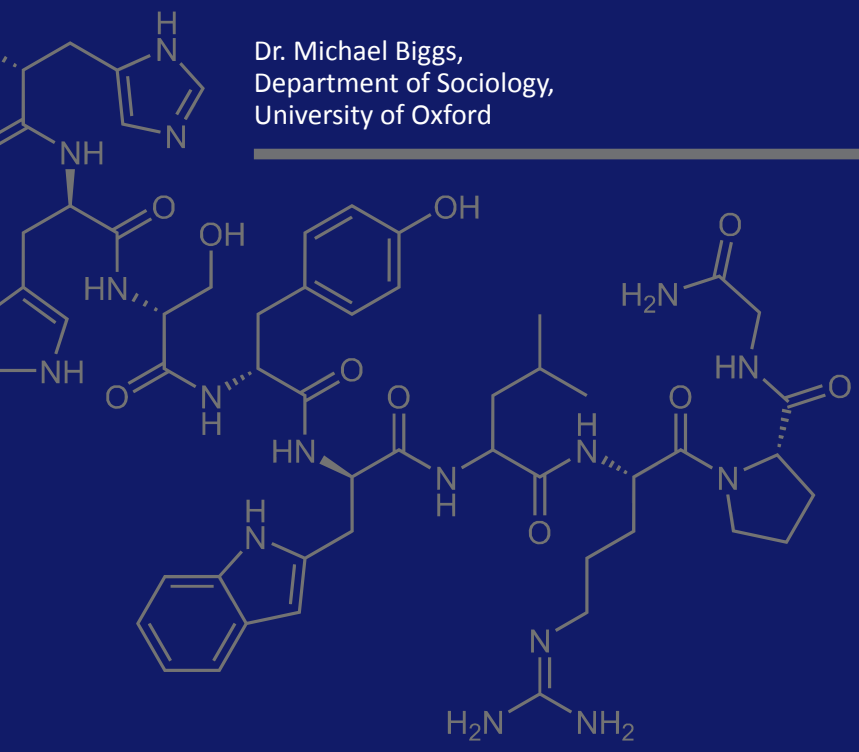
The Tavistock's Experimentation with Puberty Blockers

Dr. Michael Biggs,
Department of Sociology,
University of Oxford



Part 1: Scrutinizing the Evidence

2 March 2019

NHS transgender clinic accused of covering up negative impacts of puberty blockers on children by Oxford professor

share Save

The Tavistock ccentre is an NHS specialised clinic for transgender children in London CREDIT: JEFF BLACKLER/REX SHUTTERSCOCK

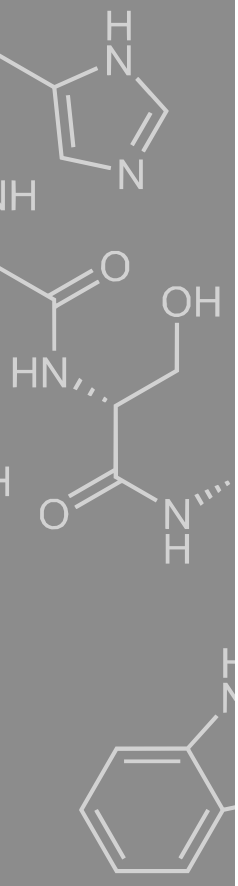
Follow By Camilla Tominey, ASSOCIATE EDITOR and Joani Walsh
7 MARCH 2019 • 9:30PM

In 2010, Tavistock and Portman NHS Trust's Gender Identity Development Service (GIDS) launched a trial of puberty blockers for children in their early teens with gender dysphoria. This was—and remains—an experimental treatment. These drugs, Gonadotropin-Releasing Hormone agonists (GnRHa), have not been certified as a safe or effective treatment for gender dysphoria by their manufacturers, nor by the National Institute for Clinical Excellence.

The Director of GIDS, Polly Carmichael, was keenly aware of the controversy over these drugs. 'The question is, if you halt your own sex hormones so that your brain is not experiencing puberty, are you in some way altering the course of nature?' (Guardian, 14 August 2008). '[T]he debate revolves around the reversibility of this intervention—physical and also psychological, in terms of the possible influence of sex hormones on brain and identity development' (Carmichael and Davidson 2009). Before 2010, GIDS administered blockers to children only when they reached 16; this is the age at which young people have the presumptive capacity to consent to medical treatment.

This cautious approach was vociferously opposed by two organizations devoted to transgendering of children, Mermaids and the Gender Identity Research and Education Society. As Carmichael later recounted: 'There was a lot of pressure coming from certain group [sic] to introduce it—families were travelling abroad because they knew it was available in Holland and America. As a service, we didn't have the evidence one way or the other, so the best way to do it was as part of a research study' (Vice, 16 November 2016).

Tavistock Trust announced the study on its website in April 2011. It stated that GnRHa treatment 'is deemed reversible'. This assertion contradicted the study's own research protocol (which I obtained under Freedom of Information from the NHS Health Research Authority). *'It is not clear* [my emphasis] what the long term effects of early suppression may be on bone development, height, sex organ development, and body shape and their reversibility if treatment is stopped during pubertal development' (Early Pubertal Suppression in a Carefully Selected Group of Adolescents with Gender Identity Disorder, 4 November 2010, Research Ethics Committee number 10/H0713/79). A paediatrician on the study team, Russell Viner, frankly acknowledged the risks. 'If you suppress puberty for three years the bones do not get any stronger at a time when they should be, and we really don't know what suppressing puberty does to your brain development. We are dealing with unknowns' (Daily Mail, 25 February 2012).



The study received considerable publicity, being reported in the *Mirror*, the *Daily Telegraph*, and the *Times*. As Carmichael observed, 'as professionals we need to be looking at the long term and making sure this treatment is safe' (Daily Telegraph, 15 April 2011). The bare outlines of the study can be gleaned from a conference presentation and a half-page published abstract (Gunn et al. 2015a; Gunn et al. 2015b). From 2010 to 2014, 61 children aged between 12 and 15 were recruited; puberty blockers were administered to 44 of them.

Even before the final patient was enrolled, Carmichael announced success to the tabloid press. 'Now we've done the study and the results thus far have been positive we've decided to continue with it' (Daily Mail, 17 May 2014). In fact the decision had already been made, at least six months earlier (Daily Mail, 17 November 2013). Tavistock Trust then embraced the drug regime with enthusiasm. Three years later, GIDS (and its satellite operation in Leeds) had prescribed puberty blockers for a total of 800 adolescents under 18, including 230 children under 14 (Daily Mail, 30 July 2017). By 2018, new prescriptions were running at 300 per year (BBC News, 2 July 2018). Freedom of Information requests have failed to elicit more recent figures because GIDS does not collate basic data on this experimental treatment—and neither does the University College London Hospitals NHS Foundation Trust, which provides its endocrinology services.

Over a thousand adolescents have been given puberty blockers on the basis that the 2010–14 study yielded 'positive' results. Tavistock is surprisingly reticent to share these results with the scientific community. GIDS has a webpage on the evidence base for puberty blockers. It notes that 'research evidence for the effectiveness of any particular treatment offered is still limited.' There is no mention of its own study; it cites only research from the Netherlands. The former director of GIDS stated last year that the 'project is ongoing and the results are yet to be published' (De Ceglie 2018).

Diligent searching does, however, uncover some unpublished results. Most revealing is an appendix within a report to Tavistock's Board of Directors (Carmichael 2015). It tracks the first 30 children on GnRHa, measuring changes after one year of the drug regime. The text is sometimes internally inconsistent and occasionally contradicts the tabulated figures, suggesting that it was prepared in haste. But we can summarize those changes that were reported as statistically significant (p-value < .05). Only one change was positive: 'according to their parents, the young people experience less internalizing behavioural problems' (as measured by the Child Behavior Checklist). There were three negative changes. 'Natal girls showed a significant increase in behavioural and emotional problems', according to their parents (also from the Child Behavior Checklist, contradicting the only positive result). One dimension of the Health Related Quality of Life scale, completed by parents, 'showed a significant decrease in Physical well-being of their child'. What is most disturbing is that after a year on blockers, 'a significant increase was found in the first item "I deliberately try to hurt or kill self"' (in the Youth Self Report questionnaire). Astonishingly, the increased risk of self-harm attracted no comment in Carmichael's report. Given that puberty blockers are prescribed to treat gender dysphoria, it is paradoxical that 'the suppression of puberty does not impact positively on the experience of gender dysphoria' (measured by the Body Image Scale). When differentiated by sex, the impact was positive for boys on one aspect of body image, but negative for girls on two aspects.

