Care pathways of children and adolescents referred to specialist gender services: a systematic review

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ABSTRACT

Background Increasing numbers of children and adolescents experiencing gender dysphoria/incongruence are being referred to specialist gender services. However, little is currently known about the proportions accessing different types of care and treatment following referral.

Aim This systematic review examines the range of care pathways of children/adolescents (under 18) referred to specialist gender or endocrinology services.

Methods Database searches were performed (April 2022), with results assessed independently by two reviewers. Peer-reviewed articles providing data for numbers of children and/or adolescents at referral/assessment and their treatment pathways were included. A narrative approach to synthesis was used and where appropriate proportions were combined in a random-effects meta-analysis.

Results 23 studies across nine countries were included, representing 6133 children and/or adolescents with a median age at assessment of 14–16 and overall a higher percentage of birth-registered females. Of those assessed, 36% (95% CI 27% to 45%) received puberty suppression, 51% (95% CI 40% to 62%) received masculinising or feminising hormones, 68% (95% CI 57% to 77%) received puberty suppression and/or hormones and 16% (95% CI 10% to 24%) received surgery. No study systematically reported information about the full pathway or psychological care received by children/adolescents. Follow-up in many studies was insufficient or unclear. Reasons for discontinuation were rarely provided.

Conclusions Prospective studies with long-term follow-up reporting information about the full range of pathways are needed to understand what happens to children and adolescents referred to specialist gender services. Information about provision of psychological care is needed considering high rates of psychosocial difficulties in this population.

PROSPERO registration number CRD42021289659.

WHAT IS ALREADY KNOWN?

⇒ Increasing numbers of children and adolescents experiencing gender dysphoria/incongruence are being referred for care at specialist paediatric gender services.

⇒ Several countries have or are modifying referral and care pathways and provision in response to increasing numbers of referrals, changing demographics and ongoing uncertainty about the benefits, risks and long-term effects of medical interventions for these children and adolescents.

⇒ Little is currently known about the trajectories and outcomes of children and adolescents referred to specialist gender services.

WHAT THIS STUDY ADDS?

⇒ Approximately two-thirds of adolescents referred to specialist gender services receive puberty suppression or hormones, although the rates vary considerably across services.

⇒ There is very little information about children/adolescents who do not receive medical intervention, or about the psychological care received by those under the care of a specialist gender service.

⇒ Studies consistently report small proportions of adolescents who discontinue medical treatment; however, systematic reporting and reasons for discontinuation are rarely provided and follow-up periods are limited.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Prospective studies that follow up children into adulthood and report information about the range of pathways followed are needed to understand longer-term outcomes for those referred to specialist paediatric gender services.

INTRODUCTION

Over the last 10-15 years, increasing numbers of children and adolescents experiencing gender incongruence are being referred to specialist paediatric gender services.1 2 Literature also highlights changes in the care pathways for those presenting with different needs,3 4 provision of psychological care by local mental health services 11 12 and expanding provision.13 14 Uncertainties in the evidence base about the benefits, risks and long-term effects of care pathways and medical interventions for this population are also driving these changes.15-23

the relationship between gender dysphoria and these co-occurring conditions is poorly understood.4-9

Specialist gender services are evolving to the changing demand for gender-related care by establishing new triage processes,10 developing multiple care pathways for those presenting with different needs,11 provision of psychological care by local mental health services11 12 and expanding provision.13 14 Uncertainties in the evidence base about the benefits, risks and long-term effects of care pathways and medical interventions for this population are also driving these changes.15-23
National and international guidelines have recently been developed or updated in response to these uncertainties and/or the changing demand for specialist care.\textsuperscript{11, 12, 24, 25} Historically, a staged pathway was outlined first involving a comprehensive gender-related and psychosocial assessment and psychoeducational support, along with provision of psychological interventions to address any co-occurring or contributory psychosocial difficulties identified.\textsuperscript{26} For adolescents experiencing gender dysphoria/incongruence that intensified during early puberty and who met the criteria for a diagnosis of gender dysphoria, puberty suppression could be considered. In later adolescence, masculinising or feminising hormones were considered for those continuing to medically transition, with surgical interventions delayed until adulthood. While this approach still broadly underpins current guidelines,\textsuperscript{11, 12, 24, 25} there is a lack of consensus regarding access to medical interventions, with the latest World Professional Association for Transgender Health guideline containing no minimum age criteria or requirement for diagnosis of gender dysphoria,\textsuperscript{26} while in contrast the latest Swedish guideline outlines much stricter eligibility criteria and recommends that medical interventions are provided under a research framework due to uncertainties in the evidence base.\textsuperscript{12}

