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Ethical dilemmas and decision-making in the healthcare for transgender minors

Vrouenraets, L.J.J.J.

Citation

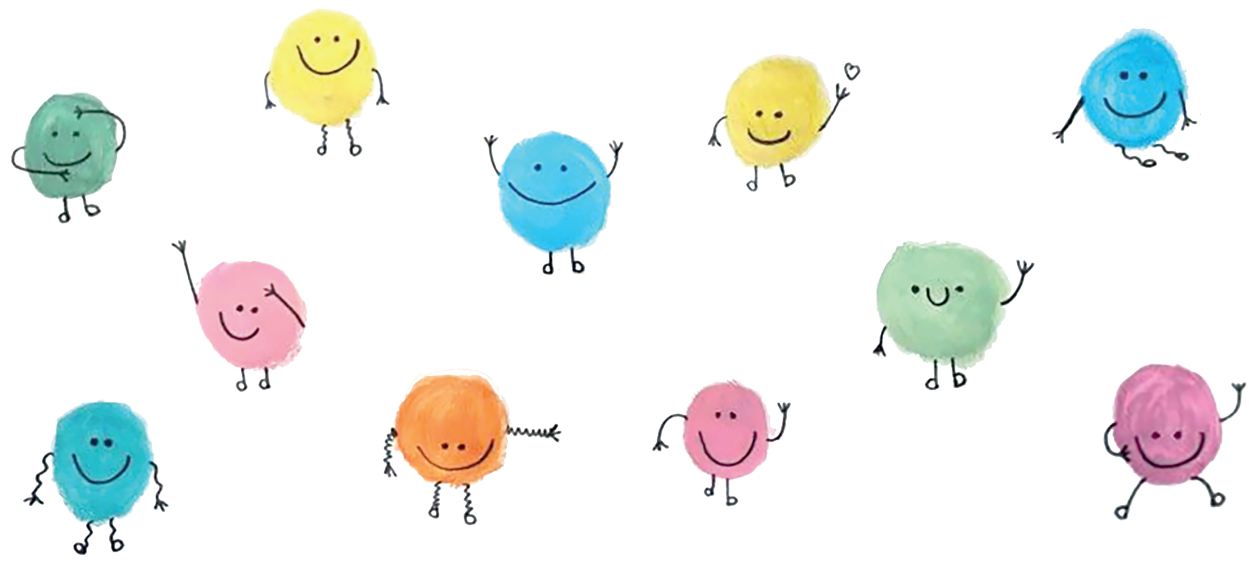
Vrouenraets, L. J. J. J. (2023, September 28). *Ethical dilemmas and decision-making in the healthcare for transgender minors*. Retrieved from <https://hdl.handle.net/1887/3642204>

Version: Publisher's Version

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Ethical dilemmas & decision-making in the healthcare for transgender minors



Lieke J.J.J. Vrouwenraets

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ISBN: 978-94-6419-895-9

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Cover design and lay-out: Douwe Oppewal, www.oppewal.nl

Printing: Gildeprint Enschede, www.gildeprint.nl

The research described in this thesis was supported by a grant from the 'Netherlands Organization for Health Research and Development' (ZonMW, projectnumber 731010002), 'Alliantie Fonds' of Amsterdam Public Health, and 'Fonds Wetenschappelijk Onderzoek Seksualiteit' (FWOS, projectnumber 18.008). Financial support for the costs associated with the publication of this thesis was provided by Sander van 't Noordende and Ferring B.V.

Ethical dilemmas & decision-making in the healthcare for transgender minors

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof. dr. ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op donderdag 28 september 2023
klokke 15.00 uur

door

Lieke Josephina Jeanne Johanna Vrouwenraets
geboren te Veldhoven
in 1989

Promotiecommissie

Promotor: Prof. dr. M.C. de Vries

Co-promotoren: Dr. A.L.C. de Vries (Amsterdam UMC, locatie VUmc)
Dr. I.M. Hein (Amsterdam UMC, locatie AMC en Levvel)

Overige leden: Prof. dr. R.R.J.M. Vermeiren
Prof. dr. G. Butler (University College Hospital London)
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- "Every revolution begins with a single act of defiance." -

Mahatma Gandhi

Voor mijn ouders

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INTRODUCTION

In the last decades, in various parts of the world, the number of children and adolescents referred to gender identity clinics has increased enormously, and minors with gender incongruent experiences have increasingly become a subject of discussion (e.g. Arnoldussen et al. 2020; Arnoldussen et al., 2022b; Kaltiala et al., 2020; Pang et al., 2020; Wiepjes et al., 2018). The question how to best organize care for these children and adolescents has become very prominent and subject of public debate (e.g. The Observer, 2022). Determining what constitutes the best care inescapably involves thinking about ethical issues and dilemmas. The research described in this thesis explores ethical issues and dilemmas surrounding early medical treatment for transgender minors. This first chapter is an introduction to the topic. It describes the clinical characteristics of gender dysphoria and its treatment options, mainly focusing on treatment that includes puberty suppression (PS). Furthermore, adolescents' medical decision-making competence (MDC) regarding starting PS, the role of media attention in referral rate and care of transgender children and adolescents, and legal and moral aspects are introduced. Finally, the overall aims and research questions of the thesis are described, and an outline of the other chapters is provided.

GENDER DYSPHORIA

Children and adolescents diagnosed with gender dysphoria experience an incongruence between their birth-assigned sex and their experienced gender, which is accompanied by distress (American Psychiatric Association, 2013). Table 1 shows the criteria for a diagnosis of gender dysphoria for children according to the 5th version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Table 2 shows the criteria for a diagnosis of gender dysphoria for adolescents and adults according to the DSM-5. Over the years and since the start of this research in 2013, terminology around gender identity related diagnoses has changed. The DSM-5 and the DSM-5-TR now use 'gender dysphoria', the 11th version of the International Statistical Classification of Diseases and Related Health Problems (ICD-11) uses 'gender incongruence', while prior to these terminologies, the term 'gender identity disorder' was used (American Psychiatric Association, 2013; American Psychiatric Association, 2022; World Health Organization, 2022). While preparing the revisions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Statistical Classification of Diseases and Related Health Problems (ICD), recommendations were made to replace 'gender identity disorder' by 'gender dysphoria', and 'transsexualism' by 'gender incongruence' respectively (Bedirhan Üstün, Jako, Çelik, Lewalle, & Kostanjsek, 2007; Cohen-Kettenis & Pfafflin, 2010; Drescher, Cohen-Kettenis, & Reed, 2016; Zachar, Regier, & Kendler, 2019). Reasons for these recommendations were that the condition can be

present to a lesser or greater extent, and that it may fluctuate over time. Furthermore, the authors aimed to make a move to depsychopathologization of the condition. They wanted the terminology to be non-stigmatizing and acceptable to those who fulfil the criteria (Cohen-Kettenis & Pfafflin, 2010; Rodríguez, Granda, & González, 2018). Whereas the DSM is a psychiatric classification system, in the ICD-11, the classification gender incongruence was moved from the chapter 'mental disorder' to a new chapter entitled 'conditions related to sexual health'. The reason for this was to avoid the mental health stigma of being diagnosed with a mental disorder (World Health Organization, 2022). Since the terms used to address this condition changed over time, and during the undertaking of this research, in this thesis several terms will be used alternating¹. In the general introduction, and in the general discussion the term 'transgender children/adolescents/individuals' is used as an umbrella term to refer to individuals who have gender incongruent experiences and/or present with questions about their gender identity, and to individuals diagnosed with gender dysphoria.

Until a couple of years ago, gender dysphoria was considered to occur rarely (Zucker & Lawrence, 2009). Over the past decades however, the number of minors seeking care regarding their gender incongruent experiences has increased tremendously throughout the Western world (Aitken et al., 2015; Chen, Fuqua, & Eugster, 2016; Pang et al., 2020; de Vries & Cohen-Kettenis, 2012; Wood et al., 2013; Handler et al., 2019). For example, by 2017, the annual number of referrals in Norway, the UK and Sweden had increased 12-, 14-, and 19-fold respectively compared to 2011 (Kaltiala et al., 2020). Finland is another example of a country with an immense increase of child and adolescent referrals. In Finland, the annual number of referrals in 2017 had increased six-fold compared to 2011, when the first two gender identity clinics for children and adolescents were introduced in this country (Kaltiala-Heino, Sumia, Työläjärvi, & Lindberg, 2015). Similarly, in the Netherlands, there was an immense increase in the number of adolescents assessed at gender identity clinics between 2000 and 2016 (Arnoldussen et al. 2020; Arnoldussen et al., 2022b).

1 Terms that will be used in the chapters 2 to 7 are 'transgender minors/children/adolescents/people/individuals', 'adolescents diagnosed with gender dysphoria', and 'identifying as transgender'. In some chapters terms are used that we would not use nowadays anymore; terms like 'gender dysphoric minors/adolescents/adults', and 'children/adolescents/individuals with gender dysphoria'. The reason for this is that, even though in many health care systems a diagnosis of gender dysphoria is used for giving access to state funded transgender health care, using these terms does reify the condition (Bouman et al., 2017). Furthermore, chapter 4 contains the following sentence: 'This article uses the term 'transgender adults/adolescents/children' to refer to persons diagnosed with gender dysphoria'. We would not use this sentence nowadays anymore, since the term 'transgender adults/adolescents/children' is used as an umbrella term, and may also be used for individuals who do not (yet) have a gender dysphoria diagnosis, but nevertheless have gender incongruent experiences and/or questions about their gender identity.

Table 1. Criteria for a diagnosis of gender dysphoria in children according to the DSM-5 *

Gender dysphoria in children is defined as a noticeable incongruence between one's experienced/expressed gender, and their birth-assigned gender. This incongruence should be lasting at least six months, as manifested by at least six of the following:

- An intense desire to be of the other gender, or an insistence that one is the other gender (or some alternative gender that is different from one's birth-assigned gender)
 - A strong preference for cross-dressing (wearing typical clothing from the gender opposite to the birth-assigned gender), and a strong resistance to wearing typical clothing from the birth-assigned gender
 - A strong preference cross-gender role in fantasy play or make-believe play
 - A strong preference to do activities, or play with toys and/or games that are stereotypically used or engaged in by the other gender
 - A strong preference for playmates of the other gender
 - A strong rejection of activities, tops, and activities that are stereotypically used or engaged in one's birth-assigned gender
 - A strong dislike of one's primary sex characteristics
 - An intense desire for the physical sex characteristics that match one's experienced gender
 - In order to meet the criteria for the diagnosis, the condition should also be associated with clinically significant distress, or it should significantly impair one's functioning socially, occupationally, and/or in other important areas of functioning
-

* American Psychiatric Association, 2013

Table 2. Criteria for a diagnosis of gender dysphoria in adolescents and adults according to the DSM-5 *

Gender dysphoria in adolescents and adults is defined as a noticeable incongruence between one's experienced/expressed gender, and their birth-assigned gender. This incongruence should be lasting at least six months, as manifested by at least two of the following:

- A noticeable incongruence between one's experienced/expressed gender, and one's primary and/or secondary sex characteristics (in young adolescents, the anticipated secondary sex characteristics)
 - An intense desire to get rid of one's primary and/or secondary sex characteristics because of the noticeable incongruence with one's experienced/expressed gender (in young adolescents, an intense desire to prevent the development of the anticipated secondary sex characteristics)
 - An intense desire to have the primary and/or secondary sex characteristics of the other gender
 - An intense desire to be of the other gender (or some alternative gender that is different from one's birth-assigned gender)
 - An intense desire for society to treat them as the other gender (or some alternative gender that is different from one's birth-assigned gender)
 - A strong conviction that one has the characteristic feelings and reactions of the other gender (or some alternative gender that is different from one's birth-assigned gender)
 - In order to meet the criteria for the diagnosis, the condition should also be associated with clinically significant distress, or significantly impair one's functioning socially, occupationally, and/or in other important areas of functioning
-

* American Psychiatric Association, 2013

TREATMENT FOR GENDER DYSPHORIA

Not only the acceptable terminology and the number of referrals changed over the years, also the recommendations regarding the (medical) treatment for these children and adolescents have been in motion. Three broad approaches regarding treatment for *pre-pubertal children* with gender incongruent experiences have been described in the

literature. A first approach in pre-pubertal children is described as the ‘therapeutic model’ (Dreger, 2009). This approach consists of direct or indirect efforts to reduce the child’s cross-gender identification. A second approach is described as the ‘affirmative model’ (Ehrensaft, 2012). This approach considers all outcomes of gender identity to be equally desirable and valid. Furthermore, it allows children who express the desire to socially transition² to do so after careful counselling. The third approach in pre-pubertal children is described by some as ‘watchful waiting’: parents are advised to keep options open about their child’s long-term gender identity and to avoid early social transition, without direct efforts to ‘prohibit’ the gender incongruent behaviour of their child (Drescher & Byne, 2012; Turban, de Vries, Zucker, & Shadianloo, 2018b). Treatment for pre-pubertal children regarding this approach is predominantly psychological, focusing on, if any, the child’s concomitant behavioural and emotional struggles and providing parent counselling (de Vries & Cohen-Kettenis, 2012). Of these three described approaches, ‘watchful waiting’ is the most commonly advised in the Netherlands in pre-pubertal children with gender incongruent experiences.

Not all pre-pubertal children with gender incongruent experiences, will be transgender adults. Of the pre-pubertal children referred to a gender identity clinic, only a minority (2-33%) return around or after the onset of puberty with the desire to undergo gender-affirming medical treatment (GAMT) (Ristori & Steensma, 2016). In contrast to these findings of clinical follow-up, a recent convenience sample of socially transitioned children showed very few retransitions after five years (Olson, Durwood, Horton, Gallagher, & Devor, 2022). In addition, not all (young) adults referred to a gender identity clinic with the desire to undergo GAMT, have had gender incongruent experiences as a child or have expressed a desire to be of a different gender as a child. Gender diversity thus may have several developmental paths (Bungener & de Vries, 2022).

When gender dysphoria continues to exist when physical changes of puberty start (Tanner stage 2-3), medical care (next to the psychological care) is possible. In the late 1990s treatment with PS (using gonadotropin-releasing hormone analogues (GnRHa)) was introduced by clinicians in the Netherlands (Cohen-Kettenis, Delemarre-van de Waal & Gooren, 2008). Two established international transgender guidelines now recommend this treatment for adolescents who meet the diagnostic criteria for gender dysphoria, and fulfil the criteria for treatment with PS after they first exhibit physical changes of puberty

2 Social transition is the process by which individuals start living according to the gender role that matches their gender identity, for example by adopting a name, pronouns, and gender expression, such as haircuts and clothing which matches their gender identity.

(at least Tanner stage 2) (Coleman et al., 2022; Hembree et al., 2017³). Any coexisting psychological, social, and/or medical problem that could interfere with the assessment or treatment should be addressed, with the underlying idea that the adolescent's functioning and situation are stable enough to assess gender dysphoria/gender incongruence and to undergo treatment. Additionally, the adolescent should have sufficient cognitive capacity to give informed consent to treatment, after being informed about the effects and possible side effects of PS. Depending on the legislation in the respective country, the legal representative(s), which are in most cases the parent(s), should give informed consent too, or on behalf of the adolescent. In addition, the parent(s) or other caretaker(s) is/are involved in the care provided to the transgender adolescent, and are offered support if desired (de Vries & Cohen-Kettenis, 2012). Table 3 shows the diagnostic criteria for treatment with PS for adolescents.

Table 3. Diagnostic criteria for treatment with puberty suppression for adolescents *

Adolescents are eligible for treatment with puberty suppression if:

- The adolescent has demonstrated an intense and long-lasting pattern of gender dysphoria or gender non-conformity (whether expressed or suppressed)
 - The gender dysphoria emerged or worsened with the onset of puberty
 - Any concurrent psychological, social, and/or medical issues that could interfere with the treatment (for example, that may compromise compliance with the treatment) have been addressed, such that the functioning and situation of the adolescent are stable enough to start the treatment
 - The adolescent is having sufficient mental capacity to give informed consent to the treatment
 - The adolescent and/or parent(s)/other caretaker(s) (depending on the adolescent's age and local laws) has/have given informed consent after being informed about the effects of the treatment and fertility preservation options
 - The parent(s)/other caretaker(s) is/are involved and supporting the adolescent throughout the treatment process
 - A paediatric endocrinologist or other clinician with experience in the assessment of puberty agrees with the indication of the clinician to start puberty suppressing treatment
 - The adolescent's puberty has started (Tanner stage \geq G2/B2)
 - The adolescent had no medical contraindications to treatment with puberty suppression
-

* Coleman et al., 2022; Hembree et al., 2017

In addition, the two established international transgender guidelines recommend the use of gender-affirming hormones (GAH; testosterone or oestrogen) after the start with treatment with PS for adolescents who still show gender dysphoria at about the age of 15-16. In the case of compelling reasons, treatment with GAH could be initiated for adolescents prior to the age of 16 years (Hembree et al., 2017). Surgery, for example

3 Very recently, Coleman et al., published a revised version of one of these guidelines, which resembles to a large extent the earlier version but also includes some significant changes regarding recommended care for transgender and gender non-conforming children and adolescents of which it is as yet not clear how they will affect clinical practice (2022). The research described in chapters 2 to 9 of this thesis is conducted at the time of the 7th version of the Standards of Care. Therefore, these chapters refer to the 7th version of these guidelines, while chapters 1 and 10 refer to the 8th version. Nevertheless, it is worth noting that the changes to the 8th version of the Standards of Care would not have changed the conclusions of the research described in chapters 2 to 9.

mastectomy, gonadectomy and/or hysterectomy, is recommended when the transgender individual and clinician(s) agree that this is medically necessary, and that it would be beneficial for the transgender individual's overall well-being and/or health (Hembree et al., 2017). The Endocrine Society clinical practice guideline and the 7th version of the Standards of Care recommend deferring surgery until the individual is at least 18 years old (Coleman et al., 2012; Hembree et al., 2017). Only with regard to mastectomy, the 7th version of the Standards of Care describes that it could be carried out before the age of 18 (Coleman et al., 2012). Therefore, the age requirement for mastectomy in some countries is below 18. For example, in the Netherlands, the minimum age has been lowered in recent years, and is now 16. The recently published 8th version of the Standards of Care does not describe any age limits for gender-affirming surgery (Coleman et al., 2022).

PUBERTY SUPPRESSION

The two established international transgender clinical guidelines outline several reasons for using PS in the early stages of puberty of transgender adolescents, which largely correspond to the reasons given in the late 1990s, when this treatment was first introduced in the Netherlands (Cohen-Kettenis et al., 2008; Coleman et al., 2022; Hembree et al., 2017). One of the reasons is that PS suppresses (further) development of secondary sex characteristics in a reversible manner (Hembree et al., 2017). It is therefore applied to extend the exploration and assessment phase. It provides the adolescents 'extra' time to make a balanced decision regarding subsequent GAMT by means of treatment with GAH, and possibly undergoing gender-affirming surgery, while creating peace of mind by relieving the adolescent's suffering caused by the development of secondary sex characteristics (Cohen-Kettenis & van Goozen, 1998). Another important reason to start PS in early puberty is that the physical outcome may be more satisfactory compared to no use or use of PS in later stages of puberty, because the masculinization or feminization of the body, which accompanies pubertal development, is suppressed (Cohen-Kettenis & van Goozen, 1997; Smith, van Goozen, Kuiper, & Cohen-Kettenis, 2005). Additionally, some surgeries such as mastectomy may not be necessary or less invasive (i.e. periareolar rather than inframammary approach) because development of secondary sex characteristics is prevented (van de Grift et al., 2020). Furthermore, PS can be used in adolescents in later stages of puberty to, among others, prevent facial hair growth in transgirls (assigned male at birth, with a female gender identity), and to stop menses in transboys (assigned female at birth, with a male gender identity) (Hembree et al., 2017). PS may therefore result in life-long advantages for adolescents (Cohen-Kettenis & van Goozen, 1997).

Little is known about how PS is perceived by the transgender adolescents themselves and their parents. More knowledge about the motivation of these stakeholders to apply for PS

will help to adequately support these adolescents in their decision-making process, and give them the information and care they need.