Preliminary results (44 children after one year on GnRHa) were also presented at a symposium at the World Professional Association for Transgender Health (Carmichael et al. 2016). Only the abstract is available. 'For the children who commenced the blocker, feeling happier and more confident with their gender identity was a dominant theme that emerged during the semi-structured interviews at 6 months. However, the quantitative outcomes for these children at 1 years time suggest that they also continue to report an *increase in internalising problems and body dissatisfaction* [my emphasis], especially natal girls.' Why were these negative results never published?

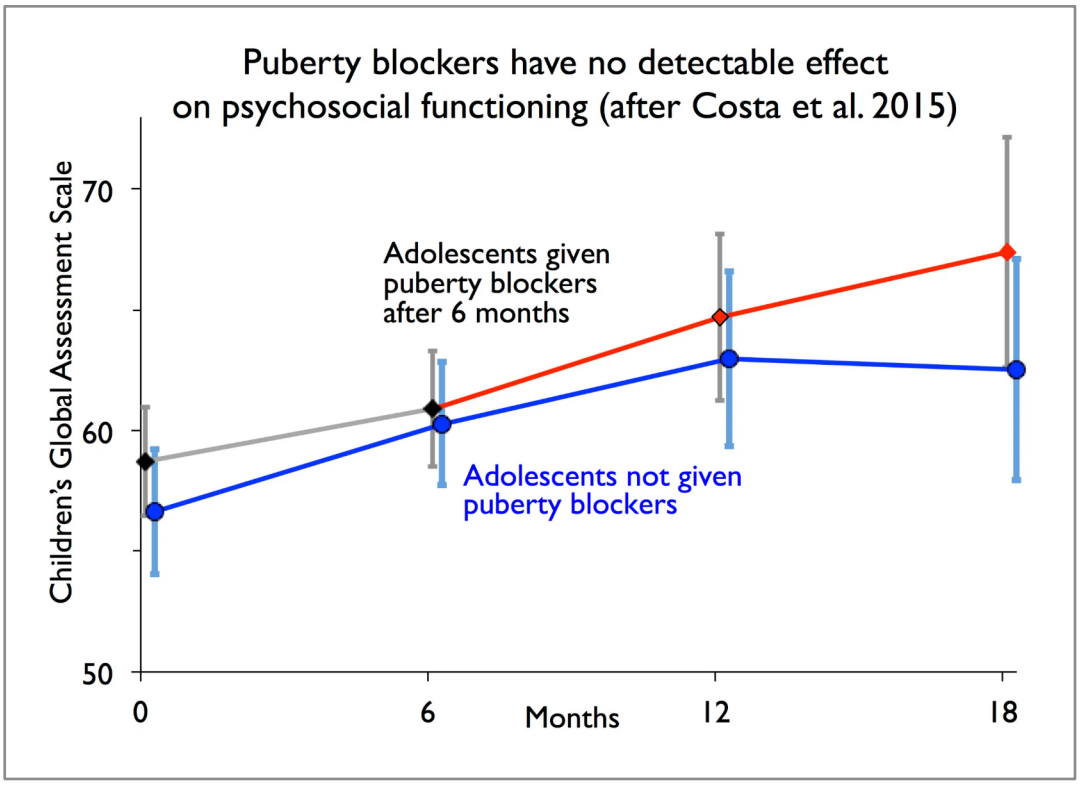
The study apparently contributed data on outcomes to one publication, coauthored by Carmichael (Costa et al. 2015). The abstract proclaims that 'adolescents receiving also

puberty suppression had significantly better psychosocial functioning after 12 months of GnRHa … compared with when they had received only psychological support'. The article is treated in the literature (e.g. Heneghan and Jefferson 2019) as providing evidence in favour of puberty blockers. But the abstract is misleading: the analysis actually *failed to detect any difference* between children who were given blockers and those who were not. To understand this, we need to scrutinize the article in detail. (Statistically minded readers will recognize the fallacy described by Gelman and Stern 2006.)

The analysis starts with 201 adolescents diagnosed with gender dysphoria. The children were divided into two groups: those deemed eligible for puberty blockers immediately, and those who needed more time due to 'comorbid psychiatric problems and/or psychological difficulties'. This second group did not receive any physical intervention during the time of this analysis, and so serves as a control group. Both groups received psychological support. The article chooses one outcome, psychosocial functioning as measured by the Children's Global Assessment Scale (CGAS). This scale was administered at the outset, and then after six, twelve, and eighteen months. It is intriguing that the article omits the outcomes that were negative in the preliminary results: the Child Behavior Checklist, the Youth Self Report Questionnaire, the Health Related Quality of Life scale, and the Body Image Scale.

The authors graph the CGAS results, but without confidence intervals—which indicate the extent of random statistical variation or noise. The smaller the sample, the greater this noise. These samples shrank over time: after eighteen months, the group getting puberty blockers numbered only 35, and the control group 36. The article does not explain why two thirds of the subjects disappeared. Presumably they did not stop the medication, because all 44 children given blockers in the 2010–14 study continued the drug regime for two years (Gunn et al. 2015b).

My graph plots the results with standard 95% confidence intervals. The group given puberty blockers from six months onwards showed improvement at eighteenth months: the average CGAS score had increased from 61 to 67 (coloured red on the graph). This improvement is statistically significant, and it is the one that the authors chose to highlight.



However, these children also received psychological support, and so attributing this improvement to medical intervention is unjustified. The crucial comparison is between the group receiving blockers and the control group. The latter's average CGAS score (coloured blue) after eighteen months was lower, 63 compared to 67. But this difference is *not statistically significant*; the 95% confidence intervals substantially overlap. (For statistically minded readers, a two-tailed *t*-test for the difference between group means yields a *p*-value of .14, far beyond the conventional .05 threshold.) In other words, the samples were so small, and there was such wide variation in scores within each group, that we can draw *no conclusions*. There is no evidence that puberty blockers improve psychosocial functioning. Presumably this is why GIDS omits the article from its own evidence base.

The abstract describing the baseline characteristics of the children in the 2010–14 study concluded: 'Assessment of growth, bone health and psychological outcomes *will* [my emphasis] be important to assess the medium and long-term safety and effectiveness of early intervention' (Gunn et al. 2015b). However, GIDS apparently failed to collect any data on its experimental subjects after they turned 18. In a startling admission, Carmichael and coauthors blame 'the frequent change in nominal and legal identity, including NHS number in those referred on to adult services'—'to date they have not been able to be followed up' (Butler et al. 2018). (Transgender activists successfully lobbied the NHS to provide new numbers to patients as well as to change the 'gender' on their medical records.)

To summarize, GIDS launched a study to administer experimental drugs to children suffering from gender dysphoria. Between 2010 and 2014, puberty blockers were given to 44 children. This study yielded only one published scientific article on outcomes. It showed no evidence for the effectiveness of GnRHa: there was no statistically significant difference in psychosocial functioning between the group given blockers and the group given only psychological support. In addition, there is unpublished evidence that after a year on GnRHa children reported greater self-harm, and that girls experienced more behavioural and emotional problems and expressed greater dissatisfaction with their body—so puberty blockers exacerbated gender dysphoria. Yet the study has been used to justify rolling out this drug regime to several hundred children aged under 16. Almost five years after the last patient was enrolled in the experiment, there is no evidence to substantiate Carmichael's claim 'that the results thus far have been positive'.

The Director of GIDS needs to answer these questions about the 2010–14 experimentation with puberty blockers:

- *On what evidence did you claim in 2014 that 'the results thus far have been positive'?*
- *When preliminary results in 2015 showed that children after a year on blockers showed a statistically significant increase in reported self-harm, was this ever investigated?*
- *Why did you never publish the negative results reported to Tavistock's Board of Directors in 2015 and to WPATH in 2016?*
- *Why did your only published article (Costa et al. 2015) using data from the study omit all the outcomes that were negative in the preliminary results (Child Behavior Checklist, Youth Self Report questionnaire, Health Related Quality of Life scale, and Body Image Scale)?*
- *In your article, why did the abstract and conclusion not report the finding that there was no statistically significant difference between the group given GnRHa and the control group?*
- *In your article, what accounts for the reduction in the number of subjects from 201 to 71 over eighteen months?*
- *What steps have you taken to monitor the 'long-term safety and effectiveness of early intervention', as these experimental subjects become adults?*

Note

How many subjects from the 2010–14 study are included in Costa et al. (2015) is unclear. The 2010–14 study gave GnRHa to 44 adolescents, referred at ages from 10 to 15. (Gunn et al. 2015a, 2015b). One would expect all of them to be included in the 'immediately eligible' group in Costa et al. (2015), along with some older adolescents to boost the sample size. The article counts 101 children in this group at 6 months when GnRHa commenced (Table 2), starting at ages from 13 to 17 (Table 1). The age range indicates the exclusion of some children from the 2010–14 study: those who commenced GnRHa from ages 10 to 12. Why? Another puzzle is worth noting. When I requested the Research Ethics Committee number from Tavistock and

Portland NHS Trust under Freedom of Information, it provided the number 10/H0718/62. According to the NHS Health Research Authority, however, this number refers to a study that was given an 'unfavourable opinion' and therefore could not proceed.

