there any changes or additions you think need to be made to this policy? Short references were allocated for the information to which each of the URLs linked. 10 URLs linked to 5 duplicate short references, leaving 246 unique short references suggested during consultation.
Action taken by Public Health lead	246 unique references were checked for relevance against the search strategy and PICO used for the evidence review and literature surveillance report and against the references detailed in the evidence review, the literature surveillance report the

	stakeholder testing Public Health Evidence Report. Where necessary, references were obtained in full text. 3 unique references were general website pages from which specific information could not be determined. 1. ONS data http://www.nomisweb.co.uk 2. St Louis https://www.stlouischildrens.org/conditions-treatments/transgender-center/puberty-blockers 3. UK Parliament Committees https://committees.parliament.uk/writtenevidence/7947/html/
Outcome for studies suggested during engagement activities	
1. Evidence already identified as part of the evidence review, literature surveillance report or stakeholder testing	1. Achille 2020 https://doi.org/10.1186/s13633-020-00078-2 2. Anacker 2020 https://pubmed.ncbi.nlm.nih.gov/32919399 3. Angus 2020 https://doi.org/10.1111/cen.14329 4. Biggs 2023 https://pubmed.ncbi.nlm.nih.gov/36120756/ 5. Boogers 2022 https://pubmed.ncbi.nlm.nih.gov/35666195/ 6. Carmichael 2021 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243894 7. Chen 2021 https://doi.org/10.1016/j.jadohealth.2020.07.033 8. Costa 2015 https://pubmed.ncbi.nlm.nih.gov/26556015/ 9. de Vries 2011 https://pubmed.ncbi.nlm.nih.gov/20646177/ 10. de Vries 2014 https://publications.aap.org/pediatrics/article-abstract/134/4/696/32932/Young-Adult-Psychological-Outcome-After-Puberty?autologincheck=redirected 11. Drummond 2008 https://psycnet.apa.org/doiLanding?doi=10.1037%2F0012-1649.44.1.34 12. Giovanardi 2019 https://pubmed.ncbi.nlm.nih.gov/30953318/ 13. Graham 2023 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10063975/ 14. Hembree 2017 https://pubmed.ncbi.nlm.nih.gov/28945902/ 15. Horton 2022 https://doi.org/10.1177/07435584221100591 16. Jensen 2019 https://pubmed.ncbi.nlm.nih.gov/31663037/ 17. Joseph 2019 https://pubmed.ncbi.nlm.nih.gov/31472062/ 18. Khatchadourian 2014 https://pubmed.ncbi.nlm.nih.gov/24315505/ 19. Klink 2015 https://pubmed.ncbi.nlm.nih.gov/25427144/ 20. Kremen 2021 https://pubmed.ncbi.nlm.nih.gov/33883246/ 21. Lee 2020 https://doi.org/10.1210/jendso/bvaa065 22. Nos 2022 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2798002 23. Panagiotakopoulos 2020 https://doi.org/10.1038/s41585-020-0372-2 24. Ramos 2020 https://link.springer.com/article/10.1007/s40618-020-01449-5 25. Rew 2021 https://doi.org/10.1111/camh.12437

	26. Schagen 2016 https://pubmed.ncbi.nlm.nih.gov/27318023/ 27. Schagen 2020 https://academic.oup.com/jcem/article/105/12/e4252/5903559?login=false 28. Staphorsius 2015 https://www.sciencedirect.com/science/article/abs/pii/S0306453015000943 29. Steensma 2013 https://doi.org/10.1016/j.yhbeh.2013.02.020 30. Tordoff 2022 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8881768/ 31. Van der Loos 2023 https://pubmed.ncbi.nlm.nih.gov/36763938/ 32. van der Miesen 2020 https://doi.org/10.1016/j.jadohealth.2019.12.018 33. Wallien 2008 https://pubmed.ncbi.nlm.nih.gov/18981931/ 34. Zucker 2010 https://www.tandfonline.com/doi/abs/10.1080/19359705.2011.530574
2.New evidence identified by stakeholders that does not fall within PICO and search methodology	1. AACAP 2020 https://www.aacap.org/AACAP/Families_and_Youth/Facts_for_Families/FFF-Guide/transgender-and-gender-diverse-youth-122.aspx 2. AACE 2022 https://pro.aace.com/recent-news-and-updates/aace-position-statement-transgender-and-gender-diverse-patients 3. AACPP 2019 https://www.aacap.org/AACAP/Latest_News/AACAP_Statement_Responding_to_Efforts-to_ban_Evidence-Based_Care_for_Transgender_and_Gender_Diverse.aspx 4. Abbruzzese 2023 https://www.tandfonline.com/doi/full/10.1080/0092623X.2022.2150346 5. Abreu 2022 https://psycnet.apa.org/record/2021-67997-001?doi=1 6. Abreu 2022a https://psycnet.apa.org/record/2022-47098-001 7. ACC 2023 https://www.acc.org/About-ACC/Press-Releases/2023/02/22/20/29/Hormone-Therapy-for-Gender-Dysphoria-May-Raise-Cardiovascular-Risks 8. ACHA https://www.acha.org/ACHA/About/Position_Statements/ACHA/About/Position_Statements.aspx?hkey=ff979452-3284-4993-8cbc-bf4abaa8b430 9. ACNM https://www.midwife.org/acnm/files/acnmlibrarydata/uploadfilename/000000000326/ACNM--PS--Care%20for%20TGNB%20People-%20Final_1.pdf 10. ACOG 2021 https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2021/03/health-care-for-transgender-and-gender-diverse-individuals

11. ACP 2023 https://www.acponline.org/advocacy/state-health-policy/attacks-on-gender-affirming-and-transgender-health-care
12. ACT 2021 https://health.act.gov.au/sites/default/files/2021-11/Guidance%20to%20support%20gender%20affirming%20care%20for%20mental%20health%20FINAL_0.pdf
13. Alegria 2016 https://pubmed.ncbi.nlm.nih.gov/27031444/
14. AMA 2019 https://www.ama-assn.org/press-center/press-releases/ama-leading-medical-organizations-fight-transgender-americans
15. AMA 2021 https://www.ama-assn.org/press-center/press-releases/ama-states-stop-interfering-health-care-transgender-children
16. ANA 2022 https://www.nursingworld.org/news/news-releases/2022-news-releases/american-nurses-association-opposes-restrictions-on-transgender-healthcare-and-criminalizing-gender-affirming-care/
17. Anacker 2021 https://pubmed.ncbi.nlm.nih.gov/32919399/
18. APA 2018 https://www.psychiatry.org/getattachment/3d23f2f4-1497-4537-b4de-fe32fe8761bf/Position-Conversion-Therapy.pdf
19. APA 2021 https://www.psychiatry.org/newsroom/news-releases/frontline-physicians-oppose-legislation-that-interferes-in-or-criminalizes-patient-care
20. Arnold 2023 https://journals.lww.com/co-pediatrics/abstract/2023/08000/transgender_and_gender_diverse_youth__an_update_on.6.aspx
21. Arnoldussen 2022 https://doi.org/10.1089/lgbt.2020.0494
22. Arnoldussen 2022a https://doi.org/10.1177/13591045221091652
23. Ashley 2023 https://www.tandfonline.com/doi/full/10.1080/26895269.2023.2218357
24. Ashley 2023a https://psycnet.apa.org/fulltext/2024-16010-001.html
25. AUA 2022 https://www.auanet.org/about-us/policy-and-position-statements/transgender-care
26. AusPath https://auspath.org.au/standards-of-care/
27. Azar 2019 https://www.aapa.org/download/50101/
28. Bailey 2003 https://www.amazon.com/Man-Would-Queen-Gender-Bending-Transsexualism/dp/0309084180
29. Bangalore Krishna 2019 https://pubmed.ncbi.nlm.nih.gov/31319416/
30. Barnes 2023 https://www.bbc.co.uk/news/health-66842352
31. Barnes 2023a https://www.amazon.com/Time-Think-Collapse-Tavistocks-Children-ebook/dp/B0BCL1T2XN
32. Bauer 2022 https://pubmed.ncbi.nlm.nih.gov/34793826/
33. Beers 2021 https://www.aap.org/en/news-room/news-releases/aap/2021/american-academy-of-pediatrics-speaks-out-against-bills-harming-transgender-youth/

34. Bhatt Murphy solicitors 2023 https://bhattmurphy.co.uk/files/SRN%20cases/Sophie%20Williams%20Press%20Release%2001.03.23.pdf
35. Bindmans 2023 https://www.bindmans.com/knowledge-hub/news/alice-litman-inquest-concludes/.
36. Blanchard 1989 https://pubmed.ncbi.nlm.nih.gov/2673136/
37. Blanchard 2008 https://www.researchgate.net/publication/5420507_Deconstructing_the_Feminine_Essence_Narrative
38. Boerner 2022 https://www.scientificamerican.com/article/what-the-science-on-gender-affirming-care-for-transgender-kids-really-shows/
39. Bradley 1990 www.researchgate.net/publication/20948042_Gender_Identity_Disorder_and_Psychosexual_Problems_in_Children_and_Adolescents
40. Bungener 2020 https://doi.org/10.1542/peds.2019-1411
41. Bustos 2021 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8099405/
42. Carter 2021 https://www.amazon.com/TransNarratives-Scholarly-Creative-Transgender-Experience/dp/0889616221
43. Castagnaro 2023 https://www.gendergp.com/new-study-confirms-benefits-of-gender-affirming-healthcare/
44. Chen 2020 https://doi.org/10.1089/TRGH.2020.0006
45. Chen 2023 https://www.nejm.org/doi/full/10.1056/NEJMoa2206297
46. Chew 2018 https://pubmed.ncbi.nlm.nih.gov/29514975/
47. Chronister 2021 https://doi.org/10.1016/j.jad.2021.07.026
48. Chudy 2023 https://www.thepinknews.com/2023/09/14/alice-litman-inquest-gender-clinic-waiting-times/
49. Clarke 2019 https://repository.tavistockandportman.ac.uk/1910/
50. Cohen-Kettenis 2008 https://pubmed.ncbi.nlm.nih.gov/18564158/
51. Cohen-Kettenis 2011 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3114100/
52. Coleman 2022 https://www.tandfonline.com/doi/pdf/10.1080/26895269.2022.2100644
53. Coyne 2023 https://skepticalinquirer.org/2023/06/the-ideological-subversion-of-biology/
54. Curtis 2020 https://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.2020.19111131
55. Davey 2023 https://amp.theguardian.com/society/2023/sep/08/fast-access-to-hormone-therapy-in-transgender-adults-lifesaving-study-

finds?fbclid=IwAR2KKTLNKBi9s7rG4_9F307IeFo3sEzuXYt7ZF9a_C_FDCFEW0IHWi9JN-Q
56. de Vries 2012 https://pubmed.ncbi.nlm.nih.gov/22455322/
57. de Vries 2020 https://pubmed.ncbi.nlm.nih.gov/32958612/
58. Diaz 2023 https://link.springer.com/article/10.1007/s10508-023-02576-9
59. Do no harm 2023 https://donoharmmedicine.org/2023/06/14/do-no-harm-expert-testifies-at-congress/
60. Eckert 2021 https://sciencebasedmedicine.org/a-critical-look-at-the-nice-review/
61. Endocrine Society 2023 https://www.endocrine.org/news-and-advocacy/news-room/2023/ama-gender-affirming-care
62. Eriksen 2018 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6148624/
63. Eugster 2019 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6486823/
64. FDA 2022 https://www.fda.gov/media/159663/download
65. Fitzsimons 2019 https://www.nbcnews.com/feature/nbc-out/prominent-transgender-activist-harassed-anti-trans-feminists-video-shows-n966061
66. GenderGP 2021 https://www.gendergp.com/detransition-facts/
67. Genspect 2023 https://genspect.org/detrans-awareness-day-2023/
68. Giedd 2012 https://doi.org/10.1186/2042-6410-3-19
69. Gill-Petersen 2018 https://en.wikipedia.org/wiki/Histories_of_the_Transgender_Child
70. Giordano 2020 https://www.tandfonline.com/doi/full/10.1080/26895269.2020.1747768
71. Giordano 2021 https://doi.org/10.1136/medethics-2020-106999
72. Giovanardi 2017 https://pubmed.ncbi.nlm.nih.gov/32258611/
73. Gitay 2009 https://pubmed.ncbi.nlm.nih.gov/19297634/
74. Glinteborg 2023 https://academic.oup.com/ejendo/article-abstract/189/3/336/7261571?redirectedFrom=fulltext
75. Godfrey 2023

https://doi.org/https://dx.doi.org/10.1016/j.psyneuen.2022.105987
76. Gonen 2023 https://pubmed.ncbi.nlm.nih.gov/36598988/
77. Good Law Project 2023 https://goodlawproject.org/warm-and-kind-alice-let-down-by-unfit-for-purpose-transgender-healthcare-provision/
78. Gosling 2022 https://sex-matters.org/wp-content/uploads/2022/12/Teenagers-medication-vs-placebo.pdf
79. GovScot 2017 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%2BPuberty%2Bblockers%2Band%2BTrans%2BYP%2B-%2BApril%2B2017.pdf
80. Green 1987 https://www.amazon.com/Sissy-Boy-Syndrome-Development-Homosexuality/dp/0300036965
81. Green 2022 https://pubmed.ncbi.nlm.nih.gov/34920935/
82. Growing up transgender 2020 https://growinguptransgender.com/2020/06/10/puberty-blockers-overview-of-the-research/
83. Gunlusoy 2017 https://pubmed.ncbi.nlm.nih.gov/28188757/
84. Guss 2022 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2798007
85. GWA 2019 https://www.health.wa.gov.au/Articles/U_Z/WA-Lesbian-Gay-Bisexual-Transgender-Intersex-Health-Strategy-2019
86. Hammes 2023 https://www.wsj.com/articles/trans-gender-affirming-care-endocrine-society-evidence-fdb8562c
87. Haugh 2017 https://pubmed.ncbi.nlm.nih.gov/27987429/
88. Hayes 2016 https://www.sciencedirect.com/science/article/abs/pii/S027753951530234X?via%3Dihub
89. Hayes 2017 https://doi.org/10.3389/fpsyg.2017.00044
90. Hayton 2022 https://debbiehayton.com/2022/05/16/my-autogynephilia-story/