MEDICAL DECISION-MAKING COMPETENCE

A major issue in paediatric ethics in general is decision-making competence for medical treatments. The right balance needs to be struck between protecting minors who are not fully capable of making the decision themselves to start or refuse a medical treatment, and respecting minors' evolving autonomy (Appelbaum, 2007). According to the international transgender guidelines, an important prerequisite to start treatment with PS is that transgender adolescents are competent to give informed consent (Coleman et al., 2022; Hembree et al., 2017; see also table 3 which can be found at page 14). There is increasing public discussion whether adolescents are actually competent to make a decision regarding PS treatment, especially because the treatment has far-reaching long-term consequences (e.g. Baron & Dierckxsens, 2021; D'Abbrera, D'Angelo, Halasz, Prager, & Morris, 2020; Giordano, Garland, & Holm, 2021; Levine, 2022; Pang, Giordano, Sood, & Skinner, 2021; Siddique, 2021; Tampier, 2022). To date, little empirical research exists regarding minors' medical decision-making (MDC) competence to decide on starting PS in the transgender context. In addition, little is known about the perceptions of transgender adolescents, their parents, and clinicians on the minors' MDC to decide on starting PS. Research regarding these aspects is needed to underpin both the ethical debate and clinical practices.

MEDIA ATTENTION

In recent years, not only the number of referrals increased enormously in various parts of the world, there has also been an explosion of media attention regarding transgender children and adolescents worldwide. Actually, one of the suggested causes for the increased number of referrals, is the increased media attention regarding transgender children and adolescents (de Graaf & Carmichael, 2019). Newspapers, television programs, magazines, movies, and the internet pay increasing attention to transgender children and adolescents (Pang et al., 2020; Sadjadi, 2013; Zucker, Bradley, Owen-Anderson, Kibblewhite, & Cantor, 2008). Most portray these children and adolescents as fascinating and sometimes somehow strange, and simultaneously as ones to feel compassion for (Sadjadi, 2013). The media have an increasingly important influence on the development of adolescents' identity, especially in western communities (Alper, Katz, & Clark 2016; Henrich, Heine, & Norenzayan, 2010). One could therefore wonder if the increasing media attention has an influence on the number of children and adolescents referred to gender identity clinics. In addition, the question can be asked whether this influence is positive or negative.

One thing that can be said, is that the increase in media coverage has also led to heated discussions between people who criticize the use of early medical treatment, and the ones who support the use of it, and to polarization of the way we conceive transgender children and adolescents. Treatment strategies are no longer private conversations between minors, their parents, and their clinicians, but have become a public debate.

LEGAL ASPECTS

Besides media attention, case law also plays an increasing role in the care and rights of transgender individuals nowadays. In various countries, e.g. the United States, Canada and England, high profile federal appellate cases have addressed transgender individuals' rights regarding for example bathroom visits, and outlawing reparative or conversion therapies (e.g. Andrade & Redondo, 2022; Byne, 2016; Fleming & McFadden-Wade, 2018; GLAD GLBTQ Legal Advocates & Defenders, 2017; Stolberg, 2017; Walch, Davidge-Pitts, Safer, Lopez, Tangpricha, & Iwamoto, 2021). In addition to these cases that promote transgender individuals' rights, there are also legal cases that seek to curtail the care of transgender individuals. One of the most prominent is the case of Keira Bell. Keira Bell is a detransitioned patient of the Tavistock and Portman National Health Service (NHS) Trust and the Gender Identity Development Service (GIDS) who started treatment with PS at the age of 16, and brought her case to court. She filed a lawsuit against the NHS and the GIDS because she was, according to herself, not challenged enough before being allowed to start PS (Barbi & Tornese, 2022). In the context of this lawsuit, the High Court of Justice in London ruled in December 2020 that transgender adolescents under the age of 16 are highly unlikely to understand the long-term effects of PS, and that they therefore are not competent to decide to start this treatment (Dyer, 2020a). In response to this verdict, it was decided nationwide that transgender minors in England could no longer start treatment with PS before the age of 16, unless a court order was obtained (Dyer, 2020b). Strikingly, the verdict and subsequent treatment restrictions were carried out even though at that time there was no empirical evidence on the MDC of transgender adolescents regarding the decision to start treatment with PS. Of note, the Court of Appeal overturned this verdict and judged that 'it was for clinicians rather than the court to decide on competence to consent', referring to the current clinical situation (Dyer, 2021; Thornton, 2021). Still, decisions such as the one that was made in England are predominantly based on age standards prescribed by law, and on MDC assessments of clinicians which are likely to be influenced by their personal subjective views of what is in the adolescent's best interest, rather than on scientific data (Hein et al., 2015d; de Vries, Wit, Engberts, Kaspers, & van Leeuwen, 2010). Therefore, more research is needed to fill in this gap in knowledge so that such decisions, with profound consequences for so many transgender children and adolescents, are based on scientific data on capacity development.

ETHICAL DILEMMAS

In the Netherlands, PS is part of the treatment protocol for transgender adolescents. Elsewhere in the world, for example in some other countries in Europe and North America, it is not always standard of care due to various ethical concerns and/or financial constraints (Gridley et al., 2016; Puckett, Cleary, Rossman, Newcomb, & Mustanski, 2019; Naiingolan, 2021). These concerns include worries about the treatment's impact on physical, cognitive, and psychosocial development, and doubts about a minors' competence to make decisions with possibly far-reaching consequences (Anacker et al., 2021; Chen et al., 2020; Kreukels & Cohen-Kettenis, 2011). Treatment teams providing PS to adolescents are inherently faced with all kinds of ethical dilemmas, which have become increasingly pressing since the exponentially growing numbers of referrals and the public attention regarding transgender care (Gerritse et al., 2018). It seems that with the increasing visibility of transgender persons, and awareness of transgender health issues, a growing polarization between two 'camps' occurs; people who criticize the use of early medical treatment state that boundaries are being crossed by the use of early medical treatment, stemming from the principle to 'first do no harm', while advocates of early medical treatment believe that the current treatment is too restrictive, stemming from the principle of 'self-determination'. Although according to the people criticizing early medical treatment, PS might entail risks, refraining the adolescents from the treatment might have harmful life-long effects as well with regard to psychological, social, and/or medical well-being of the adolescent (de Vries et al., 2021). So, in order to provide transgender minors the care they need, it is necessary that the debate moves forward by elucidating these different perspectives and by pursuing depolarization. Clinical science can help resolve controversy through profound follow-up, which is not yet thoroughly developed in this area (Levine, 2018). Additional data on the treatment and its potential effects, and elucidation of the underlying moral considerations of all stakeholders are therefore essential in order to move forward the debate and bring the necessary nuance in the field.

AIMS

The Netherlands play a pioneering role in using PS in transgender adolescents. As with other controversial medical ethical issues, like euthanasia and abortion, this stance meets both international criticism and support. Since the immense increase in the number of minors seeking professional help for their gender incongruent experiences, and since more and more people express their opinions of what, according to them, is the best care for transgender minors, this has become even more pressing (e.g. Arnoldussen et al., 2020; Arnoldussen et al., 2022b; Kaltiala-Heino et al., 2015; Kaltiala et al., 2020; Shumer & Spack, 2013). Because of the controversies surrounding the use of PS, it is essential to underpin

the Dutch treatment strategy, and to keep on formulating the moral grounds for using it. People who criticize the use of PS, and those who support this treatment option seem to have different underlying ideas about, among others, adolescents' decision-making competence, decision-making authority, and the role of concurrent psychological, social, and/or medical issues, often without openly stating them (e.g. Dubin et al., 2020; Baron & Dierckxsens, 2021; Lemma, 2018). It is an essential task to elucidate these underlying considerations. More insight in the core of the ethical dilemmas surrounding PS, and more empirical data regarding these dilemmas are needed for at least four reasons. First, to ensure that treatment for transgender minors is not only clinically, but also ethically appropriate. Second, to find common ground between various clinicians around the world regarding early medical treatment. Third, to provide the stakeholders in the field direction to deal with these ethical dilemmas in clinical practice. And fourth, to allow clinicians to safely exercise the clinical judgment to undertake the course of action which is in the child's best interests, based on objective, scientific data and not (largely) on subjective opinions.

Therefore, the first overall aim of this research is to gain more insight in the core of the ethical dilemmas that play a role in the care of transgender minors, and the underlying intuitions and considerations of stakeholders in the field regarding early medical treatment. The stakeholders are transgender adolescents who proceeded with GAMT after PS, adolescents who were diagnosed with gender dysphoria but who did not proceed with GAMT after starting treatment with PS, their parents, clinicians working in gender treatment teams, and people who are critical about the use of early medical treatment for transgender minors. The second, subsequent aim is to provide empirical data regarding these ethical dilemmas in order to give clinicians direction on how to deal with these dilemmas, and to inform and guide the minors referred to the gender identity clinics regarding these ethical dilemmas.

CENTRAL RESEARCH QUESTIONS

To provide a response to the above aims, the following questions will be addressed:

Part 1. Setting the scene: perceptions of stakeholders on ethical issues

- What are the perceptions, views, and ideas of people who criticize the use of early medical treatment for gender dysphoria, and of those who support it, regarding PS in gender dysphoria, the aetiology of gender dysphoria, and the concepts sex, gender, child competence, and best interests? And do these perceptions, views, and ideas of proponents of PS differ from those of opponents, and if so, in what sense? (chapter 2);
- What are the perceptions, views, and ideas of adolescents diagnosed with gender

dysphoria regarding PS in gender dysphoria, and regarding the concepts sex, gender, child competence, and best interests? And do the perceptions, views and ideas of these adolescents differ from those of professionals, and if so, in what sense? (chapter 3);

Part 2. Medical decision-making competence

- Are transgender adolescents eligible for starting PS treatment competent to give informed consent to this treatment, and which variables are associated with adolescents' MDC regarding starting PS? (chapter 4);
- What are the perspectives on adolescents' MDC concerning PS of transgender adolescents who proceeded with GAMT after PS, adolescents who discontinued treatment with PS, their parents, and transgender clinicians? (chapter 5);

Part 3. Significance of puberty suppression and use of fertility preservation

- How do the trajectories of transgender adolescents after the initiation of treatment with PS look like? How many adolescents discontinued PS treatment, how many adolescents had extended use of the treatment, and how long after starting PS did the adolescents start treatment with gender-affirming hormones (GAH)? And which reasons were there for extended use and discontinuation of treatment with PS? (chapter 6);
- What functions does treatment with PS have for transgender adolescents who proceeded with GAMT after PS, adolescents who discontinued treatment with PS, their parents, and transgender clinicians? (chapter 7);
- How many adolescents made use of fertility preservation in a Dutch cohort of transgirls who started treatment with PS? Had information about the risk of infertility been given to the transgirls? Was discussion of the option of fertility preservation documented in their medical files? What was the given reason for declining fertility preservation if the adolescent had not made use of fertility preservation? And what other factors were associated with the use of fertility preservation? (chapter 8);

Part 4. Clinical ethics support

- In what way can moral case deliberation (MCD) as clinical ethics support help clinicians in dealing with ethical dilemmas in transgender care? (chapter 9).

OUTLINE OF THE THESIS

This thesis consists of four parts. **Part 1** sets the scene of the ethical issues regarding the use of early medical treatment for transgender children and adolescents according to the stakeholders. *Chapter 2* explicates the considerations of people who support the use of PS and those who criticize it, regarding the use of PS in gender dysphoria. Moral intuitions on early medical treatment, and ideas, assumptions and theories about the

aetiology of gender dysphoria, the boundaries of medicine, and the concepts gender, child competence, and best interests are described. It examines whether moral intuitions, ideas, and theories of people who criticize the use of PS differ from those of people who support it, and in what sense. The considerations of 36 professionals of 17 treatment teams from 10 different countries were taken into account while using individual semi-structured interviews and open-ended questionnaires.

To do justice to the adolescents' developing autonomy to make medical decisions, especially when it concerns profound treatments such as PS, serious consideration to the opinions of transgender adolescents needs to be given. Insight into the way these adolescents perceive the concepts sex and gender, and the use of PS in the context of gender dysphoria will help to adequately support these adolescents in their decision-making process regarding this treatment and give them the care they need. *Chapter 3* therefore explores the adolescents' considerations regarding the use of PS, and regarding the concepts sex and gender. Furthermore, it describes whether these considerations differ from those of clinicians working in gender treatment teams and of people who are critical about the use of PS in gender dysphoria, and if so, in what sense. To gain this insight semi-structured interviews with 13 adolescents concerning the use of PS were conducted in the Netherlands. Eight transgender adolescents who proceeded with GAMT after PS, and five adolescents who discontinued PS (aged 13-18 years) were interviewed.

Part 2 discusses the minors' medical decision-making competence (MDC) regarding starting PS treatment. Competence is an important topic in the controversies surrounding the use of PS. There is discussion whether transgender adolescents are competent to give informed consent to start this treatment. In some countries, this doubt has even led to limited access to this treatment. We therefore examine the MDC concerning PS of transgender adolescents. To assess MDC, judgements based on the reference standard (clinical assessment) and the MacArthur Competence Assessment Tool for Treatment (MacCAT-T), a validated semi-structured interview, were used. In addition, potential associated variables on MDC, such as age, intelligence, sex, and psychological functioning, were investigated. *Chapter 4* describes the cross-sectional semi-structured interview study with 74 transgender adolescents (aged 10-18 years; 16 birth-assigned boys, 58 birth-assigned girls) within two Dutch gender identity clinics we performed.

Chapter 5 explores the perceptions concerning MDC to start PS treatment for eight transgender adolescents who proceeded with GAMT after PS, six adolescents who discontinued treatment with PS, 12 of their parents, and 10 clinicians working in gender treatment teams. For this study individual semi-structured interviews and focus groups were used. Knowing what the perspectives of the adolescents, their parents, and clinicians are regarding the adolescents' MDC will increase our understanding of the decision-making process.

Part 3 describes the significance of starting treatment with PS or refraining from the treatment, and the use of fertility preservation. Treatment with PS for transgender adolescents was developed, among others, to extend the exploration and assessment phase by providing the adolescents more time to consider their gender, the diagnosis gender dysphoria, and the potential use of GAH, without the distress associated with endogenous pubertal development. *Chapter 6* describes the minors' trajectories after the initiation of treatment with PS, and reports the reasons for extended use and discontinuation of treatment with PS in order to find out whether PS is indeed being used as a phase to further explore and assess.

Chapter 7 focuses on how PS is perceived by transgender adolescents, their parents, and clinicians. Despite PS being the current first choice treatment, little research had examined the functions of PS from the perspectives of transgender adolescents, their parents, and clinicians. Knowledge about the perceived functions of PS can help to adequately support these adolescents in their decision-making process and give them the care they need. *Chapter 7* describes the outcomes of our study using individual semi-structured interviews and focus groups to obtain insight in the perspectives of eight transgender adolescents who proceeded with GAMT after PS, six adolescents who discontinued treatment with PS, 12 of their parents, and 10 clinicians regarding the functions of PS.

One major concern regarding starting treatment with PS for transgender minors entails the consequences for the minors' fertility. As far as currently known, the effects of treatment with PS on the secondary sex characteristics' development and the gonadal function are reversible when the treatment is discontinued. However, transgender minors who start treatment with PS at a young age, and subsequently start treatment with GAH and undergo gonadectomy, cannot make use of fertility preservation since they never undergo their endogenous puberty. In order to get more insight in this currently one of the most challenging topics concerning medical treatment for transgender adolescents, *chapter 8* reports the rate of fertility preservation among a cohort of Dutch transgirls who started treatment with PS. Furthermore, the reasons why these adolescents did or did not make use of fertility preservation are described.

As has become clear of the above, clinicians frequently face ethical dilemmas arising from the care they provide. **Part 4** describes the use of clinical ethics support for clinicians who are involved in (medical) care for transgender children and adolescents, in order to support these clinicians in dealing with these challenges more effectively. The research discussed in *chapter 9* describes the treatment teams' perceived value and effectiveness

of moral case deliberation (MCD), a relatively well-established form of clinical ethics support. We offered MCD to several treatment teams of Dutch gender identity clinics. This was evaluated in a mixed methods study using individual interviews, focus groups, MCD evaluation questionnaires, and reports of MCD sessions.

In *chapter 10* the studies of this thesis are summarised and discussed. Suggestions for future studies, and implications for clinical practice are given.

2

Early medical treatment for transgender children and adolescents: an empirical ethical study

Lieke J. J. J. Vrouenraets
A. Miranda Fredriks
Sabine E. Hannema
Peggy T. Cohen-Kettenis
Martine C. de Vries

2015. *Journal of Adolescent Health*, 57, 367-373

This study was funded by the 'Netherlands Organization for Health Research and Development' (ZonMW, projectnumber 731010002)

ABSTRACT

Purpose: The Endocrine Society and the World Professional Association for Transgender Health (WPATH) published guidelines for the treatment for adolescents with gender dysphoria (GD). The guidelines recommend the use of gonadotropin-releasing hormone analogues (GnRHa) in adolescence to suppress puberty. However, in actual practice, no consensus exists whether to use these early medical interventions. The aim of this study was to explicate the considerations of proponents and opponents of puberty suppression in GD to move forward the ethical debate.

Methods: Qualitative study (semi-structured interviews and open-ended questionnaires) to identify considerations of proponents and opponents of early (medical) treatment (paediatric endocrinologists, psychologists, psychiatrists, ethicists) of 17 treatment teams worldwide.

Results: Seven themes give rise to different, and even opposing, views on treatment: (1) the (non-) availability of an explanatory model for GD; (2) the nature of GD (normal variation, social construct or [mental] illness); (3) the role of physiological puberty in developing gender identity; (4) the role of comorbidity; (5) possible physical or psychological effects of (refraining from) early medical interventions; (6) child competence and decision-making authority; and (7) the role of social context how GD is perceived. Strikingly, the guidelines are debated both for being too liberal and for being too limiting. Nevertheless, many treatment teams using the guidelines are exploring the possibility of lowering the current age limits.

Conclusions: As long as debate remains on these seven themes and only limited long-term data are available, there will be no consensus on treatment. Therefore, more systematic interdisciplinary and (worldwide) multicentre research is required.

INTRODUCTION

Gender dysphoria (GD) is a condition in which individuals experience their gender identity (the psychological experience of oneself as male, female, or otherwise) as being incongruent with their phenotype (the external sex characteristics of their body) (Besser et al., 2006). The most extreme form of GD, often called transsexualism, is accompanied by a strong wish for gender reassignment (World Health Organization, 1993). Of the individuals experiencing GD, a small number is children. Only in a minority of prepubertal children, GD will persist and manifest as an adolescent/adult GD. The percentage of ‘persisters’ appears to be between 10% and 27% (Wallien & Cohen-Kettenis, 2008; Drummond, Bradley, Peterson-Badali, & Zucker, 2008; Steensma, McGuire, Kreukels, Beekman, & Cohen-Kettenis, 2013). Treatment for prepubertal children therefore is predominantly psychological. However, those children who still experience GD when entering puberty, almost invariably will become gender dysphoric adults (de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2011a). These young adolescents may demand hormonal interventions such as puberty suppression (using gonadotropin-releasing hormone analogues (GnRHa)) to suppress the development of secondary sex characteristics. In recent years, the possibility of puberty suppression (PS) has generated a new but controversial dimension to the clinical management of adolescents with GD. The purpose of PS is to relieve suffering caused by the development of secondary sex characteristics, to provide time to make a balanced decision regarding the actual gender reassignment (by means of treatment with gender-affirming hormones (GAH) and/or surgery) and to make passing in the new gender role easier (Cohen-Kettenis, Steensma, & de Vries, 2011). In the Netherlands, PS is part of the treatment protocol and as a rule possible in adolescents aged 12 years and older who are past the early stages of puberty and still suffer from persisting GD. When there are good reasons to treat an adolescent before the age of 12 years, for example, because of the height of the adolescent, treatment at a slightly younger age is acceptable.

Although an increasing number of gender identity clinics have adopted this Dutch strategy and international guidelines exist in which PS is mentioned as a treatment option, many professionals working with gender dysphoric minors remain critical (Coleman et al., 2012; Hembree et al., 2009; Korte et al., 2008; Viner, Brain, Carmichael, & Di Ceglie, 2005). Concerns have been raised about the risk of making the wrong treatment decisions and the potential adverse effects on health and on psychological and psychosexual functioning. Proponents of PS, on the other hand, emphasize the beneficial effects of PS on the adolescents’ mental health, quality of life, and of having a physical appearance that makes it possible to live unobtrusively in the desired gender role (Kreukels & Cohen-Kettenis, 2011).

