Freedom of Information Act 2000 disclosure log entry

Reference

19-20011

Date sent

21/06/2019

Subject

GIDS Research Information

Details of enquiry

all my questions concern research study 10/H0713/79: how it gained ethical approval; in the results; and in the extension of the duration of this study.

research study 10/H0713/79 : refusal from Central London REF1 & Resubmission to REF2

The research application was refused by Central London REF1 in a letter dated 6 September 2010. They advised the researchers to reapply, taking on board their ethical concerns about the study design (which lacked any control/robust validation mechanism); and they made a special point of asking the researchers to re-apply to them - REF1 - not to another REF. However, the researchers followed neither recommendation, instead re-applying to another REF - Central London REF2 - and not implementing a control group for the study, or any of the other suggestions that REF1 made.

1. Could you please share with me a copy of the initial research application, which was sent to the HRA in July 2010 under (I believe) reference 10/H0718/62?
2. Could you please share with me the covering letter sent with the re-submitted application in November 2010?
3. Could you please share with me any internal documentation or email communications (dated between 6 September 2010 and 5 November 2010) that pertain to the unfavourable decision of REF1 and the decision to re-submit the application to a different REF, REF2? I appreciate that such searches are laborious but I hope that the very targeted subject matter and the short period of time under review would make this less onerous.
4. If the research proposal was re-submitted to REF2 because the researchers had appealed against REF1's decision, could you please state this?

   Results of research study 10/H0713/79

   In the application (section A13), the researchers stated that "at the end of the first three years the data will be analysed and an interim report will be produced giving a provisional evaluation in line with the objectives of the study. The final report will be produced at the end of the 6 years." The Trust published a news story on its website on 6 April 2011 stating that "The study has a robust system of outcome monitoring."

5. Could you please share with me both the interim report and the final report mentioned in the REF application? The Times (19 May 2014) reported "the positive results from a three-year trial involving 12 to 14 year olds" which I guess must refer to the interim report.
6. Could you kindly share with me the annual progress reports sent to the REF in relation to this research study?
7. If the results of the research study have been published, could you please point me to these publications? I am aware that there is a database of staff publications, so linking to relevant publications in this database would be very helpful. I am aware that much research is undertaken by GIDS staff so I am anxious to identify the research emanating from this particular study.

Extension of the research study 10/H0713/79 in 2013/14
According to The Sunday Times (17 November 2013), "Dr Polly Carmichael… planned to continue the programme indefinitely," referring to "the early intervention study." However, when I asked the HRA, they had no records relating to the extension of the research study. Therefore:

8. Was the duration of the study, in fact, extended beyond the 6 years specified in the application form? If so, why was additional time needed to complete the research? Answers to these questions will, I think, be found in the annual progress reports that the researchers send to the REF for, according to REF Standard Operating Procedure, para 10.10, while permission to extend is not needed from the REF, the annual progress report must give reasons for the extension. Therefore, the answer to my question 8 may already be contained within the answer to question 6.
9. If this research study was extended, when did or will it conclude?
10. I am interested to know whether all of the 12-15 year old patients of GIDS who have ever been treated with puberty blockers are deemed to be participants in this study, or are the study participants a sub-set of a larger group of 12-15 year old GIDS patients who are receiving, or have received, puberty blockers? If not all 12-15 year old GIDS patients who have been or are treated with puberty blockers are receiving that treatment as part of the research study, on what basis is that treatment taking place? Presumably there is a treatment protocol governing/permitting that treatment.

Response Sent

Research study 10/H0713/79: r**efusal from Central London REF1 & Resubmission to REF2**

The research application was refused by Central London REF1 in a letter dated 6 September 2010. They advised the researchers to reapply, taking on board their ethical concerns about the study design (which lacked any control/robust validation mechanism); and they made a special point of asking the researchers to re-apply to them - REF1 - not to another REF. However, the researchers followed neither recommendation, instead re-applying to another REF - Central London REF2 - and not implementing a control group for the study, or any of the other suggestions that REF1 made.

1. Could you please share with me a copy of the initial research application, which was sent to the HRA in July 2010 under (I believe) reference 10/H0718/62?
   This document is attached: GID Early Pubertal Suppression Ethics Form
2. Could you please share with me the covering letter sent with the re-submitted application in November 2010?
   This document is attached: Response to ethics committee 03.11.10
3. Could you please share with me any internal documentation or email communications (dated between 6 September 2010 and 5 November 2010) that pertain to the unfavourable decision of REF1 and the decision to re-submit the application to a different REF, REF2? I appreciate that such searches are laborious but I hope that the very targeted subject matter and the short period of time under review would make this less onerous.
   To enable our response to this request, we performed an electronic search of internal emails which included the following in their content or subject heading between dates 6 September 2010 and 5 November 2010:
   - "REF 1"
   - "REF 2"
   - "REC 1
   - "REC 2"
   - "10/H0718/62"
   - "Resubmission"

   This search did not produce any relevant results.
4. If the research proposal was re-submitted to REF2 because the researchers had appealed against REF1's decision, could you please state this?
   There was no appeal against the decision made by REF1.

The options after an unfavourable opinion are to submit again to the original REC or to seek an opinion from another REC, providing all information from the first application. The investigators concluded that a REC with greater experience of dealing with rare conditions in children would better understand the issues, and elected to submit a revised application to REC 2.

We wrote to the REC2 Chair outlining our responses to the decision by REC1 and why we believed that this was in error. REC2 were supplied with our original application to REC1, their decision letter and our response

Results of research study 10/H0713/79

In the application (section A13), the researchers stated that "at the end of the first three years the data will be analysed and an interim report will be produced giving a provisional evaluation in line with the objectives of the study. The final report will be produced at the end of the 6 years." The Trust published a news story on its website on 6 April 2011 stating that "The study has a robust system of outcome monitoring."

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We stated in our ethics application that some data would be analysed at the end of 3 years and an interim report produced. A number of interim outputs and reports from the study were presented and/or published:

A. Interim outcome data was presented / published from 2015 onwards

1. Gunn H, Goedhard C, Butler G, Khadr S, Carmichael P, Viner R. Early medical treatment of gender dysphoria: baseline characteristics of a UK cohort beginning early intervention. *Archives of Disease in Childhood* 2015; **100:** A198. https://adc.bmj.com/content/100/Suppl_3/A198.1

   This examined the early outcomes from 61 young people referred for consideration of early intervention. It noted that all who began GnRHa achieved full gonadatropin suppression. No young people withdrew from GnRHa treatment in the first 2 years.

2. Carmichael P, Viner R. Seminar: Physical intervention in early puberty in the UK: Report from a research study Transgender health from global perspectives. WPATH Symposium, Bangkok 14-18 Feb 2014
   This reported qualitative data on early outcomes of 44 young people who received early pubertal suppression. It noted that 100% of young people stated they wished to continue on GnRHa, that 23 (52%) reported an improvement in mood since starting the blocker but that 27% reported a decrease in mood. Noted that there was no overall improvement in mood or psychological wellbeing using standardized psychological measures.

3. Carmichael P. Time to reflect: Gender dysphoria in children and adolescents, defining best practice in a fast changing context. Plenary Lecture on 18 June 2016: WPATH 24th Scientific Symposium, Amsterdam, 17-21 June 2016.

B. Other publications and presentations

1. Impacts on bone mineral density

   Joseph T, Ting J, Butler G.
   The effect of GnRHa treatment on bone density in young adolescents with gender dysphoria: findings from a large national cohort *Endocrine Abstracts* (2018) 58 OC8.2 | DOI: 10.1530/endoabs.58.OC8.2

   Joseph T, Ting J, Butler G. The effect of GnRH analogue treatment on Bone Mineral Density in very young adolescents with gender dysphoria from a large national cohort.

   J Ped Endo Metab (In press).

   These showed that there is no actual change in bone mineral density in young transgender adolescents on long term GnRHa therapy (when measured as BMAD or tBMD). This confirms that long-term GnRHa treatment has minimal impacts upon bone health, one of the major concerns about treatment.

2. Impacts on body composition

   Rahul Ghelani, Cheryl Lim, Caroline Brain, Mary Fewtrell, Gary Butler.

   Sudden sex hormone withdrawal and the effects on body composition in late pubertal adolescents with gender dysphoria. J Ped Endo Metab (under review).

3. Impacts on growth

   Matteo Catanzano, Gary Butler. Effect of Pubertal Blockade and Cross-sex Hormone Treatment on the Growth Spurt in Young Transgender Adolescents: A First Report

   Horm Res Paediatr 2018;90(suppl 1):p505 P1-P211. DOI: 10.1159/000492307

   This showed that only 14 of the cohort of 44 in the study had reached final adult height at time of data collection. Data were therefore insufficient to comment on impact of GnRHa on final height.

C. Unpublished Interim outcome data

In addition we have reports containing progress updates and summaries of the data or aspects of the data. We cannot release these as we are going to publish the complete data set. We do not yet have a final report as data collection pertaining to the study has only recently been completed. We will be submitting the results for publication as soon as possible.

6. Could you kindly share with me the annual progress reports sent to the REF in relation to this research study?
   We do not hold these reports. We can confirm that the Trust holds the progress/update and summary reports as described at the end of the response to question 5, however under Section 22 of the FOIA Act 2000 this information is exempt from current release because it is intended for publication at a future date. Having considered the public interest in releasing this now, the Trust's decision has been to withold this data until it has been published.
7. If the results of the research study have been published, could you please point me to these publications? I am aware that there is a database of staff publications, so linking to relevant publications in this database

would be very helpful. I am aware that much research is undertaken by GIDS staff so I am anxious to identify the research emanating from this particular study.

Interim and other outcomes have been published and presented as above in response to question 5. The study was estimated to run for about 6 years in the ethics application to allow recruited subjects to reach age 16 years and be able to move to next stage of treatment. The study finished in February 2019 when the last participant in the research cohort achieved this. At time of writing (June 2019) we are finalising the database in order to produce final results. This process is dependent on using existing staff resources where available as no funding was received for this work. These data are being prepared for publication.

Extension of the research study 10/H0713/79 in 2013/14

According to The Sunday Times (17 November 2013), "Dr Polly Carmichael… planned to continue the programme indefinitely," referring to "the early intervention study." However, when I asked the HRA, they had no records relating to the extension of the research study. Therefore:

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   The duration of the study was not extended beyond the time specified in the application form.

   If this research study was extended, when did or will it conclude?

   See above the research study was not extended.

9. I am interested to know whether all of the 12-15 year old patients of GIDS who have ever been treated with puberty blockers are deemed to be participants in this study, or are the study participants a sub-set of a larger group of 12-15 year old GIDS patients who are receiving, or have received, puberty blockers? If not all 12-15 year old GIDS patients who have been or are treated with puberty blockers are receiving that treatment as part of the research study, on what basis is that treatment taking place? Presumably there is a treatment protocol governing/permitting that treatment.

   Only young people referred to the endocrine clinic within the study intake period are deemed to be participants in this research study. There has been evaluation of the emerging data and any young people referred to the endocrine clinic complete the same questionnaires as those in the research cohort. The treatment protocol can be found in our service specifications attached.

NHS STANDARD CONTRACT
FOR GENDER IDENTITY DEVELOPMENT SERVICE
FOR CHILDREN AND ADOLESCENTS

SCHEDULE 2 – THE SERVICES
A. SERVICE SPECIFICATION

Service Specification No.	E13/S(HSS)/e
Service	Gender Identity Development Service (GIDS) for Children and Adolescents
Commissioner Lead	Bernie Stocks
Provider Lead	
Period	1.4.2016 to 1.4.2020
Date of Review	30.12.2019

1. Population Needs

1.1 National/local context and evidence base

National context

1.1.1 About the service

This specification sets out the deliverables for a highly specialised service for Gender Identity Development (GID) for children and adolescents up to their 18th birthday and is for individuals who need support around their gender identity.

The service is commissioned to provide specialist assessment, consultation and care for children and young people, including psychological support and physical treatments, to help reduce the distressing feelings of a mismatch between their natal (assigned) sex and their gender identity. The service will also provide support to the family or carers of clients.

The psychological element of the service is a Tier 4 mental health service which will support children and young people to understand their gender identity.
See here for a description of tiers of mental health care:
http://www.icptoolkit.org/child_and_adolescent_pathways/about_icps/camh_service_tiers.aspx
Once accepted into the service, individuals are referred to as 'clients'.

The service will recognise a wide diversity in sexual and gender identities. It will be delivered through a highly specialist multidisciplinary team (MDT) with contributions from specialist social workers family therapists, psychiatrists, psychologists, psychotherapists, paediatric and adolescent endocrinologists and clinical nurse practitioners.

Children and young people who have disorders of sex development or intersex conditions and other endocrine conditions may be referred if there are associated concerns with gender identity development. If not, other services are available which local services can refer to.

The service will be delivered in line with:

- emerging evidence for best practice
- relevant national and international guidelines for the care of children and adolescents with GD such as the World Professional Association for Transgender Health Standards Of Care For the Health of Transsexual, Transgender and Gender Nonconforming people, (Version 7 2012) (referred to in this document as WPATH SOC v7) and the Endocrine Society's Clinical Guidelines (2009);
- NICE guidelines specific to the treatment of mental and emotional health and wellbeing including for psychosis, anxiety and depression.

Prevalence

1.1.2 Epidemiology

The incidence and prevalence of GD in adolescence is difficult to ascertain because it includes gender non-conforming individuals in whom the dysphoria subsequently partially or wholly disappears; those in which it evolves into a non-binary identity; those in whom it is the precursor to a lesbian, gay or bisexual identity (with or without a trans identity in addition), and those in whom the GD continues to be experienced.

Incidence in the UK

In the UK, a surveillance study examined the incidence and clinical presentation of GD in UK and Irish children and adolescents aged 4 to 15 years inclusive. New cases were reported by clinicians over a 19-month period (November 2011 – June 2013) and validated against DSM-IV criteria. Unpublished data from this study suggests an incidence (new cases per year) in children and adolescents aged 4-15 years (inclusive) presenting to secondary or tertiary care services of 1.6 per 100,000 in the UK.

This figure only reflects those who presented to NHS paediatric or psychological services and not those who have chosen not to, or who have been unable to access this care. The figure does not reflect the total number who may have accessed their GP regarding their gender dysphoria, or include those who have elected to seek private support.

Average age at presentation reflects referral trends to the GIDS, that is mid-adolescence (median 14.68 years [interquartile range 12.1-15.31 years]). A significant limitation of this surveillance study is that it only captured data for those presenting between their 4th and 16th birthdays - meaning that it is not possible to comment on the incidence of gender dysphoria among 16 and 17 year olds, which referral trends to the service suggest have significantly increased the overall incidence rate.

It is difficult to compare prevalence studies due to different inclusion criteria and potential underreporting. In Belgium, a population-based survey which looked at the prevalence of broader definitions of gender incongruence and gender ambivalence rather than gender dysphoria in the Flemish population, noted that the numbers were much higher than the

prevalence of gender dysphoria in clinical settings. This study identified a prevalence of gender incongruence of 0.7% and 0.6% and gender ambivalence of 2.2% and 1.9% in men and women respectively. (Van Caenegem et al. 2015).

A 2014 Dutch review reported gender dysphoria in 0.6 men and 0.2% women- based on an estimated percentage of men/women reporting ambivalent or incongruent gender identity combined with dislike of male/female body and a wish to obtain hormones/surgery. (Kuyper & Wijsen, 2014).

In the UK, the number of adolescents referred to specialised gender identity clinics for GD appears to be increasing. There also appears to be a corresponding shift in the sex ratio, from predominantly biological/assigned males to predominantly biological/assigned females. Similarly in a study at clinics in Toronto and Amsterdam, there was a significant change in the sex ratio of referred adolescents between two cohort periods: between 2006 and 2013, more assigned females were referred, but in the prior years there were more assigned males. (In Toronto there was no corresponding change in the sex ratio of 6,592 adolescents referred for other clinical problems). Sociological and sociocultural explanations have been offered to account for this recent inversion in the sex ratio of adolescents with GD (Aitken et al 2015).

1.1.4 Evidence base

The reason why some people experience GD is not fully understood. A review of the evidence supports this view. (NHS England Clinical Evidence Review: Prescribing of Cross-Sex [gender affirming] Hormones as part of the Gender Identity Development Service for Children and Adolescents E03X16/01). It is likely that the development of gender identity is multifactorial and influenced by both biological and social factors.

1.2 Gender non-conforming behaviours and continuation of GD

1.2.1 About Gender Dysphoria

The language in this area is evolving. Gender identity refers to an individual's subjective sense of being male, female, both, neither or something else.

Gender Dysphoria (GD) describes the distress that is caused by a discrepancy between a person's gender identity and that person's sex classified at birth (and the associated gender role and/or primary and secondary sex characteristics) (Fisk, 1974; Knudson, De Cuypere, & Bockting, 2010b). Assigned sex is classified at birth based on the appearance of the genitals. The term transgender is used where a person's gender identity is different to their sex assigned at birth.

GD can be more distressing in adolescence due to the pubertal development of secondary sex characteristics and increasing social divisions between genders. As a result, adolescents can be at risk of self-harm, despair and can become vulnerable to relationship difficulties, social isolation and stigma.

Gender Identity was originally defined by Stoller (1964) as "core gender identity" which reflects a person's "fundamental sense of belonging to one sex [an awareness of being male or female and]; an over-all sense of identity."

Currently a diversification of gender identifications is taking place. A person may identify with characteristics and behaviours which (their) society may recognise as not being consistent with their experienced gender, or they may identify by another descriptor such as non-binary. Binary implies that an individual identifies exclusively as a man or a woman, however there is a growing recognition that many people do not regard themselves as conforming to the binary male/female classification.

Some children experience anxiety and other forms of distress associated with the difference or incongruence between their assigned sex classified at birth and the gender characteristics and behaviours they identify with. In addition, some may strongly dislike the physical sex characteristics of their biological sex.

The WPATH SOC v7 note that not all gender variant people experience GD and those who do may not experience it persistently (on a continuing basis) throughout their lives. However, if the distress resulting from this incongruence reaches clinical levels, the diagnosis of GD according to the Diagnostic and Statistical Manual of Mental Disorders version 5 (DSM-5) is applicable.

It is recognised that there are some concerns about the DSM-5 classification, although it has a place in supporting the identification of GD. de Vries & Cohen-Kettenis (2012) of the Dutch childrens' gender service state "About one quarter of the referrals in Amsterdam do not fulfil diagnostic criteria for GID and most of them drop out early in the diagnostic procedure for this reason or because other problems are prominent".

In follow-up studies of prepubertal children (mainly boys) who were referred to clinics for assessment of gender dysphoria, the dysphoria persisted into adulthood for only 6–23% of children (Cohen-Kettenis, 2001; Zucker & Bradley, 1995). Boys in these studies were more likely to identify as gay in adulthood than as transgender (Green, 1987; Money & Russo, 1979; Zucker & Bradley, 1995; Zucker, 1984). Newer studies, also including girls, showed a 12–27% persistence rate of gender dysphoria into adulthood (Drummond, Bradley, Peterson-Badali, & Zucker, 2008; Wallien & Cohen-Kettenis, 2008).

In some children, the dysphoria will intensify and body aversion will develop or increase as they become adolescents and their secondary sex characteristics develop (Cohen-Kettenis, 2001; Cohen-Kettenis & Pfäfflin, 2003; Drummond et al., 2008; Wallien & Cohen-Kettenis, 2008; Zucker & Bradley, 1995), in WPATH SOC v7).

In contrast, GD continuing into adulthood appears to be much higher for adolescents. No formal prospective studies exist. However, in a Dutch follow-up study of 70 adolescents who were diagnosed with gender dysphoria and given puberty-suppressing hormones, all continued with gender affirming surgery, beginning with feminising/masculinizing hormone therapy (de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2010) (in WPATH SOC v7).

According to the DSM-5, rates of GD continuing into adolescence or adulthood vary. In assigned males, this has ranged from 2 to 30 percent. In assigned females, this has ranged from 12 to 50 percent. (DSM-5. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, 5th edn. Washington DC:American Psychiatric Publishing, 2013, 302.85:455). 'It's clear that, for the majority of gender-confused boys and girls, gender dysphoria desists over time as they enter adolescence'. (Zucker KJ. Measurement of

psychosexual differentiation. Arch Sex Behav 2005:34 (4):375-388.) Early introduction of puberty suppressants may mask these developmental changes.

Many adolescents may experience some disorientation and embarrassment with the physical changes of the body during puberty. Adolescence seems to be important to the way in which an individual's gender identity develops and how it is expressed.

1.2.2 Social transition

Some children state that they want to make a social transition to their preferred gender role long before puberty. 'Families vary in the extent to which they allow their young children to make a social transition to another gender role. Social transitions in early childhood do occur within some families quite smoothly. This is a controversial issue, and divergent views are held by health professionals. The current evidence base is insufficient to predict the long-term outcomes of completing a gender role transition during early childhood. Outcomes research with children who completed early social transitions would greatly inform future clinical recommendations', (WPATH SOC v7). Additional research is needed to refine estimates of its pevalence and persistence in different populations worldwide, Zucker and Lawrence (2009) in WPATH SOC v7.

The age at which adolescents transition socially has decreased in the last decade. Many young people choose to socially transition before any treatment has started, although some more anxious youngsters often prefer to wait until cross-sex hormone treatment actually commences. (Kaltiala-Heino et al. 2015).