91. Health Select Committee 2016 https://publications.parliament.uk/pa/cm201617/cmselect/cmhealth/300/30005.htm
92. Healthtalk.org https://healthtalk.org/Experiences-of-trans-and-gender-diverse-young-people/Trans-and-gender-diverse-young-peoples-experiences-of-puberty-and-puberty-blockers
93. HEIW https://heiw.nhs.wales/news/heiw-launches-new-gender-diversity-and-trans-health-training-modules/
94. Hembree 2013 https://pubmed.ncbi.nlm.nih.gov/24468758/
95. Henderson 2022 https://doi.org/10.1192/j.eurpsy.2022.2205
96. Hodgkinson 1989 https://www.amazon.com/Michael-Nee-Laura-Worlds-Female/dp/0862878721
97. Horton 2022a https://www.tandfonline.com/doi/full/10.1080/27703371.2022.2076002
98. Horton 2023 https://journals.sagepub.com/doi/10.1177/02724316221107076
99. Hough 2017 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5140006/
100. Jewett 2017 https://www.statnews.com/2017/02/02/lupron-puberty-children-health-problems/
101. Joshua 2018 https://doi.org/10.1016/J.COGNITION.2018.04.007
102. Jowett 2022 https://philpapers.org/rec/JOWCFM
103. Kallitsounaki 2022 https://pubmed.ncbi.nlm.nih.gov/35596023/
104. Kaltiala 2023 https://www.thefp.com/p/gender-affirming-care-dangerous-finland-doctor
105. Kay 2023 https://nationalpost.com/opinion/breaking-the-ideological-logjam-over-transgender-youth-health
106. Keating 2006 https://pubmed.ncbi.nlm.nih.gov/16983113/
107. KFF Health News 2017 https://kffhealthnews.org/news/women-fear-drug-they-used-to-halt-puberty-led-to-health-problems/
108. Klein 2018 https://www.aafp.org/pubs/afp/issues/2018/1201/p645.html
109. Kohls 2023 https://acamh.onlinelibrary.wiley.com/doi/10.1111/jcpp.13717
110. Kozlowska 2021 https://journals.sagepub.com/doi/full/10.1177/26344041211010777
111. Lancet 2021 https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00139-5/fulltext#figures
112. Littman https://littmanresearch.com/publications/

113. Littman 2022 https://www.jpeds.com/article/S0022-3476(22)00183-4/fulltext
114. Logic Study https://logicstudy.uk/about/
115. Mahfouda 2017 https://pubmed.ncbi.nlm.nih.gov/28546095/
116. Malone 2021 https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00235-2/fulltext
117. McNamara 2023 https://publications.aap.org/pediatrics/article-abstract/152/3/e2022060943/193719/Combating-Scientific-Disinformation-on-Gender
118. McNeil 2012 https://www.scottishtrans.org/wp-content/uploads/2013/03/trans_mh_study.pdf
119. McPherson 2023 https://www.medrxiv.org/content/10.1101/2023.05.30.23290763v3.full
120. Mehmood 2023 https://www.ncbi.nlm.nih.gov/books/NBK557435/
121. Meier 2018 https://www.amazon.com/Gender-Affirmative-Model-Interdisciplinary-Perspectives-ebook/dp/B07DKY7GFG
122. Meredith 2022 https://www.medscape.co.uk/viewarticle/1000-families-sue-tavistock-gender-service-2022a10021ac
123. Mul 2001 https://pubmed.ncbi.nlm.nih.gov/11683207/
124. Mul 2008 https://doi.org/10.1530/EJE-08-0814
125. Murphy 2023 https://www.feministcurrent.com/2023/05/03/its-the-funding-stupid/
126. Mystic sisters 2022 https://mysticsisters.substack.com/p/esg-the-hidden-reason-why-so-many
127. NASW 2023 https://www.socialworkers.org/News/News-Releases/ID/2642/Gender-Affirming-Health-Care-Saves-Lives#:~:text=WASHINGTON%2C%20D.C.%20%E2%80%93%20The%20National%20Association,transgender%20and%20gender%20diverse%20(TGD)
128. NHS 2020 https://www.nhs.uk/conditions/gender-dysphoria/
129. NHS 2022 https://www.nhs.uk/conditions/early-or-delayed-puberty/
130. NICE 2012 https://www.nice.org.uk/process/pmg6/resources/how-nice-clinical-guidelines-are-developed-an-overview-for-stakeholders-the-public-and-the-nhs-pdf-3304422725317.
131. NICE 2020 https://cass.independent-review.uk/wp-content/uploads/2022/09/20220726_Evidence-review_GnRH-analogues_For-upload_Final.pdf
132. Nuruddin 2013 https://pubmed.ncbi.nlm.nih.gov/23266521/
133. Olsen 2014 https://pubmed.ncbi.nlm.nih.gov/24972421/
134. Olson 2016 https://pubmed.ncbi.nlm.nih.gov/26921285/

135. Olson 2022 https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2021-056082/186992/Gender-Identity-5-Years-After-Social-Transition
136. Our duty https://ourduty.group/education/lifecycle-of-transgender-ideation/
137. Padula 2016 https://doi.org/10.1007/s11606-015-3529-6
138. Panagiotakopoulos 2018 https://doi.org/10.1007/s11154-018-9457-0
139. Pang 2020 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2768726
140. Pang 2022 https://pubmed.ncbi.nlm.nih.gov/35365494/
141. PATHA https://patha.nz/Guidelines
142. Pelham 2023 https://www.cedars-sinai.org/blog/puberty-blockers-for-precocious-puberty.html#:~:text=While%20puberty%20blockers%20have%20been,past%20the%20age%20of%20puberty
143. People 2020 https://people.com/health/nearly-all-transgender-children-who-socially-transition-stay-with-that-gender-study-finds/
144. Pincus 2021 https://doi.org/https://dx.doi.org/10.1016/j.psyneuen.2021.105154
145. PR Newswire 2023 https://www.benzinga.com/pressreleases/23/05/n32319924/sex-reassignment-surgery-market-report-2023-availability-of-health-insurance-coverage-to-boost-gro
146. Priest 2019 https://www.tandfonline.com/doi/abs/10.1080/15265161.2018.1557276
147. r/trans 2023 www.reddit.com/r/detrans/
148. Rafferty 2018 https://publications.aap.org/pediatrics/article/142/4/e20182162/37381/Ensuring-Comprehensive-Care-and-Support-for?autologincheck=redirected
149. RCGP 2019 https://www.rcgp.org.uk/representing-you/policy-areas/transgender-care
150. Reduxx 2021 https://reduxx.info/trans-health-authority-cites-castration-fetish-site-in-guidelines/
151. Rigg 2019 https://doi.org/10.1080/15532739.2019.1692751
152. Rigg 2020 https://spssi.onlinelibrary.wiley.com/doi/abs/10.1111/josi.12364
153. Ristori 2023 https://link.springer.com/article/10.1007/s40618-023-02173-6

154. Roberts 2022 https://academic.oup.com/jcem/article/107/9/e3937/6572526?login=false
155. Rothman 2019 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6709704/
156. Russell 2018 https://doi.org/10.1016/j.jadohealth.2018.02.003
157. Salas-Humara 2019 https://doi.org/10.1016/j.cppeds.2019.100683
158. Sapir 2023 https://www.tabletmag.com/sections/science/articles/finland-youth-gender-medicine
159. Schiappa 2021 https://doi.org/10.4324/9781003250494
160. Schillace 2021 https://www.scientificamerican.com/article/the-forgotten-history-of-the-worlds-first-trans-clinic/
161. Schneider 2017 https://doi.org/10.3389/fnhum.2017.00528
162. Schneider 2017 https://doi.org/https://dx.doi.org/10.3389/fnhum.2017.00528
163. SEGM 2021 https://segm.org/the_effect_of_puberty_blockers_on_the_accrual_of_bone_mass
164. Sex matters 2023 https://sex-matters.org/wp-content/uploads/2023/05/Social-transition-in-schools-is-not-possible.pdf
165. Shrier 2020 https://en.wikipedia.org/wiki/Irreversible_Damage
166. Singh 2021 https://www.frontiersin.org/articles/10.3389/fpsyt.2021.632784/full
167. Smith 2021 https://www.ama-assn.org/delivering-care/population-care/what-know-about-gender-affirming-care-younger-patients
168. Smothers 2021 https://www.vice.com/en/article/epnzjk/no-one-had-a-problem-with-puberty-blockers-when-only-cis-kids-took-them
169. Stanford Medicine 2022 https://med.stanford.edu/news/all-news/2022/01/mental-health-hormone-treatment-transgender-people.html
170. Stanikova 2018 https://doi.org/10.1016/j.psyneuen.2017.10.025
171. Stonewall 2018 https://www.stonewall.org.uk/lgbt-britain-trans-report
172. Stuebing 2002 https://journals.sagepub.com/doi/abs/10.3102/00028312039002469
173. Tavistock 2021

https://tavistockandportman.nhs.uk/news/early-intervention-study-shows-puberty-blockers-are-a-well-received-intervention-in-carefully-selected-patients/
174. The Gender Critical https://gcritical.org/introduction/
175. Threadreader https://threadreaderapp.com/thread/1536422533230206976.html
176. Tordoff 2023 https://doi.org/10.1089/trgh.2021.0116
177. Transgender Trend https://www.transgendertrend.com/the-suicide-myth/
178. Transgender Trend 2023 https://www.transgendertrend.com/nhs-interim-clinical-policy-public-consultation-submission-guide/
179. Transtransmedia 2023 https://www.bitchute.com/video/AEFZv6dqtERN/
180. Turban 2022 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8754307/
181. Turban 2022a https://www.psychiatry.org/patients-families/gender-dysphoria/what-is-gender-dysphoria
182. Turban 2022b https://www.psychologytoday.com/us/blog/political-minds/202201/the-evidence-trans-youth-gender-affirming-medical-care
183. US Trans Survey 2015 https://www.ustranssurvey.org/reports
184. van de Grift 2017 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5580378/
185. Van Meter 2018 https://www.youtube.com/watch?v=uC0zn0D_MyM
186. Van Meter 2019 https://christianconcern.com/wp-content/uploads/2018/10/CC-Resource-Misc-Rowes-JR-Van-Meter-20210915.pdf
187. Vandermorris 2023 https://pubmed.ncbi.nlm.nih.gov/37885600/
188. Vrouenraets 2016 https://pubmed.ncbi.nlm.nih.gov/27251640/
189. Vrouenraets 2021 https://pubmed.ncbi.nlm.nih.gov/36324881/
190. Walch 2021 https://pubmed.ncbi.nlm.nih.gov/33326028/
191. Wall Street Journal 2023 https://www.wsj.com/articles/trans-gender-affirming-care-transition-hormone-surgery-evidence-c1961e27
192. Wanta 2019 https://doi.org/10.1089/trgh.2019.0029
193. Warner 2021 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8606364/
194. WHO https://www.who.int/health-topics/gender
195. Wiepjes 2018 https://doi.org/10.1016/j.jsxm.2018.01.016
196. Wikipedia 2 https://en.wikipedia.org/wiki/Bell_v_Tavistock