Although a common care pathway is described by guidelines, little is known about the trajectories and outcomes for children or adolescents referred to specialist gender services. It is not known how many of those referred complete an assessment and access interventions, or how many leave services or discontinue treatment or subsequently ‘desist’ (no longer continue to experience gender dysphoria or incongruence), or how many who have started to medically transition will ‘de/re-transition’ (revert to living as their birth-registered sex or develop a new gender identity). This review aims to synthesise research reporting the care pathways for children and/or adolescents referred to specialist paediatric gender or endocrinology services, reporting the following:

- Number referred, assessed, diagnosed with gender dysphoria/incongruence, considered eligible for medical intervention and subsequently receiving medical intervention.
- Number who later desist or detransition/retransition.
- Reasons why they leave the service pathway or cease the assessment and/or medical intervention.
- Provision of psychological care while under the care of a specialist gender service.

**METHODS**

The review forms part of a linked series of systematic reviews examining the epidemiology, care pathways, outcomes and experiences of children and adolescents experiencing gender dysphoria/incongruence and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.\textsuperscript{28} The protocol was registered on PROSPERO (CRD42021289659).\textsuperscript{29}

**Search strategy**

A single search strategy was used comprising two combined concepts: ‘children’, which included all terms for children and adolescents; and ‘gender dysphoria’, which included associated terms such as gender incongruence and gender-related distress, and gender identity terms including transgender, gender diverse and non-binary. MEDLINE (online supplemental table S1), EMBASE and PsycINFO through OVID, CINAHL Complete through EBSCO, and Web of Science (Social Science Citation Index) were searched (13-23 May 2021, updated 27 April 2022).

**Inclusion criteria**

Peer-reviewed articles that reported, at a minimum, the number of children and/or adolescents at referral/assessment and the number progressing to treatment in paediatric or adolescent gender/endocrinology services were included (table 1).

**Selection process**

Search results were uploaded to Covidence\textsuperscript{30} and screened independently by two reviewers. Full texts for potentially relevant articles were retrieved and reviewed against the inclusion criteria by two reviewers independently. Disagreements were resolved through discussion.

**Data extraction**

Data were extracted into a pre-piloted template by one reviewer and checked by another. Data were extracted from graphs using the PlotDigitizer tool (https://plotdigitizer.com/). Study quality was not formally assessed.

**Synthesis**

A narrative approach to synthesis was used and where appropriate proportions were combined in a random-effects meta-analysis using metaprop (Stata V18), with variances stabilised using the Freeman-Tukey double arcsine transformation.\textsuperscript{31} The synthesis was performed by one reviewer and double-checked by another.

**RESULTS**

Our searches yielded 28 147 records, 3181 of which were identified as potentially relevant for the linked series of systematic reviews.
reviews and for which full texts were reviewed. From these, there were 24 papers including 23 studies that met the inclusion criteria for this review (figure 1, online supplemental table S2).

Study characteristics
Studies included specialist gender services (n=14)32–46 or endocrinology services (n=9)37–53 in Australia (n=2),32 33  Canada (n=3),34 47 48  the Netherlands (n=4),36–39 50  Spain (n=2),40 41  and the US (n=8),43–46 52–55 and single studies from Finland,49  Israel,35  Scotland51 and the UK.42  Eight studies commented on the length of follow-up, but not at standardised points and so this varied for each person.34–39 41 42 51  The longest time from assessment to follow-up was 10 years, but this study also included some patients who had only recently been assessed and so they had limited follow-up within the same study.44  Most studies reporting follow-up times had a median of 1–2 years of follow-up.35 41 42 51  Studies included referrals/assessments from 1972 to 2019, although most were from 2000 onwards. Overall, 6133 children/adolescents were included across studies, with samples ranging from 38 to 1360. Nine studies included referred adolescents only,34 37–39 42 51 whereas others included all referrals. Two US45 46 and three Dutch37–39 50 studies likely included overlapping samples. The median age at referral was 14–15 and at assessment was 14–16. Most studies reported a higher percentage of birth-registered females compared with males (online supplemental table S2).

