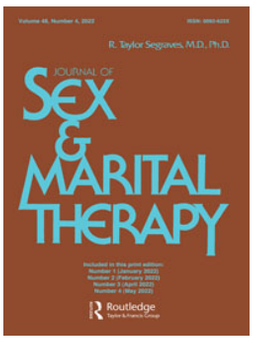

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BRIEF REPORT

Commentary on Levine: A Tale of Two Informed Consent Processes

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ABSTRACT

This commentary compares two recently published informed consent recommendations for gender dysphoria. One key difference identified is in their assessment of the strength of the evidence base for the gender affirming treatment model. An evaluation of both authors' citations supports the claims of a weak evidence base for the use of puberty blockers and gender affirming hormonal treatments in youth with gender dysphoria. This commentary then reflects on the implications of this. In particular, it asks whether it would be best practice to provide gender affirming treatments for youth only under clinical research conditions, rather than as routine clinical practice.

Introduction

"Reconsidering Informed Consent for Trans-Identified Children, Adolescents and Young Adults" (Levine, Abbruzzese, & Mason, 2022) is a timely and important paper. This Commentary asks the question: How does Levine et al.'s recommended informed consent process compare to current informed consent practices for youth with gender dysphoria? This question is addressed through an evaluation and comparison of Levine et al.'s informed consent process with those of a recently published "Informed Consent Standards of Care" (AusPATH, 2022). A key difference is the respective authors' evaluation of the strength of the evidence base for the gender affirming treatment model. This Commentary interrogates the citations these authors use for their respective claims regarding the strength of the evidence base. It finds that Levine et al.'s claims of a weak evidence base are well supported. A second question then reflected upon is: Given the weak evidence base for gender affirming treatments for youth, should these interventions be only available as part of clinical research trials, rather than implemented as routine treatments?

Terminology

Terminology in this area of medicine is varied and complex. As we are discussing clinical treatment and informed consent, I use the medical nomenclature of gender dysphoria (GD) (American Psychiatric Association, 2013). When directly reporting from other publications I generally use their preferred terminology. Levine et al.'s paper considers informed consent as it pertains to children, adolescents and young adults. I use the generic term "youth" to describe this group. Gender affirming treatment (GAT) is used to refer to a broad range of affirming health care

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approaches including: Support of, and assistance, with social gender transition, provision of puberty blockers, gender affirmative hormone treatment and surgery. Gender affirming hormones treatment (GAHT) refers to cross-sex hormones (estrogens and testosterone) and anti-androgens.

A comparison of Levine et al.'s recommended informed consent process with AusPATH's "Informed Consent Standards of Care"

Shortly after reading Levine et al.'s paper, particularly as an Australian psychiatrist, I was interested to read the Australian Professional Association for Trans Health's (AusPATH) "Australian Informed Consent Standards of Care for Gender Affirming Hormone Therapy," which were released on March 31, 2022 (AusPATH, 2022). Informed consent practices will vary across different settings. However, this recent "Informed Consent Standards of Care" provides a useful exemplar to flesh-out how Levine et al.'s recommended informed consent approach compares to current practice standards. AusPATH is an organization closely linked to WPATH (many AusPATH members, including the President and Vice-President, are also WPATH members). Thus, despite this Commentary's Australian focus, it also holds much relevance to the international context. (Of additional note, WPATH's "Standards of Care" are currently in flux, with the most recent edition not yet released in its final form, so it is not possible to evaluate any updated informed consent recommendations).

Levine et al. (2022) recommendations apply to all GAT available to GD youth. Frequent references are made to the clinical diagnoses of gender dysphoria (DSM) and gender incongruence (ICD). Levine et al. contend that an adequate informed consent process requires: Careful and thorough evaluation; assessment of capacity; involvement of parents; a full disclosure of the short and long-term risks and benefits; a discussion of the full range of alternative treatment options; and a disclosure of the weak evidence base for these interventions. The authors emphasize that informed consent needs to be a slow and thoughtful process, culminating in signed consent forms.