	197. Wojniusz 2013 https://pubmed.ncbi.nlm.nih.gov/23477973/ 198. Wojniusz 2016 https://doi.org/https://dx.doi.org/10.3389/fpsyg.2016.01053 199. Yanovski 2003 https://pubmed.ncbi.nlm.nih.gov/12621135/ 200. You tube 1 https://youtu.be/52UNfgTJBL0 201. You tube 2 https://youtu.be/Azx8e5nmc9g 202. You tube 3 https://youtu.be/v1eWIshUzr8?si=eRZLOTTeFau2tr74 203. You tube 5 https://zero.sci-hub.st/4911/9dc0c58006960fe1220b267bafa48e53/olson2016.pdf#view=FitH 204. You tube 6 www.youtube.com/watch?v=6mtQ1geeD_c 205. You tube 7 www.youtube.com/watch?v=N7_5m-AUuj4 206. Zucker 2012 https://doi.org/10.1080/00918369.2012.653309
3.New evidence identified by stakeholders that falls within PICO and search methodology but does not materially affect the conclusions of the existing evidence review	1. Lavender 2023 https://doi.org/10.1089/lgbt.2022.0201 They report a retrospective observational analysis of patients who attended an endocrine clinic. All patients in this study had been treated with puberty suppression **and** gender-affirming hormone treatment, although results are presented separately for each stage of treatment and thus it is possible to determine outcomes for patients following puberty suppression only. Number of patients in this study is small, with considerable loss to follow up (ie 109 eligible participants but full results only available for 38). Comprehensive assessment at each stage using a range of questionnaires, completed by young people and caregivers. The use of puberty suppressants resulted in statistically significant improvements in the Child Behavior Checklist but no statistically significant differences in the Youth Self Report questionnaire or the Body Image Scale questionnaire or the Utrecht Gender Dysphoria Scale. Improvements were also noted

	in self harm and suicidality statements following treatment with puberty suppressants. 2. Ludvigsson 2023 https://doi.org/10.1111/apa.16791 This is a systematic review with relevant outcomes. All contributing studies were checked and have been previously identified or are not relevant to the PICO. Note also that the authors state “Evidence to assess the effects of hormone treatment on the above fields [psychosocial and mental health, cognition, body composition, and metabolic markers of hormone treatment in children with gender dysphoria] is insufficient.” 3. Kuper 2020 https://doi.org/10.1542/peds.2019-3006 In this study a total of 148 participants completed surveys assessing body dissatisfaction, depression and anxiety at initial presentation to their clinic and at follow-up after one year. Most patients in this study were treated with feminising or masculinising hormone therapy but a small number (25/148; 17%) were treated with puberty blocking drugs and the results for this group are reported separately. Note that 90% of all the patients in this study were at a late stage of puberty (Tanner Stage IV or V). There were modest improvements in body dissatisfaction, depressive symptoms and anxiety symptoms in the group of patients treated with puberty suppressants only.
4.New evidence identified by	None

stakeholders that falls within PICO and search methodology, that does materially affect the conclusions of the existing evidence review. Updated evidence review to be undertaken (to be agreed with CET)	

Appendix D

Public Health Evidence Report Following Engagement Activity

URN	1927
Policy title	Draft Interim Clinical Policy: Puberty suppressing hormones (PSH) for children and adolescents who have gender incongruence.
CRG	Gender Dysphoria Clinical Programme
NPOC	Not applicable
Engagement activity	Post public consultation
Date	26 February 2024

Description of comments during engagement (If studies have been suggested please provide a list of references)	A query was received regarding NHSE's consideration of the The World Professional Association for Transgender Health (WPATH) Standards of Care (SOC) for the Health of Transsexual, Transgender, and Gender Nonconforming People, Version 8, during development of the draft Interim Clinical Policy: Puberty suppressing hormones (PSH) for children and adolescents who have gender incongruence.
Action taken by Public Health lead	The suggested references at stakeholder testing and public consultation during policy development and the responses to suggestions were checked for mention of the WPATH SOC Version 8. The WPATH SOC Version 8 was suggested at stakeholder testing and public consultation and a correct response was provided in both evidence reports noting that it does not fall within PICO and search methodology (because it is a guideline). To ensure comprehensive consideration of the WPATH SOC Version 8, the 200 citations within the relevant chapter, i.e. Chapter 12 Hormone Therapy, were further assessed and findings are described below.
Outcome for studies cited in Chapter 12 of WPATH SOC Vn 8	

Citation not identifiable	*Citation given in short form in Chapter 12 but full details not provided in WPATH SOC Vn8 reference list* 1. Baba, 2007 2. Finkelstein et al 1996 3. Lin et al 2021 4. Stuyver et al 2020 5. Tebbens at al 2021 6. Toorians et al 2013
Citation does not meet PICO criteria or search methodology of the NICE 2020 evidence review	*Published prior to the date limits of the literature search:* 1. Comite et al 1981 2. Laron et al 1981 3. van Kesteren et al 1997 *Published within the date limits of the literature search and either was not identified from the searches performed or was identified but sifted out because of not meeting the PICO criteria based on the title and abstract details:* 1. Adeleye et al, 2018 2. Allen et al, 2019 3. Alzahrani et al, 2019 4. Anai et al, 2001 5. Arcelus et al, 2016 6. Ashley, 2019e 7. Asscheman et al, 2013 8. Barrow & Apostle, 2018 9. Bauer et al, 2015 10. Becerra-Culqui et al, 2018 11. Beek, Kreukels et al 2015 12. Bertelloni et al, 1998 13. Bisson, 2018 14. Bockting et al, 2013 15. Borghei-Razavi, 2014 16. Bouman et al, 2016 17. Bouman et al, 2016 18. Bouman et al, 2017 19. Canonico et al, 2007 20. Carel et al, 2009 21. Klink, Caris et al, 2015 22. Carswell & Roberts, 2017 23. Chan et al 2018 24. Chen, Hidalgo et al, 2016 25. Cheng et al, 2019 26. Colebunders et al, 2017 27. Coleman et al, 2012 28. Colizzi et al, 2014 29. Coolhart et al, 2017 30. Costa et al, 2016 31. Davey et al, 2014

	32. Davis & Meier, 2014 33. De Roo et al, 2016 34. De Roo et al, 2017 35. Defreyne et al, 2018 36. Defreyne, Nota et al 2017 37. Dekker er al 2016 38. Delemarre-van de Waal & Cohen- Kettenis 2006 39. Deutsch, 2016a 40. Deutsch, Bhakri et al 2015 41. Djordjevic et al, 2008 42. Du Bois et al, 2018 43. Eisenberg et al 2017 44. Ethics committee of the American Society of Reproductive Medicine et al 2015 45. Finlayson et al 2016 46. Fisher, Castellini et al 2016 47. Fitzpatrick et al 2000 48. Frey et al 2016 49. Gaither et al 2018 50. Gava et al 2016 51. Gava et al 2018 52. Giltay & Gooren, 2000 53. Giltay et al, 2000 54. Goldstein et al 2019 55. Gomez-Gil et al, 2012 56. Gorin-Lazard et al 2012 57. Gorin-Lazard et al 2013 58. Gower, Rider, Brown et al 2018 59. Grossman & D'Augelli 2006 60. Grynberg et al 2010 61. Hembree et al 2009 62. Hendricks & Testa, 2012 63. Heylens, Elaut et al 2014 64. Horbach at al 2015 65. Irwig, 2017 66. Irwig, 2018 67. Iwamoto, Defreyne et al 2019 68. Iwamoto, T'Sjoen et al 2019 69. Jiang et al 2018 70. Jiang et al 2019 71. Kailas et al 2017 72. Keo-Meier & Ehrensaft, 2018 73. Keo-Meier & Fitzgerald, 2017 74. Keo-Meier et al 2015 75. Kerckhof et al 2019 76. Klink, Bokenkamp et al 2015 77. Kuper, Mathews et al, 2019 78. Kuper, Wright et al 2018 79. Levy et al 2003 80. Light et al 2014 81. Mamoojee et al 2017 82. Mancini et al 2018

	83. Manson, 2013 84. Maraka et al 2017 85. Marks et al 2019 86. Mattawanon et al 2018 87. Meier et al 2013 88. Merriggiola et al 2008 89. Meyer 2003 90. Millington et al 2019 91. Moody et al 2015 92. Murad et al 2010 93. Nash et al 2018 94. Newfield et al 2006 95. Neyman et al 2019 96. Nguyen et al 2018 97. Nobili et al 2018 98. Nota et al 2018 99. Nota et al 2019 100. O'Bryant et al, 2008 101. Olson-Kennedy, Garofalo et al 2019 102. Olson-kennedy, Rosenthal et al 2018 103. Ott et al 2010 104. Pelusi et al 2014 105. Pflum et al 2015 106. Pradhan & Gomez-Lobo, 2019 107. Pullen Sansfacon et al 2015 108. Rider, McMorris et al 2019 109. Rosen et al 2019 110. Rosenthal 2014 111. Rosenthal et al 2016 112. Rothernberg et al 2019 113. Rowniak et al 2019 114. Ryan 2009 115. Ryan et al 2010 116. Safer & Tangpricha 2019 117. Schagen et al 2016 118. Schechter & Safa, 2018 119. Schneider et al 2015 120. Schwartz et al 2019 121. Seal et al 2012 122. Shumer at al 2016 123. Silverberg et al 2017 124. Smith et al 2014 125. Smith et al 2018 126. Taliaferro et al 2019 127. Tangpricha & den Heijer 2017 128. Ter Wengel et al 2016 129. Tishelman & Neumann-Mascis, 2018 130. Tishelman et al 2015 131. Toorians et al 2003 132. T'Sjoen et al 2005 133. T'Sjoen et al 2019 134. van Caenegem, Verhaeghe et al 2013

	135. van Dijk et al 2019 136. Vinogradova et al 2019 137. Vlot et al 2017 138. Weinand & Safer 2015 139. White Hughto & Reisner, 2016 140. Wiepjes et al 2019 141. Wierckx et al 2013 142. Wierckx, Mueller et al, 2012 143. Wierckx, van Caenegem et al 2014 144. Wierckx, van de Peer et al, 2014 *145.* Witcomb et al 2018
Citation identified within the NICE 2020 evidence review	*Listed as an excluded study in the evidence review:* 1. de Vries et al, 2014 2. Klaver et al 2020 3. Turban, King et al 2020 *Included in the evidence review:* 1. de Vries, Steensma et al, 2011 2. Klink, Caris et al 2015
Citation identified as part of the literature surveillance report	*Identified from the literature search but sifted out because of not meeting the PICO criteria based on the title and abstract details:* 1. Angus et al, 2021 2. T'Sjoen et al 2020 *Identified from the literature search but did not meet the PICO criteria based on reading the full text:* 1. Millington et al 2020 2. Lee, Finlayson et al 2020 3. Rew et al 2020 *Identified from the literature search, did meet the PICO criteria but did not materially affect the conclusions of the NICE 2020 evidence review:* 1. Schagen et al, 2020
Citation identified as part of stakeholder testing	*Identified during stakeholder testing but did not meet the PICO criteria:* 1. Hembree et al 2017
Citation identified as part of public consultation	*Identified during public consultation but did not meet the PICO criteria or search methodology of the NICE 2020 evidence review:*

	1. Bangalore Krishna et al, 2019 2. Russell et al 2018 3. Wiepjes et al 2018
New citation that does not fall within the search methodology	*Not identified from the searches performed for the literature surveillance report, nor during stakeholder testing nor during public consultation:* 1. Aldridge et al, 2020 2. Antun et al, 2020 3. Chlebowski, 2020 4. De Blok et al, 2020 5. Defreyne, Elaut et al 2020 6. Eisenberg et al 2020 7. Gava et al 2020 8. Kuper et al 2020 9. Kvist et al 2020 10. Nobili et al 2020 11. Prince & Safer, 2020 12. Sofer et al, 2020 13. Taub et al 2020 14. Van de Grift et al 2020 15. Vereecke et al 2020 16. Wiepjes et al 2020 17. Wilson et al 2020 18. Yeung et al 2020 19. Banks et al, 2021 20. Braun et al, 2021 21. Chantrapanichkul et al, 2021 22. Dy et al 2021 23. Gezer et al 2021 24. Greenwald et al 2021 25. Irwig, 2021 26. Kozato et al 2021 27. Kuijpers et al 2021 28. Kyinn et al 2021 29. Rosenthal 2021 30. Safer, 2021 31. Weill et al 2021
New citation that falls within PICO and search methodology but does not materially affect the conclusions of the existing evidence review	None

New citation that falls within PICO and search methodology, that does materially affect the conclusions of the NICE 2020 evidence review.	None
Updated evidence review to be undertaken (to be agreed with CET)	Not applicable

Completed by:	Dr Robert Wilson
Date:	26 February 2024

Peer reviewed and supported by:	Not applicable
Date:	Not applicable

Reference List

- Adeleye, A. J., Cedars, M. I., Smith, J., & Mok-Lin, E. (2019). Ovarian stimulation for fertility preservation or family building in a cohort of transgender men. Journal of Assisted Reproduction and Genetics, 36(10), 2155–2161. https://doi.org/10.1007/s10815-019-01558-y
- Aldridge, Z., Patel, S., Guo, B., Nixon, E., Bouman, W. P., Witcomb, G., & Arcelus, J. (2020). Long term effect of gender affirming hormone treatment on depression and anxiety symptoms in transgender people: A prospective cohort study, Andrology, 1–9. https://doi.org/10.1111/ andr.12884.
- Allen, L. R., Watson, L. B., Egan, A. M., & Moser, C. N. (2019). Well-being and suicidality among transgender youth after gender-affirming hormones. Clinical Practice in Pediatric Psychology, 7(3), 302–311. https://doi. org/10.1037/cpp0000288.