Strikingly, in this debate, proponents and opponents of PS use the same ethical principles (autonomy, beneficence, nonmaleficence) but interpret them in totally different ways. Ethical discussions are often held on the level of these ethical principles only, with moral intuitions moving between extremes; for example, PS as a blessing versus treatment as an evident danger or a definite competence of the child versus incompetence because the child is simply too young and has an immature developmental level to decide on these substantial issues. What is missing in the discussions is an exploration of underlying ideas and theories about the nature of gender (dichotome or fluid) and GD (mental illness or social construct), child welfare, and child competence. Proponents and opponents seem to have different views on these issues, often without openly stating them. It is an essential task to elucidate these underlying ideas and theories because they substantially influence the judgment on GD treatment.

Strikingly, in the literature on GD, most of the times, only proponents give arguments for their treatment position. It is difficult to find arguments against the use of PS as a treatment option as opponents rarely publish in professional journals. Therefore, to date there is no clear overview of the considerations of proponents and opponents regarding the use of early medical interventions for GD. An overview explicating considerations, which underlie the different views on PS, could be the first step towards a more consistent approach recommended by clinicians across different countries. The aim of our study was to explicate the considerations of proponents and opponents of PS to move forward the ethical debate.

For this purpose, we have performed an empirical ethical study to answer the following questions: (1) what are the moral intuitions (direct thoughts or opinions) of informants on puberty suppression in GD; (2) what are the (underlying) ideas, assumptions, and theories of informants about the aetiology of GD, and the concepts 'gender', 'child competence', and 'best interests?'; and (3) do moral intuitions, ideas, and theories of proponents of PS differ from those of opponents, and in what sense?

METHODS

An empirical ethical approach was followed, using a qualitative interview and questionnaire study. The study was approved by the institutional review board of the Leiden University Medical Centre.

Fifteen professionals participating in the study were interviewed face-to-face, six by using Skype (Microsoft Corp., Redmond, WA). Some treatment teams indicated that they did not master the English language well enough for a direct interview. These teams were

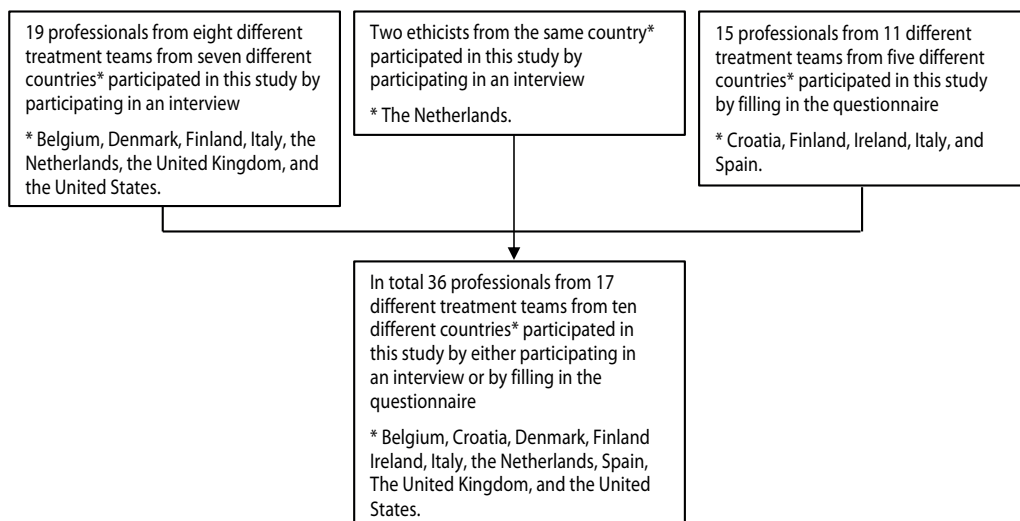
offered similar questions in a questionnaire by e-mail. The questionnaire was filled in by 15 professionals. The empirical data were obtained between October 2013 and August 2014.

Initial interview topics were formulated after examination of the relevant literature. In accordance with qualitative research techniques, the interview topics evolved as the interviews progressed through an iterative process to ensure that the questions captured all relevant emerging themes (Britten, 1995; Guest, Bunce, & Johnson 2006). The interviews contained general topics and no close ended questions.

The informants were child and adolescent psychiatrists, psychologists, and endocrinologists from diverse treatment teams in European and North American countries. Two Dutch ethicists, who are not directly related to a treatment team, were also interviewed. The treatment teams were purposefully selected on the basis of their stance in favour or against PS in the past. Interestingly, at the time this study was initiated, PS was not part of the treatment protocol for adolescents of several treatment teams. However, during this study, PS did become part of the treatment protocol of some of these teams. When interviewing these teams, extra emphasis was placed on the arguments they used to justify these treatment changes. The 36 professionals who participated in this study worked in 10 different countries (figure 1).

An extensive description of the analysis of the data is given in Appendix A (which can be found at page 222).

Figure 1. Participating informants



RESULTS

From the literature, interviews, and questionnaires, seven themes emerged that lead to different, and sometimes even opposing, views on the treatment for adolescents with GD. Representative quotations were chosen to illustrate the themes identified.

The availability or nonavailability of an explanatory model for gender dysphoria

With regard to the causes of GD, no single cause has been found so far. In the literature, genetic, hormonal, neurodevelopmental, and psychosocial factors have been suggested to play a role (de Vries & Cohen-Kettenis, 2012; Meyer-Bahlburg, 2010). Most of our informants believe that a single cause is unlikely, but they see GD as influenced by diverse factors. Some put forward the possibility of a (slightly) different aetiology for different subtypes. Others think that biological, for example, neurodevelopmental, factors play a dominant role and believe that psycho-familial factors have very little or no influence. Altered hormone exposure during foetal development was also suggested as a potential cause.

“I think that nature and nurture both contribute to the development and expression of gender dysphoria. The role of each is different in each individual and this explains the heterogeneity of gender dysphoria expression.” - Interview with an endocrinologist

“I believe biological factors play the predominant role. In my work, I have not found psycho familial or social factors that children and adolescents with gender dysphoria have in common, which is also known in scientific literature.” - Interview with a psychologist

We asked the informants whether an explanatory model for GD would affect ideas regarding treatment options for adolescents. Many, including some informants who are sceptical about early medical treatment for GD, stated that the aetiology does not affect the way adolescents with GD should be treated. Furthermore, most respondents think that not knowing the aetiology should not prevent providing care and understanding of the person's predicament.

One respondent compared it to having a broken leg:

“[It is possible to] understand that it is painful and impairs function even if you do not know exactly why or how that person has broken his leg.” - Interview with a psychiatrist

The nature of gender dysphoria

Is GD a normal variation of gender expression, a social construct, a medical disease, or a mental illness? In the DSM-5 and the to-be-released ICD-11, the main challenge in classifying GD has been to find a balance between concerns related to the stigmatization of mental disorders and the need for diagnostic categories that facilitate access to health care, payment by insurance companies, and the communication between diverse professions (American Psychiatric Association, 2013; Drescher, Cohen-Kettenis, & Winter, 2012; World Health Organization, 2022).

"I think the focus should be on getting rid of the stigma that accompanies psychiatric disorders instead of on saving specific disorders from the psychiatric disorder group."

- Interview with a psychiatrist

According to the literature, some authorities classify GD as a mental illness (Giordano, 2011; McHugh, 2004), whereas various scholars state that the diagnosis of gender-variant children with GD is a prime example of a conflict between the individual and the society in which he or she lives (Vasey & Bartlett, 2007; Drescher, 2014). The interviews and questionnaires show that most informants find it difficult to articulate their thoughts about this aspect. Most see GD as neither a disease nor a social construct, but as a normal, but less frequent variation of gender expression. However, some note that you would not need medical procedures to make the lives of people with GD more satisfying if it were merely a normal variation. The need for treatment is what defines GD as a disorder, they state. Others state that it is a disease in the sense that there is a disconnection between body and mind, which causes suffering.

"Even in the most gender dysphoria benevolent society many individuals with gender dysphoria would still need medical procedures to make their lives more satisfying, and I think that this is what makes gender dysphoria a disorder, but not a mental one." - Interview with a psychiatrist

We asked whether these diverse ideas and theories about the nature of GD affect the decision whether to use puberty suppression in adolescents with GD. Most informants state that a classification in itself should never be a factor in deciding what treatment to follow. However, one informant stated:

"I find it extremely dangerous to let an adolescent undergo a medical treatment without the existence of a pathophysiology and I consider it just a medical experimentation that does not justify the risk to which adolescents are exposed [...] Gender dysphoria is the only situation in which medical intervention does not cure a sick body, but healthy organs are mutilated in the process of adapting physical and congruent psychological identity." - Interview with a psychiatrist

The role of physiological puberty in developing a consistent gender identity

In the literature, the concern is raised that interrupting the development of secondary sex characteristics may disrupt the development of a gender identity during puberty that is congruent with the assigned gender (Korte et al., 2008). The interviews and questionnaires show that some treatment teams share this view.

"I have met gay women who identify as women who would certainly have been diagnosed gender dysphoric as children but who, throughout adolescence, came to accept themselves. This might not have happened on puberty suppression."

- Interview with a psychologist

"I believe that, in adolescence, hypothalamic inhibitors should never be given, because they interfere not only with emotional development, but [also] with the integration process among the various internal and external aspects characterizing the transition to adulthood."

- Interview with a psychiatrist

However, although most informants agreed on the fact that treatment with PS indeed may change the way adolescents think about themselves, most of them did not think that PS inhibits the spontaneous formation of a gender identity that is congruent with the assigned gender after many years of having an incongruent gender identity. Some professionals stated that, although the PS may disrupt the development of a consistent gender identity, in some cases, the very real risks of the present (the young person's distress and consequent possible suicide risk) override the possible risks for the future (the individual's uncertainty). According to them, we need to take into account what is the best for that individual person.

"I think that the distress for a child experiencing the 'wrong' puberty is so great that it overrides the opinion that the child should have the experience of 'crisis of gender'."

- Interview with a psychiatrist

Various endocrinologists made the comparison with precocious puberty; a medical condition in which PS have been used for many years, and no cases of GD have been described (at least to their knowledge). Besides, most of them emphasize that they deliberately start treatment with PS only when the minors have reached Tanner stage two or three to give them at least a kind of 'feeling' with puberty before starting with PS. Furthermore, some state that this is an issue that should be researched so that decisions can be made based on facts rather than on opinions.

The role of comorbidity

The risk of co-occurring psychiatric problems in children and adolescents with GD is high. The percentage of children referred for GD who fulfilled DSM criteria of at least one diagnosis other than GD is 52% (Wallien & Cohen-Kettenis, 2007). The psychiatric comorbidity in adolescents with GD is 32% (de Vries, Doreleijers, Steensma, & Cohen-Kettenis, 2011b). Another study shows that 43% of the children and adolescents seen in a gender identity clinic suffer from major psychopathology (Meyenburg, 2014). To date, the precise mechanisms that link GD and coexisting psychopathology are unknown. The interviews and questionnaires show that professionals think that it differs between individuals and it depends on the comorbid problem whether the GD and the co-occurring problem(s) are merely coexisting or interrelated. The impact of society is also mentioned as a mediating factor. Some professionals stress that we have to keep in mind that society marginalizes minority groups.

"This [marginalization of minority groups] can lead to internalized self-hatred and many other mental health difficulties such as self-harm, depression, anxiety, isolation, suicide etc. Being picked on or being abused as minority groups leads to fear which is a mediating variable for mental health problems." - Interview with a psychologist

"I see gender dysphoria as a cause of reactive co-occurring problems [such as anxiety and depression]; nevertheless, comorbidity with other non-reactive psychiatric problems [such as attention deficit disorder with hyperactivity, bipolar disorder] can present in parallel." - Interview with a psychiatrist

We asked whether severe coexisting psychopathology influences the treatment for the GD, and in what way. Some professionals stress the importance of addressing treatment for severe coexisting psychopathology before addressing GD-related medical interventions for minors with GD. Others state that it depends on the specific comorbid problem whether it influences the treatment for the GD and in what way. They state that, although coexisting psychopathology may interact with GD and GD-related medical interventions, the GD and the comorbid problem may result from completely different underlying processes and should therefore have separate treatment plans, goals, and strategies.

Possible physical or psychological harmful effects of early medical interventions and of refraining from interventions

The possible consequences of suppressing puberty for cognitive and brain development are unclear and debated at this moment (Cohen-Kettenis et al., 2008; Hembree et al., 2009). The normal pubertal increase in bone mineral density may be attenuated by PS, and it is uncertain if there is complete catch-up after treatment with gender-affirming hormones (GAH) (Cohen-Kettenis, Schagen, Steensma, de Vries, & Delemarre-van de Waal, 2011;

Delemarre-van de Waal & Cohen-Kettenis, 2006; Klink, Caris, Heijboer, van Trotsenburg, & Rotteveel, 2015). In the interviews and questionnaires, the loss of fertility was often mentioned as a major consequence of treatment. In addition, various informants stressed the importance of the fact that the penis and scrotum should be developed enough to be able to use this tissue to create a vagina later in life. Very early use of PS impairs penile growth and consequently makes certain surgical techniques impossible.

Although (the sparse) research until now mostly shows no negative, and even positive results regarding the consequences of treatment with PS (Cohen-Kettenis et al., 2008; de Vries et al., 2014), proponents remain cautious and opponents sceptical because of the fact that (long-term) risks and benefits of available treatments have not been fully established.

“The positive attitude of many clinicians in giving hypothalamic blockers [...] is based on the need to conform to international standards, even if they are conscious of a lack of information about medium and long-term side effects.” - Interview with a psychiatrist

In the interviews and questionnaires, harmful effects of refraining from interventions are mentioned too. Multiple professionals state that many young gender dysphoric people will harm themselves without intervention or at least the promise of future treatment options. Some professionals mention that nowadays the average age at which puberty starts is earlier than a few decades ago. This makes them wonder whether the age criterion of 12 years, that many treatment teams use, is still suitable.

“The question cannot be posed as ‘do something which may cause harm’ against ‘doing no harm’, as doing nothing results in very high levels of distress and poor outcome as well.” - Interview with a psychiatrist

“So why are we saying 12? It is arbitrary if the average age for the start of puberty in the UK or in Northern Europe is now eight or nine. [...] this is a very lively debate in our team. [...] It [lowering the age of starting with puberty suppression] is for the younger ones, who are going into puberty at 10 or 11. I mean I think we probably have to extend it to them.” - Interview with a psychologist

Ideas about child competence and the decision-making authority

Competence is an important point of disagreement when PS is discussed. In the literature, proponents have concluded that relatively young children can participate meaningfully in the consent process, whereas opponents raise doubts about what children can understand (Abel, 2014; Mann, Harmoni, & Power, 1989; Sadjadi, 2013). Most informants state that competence should be determined for every single case individually. Most state that children develop at different rates in terms of their physical, mental, emotional, and sexual

maturation. They state that the ability of adolescents to make decisions regarding their own medical treatment should be determined based on the following diverse aspects: their cognitive abilities, emotional maturity, and the presence or absence of comorbidities.

Various informants do mention the child's chronological age as a criterion; some state that the child should be at least 12, 13, or 14 years old, whereas others mention the age of 16 years as the cut-off age.

"I suppose [...] the child [should be] at least 12 or 13 [years old] but it depends on the child, their background, family and supportive systems too." - Interview with a psychologist

Some state that not a child's chronological age should count, but the fact that the child's puberty has started. One informant stated that the decision whether to start with hormones should only be made during adulthood:

"We should facilitate his or her process of integration in the society and if he or she would undergo hormone- and surgical treatments he or she could decide [on this] during adulthood." - Interview with a psychiatrist

We asked who should have authority to take decisions regarding early medical treatment. Some informants stated that the adolescent is able to give informed consent himself or herself. Others stated that minors must at least partially depend on their parents or other caregivers to make decisions regarding their treatment. Some noted that there is no discussion in other situations where minors receive medication; for example, parents making decisions about starting children on anti-epileptic medication without the child's consent. These informants therefore question why there is a discussion about the authority to decide on the start of medication in GD. It was further mentioned that a team of specialists experienced in treating transgender minors are responsible for these minors and the recommended treatment.

"People do not ask about how kids feel about going on this mood stabilization, how do you feel about going on this medication for depression. The only place where this happens is gender. [...] all kids are entering the clinic on five psychotropic medications without hesitation [of the parents and clinicians]. And nobody has this discussion."
- Interview with a paediatrician

"The fact that somebody wants something badly, does not mean that a clinician should do it for that reason; a medical doctor is not a candy seller." - Interview with a professor of health care ethics and health law

The role of the social context in the way gender dysphoria is perceived

The study shows that the way gender-variant behaviour of minors is perceived is very different in the various countries. Some informants think that the way gender-variant behaviour is approached influences to a large extent whether it is pathologized or not.

“I believe that hypothalamic blockers treatment satisfies clinicians’ anxiety, pathologizing individuals with gender dysphoria, inducing them to follow the sex-gender binarism.” - Interview with a psychiatrist

“You might think that the experience of gender dysphoria is kind of a solution [for all their problems] that is culturally available for adolescents nowadays. [...] I think that the culture is kind of offering or allowing this idea that all problems are stemming from the gender problem. And then they stick to this fixated idea and [they] seek for assessment and we readily see that they have numerous and relatively serious psychological and developmental problems and mental health disorders.” - Interview with a psychiatrist

Some informants wondered in what way the increasing media attention affects the way gender-variant behaviour is perceived by the child or adolescent with GD and by the society he or she lives in. They speculated that television shows and information on the internet may have a negative effect and, for example, lead to medicalization of gender-variant behaviour.

“They [adolescents] are living in their rooms, on the internet during night-time, and thinking about this [gender dysphoria]. Then they come to the clinic and they are convinced that this [gender dysphoria] explains all their problems and now they have to be made a boy. I think these kinds of adolescents also take the idea from the media. But of course you cannot prevent this in the current area of free information spreading.” - Interview with a psychiatrist

Furthermore, interviews and questionnaires show that treatment teams feel pressure from parents and adolescents to start with treatment at earlier ages.

DISCUSSION

Using empirical methods, our project aimed to explicate the considerations of proponents and opponents of PS in GD. A representative international group of professionals participated, enabling us to identify ideas, assumptions, and theories on GD (treatment). These data give us unique insights in the GD practice and the way ethical concepts function in this field.

The interviews and questionnaires show that the discussion regarding the use of PS goes in diverse directions and is in full swing. It touches on fundamental ethical concepts in paediatrics; concepts such as best interests, autonomy, and the role of the social context. It is striking that the Standards of Care for GD of the World Professional Association for Transgender Health and the Endocrine Society are considered too liberal and too conservative (Coleman et al., 2012; Hembree et al., 2009). Furthermore, since the start of this study, PS has been adopted as part of the treatment protocol by increasing numbers of originally reluctant treatment teams. More and more treatment teams embrace the Dutch protocol but with a feeling of unease. The professionals recognize the distress of gender dysphoric minors and feel the urge to treat them. At the same time, most of these professionals also have doubts because of the lack of long-term physical and psychological outcomes. Most informants acknowledge pro-arguments and counterarguments regarding the use of PS. Several teams, who work according to the Dutch protocol, are also exploring the possibility of lowering the current age limits for early medical treatment although they acknowledge the lack of long-term data.

For several informants, a reason to use PS was the fear of increased suicidality in untreated adolescents with GD. Research shows that transgender minors are at higher risk of suicidal ideation and suicidal attempts (Grossman & D'Augelli, 2006; Wallien & Cohen-Kettenis, 2008). Nevertheless, caution is needed when interpreting these data because they do not show causality or directionality. Another aspect mentioned by various informants is that nowadays the average age at which puberty starts is earlier than a few decades ago. Indeed, there is a research showing earlier puberty in girls in the United States and Europe (Aksglaede, Sørensen, Petersen, Skakkebaek, & Juul, 2009; Euling et al., 2008; Talma et al., 2013). In U.S. boys, data were found to be insufficient to evaluate a secular trend (Euling et al., 2008).

As still little is known about the aetiology of GD and long-term treatment consequences for children and adolescents, there is great need for more systematic interdisciplinary and (worldwide) multicentre research and debate. As long as there are only limited long-term

data in support of the guidelines, there will be no true consensus on treatment. To advance the ethical debate, we need to continue to discuss the diverse themes based on research data as an addition to merely opinions. Otherwise ideas, assumptions, and theories on GD treatment will diverge even more, which will lead to (even more) inconsistencies between the approaches recommended by clinicians across different countries.

