Assessment and support of children and adolescents with gender dysphoria

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INTRODUCTION
There has been a large increase in the number of children and adolescents who question conventional gender expectations and seek recognition and acceptance of their gender diversity, wishing to develop a body that is congruent with their gender feelings.1 Professionals may be unsure how best to provide supportive care, how to access the national Gender Identity Development Service (GIDS) for children and adolescents, or how to deal with a transgender young person presenting with another clinical problem unrelated to their gender transition. Faced with very distressed young people, they may feel under pressure to initiate physical intervention without consultation with psychosocial colleagues. It is important that all professionals are aware of the care pathway for transgender children that may be of relevance in a range of paediatric settings. The purpose of this practice review is to present an up-to-date perspective on the care of transgender children and adolescents to guide management and to enable the provision of a practical, evidence-based approach to their support.

FREQUENCY OF GENDER QUESTIONING IN CHILDREN
Gender atypical behaviour is common among young children and can be part of general development. It is difficult to determine the exact incidence and prevalence of more intense and long-standing gender dysphoria (GD) in the UK and elsewhere as the total number of children and young people referred to the GIDS has risen exponentially since 2011 (figure 1). A striking feature of this increase is the large proportion of birth-registered females from 2011 onwards. This increase and the change in sex ratio is also seen in other countries. The reasons are not fully explicable and a number of questions arise. Is this increase due mostly to the greater tolerance of gender-diverse expression in westernised society? Is male status still regarded as preferable? Are all referrals to a specialist service appropriate and do all these young people have ascertainable GD? What are the benefits, as well as the possible harms, in supporting and helping these young people at different stages of development?

THE GIDS
Support for children and adolescents up to the age of 18 years has been provided through the Tavistock and Portman NHS Trust in London for over 20 years. The GIDS was nationally commissioned by NHS England in 2009 and extended to Leeds in 2012, providing regular outreach clinics in other areas of the UK. Endocrine evaluation and support has been provided through University College Hospital London for over two decades, and Leeds Children’s Hospital since 2013. Care is provided according to an agreed service schedule,1 taking into account international guidance from the World Professional Association for Transgender Health (WPATH)4 and the recent guidelines from the Endocrine Society.5

CRITERIA FOR THE DIAGNOSIS OF GD
The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition6 provides one overarching diagnosis of GD with separate specific criteria for children and for adolescents and adults. The diagnosis involves a difference between one’s experienced/expressed gender and assigned gender, and significant distress or problems in everyday functioning. Diagnosis can be made when at least two features have been present for 6 months or more (box 1). For children, cross-gender behaviours may start between the ages 2 and 4, the same age at which most typically developing children begin showing gendered behaviours and interests. The diagnosis of GD involves at least six of the criteria and an associated significant distress or impairment in function, lasting at least 6 months (box 2).

RANGE OF GENDER VARIANT PRESENTATION TO THE GIDS
Young people referred to the GIDS are a heterogeneous group and may identify in various ways. Most young people coming to gender services report feeling more in line with the opposite gender than that in which they were registered at birth (box 3). This may be accompanied by feelings of distress, particularly around the body which does not fit with the experienced gender identity. Young people who do not identify within the two-binary model of gender, but rather hold a gender identity other than male or female, are referred to as non-binary. Around 11% of the referred adolescents report a non-binary identity and often use labels such as ‘gender neutral’ or ‘gender fluid’ (Twist and De Graaf, submitted, 2017). Some young people

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Figure 1 Referrals to the Gender Identity Development Service by birth-registered gender, April 2011–April 2017.
Leading article

Criteria for the diagnosis of gender dysphoria in adults

- A marked incongruence between one’s experienced/expressed gender and primary and/or secondary sex characteristics.
- A strong desire to be rid of one’s primary and/or secondary sex characteristics.
- A strong desire for the primary and/or secondary sex characteristics of the other gender.
- A strong desire to be of the other gender.
- A strong desire to be treated as the other gender.
- A strong conviction that one has the typical feelings and reactions of the other gender.