References to the 2010–14 GIDS Study

Carmichael, Polly, 2015, 'Preliminary Results from the Early Intervention Research', Appendix 7 in 'Service Line Report: Gender Identity Development Service (GIDS)', Tavistock and Portman NHS Trust, *Board of Directors Part One: Agenda and Papers … 23rd June 2015*, pp. 50–55.

Carmichael, Polly, Sally Phillott, Michael Dunsford, Amelia Taylor, and Nastasja de Graaf, 2016, 'Gender Dysphoria in Younger Children: Support and Care in an Evolving Context', World Professional Association for Transgender Health 24th Scientific Symposium.

Costa, Rosalia, Michael Dunsford, Elin Skagerberg, Victoria Holt, Polly Carmichael, and Marco Colizzi, 2015, 'Psychological Support, Puberty Suppression, and Psychosocial Functioning in Adolescents with Gender Dysphoria', *Journal of Sexual Medicine*, vol. 12, pp. 2206–14.

Gunn, H.M., C. Goedhart, G. Butler, S.N. Khadr, P.A. Carmichael, R.M. Viner, 2015a, 'Gender Dysphoria: Baseline Characteristics of a UK Cohort Beginning Early Intervention', presented to the Youth Health Conference, Australia.

Gunn, H.M., C. Goedhart, G. Butler, S.N. Khadr, P.A. Carmichael, R.M. Viner, 2015b, 'Early Medical Treatment of Gender Dysphoria: Baseline Characteristics of a UK Cohort Beginning Early Intervention', *Archives of Disease in Childhood*, vol. 100, supp. 3, p. A198.

Part 2: An Update

22 July 2019

Tavistock and Portman NHS Trust started an experiment in 2011, using Gonadotropin-Releasing Hormone agonist (GnRHa) to block puberty in children suffering gender dysphoria. My original investigation for Transgender Trend (posted on 5 March 2019) raised serious questions about this experiment. The outcomes were never published in a scientific journal. And I discovered unpublished evidence that initial results, after the drugs had been administered for one year, were predominantly negative.

My research was reported by the Daily Telegraph. It is elaborated in a chapter in Inventing Transgender Children and Young People, edited by Michele Moore and Heather Brunskell-Evans. It has just featured on BBC Newsnight, broadcast on 22 July.

Following my original investigation, I wrote to Professor Russell Viner at University College London (UCL), the experiment's principal investigator, and Dr Polly Carmichael, Director of the Tavistock's Gender Identity Development Service (GIDS), asking why they failed to publish results. I also contacted the Research Ethics Committee which originally granted permission, pointing out that the researchers consistently failed to provide annual progress reports. Another researcher working with Transgender Trend submitted a Freedom of Information request for further details of the experiment, and this apparently prompted GIDS to post a webpage entitled 'A statement and update on the Early Intervention Study by the Tavistock and Portman NHS Foundation Trust' at the end of June. The statement first came to notice in the *Sunday Times* on 7 July.

The statement runs to more than 4,600 words. The first 3,600 detail the origins of the experiment, emphasizing two points. First, in the years before 2011, families and transgendering organizations like Mermaids lobbied vigorously to lower the age at which GnRHa drugs were administered to children, and the Tavistock could not resist this pressure. Second, the researchers could not employ the standard randomized trial to assess the effects of blocking puberty. Both points have some justification, but one wonders why such a lengthy apologia would be necessary if the experiment's outcomes have been favourable.

The Tavistock now claims 'The study concluded in February 2019 when the last cohort member began the next stage of therapy (cross-sex hormones) at age 17 years'. When the *Daily Telegraph* asked GIDS to respond to my questions (before publication on 6 March), its spokesman did not mention that the study had just concluded. Similarly, on 26 March, Viner replied to my letter, stating 'The early intervention study cohort *remain under study*

as some of the last recruited young people have still not completed the treatment pathway' (italics added). Carmichael's reply on the same date also said nothing about the study having been concluded in February. The webpage on GIDS' *research* still describes it as 'a study that is currently underway'.

When *Lord Lucas* kindly followed my suggestion to ask a parliamentary question, he was told on 22 May that the Tavistock 'plans to publish the data once all of the young people in the study have reached the stage when a clinical decision is made about moving from pubertal suppressants to cross-sex hormones, which the Trust expects to occur in the next 12 months'. Did the Tavistock mislead the Parliamentary Under-Secretary for the Department of Health and Social Care, who answered the question? The earliest indication that the experiment had terminated came from the NHS Research Ethics Committee, which informed me on 25 June that a final report is now being drafted by the chief investigator, Viner. One suspects that this precipitous ending – which has apparently been backdated to February – was forced by Transgender Trend's scrutiny.

Whenever the study formally ended, the researchers have been collecting data for eight years. The first subject consented to GnRHa drugs in June 2011. All 44 subjects enrolled in the experiment had completed one year on the drugs by mid 2015, two years by mid 2016, and three years by mid 2017. The results should have been closely monitored and the outcomes published in a scientific journal. After all, GnRHa has never been licensed for treating gender dysphoria, not just in the United Kingdom but anywhere in the world.

Five years ago, in 2014, Carmichael told the *Mail on Sunday* that the study demonstrated favourable outcomes: 'Now we've *done* the study and the results thus far have been *positive* we've decided to continue with it' (italics added). She even appeared in a BBC television programme – 'I Am Leo', aimed at audiences aged 6 to 12 – to promote the benefits of GnRHa drugs. (*See our analysis of the programme here*).

A video clip can be found here

Credit: @STILLtish

The Tavistock's statement says remarkably little about the experiment's outcomes. It cites Carmichael and Viner's presentation to the 2014 World Professional Association for Transgender Health (WPATH) conference showing 'there was *no overall improvement* in mood or psychological wellbeing using standardized psychological measures' (italics added). This finding was presented in February 2014, but just four months later Carmichael claimed 'the results thus far have been positive'. I cannot find slides from this 2014 presentation, but Carmichael's presentation to the 2016 WPATH conference apparently recycles the same finding. It also acknowledges that 'Natal girls showed an *increase in internalising problems* from t0 to t1 [after 12 months on GnRHa] as reported by their parents' (italics added). This negative outcome is omitted from the Tavistock's statement.

The statement also omits two other statistically significant negative outcomes that I discovered buried in an appendix submitted to the Tavistock's Board of Directors in 2015. Most seriously, after a year on GnRHa, 'a significant increase was found in the first item "I deliberately try to hurt or kill self"'. Evidence that an experimental treatment raised the risk of self-harm should be a major concern, but GIDS have never addressed this finding.

There is a backhanded admission in a presentation given by the GIDS endocrinologist, Professor Gary Butler, to the 2016 WPATH conference (only the abstract is available). 'Partial suppression [of sex hormones by GnRHa] may produce more side effects due to hormone swings, and also a lowering in mood leading to clinical depression. Expectations of improvement in functioning and relief of the dysphoria are not as extensive as anticipated, and psychometric indices do not always improve nor does the prevalence of measures of disturbance such as deliberate self harm improve.' Butler's presentation is, curiously enough, not cited in the Tavistock's statement.

The Tavistock's statement also fails to mention an article coauthored by Carmichael (Costa et al. 2016), which includes data from some subjects in the Early Intervention Study. This article purported to show beneficial outcomes from GnRHa, but I have demonstrated that the authors made an elementary statistical error. The analysis actually failed to detect any difference between children who were administered GnRHa and those who were not.