AusPATH (2022) focuses on the use of GAHT, although it also includes some discussion of social and surgical interventions, for trans people of all relevant ages. The trans person is described as the expert on their own gender and needs. There is no requirement for a psychiatric "gender assessment." It is only in the context of adolescents, under the age of 18, that any reference is made to the requirement for a gender dysphoria (DSM) diagnosis and there is also scant reference to gender incongruence (ICD) diagnosis. It is noted that the outlined informed consent model can be used for adolescents under the age of 18, but a discussion is included of the more complicated clinical and legal situation, in Australia, for this group. AusPATH's recommended informed consent approach coheres with Levine et al. (2022) in advising that the risks and benefits of the treatments should be discussed with the patient and, for patients under age 18, parents or guardians. In addition, they advise the patient should be informed of the limitations of the hormones to effect certain changes (for example, height) and they note the need for lifelong monitoring and review. Examples of written information sheets and consent forms for the patient and parent to sign are provided. The process of evaluation, informed consent, and initiating hormones is described as being able to be undertaken "in just one or two appointments," although it is noted that it may require more time.

Some of the important differences between these two informed consent approaches to highlight are:

a. Levine et al. recommend a discussion of the limitations of the evidence base for GAT, whereas no mention of this is made by AusPATH.
b. Levine et al. emphasize the evaluation and informed consent processes should be a slow process. AusPATH states that the process of assessment, education, informed consent and the initiation of hormones can be completed in as little as one session.

c. Levine et al. recommend patients are informed of the risk of regret and detransition, whereas AusPATH does not mention this.
d. Levine et al. require the clinician to discuss the full range of alternative treatment options. AusPATH does not note alternative treatment options and informed consent seems to be equated with affirmation, as they state: "The informed consent model of care is sometimes called affirmation enablement or ethical affirmation."

These differences can be partly understood by differences in the authors' evaluations of the evidence base of GAT. Levine et al. (2022) claim that the evidence base for the benefits of GAT is "widely recognized" as deficient and is of very low quality and certainty. AusPATH (2022) claim that there is a "significant" and "clear" body of evidence that GAT improves quality of life and leads to better mental health outcomes.

It has previously been noted that these types of contradictory opinions can be found in the professional literature and highlighted that the merits of the various claims need to be evaluated by a close reading of the cited primary sources (Clayton et al., 2021). To that end, I will interrogate the citations and ask: Do they support the authors' claims? (Of course, the reader is free, and I would encourage it, to similarly evaluate my citations.) As both authors' citations primarily focus on puberty blockers and GAHT, this, rather than social transition and surgical treatments, will be the focus of discussion in this commentary.

Reviewing Levine et al.'s claims of very low quality evidence for puberty blockers and gender affirming hormone treatments for youth with gender dysphoria

Levine et al., in support of their claims of a deficient and very low quality evidence base for puberty blockers and GAHT for adolescents, cite Hembree et al. (2017) and the National Institute for Health and Care Excellence (NICE) (2020a, 2020b). Hembree et al. (2017) rated the evidence for the use of puberty blockers and GAHT in adolescents as being either low or very low quality. NICE (2020a, 2020b) concluded that the studies investigating the benefits or adverse effects of puberty blockers and GAHT were uncontrolled observational studies, subject to bias and confounding. The studies' quality was appraised with the Newcastle-Ottawa tool and certainty of outcomes by modified GRADE. All studies were rated as "poor quality" and all outcomes as "very low certainty."

In sum, Levine et al.'s claims of a very low quality and certainty evidence base for puberty blockers and GAHT for adolescents appears to be well supported by the cited references.

Reviewing AusPATH's claims of a clear and significant body of evidence for puberty blockers and gender affirming hormone treatments for trans people, including trans adolescents

AusPATH (2022) cite three sources to support their claim of a significant body of evidence showing that medical GAT improves psychological outcomes and improve quality of life. The first of these is a primary study reporting that access to GAHT in adolescence is associated with improved mental health outcomes among transgender adults (Turban, King, Kobe, Reisner, & Keuroghlian, 2022). This recent study has not yet been externally evaluated in a systematic review process. However, this study's design (a non-probability cross-sectional survey) puts it at high risk of bias, and, as the authors themselves noted, it cannot determine causality. Further, the limitations of the source data have been the subject of previous critiques (D'Angelo et al., 2021).