Criteria for the diagnosis of gender dysphoria in children and adolescents

- A strong desire to be of the other gender or an insistence that one is the other gender.
- A strong preference for wearing clothes typical of the opposite gender.
- A strong preference for cross-gender roles in make-believe play or fantasy play.
- A strong preference for the toys, games or activities stereotypically used or engaged in by the other gender.
- A strong preference for playmates of the other gender.
- A strong rejection of toys, games and activities typical of one’s assigned gender.
- A strong dislike of one’s sexual anatomy.
- A strong desire for the physical sex characteristics that match one’s experienced gender.

Glossary of useful terminology

Gender identity
- Gender identity is the individual’s deeply held personal sense of their own gender as male or female, neither or both.

Gender dysphoria
- Gender dysphoria, as a general descriptive term, refers to an individual’s discontent with their ‘assigned’ gender and their identification with a gender other than that associated with their birth sex based on physical sex characteristics. ‘Dysphoria’ relates to the distress and unease experienced. The term is more specifically defined when used as a diagnosis (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition).

Transgender
- Transgender refers to the broad spectrum of individuals who identify with a gender other than that associated with their birth sex.

Gender variance and gender diversity
- Gender variance and gender diversity are umbrella terms used to describe the wide range of gender identifications outside conventional gender categories.

Non-binary
- Non-binary is a lack of identification with conventional maleness or femaleness. Non-binary people may express features of both genders or neither.

Transman/transboy
- A person born phenotypically female (natal female), registered (assigned) female at birth, who identifies as male. Also known as born female/male.

Transwoman/transgirl
- A person born phenotypically male (natal male), registered (assigned) male at birth, who identifies as female. Also known as male to female.

GnRH analogue
- GnRH analogue known colloquially as ‘the blocker’. A longer acting version of the naturally occurring gonadotropin-releasing hormones (GnRH) such as triptorelin (Gonapex Depot or Decapeptyl SR) used to prevent pituitary gonadotropin (follicle stimulating hormone FSH and luteinising hormone LH) secretion by competitive inhibition of the GnRH receptor.

Cross-sex hormones
- Cross-sex hormones (also known as gender-affirming hormones): physiological doses of testosterone in transboys and oestrogens in transgirls used to induce secondary sex changes associated with the gender of identification.

Box 3 Continued

are unsure about their gender identity and seek support from professionals to help them reflect and explore. Although gender-diverse young people tend to experience some psychological or social difficulties, gender diversity is not necessarily associated with distress.4

APPROPRIATE ASSESSMENTS PRIOR TO REFERRAL

The GIDS is an unusual multidisciplinary service in that the initial assessment phase...
A bone age is routinely requested in a young person who has not completed puberty as it may be helpful for height prediction. The effect on adult height of the manipulation of the adolescent growth spurt using GnRHa and the induction of a second puberty with exogenous cross-sex hormones is not yet fully elucidated.

Bone densitometry is performed at the initial assessment and then annually until more information is known. The longer term effect of ablating sex hormone secretion is still under review, and preliminary reports from the Netherlands suggest that bone mineral content lost during treatment may not be fully recovered, although this may be dependent on the age at start of treatment. The longer term health consequences are unclear.

**Endocrine assessments**

Endocrine assessment of the reproductive axis of the birth-registered phenotypic male does not usually demonstrate any anomalies, sex hormone and gonadotropin concentrations merely reflecting the stage of puberty attained. A low testosterone concentration may result from self-medication with antiandrogens such as spironolactone to alleviate the distress of progressive virilisation. Exogenously administered oestrogen may be detectable as an abnormal oestra diol:testosterone ratio in the serum, and on examination breast development may be present and the testes may be smaller than expected for the pubertal stage.