Referral, assessment, diagnostic and treatment pathways
Ten studies reported the numbers referred, whereas all reported the numbers assessed within services (table 2). The numbers being assessed ranged from 46% to 100% of those referred. Seven studies reported both the numbers assessed and receiving a diagnosis of gender dysphoria/incongruence.32 33 36 41 42 50 53 The numbers receiving a diagnosis ranged from 44% to 100% of those assessed. Less than half of the studies (n=11) reported the reasons why individuals either discontinued during the assessment process or did not receive a diagnosis, with studies that reported these often not distinguishing between these two outcomes. Reasons included the following: being referred for other reasons than gender dysphoria/incongruence, experiencing resolution of gender dysphoria or acceptance of gender incongruence with ongoing counselling, no longer seeking medical treatment, not attending clinic after the first visit, coexisting problems interfering with the diagnostic process and/or might interfere with successful treatment, confusion about their gender identity and sexual orientation, being referred to mental health professionals, and being prepubertal and continuing with psychological counselling.

Five studies reported the numbers considered eligible or referred for further treatment out of the children/adolescents receiving a diagnosis of gender dysphoria/incongruence.32 33 36 42 50  This varied between studies, ranging from 60% to 100% of those diagnosed and considered eligible for further treatment. Eighteen studies reported the total number of adolescents who started either puberty suppression and/or masculinising or feminising hormone interventions (referred to hereon as hormones). Of the 4797 assessed in these 18 studies, 68% (95% CI 57% to 77%) received either puberty suppression and/or hormones; however, the proportions varied considerably between services (from 21%32  to 100%49) and there were differences between gender (60%; 95% CI 50% to 69%) and endocrine (83%; 95% CI 68% to 94%) services. Receipt of psychological treatment was unclear in most studies, and where it was reported the details of what this included and who received it were absent (online supplemental table S2).
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MFH, masculinising or feminising hormone interventions; PS, puberty suppression.
Interventions to suppress puberty

Twenty-one studies reported the numbers receiving hormones from 13 specialist paediatric and 8 endocrinology services. Of the referred population, the pooled estimate was 36% (95% CI 23% to 51%, n=1677, 8 studies), with similar figures reported when focusing on those completing an assessment (36%; 95%CI 27% to 45%, n=4338, 21 studies) or diagnosed with gender dysphoria/incongruence (43%; 95%CI 15% to 74%, n=938, 6 studies). Higher percentages were reported from those considered eligible for medical intervention (75%; 95%CI 49% to 94%, n=1029, 9 studies).

The age at which children/adolescents received puberty suppression was between 9 and 18 years, with an average of 15. Three studies reported age by birth-registered sex, but inconsistent results were found. Most studies did not report the reasons why individuals did not receive puberty suppression. Where the reasons were stated, they included needing more time, co-occurring psychiatric problems and/or psychological difficulties, lost to follow-up, and financial considerations, including not receiving coverage from insurance.

Seven studies reported the number of discontinuations and three reported the reasons why. Discontinuation with puberty suppression ranged from no patients to 8%. Reasons for discontinuation included emotional distress, decided on gender, reidentifying or happy being birth-registered gender, side effects, not complying with treatment protocol and difficulties attending clinic/pharmacy for injection/medication. One study reported that six (8%) young people discontinued gonadotropin-releasing hormone analogues (GnRH-a) for puberty suppression following a median duration of 6 months (range 6-18 months). Compared with those who continued with treatment, young people who discontinued had initiated treatment at an older age and included a higher proportion of those with mental health conditions and autism spectrum condition.

Masculinising and feminising hormone interventions

Nineteen studies reported the numbers receiving hormones from 11 specialist paediatric and 8 endocrinology services. Of the referred population, the pooled estimate was 43% (95% CI 19% to 69%, n=1076, 6 studies), with slightly higher figures reported when focusing on those completing an assessment (51%; 95%CI 40% to 62%, n=4028, 19 studies) or diagnosed with gender dysphoria/incongruence (52%; 95%CI 17% to 86%, n=737, 5 studies). Higher percentages were reported from those considered eligible for medical intervention (65%; 95%CI 36% to 89%, n=837, 7 studies). Few studies provided a breakdown of those who progressed to hormones following puberty suppression and those who started hormones as their first medical intervention.

The age at which adolescents received hormones was between 13 and 19 years, with an average age of 17. Three studies reported age by birth-registered sex, but inconsistent results were found. Most studies did not report the reasons why eligible individuals did not receive hormones. Where reasons were stated, they included being close to 18 when court approval is not required within the specific country, family not supporting treatment, financial considerations including not receiving coverage from insurance, delaying interventions for fertility preservation or other reasons, not wishing to receive hormone treatment, and needle phobia.

Six studies reported whether hormones were continued or discontinued, all reporting either no discontinuations or one or two individuals discontinuing. Four of these reported the reasons or context. In one study, a single person stopped treatment after 4 months as their gender dysphoria had resolved. In another, two discontinued, with one reverting to living as their birth-registered sex and the second continuing to take GnRH-a while exploring an emerging gender identity. In the third study, two birth-registered males who had been taking GnRH-a and low-dose oestrogen for 3 months decided not to transition. In the final study, three birth-registered females stopped treatment temporarily (two due to psychiatric difficulties and one due to distress over androgenic alopecia) but reported later resuming.