Several professionals mentioned that participation in the study made them think more explicitly about the various themes, and it encouraged them to discuss the issues in their teams. In the Dutch teams, we therefore introduced moral deliberation sessions to talk about these ethical topics. The first reactions of the professionals were positive; the sessions made them rethink essential aspects of the protocol. Furthermore, they had more understanding for the viewpoint of other disciplines. Moral deliberation sessions could be a valuable step in gaining more insight in the contexts of GD treatment disagreements, especially as long as treatment data are still lacking.

There are strengths and weaknesses to the present study. The qualitative nature of the study made it possible to find out, in depth, the ways in which people think or feel about specific topics. Another strength of this study is the representativeness of the participants, by interviewing 36 professionals from ten different countries. This gives a wide variety of considerations of professionals in European and North American countries. Nevertheless, the considerations explicated in this study are therefore solely Europe and North America based. The considerations of professionals are likely to be different in other parts of the world.

We encourage gathering more qualitative research data from treatment teams of additional countries, aggregating a broader range of views on the treatment for gender dysphoric minors. More empirical data from treatment teams all over the world could lead to new information and/or confirmation of the results found in this study.

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Perceptions of sex, gender, and puberty suppression: a qualitative analysis of transgender minors

Lieke J. J. Vrouenraets
A. Miranda Fredriks
Sabine E. Hannema
Peggy T. Cohen-Kettenis
Martine C. de Vries

2016. *Archives of Sexual Behavior*, 45(7), 1697-1703

This study was funded by the 'Netherlands Organization for Health Research and Development' (ZonMW, projectnumber 731010002)

ABSTRACT

International guidelines recommend the use of gonadotropin-releasing hormone analogues (GnRHa) in adolescents with gender dysphoria (GD) to suppress puberty. Little is known about the way gender dysphoric adolescents themselves think about this early medical intervention. The purpose of the present study was (1) to explicate the considerations of gender dysphoric adolescents in the Netherlands concerning the use of puberty suppression; (2) to explore whether the considerations of gender dysphoric adolescents differ from those of professionals working in treatment teams, and if so in what sense. This was a qualitative study designed to identify considerations of gender dysphoric adolescents regarding early treatment. All 13 adolescents, except for one, were treated with puberty suppression; five adolescents were transgirls and eight were transboys. Their ages ranged between 13 and 18 years, with an average age of 16 years and 11 months, and a median age of 17 years and 4 months. Subsequently, the considerations of the adolescents were compared with views of clinicians treating minors with GD. From the interviews with the gender dysphoric adolescents, three themes emerged: (1) the difficulty of determining what is an appropriate lower age limit for starting puberty suppression. Most adolescents found it difficult to define an appropriate age limit and saw it as a dilemma; (2) the lack of data on the long-term effects of puberty suppression. Most adolescents stated that the lack of long-term data did not and would not stop them from wanting puberty suppression; (3) the role of the social context, for which there were two subthemes: (a) increased media-attention, on television, and on the internet; (b) an imposed stereotype. Some adolescents were positive about the role of the social context, but others raised doubts about it. Compared to clinicians, adolescents were often more cautious in their treatment views. It is important to give voice to gender dysphoric adolescents when discussing the use of puberty suppression in GD. Otherwise, professionals might act based on assumptions about adolescents' opinions instead of their actual considerations. We encourage gathering more qualitative research data from gender dysphoric adolescents in other countries.

INTRODUCTION

Gender dysphoria (GD) is a condition in which individuals experience distress, because their gender identity (the psychological experience of oneself as male, female or otherwise) is incongruent with their gender assigned at birth (American Psychiatric Association, 2013). GD may exist in childhood, but only in a minority of prepubertal children will persist into adolescence. The percentage of 'persisters' appears to be between 10 and 27% (Drummond et al., 2008; Steensma et al., 2013; Wallien & Cohen-Kettenis, 2008). Treatment for prepubertal children consists of providing information, advice, psychological support, and/or family counselling. Those children who still experience GD when entering puberty, almost invariably will become gender dysphoric adults (de Vries et al., 2011a). They may seek hormonal interventions such as puberty suppression (using gonadotropin-releasing hormone analogues (GnRH_a)) to suppress the development of secondary sex characteristics.

In recent years, the possibility of puberty suppression (PS) has generated a new but controversial dimension to the clinical management of adolescents with GD (Vrouenraets, Fredriks, Hannema, Cohen-Kettenis, & de Vries, 2015). The purpose of PS is to relieve suffering caused by the development of secondary sex characteristics, to provide time to make a balanced decision regarding the actual gender-affirming medical treatment (GAMT; by means of treatment with gender-affirming hormones (GAH) and/or surgery), and to make passing in the new gender role easier (Cohen-Kettenis, Steensma, & de Vries, 2011). In the Netherlands, PS is part of the treatment protocol and as a rule possible in adolescents aged 12 years and older who are in or beyond the early stages of puberty and still suffer from persisting GD (Cohen-Kettenis et al., 2011). Occasionally, it is acceptable to start treatment at a (slightly) younger age than 12, if puberty has already started and is progressive. Earlier intervention might then make sense and, in fact, does already happen in practice.

An increasing number of gender identity clinics, including initially reluctant treatment teams, have adopted the Dutch strategy of PS (Vrouenraets et al., 2015), and international guidelines exist in which PS is recommended as a treatment option (Coleman et al., 2012; Hembree et al., 2009). Nevertheless, the use of PS is still controversial. Recently, we studied the opinions of 17 treatment teams worldwide. It was striking that the Standards of Care for GD of the World Professional Association for Transgender Health (WPATH) and the guidelines for the endocrine treatment for individuals with GD of the Endocrine Society were considered too liberal by some teams, but at the same time too conservative by others (Vrouenraets et al., 2015). Many professionals working with gender dysphoric minors remain critical about the use of PS because of the lack of long-term physical and psychological outcomes (Korte et al., 2008; Viner et al., 2005). Concerns have been raised

about the risk of making the wrong treatment decisions, as gender identity could fluctuate during adolescence. Furthermore, adolescents might have poor decision-making abilities. Also, there may be adverse effects on health and on psychological and psychosexual functioning. Proponents of PS on the other hand emphasize the beneficial effects of PS on the adolescents' mental health, quality of life, and of having a physical appearance that makes it possible to live unobtrusively in the affirmed gender role (Kreukels & Cohen-Kettenis, 2011). Several treatment teams, who work according to the guidelines, are exploring the possibility of lowering their current age limits for early medical treatment, even though they acknowledge the lack of long-term data (Vrouenraets et al., 2015).

In the literature on GD, it is mainly the professional view on the treatment that is available. Little is known about the way gender dysphoric adolescents themselves think about early medical intervention. However, to do justice to the developing autonomy of adolescents to make medical decisions, especially when it concerns far-reaching treatments, it seems appropriate to give serious consideration to the opinions of gender dysphoric minors themselves.

The aim of our project was to explicate the considerations and opinions of gender dysphoric adolescents in the Netherlands concerning the concept of sex and gender, and the use of PS in GD. Furthermore, we explored whether considerations and opinions on the use of PS of gender dysphoric minors themselves differ from those of professionals working in treatment teams, and if so in what sense. Therefore, we compared the results of the interviews with the adolescents to earlier data concerning the opinions of treatment teams worldwide (Vrouenraets et al., 2015). We paid extra attention to the perception of sex and gender in the media; the increased media-attention regarding transgender individuals as well as the imposed stereotype are discussed.

For this purpose, we have performed an empirical ethical study in order to answer the following questions: (1) What are the perceptions and views (direct thoughts or opinions) of gender dysphoric adolescents on PS in GD; (2) What are the (underlying) ideas, assumptions, and views of gender dysphoric adolescents about the concepts 'best interests', 'autonomy', and 'sex/gender?'; (3) Do perceptions, views, and ideas on the use of PS of gender dysphoric minors in the Netherlands differ from those of professionals, and if so in what sense?

METHOD

Participants

The interviews were conducted in the context of a larger study on controversies surrounding PS in adolescents with GD. The study was approved by the institutional review board of the Leiden University Medical Centre.

For the current part of the study, an empirical ethical approach was followed, using qualitative semi-structured interviews. Gender dysphoric adolescents were interviewed face-to-face in order to identify their considerations and opinions on the use of PS. The informants were 13 adolescents who were recruited from the Gender identity clinic in Leiden, the Netherlands. Fourteen consecutive adolescents, and their parents/guardians if the adolescent was younger than 18 years, were asked to participate when they attended their regular follow-up appointment. Thirteen adolescents and their families agreed to participate but one mother refused participation of her child. The adolescents who participated in the study were not selected in order to be representative, in characteristics (age, sex, socioeconomic status and psychopathology), of the population seen at the Curium-LUMC clinic. They were between 13 and 18 years of age, with an average age of 16 years and 11 months, and a median age of 17 years and 4 months. All adolescents, except for one, were treated with PS. The mean age at which the adolescents started treatment with PS was 15 years and 10 months. The adolescent who was not treated with PS immediately started treatment with GAH because she was above the age of 18 when treatment was indicated, which is in line with the Dutch protocol. Five adolescents were transgirls (natal boys with a female gender identity) and eight were transboys (natal girls with a male gender identity). The full-scale intelligence quotient (IQ) of the interviewed adolescents ranged between 70 and 132, with an average full-scale IQ of 99 and a median of 102.

Procedure and Measures The interviewer was not involved in the diagnostics of and treatment for these adolescents. The interviewer was a child and adolescent psychologist with a Master of Science degree and interview experience. Initial interview topics were formulated after examination of the relevant literature (see supplemental data). In accordance with qualitative research techniques, the interview topics evolved as the interviews progressed through an iterative process to ensure that the questions captured all relevant emerging themes (Britten, 1995; Guest et al., 2006). The interviews contained general topics and no close-ended questions. All interviews were audiotaped and transcribed verbatim. Before each interview informed consent for participation and tape recording was obtained from the interviewed adolescents as well as their parents in case the adolescents were younger than 18 years of age. The interviews with the adolescents took between 30 and 45 minutes. Data analysis was based on the constant comparative method (Malterud, 2001; Corbin & Strauss, 2014; Vrouenraets et al., 2015). We used an iterative process wherein we continually went back to the field and interviewed new participants to collect more data. The following

processes of data gathering and analyses were used: (1) interviews; (2) transcription of the interview data; (3) open coding, which involved identifying relevant concepts in the text; (4) constant comparison of open codes, looking for conceptual similarities and differences; (5) identification of emerging themes; (6) continued sampling and interviewing as theoretical categories emerged and novel questions arose; and (7) continued coding and comparison of codes until nothing new was added to the theoretical categories. Data collection continued as long as new information came up. After no new content was found in the interviews, subject enrolment was stopped. This process, called thematic saturation, is a well-described qualitative method to avoid unnecessarily large and repetitive data sets (Guest et al., 2006).

The methodology and results of the interviews with professionals were previously described in chapter 2 of this thesis.

RESULTS

From the interviews with the gender dysphoric adolescents three themes emerged: (1) the difficulty of determining what is an appropriate lower age limit for starting PS; (2) the lack of data on the long-term effects of PS; (3) the role of the social context; this item consisted of two subthemes: (a) increased media-attention, on television and on the internet, (b) an imposed stereotype. Representative quotations were chosen to illustrate the themes identified.

The difficulty of determining what is an appropriate lower age limit for starting puberty suppression

The guidelines published by the WPATH and the Endocrine Society recommend the use of PS in adolescents when GD persists at the beginning of puberty (Coleman et al., 2012; Hembree et al., 2009). In principle, Dutch adolescents need to be 12 years of age and in pubertal Tanner stage 2-3 to be eligible for treatment with PS.

Most adolescents found it difficult to define an appropriate lower age limit. They saw it as a dilemma. On the one hand they thought it was important that children have the possibility of treatment with PS at the moment secondary sex characteristics of the natal sex start to develop, in order to prevent irreversible body changes like growth of breasts or breaking of the voice. This opinion is illustrated by the following quote:

"I think it is hard to set an age requirement. On the one hand I think 12 years is a good age minimum, on the other hand I think that a transgender [individual] whose puberty started earlier should have the possibility to start treatment with puberty suppression before the age of 12." - Interview with a transgirl; age: 13;11

Another aspect that was mentioned was the issue of having enough time before making a decision regarding starting treatment with PS:

"In my opinion 12 is a good age minimum because then these children and adolescents have time to consider what they want before making a decision regarding starting treatment with puberty suppression." - Interview with a transgirl; age: 17;0

The opinion to define different age limits for boys and girls because most boys mature later than girls do, was raised by another adolescent:

"I would probably pick different ages for boys and girls. For girls I would put the age at I guess 11, and for boys I would put it at 13. Simply because biologically males mature later than females do." - Interview with a transboy; age: 18;5

On the other hand, the adolescents have doubts about the competence of children to make decisions regarding topics like this:

"Although a 10-year-old may realise what is going to happen in the short-term, he or she might not be fully aware of the long-term consequences." - Interview with a transboy; age: 15;9

The lack of data on the long-term effects of puberty suppression

There are limited data on the consequences of PS for bone mineral density (Klink et al., 2015) and executive brain function (Staphorsius et al., 2015) but much remains unknown about the long-term effects of this treatment.

Most adolescents stated that the lack of long-term data did not and would not stop them from wanting PS. They said that being happy in life was more important for them than any possible negative long-term consequence of PS, as described by these three adolescents:

"The possible long-term consequences are incomparable with the unhappy feeling that you have and will keep having if you do not receive treatment with puberty suppression." - Interview with a transboy; age: 18;3

"I would rather live 10 years shorter but live a very happy life being myself, than live 10 years longer and be unhappy my whole life." - Interview with a transboy; age: 17;7

"It is not a choice, even though a lot of people think that. Well, actually it is a choice: living a happy life or living an unhappy life." - Interview with a transgirl; age: 14;5

Furthermore they mentioned that in order to be able to obtain long-term data, one person needs to be the first to undergo the treatment that needs evaluation, as these adolescents described:

“If I were in charge I would definitely offer treatment with puberty suppression because that would make research feasible; people could sign up for studies in order to investigate possible consequences.” - Interview with a transgirl; age: 14;5

The adolescents who were interviewed were more than willing to be that first person.

Conceptualization of sex and gender in the media

The third theme consists of two separate aspects.

Increased media-attention, on television and on the internet

The topic regarding the increased media-attention emerged during the interviews with the gender dysphoric adolescents and during the interviews with the professionals during a previous study (Vrouenraets et al., 2015). It was not mentioned before in the relevant literature.

In the last decade transgender individuals have become visible in the media. Many television programs, films, magazines, newspapers, and the internet have paid attention to GD in children, adolescents, and adults. Recent examples are the documentary series in the Netherlands called ‘He is a she’ featured in 2014, and again in 2016; the films *The Danish Girl* (2016), *Boys Don’t Cry* (1999), and *Boys Meet Girl* (2014); and the dozens of sites on the internet that provide information on GD and transgenderism (Zucker et al., 2008). Some adolescents and professionals were positive about the increasing media-attention for transgender minors, others raised doubts about it. Some adolescents and professionals stated that this media-attention enables many transgender individuals to recognize their gender dysphoric feelings. They also stated that they had learned they were not the only ones having these feelings:

“Thanks to media coverage I learned that gender dysphoria exists; that someone can have these feelings and that you can get treatment for it. [...] Beforehand I thought I was the only one like this.” - Interview with a transboy; age: 18;11

“In my opinion the increasing media-attention is positive. I think that many transgender individuals only realise they are transgender after watching such television programs.” - Interview with a transgirl; age: 13;11

Furthermore several adolescents stated that television shows and other programs have led to more acceptance in their social environment. Yet, some adolescents and professionals raised doubts about the increasing media-attention. Some adolescents mentioned that most transgender individuals in the media are people who are functioning quite well despite their gender dysphoric feelings. They believe however that this is not a representative picture of transgender individuals. For instance, the transgender individuals who also suffer from autism spectrum disorder or depression are not shown. Furthermore, some adolescents thought that the media show a rather stereotypical picture of transgender individuals; as if all transboys were tomboys from a very early age, did not like dolls and pink, but preferred playing with cars and playing soccer. They stated that not all transgender individuals are that 'stereotypical'; and that some transboys were even 'girlish' when they were younger and preferred pink over blue. They wondered "why are not these transgender individuals in these television programs and in articles?," as illustrated by the following two quotes:

"Most of the transmen I have seen in the media...when they were younger, they always were stereotypical tomboys. I was personally quite stereotypically feminine; I liked drawing dresses with my mom, and still do. That made me feel alienated by the media." - Interview with a transboy; age: 18;5

"Television shows are never about girls that alternate between living like a girl and living like a boy. Such topics never appear. It seems such topics are simply not spectacular enough." - Interview with a transboy; age: 17;7

A binary concept of sex and gender

Since July 2014 sterilization is no longer a requirement for transgender individuals in order to be able to change their gender on their birth certificate and on other official documents in the Netherlands (art. 1:28 subsection 1 DCC Jo art. 1:20 subsection 1 DCC). During the interviews most transboys stated that they thought that they would not choose to have their ovaries/uterus removed because "it is not necessary anymore." Before this change in law, many transboys had their ovaries/uterus removed. A statement such as this one was typical among transboys:

"I do not care about hysterectomy because changing gender on official documents is nowadays possible without this surgical procedure." - Interview with a transboy; age: 18;3

The ability to change their gender on their official documents may be seen as imposing a binary phenotype on transgender individuals. Nevertheless, most adolescents thought that the concept gender is a continuum instead of a binary system, as this adolescent expressed:

“In my opinion the concept gender is a continuum. In my case it is clear, I am a woman, but I know various transgender individuals who feel they are in between men and women.” - Interview with a transgirl; age: 13;11

DISCUSSION

Using empirical methods this study aimed to explicate the considerations and opinions of gender dysphoric minors concerning the concepts of sex and gender, and the use of PS in GD. The interviews with the gender dysphoric adolescents were conducted in the context of a larger study on controversies surrounding PS in adolescents with GD. Besides the interviews with the adolescents, an extensive literature search was previously done as well as interviews with 36 professionals working in treatment teams worldwide (Vrouenraets et al., 2015). The data of the professionals enable us to compare their opinions with those of the adolescents.

Comparing the interviews of the adolescents with those of the professionals reveals that the adolescents and professionals do not agree about all topics. The lack of long-term data on possible side effects of the treatment for example was no problem for the adolescents, yet was a big issue for the professionals. In the interviews with the professionals, proponents remained cautious and opponents sceptical because of the fact that (long-term) risks and benefits of available treatments have not been fully established (Vrouenraets et al., 2015). One could explain the viewpoint of the adolescents by the fact that adolescence is a period in which short-term rewards are more important than long-term rewards, even when choosing for an immediate reward can mean a later loss or risk (Blakemore & Robbins, 2012; Crone & Dahl, 2012). However, the adolescents also showed that they seriously weighed the short- and long-term consequences, and consciously chose for the treatment. Furthermore, they showed a remarkable insight and altruism in their willingness to participate in research, which also meant they were able to look beyond their own short-term interests.

It is striking that several interviewed gender dysphoric adolescents gave arguments which were also mentioned by opponents among clinicians, for example doubts about the ability of adolescents to make decisions regarding medical treatment at the age of 12 or younger. The adolescents sometimes seemed to be even more cautious than some of the professionals. Several of the interviewed professionals work in treatment teams that use the Dutch guidelines, but are exploring the possibility of lowering the current age limit for early medical treatment. However, defining an appropriate age limit appeared to be difficult for the adolescents. They questioned the competence to take complex decisions

at a young age but also emphasize the importance of having the possibility to be treated with PS at the moment secondary sex characteristics of the natal sex develop. This made them feel setting an age limit as a dilemma.

A theme on which informants (both among professionals and adolescents) take diverging viewpoints regards the conceptualization of sex and gender in the media on television and on the internet. Some adolescents and professionals think positively about the increasing media-attention, others raise doubts about it. Some speculated that information on television shows and on the internet may have a negative effect and, for example, lead to medicalization of gender-variant behaviour (Vrouenraets et al., 2015). Furthermore, according to some informants, the media do not seem to show a representative picture of transgender individuals. According to them most transgender individuals who are shown in the media function well despite their gender dysphoric feelings, even though that is not always the case in real life. Furthermore, the picture of transgender individuals that is conveyed to the public seems to be much less varied and complicated than the existing broad spectrum of transgender phenomena (Kuyper & Wijzen, 2014). This image depicts transgender individuals as much more binary than seen in real life; a complete transition is for example not the ultimate goal for all transgender individuals (Beek, Kreukels, Cohen-Kettenis, & Steensma, 2015). If it is true that a stereotypical and binary picture is mostly shown in the media, this might contribute to more acceptance of transgender individuals in society. However, this is at the expense of an understanding by the public of the full range of transgender phenomena.