**Table 1** Karyotypes performed in young people attending GIDS England and Wales, and from Scotland and Northern Ireland (2009–2015), and frequencies of aneuploidy

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>GIDS: 1 in 446</th>
<th>Population: 1 in 426–523</th>
</tr>
</thead>
<tbody>
<tr>
<td>46,XX</td>
<td>269</td>
<td></td>
</tr>
<tr>
<td>46,XY</td>
<td>177</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>446</strong></td>
<td></td>
</tr>
<tr>
<td>New sex chromosome</td>
<td></td>
<td></td>
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<tr>
<td>aneuploidies</td>
<td></td>
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<tr>
<td>47,XXY</td>
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<tr>
<td>GIDS: 1 in 446</td>
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<tr>
<td>Population: 1 in 426–523</td>
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<tr>
<td>New autosomal</td>
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<td>aneuploidies</td>
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<tr>
<td>46XX, t(7;13) (p21;q31)mos</td>
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<tr>
<td>GIDS: 1 in 223</td>
<td></td>
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<td>Population: 1 in 138–164</td>
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</tbody>
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GIDS, Gender Identity Development Service.

**Radiological assessments**

Other diagnostic procedures employed in DSD evaluations were also routine in the GD clinic until recently. Transabdominal pelvic ultrasound scans were carried out in all phenotypic females, but between 2009 and 2013 only one congenital anomaly was found. Polycystic or multicystic ovaries were commonly seen, not necessarily associated with clinical or biochemical hyperandrogenism. Pelvic ultrasonography is therefore not required.

**Pubertal status**

It is a requirement, according to the Endocrine Society and WPATH guidelines and UK service specifications, that a young person has commenced puberty before any intervention is agreed, as the GD may resolve once puberty commences.

Figure 2 demonstrates the low absolute numbers and proportion of prepubertal children with persistent GD. Hence a clinical examination for pubertal staging is required unless confirmed as in the completed phase (eg, postmenarche from history). The majority of referrals to the GIDS and when referred on to the joint endocrine clinics in Leeds and London are postpubertal, two-thirds being over 15 years of age.

**Karyotype**

Initially the approach with GD was similar to that for disorder of sex development, with a karyotype being routinely requested. An audit of UK clinics from 2013 to 2015 (Table 1) revealed no differences from cytogenetic surveys of the UK newborn population and elsewhere. Therefore, routine karyotyping of a child or adolescent with GD is not required unless any specific clinical features determine this to be necessary.

**Figure 2** Numbers of young people presenting to the Gender Identity Development Service (GIDS) between 2010 and 2013 by age at initial referral (blue bars) and the proportion who had been referred on to the paediatric endocrinology clinics by 2017 (orange line).
A search for sources of hyperandro- 
genin in adolescent birth-registered 
phenotypic females in an attempt 
to explain the dysphoria has not elucidated 
any differences from a control population 
selected from females of similar ages 
within the same department undergoing 
evaluation of the reproductive and adrenal 
axes. Neither basal nor stimulated adrenal 
androgens or testosterone was different 
between the GD or control populations. 
It therefore appears that GD is not asso- 
ciated with excess androgen production 
in postpubertal phenotypic females. Use 
of contraceptive pill/oral contraceptives to 
halt menstruation will show the expected 
hormone suppression.

**Fertility preservation**

The initiation of GnRHa therapy halts 
gonadotropin and gonadal sex hormone 
secretion, but also suspends gonocyte 
maturati8on. Oocytes remain dormant and 
spermatogenesis is halted. Young people 
and their families are routinely counselled 
about fertility loss resulting from the phys- 
tical treatment. Various medical options 
are considered in case of a desire to 
revert to their birth gender in subsequent 
years after irreversible treatments have 
ocurred, or in case assisted conception 
techniques might be called on in adult life 
to assist with starting a family. A referral to 
specialist fertility services is always offered 
in addition.14 15

Phenotypic males are counselled about 
semen harvesting, which is possible once 
puberty is under way. By Tanner stage 
3 ejaculation can take place. Even if the 
sperm count is low at that stage, there 
may be sufficient for preservation for 
future assisted conception. The dysphoria 
however may be too extreme to consider 
semen collection by masturbation. Elec- 
troejaculation may then be helpful.