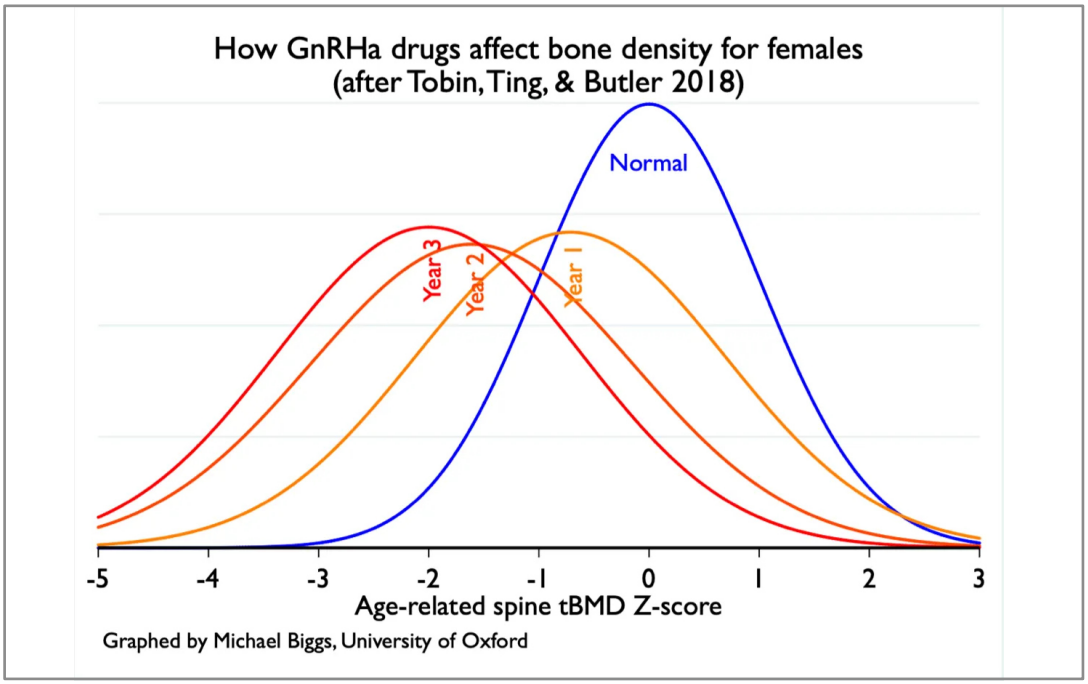
Finally, the Tavistock's statement cites a recent article on bone density, coauthored by Butler (Tobin, Ting, and Butler 2018). The article – a one-page abstract – emphasizes that bone density did not decline, in absolute terms, after GnRHa was administered. This is extremely misleading, as pointed out by Dr Michael Laidlaw and reiterated by Dr William J. Malone, both endocrinologists.

Growing children need bone density to *increase*. The article admits that the children did experience a decline relative to the normal standard for their age group, and this decline was especially marked for girls. My graph shows the distributions implied by the article's figures.

It is obvious that a substantial minority of the girls on GnRHa suffered from abnormally low bone density.

In sum, the Tavistock's statement continues the sorry record of prevarication and obfuscation that has dogged the experiment for several years. GIDS is clearly incapable of undertaking rigorous scientific research, perhaps because it has been swamped by exponentially increasing caseloads. There is no such excuse for the failure of UCL's Institute of Child Health, the experiment's lead sponsor. Neither organization can be trusted to objectively analyze the 2011 experiment.

We demand that a team of independent researchers be given access to all the data from the experiment. They will need expertise in statistics, psychiatry, and endocrinology; most importantly, they must have no vested interests in the promotion of GnRHa drugs. Given that this experiment has been used since 2014 to justify the provision of these drugs to children under the NHS, the outcomes of this experiment – on all the physical, psychological, and behavioural measures that were collected – must be published urgently.



Part 3: The Health Research Authority report

17 October 2019

The Health Research Authority (HRA) has just published its investigation into the 2010 experiment with puberty blockers, or more precisely its role in giving ethical approval and oversight. The investigation was prompted by research published on Transgender Trend in March 2019, with an update in July (the full paper is here). The HRA report's conclusions are predictably bland. Firstly, 'the research team involved in the design and delivery of the study … worked in accordance with recognised practice for health research, and in some areas such as patient involvement and transparency were ahead of normal practice at the time' (p. 11). Secondly, 'The HRA has acted within its Standard Operating Procedures and its normal practice in relation to this study' (p. 10).

On close reading, however, the report contains an astonishing admission. The paragraph deserves to be quoted in full:

> It would have reduced confusion if the purpose of the treatment had been described as being offered specifically to children demonstrating a strong and persistent gender identity dysphoria at an early stage in puberty, such that the suppression of puberty ***would allow subsequent cross-sex hormone treatment*** without the need to surgically reverse or otherwise mask the unwanted physical effects of puberty in the birth gender. The present study was ***not designed to investigate the implications on persistence or desistence of offering puberty suppression*** to a wider range of patients, it was limited to a group that had already demonstrated persistence and were actively requesting puberty blockers.
>
> *(p.5, my own emphasis added in bold).*

In fact the 2010 research protocol declared that one of its three aims was '[t]o *evaluate persistence and desistence* of the gender identity disorder and the continued wish for gender reassignment' (Early pubertal suppression in a carefully selected group of adolescents with gender identity disorder, proposal submitted to Central London REC 2, November 2010, obtained under Freedom of Information from the HRA; italics added). History is being rewritten to alter the rationale

for the experiment. It is not clear whether this revisionist history originates with the HRA, or whether the HRA is conveying the current views of the experiment's chief investigator, Professor Russell Viner (Professor in Adolescent Health at University College London) or his co-investigator, Dr Polly Carmichael (Director of the Gender Identity Development Service, GIDS).

Whatever the source, this is a clear admission that puberty blockers were the first stage on the predestined path to cross-sex hormones. After four assessment interviews, a child of 12 would be consenting in effect to a lifetime of drug dependence and the loss of fertility and the probable loss of sexual functioning. Because the "treatment" was intended to enhance the child's desire to change sex, it naturally exacerbated her or his gender dysphoria. 'Worsening behavioural and emotional symptoms of dysphoria', the HRA notes cheerily, 'would therefore not in itself be unexpected' (p. 6).

While the HRA is quite clear that puberty blockers were supposed to set the child on a course for full medical transition, it ignores one gruesome irony. For a boy who wishes to resemble a woman, puberty blockers will indeed prevent 'the unwanted physical effects of puberty' such as voice deepening. But they also leave the adolescent with the genitalia of a prepubescent boy. If he subsequently chooses (after the age of 18) to undergo genital surgery, there is insufficient for a vaginoplasty and so a piece of his bowel will have to be used. This point was underlined at a conference organized by the Gender Identity Research and Education Society in 2005:

> 'Although there are surgical means to deal [with] this difficulty, the patient and her parents or guardians should be fully informed about its implications.'

The conference was attended by Viner and Carmichael. Unaccountably they forgot to mention these implications on the Patient Information Sheet they gave to children and carers in their experiment.

Following from the HRA's admission that puberty blockers are really the start of irreversible physical transition, it makes one valuable recommendation. 'Researchers and clinical staff should consider carefully the terms that they use in describing treatments e.g. avoid referring to puberty suppression as providing a "breathing space", to avoid risk of misunderstanding.'

That phrase is common. According to Dr Gordon Wilkinson at the Young People's Gender Clinic in Glasgow—the Scottish equivalent of GIDS—GnRHa drugs 'provide breathing space to explore options'. Gendered Intelligence, a charity which trains staff in many universities, describes puberty blockers as giving 'young trans people appropriate time and breathing space to ensure that they are sure about the permanent effects of cross-sex hormones, without the adverse effects of an incorrect [sic] puberty'. (The phrase is also widely used in the USA and New Zealand.)

It is not the only misleading phrase. Carmichael went on BBC children's television in 2014 to tell one of the children in the experiment and the audience (aged 6 to 12) that puberty blockers merely pressed a pause button. We can only hope that the HRA's report will stop clinicians and charities from misleading the public—and more importantly the children and carers who are making life-changing decisions.