Secondly, AusPATH (2022) cite their own public statement (AusPATH, 2021), which stated: "Medical and surgical affirmation can frequently alleviate gender-related distress and yield a variety of other benefits to the individual." Sixteen references are cited in support of this statement, but no information is provided on the quality nor on the certainty of

findings. Three of these references are systematic reviews, one of which (White Hughto & Reisner, 2016) is the third citation in AusPATH (2022). This review of GAHT in transgender adults concluded that there was only "low quality" evidence that "suggests" GAHT "may" lead to psychological improvements and it recommended more prospective controlled trials be undertaken. All the reviewed studies were found to be at high risk of bias, and it was noted that they did not adjust for important confounders, for example concurrent psychotherapy or psychiatric medications. This conclusion does not appear to well support AusPATH's(2022) claims of a clear and significant body of evidence to support the use of medical GAT.

However, could it be that the other studies and systematic reviews cited in AusPATH (2021) provide more solid evidence? AusPATH (2021) cites seven primary studies, either on puberty blockers or GAHT in youth. Five of these were evaluated by NICE (2020a, 2020b). As already discussed, all these studies were found to be of poor quality and provide very low certainty evidence. What did the other systematic reviews cited by AusPATH (2021) report?

Multiple systematic reviews of puberty blockers and gender affirming hormonal treatments for adolescents note the weakness of the evidence

For thoroughness, and to minimize risks of "cherry-picking" the evidence, I will expand beyond the three systematic reviews cited by AusPATH (2021) (which were: Mahfouda, Moore, Siafarikas, Zepf, and Lin (2017, Mahfouda et al., 2019); White Hughto and Reisner (2016)). Two other systematic reviews, Chew, Anderson, Williams, May, and Pang (2018) and Rew Young, Monge, and Bogucka (2021a) have been recently cited as support for strong claims of the benefits of puberty blockers and/or GAHT in adolescents (Baams, 2021; Tordoff et al., 2022). There is also a review by Baker et al. (2021) which was commissioned by WPATH and included both adolescent and adults.

A reading of these reviews reveals consistent comments noting the scarce and poor quality empirical evidence base underpinning the use of puberty blockers and GAHT. These reviews emphasize that the reviewed studies are mostly subject to high risk of bias and confounding and that more rigorous evidence is required. The Baker et al. (2021) review noted there was insufficient evidence to allow conclusions to be drawn regarding the impact of hormone therapy on death by suicide in transgender people. One review, Rew, Young, Monge, and Bogucka (2021a), appeared to claim a causal link between puberty blockers and decreased adult suicidality. However, following a published critique by Clayton et al. (2021) the authors clarified they were not making any causal claims and placed emphasis on their conclusion that more rigorous studies were required (Rew, Young, Monge, Bogucka, 2021b).

In sum, the findings of these reviews do not seem consistent with any claims, including those made by AusPATH (2022), that there is a significant or clear or robust body of evidence that puberty blockers and/or GAHT for GD youth improve mental health and quality of life outcomes. Furthermore, the two reviews discussed here that addressed GAHT in adults found the evidence to be similarly weak. The findings of these systematic reviews are more consistent with Levine et al.'s claims of a weak evidence base for these treatments.

Alternative approaches

As described by Levine et al., alternative treatment options for GD youth include various forms of psychotherapy, family therapy and group therapy. These are well described in the literature (for example see: Lemma, 2021; D'Angelo et al., 2021; Kozlowska et al., 2021; Hakeem, 2012). It is important to note, as Levine et al. emphasize, that these alternatives also lack a rigorous evidence base. However, also important, they do not hold the gravity of the potential injuries that do the hormonal and surgical treatments.

Therapeutic illusions and placebo effects: what weight should be given to clinical experience as evidence?

Some clinicians seem to claim that clinical experience stands as important evidence for the use of GAT (Olson-Kennedy, 2019; Pang, Wiggins, & Telfer, 2022). However, it is important to remember clinicians' testimonies of the success of the treatments they offer is known to be unreliable (Fanaroff et al., 2020). One example, noted as long ago as 1865, is that there had long been clinical consensus that the treatment of pneumonia by bloodletting was most efficacious, but comparative experimentation in the first half of the nineteenth century showed this to be "a mere therapeutic illusion" (Lilienfeld, 1982). Humans have a tendency to overestimate the effects of their actions, often called the "illusion of control." In medicine this may manifest as a "therapeutic illusion," whereby both doctors and patients may have an unjustified enthusiasm for a treatment (Casarett, 2016).