Steensma and Cohen-Kettenis (2011) report from a clinical based sample that between 2000 and 2004, out of 121 pre-pubertal children, 3.3% had completely transitioned (clothing, hairstyle, change of name, and use of pronouns) when they were referred, and 19% were living in the preferred gender role in clothing style and hairstyle, but did not announce that they wanted a change in name and pronoun. Between 2005 and 2009, these percentages increased to 8.9% and 33.3% respectively.

Olsen et al. (2016) report data from a community based national sample of 73 transgender pre-pubescent children in the USA, suggesting that socially transitioned transgender children who were supported in their gender identity have developmentally normative levels of depression and only slightly elevated anxiety compared with population averages. They conclude that psychopathology is not inevitable within this group and that, although different samples and methods were used, compared with reports of children with GD; socially transitioned transgender children have notably lower rates of internalizing psychopathology than previously reported among children with GD living as their natal sex." (Olson et al, 2016).

It is notable that the literature looking at social transition is frequently based on a binary model of gender. Young people self-identify in increasingly diverse ways and some question traditional assumptions about stereotypical gender expression associated with gender identities.

1.2.3 Associated difficulties:

Various studies show that transgender young people may present with psychosocial difficulties. Yet it is also true that many young people who present to gender services are not acutely distressed. This may be particularly the case for adolescents who are aware of the possibility of gender transition, who live in an accepting environment, and who can have access to puberty suppressing treatments until they are able to take a decision to transition physiologically (Drescher et. al. 2012).

Some empirical studies of the mental health of gender variant young people, mostly from the US, show that adolescents are at high risk of self-harm and suicidal ideation (e.g. Grossman & D'Augelli, 2006). However, it is not helpful to generalise across the whole international population of gender variant young people given the diversity of the specific national, cultural and socio-political contexts in which young people live.

Data from the Netherlands (de Vries et al. 2014) show that there is a group of well-supported, mentally stable young people who cope well with their significant gender incongruence.

In the UK evidence suggests that experiencing GD can correlate with severe distress (Holt, Skagerberg & Dunsford 2014). The service in England identified the three most common associated difficulties which clients encountered in their daily lives were bullying (47%), low mood/depression (42%) and self-harming behaviours (39%), (Holt et al, 2014). In Holland, the Dutch team found that 67% of referred young people had no additional psychiatric diagnosis (de Vries et al 2010) but it was more common for their clients to have coexisting internalising difficulties such as anxiety and depression, than externalising presentations such as oppositional defiant disorder (de Vries et al., 2010).

In Finland, more than three quarters of 49 adolescents who were assessed over a two year period in a gender identity service had needed/or currently needed specialist level child and adolescent psychiatric services due to psychiatric problems other than GD (Kaltiala-Heino et al. 2015). The authors identified five distinctive groups of young people and adolescents amongst 49 adolescents presenting at their service: Group A: Early onset with no significant psychopathology; Group B: Early onset with considerable psychopathological difficulties; Group C: Adolescent onset with no, or very few psychopathological or developmental difficulties; Group D: Adolescent onset with severe psychopathological and developmental difficulties; and Group E: Adolescent onset with identity confused development. This last group was the largest, consisting of young people who were bullied, isolated with few friends, not attending school or not leaving the house, and frequently self-harming; they had a strong conviction that gender reassignment would solve their psychosocial difficulties.

In a more recent study, 24% of the young people referred to a specialist gender service self-harmed, 14% of the young people had thoughts of self-harming, and suicide attempts were indicated in 10% of the young people prior to attending the service (Skagerberg et. al., 2013).

The data for the assigned females and assigned males, showed that thoughts of self-harm were more common in the assigned males than in the assigned females prior to attending the specialist gender service, whereas actual self-harm was more common in the assigned females. These figures for associated difficulties appear to be increasing in line with the rise in the general population; self-harm rates in the general population tripled between 2002 and

2012 (Hawton et al 2014).
In some settings, it appears that social exclusion may be a key causal pathway for the relationship between gender identity and disadvantageous health outcomes (Hendricks & Testa 2012). This can take the form of prejudice; stigma; transphobia; individual, institutional, and societal discrimination and violence.

1.2.4 Autistic spectrum disorder conditions (ASD):

There seems to be a higher prevalence of autistic spectrum disorder (ASD) conditions in clinically referred, gender dysphoric adolescents than in the general adolescent population. Holt, Skagerberg & Dunsford (2014) found that 13.3% of referrals to the service in 2012 mentioned comorbid ASD (although this is likely to be an underestimate). This compares with 9.4% in the Dutch service; whereas in the Finnish service, 26% of adolescents were diagnosed to be on the autism spectrum (Kaltiala-Heino et al. 2015).

1.3 Physical Treatments:

It should be noted that the research evidence around the long term impacts of some treatments is limited and still developing and that by no means all clients with GD choose to have physical interventions.

Adolescents with continuing GD will be able to have physical interventions via the Service provided they fulfil the eligibility and readiness criteria for these. National and international guidelines recommend the use of hormone blockers (gonadotropin-releasing hormone agonists GnRH) in adolescence to suppress puberty,. For some individuals, this is followed later with cross-sex hormones, which are sex steroids of the experienced gender, also referred to as gender affirming hormones. If individuals fulfil additional criteria, they may have various types of gender affirming surgery from the age of 18 through adult gender identity clinics.

WPATH SOC v7 note that physical interventions should be addressed in the context of adolescent development. Some identity beliefs in adolescents may become firmly held and strongly expressed, giving a false impression of irreversibility. At the same time an adolescent's shift towards gender conformity can occur primarily to please the parents and may not persist or reflect a permanent change in gender dysphoria (Hembree et al., 2009; Steensma et al., published online ahead of print January 7, 2011).

There has been some debate about the minimum age at which puberty suppression and cross-sex hormone treatment could start. When first introduced, an age of 12 years was recommended for puberty suppression. However, boys and girls enter puberty at different stages. Please see separate NHS England Policy - Prescribing of Cross Sex Hormones as part of the Gender Identity Development Service for children and adolescents for access criteria to cross sex hormones.

In adolescents with GD, psychological support and puberty suppression have both been shown to be associated with an improved global psychosocial functioning. Both interventions may be considered effective in the clinical care of psychosocial functioning difficulties in adolescents with GD (Costa et al: in press).

Engagement in social interaction with other transgender people has been shown to help build resilience: Testa, Jimenez & Rankin (2014) demonstrated this effect empirically.

In the Dutch long-term evaluation study, it has been found that the psychological functioning of selected transgender adolescents tends to improve after a staged programme of puberty suppression, cross-sex hormones and gender reassignment surgery (de Vries et al, 2014). In this series of studies, 55 adolescents with GD were followed up at three time points: i) at intake, before the start of puberty suppression (mean age 13.6); ii) when cross-sex hormones were introduced (mean age 16.7); and iii) at least one year after gender reassignment surgery (mean age 20.7). No adolescent withdrew from puberty suppression, and all started cross-sex hormone treatment. Their psychological functioning improved steadily over time, resulting in rates of clinical problems that were indistinguishable from general population samples (e.g. numbers in the 'clinical' range dropped from 30% to 7% on the Youth Self Report (YSR) and 38% to 5% on the Child Behaviour Checklist (CBCL). Quality of life, satisfaction with life, and subjective happiness were comparable to same-age peers.

In the follow-up cohort study by the Dutch clinical team, young people were only eligible for puberty suppression if they (a) had persistent [continuing] GD from childhood, (b) lived in a supportive environment and (c) had no serious co-morbidities. These were called the 'immediately eligible' group (de Vries et al 2011).

In Holland therefore, those young people who achieve good outcomes are more likely to be those who have experienced lifelong gender non-conformity and who start off with significant social advantages: chiefly, the absence of any serious psychological difficulties and the presence of strong family support. Young people were started on puberty suppression only after a 'comprehensive psychosocial evaluation with many sessions over a longer period of time' (de Vries et al 2014). For the 'immediately eligible' group, the time from starting assessment to starting on the blocker was up to 18 months, with a mean of 9 months. If the young people did not show persistent [continuing] GD from childhood, live in a supportive environment or if they had serious co-morbidities, assessment was prolonged to up to almost two years (1.86 months). Such young people were in the 'delayed eligible' group. This delay in starting the blocker was to ensure they had adequate mental health treatment prior to medical intervention.

Spack, Edwards-Leeper and Feldman (2012), note that all the young people who were seen in the Boston service were reported to be in counselling, and the authors reference studies to show that 'those who do not receive counselling have a higher risk of behavioural and emotional problems and psychiatric diagnoses'.

Safety concerns remain regarding the impact of physical interventions. Although puberty suppression, cross-sex hormones and gender affirming surgeries are generally considered safe treatments in the short term, the long-term effects regarding bone health and cardiovascular risks are still unknown (Cohen-Kettenis & Klink, 2015).

The clinical team in Holland and the WPATH SOC v7 emphasise the importance of informed consent at each stage of treatment. This means that clients need to be informed about the possibilities and limitations of gender affirming interventions and other types of treatment, including psychological interventions. As GD may exist in many forms and intensities, gender affirming surgeries are not the only treatment option to help resolve GD. The broader impact

of gender affirming medical treatments on many aspects of their lives has to be discussed, including fertility.

2.0 Outcomes

2.1 **NHS Outcomes Framework Domains & Indicators**

Domain 1	**Preventing people from dying prematurely**	✓
Domain 2	**Enhancing quality of life for people with long-term conditions**	✓
Domain 3	**Helping people to recover from episodes of ill-health or following injury**	✓
Domain 4	**Ensuring people have a positive experience of care**	✓
Domain 5	**Treating and caring for people in a safe environment and protecting them from avoidable harm**	✓

The service will impact on the domains in the following ways:

Domain 1: Preventing people from dying prematurely
Experiencing GD can be associated with acute distress. The service will seek to reduce the distress of clients by providing high quality psychological and medical support, including physical interventions, as required on an individual basis.

Domain 2: Enhancing Quality of Life for people with long-term health conditions
Experiencing GD can be associated with significant social and emotional difficulties and distress. The service will seek to reduce the negative effects on a client's general development and build their resilience across a range of domains, including family and peer relationships, self-esteem, self-image and education, thereby improving quality of life.

Domain 3: Helping people to recover from episodes of ill-health or following injury
The service aims to reduce morbidity by providing high quality psychological and medical support through individualised health care pathways.

Domain 4: Ensuring that people have a positive experience of care
Overarching indicator: patient/client experience:
To ensure that the client and their family/carer are well-supported during the time they are in contact with the service, each client will be assigned a named Lead Worker.

The Lead Worker will be the primary source of contact for any issues arising between appointments and will be the lead for providing psychological care, supported by other staff as appropriate. Referrals will be made to the paediatric endocrine liaison service when indicated. Endocrine Consultants are the lead professionals for physical care and interventions. Care

decisions related to the commencement and continuation of hormone blockers and cross sex hormones are made jointly with psychosocial and endocrine professionals in consultation with clients and their families/carers.

As a result of interaction with the service, clients will:

- feel safe, supported and listened to by the service during their personal gender identity development experience.
- experience a reduction in the level of distress and conflict around their GD
- have an increased ability to function well in daily life in relation to their gender identification
- feel supported as a consequence of clear pathways, the availability of support materials and access to local professionals to gain information and support.
- be able to access care locally, including accessing prescribed hormone treatments by their local GP, with oversight from the Service's Paediatric and Adolescent Endocrine Liaison Team.
- know what the Service can and cannot provide, know how to access help and support from the Service between appointments, including telephone support for clients and their families/carers which are staffed on a rota basis, online literature and other support from national and local voluntary networks and community groups.
- have clarity about how to access local health care services that people with GD may want to be in contact with, for example speech and language and sexual health services. (See Appendix 3 for information on partnership working with GPs and CAMHS and Appendix 4 for more information on referral processes to local services).
- have information on fertility options and be signposted to other specialists such as gynaecologists and licensed NHS fertility experts for gamete retrieval via their GP.
- be offered support when transferring to adult gender services if this is their chosen pathway
- feel that their parents or carers are supported by the Service, so that parents/carers in turn are better able to support them.
- feel that those supporting them locally (e.g. professionals from schools, colleges, voluntary organisations, health and social care) are appropriately included and consulted with by the Service.

The Service will also provide peer support through therapeutic groups which focus on facilitating information sharing, reducing harm and promoting coping and resilience. Family days will bring together clients, families and carers who are facing similar issues, with health professionals to facilitate peer support and a safe environment to explore options and concerns.

Clients will be involved in service improvements, innovations and developments in a variety of ways which may include:

- regular feedback (including with their family/carers) about their experience of the service;
- participation in a Young Person's Stakeholder Group to influence the service based on their personal experience;
- being part of interview panels for new staff of the Service;
- attending wider provider Trust meetings to represent the views of service-users;
- requests to comment on specific issues;
- being involved in events and communications aimed at increasing awareness of needs of

young people with GD and their families and what services, professionals and communities can do to best support them.

Domain 5: Treating and caring for people in a safe environment and protecting them from avoidable harm
The Service will ensure that local systems are in place to track and manage client safety performance, including taking action when agreed standards are not met. Robust reporting of incidents will be undertaken through local procedures and reported to NHS England.

Overarching indicator: Risks will be assessed and incidents reported. Evidence of lessons learnt and subsequent improved patient safety will be required to be provided to the NHS England commissioning team.

2.2 Locally Defined Outcomes for the Gender Identity Development Service
The Service will use a number of different measures to monitor the clinical outcomes that clients achieve. The measures will capture client wellbeing and GD and hence are a proxy for the change achieved.

2.2.1 Clinically Rated Outcome Measure (CROM)
Clinically rated outcome measures will be used by the Service to monitor each client's general progress throughout their time with the Service. The Children's Global Assessment Scale (CGAS) will be used to assess adolescent global functioning after psychological support and physical treatment.

2.2.2 Patient Rated Outcome Measures (PROMs)
Patient/client rated outcome measures involve each client providing feedback on the progress they feel they are making as a result of the interventions provided by the Service.
This will include measures of GD and a self-harm questionnaire.

2.2.3 Patient Rated Experience Measure (PREMs)
The Service will measure the overall experience of clients by routinely using patient satisfaction questionnaires to gauge overall satisfaction with the interventions provided by the service.

3. Scope

3.1 Aim and objectives of service

The aim of the service is to provide a highly specialised service for children and adolescents up to their 18th birthday who are experiencing features of GD or need support to explore their gender identity.

It will do this by fostering recognition and non-judgemental acceptance of diversity in gender identities and gender expression; providing support, advice and treatment to assist in reducing behavioural, emotional and relationship difficulties and their effects; offering options for physical interventions as appropriate, and working to prevent further mental health problems such as anxiety, low mood, self-harm and suicidal thoughts. The service will consider

difficulties associated with gender identity development in the context of general developmental processes.

Objectives

The service will be provided in a timely way and will deliver the aim by working in a tiered way with other services so that the client can be supported as close to home as possible, accessing the service when specialist expertise and input is required. This will include joint-working, consultation and liaison with local Child and Adolescent Mental Health Services (CAMHS), schools, colleges and others as required.

The service will provide specialist input and consultation for GD experienced by a client. The services is not commissioned to provide care for psychiatric emergencies, as local clinical professionals are responsible for this care, and may include CAMHS, GPs and/or secondary care consultants.

The service is commissioned to improve a client's state of psychological health and social inclusion by delivering tailored treatment packages in a safe environment.

For those clients who decide to undertake physical interventions, the Service will follow a staged approach, including undertaking ongoing monitoring and therapeutic exploration of their gender identity. This approach will ensure that clients have adequate time to fully assimilate the effects of each stage of physical intervention and the different options for gender expression, recognising that the needs of each person will be different.

The objectives of the Service are to provide:

Objective Area	Aim	Deliverables – this will include:
Expert advice	To be the lead clinical service and a source of expert advice for the diagnosis and care of children and adolescents with GD within the NHS, social care and educational system.	Raised awareness and increased understanding across health, social care and educational agencies of the issues associated with GD, thereby enabling those organisations to provide improved support locally to the individual and their family/carers and a more informed, timely and effective response in referral, assessment and treatment.
Pre-referral advice	Provide consultation advice to healthcare professionals, CAMHS, schools, colleges, voluntary sector organisations prior to referral and pre-referral support where there is a complex presentation or when the young	Advice by telephone/email.

	person, parents/family or carers are not yet ready for direct contact with the service.	
Support local services	Ensure excellent joint working and effective monitoring.	Good communication, liaison and support available to GPs, local schools, colleges, health and social care providers to support young clients with GD. Support this via appropriate literature and web-based resources including guidance for schools.
Improved access	Promote equity of access and choice through the development of satellite clinics where there is a high volume of clients, following consultation and agreement with commissioners.	Ongoing review of need.

Objective Area	**Aim**	**Deliverables – this will include:**
High Quality Care	Provide expert opinion, therapeutic support and care for clients who have GD to maximise the client's experience of care, improving their long-term quality of life, social inclusion, mental and emotional health and reducing self-harm and suicidal thoughts. The service will do this through: • providing therapeutic support and care, with a client and family-centred focus; • undertaking an initial assessment process which will be specific to the person in terms of duration and will typically be over three to six meetings depending on the individual; In some complex cases, this may take longer and interim recommendations for further assessment and exploration will be made; • using the most up-to-date clinical protocols for prescribing, therapeutic interventions, control of symptoms and treatment;	An assessment report and care plan to include a history of gender development and gender identification, and a description of associated mental health issues. High quality information for clients, families or carers, schools, colleges and healthcare professionals in appropriate and accessible formats and media.

	• supporting the on-going exploration of gender identity and expression; • enabling the client and their parents/carers to make an informed choice of the treatment options; • providing an integrated service which encourages exploration of the mind-body relationship through close collaboration among professionals in different specialties, including paediatric and adolescent endocrinology for consideration of physical treatment with the hormone blocker when the client is in established puberty, (not before Tanner Stage 2) (see Appendix 5 for information on Tanner stages) and with referral via the GP to NHS specialists such as gynaecologists and fertility experts for egg and sperm retrieval advice and storage, and support; • providing a prompt, staged approach to reducing the risk of self-harming behaviour and encourage a positive self-image.	
Improved functioning of clients in their daily life	Maximise the client's daily functioning by working within the client's relationships with parents and family/carers, school and other social agencies. Help the client and their parents/carers to: • understand the nature of obstacles or adverse factors in the development of gender identity and try to minimise their negative influence; • support the client and their parents/ carers to tolerate uncertainty in gender identity	The client has an improved ability to effectively communicate and make informed choices about their life.

	development; • combat the stigma which is often associated with the experience of atypical gender identity and is at times internalised by the individual experiencing GD; • alleviate feeling of shame that some clients and their parents and family/carers' experience, and enable them to develop skills in handling social interactions and dealing with possible hostility; • promote the development of autonomy.	
Transfer	Facilitate a secure and seamless transfer to adult services for those clients in whom the GD persists and who therefore require ongoing care and support. Establish effective working relationships with providers of adult gender services and maintain supportive contact with the clients referred to those services until they are securely placed.	Supported transfer.
Audit	Undertake a rolling programme of clinical audit to test current practice and inform the evolution of care and therapeutic intervention for GD.	Audits and publications of findings.
Engagement	Collaborate and engage with community groups which deliver services to clients with GD and their family/carers.	Annual programme of engagement activities.
Service improvement and innovation	Continually develop the specialist experience, knowledge and skills of the Service's MDT to ensure high quality, sustainable provision. Continually develop clinical methods, new aspects of the Service and new ways of delivering care, while increasing the evidence base, in the area of GD.	Annual training and development programme. Attendance at National and International conferences.

3.2 Service description/care pathway

Service description

3.2.1 The Service will be provided through a highly specialist multidisciplinary approach and include the assessment and care of children and adolescents with features of GD.

It will be delivered through a network model in collaboration with specialists local to where the client lives and the organisations and agencies with whom the client and their family/ carers are interacting, including CAMHS, GP's, secondary care paediatricians, gynaecology consultants, schools and colleges. This will be holistic and tailored to the needs of the individual and their family/ carers. The Service will make recommendations to GPs for onward referral via the GP for input from other NHS healthcare professionals such as gynaecologists and licenced NHS fertility experts.

Referrals

3.2.2 Referring professionals will be encouraged to discuss the referral with the family/ carer and seek their agreement. The Service will only accept referrals for children and adolescents with features of GD which are consistent with the current diagnostic criteria as defined in DSM-5.

Referrals can be made by staff in health and social services, schools, colleges of further education and by people in voluntary organisations who may have concerns about a young person's gender identity development and associated difficulties.

Figure 1: Indicative Schematic illustration of GIDS Service pathway
Following assessment, clients follow different and individualised pathways, which may or may not include physical assessment and treatment. (In practice, pathways may be adjusted to meet individual circumstances). In some cases, clients may move between and back and forth from the various aspects of the pathway at any stage.