The situation is more complex in pheno- 
typic females. Prior to menarche, ovarian 
bioay is possible but not routinely avail- 
able at present. Mature oocyte harvesting 
prior to menarche requires the maturity to 
engage with gonadotropin pretreatment and 
transvaginal extraction. The access to 
reproductive services for transgender 
genders is very patchy at present, and 
regional National Health Service (NHS) 
funding is not always available.

Some young people, whose primary 
objective is to halt the pubertal progress, 
will choose to postpone the fertility pres- 
ervation decision until older. If they want 
to preserve fertility after having started 
GnRHa, it may take 6 months or more 
for the reproductive axis to recover, and 

### Box 4 Useful first-line 
investigations in a child or 
adolescent presenting with gender 
dysphoria

- Full blood count.
- Iron/ferritin.
- U&E, LFT, Renal and liver function tests
- Bone profile.
- Vitamin D.
- Testosterone.
- Oestradiol.
- Follicle stimulating hormone FSH and 
  luteinising hormone LH.
- Prolactin.
- Bone age in premenarchal female to 
  male or prepuberty/infancy male to 
  female.
- Bone density scan.

the reproductive capacity will only be the 
same as at the point of starting blocker 
treatment. The need to stop the GnRHa 
in itself may be a barrier to pursuing 
gamete harvesting for some young people 
as endogenous sex hormone effects will 
return, although temporarily.

### Recommended approach to initial 
investigations and monitoring of 
treatments

Investigations are purely required to 
evaluate adolescent health status and to 
measure baseline spontaneous gonado- 
tropin and sex hormone production, as our 
search for genetic, endocrine and radio- 
logical diagnostic markers of a dysphoria-
related state has proven negative. As 
reduction of sex hormone production in 
mid-adolescence to late adolescence may 
well have effects on reducing energy and 
psychological well-being, parameters such 
as full blood count, iron, vitamin D and 
thyroid status are important to ascer- 
tain (box 4). Bone mineralisation may be 
reduced on account of the GnRHa inter- 
tervention; thus, bone density evaluation is 
currently recommended. Furthermore, 
since the effect of the blockade of sex 
hormones on the intensity, duration and 
outcome of the adolescent developmental 
process is still largely unknown, height, 
weight and body proportion estimation 
should be measured with regular bone age 
estimations.

### PRIMARY INTERVENTION: GnRHa

In those whose GD is clearly established 
and long-standing and who have partici- 
pated fully in the multidisciplinary 
assessment process at the GIDS, GnRHa 
is the recommended first-stage medical 
treatment. This provides a physically 
reversible option to suspend sex hormone 
production, reduce the anxiety of ongoing 
physical development and allow further 
space for psychotherapeutic intervention 
and exploration.

This treatment is also requested in early 
pubertal children as a way to prevent the 
development of those unwanted bodily 
characteristics that may make ‘passing’ in 
the preferred sex difficult in later life (deep 
voice, facial hair and changes, breasts and 
so on) should this be their wish, and to 
render unnecessary certain surgical inter-
ventions such as mastectomy.

For children under 16, parents have 
the responsibility to agree to support any 
treatment (or not), with the clinicians 
determining the child’s capacity to give 
consent, upholding the child’s best inter-
ests in line with the UK General Medical 
Council guidance.16 Young people over 
16 are deemed as having the capacity 
to give their own consent to treatment. 
For all young people there is a require-
ment that they are helped to develop an 
adequate understanding of what is to be 
offered—both its risks and benefits, and 
the alternatives to treatment. An age-re-
lated appreciation of the potential loss of 
biological fertility is also a prerequisite. 
In practice adolescents vary greatly in their 
level of maturity, and it is important, 
when clinicians have any concern about 
the capacity to consent, that the parent/ 
carer be fully engaged to participate in the 
decision. If the parents or carers object to 
treatment, this poses a complex ethical and 
social challenge.