Placebo effects are rarely discussed by gender medicine clinicians and researchers (Clayton, 2022a). Contemporary placebo researchers describe placebo effects as the beneficial effects attributable to the brain-mind responses evoked by the treatment context rather than to the specific intervention (Wager & Atlas, 2015). Social stimuli and the whole therapeutic ritual, including medical marketing, affect the patient's neuro-psycho-biological state, and this in turn impacts, negatively or positively, on response to treatment (Benedetti, 2021). Thus, for treatments without a rigorous evidence base, especially those that are heavily promoted by clinicians, media, social media and celebrity culture, the possibility that any observed benefit may be due to the social and therapeutic milieu, rather than the specific effect of the intervention, needs to be considered. This is even more imperative if the interventions have high risk of serious and irreversible adverse effects.

Clinician experience should not be disregarded, but therapeutic illusions and placebo effects are two of the reasons why we need to have a great deal of caution in depending on clinical experience and clinical consensus as evidence for the effectiveness of medical interventions.

Implications of the weak evidence base for gender affirming treatments

Informed consent

AusPATH (2022) cite the Australian Commission on Safety and Quality in Healthcare's definition of informed consent. This notes that "accurate" and "relevant" information about the healthcare intervention, and alternative options, should be given to the patient. Levine et al. (2022) cite the American Academy of Pediatrics Committee on Bioethics and, similarly, this requires the provision of information on the risks, benefits, and uncertainties of the proposed treatments and alternative treatments. Both these definitions would seem to demand, as recommended by Levine et al., that an adequate informed consent process requires the weaknesses of the evidence base for GAT for GD youth and alternative treatment options to be carefully and thoroughly discussed in an unbiased manner with patients and parents/guardians. These definitions would also seem to necessitate a full and frank discussion of the foreseeable risks of regret and detransition.

There is a further implication of this weak evidence base that requires consideration.

Innovative clinical practice or experimental treatment?

Does the weak evidence of benefits and the adverse risks of GAT mean they should only be offered to GD youth under human research ethics committee approved clinical research conditions? Such an approach would help ensure that all involved (patients, parents and clinicians) are made fully aware of the weak evidence base, as well as contribute to the required rigorous research evidence. Of note, Sweden has recently made changes to their policies with moves in this direction (Socialstyrelsen, 2022).

A brief historical vignette might provide a stimulus to our thinking on these complex issues. From the 1960s until the 1980s, in many countries, children, many with no pathology apart from psychosocial problems considered to be due to their height were prescribed hormonal treatment by endocrinologists. At the time the hormones were declared safe, but years later disastrous long-term side effects became evident. Some of the children treated with cadaveric human growth hormone contracted Creutzfeldt-Jakob Disease (CJD), an aggressive early onset and fatal dementia (Clayton, 2022b; Cohen & Cosgrove, 2010).

In Australia, the Federal government initiated a judicial inquiry into the use of pituitary derived hormones and the Australian Human Pituitary Hormone Program. The report noted that it was a very narrow and a self- interested group, with multiple conflicts of interests, running the program. It found that "*the very power of regulation itself [was] placed in the hands of those who ought to have been the subject of regulation.*" (Allars, 1994, p. 507). One key conclusion was that: *"it is a dangerous situation if no attempt is made to draw the lines between the ordinary exercise of clinical judgment, research, experiment and clinical trial, even if those lines be blurred. The absence of lines is most dangerous when new advances in medicine are being explored*" (Allars, 1994, p. 722). It recommended that the National Health and Medical Research Council (NHMRC) review its human experimentation guidelines to ensure that: "*It provides guidance with regard to decisions as to whether treatment in a therapeutic setting constitutes an experiment*" (Allars, 1994, p.723).

The NHMRC's current statement on ethical conduct in human research includes such a statement: "*This guidance applies to research, but sometimes the distinction between research and innovative clinical practice is unclear. For example, innovative clinical practice occurs on a spectrum from minor changes at the border of established practice that pose little change in risk to patient safety to novel interventions that should only be introduced as part of an ethically approved research protocol*" (NHMRC, 2007/2018, p. 24).

Where do we consider the novel and poorly evidenced GAT approach for GD youth to be on this "spectrum": toward the end of a minor change that poses little risk, or more toward the end of a major change with significant risk of harm to the patients?