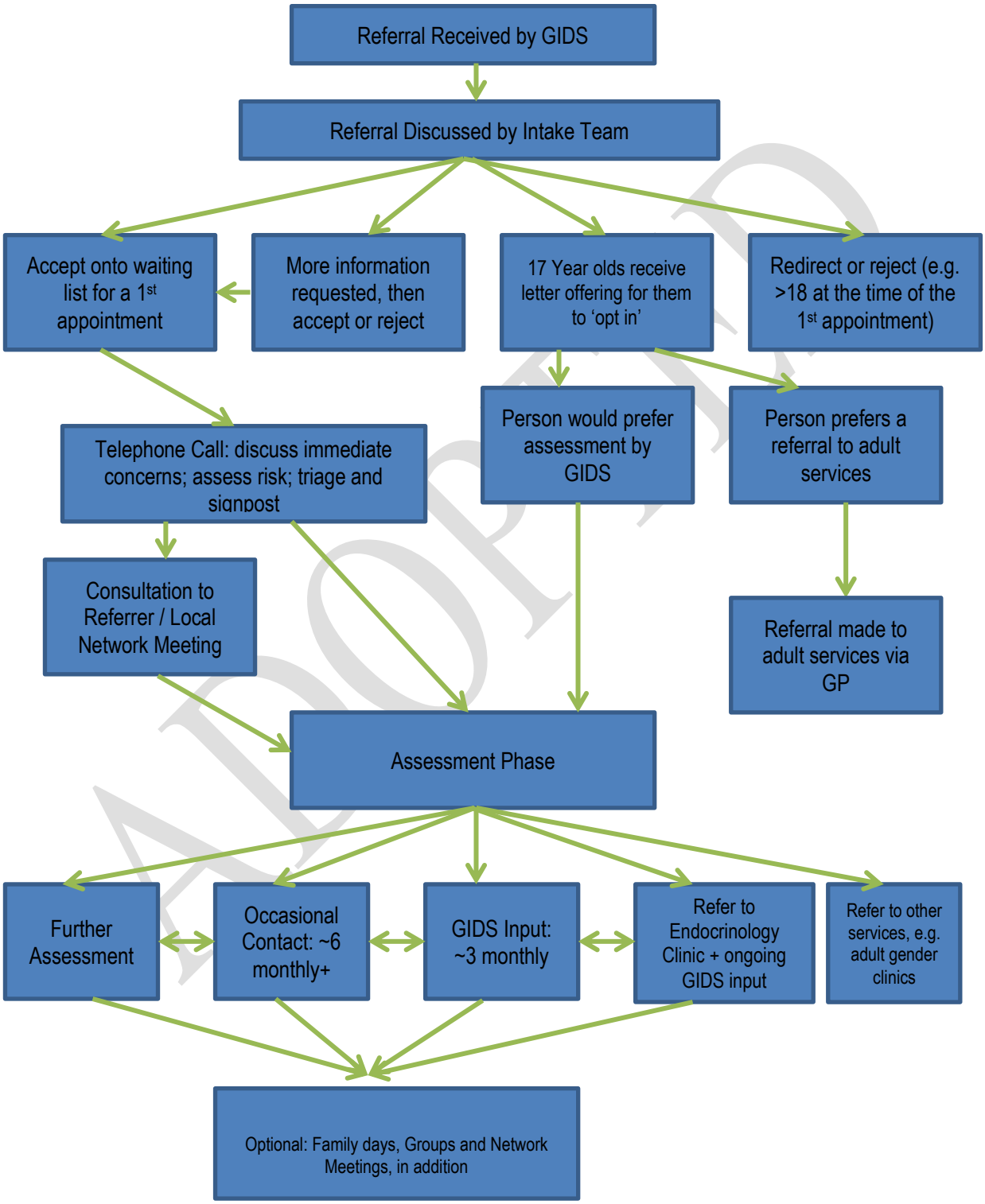
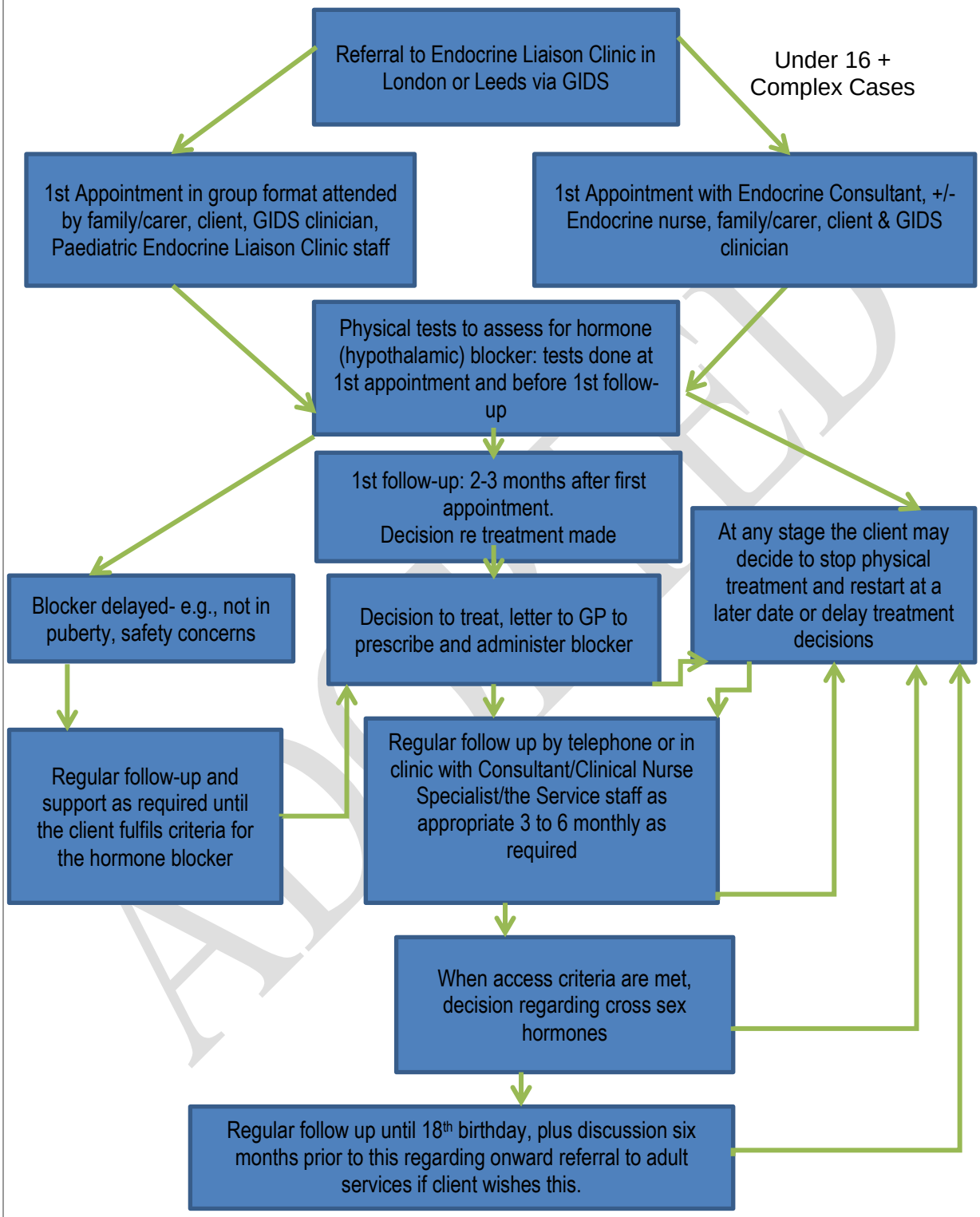


Figure 2: Indicative schematic diagram of pathways through the Paediatric Endocrine Liaison Clinic (in practice pathways may be adjusted to meet individual circumstances)
- For clients who decide to undertake physical assessment and treatment



3.2.2 Service inputs:

The service will provide:

- psychological/psychosocial support aimed at increasing the wellbeing and resilience of the client;
- therapeutic exploration of gender identity development and gender expression, including in relation to the client's familial, social and cultural situation;
- referral, when appropriate to the needs of the client, to the Service's Paediatric Endocrine Liaison Clinic for the following:
  - an initial physical assessment
  - advice for clients and their parents/carers around key decisions, such as when being offered hormone blockers or cross-sex hormones
  - ongoing review of progress with these treatments once prescribed;
  - access, via subsequent GP referral, to other medical specialists such as local secondary care gynaecologists and licenced NHS fertility specialists to provide advice to clients and their parents or carers when key decisions need to be made with regard to sperm or egg retrieval and storage.

The Service will also provide:

- consultation and teaching;
- research;
- support to children of transgender parents
- support to children with DSD (Disorder of Sex Development – also known as intersex conditions) who are experiencing GD and to professionals and families/carers making decisions about sex assignment and associated care;
- court reports;
- clinical placements.

3.2.3 Tiered model of care

The model is based on four tiers of care, with the Service managing care at Tier 4 and supporting local provision of care at the other tiers.

This will ensure that:

- appropriate care is provided as close to home as possible and,
- local professionals caring for children and adolescents can access appropriate information and support between the appointments with the Service.

See Table 1 below

Table 1: Tiers of Care

Tier	Description	Detail of support and toolkits/documentation that the Service will make available to this Tier
Tier 1	Local meetings with professionals involved in the care of the client with a diagnosis of GD including: teachers, social workers, school or college staff, secondary care consultants, GPs and others as appropriate, to identify roles and facilitate the recognition and support of the client in their local community.	The Service will support the following staff with advice in local network meetings and advise on any issues that arise: • School nurses, teachers • College lecturers • Social workers • GP's (including CCG's and LMC's) • CAMHS professionals The Service will work with primary care accreditation schemes, which support GP Practices to meet the needs of LGBT patients, and promote greater understanding through training such as the CPD accredited Gender Variance e-learning module.
Tiers 2 and 3	The client will access local generic CAMHS and GPs for general mental health needs. The service will offer advice to these staff.	The Service will support staff as follows: CAMHS – establish communication protocols and close working arrangements to enable local services to better support clients and their family or carers. CAMHS will be asked to review clients who the Service identifies as at risk. This request will be copied to the GP for information. The Service will report to NHS England on its approach to risk assessment and management and other interactions with GP's, local CAMHS teams and secondary care clinicians to provide an understanding of how/whether the issues have been addressed.
Tier 4	The Service will provide specialist assessment and care for children and adolescents with GD. The	• On a case by case basis, the service will share care and work with those who support clients locally through information giving

	Service will support generic CAMHS (Tiers 2 and 3) and other professionals (Tier 1) who are working with children for emergency and urgent care and treatment for mental illness. This will be include liaison, and where appropriate joint assessment and co-working in relation to GD.	and providing education and advice • promote a wider understanding of GD through: o Creating education materials o Undertaking and disseminating research o Creating and taking part in Continuing Professional Development opportunities

The Service is commissioned to provide assessment/consultation and the following inputs:

- continuing therapeutic exploration;
- intermittent reviews to monitor gender identity development;
- family therapy, work with parents/carers and support for siblings;
- group work and family days for clients, parents/carers and siblings;
- consultation to the network of agencies supporting the client, with or without further direct involvement with the client and their family/carers;
- network meetings in the client's locality;
- referral to the Paediatric Endocrine Liaison Clinic for physical assessment and endocrine treatment where appropriate;
- referral, via the client's GP, to other NHS healthcare professionals such as gynaecologists and licensed NHS fertility experts for discussion on gamete retrieval;
- referral to adult gender services/clinics.

Input will be agreed on a case by case basis dependent on each client's needs, including focus and frequency of contact. The Service will follow an integrated model of care involving psychosocial support, monitoring of GD and physical interventions as appropriate on a case by case basis. Where clients need more support between appointments and that support is within the expertise of local healthcare teams such as local CAMHS, the client's GP or the local acute or community paediatrician, the Service will make contact with the relevant organisation and request this.

It is recognised that a client's needs may change during their time with the Service. The Service will discuss the level of support needed with clients and their family or carers during clinic visits and other forms of contact. An individualised care plan will be created, agreed and reviewed as needs change.

3.2.4 Assessment, consultation and treatment at Tier 4:

3.2.4.1 Psychological Support:

When assessing children and adolescents who present with GD, the Service's mental health professionals will conform to the following guidelines taken from WPATH SOC v7. See Appendix 6 for more information. The service will also take into account new guidelines and evidence as they are published.

3.2.4.4 How psychological support will be offered

Pre-pubertal children, children in puberty and post pubertal children

The Service for pre-pubertal children will include initial assessment together with the family or carers to ascertain the features of GD and the nature of associated difficulties. The Service will facilitate communication in the family about the client's perceptions and behaviour regarding their gender identity to support their ongoing relationships.

In this initial assessment/consultation phase, clients and carers will be seen every one to three months, although this may be more or less frequent as needed. The Service will also provide therapeutic support and liaise with local services where appropriate to help clients and their family or carers manage any relationship difficulties. The Service may meet with parents/carers separately if requested or indicated.

The Service will organise and host Family Days to be attended by clients, their parents/ carers and siblings, and support groups for young people and for parents/carers. The aim of these will be to encourage peer support and discussion of shared experiences**.**

Children approaching puberty

For children approaching puberty, children in puberty and post-pubertal children and young people, provision will include the inputs described above, as well as individual sessions for clients.

There will be a multi-factorial assessment to enable the Lead Worker to gain a broad picture of the client's previous and current gender identification, as well as their development across a number of domains (education, family relationships, peer relationships), with a particular focus on any associated psychological difficulties that may impact on future development and response to treatment.

The work will aim to facilitate the curiosity and thoughtfulness of clients and their family or carers about the complex interactions between gender identity, gender expression, gender roles and other aspects of identity. Such conversations might also touch on the impact of living in a social world where negative attitudes towards gender variance are widespread and how these attitudes forces may be challenged.

The exact content and manner of delivery will be dependent on the developmental stage and age of the client. Where the client's situation is complex, that is, has a number of health conditions or psychosocial adversities in addition to the GD presentation, the Service will, as appropriate, undertake joint 'network' meetings with the client, their family or carers, their GP, CAMHS provider, school, secondary care paediatrician and others to ensure the appropriate care.

The Service will take particular care in assessing clients who may have social and communication difficulties or difficulties in learning, with attention paid to the client's understanding of gender and sex development and physical treatments for GD, and any issues regarding informed consent to treatment.

The Service will use a range of questionnaires as part of the assessment process to gather information on the client's gender identification and general functioning and contribute to the evidence base.

The diagnostic criteria for GD (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) will also inform the assessment regarding the child's gender identity development. The American Psychiatric Association (2013) provides further clarity on defining GD in children.

NHS England has reviewed the available evidence and concluded that as there is insufficient evidence of the long term risks and effects to inform the timing of cross sex hormones, it is appropriate to adopt a routine commissioning policy position subject to each case being assessed on the readiness of the person for further treatment and that they meet the eligibility and readiness criteria set out in the policy.

Changes to current practice should be informed by standardised data collection which develops the evidence base.

The assessment/consultation phase will involve clients and their family/carers being seen together for at least some of the time to facilitate communication about the client's perceptions of their gender identity.

Specialist assessment will take into account:

- the subjective sense of the client's identity over time;
- their expression of gender identity across different contexts over time;
- the client's and their family or carers' wishes, hopes and expectations, and their stance towards the client's gender identification;
- the capacity of the client, and their understanding of gender, puberty and fertility;
- any actual or potential risks (related to the client's physical and mental health) and how these are managed. If the risk of harm is felt to be significant, the necessary steps must be taken (i.e. immediate liaison with, or referral to, relevant agencies);
- the degree to which the client is engaging in school or work, and their experience of bullying or harassment;
- the client's psychosexual development and any sexual experiences;
- the quality of relationships within the family and wider community, and the level of support;
- the family or carers and the client's spiritual, cultural, or religious beliefs.

Factors that could influence the complexity and length of the assessment include:

- the intensity of any associated difficulties;
- on-going risk issues, including self-harm and suicidality, and safeguarding issues;
- concerns with regard to the client's capacity to understand and consent;
- family conflict (especially in a younger child) about how to proceed;
- inadequate support from the local network of agencies and services involved with the young person (where there are any concerns regarding mental health or social functioning).

The Service may liaise with CAMHS, social care and education at the assessment/ consultation stage in order to set out specific needs which local services may respond to, now

or in the future, with further psychiatric, educational and inter-disciplinary input.

The clinical work that supports identity exploration involves conversations which are focused on increasing understanding and insight. These conversations can be engaged in during the assessment period and continued subsequently when the relationship with the clinicians in the Service may become more trusting. Exploratory work will recognise the right of a client to self-define their gender identity and to make decisions about their own life and treatment, taking their developmental stage and competence into account.

Issues to do with body dissatisfaction may be broached, and hopes (which may be more or less realistic) for achieving a more settled relationship with the body. The opportunities provided by medical intervention, and the limitations of intervention will be discussed.

The Service may also support thinking about notions of masculinity and femininity and the range of possibilities around identification, whilst helping clients to tolerate the uncertainty associated with the process of exploration. Understanding the unique experience and point of view of each client will be a priority.

All aspects of the care pathways are available for clients who present with other gender identifications, including non-binary.

Liaison with CAMHS, social care, schools and colleges may be conducted at the assessment/consultation stage, identifying specific needs to which local services may respond, now or in the future, with further psychiatric and inter-disciplinary input.
If there are concerns about a client's mental health, local services will be asked to provide further psychiatric and multi-disciplinary input.

The Service will take appropriate action if harm, or the risk of harm, is felt to be significant (i.e. immediate liaison with or referral to relevant agencies).

It is noted that not all clients decide or wish to undertake physical assessment and treatment. On an individual basis therefore, clients may prefer only to access on-going support and therapeutic exploration of gender identification and/or social gender expression and not opt for physical treatment. At different times whilst in contact with the Service, clients can move between different elements of the pathway (see Figure 1).

Some children or adolescents who have socially and/or physiologically transitioned in line with their individual needs may decide to de-transition. The service will provide support for this, which may include consultation with schools, colleges and local services to ensure that the process is as smooth as possible. Support will also be provided to the young person and their family/carers in the usual way.

3.2.5 Informed consent

The Service will recognise a wide diversity in sexual and gender identities and will affirm the importance of each person to develop autonomy in relation to treatment decisions, as well as their need for care and support from their family and the professional team.

The Service will facilitate the careful consideration by clients and their family or carers of the

meaning of informed consent, as it is an important aspect of ethical assessment and intervention, including the emotional, social and factual issues, so as to enable them to make informed decisions about the treatment options, benefits, risks, and the alternatives to the treatments proposed (including the option of no treatment). The consequences of treatment decisions can be significant and life-changing.

The Service will support the client and their family or carers to jointly understand the factual information which will enable them to make informed decisions about treatment options, including hormone treatments if appropriate; initial advice about fertility options and, make a recommendation to the client's GP that a referral to a licenced NHS fertility specialist is required.

Age alone does not determine capacity to give consent. If it is concluded that a client has sufficient autonomy and understanding of what is to be offered, plus other key eligibility and readiness criteria have been met, they can consent to treatment.

The term 'competence' means that a person fully understands what is proposed; can retain an understanding of the implications; can appreciate the importance of the information and see how it applies to themselves and can assess the benefits and dis-benefits of their decision. The level of understanding that is sufficient will vary with the complexity and gravity of the decision.

The Service will assess a client's capacity or competence to consent to physical interventions. The evaluation of competence of a client for whom physical intervention is recommended within the scope of the specifications will be undertaken with special care for those under the age of 16 (see the Tavistock and Portman NHS Foundation Trust policy on 'Consent to Treatment').
http://tavistockandportman.uk/sites/default/files/files/consent-policy-and-procedure-Apr-15.pdf

All efforts will be made to ensure that clients are aware of the longer term consequences of the endocrine treatments, including implications for fertility, and the decision of the competence of the client will be jointly made by the endocrine and psychological members of the Service's integrated team.

The current context of treatment decisions about cross sex hormones in adolescence is that there is limited scientific evidence for the long-term benefits versus the potential harms of the intervention. There are also concerns that it is uncertain whether or not a young person will continue to identify as transgender in the future, given that some subsequently identify in a different way, (as referenced in Section 1.2).

Please see Appendix 7 for guidance on Informed Consent in the context of the Service.

3.2.6 Referral to the Service's Paediatric Endocrine Liaison Team

Following a detailed psychosocial assessment and consultation, a client may wish to be considered for referral to the Paediatric Endocrinology Liaison Team.

The Paediatric Endocrine Liaison Team includes Consultant Adolescent Endocrinologists and Clinical Nurse Specialists. Physical intervention is one part of the overall treatment offered by

the Service and is not offered in isolation from other aspects of the treatment provided by the MDT.

3.2.6.1 There will be two entry points:

- Early Intervention Clinic
- Standard Clinic

Early Intervention Clinic:
Physical intervention in the early stages of puberty is available via the Paediatric Endocrine Liaison Team's Early Intervention' Clinic for carefully selected clients who are at least in Tanner Stage 2 of puberty and are up to the age of 15. The Early Intervention Clinic will continue to follow the Service's 2011 research protocol, which following evaluation, has now become established practice, with the exception that hormone blockers will now be considered for any children under the age of 12 if they are in established puberty.

Standard Clinic:

These appointments will be for adolescents referred to the clinic who are aged between 15 to 18 years.

The client and their parents/carers will first attend either an educational group session or a joint appointment with a member or members of the endocrine and psychological/psychosocial care teams. Joint clinic appointments and the educational group will both include an introduction to the work of the clinic, information about physical treatments and issues relating to informed consent.