According to the WPATH and the 
recently updated Endocrine Society 
guidelines, GnRHa may be offered once 
an adolescent has demonstrated the first 
signs of physical puberty (Tanner stage 
2 in either sex).4 13 This internationally 
endorsed approach stems from the fact 
that between 73% and 88% of children 
attending gender identity clinics who 
present prepubertally, whether they have 
socially transitioned or not, are likely 
not to continue with their intention of 
changing their gender once puberty has 
started.17 Some may ‘desist’ completely, 
with their initially perceived dysphoric 
feelings pointing towards developing 
homosexuality, while others may wish 
to pursue an expression of their gender 
identity which does not require medical 
treatment.

GnRHa is prescribed in standard doses 
for a minimum of a year before additional 
medical interventions can be considered. 
This is to allow further psychotherapeutic 
assessment to take place once the anxiety
and distress related to the progression in puberty and processes such as menstruation, erections and nocturnal emissions are reduced or stopped. All young people are counselled that GnRHa cannot be considered as a contraceptive, and that additional anticonceptive methods should be used.

**Psychological benefits of GnRHa treatment**

Puberty suspension with GnRHa constitutes a treatment in its own right, meaning that it is not indicated purely as a preliminary stage before the next stage of treatment towards gender reassignment, namely gender-affirming cross-sex hormones.9 18 This puts a responsibility on the parents/carers, as well as clinicians in multidisciplinary teams, to try and ensure that time and opportunity are made for thoughtful and well-informed considerations of future options.

Most young people welcome the ‘blocker’ intervention as helping them to feel more comfortable in their bodies while holding future gender options open. However, our psychometric data suggest that although it permits further time for exploration, the impact on reducing psychological difficulties is limited. Further research is needed to determine whether GnRHa treatment is beneficial for young people of all ages, or whether some age groups may benefit more from this particular treatment than others, perhaps younger rather than older adolescents?

**Eligibility for cross-sex hormone/gender-affirming hormone treatment**

Cross-sex hormone treatment, currently referred to as gender-affirming hormone treatment (namely the induction of the opposite-sex puberty using testosterone in a phenotypic female and oestradiol in a phenotypic male), may be considered once full commitment to the preferred gender has been confirmed, and further detailed psychological exploration of the gender identity has been conducted. At the GIDS there are psychosocial criteria that need to be met, including that the young person shows some evidence of presenting coherently in the gender role with which they identify and that mental health difficulties are not escalating. Smoking and vaping are actively discouraged.

The capacity to give informed consent is an absolute requirement prior to commencing sex hormone treatment, ideally with the support of the parents, although after 16 years of age the latter is not needed under the English, Welsh and Scottish law. It is acknowledged by the Endocrine Society that a young person under the age of 16 may not have sufficient psychological maturity to commit to such a lifelong and life-changing decision, and no evidence is available to understand the effects of giving gender-affirming hormone treatment before 16 years. A systematic review of the available evidence has been published recently by NHS England Clinical Commissioning Policy.19

**Regimens for gender-affirming sex hormone treatment**

Therapeutic regimens suggested for gender-affirming hormone treatment with testosterone or oestradiol reflect the process of the induction of puberty that is traditionally done in paediatric endocrine practice to ensure maximum benefit from the gradual introduction to sex hormones.5 20 The dose increase schedule is conducted more slowly in those who have never completed puberty in their birth sex to allow emotional and social maturation, as well as the completion of the adolescent growth spurt in height. Although physical changes are the goal from the young person’s perspective, a gain in confidence is the most important marker of the success of treatment. Alterations in mood, including the development of irritability and anxiety, are risks of this treatment and are dose-dependent. However, despite the development of mood variations and anxiety, very few young people request to stop treatment at this stage.21 Fifty-five per cent of those seen initially at the GIDS and over 90% of those attending endocrinology clinics request further support from adult gender identity clinics. GnRHa is continued during feminisation in transgirls as it is difficult to suppress spontaneous testosterone production fully with exogenous oestrogen. It is usual to continue this dual therapy until gonadectomy or an alternative long-term solution is decided on. In transboys, once testosterone concentrations are elevated into the adult male range, GnRHa can be stopped as the recurrence of menses then is unlikely.