Surgical interventions

Nine studies reported the numbers receiving surgical interventions from the referred/assessed populations of eight specialist paediatric and one endocrinology service. A Dutch study reported that of those treated with hormones for at least 1.5 years and were at least 18 years old, 78.2% received surgery (actual numbers were not reported). For the remaining eight studies, the pooled estimates for those adolescents receiving surgical interventions varied from 16% to 34% across the different stages; referred 24% (95% CI 17% to 31%, n=719, 3 studies), assessed 16% (95% CI 10% to 24%, n=1488, 8 studies) and eligible for medical intervention 34% (95% CI 28% to 40%, n=236, 2 studies). Six studies reported the types of surgery received and included chest, facial feminisation and genital surgery.

Three studies commented on the age at the time of surgery. A US study reported that 57 (of 89) had surgery before they were age 18. An Israeli study reported that the median age of 15 birth-registered females who had mastectomy was 17.6 (range 15–19). In the same study, two birth-registered males had breast augmentation and two had vaginoplasty at age 18. Finally, in a Canadian study, nine people had mastectomy at a median age of 18.1 (range 15–22), six had hysterectomy and salpingooophorectomy at a median age of 18.9 (range 17–22), and two had penectomy, orchidectomy and vaginoplasty at 18 and 21 years of age.

DISCUSSION

This review of 23 studies from nine countries found that children and adolescents referred to or assessed in specialist paediatric gender and endocrinology services leave the care pathway at all stages following referral for multiple reasons. However, the numbers leaving at each possible stage of care were rarely reported, and follow-up in many studies was insufficient or unclear and in others varied considerably, with some participants followed up for several years while others had only just completed assessment, meaning their subsequent care trajectories were not reported. Few studies provided information about adolescents who completed assessment but did not subsequently receive medical intervention, estimated to be around a third of those entering assessment with differences between gender and endocrine services. No study provided clear information about psychological care received by children/adolescents under the care of gender services.

There is mixed and partial evidence about the numbers of children completing an assessment or receiving a diagnosis of gender dysphoria or incongruence. Most studies did not report the numbers referred, instead starting with the numbers assessed. Given increasing referral numbers and waiting times, a better understanding of the needs of all children/adolescents referred would provide needed insights into service provision.
Studies published more recently have systematically examined data on assessment and treatment pathways for national services in the Netherlands and the UK. However, only one reported data on those not completing assessment, which was presented for different time periods and age at first visit (range 6%–38%). Of 1401 adolescents who were eligible for puberty suppression, 882 (63%) received this, with higher rates in birth-registered females compared with males (7.3% vs 47%). Of 707 adolescents who received GnRH-a and were eligible for hormones during follow-up, 93% progressed. Only three adolescents received hormones without first receiving GnRH-a. A second Dutch study reported a similarly high progression from GnRH-a to hormones (98%).

The recent UK studies report data for a subset of adolescents who had been under the care of a national paediatric gender service and were subsequently referred onto the endocrine pathway within the service. Of 439 adolescents referred with a view to start medical intervention, 431 (98%) commenced GnRH-a and 8 (2%) commenced hormones only. At follow-up of 2–3 years, 183 (42%) had progressed to hormones after receiving GnRH-a. In this review, an average of 36% and 51% of those assessed received puberty suppression and hormones, respectively, which differ from the more recent UK and Dutch studies. Having said that, the pooled estimate presented here for those receiving either treatment was 69%, which was similar to the proportion starting GnRH-a in the Netherlands, with study authors concluding that GnRH-a may be used as the start of transition rather than being seen as an extension of the diagnostic phase. Overall, there was considerable variation between services, which likely reflects country differences in intervention criteria, regulations, insurance coverage and clinical practice, as well as whether services focus on medical interventions or provide care to children and adolescents across the care pathway.

In both the UK and the Netherlands, a similar approach is followed, with most adolescents first receiving puberty suppression before progressing to masculinising/feminising hormones. However, a recent study of 434 adolescents who had at least two encounters for gender-related care in the US Military Healthcare System found no association between GnRH-a use and subsequent hormone initiation, with 16.1% prescribed GnRH-a and 46.4% prescribed hormones within 1 year of the initial encounter and 88.3% within 4 years. Few of the reviewed studies provided clarity about which adolescents who received hormones had first received puberty suppression, although many reported a higher proportion of adolescents receiving hormones than those receiving puberty suppression. In wider research, little is known about any difference in outcomes for adolescents who start hormones with or without first receiving puberty suppression.