3.2.6.2 Assessment process for all clients

In the first or second Paediatric Endocrine Liaison clinic appointment, there will be a very short, visual and physical examination which will be done with the utmost empathy and respect for the client, in order to:

- provide the clinician(s) with a baseline assessment of the stage of pubertal development (genital stage/testicular volume in natal males and breast stage in natal females),
- enable the clinicians to ensure that the client is in good physical health and determine whether self-neglect or self-harm are present.

The need for this examination will be clearly explained to the client well in advance so that they can prepare for this and ask any questions. The client will be asked to consent to the examination. Following the examination, the client, their family or carers and clinicians will discuss further plans and reach a joint decision about whether to start the use of the hormone blocker if appropriate.

There are two separate categories of hormone treatments available:

- gonadotropin-releasing hormone analogues (GnRHa), (referred to in this document as hormone blockers). These can be prescribed to suspend puberty for clients who meet eligibility and readiness criteria. The Service will liaise with the client's GP and make the referral to the GP to prescribe these, which will be an injection given in primary care according to recommended dosage schedules. These can be taken for a limited time.

- cross-sex hormones. A client who has been on the hormone blocker for a period of time and been assessed as having continuing GD may be considered for cross-sex hormones if they meet eligibility and readiness criteria. Cross-sex hormones can be gradually introduced to mimic the physical and psychological changes of puberty.

It is expected that all treatments will be prescribed and administered in primary care services. The Service will provide support to GP's with any queries regarding this.

Hormone blockers will be considered as an appropriate treatment alongside psychological intervention, and will not necessarily be viewed as the pre-cursor to the prescribing of cross-sex hormones. The next stage of treatment, if any, should be left open for further exploration with the client.

The paediatric endocrinologist's assessment of the biological environment and the client's physical development will precede the prescribing of hormone blockers.
The decision to start hormone blockers is reached after an in-depth discussion involving the MDT. Decision-making responsibility for prescribing the hormone blocker and the physical monitoring of this treatment is with the paediatric endocrinologists, subject to periodic review by the MDT.

Fertility

All clients attending the Paediatric Endocrine Liaison clinic will receive general fertility advice including the possible effects of taking hormones for future fertility.

The Paediatric Endocrine Liaison Team will provide initial information on fertility options and signpost the client and their family or carers back to their GP who can make an onward referral to licensed NHS fertility specialists for expert advice on fertility options including gamete retrieval.

3.2.7 Staffing

The specialist MDT team will include the following professionals, with different levels of seniority providing care in each group:

- family therapists,
- child and adolescent psychiatrists,
- clinical psychologists
- social workers
- child and adolescent psychotherapists,
- clinical nurse specialists in endocrinology
- adolescent endocrinologists

3.2.8 Service hours:

The Service will operate Monday to Friday 9.30-5.30pm. If the Service cancels an appointment, a replacement slot will be booked within a week for the appointment to take place within six weeks. There should be a record kept of the number of times that a clinic appointment is cancelled before it takes place.

3.2.9 Discharge planning and possible transfer to adult services:

There are two possible outcomes for clients of the Service who are aged 17 years of age or more:

- for those clients who do not wish to proceed to the adult service for whatever reason, a referral back to the GP will be made, or
- referral to the adult gender service for those adolescents who wish to be referred. Adult gender services will accept referrals from the age of 17 years. For those clients who are being seen in the Paediatric Endocrine Liaison Clinic, the case history will be forwarded to the adult clinic at the point of onward referral, copied to the GP.

  In such cases, the Service will ensure as far as is possible, that the transfer between adolescent and adult services is achieved through liaison between these services so that treatments that have been initiated for adolescents may continue without interruption and so that where treatment has not yet been undertaken, it may be started in a timely manner, taking account of the client's clinical and social history.

The Service will ensure effective, safe, smooth and timely discharge (to local services, other NHS professionals or the adult gender service) as appropriate to the client.

To facilitate this, the Service will put in place a discharge plan to ensure that the client's needs are considered from the earliest point of contact. Discharge planning will include the needs and wishes of the client and their parents/carers. The final discharge plan will be agreed with the client and their family or carers. Discharge planning should commence from the 17th birthday or as close to this as appropriate, depending on the age at which a client is referred.

A copy of the discharge plan will be given to the client and their family or carers, the referrer, their GP and, with the permission of the family, to any other involved professionals.

The discharge documentation will include a copy of the healthcare discharge plan which is , an 'About Me' hand-held booklet, co-designed with clients to include sections which are important to them and inform other health and social care professionals about key issues, GD experiences and intentions of the person so that they do not have to unnecessarily repeat their personal experience . This should be updatable. For example: identity, pronouns, experiences with dysphoria, any experiences with self-harm or suicide attempts - if the client wishes, as these can often be very difficult to talk about.

Clients may transfer to other services where this is appropriate, such as :

- adult mental health services
- other appropriate services.

At the point of discharge, the Service will collect data on outcomes of GD and their reason for leaving, including transfer to adult service. This will be shared with the commissioners on an annual basis to inform future service development activities.

3.3 Population covered

The Service is for clients who are registered with an English General Practitioner (GP), or who are resident in Scotland or the European Union and eligible for treatment in the NHS under reciprocal arrangements.

Young people who live in Wales and Northern Ireland are not part of this commissioned service and the relevant commissioners will have separate arrangements in place with the service provider for their residents.

This contract includes provision for the Service to treat eligible patients from overseas under S2 and aligned referral arrangements. Providers are reimbursed for appropriately referred and recorded activity as part of this contract.

NHS Trusts performing procedures on patients outside of S2 arrangements and aligned referral arrangements will need to continue to make the financial arrangements directly with the governments involved, separately from their contract with NHS England.

3.4 Any acceptance and exclusion criteria

3.4.1Referral management

New clients will be seen within 18 weeks from the date the referral is received.

As a young person may or may not be experiencing distress relating to the social or physiological aspects of their GD, referrals will be assessed to ascertain the level of distress and any associated risk. If the referral is received from a health professional other than local CAMHS or from a voluntary organisation, a letter will be sent to the client's GP and the local CAMHS team to advise them of the referral and the perceived level of risk with the client.

Where the Service identifies that the client is at significant risk, it will communicate this with the GP and local CAMHS to request that the young person is assessed locally as soon as possible and an appropriate risk management plan put in place.

As a rule, referrals cannot be accepted in cases when the identified risk is not being managed locally. In such cases, the Service will liaise with local services to facilitate engagement and the development of a local care plan.

Acceptance criteria are:

- referrals will be accepted from a range of professionals including CAMHS professionals, GPs, secondary care clinicians including paediatricians and gynaecologists, schools and colleges of further education, voluntary organisations.
- referrals will be accepted if there is evidence of features consistent with a diagnosis of GD.

Following assessment, if it is apparent that the young person does not fulfil the criteria for a diagnosis of GD, or it is concluded that there are no outstanding issues with their gender identity development, they will be referred back to their GP or other referring healthcare professional, with advice regarding appropriate support and the case will be closed.

3.4.2 Age of access

The Service will be offered to children and young people aged up to their 18th birthday. If a new referral is received for a client who is already 17 years of age, the Service will contact the young person to discuss referral options, given that the 18 week timeline to be seen as a new patient followed by the appropriate duration of assessment means that they are likely to have already reached or nearly reached the exclusion criteria for the Service (that is, reached their 18th birthday) before they can commence hormone treatment, if this is indicated.

In such cases,

- If the young person's objective is to receive hormone treatment and they would instead prefer a direct referral to adult services, the referrer will be contacted and asked to do this.
- If the young person would like the opportunity to explore their gender identification and options, on their own or with their parents/carers, the Service will offer to assess the young person over two to three appointments. It will then agree an appropriate onward referral if appropriate and the young person wishes.

In all cases, referrers will be informed of the client's decision so that local health professionals can put in place support as required whilst the young person waits to access the adult gender identity clinic.

Referrals for young people who will be 18 by the time of the first assessment appointment will be promptly re directed via the referrer to adult gender services to minimise delays.

3.4.3 Criteria for referral to the Paediatric Endocrine Liaison Team for hormone blockers in the early stages of puberty and/or under the age of fifteen.

Hormone blockers will be considered as an appropriate treatment alongside psychological intervention, and will not necessarily be viewed as the pre-cursor to the prescribing of cross-sex hormones. The next stage of treatment, if any, should be left open for further exploration with the client and their parents/carers.

In reaching an overall decision regarding the prescribing of hormone blockers, the multidisciplinary clinical team will, together with the young person and their parents/ carers, consider each individual's case including the outcome of the assessment of the biological environment and the client's physical development.

Clients under the age of 16 should be assessed regarding their ability to give informed consent and whether they have appropriate autonomy to make decisions.

The decision to start hormone blockers is reached after an in-depth discussion involving the MDT, following which the final responsibility for prescribing the hormone blocker and the physical monitoring of this treatment remains with the paediatric and adolescent endocrinologists, subject to periodic review by the MDT.

The criteria for considering a referral to the Paediatric Endocrinology Liaison Team are as follows:

- the adolescent has been presenting with continuing GD and the intensity and distress has

increased with puberty;
- the adolescent presents as relatively stable psychologically as evaluated through clinical observation and questionnaires;
- there is support from the family/carers;
- where there is a need to provide information about physical development in order to allay some anxieties in the adolescent patient and the family;
- to exclude a disorder of sex development (intersex) or other endocrine conditions;

3.4.4 Criteria for considering administering hormone blockers to post-pubertal adolescents over the age of 15 years with GD:

- there is a substantial history of gender incongruence, lasting more than one year. While a diagnosis of Gender Dysphoria (DSM-5) may be made after six months of dysphoria, a move to physical treatment requires a further period of consolidation.
- the young person is judged to have sufficient understanding of what the blocker will do, and how it works, to be able to give assent, or consent, to treatment.
- if the request for blockers seems driven by a wish for no puberty or no gender, perhaps accompanied by a generalised dissatisfaction with the body, and this motivation has been carefully explored. In such a case, the young person and their parents/carers have an understanding of the limitations of what medical intervention can offer in the longer term.
- similarly, if the request, and any accompanying distress, seem linked to sexual orientation rather than gender identity, and the motivation has been carefully explored.
- there is no intense and prolonged psychological illness on the part of the young person (such as a severe eating disorder, psychotic experiences or major depression) such as might interfere with considered decision-making by the young person.
- there is no ongoing major family disruption.
- one or both parents/carers support the young person's request for puberty suppression treatment and work has been done to develop their understanding of its potential advantages and its potential disadvantages.
- where the parents are separated, it has been established who has legal parental responsibility, and careful thought has been given to involving an estranged parent in the decision-making about the young person's treatment.
- the young person and family are likely to be able to attend appointments regularly. Any likely barriers to attending have been explored prior to referral for puberty suspension.
- the young person is engaged in education and some face to face social interaction with peers.
- the young person is at least at Tanner Stage 2 i.e. 'in puberty'.

3.4.5 The eligibility and readiness criteria for prescribing cross-sex hormones

This is as set out in the separate NHS England Policy: Prescribing Cross Sex Hormones as part of the Gender Identity Development Service for Children and Adolescents.

3.5 Exclusion criteria

3.5.1 The service is not commissioned to respond to emergencies or offer treatment to associated psychological and psychiatric problems (e.g. school refusal and compulsive

symptoms). The service will, in complex cases, ensure that the client's GP and CAMHS provider are engaging with the client and are aware of any escalation in risk.

3.5.2 Care may be suspended where:

- there are abnormalities in the status or timing of pubertal development or there are other physical contraindications that require further investigation.
- the client has not met all the criteria described above.
- the client presents with a severe psychotic or other significant mental health disorder that is not adequately controlled.

In such cases, if the hormone treatments have begun, these may be paused whilst the client is being supported by other services to better manage their condition.

3.5.3 The Service does not offer shared care with private clinicians, although it is understood that some young people may wish to access hormone treatments outside of an NHS prescription or without medical supervision (e.g. from the Internet) at an earlier point than is set out in this specification.

The Service provider will make the young person and their family/carers aware of the risks, contraindications and any irreversible or partly reversible effects of any interventions, but will be unable to provide ongoing clinical supervision for the management of hormone treatments prescribed or accessed outside the service. The Service will still provide holistic psychosocial support with input from mental health professionals.

Once the client meets the access criteria set out in this specification and has been assessed by the MDT, a care plan will be agreed and if appropriate, hormones will be prescribed. If required, the Service will, with the consent of the client and their family/carers, review and evaluate the records of any prior mental health assessments or treatments, and liaise as necessary with any previous provider, to obtain the results of baseline examinations and laboratory tests.

3.6 Stopping criteria

Endocrine treatment will be suspended, following discussion with the client and their family or carers where:

- there are any concerns about the client's physical health such as low bone density
- the client and family do not attend regular follow ups at the Paediatric Endocrine Liaison Clinic and/or the GIDS general clinic as agreed in their care plan.
- the client is having a significant psychotic episode or has an exacerbation of a significant mental health condition that is not being adequately controlled with support from other agencies, as this may reduce their ability to manage the emotional issues that may arise from the changes in hormone levels from the hormone treatments and may impact on their capacity to consent.
- there are physical contraindications that require further investigation.
- the client decides to cease treatment for any reason
- gender related medications are taken without an NHS prescription.

3.7 Response time and prioritisation

The Service is required to see clients for the first time and begin the assessment process within eighteen weeks of referral.

The Service will provide equitable care for any child or young person up to their 18th birthday from any cultural background, with any protected characteristic and with any illness or disability. Every reasonable effort is to be made to make services accessible. The Service will provide accessible toilets and access for wheelchair users. When required, the Service will use interpreters and translate printed documents
The Service will undertake Equality Impact Assessments with regard to all protected characteristics as a requirement of equality legislation, promoting equality and addressing health inequalities.

The Service will:

- give due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- give regard to the need to reduce inequalities between clients in access to, and outcomes from healthcare services and to ensure that care is provided in an integrated way where this might reduce health inequalities.

3.8 Interdependencies with other services

As shown in the Tiers of Care table on page 20/21, the Service provider will be the leader in the NHS in England for the assessment and care of children and adolescents with GD even though the tiered model of care means that interaction with the Service will only be part of the client's experience.

The Service will provide advice and support to referrers and will provide education on GD within the NHS and across the education (schools and colleges), social care and voluntary sectors to raise awareness of gender identity development in child and adolescents.

The Service will form supportive relationships with local education, health, social care providers and the voluntary sector to support optimal care for clients with GD. This will include liaison with healthcare professionals such as secondary care paediatric and gynaecological consultants; GPs; community nurses; school nurses and health staff in colleges of Further Education; academies; staff in Local Education Authorities that have pupils attending the Service in any of its locations; CAMHS staff; social workers; adult gender service providers; adult endocrine services; adult surgical providers; local Clinical Commissioning Groups; helpline providers; and charities.

The Service will engage in two way communication with and seek to have robust working relationships with: local CAMHS, GP's and secondary care healthcare professionals and provide routine feedback to them of client progress, subject to appropriate information governance. This will include:

- direct consultations;

- co-working for complex cases;
- liaison and individual client care planning;
- support for transfer of clients to adult services.

In line with the tiered model of care, responsibility for managing the risk associated with gender dysphoria for all clients will reside with local services.

The Service will work in collaboration with another gender identity clinic in the Netherlands, and others in Europe, Canada and America to share and implement standardised assessments for research and evidence base practice purposes.

The Service will:
- undertake effective two-way communication with adult gender services prior to the transfer of clients to the adult service. This needs to take place with the client and their family or carers.
- provide transfer support to the adolescent in their move to the adult service

Discussions about any substantive potential change to the service model or clinical approach must take place with NHS England commissioners in order that clinical approval can be given and any changes to commissioning policies taken through the clinical governance and approvals processes.

A report to commissioners will be submitted annually on innovation and improvements in the Service.

3.9 Audit and Research

The Service will conduct research and undertake audit projects as part of ongoing service improvement and development. This will build knowledge about the profiles of the young people who are referred, their experiences at different stages in their development and at different stages of treatment and outcomes.

The Service will collaborate with adult services in the UK to follow up the outcomes for clients in a way that respects their privacy. International collaboration will also be undertaken to inform an improved understanding of the most effective treatment pathways for different groups of young people.

4. Applicable Service Standards

4.1 Applicable national standards e.g. NICE, Royal College

The Service will be fully integrated into its Trust corporate and clinical governance arrangements. Practitioners will participate in continuous professional development and networking.

The Service will develop standardised evidence base tools and training programmes, including:

- common risk assessment, care approaches and systems;
- training for gender identity development, clinical skills and specific training related to mental health;
- clinical information systems, reports to commissioners;
- child protection procedures;
- client consultation and advocacy.

Education and training

The Service will undertake a training and education role including:
- training of professionals working within it
- education (including educational materials) for professionals at Tiers 1,2,3
- education for other agencies such as schools, and colleges of further education, CAMHS and social services, voluntary organisations which support young people locally.

Documentation and Information Technology

Following each multidisciplinary clinic, the staff will produce a single clinic letter which will integrate the reports from each clinician. This will be sent out to the client and their family/ carer; the client's GP and CAMHS and other secondary care paediatric specialists.

Clinic notes and correspondence be will be stored at each centre (computerised) and included in the organisation's computerised client records of the client. The provider's administrator will have responsibility for ensuring safe storage and adherence to the Data Protection Act (1998) for computerised data. Offsite backup storage will also be arranged.

Facilities

Each centre used by the Service for the provision of care will have clinic space that is appropriate for children and adolescents and suitable for attendance by a number of multi-professional staff at one time.

Equity of access to services

Service access is paramount to success. The Service will be tiered so that care can be provided as close to home as possible, with appropriate geographic access related to demand, agreed in conjunction with commissioners.

Managing Risk

The Service provider must meet the standards set out in this specification.
It is the Trust's responsibility to notify the commissioner on an exceptional basis should there be any breaches of the standards.

5. Applicable quality requirements and CQUIN Goals
(see Schedule 4 Parts A-D)

There is a requirement to hold national audit meetings on an annual basis.

All parts of the Service must assure that:

- all practitioners participate in continuous professional development and networking
- client outcome data is recorded and audited across the Service
- all centres must participate in the NHS England annual national audit process.

Audit meetings will address:

- clinical performance and outcomes
- process-related indicators e.g. efficiency of the assessment process, prescribing policy, outpatient follow-up etc.
- service issues;
- notable events;
- treatment guidelines
- evidence based practice;
- review of learning from the year
- safety
- stakeholder satisfaction, including feedback
- client, family and carer involvement and engagement and with other stakeholders including voluntary sector support groups
- sustainability
- transfer to adult services
- review of international evidence and benchmarks to inform changes in delivery
- audit activities, service evaluation and research, including future audit programme
- potential new developments, improvements and innovations
- potential improving value schemes

Measures for monitoring the clinical benefit of the service are:

- diagnosis rate
- base unit of measurement e.g. feelings of anxiety
- informative problem-based measures
- participation in a research study.
- a minimum defined data set will be collected on all clients.
- clinically rated outcome measures (CROM)
- patient rated outcome measures (PROMs)
- patient rated experience measures (PREMS)

6. Location of Provider Premises

The Service is provided by the Tavistock and Portman NHS Foundation Trust in London and Leeds, with associated integrated Paediatric Endocrine Liaison clinics.
The community outreach service is delivered through a hub and spoke model in London and agreed outreach centres in England to ensure equity of access. The location of outreach clinics will be determined by the commissioner and will be based on referrals and following agreement with commissioners. These are currently Barnstaple, Exeter, Bristol and Bath.

Sub-contractors

The Paediatric Endocrinology Liaison Clinics which are based at the University College London Hospital NHS Foundation Trust and the Leeds Teaching Hospitals NHS Trust: Leeds General Infirmary (LGI) site, are sub-contracted, although the staff are part of the Service's MDT and there is a single, integrated clinical protocol.

7. Individual Service User Placement

Not applicable.