Conclusion

This Commentary has demonstrated the deep uncertainty and the many unknowns that face GD youth, their parents and clinicians. Any claims of certainty are premature and risk more harm than benefit, including hindering the rigorous debate and research required to improve the state of knowledge in this area of medicine. In the meantime, as recommended by Levine et al. (2022), if gender affirming treatments are to be offered as routine treatment to youth, then a thoughtful, slow and thorough evaluation and informed consent process, undertaken in a therapeutic setting, would seem optimum care for these young patients. Another option that needs to be carefully considered is whether these interventions should only be offered as part of human research ethics committee approved clinical trials, rather than be implemented as routine treatment.

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References

Allars, M. (1994). *Report of the inquiry into the use of pituitary derived hormones in Australia and Creutzfeldt-Jakob Disease*. Canberra: Australian Government Publishing Service.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Association.

AusPATH. (2021). *Public statement on gender affirming healthcare, including for trans youth – AusPATH*. https://auspath.org.au/2021/06/26/auspath-public-statement-on-gender-affirming-health-care-including-for-trans-youth/

AusPATH. (2022). *Australian informed consent standards of care for gender affirming hormone treatment*. Australia: Australian Professional Association for Trans Health. auspath.org.au

Baams L. (2021). Equity in paediatric care for sexual and gender minority adolescents. *The Lancet. Child & Adolescent Health*, *5*(6), 389–391. doi:10.1016/S2352-4642(21)00129-2

Baker, K. E., Wilson, L. M., Sharma, R., Dukhanin, V., McArthur, K., & Robinson, K. A. (2021). Hormone therapy, mental health, and quality of life among transgender people: A systematic Review. *Journal of the Endocrine Society*, *5*(4), bvab011. doi:10.1210/jendso/bvab011

Benedetti, F. (2021). *Placebo effects: Understanding the mechanisms in health and disease* (3rd ed.). Oxford: Oxford University Press.

Casarett D. (2016). The science of choosing Wisely-Overcoming the Therapeutic Illusion. *The New England Journal of Medicine*, *374*(13), 1203–1205. doi:10.1056/NEJMp1516803

Chew, D., Anderson, J., Williams, K., May, T., & Pang, K. (2018). Hormonal treatment in young people with gender dysphoria: A systematic review. *Pediatrics*, *141*(4), e20173742. doi:10.1542/peds.2017-3742

Clayton, A., Malone, W. J., Clarke, P., Mason, J., & D'Angelo, R. (2021). Commentary: The signal and the noise – Questioning the benefits of puberty blockers for youth with gender dysphoria – a commentary on Rew et al. (2021). *Child and Adolescent Mental Health*, doi:10.1111/camh.12533

Clayton, A. (2022a). The gender affirmative treatment model for gender dysphoria in youth: A perfect storm environment for the placebo effect. The implications for research and clinical practice. [Manuscript submitted for publication]

Clayton A. (2022b). The gender affirmative treatment model for youth with gender dysphoria: A medical advance or dangerous medicine?. *Archives of Sexual Behavior*, *51*(2), 691–698. doi:10.1007/s10508-021-02232-0

Cohen, S., & Cosgrove, C. (2010). Too tall, too small? The temptation to tinker with a child's height. *The Lancet*, *375*(9713), 454–455. doi:10.1016/S0140-6736(10)60185-7

D'Angelo, R., Syrulnik, E., Ayad, S., Marchiano, L., Kenny, D. T., & Clarke, P. (2021). One size does not fit all: In support of psychotherapy for gender dysphoria. *Archives of Sexual Behavior*, *50*(1), 7–16. doi:10.1007/s10508-020-01844-2

Fanaroff, A. C., Califf, R. M., Harrington, R. A., Granger, C. B., McMurray, J., Patel, M. R., Bhatt, D. L., Windecker, S., Hernandez, A. F., Gibson, C. M., Alexander, J. H., & Lopes, R. D. (2020). Randomized trials versus common sense and clinical observation: JACC review topic of the week. *Journal of the American College of Cardiology*, *76*(5), 580–589. doi:10.1016/j.jacc.2020.05.069

Hakeem, A. (2012). Psychotherapy for gender identity disorders. *Advances in Psychiatric Treatment*,*18*, 17–24, doi:10.1192/apt.bp.111.009431

Hembree, W. C., Cohen-Kettenis, P. T., Gooren, L., Hannema, S. E., Meyer, W. J., Murad, M. H., Rosenthal, S. M., Safer, J. D., Tangpricha, V., & T'Sjoen, G. G. (2017). Endocrine treatment of gender-dysphoric/gender-incongruent persons: An endocrine society clinical practice guideline. *The Journal of Clinical Endocrinology and Metabolism*, *102*(11), 3869–3903. doi:10.1210/jc.2017-01658