- Alzahrani, T., Nguyen, T., Ryan, A., Dwairy, A., McCaffrey, J., Yunus, R., Forgione, J., Krepp, J., Nagy, C., Mazhari, R., & Reiner, J. (2019). Cardiovascular disease risk factors and myocardial infarction in the transgender population. Circulation: Cardiovascular Quality and Outcomes, 12(4), e005597. https:// doi.org/10.1161/CIRCOUTCOMES.119.005597
- Anai, T., Miyazaki, F., Tomiyasu, T., Matsuo, T. (2001). Risk of irregular menstrual cycles and low peak bone mass during early adulthood associated with age at menarche. Pediatrics International, 43(5), 483–488. https://doi. org/10.1046/j.1442-200x.2001.01442.x
- Angus, L. M., Nolan, B. J., Zajac, J. D., & Cheung, A. S. (2020). A systematic review of antiandrogens and feminization in transgender women. Clinical Endocrinology, 94(5), 743–752. https://doi.org/10.1111/cen.14329.
- Antun, A., Zhang, Q., Bhasin, S., Bradlyn, A., Flanders, W. D., Getahun, D., & Goodman, M. (2020). Longitudinal changes in hematologic parameters among transgender people receiving hormone therapy. Journal of the Endocrine Society, 4(11), 1–11. https://doi.org/10.1210/ jendso/bvaa119
- Arcelus, J., Claes, L., Witcomb, G. L., Marshall, E., & Bouman, W. P. (2016). Risk factors for non-suicidal self-injury among trans youth. Journal of Sexual Medicine, 13(3), 402–412. https://doi.org/10.1016/j.jsxm.2016.01.003.
- Ashley, F. (2019e). Thinking an ethics of gender exploration: Against delaying transition for transgender and gender creative youth. Clinical Child Psychology and Psychiatry, 24(2), 223–236. https://doi.org/10.1177/1359104519836462
- Asscheman, H., T'Sjoen, G., Lemaire, A., Mas, M., Meriggiola, M. C., Mueller, A., Kuhn, A., Dhejne, C., Morel-Journel, N., & Gooren, L. J. (2014). Venous thrombo-embolism as a complication of cross-sex hormone treatment of male-to-female transsexual subjects: A review. Andrologia, 46(7), 791–795. https://doi. org/10.1111/and.12150
- Bangalore Krishna, K., Fuqua, John S., Rogol, Alan D., Klein, Karen O., Popovic, J., Houk, Christopher P., Charmandari, E., & Lee, Peter A. (2019). Use of gonadotropin-releasing hormone analogs in children: Update by an international consortium. Hormone Research in Paediatrics, 91(6), 357–372. https://doi. org/10.1159/000501336.
- Banks, K., Kyinn, M., Leemaqz, S. Y., Sarkodie, E., Goldstein, D., & Irwig, M.S. (2021). Blood pressure fffects of gender-affirming hormone therapy in transgender and gender-diverse adults. Hypertension, 77(6), 2066–2074. https://doi.org/10.1161/HYPERTENSIONAHA.120.16839
- Barrow, K., & Apostle, D. (2018). Addressing mental health conditions often experienced by transgender and gender expansive children. In C. E. Keo-Meier & D. E. Ehrensaft (Eds.), The gender affirmative model: An interdisciplinary approach to supporting transgender and gender expansive International Journal of Transgender Health S183 children. American Psychological Association. https:// www.jstor.org/stable/j.ctv1chrwv9
- Bauer, G. R., & Hammond, R. (2015). Toward a broader conceptualization of trans women's sexual health. The Canadian Journal of Human Sexuality, 24(1), 1–11. https://doi.org/10.3138/cjhs.24.1-CO1.
- Becerra-Culqui, T. A., Liu, Y., Nash, R., Cromwell, L., Flanders, W. D., Getahun, D., Giammattei, S. V., Hunkeler, E. M., Lash, T. L., Millman, A., Quinn, V. P., Robinson, B., Roblin, D., Sandberg, D. E., Silverberg, M. J., Tangpricha, V., & Goodman, M. (2018). Mental health of transgender and gender nonconforming youth compared with their peers. Pediatrics, 141(5), e20173845. https://doi.org/10.1542/peds.2017-3845.
- Beek, T. F., Kreukels, B. P. C., Cohen-Kettenis, P. T., & Steensma, T. D. (2015). Partial treatment requests and underlying motives of applicants for gender affirming interventions. The Journal of Sexual Medicine, 12(11), 2201–2205. https://doi.org/10.1111/jsm.13033.

- Bertelloni, S., Baroncelli, G. I., Ferdeghini, M., Menchini-Fabris, F., & Saggese, G. (2000). Final height, gonadal function and bone mineral density of adolescent males with central precocious puberty after therapy with gonadotropin-releasing hormone analogues. European Journal of Pediatrics, 159(5), 369–374. https://doi. org/10.1007/s004310051289.
- Bisson, J. R., Chan, K. J., & Safer, J. D. (2018). Prolactin levels do not rise among transgender women treated with estradiol and spironolactone. Endocrine Practice, 24(7), 646–651. https://doi.org/10.4158/EP-2018-0101.
- Bockting, W. O., Miner, M. H., Swinburne Romine, R. E., Hamilton, A., & Coleman, E. (2013). Stigma, mental health, and resilience in an online sample of the US transgender population. American Journal of Public Health, 103(5), 943–951. https://doi.org/10.2105/ AJPH.2013.301241.
- Borghei-Razavi, H., Fragoza-Padilla, V., Hargus, G., Bakhti, S., & Schick, U. (2014). Meningioma: The unusual growth in a transsexual patient after estrogen-progesterone therapy. SOJ Neurology, 1(1), 1–3. https://doi.org/10.15226/ 2374-6858/1/2/00109
- Bouman, M. B., van der Sluis, W. B., van Woudenberg Hamstra, L. E., Buncamper, M. E., Kreukels, B. P. C., Meijerink, W., & Mullender, M. G. (2016). Patient-reported esthetic and functional outcomes of primary total laparoscopic intestinal vaginoplasty in transgender women with penoscrotal hypoplasia. Journal of Sexual Medicine, 13(9), 1438–1444. https://doi.org/10.1016/j. jsxm.2016.06.009.
- Bouman, W. P., Claes, L., Brewin, N., Crawford, J. R., Millet, N., Fernandez-Aranda, F., & Arcelus, J. (2017). Transgender and anxiety: A comparative study between transgender people and the general population. International Journal of Transgenderism, 18(1), 16–26.
- Bouman, W. P., Davey, A., Meyer, C., Witcomb, G. L., & Arcelus, J. (2016). Predictors of psychological well-being among treatment seeking transgender individuals. Sexual and Relationship Therapy, 31(3), 359–375. https://doi.org /10.1080/14681994.2016.1184754.
- Braun, H., Zhang, Q., Getahun, D., Silverberg, M. J., Tangpricha, V., Goodman, M., & Yeung, H. (2021). Moderate-to-severe acne and mental health symptoms in transmasculine persons who have received testosterone. JAMA Dermatology, 157(3), 344–346. https://doi. org/10.1001/jamadermatol.2020.5353.
- Canonico, M., Oger, E., Plu-Bureau, G., Conard, J., Meyer, G., Lévesque, H., & Scarabin, P. Y. (2007). Hormone therapy and venous thromboembolism among postmenopausal women: Impact of the route of estrogen administration and progestogens: The ESTHER study. Circulation, 115 (7), 840–845. https://doi.org/10.1161/ CIRCULATIONAHA.106.642280.
- Carel, J. C., Eugster, E. A., Rogol, A., Ghizzoni, L., & Palmert, M. R. (2009). Consensus statement on the use of gonadotropin-releasing hormone analogs in children. Pediatrics, 123(4), e752–e762. https://doi.org/10.1542/ peds.2008-1783.
- Carswell, J. M., & Roberts, A. L. (2017). Induction and maintenance of amenorrhea in transmasculine and nonbinary adolescents. Transgender Health, 2, 195–201. https://doi.org/10.1089/trgh.2017.0021.
- Chan, K. J., Liang J. J., Jolly, D., Weinand, J. D., & Safer J. D. (2018). Exogenous testosterone does not induce or exacerbate the metabolic features associated with PCOS among transgender men. Endocrine Practice 24(6), 565– 572. https://doi.org/10.4158/EP-2017-0247.
- Chantrapanichkul, P., Stevenson, M. O., Suppakitjanusant, P., Goodman, M., & Tangpricha, V. (2021). Serum hormone concentrations in transgender individuals receiving gender-affirming hormone therapy: A longitudinal retrospective cohort Study. Endocrine Practice, 27(1), 27–33. https://doi.org/10.4158/EP-2020-0414.

- Chen, D., Hidalgo, M. A., Leibowitz, S., Leininger, J., Simons, L., Finlayson, C., & Garofalo, R. (2016). Multidisciplinary care for gender-diverse youth: A narrative review and unique model of gender-affirming care. Transgender Health, 1(1), 117–123. https://doi.org/10.1089/ trgh.2016.0009.
- Cheng, P. J., Pastuszak, A. W., Myers, J. B., Goodwin, I. A., & Hotaling, J. M. (2019). Fertility concerns of the transgender patient. Translational Andrology and Urology, 8(3), 209–218. https://doi.org/10.21037/tau.2019.05.09.
- Chlebowski, R. T., Anderson, G. L., Aragaki, A. K., Manson, J. E., Stefanick, M. L., Pan, K., Barrington, W., Kuller, L. H., Simon, M. S., Lane, D., Johnson, K. C., Rohan, T. E., Gass, M., Cauley, J. A., Paskett, E. D., Sattari, M., & Prentice, R. L. (2020). Association of menopausal hormone therapy with breast cancer incidence and mortality during long-term follow-up of the women's health initiative randomized clinical trials. JAMA, 324(4), 369– 380. https://doi.org/10.1001/jama.2020.9482.
- Colebunders, B., Brondeel, S., D'Arpa, S., Hoebeke, P., & Monstrey, S. (2017). An update on the surgical treatment for transgender patients. Sexual Medicine Reviews, 5(1), 103–109. https://doi.org/10.1016/j.sxmr.2016.08.001.
- Coleman, E., Bockting, W., Botzer, M., Cohen-Kettenis, P., DeCuypere, G., Feldman, J., Fraser, L., Green, J., Knudson, G., Meyer, W. J., Monstrey, S., Adler, R. K., Brown, G. R., Devor, A. H., Ehrbar, R., Ettner, R., Eyler, E., Garofalo, R., Karasic, D. H., Lev, A. I., Mayer, G., Meyer-Bahlburg, H., Hall, B. P., Pfaefflin, F., Rachlin, K., Robinson, B., Schechter, L. S., Tangpricha, V., van Trotsenburg, M., Vitale, A., Winter, S., Whittle, S., Wylie, K. R., & Zucker, K. (2012). Standards of care for the health of transsexual, transgender, and gender-nonconforming people, Version 7. International Journal of Transgenderism, 13(4), 165–232. https://doi.org/10.1080/15532739.2011.700873
- Colizzi, M., Costa, R., & Todarello, O. (2014). Transsexual patients' psychiatric comorbidity and positive effect of cross-sex hormonal treatment on mental health: Results from a longitudinal study. Psychoneuroendocrinology, 39, 65–73. https://doi.org/10.1016/j.psyneuen.2013.09.029
- Comite, F., Cutler, G. B., Jr., Rivier, J., Vale, W. W., Loriaux, D. L., & Crowley, W. F., Jr. (1981). Short-term treatment of idiopathic precocious puberty with a long-acting analogue of luteinizing hormone-releasing hormone. A preliminary report. New England Journal of Medicine, 305(26), 1546–1550. https://doi.org/10.1056/ nejm198112243052602
- Coolhart, D., Ritenour, K., & Grodzinski, A. (2017). Experiences of ambiguous loss for parents of transgender male youth: A phenomenological exploration. Contemporary Family Therapy, 40(1), 28–41. https://doi. org/10.1007/s10591-017-9426-x.
- Costa, R., Carmichael, P., & Colizzi, M. (2016). To treat or not to treat: Puberty suppression in childhood-onset gender dysphoria. Nature Reviews Urology, 13(8), 456–462. https://doi.org/10.1038/nrurol.2016.128
- Davey, A., Bouman, W. P., Arcelus, J., Meyer, C. (2014). Social support and psychological wellbeing: A comparison of patients with gender dysphoria and matched controls. Journal of Sexual Medicine, 11(12), 2976–2985. https:// doi.org/10.1111/jsm.12681
- Davis, S. A., & Meier, S. C. (2014). Effects of testosterone treatment and chest reconstruction surgery on mental health and sexuality in female-to-male transgender people. International Journal of Sexual Health, 26(2), 113–128. https://doi.org/10.1080/19317611.2013.833152
- de Blok, C. J. M., Staphorsius, A. S., Wiepjes, C. M., Smit, J. M., Nanayakkara, P. W. B., & den Heijer, M. (2020). Frequency, determinants, and satisfaction of breast augmentation in trans women receiving hormone treatment. The Journal of Sexual Medicine, 17(2), 342–348. https:// doi.org/10.1016/j.jsxm.2019.10.021.