The HRA's investigation repeats a familiar misconception: because Gonadotropin-Releasing Hormone agonist (GnRHa) drugs are licensed for the postponement of central precocious puberty, therefore 'the treatment was licensed for the purpose of blocking progression of puberty' (p. 4). In the case of precocious puberty, a child starts to go through puberty at an abnormally young age—a girl starts menstruating at five, for example. This condition has an objective physical diagnosis. GnRHa drugs are then prescribed in order to *postpone* puberty until the normal age of puberty is reached, when the drugs are stopped and puberty resumes normally. There is no similarity at all for the case of a child with gender dysphoria. This condition has no objective physical diagnosis. GnRHa drugs are prescribed in order to prevent the child from ever experiencing puberty. The adolescent never develops the ability to conceive a baby and might never develop the capacity to orgasm.

When it comes to the HRA's own ethical

procedures, its investigation throws some intriguing findings. The experiment was first rejected by one Research Ethics Committee (REC 1), and was then submitted to another Committee (REC 2). 'A number of members' on the latter 'had connections with University College London', which by coincidence was Viner's own institution. The committee also co-opted a member who had co-authored with Viner. 'It is not clear whether the potential conflict of interest was declared, whether this committee discussed this potential conflict of interests and agreed that it was not a concern, or whether the other members agreed that the individual concerned could contribute but that they would ensure that it did not influence their decision-making' (p. 9). It is unfortunate that the minutes provide no information.

The Research Ethics Committee made the submission of annual progress reports 'a condition of the favourable ethical opinion', as it stressed in its letters (e.g. letter of 29 April 2013, obtained under Freedom of Information from the HRA). Viner failed to submit such reports in 2013, 2014, and 2015. The HRA reassures us that 'it is common for researchers not to supply annual progress reports' (p. 10). Rules, after all, are made to be broken.

After 2015, the Research Ethics Committee forgot about the experiment, as apparently did Viner and Carmichael. It had served its purpose, for what had been 'research' now became policy at GIDS: puberty blockers are routinely given to children from the age of 12, and in some cases as to children as young as 10.

Let us leave the last word to Viner, who spoke with remarkable candour in 2012:

> If you suppress puberty for three years the bones do not get any stronger at a time when they should be, and we really don't know what suppressing puberty does to your brain development. We are dealing with unknowns. (Daily Mail, 25 February 2012)

We know no more now than we did then.

The HRA should review how effectively declarations of interest by REC members are managed, and seen to be managed.

The Tavistock and Portman NHS Trust should provide greater clarity both internally and externally about the boundaries between research and clinical service.

Researchers and clinical staff working in gender identity development should consider carefully the terms that they use in describing treatments e.g. avoid referring to puberty suppression as providing a 'breathing space', to avoid risk of misunderstanding.

UCL should ensure it has mechanisms to oversee version labeling of documents used in research.

NHS England should provide guidance to NHS organisations on appropriate and transparent oversight and governance of innovative practice undertaken outside research.

From: Investigation into the study 'Early pubertal suppression in a carefully selected group of adolescents with gender identity disorders'

NHS Health Research Authority

Part 4: The Judicial Review

3 December 2020

Keira Bell's and Mrs A's claim against the Tavistock and Portman NHS Foundation Trust led to a momentous judgment on 1 December 2020. The judgment places significant constraints on the use of GnRHa (Gonadotropin-Releasing Hormone agonist) to suppress puberty in children suffering from gender dysphoria, as adopted by the Tavistock's Gender Identity Development Service (GIDS) in 2011.

1. Puberty suppression is an experimental treatment

The judgment is unequivocal that puberty suppression for gender dysphoria is an experiment: 'it is right to call the treatment experimental or innovative in the sense that there are currently limited studies/evidence of the efficacy or long-term effects of the treatment' (para 148). This finding should finally dispose of the claim—frequently made by the GIDS—that the treatment is not experimental because GnRHa drugs are licensed for precocious puberty. Treating a child whose puberty arrives abnormally early (under the age of 8) so that he or she can experience puberty at a normal age cannot be compared to stopping puberty at the normal age so that a child can proceed to cross-sex hormones at the age of 16.

Puberty suppression is an experiment whose aims are ambiguous. The judgment highlights the 'lack of clarity over the purpose of the treatment: in particular, whether it provides a "pause to think" in a "hormone neutral" state or is a treatment to limit the effects of puberty, and thus the need for greater surgical and chemical intervention later' (para 134).

2. GIDS fails to collect basic data and to report outcomes

At several points the judges express surprise at the failure of the GIDS to provide data to the court. The GIDS could not provide comprehensive figures on the ages at which children have been prescribed GnRHa (para 28). It had no information on how many were diagnosed with Autism Spectrum Disorder (para 35). It could not say how many proceeded from GnRHa to cross-sex hormones (paras 59). This failure—or perhaps reluctance—to collect basic data has been highlighted by Transgender Trend.

During the proceedings, the judges asked the GIDS to produce results from their initial experiment with puberty blockers on 44 children from 2011 to 2014. This initial experiment had been conveniently forgotten by GIDS—and even by the Principal Investigator, Professor Russell Viner—until it was brought to light by Transgender Trend in March 2019. We called then for the outcomes of the treatment on all 44 subjects to be published immediately.

When the judges asked for these results during the hearing, the GIDS refused. As the judges explain, 'we note that though this research study was commenced some 9 years ago, at the time of the hearing before us the results of this research had yet to be published. Dr Carmichael says in her witness statement dated 2 February 2020 that a paper is now being finalised for publication. At the hearing we were told that that this paper had been submitted for peer-review but that Professor Viner, one of the authors of it, had yet to respond to issues raised by the reviewers, as he has been otherwise engaged in working on issues relating to the coronavirus pandemic' (para 24).

Using the pandemic as an excuse is not plausible given that Professor Viner and Dr Carmichael promised (in their protocol given ethical approval in 2010) to provide outcomes after the patients had been on GnRHa for two years, which would have been in 2016. (The only peer-reviewed publication on the experiment's outcomes for psychological functioning and gender dysphoria is my letter in Archives of Sexual Behavior.) If the longer-term outcomes of the 2011-14 experiment were positive, why would Dr Carmichael and Professor Viner refuse to produce this evidence for the judges?

The failure to publish cannot be blamed on lack of resources. In 2019 the GIDS won a £1.3 million grant to research outcomes for children treated for gender dysphoria.

3. Puberty suppression inexorably leads to cross-sex hormones

The judgment should finally dispose of the illusion that puberty suppression simply provides a "breathing space" or pushes a "pause" button (as Dr Carmichael claimed on BBC Children's Television in 2014). As I have said, it is more like pressing fast forward into cross-sex hormones and ultimately surgery. The Health Research Authority has acknowledged that the rationale for puberty suppression is lifelong physical transition. The judges emphasized that 'the vast majority of children who take PBs [puberty blockers] move on to take cross-sex hormones, that Stages 1 and 2 are two stages of one clinical pathway and once on that pathway it is extremely rare for a child to get off it' (para 136).

Therefore for a child to actually consent, he or she 'would have to understand, retain and weigh up' the following information: '(i) the immediate consequences of the treatment in physical and psychological terms; (ii) the fact that the vast majority of patients taking PBs go on to CSH [cross-sex hormones] and therefore that s/he is on a pathway to much greater medical interventions; (iii) the relationship between taking CSH and subsequent surgery, with the implications of such surgery; (iv) the fact that CSH may well lead to a loss of fertility; (v) the impact of CSH on sexual function; (vi) the impact that taking this step on this treatment pathway may have on future and life-long relationships; (vii) the unknown physical consequences of taking PBs; and (viii) the fact that the evidence base for this treatment is as yet highly uncertain' (para 138).

4. Can children consent to sterility and potentially losing sexual function?

The judges remarked on the curious fact that the GIDS could not recall any child ever being considered to lack "Gillick competence" to consent to GnRHa drugs (para 44). Gillick competence requires the child to have 'sufficient maturity and intelligence to understand the nature and implications of the proposed treatment' (para 105). Even when treating children as young as 10, the GIDS invariably assessed them as having the ability to consent, 'on the assumption that if they give enough information and discuss it sufficiently often with the children, they will be able to achieve Gillick competency'. The judges concluded laconically, 'we do not think that this assumption is correct' (para 150).

One of the GIDS' witnesses, "J" embarked on puberty suppression at the age of 12. According to J's recollection of the consent process: "We discussed sex and I told them the idea of it disgusted me. I knew I would be unable to consider having a sexual relationship as an adult with my body so wrongly formed' (para 86). Such testimony heightened the judges' concerns about consent. 'Some of the children and young people who have been treated at GIDS say in their witness statements that the thought of sex disgusted them, or they did not really think about fertility. These normal reactions do not detract from the difficulties surrounding consent and treatment with PBs. That adolescents find it difficult to contemplate or comprehend what their life will be like as adults and that they do not always consider the longer-term consequences of their actions is perhaps a statement of the obvious.' (para 141).