Discontinuation of medical treatments was similar across reviewed studies. In the seven studies reporting data for puberty suppression, discontinuation ranged from no patients to 8%. In the recent Dutch study, five (0.8%) birth-registered females and nine (3.4%) birth-registered males discontinued treatment during follow-up, and in the UK 30 (7%) adolescents consenting to GnRH-a did not start or discontinued treatment. For masculinising/feminising hormones, six studies reported discontinuation, with very low rates (0–2 individuals) reported. High rates of continuation were also reported in the recent Dutch study, with 98% still prescribed them at follow-up (average 3.2 years for birth-registered females, 6.1 years for birth-registered males), and the UK study which found no discontinuation at 2–3 years of follow-up. A second UK study which reported discharge outcomes (length of follow-up unclear) found that of 1089 adolescents referred to the endocrine pathway, 90 (8.3%) stopped identifying as gender incongruent, 58 (5.3%) of whom had started puberty suppression or hormones and subsequently stopped these and reverted to their birth-registered sex. The lack of reporting on reasons for discontinuation makes drawing conclusions problematic. Longer-term follow-up into adulthood is necessary to understand trajectories more comprehensively. Detransitioning has been reported to occur on average around 3.9 years later, with expressions of regret reported as ranging between 3.8 and 22 years after transition.

There was variation in the percentages of referred, assessed and eligible for medical intervention populations receiving surgical interventions (16%–34%). However, the numbers receiving surgery were only at the observation point, which was often unclear and/or relatively short, and therefore unlikely to include surgery received later in adulthood, which is often when it occurs. A Spanish study reported the numbers receiving and waiting for surgery (36 received surgery and 46 were awaiting surgery), which combined would lead to a much higher proportion of adolescents going on to receive surgery. Numbers receiving surgery are also likely to differ by country due to different regulations, insurance coverage, service provision and the clinical guideline informing practice. A key difference is whether adolescents under the age of 18 are considered for surgery. However, only three of the nine studies reporting on surgery provide this detail. These studies suggest surgery is relatively common among adolescents under the age of 18. However, in the recently published Dutch study, surgery is only provided to young people aged 18 or over. Longer-term follow-up is therefore required to gain a fuller picture about the proportion of children/adolescents who go on to request and receive surgery to modify their bodies.

Like the studies reviewed here, these more recent studies do not report systematic information about any psychological care provision. In some countries, there is now an expectation that psychological care is provided by local mental health services, in part due to increasing demand for specialist gender services. At the same time, clinical guidelines recommend that psychological care for this population is provided by professionals with expertise in gender development and gender dysphoria/congruence. Currently, there is limited understanding about the provision of psychological care for children and adolescents experiencing gender dysphoria/congruence by specialist gender or local mental health services, or about professional competence in this area of practice. There is also little evidence about the effectiveness of psychosocial interventions for this population.

Strengths and limitations
Strengths include a published protocol with robust search strategies and comprehensive synthesis. As searches were conducted to April 2022 this review does not include more recently published studies; as this is a rapidly evolving area this is a limitation. Pooled estimates for each stage of the care pathway must be interpreted with caution due to inadequate and/or unclear reporting of follow-up and studies not reporting data on the full care pathway, in particular not reporting the numbers referred. This review did not extract information about fertility care for adolescents, which was reported by few of the identified studies and has been examined in separate studies.
CONCLUSION

This review aids our understanding of the assessment and treatment trajectories of children and adolescents who are referred to specialist gender and endocrinology services, showing children/adolescents leave at different stages, suggesting there is not just one care pathway. However, prospective studies that follow up children into adulthood and report information about all possible trajectories and outcomes are needed. A better understanding is also needed about what care is provided to around a third of adolescents who undergo assessment within a gender service but do not go on to receive medical intervention. Information about provision of psychological care is needed, particularly considering the high prevalence of mental health and psychosocial difficulties in this population.

Contributors JT and CEH conducted the selection, extraction and synthesis, and drafted the manuscript. All authors contributed to the design of the review, assisted with interpretation of synthesis, and contributed to and reviewed the manuscript before submission. CEH accepts full responsibility for the finished work and the conduct of the study, had access to the data, and controlled the decision to publish.

Funding This work was funded by NHS England to inform the Cass Review (Independent review of gender identity services for children and young people). The funder and Cass Review team had a role in commissioning the research programme but no role in the study conduct, interpretation or conclusion.

Competing interests None declared.

Patent consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

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