After a change in the law, sterilization is no longer a requirement for transgender individuals to be able to change their gender in official documents in the Netherlands. Most interviewed transboys thought that, after this change in the law, they would not choose to remove their ovaries and uterus because “it is not necessary anymore.” It should be noted that the requirement for transgender individuals to be able to change their legal gender is and was not the only reason for transgender individuals to remove their ovaries/uterus. Other reasons for desiring hysterectomy and/or oophorectomy are for example that transgender men may feel less female and more satisfied about their bodies after this type of surgery, may avoid problems with menstrual bleeding once PS is stopped or do not need to undergo investigations such as cervical smears to screen for cervical cancer. These reasons to undergo this type of surgery are discussed with the adolescents during the diagnostic and treatment phase. Yet, before the law change, many transgender individuals had their ovaries and uterus removed and may not have felt they had a true choice to undergo this surgery or not. Many may have felt forced to make the step in order to become their true gendered selves.

It is important to give voice to the gender dysphoric adolescents themselves, hearing their views on topics like gender, autonomy, and best interests, when discussing the use of PS in GD. As professionals publish their pleas for or against this treatment it only seems fair to add the views of those involved, the adolescents themselves, to the literature. This is important because otherwise professionals act upon assumptions on the adolescents' views, rather than on the actual considerations and opinions of the adolescents. This is illustrated by the fact that the adolescents seem to have more concerns about lowering age limits than professionals. In order to advance the ethical debate, we need to continue discussing the various themes based on research data in addition to mere opinions. If not based on empirical data, ideas on GD treatment may diverge even more, which eventually may lead to (even more) inconsistencies between the approaches recommended by clinicians across different centres.

There are strengths and weaknesses to the present study. The qualitative nature of the study made it possible to find out, in depth, the ways in which the adolescents think or feel about specific topics. Nevertheless, the considerations explicated in this study are solely from a relatively small sample of adolescents from the treatment team in Leiden, the Netherlands. The considerations of adolescents are likely to be different in other adolescents and in other countries or other clinics. Furthermore, all adolescents, except for one, started treatment with PS when they were older than 12, at an average age of 15 years and 10 months. This could have had an effect on the way these adolescents think about the current age limit of 12 years of age. These adolescents were never confronted with this limit which possibly did not make them feel the urge to lower the current age limit. It calls for studies among a larger group of adolescents who started treatment at younger ages and adolescents who were not treated with PS at all. Furthermore the adolescents in our study come from a society with a relatively high acceptance of transgender individuals (Keuzenkamp & Kuyper, 2013). Studies in other countries should be done, not only to investigate differences between minors that had different treatment regimens but also to investigate the relationship between their views and the culture they live in. Until more research data become available, the optimal timing of treatment for GD will remain unclear (Olson-Kennedy et al., 2016).

4

Assessing medical decision-making competence in transgender minors

Lieke J. J. J. Vrouwenraets
Annelou L. C. de Vries
Martine C. de Vries
Anna I. R. van der Miesen
Irma M. Hein

2021. *Pediatrics*, 148(6), e2020049643

This study was funded by 'Alliantie Fonds' of Amsterdam Public Health

ABSTRACT

Background: According to international transgender care guidelines, an important prerequisite abstract for puberty suppression (PS) is transgender adolescents' competence to give informed consent (IC). In society, there is doubt whether transgender adolescents are capable of this, which in some countries has even led to limited access to this intervention. Therefore, this study examined transgender adolescents' medical decision-making competence (MDC) to give IC for starting PS in a structured, replicable way. Additionally, potential associated variables on MDC, such as age, intelligence, sex, psychological functioning, were investigated.

Methods: A cross-sectional semistructured interview study with 74 transgender adolescents (aged 10-18 years; 16 birth-assigned boys, 58 birth-assigned girls) within two Dutch specialized gender identity clinics was performed. To assess MDC, judgements based on the reference standard (clinical assessment) and the MacArthur Competence Assessment Tool for Treatment (MacCAT-T), a validated semistructured interview, were used.

Results: Of the transgender adolescents, 93.2% (reference standard judgements; 69 of 74) and 89.2% (MacCAT-T judgements; 66 of 74) were assessed competent to consent. Intermethod agreement was 87.8% (65 of 74). Interrater agreements of the reference standard and MacCAT-T-based judgements were 89.2% (198 of 222) and 86.5% (192 of 222), respectively. IQ and sex were both significantly related to MacCAT-T total score, whereas age, level of emotional and behavioural challenges, and diagnostic trajectories duration were not.

Conclusions: By using the MacCAT-T and clinicians' assessments, 93.2% and 89.2%, respectively, of the transgender adolescents in this study were assessed competent to consent for starting PS.

INTRODUCTION

In December 2020, the High Court of Justice in London ruled that, in the United Kingdom, transgender minors aged ≤ 15 years are highly unlikely to fully understand the long-term effect of puberty suppression (PS; using gonadotropin-releasing hormone analogues (GnRHa)) and to give informed consent (IC) (Dyer, 2020b). Other countries and states have considered or applied similar age-based restrictions in access to this care as well (Walch et al., 2021). However, evidence regarding transgender minors' medical decision-making competence (MDC) was lacking until now. To our knowledge, the current study is the first to present empirical outcomes of assessment of transgender minors' MDC.

Transgender people have a feeling of discrepancy between their birth-assigned sex and gender identity (World Health Organization, 2022). In this article, the term '(birth-assigned) sex' is used for an anatomic or chromosomal determination, as opposed to gender, which refers to an internal sense of self as man, woman, another gender or no gender. When puberty starts, transgender minors have to deal with body changes they abhor. In the 1990s, the Dutch introduced treatment with PS, which allows transgender adolescents to further mature and accrue life experience before decisions are made regarding successive gender-affirming medical treatment (GAMT) with permanent physical changes (Cohen-Kettenis, Steensma, & de Vries, 2011; Delemarre-Van De Waal & Cohen-Kettenis, 2006; Hembree et al., 2017).

In the Netherlands, transgender adolescents undergo a diagnostic trajectory, including a psycho-diagnostic assessment and several monthly sessions with a mental health provider over a longer period of time (usually ~ 6 months), when assessing eligibility for PS. PS at early stages of puberty improves psychological functioning and ameliorates general functioning, and physical outcome may be better (Anacker et al., 2021; de Vries et al., 2011a; van der Miesen, Steensma, de Vries, Bos, & Popma, 2020). As far as currently known, the effects of this treatment are fully reversible when discontinued (Hembree et al., 2017). However, there are worries about the impact of PS on physical, cognitive, and psychosocial development and the capability of making decisions about this treatment with profound implications (e.g., regarding fertility) at this young age (Anacker et al., 2021; Chen et al., 2020; Kreukels & Cohen-Kettenis, 2011). Minors' MDC for interventions is a major issue in paediatric ethics. Therefore, according to the international guidelines, one of the criteria for transgender adolescents to start PS is having sufficient mental capacity to give IC (Coleman et al., 2012; Hembree et al., 2017). Of note, GnRHa are standard of care for treatment for children with precocious puberty (Carel et al., 2009).

Minors are a protected population and, in most circumstances, not accorded the legal right to consent. Local jurisdictions determine age limits for minors' alleged MDC, which vary

widely between countries (Hein et al., 2012; Stultiëns, Dierickx, Nys, Goffin, & Borry, 2007). Research reveals that minors who have not yet reached the legally set age for MDC often have the mental capacity to understand the implications of a decision (Hein et al., 2014). In contrast, minors may differ from adults by not yet having developed stable long-term goals in life and basing their decisions on values that might change (Cohen & Cohen, 1996).

Additionally, minors are not as likely as adults to consider the benefits and risks associated with a decision (Halpern-Felsher & Cauffman, 2001). In our study, to deal with discrepancies between local laws and international jurisdictions, we focused on adolescents' decision-making competence or capacity for giving consent regarding the decision to start treatment with PS, regardless of the legal age to give IC (alone or together with their parents). In the context of our study, legally, parents have to give consent when the child is aged <12 years; between the ages of 12 and 15 years, parents and child both have to give consent; and at age ≥ 16 years, the child is allowed to give consent independently.

MDC describes the capacities needed for making an autonomous medical decision (Grisso, Appelbaum, & Hill-Fotouhi, 1997). To reach MDC, a person needs to fulfil four criteria: (1) understand the information relevant to one's condition and the proposed treatment; (2) appreciate the nature of one's circumstances, including one's current medical situation and the underlying values; (3) reason about benefits and potential risks of the options; and (4) be able to express a choice (Appelbaum & Grisso, 1988). MDC is relative to a specific task and context. It is one of the three prerequisites for giving a valid IC, next to being well-informed and without coercion (Beauchamp & Childress, 2008; Grisso & Appelbaum, 1995).

In paediatric daily practice, MDC is generally assessed implicitly and in an unstructured way, which may lead to inconsistencies (Appelbaum, 2007). A study in which researchers reviewed 23 existing measures reveals that the MacArthur Competence Assessment Tool for Treatment (MacCAT-T) has the most empirical support for assessing MDC (Dunn, Nowrangi, Palmer, Jeste, & Saks, 2006; Grisso et al., 1997; Kim, Caine, Currier, Leibovici, & Ryan, 2001; Kim et al., 2007). The MacCAT-T proved reliable in assessing mental competence in adult patients with dementia, schizophrenia, and other psychiatric conditions (Cairns et al., 2005; Owen et al., 2008; Palmer et al., 2005).

The cognitive, emotional, and social abilities of minors develop over time and so do their decision-making capacities (Hein et al., 2012). Age is often considered to be the best determinant for assessing MDC (Dorn, Susman, & Fletcher, 1995). Some research reveals that 12 years is a common age to reach MDC (Billick, Burgert 3rd, Friberg, Downer, & Brunis-Solhkhah, 2001). Other research reveals that minors <12 years of age may be capable of

making well-considered decisions and that minors from the age of nine years are capable of understanding the issues involved in clinical trials (Billick, Edwards, Burgert, & Bruni, 1998; Mårtenson & Fägerskiöld, 2008). Contributing factors for MDC are intelligence and psychological functioning (Dorn et al., 1995; Grisso, & Appelbaum, 1998). People with limited cognitive capacities may have more difficulty understanding information (Grisso, & Appelbaum, 1998). Research suggests that psychiatric conditions and psychopathology might impair MDC (Cairns et al., 2005; Owen et al., 2008; Palmer et al., 2005).

Little research exists regarding minors' MDC (Hein et al., 2015d). Specifically, there is no empirical evidence on transgender adolescents' MDC to decide on PS. In clinical practice and policy making, age standards prescribed by law may have too much influence on the clinicians' assessments (Hein et al., 2015d). In addition, clinicians' assessments of MDC are influenced by their personal subjective views of what is in the adolescent's best interest (de Vries, Wit, Engberts, Kaspers, & van Leeuwen, 2010). The right balance needs to be struck between respecting transgender adolescents' autonomy and protecting adolescents who are not fully capable of making these decisions themselves (Appelbaum, 2007).

To fill the gaps in knowledge regarding transgender adolescents' MDC, in this cross-sectional semistructured interview study, we aimed to answer the following questions:

1. Are transgender adolescents competent to give IC for starting PS, according to the standard IC procedure and the MacCAT-T?
2. What is the intermethod agreement between MDC judgements based on the standard IC procedure and the MacCAT-T?
3. What is the interrater agreement regarding MDC judgements between raters using the standard IC procedure and the MacCAT-T?
4. To what extent are age, intelligence, psychological functioning, duration of the diagnostic trajectory, sex, and family situation associated with transgender adolescents' MDC regarding starting PS?

METHODS

Participants

Participants were transgender adolescents visiting the Centre of Expertise on Gender Dysphoria of the Amsterdam University Medical Centres, Location VUmc in Amsterdam, the Netherlands, between January 1, 2016, and December 31, 2017, or visiting the gender-identity clinic of Leiden University Medical Centre, Leiden University Medical Centre Curium, in Leiden, the Netherlands, between March 1, 2017, and December 31, 2017. The researchers identified the adolescents who were about to start PS through the medical

files, and the adolescents and their parents were invited by the involved clinician to participate. The study protocol was approved by the institutional review boards of the participating institutions. Written information was provided, and signed IC for participation was obtained from all participants and their parents.

All adolescents visiting the clinics were eligible for study participation; there was no selection process. Not speaking Dutch and being cisgender were exclusion criteria. In this study, no distinction was made in describing the gender identity of the participants other than being transgender. The adolescents who participated in the study were, as recommended by the Standards of Care, at least at Tanner stage 2 (Coleman et al., 2012). The clinics' protocols use PS until age 17 years to prepare for more definite affirming treatment by hormones and, in some individual cases, >17 years when creating rest and time for further gender-identity exploration are indicated. Seventy-four adolescents participated, whereas 206 eligible adolescents were not reached or did not want to or could not participate (figure 2). There were no significant differences between the participating and non-participating adolescents with regard to demographics (table 4).

Figure 2. Flowchart of adolescent participation

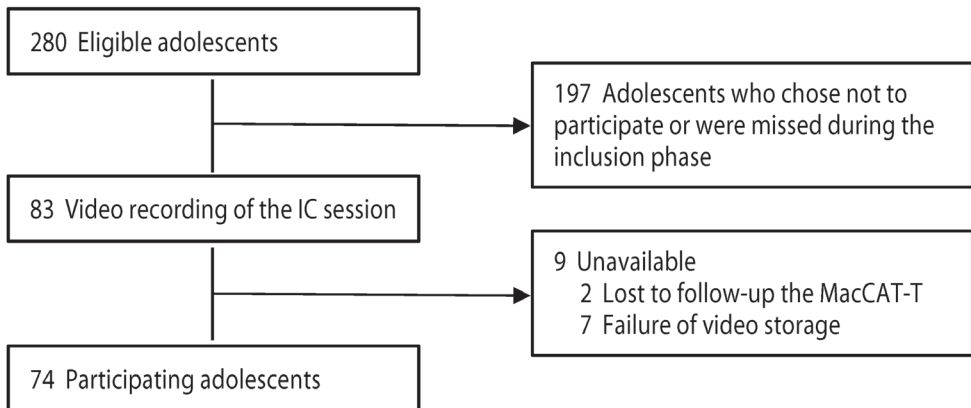


Table 4. Comparison of characteristics of participating and non-participating adolescents MacCAT-T

Variables	Participating adolescents	Non-participating adolescents	p-value
Age (in years)			.09
<i>n</i>	73 ^a	206	
M	14.71	15.18	
Range	10.63 - 18.34	10.10 - 18.36	
Total IQ			.65
<i>n</i>	70 ^b	195 ^c	
M	100.21	99.17	
Range	66 - 144	61 - 144	
Sex, <i>n</i> (%)			.39
Birth-assigned girl	58 (78.4)	151 (73.3)	
Birth-assigned boy	16 (21.6)	55 (26.7)	
CBCL's total problem <i>T</i> -score			.25
<i>n</i>	57 ^d	183 ^e	
M	60.42	58.78	
Range	42 - 77	34 - 80	
Duration of diagnostic trajectory (in months)			.43
<i>n</i>	73 ^a	206	
M	9.55	10.29	
Range	4 - 26	3 - 59	
Family situation, <i>n</i> (%)			.16
With both parents	39 (52.7)	128 (62.1)	
Other	35 (47.3)	78 (37.9)	

Age refers to age at the informed consent session; total IQ refers to full-scale intelligence quotient; CBCL refers to Child Behaviour Checklist.

^a Date of starting with puberty suppressing treatment was unknown for one participating adolescent.

^b Total IQ was missing of four participating adolescents.

^c Total IQ was missing of 11 non-participating adolescents.

^d CBCL's total problem *T*-score was missing of 17 participating adolescents.

^e CBCL's total problem *T*-score was missing of 23 non-participating adolescents.

Measures

Demographics

Adolescents' demographic characteristics obtained from the medical files were date of birth, sex, family situation, date of the first contact at the clinic, and date of the IC session. Family situation was categorized into (1) living with both parents and (2) other.

Medical decision-making competence

The MacCAT-T is a quantitative, semistructured interview used to assess the four MDC criteria and takes 15 to 20 minutes (Grisso et al., 1997; Appelbaum & Grisso, 1988). In this study, the Dutch version modified for children and adolescents was used (Hein et al., 2015c). In the current study, the disclosure of information was adapted to treatment with PS for transgender adolescents (Grisso et al., 1997; Hein et al., 2012; Hein et al., 2015d). Examples of interview-questions are “what would be possible consequences if you would choose to undergo this intervention, and what if you would not?”. The tool provides a total score and subscale scores for each of the four MDC criteria. An overall cut-off score for MDC is not provided. The assessor weighs the subscale scores, along with contextual information (e.g., substantial risks of treatment, far-reaching consequences, and whether there is support of caregivers), and judges MDC in each individual case. Recent research revealed that the four MDC criteria constitute a continuum or single trait in children (Hein et al., 2014).

Full-scale intelligence quotient

The full-scale intelligence quotient (IQ) was assessed by the Dutch Wechsler Intelligence Scale for Children in adolescents aged ≤ 16 years and by the Dutch Wechsler Adult Intelligence Scale in adolescents aged >16 years (Wechsler, 1997; Wechsler, 2005).

Child Behaviour Checklist

The parent-reported Child Behaviour Checklist (CBCL) was used to assess behavioural and emotional difficulties (Achenbach & Rescorla, 2001; Verhulst & van der Ende, 2013). The total-problem *T*-score was calculated as age standardized measure of total behavioural and emotional difficulties.

Procedures

Both gender identity clinics that participate in the study follow the Standards of Care and the Endocrine Society clinical practice guideline (Coleman et al., 2012; Hembree et al., 2017). The diagnostic trajectory, which is spread over a longer period of time, concludes with a session for signing a printed IC statement by adolescents and parents. This standard IC session was videotaped and used to establish the reference standard for MDC in this study (see below), similar to previous studies.^{16,35} After the IC session, the MacCAT-T interview was administered by one of the researchers, which was also videotaped, to provide the MacCAT-T-based judgements of MDC.

A panel of 12 experts (including child psychiatrists, paediatric endocrinologists, child psychologists, and master thesis medical students) was trained in judging MDC on the basis of the four criteria, which are currently considered the generally accepted reference standard (Carney, Neugroschl, Morrison, Marin, & Siu, 2001; Etchells et al., 1999; Hein et al., 2014; Kim et al., 2001).

Reference standard

Of each IC video, three MDC judgements were performed: two by experts and one by the clinician involved in the diagnostic trajectory. These judgements were used for establishing the reference standard.

MacArthur Competence Assessment Tool for Treatment (MacCAT-T)

Each MacCAT-T video was also judged by three different experts, who rated the subscale scores, total score, and their MDC judgement. These assessments were used for the MacCAT-T-based judgements. The experts received the videos in random order, blinded to other judgements or adolescents' characteristics.

Statistical analyses

All statistical analyses were performed by using SPSS, version 26 (IBM Corporation, 2019). Both for the reference standard and MacCAT-T-based judgements, MDC was considered present when at least two out of three judgements were positive (Hein et al., 2015d).

The proportion of adolescents assessed positive on MDC was described as a raw percentage. The correlation between the reference standard and MacCAT-T-based judgements, as a measure of intermethod agreement, was also described as a raw percentage. Interrater agreement of the three reference standard and three MacCAT-T-based judgements, which is the overall percentage of mean fractions of agreement between the three raters, were calculated as raw percentages.

To discern potential associations between MacCAT-T total-scale scores and our main variables of interest (age, intelligence, CBCL total-problem *T*-score, and duration of the diagnostic trajectory), demographic characteristics were identified as relevant control variables (e.g., gender, family situation, and clinic location) as a first step. Second, multiple linear regression was used to identify variables correlated to the MacCAT-T total scores with pairwise deletion of missing variables.

RESULTS

Baseline characteristics

Participants' baseline characteristics are listed in table 5.