Remarkably little is known about the effect of puberty suppression on the development of sexual desire and the capacity to orgasm. This was revealed in the proceedings, when the judges asked for evidence that the development of sexuality was unimpaired by GnRHa. The question stumped the barrister for University College London Hospitals NHS Foundation Trust, which prescribes the drugs on behalf of the GIDS. One clue is that GnRHa is prescribed to chemically castrate sex offenders in Broadmoor—a use for which it is licensed, unlike for gender dysphoria. It seems implausible that an adolescent's sexuality would be unaffected by several years of chemical castration.

5. Who can consent to puberty suppression?

The judges concluded by emphasizing the 'enormous difficulties in a child under 16 understanding and weighing up this information and deciding whether to consent to the use of puberty blocking medication' (para 150). Therefore GIDS—and private clinicians who wish to prescribe GnRHa for treating gender dysphoria—will have to seek a court order for each individual patient. The judgment sets a high bar for meeting Gillick competence: for a child aged 13 or under, this would be 'highly unlikely'; for a child aged 14 or 15, it would be 'very doubtful'. Even for a child aged 16 or 17, for whom there is a presumption of consent, the judges recommend that clinicians 'may well regard these as cases where the authorisation of the court should be sought' (para 151). The judgment closes the era of unconstrained experimentation on children suffering from gender dysphoria, when the GIDS could flout ethical rules and ignore scientific principles.

Part 5: The belated results

18 December 2020

The Tavistock's Gender Identity Development Service (GIDS) and University College London have finally released the results of their experiment on puberty blockers, albeit not in a scientific journal. The timing is curious. The paper's first author, Dr Polly Carmichael (Director of GIDS) refused to provide it to the judicial review brought by Keira Bell and Mrs A, on a flimsy pretext. On the day after the judgement was handed down, the paper appeared on a preprint server, medRxiv (Carmichael et al., 2020). It was not discovered for some days because the authors were too modest to seek publicity. The event has not been mentioned on the website of the Tavistock and Portman NHS Foundation Trust, which had originally announced the experiment in 2011 with some fanfare: 'It is hoped that the results of this study will contribute to improving the standards of care offered to this group of young people and their families.'

The fact that the Carmichael et al. have only now published results that were available in 2016—for outcomes after one year—and in 2017—after two years—shows their lack of concern for the standards of care offered to this group of young people. Indeed, it is almost certain that the experiment would have been conveniently forgotten without Transgender Trend's sustained scrutiny. This website first called on the Tavistock to publish the results of its 'Early Intervention Study' in March 2019. I made a formal complaint to the Health Research Authority, which oversees the Research Ethics Committee that had approved this experiment. The report of its investigation was sent to me (embargoed before publication) on 11 October 2019. Carmichael et al.'s statistical analysis plan was 'lodged with the Research Ethics Committee of the Health Research Authority on 9 October 2019' (Appendix S2, p. 1).

The long-delayed paper provides results for 44 subjects—aged 12 to 15—who were prescribed Gonadotropin-releasing Hormone agonist (GnRHa). They were followed up at three time points: after one year, two years, and three years. Because the subjects could progress to cross-sex hormones soon after their sixteenth birthday, only 24 remained on GnRHa after two years, and only 14 at three years.

Managing expectations

The authors' statistical analysis plan, written in 2019 after they had come under scrutiny from Transgender Trend, is remarkable for its low expectations. It is far more pessimistic than the original research protocol from 2010.

- *2010:* 'Going through puberty in what is perceived to be the wrong body can be very distressing and in some cases contribute to self-harm and suicide attempts …. It is important to evaluate whether intervention early in puberty reduces self harm and suicide attempts' (Viner et al., 2010, p. 15).
- *2019:* 'We hypothesise no change in self-harm across the study' (Carmichael et al., 2020, S2, p. 9).
- *2010:* 'Early intervention is also associated with a reduction in the gender dysphoria experienced by these adolescents …' (Viner et al., 2010, p. 15).
- *2019:* 'It is therefore unlikely that GnRHa treatment will result in significant reduction in body dissatisfaction' (Carmichael et al., 2020, S2, pp. 12-13).

The authors have provided a perfect illustration of what psychologists call 'HARKing': hypothesizing after the results are known (Kerr, 1998). Aside from this being a questionable research practice, one wonders how it could be ethical to give an experimental treatment to children if the experimenters themselves expect the treatment not to lead to any improvement.

Psychological functioning does not change

The paper's headline finding is that 'GnRHa treatment brought no measurable benefit nor harm to psychological function in these young people with GD [gender dysphoria]' (p. 45). This seems reassuring given that the first 30 subjects enrolled in the GIDS experiment reported more negative than positive effects after one year (GIDS, 2015; Biggs, 2020).

The paper's findings might partly reflect the authors' choice to present results only for girls and boys combined, and to test sex differences (Table 6) for only 2 measures out of 26. 'Our statistical analysis plan restricted testing all outcomes for differences by sex due to the type 1 error risk', they explain (p. 46). This risk is a legitimate concern, which will be discussed below. There is no justification, however, for not tabulating the results disaggregated by sex, as done by the landmark Dutch study on which the Tavistock's experiment was modelled (de Vries et al., 2011), and by Carmichael's presentation of the preliminary results (GIDS, 2015). My article (Biggs, 2020) shows that the measures for boys and for girls are uncorrelated, in the preliminary GIDS results and likewise in the Dutch study. In both data sets, to take the clearest example, girls' body image worsened following GnRHa, while boys' body image improved. By combining both sexes, the authors make it impossible to discern such patterns.

The authors also provide frustratingly little information on self-harm. There are two indexes, one created from the child's answers and one from the parent's. Each index sums two questions, each scored as 0, 1, or 2. The authors report only the median and the interquartile range (Table 4). The median is always 0 because most children do not harm themselves. The lower quartile is 0, of course; the upper quartile is 1 in every measure except the index for Youth Self Report after twelve months, when it is 2. (The difference between this measure at baseline and at one year is apparently not statistically significant; $p = .4$.) Why not report the mean, as they had previously (GIDS, 2015)? Or tabulate the frequency? Disaggregating by sex would also be informative, because their own preliminary results for the first 30 subjects showed that the increase in self-harm—on the question 'I deliberately try to hurt or kill myself'—was greater for girls than for boys (the sex difference was statistically significant, $p = .014$).

The lack of discernible improvement is quite surprising because children and their parents must have been enthusiastic about puberty blockers and would have considered themselves fortunate to be in the first group of British adolescents to receive them. After all, this treatment had been demanded for years by Mermaids and GIRES, as a lifesaving elixir for children who identify as transgender (Biggs, 2019). This context should have created a powerful placebo response, even if the specific physical effects of GnRHa were minimal. We know that almost all or all the benefit of anti-depressants comes from placebo response (Kirsch, 2019).

The sample is too small

The authors are right to be wary of conducting too many statistical tests on a small sample, comprising only 44 individuals. I will try to explain this simply. Let us say we find a sample statistic—like the average change in one measure after these particular patients have been treated for a year—to be statistically significant at the .05 level. This means that if the population parameter were truly zero—if there were really no effect—we would then have only a 5% probability of getting a statistic of that magnitude in a sample of that size, simply due to random variability. In other words, the probability of a 'Type I error' is 5%. The more measures we test, however, the greater the probability of finding one to be statistically significant. If we were to carry out 20 statistical tests on completely random variables, on average 1 in 20 would be statistically significant at the .05 level.

The authors point out that my analysis (Biggs, 2020) of their preliminary results does not adjust for the number of statistical tests. I replicated the procedure used in the Dutch article (de Vries et al., 2011) which provides the only significant evidence for the benefits of puberty blockers. The authors' critique therefore applies equally to that article, whose sample was almost as small, ranging from 41 to 57 (depending on the measure). Statistical tests were conducted on 14 measures. Applying the Bonferroni correction, as the authors advocate (Carmichael et al., 2020, p. 18), would also eliminate 3 out 8 of the positive Dutch findings. Most importantly, the improvement in overall psychological functioning (captured the Children's Global Adjustment Scale) and the reduction in depression would no longer be statistically significant ($p > .05 / 14$).