**Further supportive treatments**

The GIDS is commissioned to look after young people up to the age of 18 years, after which referral may be offered by one of the currently nationally commissioned UK adult gender identity clinics. There, after further assessment, the treatment schedule will usually be reauthorised and the young person may at their own request be referred for surgical interventions. This can include mastectomy, frequently requested by transboys, and gender affirmation surgery less often. Male-to-female feminising genitoplasty is a well-established procedure where the penoscrotal skin is refashioned to produce the vagina and labia with preservation of the clitoris capable of orgasm. Concern now exists that the early blockade of puberty may result in insufficient genital skin being available for this procedure.

Female-to-male surgery is more complex. Options include metoidioplasty, where the testosterone-enhanced clitoris is tubularised and a scrotum is constructed from the labia. In full male genital reconstruction, a penis can be formed from either abdominal, thigh or forearm skin flaps. A hydraulic implant is inserted in a newly fashioned scrotum to provide controllable erectile function. This approach requires several surgical procedures and leaves extensive scarring.

**Long-term outcomes of GD management**

In the UK, as yet there is little evidence of the longitudinal outcome from the GIDS. One published study showed that psychological support and puberty suppression were both associated with an improved global psychosocial functioning in adolescents with GD.22 One clear difficulty in tracking people is the frequent change in nominal and legal identity, including NHS number in those referred on to adult services and thus to date they have not been able to be followed up. The few longitudinal follow-up studies that have been published in the Netherlands have generally shown a high satisfaction outcome, particularly from those who have gone through surgical affirmation of their identified gender.23 24 These reported outcomes however are only from a highly selected group of fully dysphoric, well-adjusted individuals with few comorbidities and may not represent the full spectrum of gender diversity. Much further work needs to be done in this area.

**Alternative treatments which can be offered to a gender variant or non-binary gender-identifying person**

GD has typically been associated with a full identification with the opposite gender, and until recently a full social and legal transition was a requirement before receiving gender-affirming hormones. However, a significant number of young people are unsure of their eventual gender status or may retain feelings related to
their birth sex/gender as well as to their preferred gender, that is, a mixture of both. Non-binary gender identification is now increasingly encountered in clinical settings.

In some situations, simple management of the anxiety generated by birth-sex features in transboys such as menstruation with commonly used gynaecological treatments is a good solution. The combined contraceptive pill/oral contraceptive pills taken continuously with a break one to two times a year for a menstrual bleed, or a continuous progestogen such as norethisterone, may be prescribed. Depot progesterone implants, either subcutaneously or intrauterine, have variable success in halting menstruation. In young transgirls, alternative antiandrogen therapies such as spironolactone or cyproterone acetate are not recommended due to the high incidence of side effects and low efficacy, but topical treatments such as eflohithione cream (Vaniqa) may help to reduce unwanted facial and body hair growth.

CONCLUSION
The UK, along with other developed countries, is seeing an increase in the number of young people who are questioning their gender and taking the decision to pursue social and medical transition in line with their identified gender which may be non-binary. While professionals need to treat young people with respect and to acknowledge the intensity of their gender identification, much is still to be ascertained about the impact of medical intervention. The best practice in this field currently involves close collaborative working in multidisciplinary teams.

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Contributors GB conceived the idea, analysed the biological data and wrote the paediatric medical sections. NDG analysed the demographic and psychological data and cowrote those sections with BW. PC has had significant input to the final document.

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