- de Roo, C., Lierman, S., Tilleman, K., Peynshaert, K., Braeckmans, K., Caanen, M., Lambalk, C. B., Weyers, S., T'Sjoen, G., Cornelissen, R., & De Sutter, P. (2017). Ovarian tissue cryopreservation in female-to-male transgender people: Insights into ovarian histology and physiology after prolonged androgen treatment. Reproductive Biomedicine Online, 34(6), 557–566. https://doi. org/10.1016/j.rbmo.2017.03.008
- de Roo, C., Tilleman, K., T'Sjoen, G., & De Sutter, P. (2016). Fertility options in transgender people. International Review of Psychiatry, 28(1), 112–119. https://doi.org/10. 3109/09540261.2015.1084275
- de Vries, A. L. C., McGuire, J. K., Steensma, T. D., Wagenaar, E. C. F., Doreleijers, T. A. H., & Cohen-Kettenis, P. T. (2014). Young adult psychological outcome after puberty suppression and gender reassignment. Pediatrics, 134(4), 696–704. https://doi.org/10.1542/peds.2013-2958.
- de Vries, A. L. C., Steensma, T. D., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2011). Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. The Journal of Sexual Medicine, 8(8), 2276–2283. https://doi.org/10.1111/j.1743-6109. 2010.01943.x.
- Defreyne, J., Elaut, E., Kreukels, B., Fisher, A. D., Castellini, G., Staphorsius, A., & T'Sjoen, G. (2020). Sexual desire changes in transgender individuals upon initiation of hormone treatment: Results from the longitudinal European Network for the Investigation of Gender Incongruence. The Journal of Sexual Medicine, 17(4), 812–825. https://doi.org/10.1016/j.jsxm.2019.12.020.
- Defreyne, J., Nota, N., Pereira, C., Schreiner, T., Fisher, A. D., den Heijer, M., & T'Sjoen, G. (2017). Transient elevated serum prolactin in trans women is caused by Cyproterone Acetate treatment. LGBT Health, 4(5), 328– 336. https://doi.org/10.1089/lgbt.2016.0190.
- Defreyne, J., Vantomme, B., Van Caenegem, E., Wierckx, K., De Blok, C. J. M., Klaver, M., & T'Sjoen, G. (2018). Prospective evaluation of hematocrit in gender-affirming hormone treatment: Results from European Network for the Investigation of Gender Incongruence. Andrology, 6(3), 446–454. https://doi.org/10.1111/andr.12485.
- Dekker, M. J., Wierckx, K., Van Caenegem, E., Klaver, M., Kreukels, B. P., Elaut, E., & T'Sjoen, G. (2016). A International Journal of Transgender Health S195 European Network for the investigation of gender incongruence: Endocrine part. The Journal of Sexual Medicine, 13(6), 994–999. https://doi.org/10.1016/j.jsxm.2016.03.371.
- Delemarre-van de Waal, H. A., & Cohen-Kettenis, P. T. (2006). Clinical management of gender identity disorder in adolescents: A protocol on psychological and paediatric endocrinology aspects. European Journal of Endocrinology, 155(Suppl. 1), S131–S137. https://doi. org/10.1530/eje.1.02231.
- Deutsch, M. B. (2016a). Guidelines for the primary and gender-affirming care of transgender and gender nonbinary people (2nd ed.). University of California, San Francisco, Department of Family and Community Medicine Center of Excellence for Transgender Health. https://transcare.ucsf.edu/guidelines
- Deutsch, M. B., Bhakri, K., & Kubicek, K. (2015). Effects of cross-sex hormone treatment on transgender women and men. Obstetric Gynecology, 125(3), 605–610. https:// doi.org/10.1097/AOG.0000000000000692.
- Djordjevic, M. L., Majstorovic, M., Stanojevic, D., Bizic, M., Ducic, S., Kojovic, V., & Perovic, S. (2008). One-stage repair of severe hypospadias using combined buccal mucosa graft and longitudinal dorsal skin flap. European Journal of Pediatric Surgery, 18(6), 427–430. https://doi. org/10.1055/s-2008-1038929.
- Du Bois, S. N., Yoder, W., Guy, A. A., Manser, K., & Ramos, S. (2018). Examining associations between state-level transgender policies and transgender health. Transgender Health, 3(1), 220–224. https://doi.org/10.1089/ trgh.2018.0031

- Dy, G. W., Granieri, M. A., Fu, B. C., Vanni, A. J., Voelzke, B., Rourke, K. F., Elliott, S. P., Nikolavsky, D., & Zhao, L. C. (2019). Presenting complications to a reconstructive urologist after masculinizing genital reconstructive surgery. Urology, 132, 202–206. https://doi.org/10.1016/j. urology.2019.04.051.
- Eisenberg, M. E., Gower, A. L., McMorris, B. J., Rider, G. N., Shea, G., & Coleman, E. (2017). Risk and protective factors in the lives of transgender/gender nonconforming adolescents. Journal of Adolescent Health, 61(4), 521–526. https://doi.org/10.1016/j.jadohealth.2017.04.014.
- Eisenberg, M. E., McMorris, B. J., Rider, G. N., Gower, A. L., & Coleman, E. (2020). “It’s kind of hard to go to the doctor’s office if you’re hated there.” A call for gender-affirming care from transgender and gender diverse adolescents in the United States. Health & Social Care in the Community, 28(3), 1082–1089. https://doi. org/10.1111/hsc.12941
- Ethics Committee of the American Society for Reproductive Medicine. (2015). Access to fertility services by transgender persons: An Ethics Committee opinion. Fertility and Sterility, 104(5), 1111–1115. https://doi.org/10.1016/j. fertnstert.2015.08.021.
- Finlayson, C., Johnson, E. K., Chen, D., Dabrowski, E., Gosiengfiao, Y., Campo-Engelstein, L., & Woodruff, T. K. (2016). Proceedings of the working group session on fertility preservation for individuals with gender and sex diversity. Transgender Health, 1(1), 99–107. https://doi. org/10.1089/trgh.2016.0008.
- Fisher, A. D., Castellini, G., Ristori, J., Casale, H., Cassioli, E., Sensi, C., & Maggi, M. (2016). Cross-sex hormone treatment and psychobiological changes in transsexual persons: Two-year follow-up data. The Journal of Clinical Endocrinology & Metabolism, 101(11), 4260–4269. https:// doi.org/10.1210/jc.2016-1276
- Fitzpatrick, L. A., Pace, C., Wiita, B. (2000). Comparison of regimens containing oral micronized progesterone or medroxyprogesterone acetate on quality of life in postmenopausal women: A cross-sectional survey. Journal of Womens Health & Gender-Based Medicine. 9(4), 381–387. https://doi.org/10.1089/15246090050020691
- Frey, J. D., Poudrier, G., Thomson, J. E., & Hazen, A. (2017). A historical review of gender-affirming medicine: Focus on genital reconstruction surgery. Journal of Sexual Medicine, 14(8), 991–1002. https://doi.org/10.1016/j. jsxm.2017.06.007.
- Gaither, T. W., Awad, M. A., Osterberg, E. C., Murphy, G. P., Romero, A., Bowers, M. L., & Breyer, B. N. (2018). Postoperative complications following primary penile inversion vaginoplasty among 330 male-to-female transgender patients. Journal of Urology, 199(3), 760–765. https://doi.org/10.1016/j.juro.2017.10.013.
- Gava, G., Cerpolini, S., Martelli, V., Battista, G., Seracchioli, R., & Meriggiola, M. C. (2016). Cyproterone acetate vs leuprolide acetate in combination with transdermal oestradiol in transwomen: A comparison of safety and effectiveness. Clinical Endocrinology, 85(2), 239–246. https:// doi.org/10.1111/cen.13050.
- Gava, G., Mancini, I., Alvisi, S., Seracchioli, R., & Meriggiola, M. C. (2020). A comparison of 5-year administration of cyproterone acetate or leuprolide acetate in combination with estradiol in transwomen. European Journal of Endocrinology, 183(6), 561–569. https://doi.org/10.1530/ EJE-20-0370
- Gava, G., Mancini, I., Cerpolini, S., Baldassarre, M., Seracchioli, R., & Meriggiola, M. C. (2018). Testosterone undecanoate and testosterone enanthate injections are both effective and safe in transmen over 5 years of administration. Clinical Endocrinology, 89(6), 878–886. https://doi.org/10.1111/cen.13821
- Gezer, E., Piro, B., Cantürk, Z., Çetinarslan, B., Sözen, M., Selek, A., Işik, A. P., & Seal, L. J. (2021). The comparison of gender dysphoria, body image satisfaction and quality of life between treatment-naive transgender males with and without polycystic ovary syndrome. Transgender Health. Advance online publication. https://doi. org/10.1089/trgh.2021.0061

- Giltay, E. J., & Gooren, L. J. (2000). Effects of sex steroid deprivation/administration on hair growth and skin sebum production in transsexual males and females. Journal of Clinical Endocrinology and Metabolism, 85(8), 2913– 2921. https://doi.org/10.1210/jcem.85.8.6710.
- Giltay, E. J., Gooren, L. J. G., Emeis, J. J., Kooistra, T., & Stehouwer, C. D. A. (2000). Oral, but not transdermal, administration of estrogens lowers tissue-type plasminogen activator levels in humans without affecting endothelial synthesis. Arteriosclerosis, Thrombosis, and Vascular Biology, 20(5), 1396–1403. https://doi.org/10.1161/01. ATV.20.5.1396.
- Goldstein, Z., Khan, M., Reisman, T., & Safer, J. D. (2019). Managing the risk of venous thromboembolism in transgender adults undergoing hormone therapy. Journal of Blood Medicine, 10, 209–216. https://doi.org/10.2147/JBM. S166780.
- Gómez-Gil, E., Zubiaurre-Elorza, L., Esteva, I., Guillamon, A., Godás, T., Cruz Almaraz, M., & Salamero, M. (2012). Hormone-treated transsexuals report less social distress, anxiety and depression. Psychoneuroendocrinology, 37(5),
- Gorin-Lazard, A., Baumstarck, K., Boyer, L., Maquigneau, A., Gebleux, S., Penochet, J., Pringuey, D., Albarel, F., Morange, I., Loundou, A., Berbis, J., Auquier, P., Lançon, C., & Bonierbale, M. (2012). Is hormonal therapy associated with better quality of life in transsexuals? A cross-sectional study. The Journal of Sexual Medicine, 9(2), 531–541. https://doi.org/10.1111/j.1743-6109.2011.02564.x.
- Gorin-Lazard, A., Baumstarck, K., Boyer, L., Maquigneau, A., Penochet, J. C., Pringuey, D., & Auquier, P. (2013). Hormonal therapy is associated with better self-esteem, mood, and quality of life in transsexuals. The Journal of Nervous and Mental Disease, 201(11), 996–1000. https:// doi.org/10.1097/nmd.0000000000000046
- Gower, A. L., Rider, G. N., Brown, C., McMorris, B. J., Coleman, E., Taliaferro, L. A., & Eisenberg, M. E. (2018). Supporting transgender and gender diverse youth: Protection against emotional distress and substance use. American Journal of Preventive Medicine, 55(6), 787–794. https://doi.org/10.1016/j.amepre.2018.06.030.
- Greenwald, P., Dubois, B., Lekovich, J., Pang, J. H., & Safer, J. D. (2021). Successful in vitro fertilization in a cisgender female carrier using oocytes retrieved from a transgender man maintained on testosterone. AACE Clinical Case Reports, 8(1), 19–21. https://doi.org/10.1016/j. aace.2021.06.007.
- Grossman, A. H., & D'Augelli, A. R. (2006). Transgender youth: Invisible and vulnerable. Journal of Homosexuality, 51(1), 111–128. https://doi.org/10.1300/J082v51n01_06.
- Grynberg, M., Fanchin, R., Dubost, G., Colau, J. C., Bremont-Weil, C., Frydman, R., & Ayoubi, J. M. (2010). Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. Reproductive Biomedicine Online, 20(4), 553–558. https://doi.org/10.1016/j.rbmo.2009.12.021.
- Hembree, W. C., Cohen-Kettenis, P. T., Gooren, L., Hannema, S. E., Meyer, W.J, Hassan Murad, M, Rosenthal, S. M., Safer, J. D., Tangpricha, V., & T'Sjoen, G. G. (2017). Endocrine treatment of gender-dysphoric/ gender-incongruent persons: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, 102(11), 3869–3903. https:// doi.org/10.1210/jc.2017-01658.
- Hembree, W. C., Cohen-Kettenis, P., Delemarre-van de Waal, H. A., Gooren, L. J., Meyer, W. J., Spack, N. P., Tangpricha, V., & Montori, V. M. (2009). Endocrine treatment of transsexual persons: An endocrine society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism, 94(9), 3132–3154. https:// doi.org/10.1210/jc.2009-0345.
- Hendricks, M. L., & Testa, R. J. (2012). A conceptual framework for clinical work with transgender and gender nonconforming clients: An adaptation of the Minority Stress

