

Drs Mike and Helen Webberley

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Dear Sir, we wish to complain about the BMJ post on the treatment of gender dysphoric children entitled 'Gender-affirming hormone in children and adolescents', funded by the BBC. <https://blogs.bmj.com/bmjebmspotlight/2019/02/25/gender-affirming-hormone-in-children-and-adolescents-evidence-review/> authored by Carl Heneghan and Tom Jefferson.

Although we fully accept that there is always more research that would be welcome, we have several criticisms of this paper which we believe provides an unbalanced view, cherry-picks and is often factually incorrect. Their biased view supports transphobia and has the potential to cause harm to this group who are protected under the Equality Act 2010.

GMC Good Medical Practice requires that doctors 'must conduct research honestly. If you are concerned about the quality or integrity of the research, including allegations of fraud or misconduct, you must follow the guidance in paragraph 19 on raising concerns. You must report evidence of financial or scientific fraud, or other breaches of this guidance, to an appropriate person in your employing or contracting body, and where appropriate to the GMC or other statutory regulatory bodies.' https://www.gmc-uk.org/-/media/documents/good-practice-in-research-and-consent-to-research_pdf-58834843.pdf

Heneghan and Jefferson refer their figures to the UK "rare disease" website which is highly insulting and pathologising for transgender people. The prevalence data quoted in this paper, significantly underestimates the likely prevalence. A large population-based study from the Williams Institute in the US (2014) has shown prevalence rates of up to 1.4% nationally and as can be seen from the quoted GIDS figures, UK referral rates have tripled since 2014, suggesting that the actual prevalence is very likely to be significantly higher. <https://williamsinstitute.law.ucla.edu/wp-content/uploads/TransAgeReport.pdf>

Pubertal Suppression

Pubertal suppression with Gonadotropin-releasing hormone agonists (GnRHa) has been used as a means of pausing puberty in children with gender dysphoria for 20 years and has been shown to be safe and effective. There was a large and excellent review of 96 papers examining puberty suppression treatment in transgender youth <https://www.sciencedirect.com/science/article/pii/S2213858717300992> and the conclusions drawn were that;

'The limited available evidence suggests that puberty suppression, when clearly indicated, is reasonably safe. The few studies that have examined the psychological effects of suppressing puberty, as the first stage before possible future commencement of CSH therapy, have shown benefits.'

Persistence

Heneghan and Jefferson then misrepresent desistance rates in trans youth by claiming that *'approximately ¾ of pre-pubescent children attending gender identity clinics will not want to change their gender once puberty starts.'*

This claim is based on a highly criticised paper (Wallien 2008) examining desistance rates in an Amsterdam clinic. The authors fail to address the serious flaws in this paper which include the fact that only 77 children out of a cohort of 200 were 'selected' for the study, 19 of those included did not even meet the diagnostic criteria for gender dysphoria and 23 were 'lost to follow up'. These 42 children were all labelled as 'desistors' in this paper. A rather astounding assumption. However Wallien did state that;

'Clinicians should therefore take child and parent reports of cross-gender identification and behaviour seriously, to address them in a timely manner when the subjects enter adolescence. It is conceivable that, in the future, persisting children will be identified and treated with GnRH analogs, even before the actual beginning of puberty'

Most importantly, those numbers are irrelevant to puberty blockers and hormone replacement therapy. The ¾ statistic only refers to pre-pubertal youth, whereas puberty blockers and hormone replacement therapy are only offered after the beginning of puberty.

The authors also cite Schagens paper (2016) and immediately misquote it by saying that *'treatment (with triptorelin) **did** require adjusting because of insufficient suppression'*

However the paper states *'Treatment **did not** have to be adjusted because of insufficient suppression in any subject.'* Furthermore the authors quoted *'further studies should evaluate whether the effects on height and body composition can be reversed during subsequent GAH treatment'* but omitted *'routine monitoring of gonadotropins, sex steroids, creatinine, and liver function is not necessary'* because triptorelin was found to be safe.