Table 5. Descriptive statistics for characteristics of the participants

Variables	Birth-assigned boys	Birth-assigned girls	Total	<i>p</i> -value
Age (in years)				.15
<i>n</i>	16	58	74	
M	14.02	14.87	14.69	
Range	12.02 - 17.11	10.63 - 18.34	10.63 - 18.34	
Total IQ				.82
<i>n</i>	15	55	70 ^a	
M	99.47	100.42	100.21	
Range	82 - 131	66 - 144	66 - 144	
CBCL's total problem <i>T</i> -score				.91
<i>n</i>	13	48	61 ^b	
M	60.62	60.94	60.87	
Range	44 - 72	42 - 77	42 - 77	
Percentage in clinical range (%) ^c	38.5	43.7	42.6	0.73
Duration of diagnostic trajectory (in months)				.64
<i>n</i>	16	58	74	
M	9.25	8.69	8.81	
Range	4 - 18	2 - 26	2 - 26	
Family situation, <i>n</i> (%)				.71
With both parents	8 (50.0)	32 (55.2)	40 (54.1)	
Other	8 (50.0)	26 (44.8)	34 (45.9)	

Age refers to age at the informed consent session; total IQ refers to full-scale intelligence quotient; CBCL refers to Child Behaviour Checklist.

^a Total IQ was missing of four participants.

^b CBCL total-problem *T*-score was missing of 13 participants.

^c Clinical range: $t \geq 64$ (Achenbach & Rescorla, 2001).

Medical decision-making competence

After the reference standard and MacCAT-T-based judgements, respectively, 93.2% (69 of 74) and 89.2% (66 of 74) of the adolescents were positive on MDC regarding starting PS. Table 6 shows characteristics of participants who were judged not competent.

Table 6. Characteristics of participants judged not competent using the reference standard and/or MacCAT-T

Participant	Assigned sex	Reference standard	MacCAT-T	Age (in years)	Total IQ	Duration of diagnostic trajectory (in months)
1	Female	Incompetent	Incompetent	12	69	7
2	Male	Incompetent	Incompetent	12	84	10
3	Female	Competent	Incompetent	11	93	15
4	Male	Competent	Incompetent	13	Missing	5
5	Male	Competent	Incompetent	12	96	12
6	Female	Competent	Incompetent	12	79	8
7	Female	Competent	Incompetent	17	66	10
8	Female	Competent	Incompetent	11	79	10
9	Female	Incompetent	Competent	11	Missing	7
10	Male	Incompetent	Competent	12	101	8
11	Female	Incompetent	Competent	10	110	13

Age refers to age at the informed consent session; total IQ refers to full-scale intelligence quotient.

Intermethod agreement

The reference standard and MacCAT-T-based judgements correlated in 87.8% (65 of 74) of the cases (table 7).

Table 7. Percentage competent / incompetent according to the reference standard based judgements and the MacCAT-T based judgements of transgender adolescents' medical decision-making competence

Reference standard (<i>n</i> = 74)	MacCAT-T (<i>n</i> = 74)		
	Competent	Incompetent	Total
Competent (<i>n</i>)	85.1% (63)	8.1% (6)	69
Incompetent (<i>n</i>)	4.1% (3)	2.7% (2)	5
Total	66	8	74

MacCAT-T refers to MacArthur Competence Assessment Tool for Treatment.

Interrater agreement

The interrater agreement of the reference standard and MacCAT-T-based judgements for the three experts were 89.2% (198 of 222) and 86.5% (192 of 222), respectively.

Variables related to MacCAT-T scores

Sex was significantly associated with MacCAT-T score ($t[72] = -3.045$; $p = .003$); birth-assigned girls showed a higher total score. Both family status and clinic location were not significantly associated with MacCAT-T score. Therefore, a multiple linear regression analysis was conducted with only sex as control variable and age, intelligence, psychological functioning, and duration of the diagnostic trajectory as the main variables of interest, with the MacCAT-T score as the dependent variable. Table 8 shows the results of the multiple linear regression analysis. A significant regression equation was found ($F(5,52) = 3.685$; $p = .006$). Sex and full-scale intelligence quotient (IQ) are both significantly related to the MacCAT-T score when each one was corrected for the other three variables (respectively, $\beta = 3.636$; $t(52) = 2.685$; $p = .010$; and $\beta = 0.088$; $t(52) = 2.381$; $p = .02$). Age at the IC session, CBCL total-problem T -score and duration of the diagnostic trajectory were not significantly correlated.

Table 8. Multiple linear regression analysis comparing the effect of age, full-scale intelligence quotient, psychological functioning, duration of the diagnostic trajectory associated and sex with the MacCAT-T score

	B	p-value	95% Confidence Interval for B	
			Lower bound	Upper bound
Step 1:				
Constant	29.177	-	24.211	34.142
Sex	3.636	.01*	0.923	6.348
Step 2:				
Constant	18.560	-	4.977	32.143
Age	0.476	.08	-0.056	1.008
Total IQ	0.088	.02*	0.014	0.161
CBCL's total problem T -score	-0.080	.19	-0.201	0.040
Duration of diagnostic trajectory	0.056	.67	-0.210	0.322

Age refers to age at the informed consent session; total IQ refers to full-scale intelligence quotient; CBCL refers to Child Behaviour Checklist; '-' refers to not applicable.

* p -value $< .05$

DISCUSSION

The current study revealed that 93.2% and 89.2% of the transgender adolescents who were about to start PS and were participating in this study were competent to give IC on the basis of the standard clinical assessment and when using the MacCAT-T interview, respectively. This is a reassuring finding, which reveals that guidelines that require understanding the pros and cons of the treatment and capacity for IC for starting PS are followed for these participants (Coleman et al., 2012; Hembree et al., 2017). This study was performed after several sessions with adolescents and parents aimed at obtaining understanding of the consequences of PS, including not only the short-term, with regard to suppression of further feminization or virilization, but also long-term considerations of bone development, surgical options, and fertility (Di Ceglie, 2018).

This study further looked into several variables potentially associated with MDC. Of the examined variables, higher full-scale intelligence quotient (IQ) and sex (birth-assigned girls) were associated with higher MacCAT-T scores. The association of a higher intelligence with MDC is in line with other research (Hein et al., 2015c; Miller, Drotar, & Kodish, 2004). The birth-assigned girls in our study might have had a more advanced puberty compared with the birth-assigned boys, which might be related to a deeper understanding of the consequences of PS (Koerselman & Pekkarinen, 2017). Contrary to our expectations and earlier research, age was not correlated to MacCAT-T scores in this study. Although the participants seem like a representative sample, it may be too homogeneous, with regard to age, to detect a significant effect because the sample included few participants aged ≤ 11 years. Most research suggests that MDC is reached little before the age of 12 years (Billick et al., 1998; Hein et al., 2014; Mårtenson & Fåggerskiöld, 2008). Finally, no association between MDC and duration of the diagnostic trajectory, and between MDC and behavioural and/or emotional difficulties was found. This finding was also against our expectation because psychological difficulties can interfere with MDC. However, one of the criteria for starting PS applied at the Dutch gender identity clinics is 'having no interfering psychosocial difficulties' (Coleman et al., 2012; Hembree et al., 2017). Therefore, by protocol, adolescents with severe psychosocial difficulties might have been referred for appropriate treatment before deciding on PS.

The results of this study confirm the feasibility of the Dutch version of the MacCAT-T for children and adolescents in assessing transgender adolescents' MDC; the interrater agreement of the reference standard and MacCAT-T-based judgements were both high (respectively, 89.2% and 86.5%). Furthermore, the results of this study offer first indications of validity of the MacCAT-T for judging transgender adolescents' MDC (intermethod agreement was 87.8%), and the MacCAT-T could therefore be used in clinical practice when MDC assessment is difficult. The MacCAT-T should not necessarily replace (a part

of) the usual implicit assessment of MDC. However, in individual cases of doubt on MDC, the MacCAT-T could be used as a structured tool to underpin MDC assessment more objectively. Therefore, the tool will not be a barrier for access to care but can be used for due diligence. In the MacCAT-T, contextual information is weighted in the assessment, which may include parental support. It is expected that these results will be generalizable to other clinics because findings are in line with other research on the use of the MacCAT-T in minors (e.g., in a population deciding on predictive genetic testing, in minors with HIV infection, and in a sample of adolescents with psychiatric conditions) (Chenneville et al., 2014; Hein et al., 2015d; Mandarelli et al., 2017). Findings regarding the age for established MDC are congruent.

Although the study results reveal that most adolescents are considered competent to give IC for starting PS, nevertheless 6.8% to 10.8% are not, respectively, reference standard-based and MacCAT-T based. In all of these 11 adolescents assessed incompetent, except for one, the involved clinician had no doubts about the MDC. Possibly, the more positive judgement by these clinicians may be explained by their judgement on the basis of several sessions and not on a single assessment. In the one adolescent that was assessed incompetent by the involved clinician, the clinician added that she considered the adolescent's mother competent to give (proxy) consent. So, in cases in which there is doubt regarding adolescents' MDC, clinicians may more heavily depend on the parents' IC (Giordano et al., 2021). Subsequently, time on PS could more explicitly be used to prepare MDC for treatment with lasting effects of gender-affirming hormones (GAH).

This is in line with statements in a recent qualitative study that the best interest for an individual should be taken into account when deciding whether to start PS (Vrouenraets et al., 2015). Other research reveals also that MDC assessment is regularly influenced by the clinicians' ideas of what is in the child's best interest (de Vries, de Wit, Engberts, Kaspers, & van Leeuwen, 2010). This might mean that some clinicians start PS in transgender adolescents who are assessed incompetent to consent on the basis of the principle of best interest.

In addition, the results of the current study do not answer questions on how to respect the developing autonomy of incompetent adolescents ethically. In the aforementioned qualitative interview study, some clinicians stated that transgender minors should at least partially depend on their parents to make decisions regarding PS (Vrouenraets et al., 2015). It could be that the parents' role and responsibility should be more pronounced when an adolescent is deemed incompetent to consent (Giordano et al., 2021).

Of note, the focus of this study was not on the putative association between MDC and having no regrets later in life about the decision to start PS. Competent transgender adolescents who begin PS may still potentially have regrets about the decision.

There are strengths and limitations to the current study. The study's standardized nature provided a reproducible and interrater-reliable method for assessing MDC in transgender adolescents who were about to start PS. Nevertheless, because of the study's design to only include adolescents who were about to start PS after a diagnostic trajectory, the sample contained relatively few adolescents aged <12 years, with low intelligence, showing serious (interfering) psychiatric conditions or psychopathology, and relatively few birth-assigned boys. Additionally, adolescent's Tanner stage was not investigated in this study as a potential associated variable on MDC. Furthermore, on the basis of the current results, one cannot conclude with certainty whether the exploration and explanation during the diagnostic trajectory is essential in helping the transgender adolescents becoming competent to consent to PS or that MDC was already reached before the diagnostic trajectory.

In future work, researchers should especially focus on transgender adolescents aged <12 years starting this treatment, particularly birth-assigned girls who may benefit from PS as early as nine years of age. Additional research is needed for adolescents with lower intelligence, serious developmental conditions, or psychopathology, for birth-assigned boys, and participants in early stages of puberty. More research is needed regarding the question what to do when an adolescent is incompetent to consent to the treatment; for example, what are the parents' and the involved clinician's role and responsibility in such a situation? In addition, qualitative research focused on the role of MDC in clinical practice and the principle of best interest are encouraged.

CONCLUSION

It is reassuring that the majority of the transgender adolescents participating in this study seem to have thoroughly thought about PS, understand what PS involves, and are deemed competent to decide. However, this might not be similar for all other contexts, particularly because our study cohort had extensive and thorough diagnostic evaluation before the MDC assessment as opposed to adolescents without this support. Additionally, the study results indicate feasibility and validity of the MacCAT-T in clinical practice. Nevertheless, as long as there are only limited data on transgender adolescents' MDC regarding starting PS, an individualized approach is highly important for this group.

5

Medical decision-making competence regarding puberty suppression: perceptions of transgender adolescents, their parents and clinicians

Lieke J. J. J. Vrouwenraets
Annelou L. C. de Vries
Marijn Arnoldussen
Sabine E. Hannema
Ramón J. L. Lindauer
Martine C. de Vries
Irma M. Hein

2022. *European Child & Adolescent Psychiatry*, 1-19

This study was funded by 'Fonds Wetenschappelijk Onderzoek Seksualiteit' (FWOS, projectnumber 18.008)

ABSTRACT

According to international transgender care guidelines, transgender adolescents should have medical decision-making competence (MDC) to start puberty suppression (PS) and halt endogenous pubertal development. However, MDC is a debated concept in care for transgender adolescents and little is known about the transgender adolescents', their parents', and clinicians' perspectives on this. Increasing our understanding of these perspectives can improve transgender adolescent care. A qualitative interview study with adolescents attending two Dutch gender identity clinics (eight transgender adolescents who proceeded to gender-affirming hormones (GAH) after PS, and six adolescents who discontinued PS) and 12 of their parents, and focus groups with ten clinicians was conducted. From thematic analysis, three themes emerged regarding transgender adolescents' MDC to start PS: (1) challenges when assessing MDC, (2) aspects that are considered when assessing MDC, and (3) MDC's relevance. The four criteria one needs to fulfil to have MDC - understanding, appreciating, reasoning, communicating a choice - were all, to a greater or lesser extent, mentioned by most participants, just as MDC being relative to a specific decision and context. Interestingly, most adolescents, parents and clinicians find understanding and appreciating PS and its consequences important for MDC. Nevertheless, most state that the adolescents did not fully understand and appreciate PS and its consequences, but were nonetheless able to decide about PS. Parents' support of their child was considered essential in the decision-making process. Clinicians find MDC difficult to assess and put into practice in a uniform way. Dissemination of knowledge about MDC to start PS would help to adequately support adolescents, parents and clinicians in the decision-making process.

INTRODUCTION

The World Professional Association for Transgender Health (WPATH) Standards of Care (7th version) and the Endocrine Society clinical practice guideline on care for transgender children and adolescents recommend treatment with puberty suppression (PS; using gonadotropin-releasing hormone analogues (GnRHa)) provided that certain criteria are fulfilled⁴ (table 3 which can be found at page 14 shows the diagnostic criteria for treatment with PS for adolescents) (Coleman et al., 2012; Hembree et al., 2017). It is recommended to start PS when, among other criteria, adolescents suffer from an intense and long-lasting pattern of gender dysphoria/gender incongruence and after they first exhibit physical changes of puberty (at least Tanner stage 2). The aim of using PS in this context is to suppress, in a reversible manner, further development of secondary sex characteristics to allow the adolescent more time and rest to explore their gender before decisions are made on gender-affirming hormones (GAH) with more irreversible effects. Besides, it prevents psychological distress associated with the undesired endogenous pubertal development, as several adolescents stated in an interview study regarding the function of PS (Vrouenraets, de Vries, Hein, Arnoldussen, Hannema, & de Vries, 2022b). In addition, the physical outcome may be more satisfactory when using PS in the early stages of puberty because some surgeries, such as mastectomy, may then not be necessary or less invasive (i.e. periareolar rather than inframammary approach) because the development of secondary sex characteristics is prevented (van de Grift et al., 2020). Currently, the evidence base for the positive implications of treatment is still limited and treatment teams applying PS may experience feelings of unease (Vrouenraets et al., 2015). Their concerns regard the lack of data on its impact on physical, psychosocial, and cognitive development in the long-term, and the consequences for fertility (Chen et al., 2020; Laidlaw, van Meter, Hruz, van Mol, & Malone, 2019b). In an interview study, clinicians report worries about the risk of regret and the lack of long-term data on possible side effects of PS (Vrouenraets et al., 2015). Transgender adolescents themselves express some hesitations to start treatment with PS too, e.g. about the ability of adolescents to make informed decisions regarding medical treatment at the age of 12 or younger (Vrouenraets, Fredriks, Hannema, Cohen-Kettenis, & de Vries, 2016). Research shows that transgender people, after sex reassignment, have significantly higher risks for suicidal behaviour, psychiatric morbidity, and mortality compared to the general population (Dhejne et al., 2011; Wiepjes et al., 2020). Nevertheless, it is unknown whether these results are the same for transgender people who started treatment with PS in the early stages of their puberty. Besides, it is

4 According to the WPATH Standards of Care and the Endocrine Society clinical practice guideline, transgender adolescents undergo a diagnostic trajectory with a psychologist or psychiatrist over a longer period of time in order to assess eligibility for PS, discusses the benefits and potential risks of treatment, and be able to make a shared decision in a multidisciplinary team (adolescent, parents, clinicians).

good to keep in mind that these studies do not tell us anything about the exact causes of these increased risks; some of the outcomes might be related to, for example, transgender people's experiences of living in a discriminatory and rejecting society (i.e. minority stress) instead of solely being related to post-surgical outcomes (e.g. Poštuvan, Podlogar, Šedivy, & Leo, 2019).

Adolescents may present or be diagnosed with gender dysphoria during or after the completion of endogenous puberty and may therefore start PS at various stages of pubertal development. Most adolescents who start treatment with PS subsequently start treatment with GAH and surgery afterwards (Brik, Vrouenraets, de Vries, & Hannema, 2020). Some adolescents discontinue their PS treatment. Of the latter group, most no longer wish gender-affirming medical treatment (GAMT), while some commence treatment with GAH and/or surgery later in life, such as in adulthood (Brik et al., 2020). Besides, providing solely psychological support, and see if adolescents can accept themselves without any medical intervention, is always considered when working according to the international guidelines too (Coleman et al., 2012; Hembree et al., 2017). Research shows that about 22 percent of the minors referred to a Dutch specialized gender identity clinic do not start affirmative medical treatment, being PS and/or GAH (Arnoldussen et al., 2020; Arnoldussen et al., 2022b).

As far as currently known, the effects of PS on the development of secondary sex characteristics and gonadal function are reversible when discontinued (Hembree et al., 2017). Nevertheless, transgender adolescents who start PS at a young age and subsequently start treatment with GAH and undergo a gonadectomy, may not be able to pursue fertility preservation since these adolescents never undergo their endogenous puberty (Brik et al., 2019; Health, 2021; Hudson, Nahata, Dietz, & Quinn, 2018). On the other hand, one should keep in mind that refraining from PS could be harmful as well, with potential life-long psychological, medical, and social consequences, such as personal physical discomfort, stigmatization, and difficulties with social integration and social function (de Vries et al., 2021; Giordano, 2008b; Giordano & Holm, 2020; Kreukels & Cohen-Kettenis, 2011). So, these young adolescents make decisions that may have life-long consequences. Even though it is recommended to involve parents when adolescents decide on starting PS, the issue whether these adolescents are capable of making these decisions is an important one (Coleman et al., 2012; Byne et al., 2012). According to international guidelines, one of the criteria for treatment with PS is that adolescents are competent to give informed consent (Coleman et al., 2012; Hembree et al., 2017). However, in society, there is doubt about this competence (e.g. Baron & Dierckxsens, 2021; d'Abrera et al., 2020; Giordano et al., 2021; Health, 2021; Levine, 2019; Levine, Abbruzzese, & Mason, 2022; Pang et al., 2021). Furthermore, both transgender adolescents themselves and clinicians mention medical decision-making competence (MDC) as one of the main topics in the debate regarding treatment with PS (Kerman et al., 2021; Vrouenraets et al., 2015; Vrouenraets et al., 2016).

MDC describes the capacities that a person needs to make an autonomous medical decision (Grisso et al., 1997). To have MDC, one needs to fulfil the following four criteria: (1) understanding the information relevant to one's condition and the proposed treatment; (2) appreciating the information and relating it to one's circumstances including one's current medical situation and one's values; (3) reasoning about benefits and potential risks of the options; and (4) communicating a choice (Appelbaum & Grisso, 1988). MDC is relative to a specific decision and context. It is one of the three prerequisites to give valid informed consent, besides being well-informed and without coercion (Beauchamp & Childress, 2008; Grisso & Appelbaum, 1995).