The authors make a convincing argument that their sample was too small to really detect changes in so many measures. Why did they not realize this earlier? When the experiment was designed, the GIDS had a caseload of only 29 teenagers aged between 12 and 15 (Viner et al., 2010, pp. 8–9), and so they planned to enrol 30–45 patients over three years. Referrals subsequently grew exponentially, perhaps helped by Dr Carmichael's promotion of puberty blockers in newspaper interviews and on BBC Children's Television. In 2014/15, the final year of enrolment on to the experiment, the GIDS received referrals for 282 teenagers in the 12-15 age bracket. In other words, the *annual increase* was by then ten times greater than the *total* number of patients just four years earlier. After enrolment in the experiment finished, the GIDS recruited over 50 children aged 10-14 each year to its GnRHa programme. The GIDS therefore should now possess data on the effect of puberty suppression—after one year—on at least 250 more children (counting those referred to the endocrine clinic from January 2015 to December 2018). A sample size of around 300 would provide sufficient statistical power to really test whether adolescents undergoing puberty suppression improve or deteriorate. Unfortunately, the GIDS chose either not to collect or not to report these data, despite winning £1.3 million in research funding. Why?

No information on autism

In the case brought by Keira Bell and Mrs A, the judges asked for the number of children on the autism spectrum who were administered puberty blockers. They were told that these data could not be obtained. The judgment 'found this lack of data analysis—and the apparent lack of investigation of this issue—surprising' (para 35). The authors mention that they used the Social Responsiveness Scale to assess autism but simply promise that 'these data will be analysed in the future' (Carmichael et al., 2020, p. 17). We know only that out of the first 30 experimental subjects, 16 were in the normal range, 10 had 'mid to moderate' Autism Spectrum Disorder traits, and 5 had 'severe' traits as measured by SRS-2 (GIDS, 2015, p. 50).

Bone density

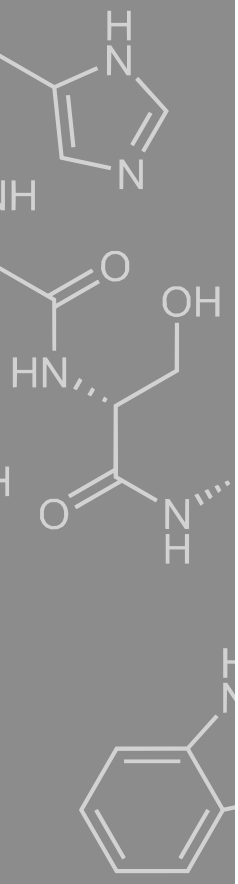
An American endocrinologist, Dr Michael Laidlaw, raised the alarm about the effects of GnRHa on bone density, which must accrue rapidly during puberty to avoid osteoporosis later in life. This paper confirms his fears. At baseline the subjects were already half a standard deviation below the norm for their age and sex (Table 3). After one year, they were one standard deviation below the norm; at two years, more than one standard deviation below. (The authors chose not to statistically test these changes in *Z*-scores, for reasons which are unclear.) The paper omits the range of bone density, which is crucial: given that after one year the *average* was a standard deviation below the norm, many of the subjects would fall more than two standard deviations below the norm—which is a warning sign 'that your bone density is lower than it should be for someone of your age' (NHS, 2020). In the overall population, only 2% of individuals will experience such low bone density to meet this warning threshold (*Z*-score < -2). After two years on GnRHa, perhaps 30% of those with puberty suppression could meet this threshold for spine bone density, even adjusting for height. (My calculation assumes the Normal distribution and necessarily estimates the standard deviation of the *Z*-score from the authors' confidence intervals.)

Whether the failure to accrue bone density increases the risk of fractures is unclear. The authors collected data on various 'adverse events', but these did not include broken bones.

Puberty blockers lead inexorably to cross-sex hormones

The most important outcome—but the least surprising—is that 43 out of 44 subjects continued to cross-sex hormones. Although puberty blockers are promoted as a diagnostic aid, since 2006 (if not before) we have known that in almost every case they lead to cross-sex hormones and eventually surgery. It is therefore astonishing that the authors continue to claim that 'pubertal suppression may be both a treatment in its own right and also an intermediate step' (p. 48).

Considered as a treatment in its own right, the suppression of puberty with GnRHa might be the only treatment provided by the NHS for which the costs clearly exceed the benefits. The sole justification for GnRHa is to prepare a child for lifelong medicalization with cross-sex hormones and surgeries, with irreversible consequences for sexuality and fertility. After all, the paper that introduced puberty suppression was entitled 'The Feasibility of Endocrine Interventions in Juvenile Transsexuals' (Gooren & Delemarre-van de Waal, 1996). The question is whether the GIDS has the moral authority and scientific expertise to designate children as young as 10 as juvenile transsexuals. As the judges ruled in the case of Keira Bell and Mrs A, 'Apart perhaps from life-saving treatment, there will be no more profound medical decisions for children than whether to start on this treatment pathway' (para 149).



References

Biggs, M. (2019). *The Tavistock's experiment with puberty blockers*. https://users.ox.ac.uk/~sfos0060/Biggs_ExperimentPubertyBlockers.pdf

Biggs, M. (2020). Gender dysphoria and psychological functioning in adolescents treated with gnrha: comparing Dutch and English prospective studies. *Archives of Sexual Behavior*, 49, 2231–2236. https://doi.org/10.1007/s10508-020-01764-1

Carmichael, P., Butler, G., Masic, U., Cole, T. J., De Stavola, B. L., Davidson, S., Skageberg, E. M., Khadr, S., & Viner, R. (2020). *Short-term outcomes of pubertal suppression in a selected cohort of 12 to 15 year old young people with persistent gender dysphoria in the UK*. https://doi.org/10.1101/2020.12.01.20241653

de Vries, A. L. C., Steensma, T. D., Doreleijers, T. A. H., & Cohen- Kettenis, P. T. (2011). Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *Journal of Sexual Medicine*, 8, 2276–2283. https://doi.org/10.1111/j.1743-6109.2010.01943.x

Gender Identity Development Service. (2015). Preliminary results from the early intervention research. Tavistock and Portman NHS Foundation Trust, Board of Directors, *Part One: Agenda and Papers ... 23rd June* 2015, 50–55. https://tavistockandportman.nhs.uk/documents/142/board-papers-2015-06.pdf

Gooren, L., & Delemarre-van de Waal, H. (1996). The feasibility of endocrine interventions in juvenile transsexuals. *Journal of Psychology & Human Sexuality*, 8, 69–74. https://doi.org/10.1300/J056v08n04_05

Kerr, N. L. (1998). HARKing: Hypothesizing after the results are known. *Personality and Social Psychology Review*, 2, 196–217. https://doi.org/10.1207/s15327957pspr0203_4

Kirsch, I. (2019). Placebo effect in the treatment of depression and anxiety. *Frontiers in Psychiatry*, 10. https://doi.org/10.3389/fpsyt .2019.00407

NHS (2019). *Bone density scan (DEXA scan): How it is performed*. https://www.nhs.uk/conditions/dexa-scan/what-happens/

Viner, R., Carmichael, P., Di Ceglie, D., Butler, G., Brain, C., Holt, V., Khadr, S., & Skagerberg, E. (2010). A*n evaluation of early pubertal suppression in a carefully selected group of adolescents with gender identity disorder (v1.0*, 6 October 2010). Obtained from the Health Research Authority under Freedom of Information.

Part 6: The effects on bone density

3 May 2021

Transgender Trend first examined the effects of Gonadotropin-Releasing Hormone agonist (GnRHa) on bone density in 2019. This was prompted by a study co-authored by Professor Gary Butler, the lead clinical endocrinologist for the Gender Identity Development Service (GIDS) at the Tavistock and Portman NHS Foundation Trust (Joseph, Ting, and Butler 2018; Joseph, Ting, and Butler 2019).

The authors emphasized that adolescents administered with GnRHa had not experienced any decline in absolute bone density. As endocrinologists Dr William J. Malone and Dr Michael Laidlaw pointed out on Twitter, however, adolescence is a period of increasing bone density—this is the developmental stage when an individual lays down the bone mass that will last them the rest of their life. What matters, then, is the individual's bone density relative to the norm for their age and sex, which is measured by the Z-score (standardized deviation from the population mean). The Z-scores of the patients at the GIDS had fallen significantly. Spurred by Laidlaw's and Malone's comments, I produced a graph to illustrate how these Z-scores had declined (the graph was crude because it had to be derived from the mean and standard deviation of Z-scores alone, because nothing more was reported by Butle's study). My conclusion: 'It is obvious that a substantial minority of the girls on GnRHa suffered from abnormally low bone density.'