Heneghan and Jefferson then cited 3 further papers (Costa, Delamarre-Van de Waal, Staphorsius) in 307 patients, which demonstrate that GnRHa significantly improved global and psychological functioning with no adverse effects on growth, bone density and executive functioning. However rather than dwell on these benefits they then cite a single letter to BMJ expressing the personal and unsubstantiated opinions from three non-practitioners in gender care (momentous step in the dark).

Gender affirming hormones (GAH)

Heneghan and Jefferson allude to potential complications of GAH, including polycythaemia in trans masculine patients and venous thromboembolism (VTE) in trans feminine patients. What they fail to say is that although increases in haematocrit are commonly seen in trans masculine (to reach those of the male phenotype) rarely do they become supra-physiological. Large meta-analysis in hypogonadal men on TRT have shown no increased risk in VTE with [testosterone](https://www.ncbi.nlm.nih.gov/pubmed/28495861)<https://www.ncbi.nlm.nih.gov/pubmed/28495861>

In trans feminine young people, transdermal estradiol valerate is routinely prescribed. There is a very small risk of VTE with this medication which is age dependent and virtually never occurs under the age of 55 and no reports worldwide of VTE in transfeminine children and adolescents. However we do agree that careful monitoring with three monthly bloods is advisable.

In Burke's study, contrary to the misleading evaluation by the authors, this study demonstrated that trans masculine adolescents had very similar results for the magnetic resonance tomography (MRT) to natal males (and different from natal females) and that treatment with testosterone evoked similar changes in the MRT over a period of 10 months treatment to that seen in natal males. In other words, treatment was not associated with a detrimental effect on this higher-order cognitive process.

Heneghan and Jefferson finally discuss the dangers of 'off-label' anti-androgen treatments and in particular spironolactone and cyproterone acetate which they state 'can cause substantial harms and even death'. However they fail to explain that these treatments are used rarely in the UK in adults and never in children and adolescents, where GnRH analogues are the testosterone suppressors of choice.

They finally state that *the current evidence base does not support informed decision making and safe practice.*'

This is fundamental and demonstrates the complete lack of understanding by Heneghan and Jefferson of the issues around treating trans youth and the psychological impact and mental anguish that occurs if treatment is delayed or even refused. Evidence to date suggests that medical treatment of transgender youth is safe and beneficial. There has not been a single published study that had demonstrated significant harm from the use of GnRH agonists and GAH in adolescents. However there is plenty of evidence to show the frequency of self harm and suicide if treatment is delayed.

Although hormonal interventions raise some safety concerns and better studies are needed in elucidating the comparative benefits of different regimens, they are sufficiently safe for current practices. According to the systematic review, Hormonal Treatment in Young People With Gender Dysphoria <https://www.ncbi.nlm.nih.gov/pubmed/29514975> which the blog authors relied upon: "Overall, hormonal treatments for transgender youth were observed to be relatively safe but not without potential adverse effects." <http://www.bioethics.net/2019/03/an-evidence-based-affirmative-perspective-on-hormonal-interventions-for-trans-youth/>

The current international guidance (listed below) is evidence-based and balanced, acknowledging the quality of available evidence when making recommendations. Heneghan and Jefferson have not referred to this guidance, and have instead written a very unbalanced and biased, inaccurate review which does not balance the risk of not treating a trans person.

WPATH - https://www.wpath.org/media/cms/Documents/SOC%20v7/Standards%20of%20Care_V7%20Full%20Book_English.pdf

ENDOCRINE SOCIETY - <https://academic.oup.com/jcem/article/102/11/3869/4157558>

AUSTRALIA - <https://www.rch.org.au/uploadedFiles/Main/Content/adolescent-medicine/australian-standards-of-care-and-treatment-guidelines-for-trans-and-gender-diverse-children-and-adolescents.pdf>

UCSF - <http://transhealth.ucsf.edu/pdf/Transgender-PGACG-6-17-16.pdf>

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