Lemma, A. (2021). *Transgender identities: A contemporary introduction*. Oxon: Routledge

Kozlowska, K., McClure, G., Chudleigh, C., Maguire, A. M., Gessler, D., Scher, S., & Ambler, G. R. (2021). Australian children and adolescents with gender dysphoria: Clinical presentations and challenges experienced by a multidisciplinary team and gender service. *Human Systems*, *1*(1):70–95. doi:10.1177/26344041211010777

Levine, S. B., Abbruzzese, E., & Mason, J. W. (2022). Reconsidering informed consent for trans-identified children, adolescents, and young adults. *Journal of Sex & Marital Therapy*, 1–22. Advance online publication. doi:10.1080/0092623X.2022.2046221

Lilienfeld, A. M. (1982). The Fielding H. Garrison Lecture: Ceteris paribus: the evolution of the clinical trial. *Bulletin of the History of Medicine*, *56*(1), 1–18.

Mahfouda, S., Moore, J. K., Siafarikas, A., Zepf, F. D., & Lin, A. (2017). Puberty suppression in transgender children and adolescents. *The Lancet. Diabetes & Endocrinology*, *5*(10), 816–826. doi:10.1016/S2213-8587(17)30099-2

Mahfouda, S., Moore, J. K., Siafarikas, A., Hewitt, T., Ganti, U., Lin, A., & Zepf, F. D. (2019). Gender-affirming hormones and surgery in transgender children and adolescents. *The Lancet. Diabetes & Endocrinology*, *7*(6), 484–498. doi:10.1016/S2213-8587(18)30305-X

National Health and Medical Research Council and the Australian Research Council Universities Australia. (2007/2018). *National statement on ethical conduct in human research*. Canberra: NHMRC. https://www.nhmrc.gov.au

National Institute for Health and Care Excellence. (2020a). Evidence review: Gonadotrophin releasing hormone analogues for children and adolescents with gender dysphoria. https://arms.nice.org.uk/resources/hub/1070905/attachment

National Institute for Health and Care Excellence. (2020b). Evidence review: Gender-affirming hormones for children and adolescents with gender dysphoria. https://arms.nice.org.uk/resources/hub/1070871/attachment

Olson-Kennedy, J. (2019). Treating trans youth with Dr Johanna Olson-Kennedy. *Gender GP Medical Podcast*, Jan 17. https://gendergp.com

Pang, K. C., Wiggins, J., Telfer, M. M. (2022). Gender identity services for children and young people in England: Landmark review should interrogate existing international evidence and consensus. *British Medical Journal 377*:o825 doi:10.1136/bmj.o825

Rew, L., Young, C. C., Monge, M., & Bogucka, R. (2021a). Review: Puberty blockers for transgender and gender diverse youth-a critical review of the literature. *Child and Adolescent Mental Health*, *26*(1), 3–14. doi:10.1111/camh.12437

Rew, L., Young, C. C., Monge, M., & Bogucka, R. (2021b). Response: "The Signal and the Noise"–A response to Clayton et al. (2021). *Child and Adolescent Mental Health*. Advance online publication. doi:10.1111/camh.12534

Socialstyrelsen, The National Board of Health and Welfare. (2022). Care of children and adolescents with gender dysphoria. https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/kunskapsstod/2022-3-7799.pdf

Tordoff, D. M., Wanta, J. W., Collin, A., Stepney, C., Inwards-Breland, D. J., & Ahrens, K. (2022). Mental health outcomes in transgender and nonbinary youths receiving gender-affirming care. *JAMA Network Open*, *5*(2), e220978. doi:10.1001/jamanetworkopen.2022.0978

Turban, J. L., King, D., Kobe, J., Reisner, S. L., & Keuroghlian, A. S. (2022). Access to gender-affirming hormones during adolescence and mental health outcomes among transgender adults. *PloS One*, *17*(1), e0261039. doi:10.1371/journal.pone.0261039

Wager, T. D., & Atlas, L. Y. (2015). The neuroscience of placebo effects: Connecting context, learning and health. *Nature Reviews. Neuroscience*, *16*(7), 403–418. doi:10.1038/nrn3976

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. doi:10.1089/trgh.2015.0008]