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Glossary of Terms

	Term	Initials	Description
1	Analogue		See GnRH below
2	Autonomy		Term used to describe a person's ability to give informed consent.
3	Biological sex		See 'natal' sex below.
4	Child and Adolescent Mental Health Services	CAMHS	CAMHS are specialist NHS children and young people's mental health services See http://www.youngminds.org.uk/for_parents/services_children_young_people/camhs
5	Child Behaviour Checklist	CBCL	The Child Behaviour Checklist (CBCL) is a parent-report questionnaire on which the child is rated on various behavioural and emotional problems.
6	Cross Sex Hormone [gender affirming] (therapy)	CSH	Hormone replacement therapy for gender variant individuals, where sex hormones (androgens for trans male) and oestrogens for trans female) are administered for the purpose of inducing physical changes which are more in line with the experienced gender identity – also called gender affirming hormone therapy.
7	Diagnostic and Statistical Manual of Mental Disorders Fifth edition	DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, http://journals.lww.com/co-psychiatry/Abstract/2007/01000/Dimensional_models_of_personality_disorder_.11.aspx
8	Gamete		Reproductive or sex cells. Female gametes are called ova or egg cells and male gametes are called sperm.
9	Gender Dysphoria	GD	Where a person experiences discomfort or distress due to a mismatch between their biological sex and the gender as which they identity. Biological sex is classified at birth, depending on the appearance of the genitals. www.nhs.uk/conditions/Gender-dysphoria/Pages/Introduction.aspx
10	Gender Identity		In simplest terms Gender Identity refers to an individual's internal sense of being male, female, both, neither, or something else. A person's "fundamental sense of belonging to one sex [an awareness of being male or female and] an over-all sense of identity." Stoller RJ. A contribution to the study of Gender Identity. J Psychoanal 1964; 45: 220-6.
11	Gender Identity		The emotional and intellectual experiences of a child or young person in seeking to understand

	Development		their gender identity
12	Gender Identity Development Service	GIDS	The abbreviation used for the service that NHS England commissions for children and adolescents with GD.
13	Gender role		Characteristics in personality, appearance, and behavior that in a given culture and historical period are designated as masculine or feminine (that is, more typical of the male or female social role) (Ruble, Martin, & Berenbaum, 2006). While most individuals present socially in clearly masculine or feminine gender roles, some people present in an alternative gender role such as genderqueer or specifically transgender. All people tend to incorporate both masculine and feminine characteristics in their gender expression in varying ways and to varying degrees (Bockting, 2008) in WPATH SOC v7. see http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351
14	Gillick competence/ Fraser guidelines		A term used in medical law to decide whether a child or young person up to the age of 16 years is able to consent to his or her own medical treatment, without the need for parental permission or knowledge. Based on the names of cases. https://www.nspcc.org.uk/preventing-abuse/child-protection-system/legal-definition-child-rights-law/gillick-competency-fraser-guidelines/ 'Gillick competency and Fraser guidelines' refers to a legal case which looked specifically at whether doctors should be able to give contraceptive advice or treatment to under 16-year-olds without parental consent. But since then, they have been more widely used to help assess whether a child has the maturity to make their own decisions and to understand the implications of those decisions'. '...whether or not a child is capable of giving the necessary consent will depend on the child's maturity and understanding and the nature of the consent required. The child must be capable of making a reasonable assessment of the advantages and disadvantages of the treatment proposed, so the consent, if given, can be properly and fairly described as true consent." (Gillick v West Norfolk, 1984).

15	Gonadotropin - releasing hormone (also known as the hormone blocker/s)	GnRH	A gonadotropin-releasing hormone analogue (GnRHa), also known as a luteinizing hormone releasing hormone agonist (LHRH agonist) or LHRH analogue or hormone blocker. This is a synthetic peptide drug modelled after the human hypothalamic gonadotropin-releasing hormone (GnRH). This is designed to 'competitively block' the GnRH receptor and prevent the release of pituitary gonadotropins FSH and LH for therapeutic purposes. It is used by the Service to halt puberty in order that the client can further explore their GD without the fear of puberty progressing.
16	General Practitioner	GP	http://www.nhs.uk/NHSEngland/AboutNHSservices/doctors/Pages/NHSGPs.aspx GPs deal with a whole range of health problems and manage the care of their patients, referring onto specialists as appropriate.
17	Multi-Disciplinary Team	MDT	The identified group of professional staff who provide the service.
18	Natal sex (see also biological sex)		The biological sex that a person is born as, which is male - 'natal male', female - 'natal female' or Intersex and is most often based on identification of genitals at birth.
19	Non-binary, agender, Bigender, non-gendered or gender fluid		An umbrella term for any gender identity that does not fit into the traditional gender binary of male and female. Can also be a discrete gender identity. Also: Agender: a gender identity characterised by having no feeling of gender, or a specific identity of no gender. Bigender: experiencing two genders simultaneously. These two genders are often, but not always, male and female, and are not necessarily split evenly. Genderfluid: an experience of gender that is not fixed, but changes between two or more identities. For example, someone may feel female some days and non-binary on others.
20	Tanner Stage		Specialist classification of puberty by stage at which adolescents experience maturation. Used by specialists only. The complex series of biologic transitions are known as puberty, and these changes may impact psychosocial factors. See http://www.childgrowthfoundation.org/CMS/FILES/Puberty_and_the_Tanner_Stages.pdf

			For a simpler classification of pubertal development – puberty phases, see http://www.rcpch.ac.uk/child-health/research-projects/uk-who-growth-charts/uk-growth-chart-resources-2-18-years/school-age#cpcm
21	Transgender	trans	A person whose gender identity is different to the sex assigned at birth.
22	US	USA	United States of America
23	World Professional Association for Transgender Health (2012)	WPATH SOC v7	World Professional Association for Transgender Health: Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People 2012 (WPATH SOC v7) see http://www.wpath.org/site_page.cfm?pk_association_webpage_menu=1351

Appendices

Appendix 1: Children's Insert to NHS England specifications –
(standard NHS England wording/ subject to revision)
Appendix 2: Quality standards specific to the service:
Appendix 3: Description of partnership working with GPs and local CAMHS
Appendix 4: Referral processes and funding arrangements to access associated treatments for children and adolescents with Gender Dysphoria
Appendix 5: Definitions of Tanner Stages
Appendix 6: Description of the psychological support that the Service will offer
Appendix 7: Informed consent in the context of GIDS

Appendix 1: Children's Insert – Provision of services to children

Aims and objectives of service

This specification annex applies to all children's services and outlines generic standards and outcomes that would fundamental to all services.

The generic aspects of care:

The Care of Children in Hospital (Health Service Circular 1998/238) requires that:

• Families with children have easy access to hospital facilities for children without needing to travel significantly further than to other similar amenities.

• Good child health care is shared with parents/carers and they are closely involved in the care of their children at all times unless, exceptionally, this is not in the best interest of the child.

Service description/care pathway

All paediatric specialised services have a component of primary, secondary, tertiary and even quaternary elements.

The efficient and effective delivery of services requires children to receive their care as close to home as possible dependent on the phase of their disease/condition.

Services should therefore be organised and delivered through "integrated pathways of care" (National Service Framework for children, young people and maternity services (Department of Health & Department for Education and Skills, London 2004)

Interdependencies with other services

All services will comply with Commissioning Safe and Sustainable Specialised Paediatric Services: A Framework of Critical Inter-Dependencies – Department of Health (DH)

References

Continuing Professional Development (CPD) matrix level 3

Taking account of the differences in client profiles the principles and standards set out in this specification apply with modifications to the recommendations regarding the following:

• Facilities and environment – essential Quality Network for In-patient CAMHS (QNIC) standards should apply (http://www.rcpsych.ac.uk/quality/quality,accreditationaudit/qnic1.aspx)

• Staffing profiles and training - essential QNIC standards should apply.

• Parents/carers are involved in the child/young person's care except where this is not in the best interests of the child / young person and in the case of young people who have the capacity to make their own decisions is subject to their consent.

• Applicable national standards e.g. NICE, Royal College

Children and young people must receive care, treatment and support by staff registered by the Nursing and Midwifery Council on the parts of their register that permit a nurse to work with children (Outcome 14h Essential Standards of Quality and Safety, Care Quality Commission, London 2010)

• There must be at least two Registered Children's Nurses (RCNs) on duty 24 hours a day in all hospital children's departments and wards.
• There must be an Registered Children's Nurse available 24 hours a day to advise on the nursing of children in other departments (this post is included in the staff establishment of 2RCNs in total).

Accommodation, facilities and staffing must be appropriate to the needs of children and separate from those provided for adults. All facilities for children and young people must comply with the Hospital Build Notes HBN 23 Hospital Accommodation for Children and Young People NHS Estates, The Stationary Office 2004.

All staff who work with children and young people must be appropriately trained to provide care, treatment and support for children, including Children's Workforce Development Council Induction standards (Outcome 14b Essential Standards of Quality and Safety, Care Quality Commission, London 2010).

Staff must carry out sufficient levels of activity to maintain their competence in caring for children and young people, taking account of guidance from relevant expert or professional bodies (Outcome 14g Essential Standards of Quality and Safety, Care Quality Commission, London 2010).

Providers must have systems in place to gain and review consent from people who use services, and act on them (Outcome 2a Essential Standards of Quality and Safety, Care Quality Commission, London 2010). These must include specific arrangements for seeking valid consent from children while respecting their human rights and confidentiality and ensure that where the person using the service lacks capacity, best interest meetings are held with people who know and understand the person using the service. Staff should be able to show that they know how to take appropriate consent from children, young people and those with learning disabilities (Outcome 2b) (Seeking Consent: working with children Department of Health, London 2001).

Children and young people must only receive a service from a provider who takes steps to prevent abuse and does not tolerate any abusive practice should it occur (Outcome 7 Essential Standards of Quality and Safety, Care Quality Commission, London 2010 defines the standards and evidence required from providers in this regard). Providers minimise the risk and likelihood of abuse occurring by:
• Ensuring that staff and people who use services understand the aspects of the safeguarding processes that are relevant to them
• Ensuring that staff understand the signs of abuse and raise this with the right person when those signs are noticed.
• Ensuring that people who use services are aware of how to raise concerns of abuse.
• Having effective means to monitor and review incidents, concerns and complaints that have the potential to become an abuse or safeguarding concern.
• Having effective means of receiving and acting upon feedback from people who use services and any other person.
• Taking action immediately to ensure that any abuse identified is stopped and suspected abuse is addressed by:

a. Having clear procedures followed in practice, monitored and reviewed that take account of relevant legislation and guidance for the management of alleged abuse
b. Separating the alleged abuser from the person who uses services and others who may be at risk or managing the risk by removing the opportunity for abuse to occur, where this is within the control of the provider
c. Reporting the alleged abuse to the appropriate authority
d. Reviewing the person's plan of care to ensure that they are properly supported following the alleged abuse incident.
• Using information from safeguarding concerns to identify non-compliance, or any risk of non-compliance, with the regulations and to decide what will be done to return to compliance.
• Working collaboratively with other services, teams, individuals and agencies in relation to all safeguarding matters and has safeguarding policies that link with local authority policies.
• Participates in local safeguarding children boards where required and understand their responsibilities and the responsibilities of others in line with the Children Act 2004.
• Having clear procedures followed in practice, monitored and reviewed in place about the use of restraint and safeguarding.
• Taking into account relevant guidance set out in the Care Quality Commission's Schedule of Applicable Publications
• Ensuring that those working with children must wait for a full CRB disclosure before starting work.
• Training and supervising staff in safeguarding to ensure they can demonstrate the competences listed in Outcome 7E of the Essential Standards of Quality and Safety, Care Quality Commission, London 2010

All children and young people who use services must be:
• Fully informed of their care, treatment and support.
• Able to take part in decision making to the fullest extent that is possible.
• Asked if they agree for their parents or carers to be involved in decisions they need to make.

(Outcome 4I Essential Standards of Quality and Safety, Care Quality Commission, London 2010)

Key Service Outcomes
Evidence is increasing that implementation of the national Quality Criteria for Young People Friendly Services (Department of Health, London 2011) have the potential to greatly improve client experience, leading to better health outcomes for young people and increasing socially responsible life-long use of the NHS.

Implementation is also expected to contribute to improvements in health inequalities and public health outcomes e.g. reduced teenage pregnancy and STIs, and increased smoking cessation. All providers delivering services to young people should be implementing the good practice guidance which delivers compliance with the quality criteria.

Poorly planned transfer from young people's to adult-oriented health services can be

associated with increased risk of non-adherence to treatment and loss to follow-up, which can have serious consequences. There are measurable adverse consequences in terms of morbidity and mortality as well as in social and educational outcomes. When children and young people who use paediatric services are moving to access adult services (for example, during transfer for those with long term conditions), these should be organised so that:
• All those involved in the care, treatment and support cooperate with the planning and provision to ensure that the services provided continue to be appropriate to the age and needs of the person who uses services.

The National Minimum Standards for Providers of Independent Healthcare, (Department of Health, London 2002) require the following standards:
• A16.1 Children are seen in a separate out-patient area, or where the hospital does not have a separate outpatient area for children, they are seen promptly.
• A16.3 Toys and/or books suitable to the child's age are provided.
• A16.8 There are segregated areas for the reception of children and adolescents into theatre and for recovery, to screen the children and adolescents from adult patients; the segregated areas contain all necessary equipment for the care of children.
• A16.9 A parent is to be actively encouraged to stay at all times, with accommodation made available for the adult in the child's room or close by.
• A16.10 The child's family is allowed to visit him/her at any time of the day, except where safeguarding procedures do not allow this (?does not apply)
• A18.10 There are written procedures for the assessment of pain in children and the provision of appropriate control.

There should be age specific arrangements for meeting Regulation 14 of the Health and Social Care Act 2008 (Regulated Activities) Regulations 2010. These require: (we will need to delete those that do not apply)
• A choice of suitable and nutritious food and hydration, in sufficient quantities to meet service users' needs
• Food and hydration that meet any reasonable requirements arising from a service user's religious or cultural background
• Support, where necessary, for the purposes of enabling service users to eat and drink sufficient amounts for their needs
• For the purposes of this regulation, "food and hydration" includes, where applicable, parenteral nutrition and the administration of dietary supplements where prescribed
• Providers must have access to facilities for infant feeding, including facilities to support breastfeeding (Outcome 5E, of the Essential Standards of Quality and Safety, Care Quality Commission, London 2010)

All paediatric clients should have access to appropriately trained paediatric trained dieticians, physiotherapists, occupational therapists, speech and language therapy, psychology, social work and CAMHS services within nationally defined access standards.

All children and young people should have access to a professional who can undertake an assessment using the Common Assessment Framework and access

support from social care, housing, education and other agencies as appropriate.

All registered providers must ensure safe use and management of medicines, by means of the making of appropriate arrangements for the obtaining, recording, handling, using, safe keeping, dispensing, safe administration and disposal of medicines (Outcome 9 Essential Standards of Quality and Safety, Care Quality Commission, London 2010). For children, these should include specific arrangements that:

• They are supported to have a health action plan

• Facilities meet the appropriate requirements of the Disability Discrimination Act 1995

They meet the standards set out in Transfer: getting it right for young people. Improving the transfer of young people with long-term conditions from children's to adult health services. Department of Health, 2006.

Appendix 2: Quality standards specific to the service:

Quality Requirement	Threshold	Method of Measurement	Consequence of breach
Domain 1: Preventing people dying prematurely			
The Service will seek to reduce distress by providing high quality psychological and medical support, including physical interventions as required on an individual basis.	100% of people accepted into the Service will commence the assessment process within the first one to one appointment.	National database Annual Returns	To be addressed in annual service audit meeting
Domain 2: Enhancing the quality of life of people with long-term conditions			
The Service will seek to ameliorate the negative effects on the client's general development and build their resilience across a number of domains, (including family and peer relationships, self-esteem, self-image and education), including thereby improving their quality of life.	100% of clients will have a personalised care plan which sets out a pathway through the Service, recognising that this may change over time depending on need.	National database Annual Returns	To be addressed in annual service audit meeting
Domain 3: Helping people to recover from episodes of ill-health or following injury			
The Service will help to reduce	See care plan note above	National Database –	To be addressed in annual service

Quality Requirement	Threshold	Method of Measurement	Consequence of breach
morbidity by providing high quality psychological and medical support through individualised health care pathways.		Annual Returns	audit meeting
Domain 4: Ensuring that people have a positive experience of care			
The Service will support the client and their family/carer, which will be led and co-ordinated by a named Lead Worker who will support them during their time with the Service.	100% of clients will have a named Lead Worker who, when possible, will be introduced at the first one to one meeting with the Service.	National database – Annual Returns	To be addressed in annual service audit meeting
Domain 5: Treating and caring for people in a safe environment and protecting them from avoidable harm			
The Service will ensure that local systems are in place to track and manage client safety performance, including taking action when agreed standards are not met. Robust reporting of incidents will be undertaken through local procedures and reported to NHS England.	Risk reporting processes will be in place for all clients. 100% of incidents will be reported to NHS England, together with a report of lessons learned and amendments to safety systems, process and clinical practice where appropriate.	National database – Annual Returns	To be addressed in annual service audit meeting

Quality Requirement	Threshold	Method of Measurement	Consequence of breach
Overarching indicator: Risks will be identified and incidents reported. Evidence of lessons learnt and subsequent improved patient safety will be required to be provided to the commissioning team.			

Appendix 3: Description of partnership working with GPs and local CAMHS

The service will work with General Practitioners (GP's) and local CAMHS to promote clarity about respective responsibilities and good communication on both sides.

When referrals are accepted by the service, it will ensure that both the client's GP and the CAMHS team which is local to where the client lives, are made aware of the referral with the client's knowledge. The CAMHS team will be advised that they retain responsibility for monitoring and managing risk and associated difficulties. Any change in risk will be communicated to the GP and to CAMHS by telephone and/or letter as appropriate.

The service will confirm to the GP and CAMHs team that it is responsible for the individualised care plan that has been agreed with the client (and their family or carer if appropriate).

GPs prescribe and monitor any physical treatments and the Paediatric Endocrine Liaison Clinic will supply a shared care agreement and respond to any queries or concerns around this.

In complex cases, the service will convene local network meetings with CAMHS teams to review and discuss the needs of the client and agree roles. GPs will be kept informed.

If risk is identified with a client at any stage in their time with the service and there is no local CAMHS involvement, the service will facilitate an appropriate referral in order that the risk is understood locally and so that the CAMHS can provide support to the young person.

The service will be as active as possible where there is a client is at significant risk by ensuring that the client's GP and CAMHS are made aware.

The service will respond promptly to enquiries and concerns raised by CAMHS teams.

CAMHS teams will be asked to keep the service informed of their contact with clients by letter and/or telephone as appropriate.
With the permission of the client, the service will copy CAMHS into correspondence including the assessment report.

Work will be undertaken with GPs and local CAMHS providers to build relationships and the support offer from the service.

The service will provide advice to GPs as required with regard to issues in managing prescriptions which have been issued for a young person **in accordance with the GMC's requirements**
http://www.gmc-uk.org/guidance/ethical_guidance/28851.asp

Appendix 4: Definition of Tanner Stages

Adolescents experience several types of maturation, including cognitive (the development of formal operational thought), psychosocial (the stages of adolescence), and biologic. The complex series of biologic transitions are known as puberty, and these changes may impact psychosocial factors.

The most visible changes during puberty are growth in stature and development of secondary sexual characteristics. Equally profound are changes in body composition; the achievement of fertility; and changes in most body systems, such as the neuroendocrine axis, bone size, and mineralization; and the cardiovascular system. As an example, normal cardiovascular changes, including greater aerobic power reserve, electrocardiographic changes, and blood pressure changes, occur during puberty.

The normal sequence of pubertal events and perils of puberty are reviewed here. This is within the normal ranges and does not take into account Precocious Puberty or Delayed Puberty. See
http://www.childgrowthfoundation.org/CMS/FILES/Puberty_and_the_Tanner_Stages.pdf
See
http://www.rcpch.ac.uk/child-health/research-projects/uk-who-growth-charts/uk-growth-chart-resources-2-18-years/school-age#cpcm for a simpler classification and explanation of puberty development.

Appendix 5: Referral processes and funding arrangements to access associated treatments for children and adolescents with GD

There are a range of other services which children and adolescents with GD may require access to, but are funded outside of this specification, commissioned by NHS England Clinical Commissioning Groups (CCG's) rather than the Highly Specialised Commissioning Team.

For clarity, the means of accessing these is as follows:

		Funded by	Requirement
1	CAMHS – Local services	Clinical Commissioning Groups	Where not involved, may be made via the GP or the Service to the local CAMHS team.
2	Fertility advice and preservation	CCGs	GIDS to signpost, via GP, to other Medical specialists such as gynaecologists, and licensed NHS fertility experts who will be able to assist clients in making key decisions regarding gamete retrieval. This will include being made aware of the full facts of the implications of extracting or not extracting the eggs or sperm and what happens, before, during, and after the procedure. Also discussion on subsidiary issues such as storage of gametes, how long they can be kept for, what happens if you want to use these at a future date if you want to use them, and the additional future consequences and treatments required if gametes haven't been extracted before hormone therapy is started.
3	Gynaecological advice	CCGs	GIDS to clarify access routes to other medical specialists, i.e. gynaecologists to assist clients and their family or carers in making key decisions. GIDS to write to GP proposing that a referral is made to local clinician.
4	Occupational therapy	CCGs	GIDS to write to GP proposing that a referral is made to local team.
5	Physiotherapy	CCGs	GIDS to write to GP proposing that a referral is made to local teams.
6	Sexual health services	CCGs	GIDS to write to GP proposing that a referral is made to local teams
7	Speech and language therapy (SaLT)	CCGs	GIDS to write to GP proposing that a referral is made to local team.

Appendix 6: Informed consent in the context of GIDS – a description

Thinking carefully about informed consent is an important aspect of assessing and intervening ethically. The aim is to enhance the young person's and the family/carer's grasp of the available factual information about the interventions they are offered, including hormone treatments, and the emotional and social issues involved in undertaking treatment, so as to enable them to make informed decisions about the options.

Children's competence relies on them having access to good information tailored to their comprehension level: they need to understand fully what is proposed, retain an understanding of the implications, appreciate the importance of the information and see how it applies to them. Therefore young people and their parents/carers are offered a thorough discussion of the treatments offered, the benefits and risks, and alternatives to the treatment proposed (including the option of no treatment. Information sheets are provided prior to attending the service's endocrinology clinics explaining available physical treatments, and Consent Forms need to be signed prior to medical intervention.