This claim can be vindicated now that the Tavistock finally released a subset of data from their experiment with GnRHa on children aged 12 to 15. The data were released following Transgender Trend's lengthy campaign to disclose the outcomes of the experiment, which included a formal complaint to the Health Research Authority. My reanalysis of these data is now published by the Journal of Paediatric Endocrinology and Metabolism. I find that after two years on GnRHa, the Z-scores for up to a third of the children had declined to below -2. Only about 2% of the population fall below this threshold, and this is the threshold of clinical concern. Indeed, the Tavistock's 2011 experimental protocol initially excluded any child with a Z-score below -2. This restriction was subsequently relaxed, with the stipulation that the patient must understand the 'risks of later osteoporosis' (Amendment 1.2, 3 July 2012). The Patient Information Sheet, however, never mentioned osteoporosis; it stated merely 'We do not know how blocker treatment in early puberty will affect bone strength …'. The experimental protocol provides evidence that Butler—one of the investigators in the project, led by Professor Russell Viner and Dr Polly Carmichael—understood that such low bone density indicates a risk of osteoporosis.

The graphs show my results in detail. The blue line shows the normal distribution of bone density in the population. For hip bone mineral density, the Z-scores of one third of the patients had fallen below -2. For spine bone mineral density, over a quarter of Z-scores had declined below this threshold. Some had even fallen below 3; such low bone density is extremely rare, found in only 0.13% of the population. Adjusting for height—bone mineral apparent density—does not attenuate the lowest values.

Does such abnormally low bone density increase the risk of bone fractures? One of the Tavistock's patients who started GnRHa at age 12 then experienced four broken bones by the age of 16. We have no idea whether this was unusual because Butler and the other researchers collected no data on fractures. Dutch studies show that the accrual of bone density recommences when cross-sex hormones are taken from age 16, and so Z-scores increase (Klink et al 2015; Stoffers et al. 2019).

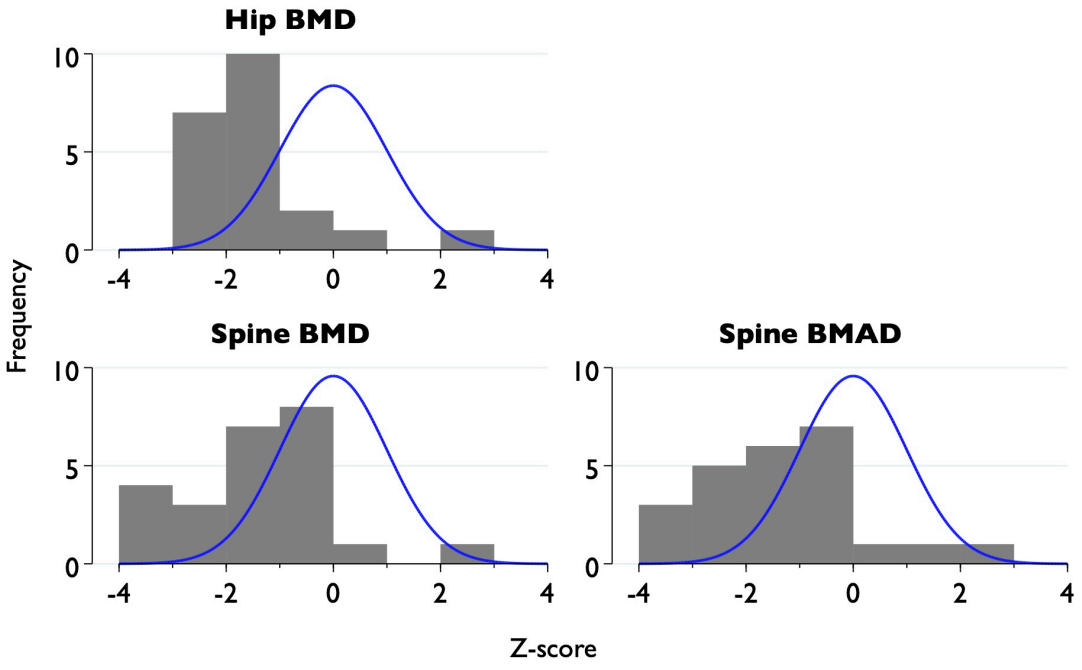
But in many cases the recovery is partial, and the Z-scores do not return to the level registered at the onset of GnRHa. The Tavistock has given GnRHa to a child as young as 10 years old, and so the failure to accrue bone mass could last up to five years. The Tavistock never follow up GIDS patients once they turn 18—not even those who graduate to the adult Gender Identity Clinic in the Tavistock Trust itself—and so there is no way of knowing whether patients who experience abnormally low Z-scores for years in adolescence have experienced osteoporosis as dults.

The fact that adolescents undergoing puberty suppression failed to accrue bone mass—to the point where a significant minority ended up with abnormally low bone density—inspired Butler and his coauthors to make two recommendations (Joseph, Ting, and Butler 2019). One is to reduce the monitoring of bone density, which has 'significant financial implications for healthcare providers'. The other is to change the computation of Z-scores; 'reference ranges may need to be re-defined for this select patient cohort'. When a measure provides inconvenient results, stop measuring or choose another scale: that is how transgender medicine is practiced at the Tavistock.

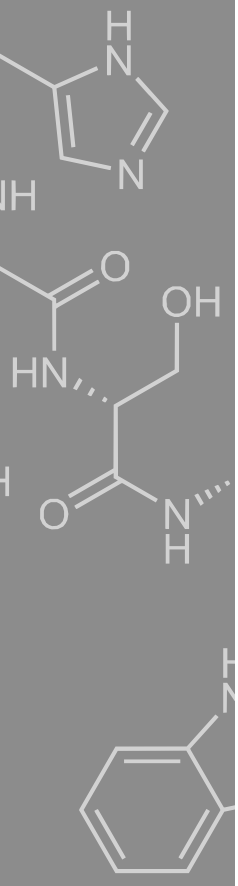
The Tavistock's Dutch counterparts at least provide practical advice: 'Adolescents should be counseled on the importance of weight-bearing exercise, an adequate dietary calcium intake, sufficient sunlight exposure to ensure adequate vitamin D levels, or vitamin D supplementation' (Schagen et al. 2020). But the Dutch researchers also apparently omitted to collect data on fractures. Their latest article (which acknowledges a research grant from Ferring Pharmaceuticals, the manufacturer of the GnRHa drug used in the Netherlands and Britain) suggests that future studies should 'investigate clinically important outcomes such as fracture risk' (Schagen et al. 2020).

Fifteen years ago the exponents of the Dutch protocol for transgendering children admitted that their patients could 'end with a decreased bone density, which is associated with a high risk of osteoporosis' (Delemarre-van de Waal & Cohen-Kettenis 2006). It is remarkable that the proponents of puberty suppression are only now contemplating collecting evidence on this key clinical outcome at some future date.

Fig. 1. Bone density after 24 months of puberty suppression



N = 24 for spine, 21 for hip. BMD, bone mineral density; BMAD, bone mineral apparent density.



Acknowledgements

I am indebted to help from Stephanie Davies-Arai, Elin Lewis, Susan Matthews, Heather Brunskell-Evans, and a former GIDS employee.

Further reading

The Tavistock's experiment with puberty blockers. 2019. 1 http://users.ox.ac.uk/~sfos0060/Biggs_ExperimentPubertyBlockers.pdf

Britain's experiment with puberty blockers. In M. Moore & H. Brunskell-Evans (Eds.), *Inventing transgender children and young people* (pp. 40–55). Newcastle, England: Cambridge Scholars Press, 2019.

Puberty blockers for gender dysphoria: The Dutch protocol, YouTube, 2020 https://www.youtube.com/watch?v=9VHlkE40cFk

A letter to the editor regarding the original article by Costa et al: Psychological support, puberty suppression, and psychosocial functioning in adolescents with gender dysphoria. *Journal of Sexual Medicine, 16*, 2019, p. 2043. https://doi.org/10.1016/j.jsxm.2019.09.002

Gender dysphoria and psychological functioning in adolescents treated with GnRHa: comparing Dutch and English prospective studies. *Archives of Sexual Behavior, 49*, 2020, pp. 2231–2236. https://doi.org/10.1007/s10508-020-01764-1

A collection of articles by Dr. Michael Biggs for

Transgender TREND

Questioning the trans narrative