Model. Professional Psychology: Research and Practice, 43(5), 460–467. https://doi.org/10.1037/a0029597
- Heylens, G., Elaut, E., Kreukels, B. P. C., Paap, M. C. S., Cerwenka, S., Richter-Appelt, H., Cohen-Kettenis, P. T., Haraldsen, I. R., & De Cuypere, G. (2014). Psychiatric characteristics in transsexual individuals: Multicentre study in four European countries. British Journal of Psychiatry, 204(2), 151–156. https://doi.org/10.1192/bjp. bp.112.121954.
- Horbach, S. E., Bouman, M. B., Smit, J. M., Ozer, M., Buncamper, M. E., & Mullender, M. G. (2015). Outcome of vaginoplasty in male-to-female transgenders: A systematic review of surgical techniques. The Journal of Sexual Medicine, 12(6), 1499–1512. https://doi.org/10.1111/ jsm.12868.
- Irwig, M. S. (2018). Cardiovascular health in transgender people. Reviews in Endocrine and Metabolic Disorders, 19(3), 243–251. https://doi.org/10.1007/s11154-018-9454-3.
- Irwig, M. S. (2021). Is there a role for 5α-reductase inhibitors in transgender individuals? Andrology, 9(6), 1729– 1731. https://doi.org/10.1111/andr.12881.
- Irwig, M. S., Childs, K., & Hancock, A. B. (2017). Effects of testosterone on the transgender male voice. Andrology, 5(1), 107–112. https://doi.org/10.1111/andr.12278.
- Iwamoto, S. J., Defreyne, J., Rothman, M. S., Van Schuylenbergh, J., Van de Bruaene, L., Motmans, J., & T'Sjoen, G. (2019). Health considerations for transgender women and remaining unknowns: A narrative review. Therapeutic Advances in Endocrinology and Metabolism, 10, 204201881987116. https:// doi.org/10.1177/2042018819871166.
- Iwamoto, S. J., T'Sjoen, G., Safer, J. D., Davidge-Pitts, C. J., Wierman, M. E., Glodowski, M. B., & Rothman, M. S. (2019). Letter to the editor: "Progesterone is important for transgender women's therapy—Applying evidence for the benefits of progesterone in ciswomen". The Journal of Clinical Endocrinology & Metabolism, 104(8), 3127–3128. https://doi.org/10.1210/jc.2019-00249.
- Jiang, D. D., Gallagher, S., Burchill, L., Berli, J., & Dugi, D., 3rd. (2019). Implementation of a pelvic floor physical therapy program for transgender women undergoing gender-affirming vaginoplasty. Obstetrics and Gynecology, 133(5), 1003–1011. https://doi.org/10.1097/ AOG.0000000000003236.
- Jiang, D., Witten, J., Berli, J., & Dugi, D., 3rd. (2018). Does depth matter? Factors affecting choice of vulvoplasty over vaginoplasty as gender-affirming genital surgery for transgender women. The Journal of Sexual Medicine, 15(6), 902–906. https://doi.org/10.1016/j.jsxm.2018.03.085.
- Kailas, M., Lu, H. M. S., Rothman, E. F., & Safer, J. D. (2017). Prevalence and types of gender-affirming surgery among a sample of transgender endocrinology patients prior to state expansion of insurance coverage. Endocrine Practice, 23(7), 780–786. https://doi.org/10.4158/EP161727. OR.
- Keo-Meier, C. L., & Ehrensaft, D. (2018). Introduction to the gender affirmative model. In C. Keo-Meier & D. Ehrensaft (Ed.), The gender affirmative model: An interdisciplinary approach to supporting transgender and gender expansive children (pp. 3–19). Washington, DC: American Psychological Association
- Keo-Meier, C. L., & Fitzgerald, K. M. (2017). Affirmative psychological testing and neurocognitive assessment with transgender adults. The Psychiatric Clinics of North America, 40(1), 51–64. https://doi.org/10.1016/j. psc.2016.10.011
- Keo-Meier, C. L., Herman, L. I., Reisner, S. L., Pardo, S. T., Sharp, C., & Babcock, J. C. (2015). Testosterone treatment and MMPI-2 improvement in transgender men: A prospective controlled study. Journal of Consulting and Clinical Psychology, 83(1), 143–156. https://doi. org/10.1037/a0037599.
- Kerckhof, M. E., Kreukels, B. P. C., Nieder, T. O., Becker-Hébly, I., van de Grift, T. C., Staphorsius, A. S., Elaut, E. (2019). Prevalence of sexual dysfunctions in transgender

persons: Results from the ENIGI follow-up study. The Journal of Sexual Medicine, 16(12), 2018–2029. https://doi.org/10.1016/j.jsxm.2019.09.003.
- Klaver, M., de Mutsert, R., van der Loos, M., Wiepjes, C. M., Twisk, J. W. R., den Heijer, M., & Klink, D. T. (2020). Hormonal treatment and cardiovascular risk profile in transgender adolescents. Pediatrics, 145(3), e20190741. https://doi.org/10.1542/peds.2019-0741.
- Klink, D., Bokenkamp, A., Dekker, C., & Rotteveel, J. (2015). Arterial hypertension as a complication of triptorelin treatment in adolescents with gender dysphoria. Endocrinology and Metabolism International Journal, 2(1), 36–38. https://doi.org/10.15406/emij.2015.02.00008.
- Klink, D., Caris, M., Heijboer, A., van Trotsenburg, M., & Rotteveel, J. (2015). Bone mass in young adulthood following gonadotropin-releasing hormone analog treatment and cross-sex hormone treatment in adolescents with gender dysphoria. The Journal of Clinical Endocrinology & Metabolism, 100(2), E270–E275. https://doi.org/10.1210/jc.2014-2439.
- Klink, D., Caris, M., Heijboer, A., van Trotsenburg, M., & Rotteveel, J. (2015). Bone mass in young adulthood following gonadotropin-releasing hormone analog treatment and cross-sex hormone treatment in adolescents with gender dysphoria. The Journal of Clinical Endocrinology & Metabolism, 100(2), E270–E275. https://doi.org/10.1210/jc.2014-2439.
- Kozato, A., Fox, G. C., Yong, P. C., Shin, S. J., Avanessian, B. K., Ting, J., Yiwei, L., Subha, K., Safer, J. D., & Pang, J. H. (2021). No venous thromboembolism increase among transgender female patients remaining on estrogen for gender-affirming surgery. The Journal of Clinical Endocrinology & Metabolism, 106(4), e1586–e1590. https://doi.org/10.1210/clinem/dgaa966
- Kuijpers, S., Wiepjes, C. M., Conemans, E. B., Fisher, A. D., T'Sjoen, G., & den Heijer, M. (2021). Toward a lowest effective dose of cyproterone acetate in trans women: Results from the ENIGI study. The Journal of Clinical Endocrinology & Metabolism, 106(10), e3936–e3945. https://doi.org/10.1210/clinem/dgab427.
- Kuper, L. E., Mathews, S., & Lau, M. (2019). Baseline mental health and psychosocial functioning of transgender adolescents seeking gender-affirming hormone therapy. Journal of Developmental & Behavioral Pediatrics, 40(8), 589–596. https://doi.org/10.1097/DBP.0000000000000697
- Kuper, L. E., Stewart, S., Preston, S., Lau, M., & Lopez, X. (2020). Body dissatisfaction and mental health outcomes of youth on gender-affirming hormone therapy. Pediatrics, 145(4). https://doi.org/10.1542/peds.2019-3006.
- Kuper, L. E., Wright, L., & Mustanski, B. (2018). Gender identity development among transgender and gender nonconforming emerging adults: An intersectional approach. International Journal of Transgenderism, 19(4), 436–455. https://doi.org/10.1080/15532739.2018.1443869.
- Kvist, O., Luiza Dallora, A., Nilsson, O., Anderberg, P., Sanmartin Berglund, J., Flodmark, C. E., & Diaz, S. (2021). A cross-sectional magnetic resonance imaging study of factors influencing growth plate closure in adolescents and young adults. Acta Paediatrica, 110(4), 1249–1256. https://doi.org/10.1111/apa.15617.
- Kyinn, M., Banks, K., Leemaqz, S. Y., Sarkodie, E., Goldstein, D., & Irwig, M. S. (2021). Weight gain and obesity rates in transgender and gender-diverse adults before and during hormone therapy. International Journal of Obesity, 45(12), 2562–2569. https://doi.org/10.1038/s41366-021-00935-x.
- Laron, Z., Zeev, Z., Kauli, R., Comaru-Schally, A., & Schally, A. (1981). D-Trp6-analogue of luteinising hormone releasing hormone in combination with cyproterone acetate to

treat precocious puberty. The Lancet, 318(8253), 955– 956. https://doi.org/10.1016/s0140-6736(81)91155-7.
- Lee, J. Y., Finlayson, C., Olson-Kennedy, J., Garofalo, R., Chan, Y. M., Glidden, D. V., & Rosenthal, S. M. (2020). Low bone mineral density in early pubertal transgender/ gender diverse youth: Findings from the Trans Youth Care Study. Journal of Endocrine Society, 4(9), https:// doi.org/10.1210/jendso/bvaa065
- Levy, A., Crown, A., & Reid, R. (2003). Endocrine intervention for transsexuals. Clinical Endocrinology, 59(4), 409–418. https://doi.org/10.1046/j.1365-2265.2003.01821.x.
- Light, A. D., Obedin-Maliver, J., Sevelius, J. M., & Kerns, J. L. (2014). Transgender men who experienced pregnancy after female-to-male gender transitioning. Obstetrics and Gynecology, 124(6), 1120–1127. https://doi. org/10.1097/AOG.0000000000000540.
- Mamoojee, Y., Seal, L. J., & Quinton, R. (2017). Transgender hormone therapy: Understanding international variation in practice. Lancet Diabetes & Endocrinology, 5(4), 243–246. https://doi.org/10.1016/ S2213-8587(17)30068-2.
- Mancini, I., Rotilio, A., Coati, I., Seracchioli, R., Martelli, V., & Meriggiola, M. C. (2017). Presentation of a meningioma in a transwoman after nine years of cyproterone acetate and estradiol intake: Case report and literature review. Gynecological Endocrinology, 34(6), 456–459. https://doi.org/10.1080/09513590.2017. 1395839
- Manson, J. E., Chlebowski, R. T., Stefanick, M. L., Aragaki, A. K., Rossouw, J. E., Prentice, R. L., Anderson, G., Howard, B. V., Thomson, C. A., LaCroix, A. Z., Wactawski-Wende, J., Jackson, R. D., Limacher, M., Margolis, K. L., Wassertheil-Smoller, S., Beresford, S. A., Cauley, J. A., Eaton, C. B., Gass, M., …& Wallace, R. B. (2013). Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. The Journal of
- Maraka, S., Singh Ospina, N., Rodriguez-Gutierrez, R., Davidge-Pitts, C. J., Nippoldt, T. B., Prokop, L. J., & Murad, M. H. (2017). Sex steroids and cardiovascular outcomes in transgender individuals: A systematic review and meta-analysis. The Journal of Clinical Endocrinology & Metabolism, 102(11), 3914–3923. https://doi. org/10.1210/jc.2017-01643.
- Marks, D. H., Peebles, J. K., & Dommasch, E. (2019). Hair reduction for transgender persons: What dermatologists should know and how they can help. JAMA Dermatology, 155(5), 525–526. https://doi.org/10.1001/jamadermatol.2019.0149.
- Mattawanon, N., Spencer, J. B., Schirmer, D. A., & Tangpricha, V. (2018). Fertility preservation options in transgender people: A review. Reviews in Endocrine and Metabolic Disorders, 19(3), 231–242. https://doi. org/10.1007/s11154-018-9462-3.
- Meier, S. C., Sharp, C., Michonski, J., Babcock, J. C., & Fitzgerald, K. (2013). Romantic relationships of female-tomale trans men: A descriptive study. International Journal of Transgenderism, 14(2), 75–85. https://doi.org/10.1080/ 15532739.2013.791651.
- Meriggiola, M. C., Armillotta, F., Costantino, A., Altieri, P., Saad, F., Kalhorn, T., & Pelusi, G. (2008). Effects of testosterone undecanoate administered alone or in combination with letrozole or dutasteride in female to male transsexuals. The Journal of Sexual Medicine, 5(10), 2442–2453. https://doi.org/10.1111/j.1743-6109. 2008.00909.x
- Meyer, I. H. (2003). Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: conceptual issues and research evidence. Psychological Bulletin, 129(5), 674–697. https://doi.org/10.1037/0033- 2909.129.5.674
- Millington, K., Liu, E., & Chan, Y. M. (2019). The utility of potassium monitoring in gender-diverse adolescents taking spironolactone. Journal of the Endocrine Society, 3(5), 1031–1038. https://doi.org/10.1210/js.2019-00030.
- Millington, K., Schulmeister, C., Finlayson, C., Grabert, R., Olson-Kennedy, J., Garofalo, R., & Chan, Y. M. (2020). Physiological and metabolic characteristics of a cohort of