Age alone does not determine capacity to give consent: there is no international consensus on the lower age limit for presuming competence.
For young people under 16, consent to treatment should usually be sought from the child and from one or both parents/carers, except under exceptional circumstances. Under the law, adolescents over 16 may consent to treatment if capacity is demonstrated. A clinician(s) should assess a young person's capacity to give consent. While we may think of a young person expressing their 'autonomy' by deciding on their own, with good understanding and without undue constraint, in reality a number of contextual factors are likely to influence a child or young person's decision-making competence.

These will include their developmental stage, the quality of information provided (as discussed above, the influence of peers, parents/carers and their life experience. For instance, young children face cognitive limitations: they may view the world in concrete terms and struggle to reason about abstract or hypothetical problems. In adolescence, new cognitive and social skills are acquired which lead to increased maturity in reasoning about complex issues. Yet adolescents may still find it difficult to restrain impulsiveness and to see a given decision in a larger temporal context.

Competence in children and young people may also be related to life experience: children who have personal experiences with particular kinds of challenge may show greater insight and understanding than children of comparable age who lack this experience. Finally, children and young people are still dependant on their parents/ carers (and their clinicians) to define the meaning of the situation they are in, and so the quality of those relationships may also influence the young person's capacity for autonomous decision-making. (See Hein et al 2015).

Reference: Hein I.M., De Vries M.C., Troost P.W., Meynen G., Van Goudoever J.B. and Lindauer R.J.L (2015) Why is it hard to make progress in assessing children's decision-making competence? BMC Medical Ethics 16:1

Appendix 7: Description of the psychological support that the Service will offer:

7.1 When assessing children and adolescents who present with GD, the service's mental health professionals will broadly conform to the following guidelines taken from the WPATH SOC v7:

7.1.1 Mental health professionals should not dismiss or express a negative attitude towards nonconforming gender identities or indications of gender dysphoria. Rather, they should acknowledge the presenting concerns of children, adolescents, and their families; offer a thorough assessment for gender dysphoria and any coexisting mental health concerns; and educate clients and their families about therapeutic options, if needed. Acceptance, and alleviation of secrecy, can bring considerable relief to gender dysphoric children/adolescents and their families.

7.1.2 Assessment of gender dysphoria and mental health should explore the nature and characteristics of a child's or adolescent's gender identity. A psychodiagnostic and psychiatric assessment—covering the areas of emotional functioning, peer and other social relationships, and intellectual functioning/school achievement—should be performed. Assessment should include an evaluation of the strengths and weaknesses of family functioning. Emotional and behavioral problems are relatively common, and unresolved issues in a child's or youth's environment may be present (de Vries, Doreleijers, Steensma, & Cohen-Kettenis, 2011; Di Ceglie & Thümmel, 2006; Wallien et al., 2007).

7.1.3 For adolescents, the assessment phase should also be used to inform youth and their families about the possibilities and limitations of different treatments. This is necessary for informed consent, but also important for assessment. The way that adolescents respond to information about the reality of sex reassignment can be diagnostically informative. Correct information may alter a youth's desire for certain treatment, if the desire was based on unrealistic expectations of its possibilities.

7.1.4 Roles of Mental Health Professionals Working with Children and Adolescents with Gender Dysphoria
Mental health professionals will:
• Directly assess gender dysphoria in children and adolescents (see general guidelines for assessment, below).
• Provide family counselling and supportive psychotherapy to assist children and adolescents with exploring their gender identity, alleviating distress related to their gender dysphoria, and ameliorating any other psychosocial difficulties.
• Assess and treat any coexisting mental health concerns of children or adolescents (or refer to another mental health professional for treatment). Such concerns should be addressed as part of the overall treatment plan.
• Refer adolescents for additional physical interventions (such as puberty-suppressing hormones) to alleviate gender dysphoria. The referral should include

documentation of an assessment of gender dysphoria and mental health, the adolescent's eligibility for physical interventions (outlined below), the mental health professional's relevant expertise, and any other information pertinent to the youth's health and referral for specific treatments.
• Educate and advocate on behalf of gender dysphoric children, adolescents, and their families in their community (e.g., day care centers, schools, camps, other organizations). This is particularly important in light of evidence that children and adolescents who do not conform to socially prescribed gender norms may experience harassment in school (Grossman, D'Augelli, & Salter, 2006; Grossman, D'Augelli, Howell, & Hubbard, 2006; Sausa, 2005), putting them at risk for social isolation, depression, and other negative sequelae (Nuttbrock et al., 2010)
• Provide children, youth, and their families with information and referral for peer support, such as support groups for parents of gender-nonconforming and transgender children (Gold & MacNish, 2011; Pleak, 1999; Rosenberg, 2002).

7.1.5 Psychological and Social Interventions for Children and Adolescents
When supporting clients, the service's health professionals will broadly conform to the following guidelines as set out in the World Professional Association for Transgender Health: Standards of Care V7 (2012):
• help families to have an accepting and nurturing response to the concerns of their gender dysphoric child or adolescent. Families play an important role in the psychological health and well-being of youth (Brill & Pepper, 2008; Lev, 2004). This also applies to peers and mentors from the community, who can be another source of social support.
• psychosocial support should focus on reducing a child's or adolescent's distress related to the gender dysphoria and on ameliorating any other psychosocial difficulties. For youth pursuing sex reassignment, psychotherapy may focus on supporting them before, during, and after reassignment. Formal evaluations of different psychotherapeutic approaches for this situation have not been published, but several counseling methods have been described (de Vries, Cohen-Kettenis, & Delemarre-van de Waal, 2006; Di Ceglie & Thümmel, 2006; Hill, Menvielle, Sica, & Johnson, 2010; Malpas, in press; Menvielle & Tuerk, 2002; Rosenberg, 2002; Vanderburgh, 2009; Zucker, 2006).
• treatment aimed at trying to change a person's gender identity and expression to become more congruent with sex assigned at birth has been attempted in the past without success (Gelder & Marks, 1969; Greenson, 1964), particularly in the long term (Cohen-Kettenis & Kuiper, 1984; Pauly, 1965). Such treatment is no longer considered ethical.
• families should be supported in managing uncertainty and anxiety about their child's or adolescent's psychosexual outcomes and in helping youth to develop a positive self-concept.
• mental health professionals should not impose a binary view of gender. They should give ample room for clients to explore different options for gender expression.
• hormonal treatments are appropriate for some adolescents, but not for others.
• clients and their families should be supported in making difficult decisions regarding the extent to which clients are allowed to express a gender role that is consistent

with their gender identity, as well as the timing of changes in gender role and possible social transition. For example, a client might attend school while undergoing social transition only partly (e.g., by wearing clothing and having a hairstyle that reflects gender identity) or completely (e.g., by also using a name and pronouns congruent with gender identity). Difficult issues include whether and when to inform other people of the client's situation, and how others in their lives might respond.

• health professionals should support clients and their families as educators and advocates in their interactions with community members and authorities such as teachers, school boards, and courts.

• mental health professionals should strive to maintain a therapeutic relationship with gender-nonconforming children/adolescents and their families throughout any subsequent social changes or physical interventions. This ensures that decisions about gender expression and the treatment of gender dysphoria are thoughtfully and recurrently considered. The same reasoning applies if a child or adolescent has already socially changed gender role prior to being seen by a mental health professional.

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please enter a short title for this project (maximum 70 characters)
Early pubertal suppression in a selected group of adolescents with GID

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product
( ) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial or clinical investigation
( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples, other human biological samples and/or data *(specific project only)*
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

(●) Other study

2a. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation?	(●) Yes	( ) No
b) Will you be taking new human tissue samples (or other human biological samples)?	( ) Yes	(●) No
c) Will you be using existing human tissue samples (or other human biological samples)?	( ) Yes	(●) No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

[x] England
[ ] Scotland
[ ] Wales
[ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

(●) England
( ) Scotland

- ○ Wales
- ○ Northern Ireland
- ○ This study does not involve the NHS

4. Which review bodies are you applying to?

- ☑ NHS/HSC Research and Development offices
- ☐ Social Care Research Ethics Committee
- ☑ Research Ethics Committee
- ☐ National Information Governance Board for Health and Social Care (NIGB)
- ☐ Ministry of Justice (MoJ)

5. Will any research sites in this study be NHS organisations?

◉ Yes ○ No

5a. Do you want your application to be processed through the NIHR Coordinated System for gaining NHS Permission?

○ Yes ◉ No

If yes, you must complete and submit the NIHR CSP Application Form immediately after completing this project filter, before proceeding with completing and submitting other applications.

6. Do you plan to include any participants who are children?

◉ Yes ○ No

7. Do you plan to include any participants who are adults unable to consent for themselves through physical or mental incapacity? *The guidance notes explain how an adult is defined for this purpose.*

○ Yes ◉ No

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service in England or Wales?

○ Yes ◉ No

9. Is the study, or any part of the study, being undertaken as an educational project?

○ Yes ◉ No

10. Is this project financially supported by the United States Department for Health and Human Services?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the clinical care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

Integrated Research Application System
Application Form for Other research

NHS
National Patient Safety Agency
National Research Ethics Service

Application to NHS/HSC Research Ethics Committee

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
Early pubertal suppression in a selected group of adolescents with GID

Please complete these details after you have booked the REC application for review.

REC Name:
Central London REC 1

REC Reference Number:
10/H0718/62

Submission date:
14/07/2010

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

An evaluation of early pubertal suppression in a carefully selected group of adolescents with Gender Identity Disorder

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Dr.	Russell	Viner
Post	Reader in Adolescent Health		
Qualifications	MBBS FRACP FRCPCH FRACP PhD		
Employer	University College London		
[redacted]	[redacted]		

Fax

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and R&D reviewers that is sent to the CI.

	Title	Forename/Initials	Surname
	Dr.	Tracy	Assari
Address	Joint R&D Office for GOSH & UCL ICH		
	[redacted]		
	[redacted]		
[redacted]	[redacted]		
[redacted]	[redacted]		
[redacted]	[redacted]		
[redacted]	[redacted]		

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):
Sponsor's/protocol number: 1.0
Protocol Version: 1.0
Protocol Date: 25/06/2010
Funder's reference number: N/A
International Standard Randomised Controlled Trial Number (ISRCTN): N/A
ClinicalTrials.gov Identifier (NCT number): N/A
European Clinical Trials Database (EudraCT) number: N/A
Project website: N/A

Ref.Number Description	Reference Number
Central London REC 1	10/H0718/62

A5-2. Is this application linked to a previous study or another current application?

○ Yes ◉ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. This summary will be published on the website of the National Research Ethics Service following the ethical review.*

This study aims to evaluate the psychological, social and physical effects of pubertal suppression in a carefully

selected group of adolescents with Gender Identity Disorder. Gender Identity Disorder in young people is a complex and rare condition where there is an incongruence or discordance between the young person's perceived gender identity and their biological gender. Gender Identity Disorder is often associated with distress levels which tend to increase considerably during puberty with the development of secondary sex characteristics. Because of the association between distress and pubertal development there has been increasing pressure to provide early pubertal suppression from some young people, their families and some professionals. Professional Guidelines allow this intervention in carefully selected cases. Pubertal suppression in early puberty is now offered in some countries. The research evidence for this treatment is currently low. The current situation where early treatment is offered only in some centres is unsatisfactory. Current Guidelines (2009) by the British Society for Paediatric Endocrinology and Diabetes (BSPED) recommend that early intervention should ideally be implemented as a research study. This study proposes offering intervention in the early stages of puberty to a carefully selected group of adolescents with the following aims:
To evaluate the benefits and risks for physical and mental health of early medical intervention in adolescents with GID.
To add to the evidence base regarding the efficacy of this treatment for young people and to evaluate the impact of this intervention on the young people's well-being.
To evaluate persistence and desistence of the gender identity disorder and the continued wish for gender reassignment within this early intervention group.

A6-2. Summary of main issues. *Please summarise the main ethical and design issues arising from the study and say how you have addressed them.*

Early pubertal supression using a drug which blocks sex hormone production is already offered in some centres around the world. The current situation where treatment is offered in some centres but not others is unsatisfactory and can add further distress to the young people and their families. However because of the uncertainty regarding the reversibility of hormone blockers introduced in early puberty for a number of years, it is advisable that the offer of early intervention should be implemented as a research study (BSPED, 2009). Therefore this study proposes offering intervention in the early stages of puberty to a carefully selected group of adolescents with the following aims:

• To evaluate the benefits and risks for physical and mental health of early medical intervention in adolescents with GID.
• To add to the evidence base regarding the efficacy of this treatment for young people and to evaluate the impact of this intervention on the young people's well-being.
• To evaluate persistence and desistence of the gender identity disorder and the continued wish for gender reassignment within this early intervention group.

This research protocol has been developed by a core group of professionals working within the nationally designated Gender Identity Development Service (GIDS) at the Tavistock Centre which is linked with the Department of Peadiatric Endocrinology at UCLH. The core group includes professionals who have long-term experience in working with children and adolescent with Gender Identity Disorders. Four of these professionals have a background in mental health (Dr. Domenico Di Ceglie, Dr. Polly Carmichael, Dr. Vicky Holt and Dr. Elin Skagerberg) and four professionals have a background in Paediatric Endocrinology (Dr. Caroline Brain, Dr. Russell Viner, Dr. Gary Butler and Dr. Sophie Khadr). The group has sought consultation from eminent academics such as Professor Peter Fonagy (UCL) and Professor Ieuan Hughes (University of Cambridge).

Issues relating to this treatment have been widely debated in two recent international conferences at the Royal Society of Medecine and at Imperial College. These conferences have been attended by user group representatives and there have been presentations by the staff at the GIDS and UCLH. From the debates it has emerged that there is strong support from service users and some professionals that this treatment should be offered as a choice to young people and their families who can consent. We have also discussed the protocol with some adolescents and families attending the service and have sought their views.

Historically, physical interventions for GID were conceptualised in the guidance of the Royal College of Psychiatrists published in 1998 and then adopted in the Standards of Care of the Harry Benjamin Gender Dysphoria association, now WPATH.

In the Royal College of Psychiatrists Guidelines physical interventions were classed in three groups:
1) Wholly reversible intervention: this includes the use of hypothalamic blockers which suppress the production of estrogens or testosterone.
2) Partially reversible interventions, such as hormonal treatment that masculinises or feminises the body.
3) Irreversible interventions such as surgical procedures.
These guidelines state that surgical intervention should not be carried out prior to adulthood, which is interpreted as over the age of 18 years.
The Royal College of Psychiatrists Guidelines recommend that young people have "some experience of themselves in the post-pubertal state of their biological sex". However, these guidelines do not explicitly refer to a specific Tanner Stage of pubertal development. By contrast, the Harry Benjamin Standards of care (February, 2001) state specifically

that hormonal blockers should not be given before Tanner Stage 2 of puberty.
Whilst a number of specialist gender services offer hormonal blockers as the first stage of physical intervention, the timing differs. For example, the team at the Amsterdam Gender Clinic offers intervention at Tanner Stage 2/3 to selected cases fulfilling their inclusion criteria (described in the method section), while in the UK hormonal blockers have been offered at Tanner Stage 5 in line with previous guidelines issued by the British Society for Paediatric Endocrinology and Diabetes (BSPED, 2004).
The Royal College guidelines do not give any specific recommendations regarding age at which hormonal blockers could be offered or cross sex hormones introduced while the Harry Benjamin Guidelines state that the age for the eligibility for cross sex hormones is sixteen.

The Endocrine Society Clinical Practice Guidelines (Hembree et al., 2009) recommend that “adolescents who fulfil eligibility and readiness criteria for gender reassignment initially undergo treatment to suppress pubertal development” and that “suppression of pubertal hormones starts when girls and boys first exhibit physical changes of puberty (confirmed by pubertal levels of estradiol and testosterone, respectively), but no earlier than Tanner stages 2-3” (p. 3133).

Recent guidelines by the British Society for Paediatric Endocrinology and Diabetes (December 2009) recommend that “any deviation from current practice should be made by the specialist MDT [multi-disciplinary team]. Such a change in management should include comprehensive multidisciplinary assessment, informed consent, a system for monitoring outcome and ideally should be implemented as a research study”.
As considerable distress can be associated with the development of secondary physical sex characteristics in some young people entering puberty there has been increasing pressure to provide early physical intervention (at Tanner stage 2) from some young people, their families and some professionals. Pubertal suspension in early puberty is now offered in some countries by multidisciplinary teams or individual paediatricians supported by a colleague offering a psychological assessment. The rationale for early suppression of sex hormones during pubertal development is as follows:
1. It is argued that early suppression of sex hormones is associated with improved physical and psychological adaptation and well-being during adolescence and adulthood (Delemarre-van de Waal & Cohen-Kettenis, 2006).
2. It is argued that there is a positive impact on any sex-reassignment surgery in adulthood (Delemarre-van de Waal & Cohen-Kettenis, 2006).
3. It is argued that the introduction of hypothalamic blockers at Tanner stage 2 is fully reversible (Hembree, Cohen-Kettenis, Delemarre-van de Waal, Gooren, Meyer, Spack, Tangpricha, & Montori, 2009) and that it does not have an adverse effect on either physical or psychological development.
4. It is argued that it is possible to select a sub-group of adolescents with GID who will persist in their GID and wish to pursue gender reassignment (see De Vries et al., 2006).
5. It is argued that reducing anxieties and conflicts associated with pubertal development allows space to explore the cross gender identification (Delemarre-van de Waal & Cohen-Kettenis, 2006).
6. It is argued that preliminary results show that “this policy is promising” (Cohen-Kettenis et al., 2008, p.1892).

On the other hand, concerns have been expressed in the following areas:

1. It is not clear 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.

2. It is argued that it is possible that early suppression may affect brain functioning and gender identity development by influencing the persistence of the GID and fixing transgender beliefs. Evidence suggests that GID does not persist in about 80% of young people presenting pre-pubertally with GID (Green, 1987; Zucker & Bradley, 1995; Drummond et al., 2008; Wallien & Cohen-Kettenis, 2008).

3. It is unclear how early intervention affects cognitive function and mood or affect. Studies on Androgen Deprivation Therapy (ADT) in adults with prostate cancer showed some adverse changes in cognitive function and mood (Cherrier, Aubin, & Higano, 2009; Nelson, Lee, Gamboa, & Roth, 2008). However, this may not apply to adolescents.

4. Issues regarding fertility e.g. adolescents on blockers cannot produce sperm or eggs to be frozen. In biological boys, who commence the blocker in late puberty in order for sperm to be produced suspension of the analogue treatment needs to occur for a period of up to 6-12 months. No data is available on when ovulation could resume in girls (Hembree et al., 2009). In the case of pubertal suppression in the early stages of puberty, from Tanner stage 2, a significant period off the blockers would be required, with associated physical development, for the possibility of egg or sperm production.

5. There is little research evidence on the long-term physical and psychological consequences of early intervention. It is therefore difficult to assess if the proposed benefits of early intervention outweigh the possible risks. The Endocrine Society Clinical Practice Guidelines (2009) state that the research evidence on endocrine treatment is currently low or very low in this area using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system.

Recruitment:
Participants will be recruited from the adolescents attending the Gender Identity Development Service. The entry criteria will be consistent with the protocol used at the Amsterdam Gender Clinic (Cohen-Kettenis & Delemarre-van De Waal, 2008; Delemarre-van De Waal & Cohen-Kettenis, 2006; De Vries et al., 2006). All adolescents and their families attending the service will receive information about this study included in the general information leaflet of the service. Adolescents and their parents who seek this treatment and meet the eligibility criteria will be considered for inclusion in the study.

The ethical issue which has arisen is that users wish to exercise choice in a treatment which is already offered in some centres but for which the evidence base is currently low. This protocol offers service users a choice within a framework with a robust system of outcome monitoring and in the safest possible way. As there are well-defined inclusion and exclusion criteria (see section A17-1 and A17-2) it is possible to that a small number of service users may be disappointed. Every effort will be made to support these families in understanding why at the time of the decision they were not able to take part in the project. They will continue to be offered standard treatment and will be reconsidered to be included in the project if they so wish and if the clinical presentation has changed.

Consent:
Consent will be sought from the adolescents and his/her parent/carer. The capacity of the adolescent to understand the nature of the treatment and the possible consequences will be carefully assessed by the treating clinician and a detailed information sheet will be given and its content fully discussed with the adolescent and his/her carer.

Risk/benefits:
The benefits and risks to the patients have been highlighted above. This will be described in the information sheet and fully discussed with the adolescent and his/her family in order to make sure that they have been fully undetstood. This will minimise the risk of adolescents and parents/carers making a choice without an understanding of the potential negative consequences.

Confidentiality:
The service will adhere to the Caldicott Principles and the data will be safely stored at the Tavistock Centre and at UCLH as appropriate. The Chief Investigator (UCLH) and principal investigator at the Tavistock will be responsible for the maintenance of confidentiality, safety, and proper handling of the data.

Conflict of interest:
There is no conflict of interest in conducting this research as no funding will be soiught from drug companies or other groups interested in achieving a particular result.

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

The main aim of the present study is to evaluate some of the psychological, social and physical benefits and risks involved in blocking sex hormone production in a carefully selected group of biological girls and boys with Gender Identity Disorder in the early stages of puberty.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

• To add to the evidence base regarding the efficacy of this treatment for young people and to evaluate the impact of this intervention on the young people's well-being.

• To evaluate persistence and desistence of the gender identity disorder and the continued wish for gender reassignment within this early intervention group.