In December 2020, the High Court of Justice in London ruled that transgender minors under the age of 16 are highly unlikely to fully understand the long-term effects of PS, and therefore are not competent to decide on treatment with PS (Dyer, 2020a). As a result of this verdict transgender adolescents in England could no longer start PS before age 16 unless a court order was obtained (Dyer, 2020b). However, in September 2021 the Court of Appeal overturned the High Court's ruling of December 2020 (Thornton, 2021). Furthermore, in Sweden paediatric endocrinologists stopped providing PS to newly referred transgender adolescents in May 2021 because of, among others, concerns regarding harmful long-term consequences (Naiingolan, 2021). In summary, adolescents' MDC to start PS is and has been under discussion for some time among both advocates and opponents of the use of PS in transgender adolescents (e.g. Armitage, 2021; de Vries et al., 2021; Moreton, 2021; Pang et al., 2021; Wheeler, 2021).

Adolescents' MDC has often proved difficult to assess and is usually evaluated implicitly in clinical settings (Hein et al., 2015b). Additionally, there is little empirical evidence on transgender adolescents' competence to decide on PS. To our knowledge, there is only one study, from the Netherlands performed in our centres, that has examined this by a structured replicable interview. That study shows that the vast majority (89%) of transgender adolescents (aged 10-18 years) about to start PS treatment are competent to consent to this treatment (Vrouenraets et al., 2022b).

Little research has examined the ideas and considerations of adolescents themselves and their parents regarding adolescents' MDC to start PS. An interview study showed that clinicians stated that they find it important that the adolescents mature a little further during the period they receive PS so that they will be better able to decide about proceeding to GAH and carefully consider their decision's consequences. This implies that these clinicians assume that the adolescents, when they decide on PS, are not always competent yet to decide on GAH (Vrouenraets et al., 2022b). Insight into the stakeholders' perceptions of adolescents' MDC will help to further improve care and support for adolescents in their decision-making process. Therefore, we performed an interview and focus group study to

investigate the perceptions of transgender adolescents who proceeded to GAH after PS, adolescents who discontinued treatment with PS, their parents, and clinicians regarding transgender adolescents' MDC concerning PS.

METHODS

Participants

The interviews and focus groups were conducted in the context of a larger study on transgender adolescents' competence to consent to PS and the function of this treatment. Study methods are described in full in the article about the perceptions of the various informants on the function of PS (Vrouenraets et al., 2022b). Briefly, transgender adolescents who proceeded to GAH after treatment with PS ('continuers'), adolescents who discontinued treatment with PS ('discontinuers'), and their parents were recruited from the gender identity clinics in Amsterdam and Leiden between January and September 2019. The informants were interviewed using a topic list (see Appendix B, which can be found at page 223) to explore their considerations and experiences. The same topics were discussed in focus groups with clinicians of the two Dutch gender teams.

Semi-structured individual interviews were conducted with 14 adolescents and 12 parents. The informants consisted of:

1. Eight transgender adolescents who were treated with PS and subsequently with GAH;
2. Six adolescents who had been treated with PS and had discontinued this treatment;
3. Eight parents of adolescents who were treated with PS and subsequently with GAH;
4. Four parents of adolescents who had discontinued treatment with PS.

Inclusion criteria for the adolescents who had continued treatment (group 1) were: (a) diagnosis of gender dysphoria according to DSM-IV or DSM-5, depending on which version of the DSM was used at the time of diagnosis (American Psychiatric Association, 2013), (b) had started PS at age 10-15 years, (c) had used PS for at least 12 months, (d) had used GAH for at least six months, and (e) age at the time of the interview between 15 and 20 years. The aim was to have at least as many adolescents in group 1 as in group 2. Therefore, thirteen consecutive adolescents were asked to participate when they attended their regular follow-up appointment. Eight adolescents agreed to participate. Five adolescents declined for various reasons.

Inclusion criteria for the adolescents who had discontinued treatment (group 2) were: (a) diagnosis of gender dysphoria according to DSM-IV or DSM-5, depending on which version of the DSM was used at the time of diagnosis (American Psychiatric Association, 2013), (b) had started PS at age 10-17 years (a wider age range was chosen for those that discontinued PS to allow the inclusion of as many participants as possible given the limited

number of individuals that discontinued PS), and (c) had discontinued PS treatment. Out of 1015 adolescents diagnosed with gender dysphoria between 2000 and 2018 at the Amsterdam or Leiden gender identity clinic, twenty adolescents in total were eligible. Eight adolescents could not be reached, mostly because their contact details were no longer up to date. One was not contacted because he had previously indicated that he did not want to be approached for research purposes. Two adolescents were not contacted because their clinician thought this was inappropriate due to, among others, comorbid mental health difficulties. Nine adolescents were asked to participate. Two adolescents declined without giving a reason, one parent did not want her child to participate because she did think that was not in the child's best interest, and six adolescents agreed to participate. Characteristics of the two groups of adolescents are presented in table 9.

Table 9. Characteristics of participating adolescents

Variables	Adolescents who discontinued treatment	Adolescents who continued treatment
<i>n</i>	6	8
Birth-assigned girls	5 ^a	4
Birth-assigned boys	1 ^b	4
Age during interview (median; range) (years)	17.5; 14-27	17.9; 15-18
Age when visiting gender identity clinic for the first time (median; range) (years)	14.3; 11-15	11.3; 10-13
Age start PS (median; range) (years)	15.2; 12-17	12.3; 10-14
Duration of PS (median; range) (months)	10; 1-14	35; 21-48
Duration diagnostic trajectory before starting PS treatment (median; range) (months) ^c	10; 6-22	9; 6-12
Full-scale IQ (median; range)	100; 98-124	104; 76-132

PS refers to treatment with puberty suppression.

^a Two adolescents identified as transboy, one as a-gender, one as genderfluid, and one as cis-gender girl at the time of the interview.

^b Gender identity at the time of the interview: a-gender.

^c Diagnostic trajectory before starting PS treatment; In the Netherlands, transgender adolescents undergo a diagnostic trajectory, consisting of psycho-diagnostic assessment and several sessions with a mental health provider over a longer period of time, when assessing eligibility for PS.

The parents of all interviewed adolescents who continued treatment were asked to participate (group 3). Eight parents (seven biological mothers and one biological father) agreed. Four parents (group 4; three biological mothers and one adoptive mother) of adolescents who had discontinued treatment were asked to participate in the study and all agreed. The other parents were not asked because of logistic reasons (e.g. they could not be reached by phone in time prior to the appointment).

In addition, two focus groups with clinicians working at the two treatment teams were held. The informants were purposefully selected based on their discipline (all different disciplines working within both teams participated to assure representativeness for the complete treatment team; i.e. three child and adolescent psychiatrists, four child and adolescent psychologists and three paediatric endocrinologists).

Procedure

Two authors of this study conducted the interviews. Both had interview experience and worked as a clinician at one of the gender identity clinics (MA and LV). They had not been involved in the diagnostic assessments of the adolescents they interviewed. Initial interview questions were formulated after review of the relevant literature and discussion within the research team involving all authors. The interview guide contained no closed-ended questions (see Appendix B, which can be found at page 223).

One of the authors (MV) facilitated the two focus groups. During the focus groups the questions asked in the interviews were presented along with several anonymous quotes from the interviews to get the conversation started. The participants were asked whether they agreed with and/or identified with the quotes. Furthermore, the participants were invited to express possible other views they held on these topics.

All interviews and focus groups were conducted in Dutch, and were audio-taped and transcribed verbatim. Written informed consent for participation and tape recording was obtained before each interview and each focus group. The study was approved by the institutional review board of the Amsterdam University Medical Centres, location VUmc, and the Leiden University Medical Centre.

Analysis

Data analysis was based on hermeneutic analysis (Miles & Huberman, 1994; Stake, 2005). After an initial open reading of the data, two of the authors presented some preliminary (sub)themes (MA and LV). Besides, one of these authors analysed the transcripts by selecting representative quotations for each of the defined themes, taking care to draw quotations from all data sources. Then, the same two authors conducted an additional round of analyses to assess whether the (sub)themes enabled them to accurately subdivide the outcome of the data. They also re-analysed the transcripts to select representative quotations. Then, through a deliberative process, the authors redefined the initial (sub) themes until they reached a consensus. The quotations were initially translated from Dutch into English by one of the authors (LV). The other authors, who are all bilingual, checked, and if necessary, revised these translations (they were also provided with the original Dutch quotations).

RESULTS

From the interviews and focus groups, 10 themes emerged regarding transgender adolescents' MDC to start PS. These 10 themes can be merged into three main themes: (1) challenges when assessing MDC to start PS, (2) aspects that are considered when assessing the adolescent's MDC, and (3) relevance of MDC. Representative quotations are presented to illustrate the themes identified.

Challenges when assessing medical decision-making competence to start puberty suppression

During the interviews and focus groups the informants mentioned several aspects that challenged the assessment of MDC to start PS. Six subtopics further emerged from the data.

Understanding and appreciating consequences of puberty suppression

Most adolescents and parents mentioned that certain aspects of (the impact of) the treatment simply cannot be understood and appreciated by adolescents below a certain age.

"I think I had thought about it [starting treatment with puberty suppression or not starting this treatment] pretty well. But as a 12 or 13 year-old, you cannot really judge what it is all about. So I had thought about it [starting the treatment or not], but only as much as I was able to at the time [I decided to start with the treatment]." - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

"It does not really mean much to a 12 year-old when you're talking about osteoporosis. She [my daughter] understood [what osteoporosis meant], but she thought 'what does it matter', we'll see about that later." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

Some adolescents, both continuers and discontinuers, wondered whether they were able to understand and appreciate the consequence of possible loss of fertility if they were to proceed to GAH and possibly gonadectomy, and whether they were able to carefully consider the possibility to freeze sperm or store oocytes before they started the treatment with PS. Some adolescents stated that during the period they were treated with PS, they started to realise what the impact of some consequences could be. Worth mentioning is that one parent whose child froze sperm mentioned the impact which the process of fertility preservation had on her child and on herself, instead of the impact of the possible loss of fertility.

“The first few months I was very happy with it [the inhibition of secondary sexual characteristics] until I realised what if I will not be fertile anymore.” - Interview with an assigned female at birth who had discontinued PS; age at start PS: 17.0; age at discontinuation PS: 17.9; age at interview: 27.8

“At the moment I know that I would like to have children when I grow older [while at the time I made the decision regarding starting treatment with puberty suppression, I did not have a desire to have children] [...] That’s the only thing I wonder about, whether I was able enough to make that decision at the time.” - Interview with an assigned female at birth who had discontinued PS; age at start PS: 17.0; age at discontinuation PS: 17.9; age at interview: 27.8

“Before she [my daughter] started treatment with puberty suppression, she had frozen sperm. I found that very intense. Ehm... for her too of course. [...] I thought it had quite an impact on such a young child, who had to go into that room to fill up a jar [with sperm]. [...] I found that quite difficult to deal with [as a parent].” - Interview with a parent of a transgirl who continued PS; age at start PS: 14.2; age at interview: 17.9

The clinicians mentioned several consequences of PS which give them a feeling of unease when treating adolescents with PS. One of these consequences, a concern that all clinicians shared and which was mentioned by adolescents and parents too, is the possible loss of fertility if adolescents proceed to GAH and possibly gonadectomy.

“I think that the part regarding wanting to have children is a tricky one. They [the adolescents] just cannot understand and appreciate that [the impact of possible infertility].” - Focus group with clinicians

The clinicians, just as most adolescents and parents, stated that not being able to understand and appreciate the impact of certain consequences of PS is inherent to the adolescent’s age and/or developmental stage, for example, the possible consequence of loss of fertility for one’s future life and relationships. Furthermore, they stated that even some adults are unable to understand and appreciate the impact of such consequences.

“How can you leave such a choice [whether or not you want biologically related children when you are older] to these children?” - Focus group with clinicians

“That [possible infertility due to treatment with puberty suppression and subsequent gender-affirming hormones and/or surgery] is a very complicated one. As if children of that age [12 or 13 years old] can even begin to imagine what it [infertility] really implies.” - Focus group with clinicians

Apart from the possible loss of fertility, adolescents, both continuers and discontinuers, parents, and clinicians mentioned other consequences of PS that are difficult to understand and appreciate for adolescents prior to the start of treatment. For example, several adolescents mentioned that they had not realised their peers would undergo pubertal development while they stood 'still' as their puberty was suppressed and that they found this difficult to cope with. This had a negative psychological impact.

"I did have the feeling that I stood still while the rest [my peers who did go through pubertal development] went on [...] [Before starting the treatment with puberty suppression] I had not thought very much about what that could do to you mentally. [...] I was quite depressed during that time. And [...] I think that it [the fact that I had the feeling I stood still while my peers went through their pubertal development] also played a part in how I felt [depressed] at the time. I had not foreseen that beforehand." - Interview with a transgirl who continued PS; age at start PS: 12.0; age at interview: 18.1

Additionally, some clinicians stated that they think that it is difficult for an obese adolescent to understand and appreciate the impact of not being eligible to undergo certain surgeries following PS and GAH if they were to remain obese.⁵

Uncertainties regarding the long-term effects of puberty suppression

Some parents stated that they themselves knew little about the consequences of the treatment. One parent indicated that it is a challenge that no one can ever tell what the outcome would have been without medical treatment. Furthermore, some parents stated that they themselves would never take medication with unknown long-term effects.

"[Starting the treatment with puberty suppression was] a bit scary for all of us in the sense that we did not know whether we were doing the right thing or whether we were going to stuff our child full of things of which you do not know the consequences yet." - Interview with a parent of a transboy who continued PS; age at start PS: 10.9; age at interview: 17.6

"What I think is difficult about puberty suppression is that you do not know exactly what you're suppressing; you do not know what she [my daughter] would have become if she had not used that [treatment with pubertal suppression] [...] you do not know what you're inhibiting. [...] Yes, you [know that you] suppress puberty, but

5 According to the protocol as used in the Dutch gender identity clinics the upper limit of the person's body mass index (BMI) to be eligible for for example mastectomy is 35 kg/m², and for phalloplasty and vaginoplasty the upper limit is a BMI of 30 kg/m².

you do not know what it [my daughter's puberty] would have looked like [without the treatment with puberty suppression]." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.4; age at interview: 18.6

"You would never do that to yourself; you would never inject yourself with something you do not know the long-term consequences of." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.4; age at interview: 18.6

Clinicians stated that it is difficult to inform adolescents and their parents about possible consequences of PS which are not yet known. In addition, they mentioned that no one can foresee what impact certain consequences will have on the quality of life of the adolescent.

"You cannot properly inform people about what is not known [regarding (possible consequences of) the treatment], except that there are uncertainties. That's very difficult." - Focus group with clinicians

"Of course, you do not exactly know that [what the consequences of treatment with puberty suppression may be]. And you do not exactly know what effect that [those consequences] will have on the person's well-being later in life either." - Focus group with clinicians

The parents' role, influence and responsibility

Some adolescents, both continuers and discontinuers, and parents mentioned the substantial role some parents play in the diagnostic trajectory and decision-making, whereas other adolescents were not sure to what extent their parents had weighed the pros and cons of the treatment.

"My parents mostly investigated it [what treatment with puberty suppression entails] for me, because I really did not want to know anything about it [...] I just could not talk about it and I did not want to look anything up [regarding the treatment] because doing so reminded me of being [a] transgender [person]. But because my parents are like that, I ended up where I am now. Otherwise, it would have been a different story." - Interview with a transgirl who continued PS; age at start PS: 12.0; age at interview: 18.1

"Yes, we as parents and I [the mother] in particular [have weighed the pros and cons of the treatment]. [...] I like to know what to expect, so I read up on things a bit more. My son is not like that; he hears it [the possibility to start the treatment], accepts it, and goes on." - Interview with a parent of a transboy who continued PS; age at start PS: 11.9; age at interview: 18.5

One adolescent mentioned that his parents were involved and supported him in the decision-making process, but that the decision whether or not to start the treatment was made entirely by himself.

"It was entirely my own choice [to start treatment with puberty suppression]. My father and mother had virtually nothing to do with it. Yeah, of course they were there for support and things like that, but the choice was really my own." - Interview with a transboy who continued PS; age at start PS: 12.0; age at interview: 16.3

All clinicians stated that most children and adolescents need support when going through the decision-making process, from either their parents or clinicians, and that parents and/or clinicians have an important role in the decision-making.

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"The point is that you [the adolescent deciding about puberty suppressing treatment] are then at an age at which you cannot yet understand and appreciate [the consequences of the treatment], and [that you as a clinician] basically make a choice for them [the adolescents]." - Focus group with clinicians

Clinicians mentioned the role and sometimes strong influence parents can have in the diagnostic process and in decision-making.

"It is more the anticipated fear or agony of the parents. In these cases, I sometimes feel that the parents are urging to start the treatment [with puberty suppression] more than the adolescents themselves, because they [the adolescents] are not yet so concerned with the puberty suppression, and whether or not it [starting this treatment] is possible. Sometimes it is difficult when I have the feeling that the parents are very much in a hurry and 'pushing'." - Focus group with clinicians

"I think that parents are very influential in that. How do parents talk about it [the treatment with puberty suppression]? How do they talk to each other [parents together]? I think that at that age [when the child is 10 or 11] that is very closely connected to how the child thinks about treatment." - Focus group with clinicians

The clinicians stated that in some of these cases they find it hard to distinguish between the adolescent's wishes and the parents' suffering or anticipated fear.

"On the other hand, it is very complicated [...] when parents have already started that [social] transition against the advice [of the clinicians] and when they are so on top of it [starting the treatment with puberty suppression], that you wonder to what extent the child's agony is his/her own." - Focus group with clinicians

“Aren’t we [clinicians] reading into it, or aren’t parents reading into it? Where are these signals coming from? Are they [these signals] coming from the adolescents themselves or are they coming from the people around them? Are they [the adolescents] being coloured [by the thoughts and opinions of the people around them]? These are all pretty complicated things.” - Focus group with clinicians

Additionally, the clinicians asked themselves what role parents and clinicians should have in the decision-making process. Who is responsible for the decision and its consequences? Some stated that, on the one hand, parents are responsible, since they are the ones giving informed consent according to the law (for adolescents < 12 years of age; for those aged 12-16 together with the adolescents). On the other hand, some clinicians wondered how parents can make a decision based on the interpretation of the feelings and behaviour of their child. Furthermore, they pointed out the large role of clinicians in assessing which adolescents would benefit from treatment.

“I feel with those young children [about 11 years old] that the parents take over the medical decision-making competence from the children. [...] Legally that’s also the case; they [the parents] decide for the child.” - Focus group with clinicians

“Do we [the clinicians] consider ourselves most competent in medical decision-making in the whole process [diagnostic trajectory] of gender dysphoria? Considering all people involved, who are most competent in medical decision-making? Especially when you think about the fact that we [the clinicians] have such an important role in decisions about the treatment. Does that then imply, that we consider ourselves most competent to understand and appreciate what is best for the adolescent [whether or not to start treatment with puberty suppression]?” - Focus group with clinicians

Choosing between two negatives; is there really any choice?

Most adolescents who proceeded to GAH after PS and their parents stated that they did not feel they had a choice whether or not to start PS. Strikingly, none of the adolescents who discontinued PS or their parents explicitly stated that they had the feeling that they did not have a choice whether or not to start PS.

“For me [...] it was never really a choice. [...] Of course it is a choice in the way that you can choose to do it [start treatment with puberty suppression or not], but in my mind it was never really a choice, but just something I wanted to do to move forward in the journey.” - Interview with a transgirl who continued PS; age at start PS: 12.4; age at interview: 18.5

"We [the parents] said to each other, we would not have let her [our daughter] make any other radical decision at the age of twelve. If she had said 'well I really do not need any more schooling' at the age of twelve [...] [then we would have said] that's out of the question, because we are your parents and we decide that you do have to go to school [...] You feel like you do not have a choice [about whether or not to start treatment with puberty suppression]. I'm glad it [this treatment] is available, but we did not really experience it as having any choice. [...] My husband and I felt we had to choose between two evils and concluded we'd better choose the puberty suppressing treatment. [...] Of course it is sad that she might die sooner because of all the chemicals that she has to take, but on the other hand there's no point in living your life if you're not able to be yourself." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.4; age at interview: 18.6

On the other hand, many adolescents, both continuers and discontinuers, and their parents mentioned that they simply accepted possible negative consequences of the treatment and did not really take them into consideration.