transgender and gender-diverse youth in the United States. Journal of Adolescent Health, 67(3), 376–383. https://doi.org/10.1016/j.jadohealth.2020.03.028.
- Moody, C., Fuks, N., Peláez, S., & Smith, N. G. (2015). “Without this, I would for sure already be dead”: A qualitative inquiry regarding suicide protective factors among trans adults. Psychology of Sexual Orientation and Gender Diversity, 2(3), 266. https://doi.org/10.1037/sgd0000130.
- Murad, M. H., Elamin, M. B., Garcia, M. Z., Mullan, R. J., Murad, A., Erwin, P. J., & Montori, V. M. (2010). Hormonal therapy and sex reassignment: A systematic review and meta-analysis of quality of life and psychosocial outcomes. Clinical Endocrinology, 72(2), 214–231. https://doi.org/10.1111/j.1365-2265.2009.03625.x
- Nash, R., Ward, K. C., Jemal, A., Sandberg, D. E., Tangpricha, V., & Goodman, M. (2018). Frequency and distribution of primary site among gender minority cancer patients: An analysis of U.S. national surveillance data. Cancer Epidemiology, 54, 1–6. https://doi.org/10.1016/j. canep.2018.02.008
- Newfield, E., Hart, S., Dibble, S., & Kohler, L. (2006). Female-to-male transgender quality of life. Quality of Life Research, 15(9), 1447–1457. https://doi.org/10.1007/ s11136-006-0002-3
- Neyman, A., Fuqua, J. S., & Eugster, E. A. (2019). Bicalutamide as an androgen blocker with secondary effect of promoting feminization in male-to-female transgender adolescents. The Journal of Adolescent Health, 6 4 (4), 544–546. https://doi.org/10.1016/j. jadohealth.2018.10.296
- Nguyen, H. B., Chavez, A. M., Lipner, E., Hantsoo, L., Kornfield, S. L., Davies, R. D., & Epperson, C. N. (2018). Gender-affirming hormone use in transgender individuals: Impact on behavioral health and cognition. Current Psychiatry Reports, 20(12), 1–9. https://doi.org/10.1007/ s11920-018-0973-0
- Nobili, A., Glazebrook, C., & Arcelus, J. (2018). Quality of life of treatment-seeking transgender adults: A systematic review and meta-analysis. Reviews in Endocrine and Metabolic Disorders, 19(3), 199–220. https://doi. org/10.1007/s11154-018-9459-y.
- Nobili, A., Glazebrook, C., Bouman, W. P., Baron-Cohen, S., & Arcelus, J. (2020). The stability of autistic traits in transgender adults following cross-sex hormone treatment. International Journal of Transgender Health, 21(4)
- Nota, N. M., Wiepjes, C. M., de Blok, C. J. M., Gooren, L. J. G., Kreukels, B. P. C., & den Heijer, M. (2019). Occurrence of acute cardiovascular events in transgender individuals receiving hormone therapy. Circulation, 139(11), 1461–1462. https://doi.org/10.1161/circulationaha.118.038584.
- Nota, N. M., Wiepjes, C. M., de Blok, C. J. M., Gooren, L. J. G., Peerdeman, S. M., Kreukels, B. P. C., & den Heijer, M. (2018). The occurrence of benign brain tumours in transgender individuals during cross-sex hormone treatment. Brain, 141(7), 2047–2054. https://doi.org/10.1093/ brain/awy108.
- O’Bryant, C. L., Flaig, T. W., & Utz, K. J. (2008). Bicalutamide-associated fulminant hepatotoxicity. Pharmacotherapy, 28(8), 1071–1075. https://doi. org/10.1592/phco.28.8.1071
- Olson-Kennedy, J., Chan, Y.-M., Garofalo, R., Spack, N., Chen, D., Clark, L., Ehrensaft, D., Hidalgo, M., Tishelman, A., & Rosenthal, S. (2019). Impact of early medical treatment for transgender youth: Protocol for the longitudinal, observational Trans Youth Care Study. JMIR Research Protocols, 8(7), e14434. https://doi.org/10. 2196/14434
- Olson-Kennedy, J., Rosenthal, S. M., Hastings, J., & Wesp, L. (2018). Health considerations for gender non-conforming children and transgender adolescents. Guidelines for the primary care of transgender and gender nonbinary people. http://transhealth.ucsf.edu/guidelines/youth

- Ott, J., Kaufmann, U., Bentz, E. K., Huber, J. C., & Tempfer, C. B. (2010). Incidence of thrombophilia and venous thrombosis in transsexuals under cross-sex hormone therapy. Fertility and Sterility, 93(4), 1267–1272. https://doi. org/10.1016/j.fertnstert.2008.12.017.
- Pelusi, C., Costantino, A., Martelli, V., Lambertini, M., Bazzocchi, A., Ponti, F., & Meriggiola, M. C. (2014). Effects of three different testosterone formulations in female-to-male transsexual persons. The Journal of Sexual Medicine, 11(12), 3002–3011. https://doi.org/10.1111/ jsm.12698
- Pflum, S. R., Testa, R. J., Balsam, K. F., Goldblum, P. B., & Bongar, B. (2015). Social support, trans community connectedness, and mental health symptoms among transgender and gender nonconforming adults. Psychology of Sexual Orientation and Gender Diversity, 2(3), 281–286. https://doi.org/10.1037/sgd0000122.
- Pradhan, S., & Gomez-Lobo, V. (2019). Hormonal contraceptives, intrauterine devices, gonadotropin-releasing hormone analogues and testosterone: Menstrual suppression in special adolescent populations. Journal of Pediatric and Adolescent Gynecology, 32(5S), S23–S29. https://doi. org/10.1016/j.jpag.2019.04.007.
- Prince, J. C. J., & Safer, J. D. (2020). Endocrine treatment of transgender individuals: Current guidelines and strategies. Expert Review of Endocrinology & Metabolism, 15(6), 395–403. https://doi.org/10.1080/17446651.2020.18 25075.
- Pullen Sansfaçon, A., Robichaud, M.-J., & Dumais-Michaud, A.-A. (2015). The experience of parents who support their children's gender variance. Journal of LGBT Youth, 12, 39–63. https://doi.org/10.1080/19361653.2014. 935555.
- Rew, L., Young, C. C., Monge, M., & Bogucka, R. (2021). Puberty blockers for transgender and gender diverse youth—A critical review of the literature. Child and Adolescent Mental Health, 26(1), 3–14. https://doi. org/10.1111/camh.12437.
- Rider, G. N., Vencill, J. A., Berg, D. R., Becker-Warner, R., Candelario-Pérez, L., & Spencer, K. G. (2019). The gender affirmative lifespan approach (GALA): A framework for competent clinical care with nonbinary clients. International Journal of Transgenderism, 20(2-3), 275–288. https://doi.org/10.1080/15532739.2018.1485069
- Rosen, H. N., Hamnvik, O. R., Jaisamrarn, U., Malabanan, A. O., Safer, J. D., Tangpricha, V., Wattanachanya, L., & Yeap, S. S. (2019). Bone densitometry in transgender and gender non-conforming (TGNC) individuals: 2019 ISCD official position. Journal of Clinical Densitometry, 22(4), 544–553. https://doi.org/10.1016/j.jocd.2019.07.004.
- Rosenthal, S. M. (2014). Approach to the patient: Transgender youth: endocrine considerations. The Journal of Clinical Endocrinology & Metabolism, 99(12), 4379– 4389. https://doi.org/10.1210/jc.2014-1919.
- Rosenthal, S. M. (2016). Transgender youth: Current concepts. Annals of Pediatric Endocrinology & Metabolism, 21(4), 185–192. https://doi.org/10.6065/apem.2016.21.4.185.
- Rosenthal, S. M. (2021). Challenges in the care of transgender youth: An endocrinologist's view. Nature Reviews Endocrinology, 17(10), 581–591 https://doi.org/10.1038/ s41574-021-00535-9
- Rothenberg, S. S., Witchel, S. F., & Menke, M. N. (2019). Oocyte cryopreservation in a transgender male adolescent. New England Journal of Medicine, 380(9), 886–887. https://doi.org/10.1056/NEJMc1813275.
- Rowniak, S., Bolt, L., & Sharifi, C. (2019). Effect of cross-sex hormones on the quality of life, depression and anxiety of transgender individuals: A quantitative systematic review. JBI Evidence Synthesis, 17(9), 1826–1854. https:// doi.org/10.11124/JBISRIR-2017-003869.
- Russell, S. T., Pollitt, A. M., Li, G., & Grossman, A. H. (2018). Chosen name use is linked to reduced depressive symptoms, suicidal ideation, and suicidal behavior among