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

The current situation where early treatment is offered only in some centres is unsatisfactory. There is little research evidence regarding the short-term and long-term benefits and risks of this treatment. Current BSPED Guidelines (2009) recommend that early intervention should ideally be implemented as a research study. This study therefore proposes offering intervention in the early stages of puberty to a carefully selected group of adolescents. Additionally, there is a strong wish from users that our service offers a choice of treatment.

This study has a robust system of outcome monitoring (physically and psychologically)and therefore provides the safest possible way to offer this treatment to GID service users.

The offer of treatment options with informed consent is also strongly recommended by the World Congress on Family

Law and Children's Rights, 2009 (Resolution 19).

A13. Please give a full summary of your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

In designing the project the research group carefully considered a randomised control design. However it is not feasible as the effect of the intervention would make it obvious to participants whether or not they were receiving the blocker or a placebo. Additionally it is very unlikely to be acceptable to prospective participants to take part in a research design in which there is a chance they will not receive hormonal treatment. Further, as the numbers are small this would make it difficult to collect sufficient data. Additionally it is highly likely that those in the no treatment group would drop out of the study and seek private treatment.

The design of the protocol should interfere as little as possible with the clinical model of care of the GIDS (treatment as usual). This involves carrying out the research at the two sites of the service: The GIDS Tavistock clinic and University College London Hospital (UCLH) for the paediatric and endocrinology components. This should allow for service users who wish to withdraw from the research protocol to continue to receive treatment as usual.

The design of the protocol should be applicable to other countries in Europe or outside Europe so that it can be added to their model of care without too much interference if European cooperation for this project becomes feasible.

The system for monitoring outcomes should be manageable i.e. where possible, follow-up research appointments should be arranged to coincide with the administration of the analogue and follow-up physical investigations.

Young people and their families will receive information about this research project through a GIDS general information leaflet given to the service users at the beginning of their contact with the service. Young people (between the age of 12 and 15) and their families who have attended the service for at least 6 months and attended at least four interviews, who actively request intervention in early puberty, and who are deemed to meet the other psychosocial eligibility criteria by the treating clinician/s will be given further written information about the project.

If they meet the eligibility criteria they will be asked to fill in the following questionnaires if they have not already been fully completed within the last 3 months.

General Psychological Functioning
- Child Behaviour Checklist
- Youth Self Report
- Teacher’s Report Form
- The Children’s Global Assessment Scale
- Social Responsiveness Scale
- Kidscreen- 52 (well-being questionnaire)

Gender Identity / Dysphoria
- Gender Identity Interview
- Utrecht Gender Dysphoria Scale
- Body Image Scale
- Recalled Childhood Gender Identity Scale
- Dimensional DSM Criteria-GID List

Endocrine evaluation
Young people meeting the psychosocial eligibility criteria will be offered a physical assessment at the UCLH site by the research paediatrician to determine the Tanner stage of pubertal development. Only young people who have reached the Tanner stage 2/3 of pubertal development will be eligible from the physical point of view. Young people at stage 3 or 4 would also be eligible. Informed consent will be sought from the adolescent and a legal guardian.

The following baseline investigations will be carried out at UCLH (detailed in full in Appendix 2 of the protocol):
1. Karyotype (to confirm genetic make up in terms of biological sex)
2. Baseline blood tests and hormone profile
3. Synacthen test in biological girls (to exclude congenital adrenal hyperplasia, a rare inherited endocrine condition)
4. Hand and wrist Xray to check bony maturity (or 'bone age')
5. Dual X-ray absorptiometry (DXA) scan to check bone density (bone strength)
6. Pelvic ultrasound in biological females to check that the womb and ovaries are present - as we would expect - and appear normal

On the basis of this information the chief and principal investigators in consultation with the key clinicians will make a decision as to whether the criteria have been fulfilled and whether analogue treatment can be offered. The analogue treatment will be administered at UCLH where possible but may be delivered locally by appropriately trained individuals if required.

It is envisaged that approximately 10-15 young people per year will meet the eligibility criteria. It is expected that the project will be run for about 6 years and that the recruitment will stop after 3 years. The people who were recruited in the third year will then have enough time to complete the treatment with the hypothalamic blocker before returning to standard protocol- outside the research study.

The study questionnaires will be administered on a yearly basis from the commencement of the analogue treatment until the age of 16. Young people and their families who agree to be involved in the study will also commit themselves to be seen for a clinical interview with their key clinician and a follow-up semi-structured interview by a member of the clinical research team once every 6 months until the age of 16 when they will become eligible to start cross-hormone treatment. The clinical interview will be managed in whatever way the therapist feels is appropriate. The aim of the semi-structured research interview will be to monitor the psychological effects of the analogue and the persistence of the gender identity disorder and the wish to continue with the treatment so that the data collected will be recorded in a standardised way. At the age of 16 after completing the project the young people will receive treatment within the standard protocol and continue to be monitored under the audit procedures of the service. All participants in the study will be encouraged to participate in the therapeutic program of the GIDS as deemed appropriate in discussion with the clinician involved. This could involve family work, individual work and network-liaison meetings with local services. These additional psycho-social interventions, which are part of the treatment as usual by the GIDS, will be carefully recorded as they may be useful for future single case studies regarding possible mechanisms contributing to particular outcomes.

There will be review appointments with the Paediatric Endocrinologist every 3 months for the first year and then bi-annually until the age of 16. These will include a physical examination to monitor the Tanner stage of pubertal development and other aspects of physical development, and to exclude other medical conditions. Safety monitoring will include evaluation of the following (detailed in full in Appendix 2 of the protocol):
1. Linear growth, 3-monthly
2. DXA scan, yearly, to check bone density
3. Blood hormone profile, 3-monthly for the first year then bi-annually
4. Blood tests to check kidney and liver function, blood count, bone profile and vitamin D levels, 3-monthly for the first year then bi-annually.

The progress of the treatment will be reviewed at least once every 6 months by the study steering group and by the research team and the clinical team at the regular clinical meetings of the GIDS. An early review can be called at any time by any member of the team.

At the end of the first three years the data will be analysed and an interim report will be produced giving a provisional evaluation in line with the objectives of the study. The final report will be produced at the end of the 6 years.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- [x] Design of the research
- [ ] Management of the research
- [ ] Undertaking the research
- [ ] Analysis of results
- [x] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
Families attending the Gender Identity Development Service at the Tavistock Centre were asked to read the research protocol and to make comments. These comments were then implemented into the research protocol where deemed appropriate.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

The entry criteria will be consistent with the protocol used at the Amsterdam Gender Clinic (Cohen-Kettenis & Delemarre-van De Waal, 2008; Delemarre-van De Waal & Cohen-Kettenis, 2006; De Vries et al., 2006).

A. Psychological criteria
Before the adolescent can be considered for inclusion in the research protocol s/he should have been seen by the service at the Tavistock clinic site for at least 6 months and should have attended at least 4 interviews for assessment and therapeutic exploration of their gender identity development.

1. Standard readiness criteria relating to psychological stability sufficient to withstand the stresses of sex re-assignment. These are standard within the current clinical service at the Tavistock.

2. Fulfils the following criteria relating to GID:
a) Throughout childhood (defined as over 5 years) the adolescent has demonstrated an intense pattern of cross-gendered behaviours and cross-gender identity.

b) The adolescent has gender dysphoria that is significantly increased with the onset of puberty. Following assessment the clinician(s) working with the young person deems that there is a high likelihood of the young person experiencing severe psychological distress consequent on experiencing full pubertal development before the blocker is implemented.

3. The young person and parents/guardians are actively requesting blockers.

4. The young person is able to give informed consent.
(Note that so called “real life experience” of living in a trans-gender role is not required, de Vries (2006, p. 91).

B. Physical/medical criteria
1. In established puberty:
• For biological males Tanner (Genital and pubic hair (PH)) stage 3 and above.
• For biological females, Tanner (Breast and PH) stage 2 and above.
Note that these pubertal criteria match those used by the Dutch. The rationale for the sex difference is that the pubertal growth spurt which early intervention aims to avoid occurs earlier in females (Tanner 2-3) than in males (Tanner 3-4), thus earlier intervention is required in females but is not necessary in males to avoid unwanted growth (in males) or growth termination (in females).

2. Normal endocrine function and karyotype consistent with biological sex.
Note that the presence of mild elevations of androgens in biological females consistent with polycystic ovarian syndrome is not an exclusion criterion.

3. Age 12 and above (Delemarre-van de Waal & Cohen-Kettenis, 2006).

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

1. Low spine or hip bone mineral density (BMD) on dual X-ray absorptiometry (DXA) scan (>1 z-score below expected BMD for age and biological sex).

2. Inability to participate with full investigatory protocol e.g. needle phobia, failure to attend for tests and scans.

3. Low body mass index (BMI, less than 15th centile for age and biological sex)

4. Mental health exclusions associated with serious psychiatric conditions (e.g. psychosis, bipolar condition, anorexia nervosa, severe body-dysmorphic disorder unrelated to GID).

5. Inability of the young person to give informed consent (all young people must be fully competent to give consent according to the Fraser Guidelines).

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
seeking consent	1	1	60 mins	The consent will be sought from the adolescent and a legal guardian by a member of the clinical research team at the Tavistock Centre.
Questionnaires	11	9	90 mins	The questionnaires will be administered at the Tavistock Centre by a member of the clinical research team.
semi-structured interview	1	N/A	30 mins	The semi-structured interview will be administered at the Tavistock Centre by a member of the clinical research team.

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. *These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Initial Paed. Endocrinology assessment to check eligibility, including a history, physical examination, Tanner staging of puberty, blood tests, hand and wrist X-ray, DXA & pelvic ultrasound in girls	1	All	1-3h	The assessment will be undertaken by a Paediatric Endocrinologist at UCLH. All investigations will be carried out at UCLH, where possible on the same day as an existing Paediatric Endocrinology appointment (boys). Girls will attend UCLH on 1 separate occasion for the pelvic ultrasound and synacthen test (both to be performed on the same day).
Clinical interview	4/y	4/y	1h	The clinical interview will be administered by the patient's key clinician at the Tavistock Centre.
Paediatric Endocrinology appointment for assessment and monitoring. This will include a short history, standard physical examination, Tanner staging of puberty, blood tests - plus an annual DXA scan.		All	1h	The follow-up assessments will be administered by a Paediatric Endocrinologist at UCLH. Subjects will be seen 3 monthly for the first year then 6 monthly. Where possible, annual DXA scans will be booked on the same day as a Paediatric Endocrinology appointment.
Intramuscular hormone blocker injections		All	15 min	The hormone blocker will be administered by the Paediatric Endocrine Clinical Nurse Specialist on a monthly basis at UCLH, where possible coinciding with a Paediatric Endocrinology monitoring appointment. Under some circumstances, injections may be delivered locally by appropriately trained individuals.

A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?

○ Yes ◉ No

A21. How long do you expect each participant to be in the study in total?

4 years or less (up to the age of 16)

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

In the short-term, it is expected that the adolescent will experience a relief of their distress generated by their unwanted pubertal development. In fact, the adolescent entering the study will be actively seeking this treatment with parental consent and will be highly motivated. However, patients who do not experience this benefit will be able to stop the treatment. If an adolescent experiences problems with concentration or mood swings or any other unpredicted symptoms the treating clinician and the Paediatric Endocrinologist will discuss the balance between benefits and discomforts involved in this treatment option with the adolescent and the parent/s. The clinicians will also discuss possible ways of aleviating the discomfort. The stopping rules describe conditions where the treatment will be stopped in the best interest of the patient. All participants and their parents/carers will receive a patient information sheet which will be carefully discussed with the clinicians before they decide whether to take part. The patient information sheet describes the benefits and potential risks involved in this treatment option.

The potential risks include:

1.It is not clear 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.

2.It is possible that early suppression may affect brain functioning and gender identity development by influencing the persistence of the adolescent's perceived gender identity.

3.It is unclear how early intervention affects cognitive functioning (e.g. memory and concentration) and mood.

4.There are issues regarding fertility e.g. adolescents on blockers cannot produce sperm or eggs to be frozen. The treatment with blockers would need to be stopped for a long period in order for sperm or eggs to be produced. For biological boys this period is likely to be 6-12 months but it is not clear how long it will take to resume egg production in biological girls.

5.There may be long-term consequences associated with this treatment which cannot be foreseen at present.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

◉ Yes ○ No

If Yes, please give details of procedures in place to deal with these issues:

The interviews/questionnaires may include topics that might be sensitive for the participants, however, they will be administered by experienced clinicians who will be able to provide support as appropriate. On the other hand, this information is routinly collected in the service for the clinical management and audit purposes. The patient information sheet explains that if child protection issues emerge or the risk of harm to the self or other is present appropriate action will be taken by the clinician according to the trust procedures and this may involve, after careful consideration, informing the appropriate statutory agencies.

A24. What is the potential for benefit to research participants?

The preliminary results from the data on puberty-delaying treatment by the centres that have used it are considered encouraging and it is assumed that:

1.Early suppression of sex hormones is associated with improved physical and psychological adaptation and well-being during adolescence and adulthood.

2.There is a positive impact on any sex-reassignment surgery in adulthood.

3.The introduction of hypothalamic blockers at Tanner stage 2 is considered reversible and that it does not have an adverse effect on either physical or psychological development.

4.Reducing anxieties and conflicts associated with pubertal development may allow space to explore the cross gender identification.

A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? *May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.*

After completing the project the participants will receive standard psychosocial and physical interventions provided by the service and they will continue to be monitored under the audit procedures of the service. The physical interventions involve hormonal treatment as appropriate. At the age of 18 the young people can be referred to an adult service for further treatment as appropriate and according to the usual procedures of the Gender Identity Development Service.

A26. What are the potential risks for the researchers themselves? *(if any)*

The adolescents and their parents/carers may find the experience of Gender Identity Disorder painful and unbearable and this may lead to pressures being placed on clinicians to provide physical interventions which may not be clinically appropriate at the time of the request (e.g. the use of cross-sex hormones). In such cases, a detailed discussion with the adolescent and the family of the treatment as a staged process may be containing, by creating space for thinking. Additionally, the GIDS will provide a space for discussion of potential difficulties and support to the professionals involved in the study.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Participants will be recruited from young people attending the Gender Identity Development Service (GIDS). Young people and their families will receive information about this research project through a GIDS general information leaflet given to the service users at the beginning of their contact with the service. Young people (between the age of 12 and 15) and their families who have attended the service for at least 6 months and attended at least four interviews, who actively request intervention in early puberty, and who are deemed to meet the other psychosocial eligibility criteria (as described in section A17-1) by the treating clinician/s will be given further written information about the project.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

○ Yes ◉ No

Please give details below:

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

○ Yes ◉ No

A29. How and by whom will potential participants first be approached?

Potential participants who are actively requesting this treatment will first be approached by their treating clinician.

A30-1. Will you obtain informed consent from or on behalf of research participants?

(•) Yes ( ) No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

All the participants and their legal guardians who are actively seeking this treatment option and who meet the eligibility criteria will receive information sheets about the project which will be carefully discussed with their clinician and will be asked to sign a consent form if they agree to take part in the project. Both the adolescent and the parents/legal guardians will have to agree to enter the study. The information sheet will explain what the research involves and what the potential risks and benefits of taking part are. The information sheet and the clinician will explain that participation in the research project is entirely voluntary and the young person and guardian will be given up to a month to decide whether they would like to take part. A copy of the information sheet will be given to all participants to keep.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

(•) Yes ( ) No

A31. How long will you allow potential participants to decide whether or not to take part?

In order for the participants and their parents/legal guardians to be able to fully consider the benefits and risks of taking part and to be able to ask questions they will be given up to 1 month to decide whether or not to take part. However, they may seek to enter the study at a later stage if they still meet the eligibility criteria.

A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?

(•) Yes
( ) No
( ) Not Known

If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?

It is possible that some of the potential participants are involved or have recently been involved in other research prior to recruitment, but we expect that this will not be the case for the majority of them. It is unlikely that participation in this study presents a conflict with participation in another project, however, this will be discussed by the research team to see if participation in another project affects the eligibility criteria.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

Interpreters will be arranged for persons who might not adequately understand written or verbal information in English or who have special communication needs. All the material will be translated and administered with the use of an interpreter.

A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?

If information that may be relevant to their continued participation in the project becomes available during the course of the research they will be informed verbally by their treating clinician if possible and will also be provided with written information about this. Any attempt will be made to provide this information as soon as possible.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

- ○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ◉ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ○ The participant would continue to be included in the study.
- ○ Not applicable – informed consent will not be sought from any participants in this research.

Further details:

This occurence is highly unlilkely in this study, however, participants will be given information about this and will be asked to tick a box in the consent form.

If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)? *(Tick as appropriate)*

- ☐ Access to medical records by those outside the direct healthcare team
- ☐ Electronic transfer by magnetic or optical media, email or computer networks
- ☐ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☑ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☑ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☑ Use of audio/visual recording devices
- ☐ Storage of personal data on any of the following:
  - ☑ Manual files including X−rays
  - ☑ NHS computers
  - ☐ Home or other personal computers
  - ☑ University computers
  - ☐ Private company computers
  - ☐ Laptop computers

Further details:
Data will be stored as per the usual clinical practice within the two Trusts, the Tavistock and UCLH. This may include audiovisual recording of therapy sessions. Research data will further be stored on research computers belonging to the Trusts or University.

If publications of direct quotations will be made it will be anonymised.

Appropriate access controls will be in place to ensure that access to confidential research information is restricted to those who need access.

Paper and other manual files will be appropriately filed and stored securely in a locked cupboard and according to both trusts' security procedures.

A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

A different number from the NHS number will be used when storing data for research purposes, in order to ensure confidentiality and we will adhere to the NHS Code of Confidentiality and both trusts' confidentiality procedures.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

The research team and key clinicians from the multi-disciplinary team will have access to participants' personal data during the study.

Storage and use of data after the end of the study

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ○ 6 – 12 months
- ○ 12 months – 3 years
- ◉ Over 3 years

If longer than 12 months, please justify:
As service users entering the research protocol may continue to receive treatment under the service treatment as usual and be audited it will be useful to retain the original data for comparison and outcome monitoring. The confidentiality of these data will be protected in line with the procedures described in section A38.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

◉ Yes ○ No

If Yes, please give details. For monetary payments, indicate how much and on what basis this has been determined.
Not directly for participation in research. However as this will constitute clinical care for participants, they will be eligible to be reimbursed for travel costs according to the Healthcare Travel Costs Scheme issued by the Department of Health.

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

◉ Yes ○ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?

◉ Yes ○ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

○ Yes ◉ No

Please give details, or justify if not registering the research.
As the participants eligible for this study will come from the population referred to the Gender Identity Development Service the information will be available to them through the general information sheet provided to new patients at the beginning of the contact, thus publishing this information on a public register will not be necessary nor in the subjects' interest.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

- ☑ Peer reviewed scientific journals
- ☑ Internal report
- ☑ Conference presentation
- ☑ Publication on website
- ☐ Other publication
- ☐ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☐ Other (please specify)

A53. Will you inform participants of the results?

◉ Yes ○ No

Please give details of how you will inform participants or justify if not doing so.
All participants will be informed of the results of the study and any relevant published material will be sent to them by post.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? *Tick as appropriate:*

- [x] Independent external review
- [ ] Review within a company
- [x] Review within a multi−centre research group
- [x] Review within the Chief Investigator's institution or host organisation
- [x] Review within the research team
- [ ] Review by educational supervisor
- [ ] Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
The scientific quality of the research has been reviewed within our research multidisciplinary team, by the Research and Development department at the Tavistock Centre and at UCLH and by independent academics in the field of Endocrinology (Professor Ieuan Hughes) and Psychology (Professor Peter Fonagy). The project has been widely discussed with the clinical team at the Gender Idenity Development Service and with the team at UCLH.

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

- [ ] Review by independent statistician commissioned by funder or sponsor
- [ ] Other review by independent statistician
- [ ] Review by company statistician
- [ ] Review by a statistician within the Chief Investigator's institution
- [ ] Review by a statistician within the research team or multi−centre group
- [ ] Review by educational supervisor
- [x] Other review by individual with relevant statistical expertise
- [ ] No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
	Dr.	Elin	Skagerberg
Department	Gender Identity Development Service		
Institution	Tavistock and Portman NHS Foundation Trust		
[redacted]	[redacted]		
[redacted]	[redacted]		
[redacted]	[redacted]		
[redacted]	[redacted]		
[redacted]			
[redacted]	[redacted]		

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

This is observational research concerning a timing modification of an established treatment. We feel it is inappropriate to therefore identify a single primary outcome.

The primary outcomes will be the benefits and risks for physical and mental health of early medical intervention in adolescents with GID. This will be achieved through comparing the scores on the questionnaires, the results on the medical tests and the information collected in the semi-structured interviews.

A58. What are the secondary outcome measures? *(if any)*

1. To add to the evidence base regarding the efficacy of this treatment for young people and to evaluate the impact of this intervention on the young people's wellbeing. The young people's wellbeing will be evaluated by the Kidscreen questionnaire and the change in the young people's mental states will be evaluated through the other questionnaires and the semi-structured interview. An improvement in mental states and overall wellbeing will support the view that the treatment is effective.

2. To evaluate the persistance and desistence of the gender identity disorder and the continued wish for gender reassignment within this early intervention group. This will be measured by the recorded adolescents' statements regarding their continued wish for physical intervention and gender reassignment in the 6- monthly semi-structured interview.