transgender youth. Journal of Adolescent Health, 6 3 (4), 503–505. https://doi.org/10.1016/j. jadohealth.2018.02.003.
- Ryan, C. (2009). Supportive families, healthy children: Helping families with lesbian, gay, bisexual & transgender (LGBT) children. http://familyproject.sfsu.edu
- Ryan, C., Russell, S. T., Huebner, D., Diaz, R., & Sanchez, J. (2010). Family acceptance in adolescence and the health of LGBT young adults. Journal of Child and Adolescent Psychiatric Nursing, 23(4), 205–213. https://doi. org/10.1111/j.1744-6171.2010.00246.x
- Safer, J. D. (2021). Research gaps in medical treatment of transgender/nonbinary people. The Journal of Clinical Investigation, 131(4), e142029. https://doi.org/10.1172/JCI142029.
- Safer, J. D., & Tangpricha, V. (2019). Care of the transgender patient. Annals of Internal Medicine, 171(1), ITC1– ITC16. https://doi.org/10.7326/aitc201907020.
- Safer, J. D., Coleman, E., Feldman, J., Garofalo, R., Hembree, W., Radix, A., & Sevelius, J. (2016). Barriers to healthcare for transgender individuals. Current Opinion in Endocrinology & Diabetes and Obesity, 23(2), 168–171. https://doi.org/10.1097/med.0000000000000227.
- Schagen, S. E. E., Wouters, F. M., Cohen-Kettenis, P. T., Gooren, L. J., & Hannema, S. E. (2020). Bone development in transgender adolescents treated with GnRH analogues and subsequent gender-affirming hormones. The Journal of Clinical Endocrinology & Metabolism, 105(12). https://doi.org/10.1210/clinem/dgaa604.
- Schechter, L. S., & Safa, B. (2018). Introduction to phalloplasty. Clinics in Plastic Surgery, 45(3), 387–389. https:// doi.org/10.1016/j.cps.2018.03.014.
- Schneider, F., Neuhaus, N., Wistuba, J., Zitzmann, M., Heß, J., Mahler, D., & Kliesch, S. (2015). Testicular functions and clinical characterization of patients with gender dysphoria (GD) undergoing sex reassignment surgery (SRS). Journal of Sexual Medicine, 12(11), 2190–2200. https:// doi.org/10.1111/jsm.13022.
- Schwartz, A. R., Russell, K., & Gray, B. A. (2019). Approaches to vaginal bleeding and contraceptive counseling in transgender and gender nonbinary patients. Obstetrics and Gynecology, 134(1), 81–90. https://doi. org/10.1097/aog.0000000000003308
- Seal, L. J., Franklin, S., Richards, C., Shishkareva, A., Sinclaire, C., & Barrett, J. (2012). Predictive markers for mammoplasty and a comparison of side effect profiles in transwomen taking various hormonal regimens. The Journal of Clinical Endocrinology & Metabolism, 97(12), 4422–4428. https://doi.org/10.1210/jc.2012-2030
- Shumer, D. E., Nokoff, N. J., & Spack, N. P. (2016). Advances in the care of transgender children and adolescents. Advances in Pediatrics, 63(1), 79–102. https://doi. org/10.1016/j.yapd.2016.04.018.
- Silverberg, M. J., Nash, R., Becerra-Culqui, T. A., Cromwell, L., Getahun, D., Hunkeler, E., & Goodman, M. (2017). International Journal of Transgender Health. Cohort study of cancer risk among insured transgender people. Annals of Epidemiology, 27(8), 499–501. https:// doi.org/10.1016/j.annepidem.2017.07.007.
- Smith, A. J., Hallum-Montes, R., Nevin, K., Zenker, R., Sutherland, B., Reagor, S., & Brennan, J. M. (2018). Determinants of transgender individuals' well-being, mental health, and suicidality in a rural state. Journal of Rural Mental Health, 42(2), 116. https://doi.org/10.1037/ rmh0000089.
- Smith, N. L., Blondon, M., Wiggins, K. L., Harrington, L.B/, van Hylckama Vlieg, A., Floyd, J. S., Hwang, M., Bis, J. C., McKnight, B., Rice, K.M, Lumley, T., Rosendaal, F. R., Heckbert, S. R., & Psaty, B. M. (2014). Lower risk of cardiovascular events in postmenopausal women taking oral estradiol compared with oral conjugated equine estrogens. JAMA Internal Medicine, 174(1), 25–31. https:// doi.org/10.1001/jamainternmed.2013.11074.

- Sofer, Y., Yaish, I., Yaron, M., Bach, M. Y., Stern, N., & Greenman, Y. (2020). Differential endocrine and metabolic effects of testosterone suppressive agents in transgender women. Endocrine Practice, 26(8), 883–890. https://doi.org/10.4158/EP-2020-0032.
- T'Sjoen, G. G., Beguin, Y., Feyen, E., Rubens, R., Kaufman, J. M., & Gooren, L. (2005). Influence of exogenous oestrogen or (anti-) androgen administration on soluble transferrin receptor in human plasma. Journal of Endocrinology, 186(1), 61–67. https://doi.org/10.1677/joe.1.06112
- T'Sjoen, G., Arcelus, G., Gooren, L., Klink, D. T., & Tangpricha, V. (2019). Endocrinology of transgender medicine. Endocrine Reviews, 40(1), 97–117.https://doi.org/10.1210/er.2018-00011.
- T'Sjoen, G., Arcelus, J., De Vries, A. L. C., Fisher, A. D., Nieder, T. O., Özer, M., & Motmans, J. (2020). European Society for Sexual Medicine position statement "Assessment and hormonal management in adolescent and adult trans people, with attention for sexual function and satisfaction." The Journal of Sexual Medicine, 17(4), 570–584. https://doi.org/10.1016/j.jsxm.2020.01.012.
- Taliaferro, L. A., McMorris, B. J., Rider, G. N., & Eisenberg, M. E. (2019). Risk and protective factors for self-harm in a population-based sample of transgender youth. Archives of Suicide Research, 23(2), 203–221. https://doi.org/10.1080/13811118.2018.1430639.
- Tangpricha, V., & den Heijer, M. (2017). Oestrogen and anti-androgen therapy for transgender women. Lancet Diabetes & Endocrinology, 5(4), 291–300. https://doi.org/10.1016/S2213-8587(16)30319-9.
- Taub, R. L., Ellis, S. A., Neal-Perry, G., Magaret, A. S., Prager, S. W., & Micks, E. A. (2020). The effect of testosterone on ovulatory function in transmasculine individuals. American Journal of Obstetrics and Gynecology, 223(2), 229–e1. https://doi.org/10.1016/j.ajog.2020.01.059.
- Ter Wengel, P. V., Martin, E., Gooren, L., Den Heijer, M., & Peerdeman, S. M. (2016). Meningiomas in three male-to-female transgender subjects using oestrogens/progestogens and review of the literature. Andrologia, 48(10), 1130–1137. https://doi.org/10.1111/and.12550.
- Tishelman, A. C., Kaufman, R., Edwards-Leeper, L., Mandel, F. H., Shumer, D. E., & Spack, N. P. (2015). Serving transgender youth: Challenges, dilemmas, and clinical examples. Professional Psychology: Research and Practice, 46(1), 37–45. https://doi.org/10.1037/a0037490.
- Tishelman, A., & Neumann-Mascis, A. (2018). Gender-related trauma. In The gender affirmative model: An interdisciplinary approach to supporting transgender and gender expansive children (pp. 85–100). American Psychological Association.
- Toorians, A. W. F. T., Thomassen, M. C. L. G. D., Zweegman, S., Magdeleyns, E. J. P., Tans, G., Gooren, L. J. G., & Rosing. (2003). Venous thrombosis and changes of hemostatic variables during cross-sex hormone treatment in transsexual people. The Journal of Clinical Endocrinology & Metabolism, 88(12), 5723–5729. https://doi.org/10.1210/jc.2003-030520.
- Turban, J. L., King, D., Carswell, J. M., & Keuroghlian, A. S. (2020). Pubertal suppression for transgender youth and risk of suicidal ideation. Pediatrics, e20191725. https://doi.org/10.1542/peds.2019-1725.
- Van Caenegem, E., Taes, Y., Wierckx, K., Vandewalle, S., Toye, K., Kaufman, J. M., Schreiner, T., Haraldsen, I., & T'Sjoen, G. (2013). Low bone mass is prevalent in male-to-female transsexual persons before the start of cross-sex hormonal therapy and gonadectomy. Bone, 54(1), 92–97. https://doi.org/10.1016/j.bone.2013.01.039.

- Van de Grift, T., Van Gelder, Z., Mullender, M., Steensma, T., de Vries, ALC., & Bouman, M. (2020). Timing of puberty suppression and surgical options for transgender youth. Pediatrics, 146(5), e20193653. https://doi. org/10.1542/peds.2019-3653.
- Van Dijk, D., Dekker, M., Conemans, E. B., Wiepjes, C. M., de Goeij, E. G. M., Overbeek, K. A., & T'Sjoen, G. (2019). Explorative prospective evaluation of short-term subjective effects of hormonal treatment in trans people—Results from the European Network for the Investigation of Gender Incongruence. The Journal of Sexual Medicine, 16(8), 1297–1309. https://doi. org/10.1016/j.jsxm.2019.05.009
- Van Kesteren, P. J., Asscheman, H., Megens, J. A., & Gooren, L. J. (1997). Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Clinical Endocrinology, 47(3), 337–342. https://doi.org/10.1046/ j.1365-2265.1997.2601068.x
- Vereecke, G., Defreyne, J., Van Saen, D., Collect, S., Van Dorpe, J., T'Sjoen, G., & Gooseens, E. I. (2021). Characterisation of testicular function and spermatogenesis in transgender women. Human Reproduction, 36(1), 5–15. https://doi.org/10.1093/humrep/deaa254.
- Vinogradova, Y., Coupland, C., & Hippisley-Cox, J. (2019). Use of hormone replacement therapy and risk of venous thromboembolism: Nested case-control studies using the QResearch and CPRD databases. British Medical Journal, 364, k4810. https://doi.org/10.1136/bmj.k4810.
- Vlot, M. C., Klink, D. T., den Heijer, M., Blankenstein, M. A., Rotteveel, J., & Heijboer, A. C. (2017). Effect of pubertal suppression and cross-sex hormone therapy on bone turnover markers and bone mineral apparent density (BMAD) in transgender adolescents. Bone, 95, 11–19. https://doi.org/10.1016/j.bone.2016.11.008.
- Weill, A., Nguyen, P., Labidi, M., Cadier, B., Passeri, T., Duranteau, L., Bernat, A. L., Yoldjian, I., Fontanel, S., Froelich, S., & Coste, J. (2021). Use of high dose cyproterone acetate and risk of intracranial meningioma in women: Cohort study. British Medical Journal (Clinical Research Edition.), 372, n37. https://doi.org/10.1136/bmj. n37.
- Weinand, J. D., & Safer, J. D. (2015). Hormone therapy in transgender adults is safe with provider supervision; A review of hormone therapy sequelae for transgender individuals. Journal of Clinical and Translational Endocrinology, 2(2):55–60. https://doi.org/10.1016/j. jcte.2015.02.003.
- White Hughto, J. M., & Reisner, S. L. (2016). A systematic review of the effects of hormone therapy on psychological functioning and quality of life in transgender individuals. Transgender Health, 1(1), 21–31. https://doi. org/10.1089/trgh.2015.0008.
- Wiepjes, C. M., de Blok, C. J., Staphorsius, A. S., Nota, N. M., Vlot, M. C., de Jongh, R. T., & den Heijer, M. (2020). Fracture risk in trans women and trans men using long-term gender-affirming hormonal treatment: A nationwide cohort study. Journal of the American Society for Bone and Mineral Research, 35(1), 64–70. https://doi. org/10.1002/jbmr.3862
- Wiepjes, C. M., den Heijer, M., & T'Sjoen, G. G. (2019). Bone health in adult trans persons: An update of the literature. Current Opinion in Endocrinology, Diabetes and Obesity, 26(6), 296–300. https://doi.org/10.1097/ MED.0000000000000502.
- 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). The Amsterdam cohort of Gender Dysphoria study (1972-2015): Trends in prevalence, treatment, and regrets. Journal of Sexual Medicine, 15(4), 582–590. https://doi.org/10.1016/j.jsxm.2018.01.016
- Wierckx, K., Elaut, E., Declercq, E., Heylens, G., De Cuypere, G., Taes, Y., Kaufman, J. M., & T'Sjoen, G. (2013). Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: A case-control study. European Journal of Endocrinology, 169(4), 471–478. https://doi.org/10.1530/ EJE-13-0493.

- Wierckx, K., Mueller, S., Weyers, S., Van Caenegem, E., Roef, G., Heylens, G., & T'Sjoen, G. (2012). Long-term evaluation of cross-sex hormone treatment in transsexual persons. Journal of Sexual Medicine, 9(10), 2641–2651. https://doi.org/10.1111/j.1743-6109.2012.02876.x
- Wierckx, K., Van Caenegem, E., Schreiner, T., Haraldsen, I., Fisher, A. D., Toye, K., Kaufman, J. M., & T'Sjoen, G. (2014). Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: Results from the European network for the investigation of gender incongruence. Journal of Sexual Medicine, 11(8), 1999– 2011. https://doi.org/10.1111/jsm.12571.
- Wierckx, K., Van de Peer, F., Verhaeghe, E., Dedecker, D., Van Caenegem, E., Toye, K., & T'Sjoen, G. (2014). Shortand long-term clinical skin effects of testosterone treatment in trans men. Journal of Sexual Medicine, 11(1), 222–229. https://doi.org/10.1111/jsm.12366.
- Wilson, L. M., Baker, K. E., Sharma, R., Dukhanin, V., McArthur, K., & Robinson, K. A. (2020). Effects of antiandrogens on prolactin levels among transgender women on estrogen therapy: A systematic review. International Journal of Transgender Health, 21(4), 391–402. https:// doi.org/10.1080/15532739.2020.1819505.
- Witcomb, G. L., Bouman, W. P., Claes, L., Brewin, N., Crawford, J., & Arcelus, J. (2018). Levels of depression in transgender people and its predictors: Results of a large matched control study with transgender people accessing clinical services. Journal of Affective Disorders, 235, 308–315. https://doi.org/10.1016/j.jad.2018.02.051.
- Yeung, H., Ragmanauskaite, L., Zhang, Q., Kim, J., Tangpricha, V., Getahun, D., & Goodman, M. (2020). Prevalence of moderate to severe acne in transgender adults: A cross-sectional survey. Journal of the American Academy of Dermatology, 83(5), 1450–1452. https://doi. org/10.1016/j.jaad.2020.02.053.