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:	45
Total international sample size (including UK):	0
Total in European Economic Area:	0

Further details:
We excpect that between 10-15 adolescents per year will be eligible to enter this study and that the recruitment will continue for 3 years.

It is envisaged that we might at a later stage seek collaboration with other countries in Europe and the study has been designed with this possibility in mind.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

The sample size was decided based on the current caseload of young people between the age of 12-15 attending the service. The current caseload in this age range is approximately 45 and we estimate that about one third will fulfill the eligibility criteria. A formal power calculation was not undertaken.

A61. Will participants be allocated to groups at random?

○ Yes ◉ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Descriptive statistics including means and standard deviations will be reported as well as parametric and non-parametric tests as appropriate.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

Title	Forename/Initials	Surname
Dr.	Polly	Carmichael

Post	Service Director GIDS and Clinical Psychologist
Qualifications	DClinPsy PhD
Employer	The Tavistock and Portman NHS Foundation Trust
[redacted]	[redacted]

Title	Forename/Initials	Surname
Dr.	Domenico	Di Ceglie

Post	Director of training, development and research GIDS and Honorary Senior Lecturer at UCL
Qualifications	MD DipPsych (IT) FRCPsych
Employer	Tavistock and Portman NHS Foundation Trust
[redacted]	[redacted]

Title	Forename/Initials	Surname
Dr.	Vicky	Holt

Post	Consultant Child and Adolescent Psychiatrist
Qualifications	MD MRCPsych
Employer	The Tavistock and Portman NHS Foundation Trust
[redacted]	[redacted]

Title	Forename/Initials	Surname
Dr.	Sophie	Khadr

Post	NIHR Clinical Lecturer in Adolescent Medicine
Qualifications	MB CHB MD MRCPCH
Employer	University College London
Work Address	University College London Hospital [redacted]

Title	Forename/Initials	Surname
Dr.	Caroline	Brain

Post	Consultant in Paediatric Endocrinology
Qualifications	MB BF FRCP MD
Employer	University College London Hospital
	[redacted]

Title	Forename/Initials	Surname
Prof.	Gary	Butler

Post	Consultant in Paediatric and Adolescent Endocrinology
Qualifications	MB BS MD MRCP FRCPCH FRCP
Employer	University College London Hospital
Work Address	235, Euston road [redacted]

Title	Forename/Initials	Surname
Dr.	Elin	Skagerberg

Post	Research Psychologist
Qualifications	PhD
Employer	The Tavistock and Portman NHS Foundation Trust
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status:
- ○ NHS or HSC care organisation
- ◉ Academic
- ○ Pharmaceutical industry
- ○ Medical device industry
- ○ Local Authority
- ○ Other social care provider (including voluntary sector or private organisation)
- ○ Other

Commercial status: Non-Commercial

If Other, please specify:

Contact person

Name of organisation	University College London, Institute of Child Health
Given name	Tracy
Family name	Assari
Address	Joint R&D Office for GOSH and UCL ICH, Institute of Child Health, 30 Guilford St.,
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Is the sponsor based outside the UK?

○ Yes ◉ No

Where the lead sponsor is not established within the UK, a legal representative in the UK may need to be appointed. Please consult the guidance notes.

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another

country?

○ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68. Give details of the lead NHS R&D contact for this research:

	Title	Forename/Initials	Surname
		Philip	Diamond
Organisation		University College London Hospitals NHS Trust	
[redacted]		[redacted]	
Fax			
Mobile			

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/09/2010
Planned end date: 31/08/2016
Total duration:
Years: 6 Months: 0 Days: 0

A71-1. Is this study?

○ Single centre
◉ Multicentre

A71-2. Where will the research take place? *(Tick as appropriate)*

☑ England
☐ Scotland
☐ Wales
☐ Northern Ireland
☐ Other countries in European Economic Area

Total UK sites in study 2

Does this trial involve countries outside the EU?
○ Yes ◉ No

A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? *Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:*

- [x] NHS organisations in England 2
- [ ] NHS organisations in Wales
- [ ] NHS organisations in Scotland
- [ ] HSC organisations in Northern Ireland
- [ ] GP practices in England
- [ ] GP practices in Wales
- [ ] GP practices in Scotland
- [ ] GP practices in Northern Ireland
- [ ] Social care organisations
- [ ] Phase 1 trial units
- [ ] Prison establishments
- [ ] Probation areas
- [ ] Independent hospitals
- [ ] Educational establishments
- [ ] Independent research units
- [ ] Other (give details)

Total UK sites in study:

A75-1. Will a data monitoring committee (DMC) be convened?

○ Yes ◉ No

If Yes, please forward details of the membership of the DMC, its standard operating procedures and summary reports of interim analyses to the Research Ethics Committee which gives a favourable opinion of the study (or to GTAC if applicable).

A75-2. What are the criteria for electively stopping the trial or other research prematurely?

If an unforseen and serious adverse event occurs during the course of the research the research team will have a full discussion of the event and seek advice from the advisory committee and the R&D Directors at the Tavistock Centre and UCLH and a decision to electively stop the research prematurely may be taken.

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:* in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland**

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- [ ] NHS indemnity scheme will apply (NHS sponsors only)
- [x] Other insurance or indemnity arrangements will apply (give details below)

UCL Insurance. See attached letter

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

- [x] NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- [ ] Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

- [x] NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)
- [ ] Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

○ Yes ◉ No

Please enclose a copy of relevant documents.

PART B: Section 3 – Exposure to ionising radiation

Complete sub-sections A and/or B as applicable with input from relevant experts. It is advisable to discuss the proposed research at an early stage with (a) a Medical Physics Expert and (b) a Clinical Radiation Expert, who will carry out the required assessments for sub-sections C and D. The lead MPE can also facilitate the completion of sub-sections A and/or B if necessary.

1. Does the study involve exposure to radioactive materials?

○ Yes ◉ No

2. Does the study involve other diagnostic or therapeutic ionising radiation?

◉ Yes ○ No

A. Radioactive materials

Details of radioactive materials

B. Other ionising radiation

B1. Details of other ionising radiation

Give details by completing the table below:

Procedure	No of procedures	Estimated procedure dose *(use national Diagnostic Reference Levels where available)*
hand and wrist Xray	1 per subject (at recruitment)	0.17 uSv
hip and lumbar spine DXA	1 study at recruitment and then annually (upto three further studies)	11 uSv (at age 10), 7.6 uSv (at age 15), 6.8 uSv (at adult) please refer to MPE dose and risk assessment

C. Dose and risk assessment

C1. What is the total research protocol dose from the exposures in A1 and/or B1, and what component of this is the additional dose over and above standard practice? What are the risks associated with these two doses (total and additional)?

The dose and risk assessment should be set out below. This should be prepared by a Medical Physics Expert (MPE) who is a registered health care professional and has expertise relevant to the planned exposures. Where the study involves different types of exposure (for example, both radioactive materials and other ionising radiation, or more than one imaging method), advice may need to be sought from other MPEs with relevant expertise. The lead MPE should produce a combined assessment for the ethics committee, giving the names of any other MPEs who have contributed to the assessment. Further guidance is available by clicking on the information button or in the document "Approval of research involving ionising radiation", available here: http://www.nres.npsa.nhs.uk/applicants/guidance/

Nil in addition to standard clinical practice for pubertal suppression, which includes a baseline hand and wrist X-ray and dual X-ray absorptiometry (DXA) scan followed by yearly assessment of bone mineral density by DXA.

Research patients will be recruited into the trial from age 12 years, and will be followed until age 16. They will receive a baseline DXA hip and lumbar spine study to determine bone mineral density at the outset of the trial, with further DXA studies annually. Thus they may receive a maximum of four such DXA studies. Each patient will also receive a plain X-ray study of the hand and wrist at recruitment to determine bone age.

Each DXA study will result in an effective radiation dose dependent upon the DXA instrument itself, the DXA procedure undertaken and the age and body habitus of the adolescent patient. All studies will be performed on the same Hologic Discovery-A DXA system at the Institute of Nuclear Medicine, UCL Hospitals, and all studies will comprise a combined hip and (L1-L4) lumbar spine DXA procedure, performed to the same standard institutional protocol.

Published data (Blake GM et al, Bone 2006; 38: 935-942) states that the mean effective dose arising from a combined hip and lumbar spine DXA study performed on a Hologic Discovery-A system is 11 uSv, 7.6 uSv and 6.8 uSv for a 10 year old, 15 year old and adult patient respectively. Data is presented for the DXA system operated in Express mode with the scan range scaled appropriately to the patient's size. Effective dose here has been determined using the most recent ICRP 103 Recommendations for tissue weighting factor wT, published in 2007.

Thus the total effective dose for a maximum of four DXA procedures is 44 uSv, 30.4 uSv and 27.2 uSv for the 10 year old, 15 year old and adult patient.

Published data for effective dose resulting from a plain X-ray study of the hand and wrist indicates a figure of only 0.17 uSv (Huda W and Gkanatsios NA, Health Physics 1998; 75(5): 492-499).

Thus, a maximum radiation dose of 44 uSv will be received by any trial patient.

The relevant risk to consider for exposure to ionising radiation is that of the late risk of a malignancy induced by the exposure. For the age range 10-19 years, the mean lifetime risk of an induced fatal cancer in a UK population is 9.9x10-8 per uSv (Documents of the NRPB, 1993; vol4 no4). This equates to a risk of 1 in 230,000 throughout the patient's lifetime for the 44 uSv maximum radiation dose quoted here. This maximum dose can also be compared

with the UK average radiation dose from natural background radiation of 7 uSv per day, and an effective dose of 20 uSv for a chest X-ray.

Wendy Waddington
14 July 2010

Special attention must be paid to pregnant/potentially pregnant women or those who are breast feeding, or other potentially vulnerable groups.

C2. Declaration by lead Medical Physics Expert

I am satisfied that the information in sub-sections A and/or B and the assessment in sub-section C provide a reasonable estimate of the ionising radiation exposure planned in this research and the associated risks.

Signature:…….. Date: 14/07/2010

C3. Details of person acting as lead Medical Physics Expert

	Title	Forename/Initials	Surname
	Ms	Wendy	Waddington
Post	Consultant Clinical Scientist, Head of Clinical Nuclear Medicine Physics		
Details of professional registration	HPC Registration: CS 02349		
Organisation	UCL Institute of Nuclear Medicine, UCL Hospitals NHS Foundation Trust		
[redacted]	[redacted]		

D. Clinical assessment

This sub-section should be completed by a Clinical Radiation Expert (CRE) who is a registered health professional with clinical expertise relevant to the planned exposures. The assessment should cover potential exposure at all research sites, taking account of possible variation in normal clinical practice. Where the study involves different types of exposure (for example, both radiotherapy and other ionising radiation), advice may need to be sought from other CREs with relevant expertise. The lead CRE should produce a combined assessment for the ethics committee, giving the names of any other CREs who have contributed to the assessment. The guidance notes give advice to Chief Investigators on who can act as lead Clinical Radiation Expert (CRE) and advice for the CRE on the assessment of exposures having regard to IRMER.

Special attention must be paid to pregnant/potentially pregnant women or those who are breast feeding, or other potentially vulnerable groups.

D1. Will the exposure exceed the exposure that might be received as part of normal care at any proposed research site?

○ Yes ◉ No

D3. Declaration by lead Clinical Radiation Expert

I am satisfied that the exposure to ionising radiation planned in this research study (as defined in A1 and/or B1) is reasonable and that the risks are adequately described in the participant information sheet for the study.

Signature:…….. Date: 14/07/2010

D4. Details of lead Clinical Radiation Expert

	Title	Forename/Initials	Surname
	Professor	Peter Josef	Ell
Post	Consultant Nuclear Medicine Physician, NIHR Senior Investigator		
Details of professional registration	FRCP GMC 2473453		
Organisation	UCL Institute of Nuclear Medicine, UCL Hospitals NHS Foundation Trust		
Address	University College Hospital		

Employers responsible for radiation facilities at research sites must have written procedures to meet the requirements of the Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER). R & D offices for NHS sites will seek confirmation from local radiation experts that local IRMER authorisation procedures have been followed. Where the local Medical Physics Expert or IRMER Practitioner disagrees with the assessments made in this Section and/or the care organisation is unable to adhere to the protocol, this should be discussed with the Chief Investigator and the lead experts for the study. Any necessary variation in the protocol or participant information sheet at particular sites should be notified to the main REC as a substantial amendment and an ethical opinion sought.

PART B: Section 7 - Children

1. Please specify the potential age range of children under 16 who will be included and give reasons for carrying out the research in this age group.

12-15

It is at the core of this research project that early hormonal intervention is offered to a carefully selected group of adolescents as described in section A12.

2. Indicate whether any children under 16 will be recruited as controls and give further details.

No

3-2. Please describe the arrangements for seeking informed consent from a person with parental responsibility and/or from children able to give consent for themselves.

Informed consent will be sought from the adolescent and from the parents/legal guardians as described in section A30-1. The adolescent will need to be Fraser competent as assessed by the treating clinician and in discussion with the Prinicpal Investigators.

4. If you intend to provide children under 16 with information about the research and seek their consent or agreement, please outline how this process will vary according to their age and level of understanding.

An information sheet which describes the research in a language appropriate to the adolescent will be given to them. The information offered will be fully discussed with the treating clinician during the assessment interviews who will make sure that the adolescent understands the benefits and potential risks of undertaking this treatment. A similar process will be undertaken with the parents/legal guardians.

Copies of written information sheet(s) for parents and children, consent/assent form(s) and any other explanatory material should be enclosed with the application.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.*

Research site		Investigator/ Collaborator/ Contact	
Institution name	The Tavistock and Portman NHS Trust	Title	Dr.
Department name	Gender Identity Development Service	First name/ Initials	Polly
Street address	120, Belsize lane	Surname	Carmichael
Town/city	London		
Post Code	NW3 5BA		
Institution name	University College London Hospital	Title	Dr.
Department name	Department of Adolescent Medicine	First name/ Initials	Russell
Street address	250, Euston Road	Surname	Viner
Town/city	London		
Post Code	NW1 2PQ		

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.

9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the main REC or the GTAC (as applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the main REC, in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs.
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.

10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.

11. I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- [x] Chief Investigator
- [ ] Sponsor
- [ ] Study co-ordinator

☐ Student

☐ Other – please give details

☐ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

Signature: .....

Print Name: Russell Viner

Date: 14/07/2010 *(dd/mm/yyyy)*

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

4. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

5. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.

6. I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Signature: .....

Print Name: Tracy Assari

Post: Research Governance Co-ordinator

Organisation: UCL (Joint R&D Office for GOSH and UCL Institute of Child Health)

Date: 14/07/2010 *(dd/mm/yyyy)*

[redacted]

Dear [redacted]

Following the outcome of the Central London REC 1 meeting on the 25th of August, which gave an unfavourable opinion, we have decided, after careful consideration, to submit our application for ethical approval from your committee.

We appreciate the Central London Research Ethics Committee 1's dilemmas in granting approval for this study given the unusual presentation of Gender Identity Disorder and the sensitive and controversial nature of research in this area. We are aware of the ethical tensions involved in determining what the best interests of this group of children might be.

The following comments are our response to the reasons for the unfavourable ethical opinion in the letter from [redacted] Chair of Central London REC 1 dated 06-09-10 (see attached letter):

a. The committee's main concern was the lack of a control group for this study. As described on page 9 of our research protocol we considered in detail a randomised control design and sought advice from other researchers about this. Obviously a randomised control trial would be the ideal way of comparing two treatment options.

   The main reason why we reached the conclusion that a randomised control trial is not feasible was that this treatment would be offered only to highly motivated individuals who have demonstrated persistence in their gender identity disorder, that is, in their belief and wish to change their body to match their internal perception. People in this state of mind and with this level of conviction about their identity are therefore highly unlikely to accept to enter a project which faces them with the uncertainty of whether or not they will receive this treatment based on chance. Their ultimate aim is to harmonise their body to their perceived identity. The same conclusion was reached by de Vries et al. who are the only people who have published a longitudinal follow-up study on pubertal suppression in adolescents with Gender Identity Disorder (in press, see **appendix 1** page 7). This study received ethical approval from the VWMC ethics committee in Amsterdam.

The main aim of this study is not to compare two groups but to provide a prospective longitudinal follow-up study comparing the psychological and physical wellbeing in this group of teenagers before and after puberty suppression.

The study offers a choice to service users, who actively seek this treatment, within a safe framework of monitoring and informed consent in line with the recommendations of the British Society for Paediatric Endocrinology and Diabetes (2009) and the previous guidelines of the Royal College of Psychiatrists (1998) (see **appendix 2**). The study also aims at evaluating the impact of this intervention on young people's well being and their persistence in pursuing gender reassignment. The service users who decide not to go ahead with the hormone blockers at this stage or those who are not eligible would not be comparable to the group who intensely wishes to start the blockers because of a number of confounding factors such as having different psychological characteristics. No other study in this area, as far as we know, uses a randomised control group or any other control group (see de Vries et al., in press). However, we think that it would still be useful to use the group of teenagers who are not eligible or who choose not to go ahead with hormone blockers as a comparison group (see point f) to see whether any major differences emerge between the groups which can direct further studies.

b. We try to be caring and trusted clinicians with all of our service users. However, for the reasons described above hardly any of the eligible service users would accept a randomised control trial, as the main aim of the people who are eligible is to adapt their body to their strong self-perception. This judgment is based on our long-term clinical experience and discussions with user groups.

c. Some service users to whom we could not offer an option of early intervention, and who could afford it, have gone for treatment abroad. We know of three or four cases, but there might be more. They resented having to pay for this treatment and some have complained to their local PCT for not funding their treatment which is not available in this country. This also raises the issue of equity, as only well off people are able to afford it. One of the reasons for this study is to offer a choice to service users who are highly motivated and who meet the eligibility criteria and not to loose service users to follow up. We do not have any information about the outcome of service users who went abroad. This approach would be in line with resolution 19 of the World Congress on Family Law and Children's Rights (2009, see **appendix 3**).

d. From our experience, adolescents who enter puberty and who persist in their cross identification with the other gender find puberty unbearable and convey their high level of distress to their parents, who in turn may become distressed themselves and consequently find it hard to cope with their child's distress. Our service addresses these issues through psychological and social interventions, but there is a need to have physical interventions as an option in carefully selected cases. De Vries et al. (in press) found that in their study in

Holland "behavioural and emotional problems and depressive symptoms decreased, while general functioning improved significantly during puberty suppression".

e. Current studies show that about 80% of prepubertal children with gender identity disorder change their mind **before or at the onset of puberty** (Green, 1987; Zucker & Bradley, 1995; Drummond et al., 2008; Wallien & Cohen-Kettenis, 2008). However, after the onset of puberty, at the age of 12 or 13, the condition tends to crystallise and people are less likely to change their mind. This study aims to evaluate the persistence or desistence of the gender identity disorder. The Dutch group reports that noone entered in their study has changed their mind during the eight years in which the Dutch group has offered hormone blockers (de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2010). Their eligibility criteria are similar to those of our study. It will therefore be useful to see if the data from this study regarding persistence and desistence confirms the Dutch data as there may be a differences between the two services in terms of psychological and social interventions.

f. If the study is ethically approved the service will certainly continue to offer alternatives to service users such as the current standard of care and a delayed start of hormonal blockers. It is not intended that this service will offer early hormonal intervention if service users are not actively asking for it or do not meet the eligibility criteria. For all of our service users, we are using the same assessment criteria and standardised questionnaires for audit purposes. This set of questionnaires (except the well-being questionnaire -Kidscreen-52 and the Social Responsiveness Scale) were agreed for standardised monitoring by an international group of professionals working in this area including ourselves, Holland, Germany, Belgium, Norway, Canada and USA. We could use this data from young people who choose not to start the treatment with blockers or who are referred to the service late in adolescence as a comparison group to see whether there are any significant differences between these groups. However, this comparison will not have the same strength as a randomised control trial.

We very much hope that this response addresses the concerns raised by the Central London REC 1 and we would be very happy to discuss any issues further with you.

With best wishes,

[redacted]
On behalf of the research team

References:

British Society for Pediatric Endocrinology and Diabetes (BSPED) Statement on the management of Gender Identity Disorder (GID) in Children and Adolescents (December 2009).

De Vries, A. L., Steensma, T. D., Doreleijers, T. A. and Cohen-Kettenis, P. T. (in press). Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *The Journal of Sexual Medicine*.

Drummond, K. D., Bradley, S. J., Peterson-Badali, M., & Zucker, K. J. (2008). A follow up study of girls with gender identity disorder. *Developmental Psychology*, **44**, 34-45.

Green. R. (1987). The 'sissy boy syndrome' and the development of homosexuality. New Haven, CT: Yale University Press.

Royal College of Psychiatrists (1998). *Gender Identity Disorders in Children and Adolescents- Guidance for Management.* Council Report CR63. London: Royal College of Psychiatrists.

Wallien, M. S. C. & Cohen-Kettenis, P. T. (2008). Psychosexual outcome of gender dysphoric children. *Journal of the American Academy of Child & Adolescent Psychiatry*, **47**, 1413-1423.

World Congress on Family Law and Children's Rights (2009). Halifax- Canada. Resolution 19. http://www.lawrights.asn.au/

Zucker, K. J. & Bradley, S. J. (1995). Gender identity disorder and psychosexual problems in children and adolescents: New York Plenum Press.