"At the time I did not think very much about the pros and cons of puberty suppression [...] I had really already made up my mind [even before I had heard about the disadvantages of the treatment]." - Interview with an assigned female at birth who had discontinued PS; age at start PS: 16.7; age at discontinuation PS: 17.0; age at interview: 19.5

"No, because for her there were no disadvantages, only advantages [of the treatment]. [...] We [the parents and daughter] never actually talked about the disadvantages, except that the injections are annoying and that sometimes you can feel unwell [because of the injections]. But she did not take that into consideration. [...] The other way [not starting treatment with puberty suppression] was not an option. [...] So to what extent can one even speak of a consideration? The disadvantages are just part of the deal." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.0; age at interview: 18.1

Defining medical decision-making competence

The term MDC per se was only discussed during the focus groups with the clinicians. Most clinicians encounter difficulties defining MDC: exactly what should an adolescent understand regarding the treatment, or what should one be able to explain to be considered competent to consent? Additionally, they wondered what the term 'understanding' means in this context.

“What does medical decision-making competence entail? [...] You can talk about medical decision-making competence as in ‘do you know what happens when you use puberty suppressing treatment and do you know what the full medical trajectory entails’, so that you are aware that if you start treatment with puberty suppression, you will have to have surgeries in the future to get a penis. Is that what it [medical decision-making competence] entails? Or is it [medical decision-making competence] about the fact that if you use puberty suppression, that will stop [pubertal development] and might negatively impact the strength of your bones? According to me, there’s quite a difference between these two [ways of describing what medical decision-making competence entails].” - Focus group with clinicians

Assessing medical decision-making competence

Some clinicians stated that they assess MDC differently depending on the adolescent’s developmental age. They wondered what one can expect from an X-year-old child or adolescent with regard to, for example, understanding and appreciating what the treatment and its consequences entail. Some parents mention this too.

“That’s what I find difficult about medical decision-making competence: you verify whether someone has understood the information and to what extent someone can appreciate the consequences of the treatment in the future, but to what extent can an 11 year-old understand and appreciate that future properly? I think most 11 year-olds are not quite able to do that yet. But that does not mean someone lacks decision-making competence, that’s simply appropriate for the [child’s] developmental age.” - Focus group with clinicians

“Of course we do not know to what extent a child of that age can already understand and appreciate an entire lifetime. [...] That [not being able to understand and appreciate things when you have not experienced them] is not only inherent to being a child [this is also true for adults], but when you are older you have seen a lot more of the world and you know what the impact can be on a person’s life and a child does not.” - Interview with a parent of a transgirl who continued PS; age at start PS: 12.0; age at interview: 18.1

Some parents mentioned that no matter how much information you receive prior to starting treatment, and no matter how much thought you put into this, there are some things that you simply cannot know or understand before you experience it.

“Some things you just do not and cannot know until you’ve experienced it. Some things you need to experience before you know.” - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

In addition, some clinicians mentioned that sometimes an adolescent may not have MDC regarding a specific part or consequence of the treatment.

"In that case the adolescent does not have medical decision-making competence regarding that aspect [the ability to decide about possible loss of fertility] [...] that [medical decision-making competence] develops much later in this area. [...] And are you then going to postpone the start of treatment in the meantime [until the adolescent has medical decision-making competence regarding this aspect]? That's pretty complicated." - Focus group with clinicians

Furthermore, the clinicians stated that in their daily practice, MDC is generally assessed implicitly and not in a structured way.

"We [as clinicians] have not quite formalized it [the assessment of medical decision-making competence] as some kind of medical decision-making competence measurement. Nevertheless, of course you do it [assess one's medical decision-making competence]; you look at what exactly did the person tell me, what were his/her thoughts about it, and what can he/she tell me about the idea of how it [life after the start with puberty suppression] will go forward. And as a matter of fact, that also includes an assessment of the extent to which this person can understand and appreciate it [starting treatment with puberty suppression and its consequences]." - Focus group with clinicians

Aspects that are considered when assessing the adolescent's medical decision-making competence

The adolescents, their parents and clinicians described several aspects they take into account when assessing MDC to start PS. From the interviews and the focus groups, three subtopics emerged.

Understanding and appreciating what the treatment and its (long-term) consequences entail, and making the decision deliberately

The informants stated that understanding relevant information regarding the treatment is necessary for MDC. Nevertheless, only a few adolescents and their parents stated that the adolescent fully understood what PS entailed before starting the treatment. Some adolescents mentioned that they were able to understand most of what the treatment entailed.

"You receive so much explanation about it [the treatment with puberty suppression and its (possible) consequences] and you also have to fill in several forms. So you really know what it entails." - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

"I do not know if I understood it [what the treatment and its consequences entail] for 100 percent. But I knew that I could always stop it [the treatment] and that the male hormones would then come back. I knew that they were monthly injections, that they would stop [the release of] my male hormones in terms of physical aspects.. [like] hair growth or lowering of the voice. So in that respect, I was aware of what it [the treatment and its consequences] did and what it [the treatment and its consequences] was [were]." - Interview with a transgirl who continued PS; age at start PS: 12.4; age at interview: 18.5

"I do not think so [that my child made a deliberate decision to start puberty suppression], because we actually did not even know what the disadvantages [of the treatment] were." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.4; age at interview: 18.6

Three adolescents who proceeded to GAH after PS stated that during the time that they received treatment with PS, they began to better understand what the treatment involved.

"I think that I did take it in [the information about puberty suppression] back then [when I thought about starting the treatment with puberty suppression], but that I did not understand it very well. However, over the years, let's say between 13 and 15 [or] 16 [years of age], I started to really understand the consequences that [the treatment] has, why I was doing it, why this was helping me, why it could also serve as extra time for reflection. Basically, everything to do with it [the treatment and its (possible) consequences]." - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

"[I] maybe [understood] for about three quarters [what the treatment entailed before I started the treatment]. After the first injection [with puberty suppression] I was like, well I understand what they mean. And when I really noticed that nothing changed, I was like, I think I fully understand it now. So I understood most of it [what the treatment entailed before I started the treatment]." - Interview with a transboy who continued PS; age at start PS: 12.0; age at interview: 16.3

Some clinicians wondered to what extent adolescents should be able to understand the information regarding the treatment to be decision-making competent.

"Are you [the adolescent] able to understand the information I provide? [The question then is] Where do you draw the line?" - Focus group with clinicians

The informants stated that, besides being able to understand the relevant information about the treatment, adolescents need to be able to understand and appreciate the (long-term) consequences of the treatment to be decision-making competent. However, most adolescents and parents indicated that they/their children were not actually able to understand and appreciate all the (long-term) consequences.

"I was aware of all the disadvantages [of the treatment with puberty suppression]. Especially the mood swings, and I did underestimate those I think [the adolescent laughs]." - Interview with a transboy who continued PS; age at start PS: 10.9; age at interview: 17.6

"She [my daughter] was well informed [about the treatment with puberty suppression and its (possible) consequences], she really understood, but neither we as parents nor X [my daughter] knew [beforehand] what it would be like." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

"When they are so small [younger than 12 years old] they [...] only have one goal in mind, namely: to become the woman you feel you are. I find it hard to assess whether she [my daughter] had really understood and appreciated that [the effects of the treatment and its (possible) consequences]. I do not think that they [adolescents of that age] are able to understand and appreciate all of it." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.0; age at interview: 18.1

In addition to understanding the relevant information, and being able to understand and appreciate the (long-term) consequences, the informants wondered about how deliberate the adolescent's decision to start with PS was. Clinicians stated that adolescents should be able to appreciate the impact of the treatment on their own situation. Of importance, most parents of adolescents who proceeded to GAH, as well as a few parents of adolescents who discontinued PS, thought that their child's decision to start with PS was made deliberately. In contrast, most adolescents themselves, both continuers and discontinuers, thought they were not aware of the importance and impact of the decision.

"Of course, I was very young at the time [when I decided about starting the treatment with puberty suppression], but I had been whining about it for a long time already. It was more like: 'I have to do it, I have to do it'. Did I think it through [what the treatment with puberty suppression and its (possible) consequences entailed]? No. Was I eventually satisfied with it [the treatment with puberty suppression]? Yes." - Interview with a transgirl who continued PS; age at start PS: 14.2; age at interview: 17.9

"I think X [my daughter] understood that [what the treatment with puberty suppression and its (possible) consequences entailed] very well. [...] She did really make a deliberate decision [about whether or not to start treatment with puberty suppression]: 'this is what I want'." - Interview with a parent of an assigned female at birth who had discontinued PS; age at start PS: 16.7; age at discontinuation PS: 17.0; age at interview: 19.5

"Especially when it regards gender dysphoria, you [as a clinician] want to hear from that person [who's having gender incongruent feelings] what that person needs to feel good. And that does not necessarily involve [a treatment with] testosterone and surgery and this and that. So then you need that person to be able to explain 'well you know, this is what bothers me, and I do not need this [kind of treatment]'. So you need to be able to have a kind of meaningful conversation about that." - Focus group with clinicians

Reversibility of puberty suppression

The adolescents had diverging views regarding the way the fact that effects of PS are largely medical reversible influenced their decision-making process.

"I think that the fact that it [the effects of the treatment with puberty suppression] was [were] reversible lowered the threshold [to start the treatment]. And I think if it had immediately been about testosterone, then that doubt that subconsciously was already there, might have come to the surface, because that threshold [to start testosterone treatment] would have been higher, so I do not know if I would still have started [the medical treatment] at that point. The fact that it [the effects of the treatment with puberty suppression] was [were] reversible definitely made it much easier for me to just think, yeah, I'm going to do this [start treatment with puberty suppression]." - Interview with an assigned female at birth who had discontinued PS; age at start PS: 16.7; age at discontinuation PS: 17.0; age at interview: 19.5

"I did not care whether it [the effects of the treatment with puberty suppression] was [were] irreversible or not. [...] I did not really think about that at all. It was just something that I wanted so badly, one of my greatest wishes that would finally become true. So no, you do not really think about that. I have had plenty of time beforehand [before I decided about starting the treatment] to think about it [the treatment and (possible) consequences]. They had already given me more than enough information. It was just something that felt right." - Interview with a transboy who continued PS; age at start PS: 12.0; age at interview: 16.3

Some adolescents and clinicians thought that parents find it a reassuring idea that the first medical step has effects that are largely medical reversible. Some parents confirmed this idea whereas others did not.

"I think that especially for my parents, the decision to start treatment with puberty suppression was easier [compared to the decision to start treatment with gender-affirming hormones]." - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

"Especially for ourselves [as parents] it was extra time to reflect and think. I liked the idea that it [the effects of the treatment with puberty suppression] was [were] still reversible, even though I did not doubt her [gender incongruent] feelings or think that would ever be necessary. But I liked that about it [the treatment]. So I think the way we [as parents] experienced it [the fact that the effects of the treatment with puberty suppression are reversible] was different from the way she [our daughter] did; for her it was more like the beginning of [gender-affirming medical] treatment." - Interview with a parent of a transgirl who continued PS; age at start PS: 12.0; age at interview: 18.1

The clinicians had diverging views on the fact that effects of PS are largely medical reversible and the role this should play in the decision-making process.

"I also think, even though it [the effects of the treatment with puberty suppression] is [are] reversible, it is still an invasive treatment with substantial disadvantage." - Focus group with clinicians

"You wonder if 11, 12, [and] 13 year-olds can really understand and appreciate what they are getting into [when starting treatment with puberty suppression]. But especially for ourselves, as psychologists, it is helpful that it [the effects of the treatment with puberty suppression] is [are] reversible." - Focus group with clinicians

The role of age, intelligence, and mental health problems

The informants mentioned several factors they consider when assessing the adolescent's MDC, among others, the adolescent's developmental age, intelligence, and the presence of mental health problems. Clinicians stated that the younger the adolescent is when deciding about PS, the less likely to understand and appreciate what the treatment and its consequences entail.

"I also find very young children [...] aged 10 or 11 [...] tricky, the ones who do not necessarily have a low IQ, but are just very young. And how they consider it [the treatment with puberty suppression and its (possible) consequences]." - Focus group with clinicians

Adolescents and parents mentioned the role age plays when deciding about PS as well. Several adolescents stated that they thought they were not too young to decide about starting the treatment, but that as they grew older, their ability to make the decision improved.

"In that case [if I had made the decision to start treatment with puberty suppression when I was 16 or above] it would have been different. Then I would have had better abstract reasoning, better than when I was, say 13 years of age." - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

"I do not really think that I was too young to decide whether or not to start treatment with puberty suppression. Especially because that [the effects of the treatment] was [were] just reversible. Nevertheless, I do think that I was too young to completely understand it; the whole concept of transitioning, the social transition and the medical transition. Especially because I was only 14 [years of age] at the time, it was just like 'this [treatment with puberty suppression] is the holy grail'. And only when I got older I grasped 'hmm.. there is also another side to it [the treatment].'" - Interview with an assigned female at birth who had discontinued PS; age at start PS: 16.7; age at discontinuation PS: 17.0; age at interview: 19.5

In addition, clinicians mentioned that adolescents with lower intelligence might be less likely to be able to understand and appreciate what the treatment and its consequences entail. For several clinicians, low intelligence might even be a reason not to start PS, despite the presence of gender incongruent feelings. One adolescent and one parent mentioned the role of intelligence too. They stated that she/her child was smart enough to be able to understand and appreciate the consequences of PS prior to starting the treatment.

"I'm pretty smart so to say. So I could think of that [the effects of treatment and its (possible) consequences]." - Interview with an assigned female at birth who had discontinued PS; age at start PS: 12.1; age at discontinuation PS: 13.3; age at interview: 14.3

"How smart they [the adolescents] are, is of course an important part of their competence to make medical decisions." - Focus group with clinicians

“Especially those who have a disharmonic intelligence profile, who are verbally quite strong, but of whom you can wonder whether he/she is able to reason, and understand and appreciate the information [about the treatment and its (possible) consequences]. We do take more time for these cases [even though] we do not doubt the diagnosis [of gender dysphoria].” - Focus group with clinicians

Furthermore, clinicians mentioned that the presence of (serious) mental health problems and/or other developmental (like autism spectrum disorder) or physical differences (like deafness) might affect the adolescent’s MDC. Some wondered how MDC should be assessed in those circumstances.

“I think that, when you’re dealing with for example [someone with an] autism spectrum disorder, a deaf person, or someone with a very low intelligence, you have the idea that it almost becomes a black box; that you almost have to deduce the behaviour [of the adolescent] to have an idea of what is happening inside that black box and how plausible is it that the adolescent has ‘authentic’ gender dysphoria?”
- Focus group with clinicians

Relevance of medical decision-making competence

Finally, one of the clinicians questioned why MDC to start PS is seen as such an important aspect to be eligible to start the treatment. The clinician wondered whether some people might assume that there is a direct correlation between MDC and the chance of having regrets about the decision to start the treatment later in life, even though competent adolescents who start PS may potentially still have regrets about this decision.

“Why do we insist on medical decision-making competence, if it were about regret [of the treatment], could we argue that if it [what the treatment with puberty suppression and its (possible) consequences entails] has been discussed, it has become some kind of a deliberate choice, which makes it less likely you will regret it?” - Focus group with clinicians

This theme did not feature in any of the interviews with the adolescents or the parents.

DISCUSSION

Using qualitative methods, this study aimed to explicate and compare the perceptions of transgender adolescents who had continued or discontinued PS, their parents, and clinicians regarding adolescent’s MDC to start PS. From thematic analysis three themes emerged, being: challenges when assessing MDC to start PS, aspects that are considered when assessing the adolescent’s MDC, and relevance of MDC.

Challenges when assessing medical decision-making competence to start puberty suppression

Several aspects the participants mentioned illustrate ethical challenges surrounding assessing adolescents' MDC to start PS. One of these aspects is the fact that certain consequences of PS and uncertainty about long-term effects cause doubts. Similar ethical challenges play a role in other fields. For example, in children with limited treatment options for serious conditions, 'experimental' interventions such as gene therapy may be seen as the best available option (Lyer et al., 2021). GnRHa are used as standard care for children with precocious puberty and an increasing number of other indications, and adverse psychological and physical effects have been rare (Krishna et al., 2019; Lee et al., 2014; Yu, Yang, & Hwang, 2019). Nevertheless, several adolescents, parents and clinicians in the current study share a feeling of unease regarding PS. They try to find a balance between the need to relieve the distress associated with the undesired endogenous pubertal development of the transgender adolescent, and the wish to avoid potential long-term negative effects of PS (Butler, Wren, & Carmichael, 2019). This is difficult since what the best care is, depends also on individual preferences. Even though more evidence-based outcomes of treatment is important, it remains impossible to predict the treatment's effects and impact on a particular individual.

One of the consequences mentioned by the participants was the possible loss of fertility. Interestingly, several adolescents, most of whom were continuers, parents, and all clinicians had a specific feeling of unease about this. One could therefore question to what extent or in what way potential loss of fertility should already be taken into account when assessing adolescents' MDC to start PS.

Although the effects of PS on the development of secondary sex characteristics and gonadal function are reversible when the treatment is discontinued, as far as is currently known, if adolescents subsequently undergo treatment with GAH and gonadectomy, this will result in loss of fertility (Hembree et al., 2017). If they start PS at a young age, they may never undergo their endogenous puberty and may therefore not be able to pursue fertility preservation (Brik et al., 2019; Hudson et al., 2018). However, not all adolescents pursue gonadectomy, and depending on birth-assigned sex and the type of treatment individuals choose to undergo, fertility outcomes may vary (Cheng, Pastuszak, Myers, Goodwin, & Hotaling, 2019). Research shows that very few (1.9-6%) adolescents discontinue PS (e.g. Brik et al., 2020; Khatchadourian, Amed, & Metzger, 2014; Wiepjes et al., 2018). A subset of these adolescents (3.5-3.7%) no longer wish gender-affirming medical treatment (GAMT) (Brik et al., 2020, Khatchadourian et al., 2014). That means that the vast majority of the adolescents who start PS subsequently proceed to GAH, with possible loss of fertility as a result. Providing adequate information about the impact of treatment on future fertility and about fertility preservation is therefore highly recommended (Armund, Wettergren, Rodriguez-Wallberg, & Lampic, 2014; Stein et al., 2014).

However, the adolescents, parents and clinicians wondered to what extent an adolescent should and can be able to understand and appreciate some possible (long-term) consequences of the treatment. According to clinicians and parents, not being able to understand and appreciate the impact of the loss of fertility on one's future life and relationships is inherent to an adolescent's age and developmental stage. Some clinicians mentioned that even some adults are not able to understand and appreciate the impact of certain consequences of the treatment. Thus, one might question whether it is reasonable to expect adolescents to be able to understand and appreciate all possible consequences of medical treatment. Yet we often seem to assess adults' MDC in these situations as 'sufficient', while we question that of adolescents. Infertility and concerns about (future) fertility may have a major negative impact on quality of life and mental health (Carter et al., 2010; Trent, Rich, Austin, & Gordon, 2003). Research focusing on survivors of paediatric cancer shows that plans of minors for future children may change over the years (Armund et al., 2014; Stein et al., 2014). Although there is, as far as we know, no similar published data regarding transgender minors deciding on PS, data from a Dutch study with transgender adults shows that views regarding parenthood might change over time (Van Mello et al., 2022). Other research shows that vitality and self-perceived mental health status is significantly better among adult transmen with children than for those without (Wierckx et al., 2012). Offering the possibility of fertility preservation is therefore important. However, that in turn might bring its own difficulties. For example, the fertility preservation process might have a psychological impact on the adolescent and/or the parent(s), as mentioned by one of the parents in this study. In our clinical practice, all adolescents and their families are offered fertility counselling, but some families refuse because they consider even just the counselling too psychologically burdensome for their young child.

Up until now little is known about the possible psychological impact of the procedures and the process of fertility preservation on transgender adolescents (Baram, Myers, Yee, & Librach, 2019). Further research regarding not only the benefit but also the possible harm of a fertility preservation process on transgender adolescents and their families would therefore be valuable (Baram et al., 2019; Chen & Simons, 2018). Besides, we recommend future research examining the impact of the loss of fertility later in the adolescents' lives, and investigating the best way to communicate information regarding fertility (preservation) to these young adolescents. Of note, in the Netherlands fertility preservation continues to be a topic of conversation throughout the diagnostic and treatment phases, and in any case before decisions about GAH and surgery are made, since fertility preservation remains possible even after adolescents have started treatment with PS, for example, by temporarily interrupting treatment.

Another aspect participants mentioned regarding assessing MDC to start PS was the parents' role. Involvement and help of parents with regard to making medical decisions for

minors is important, just as most adolescents, both continuers and discontinuers, parents, and clinicians mentioned, and as stated in laws and in international guidelines on care for transgender children and adolescents (Coleman et al., 2012; Vrouenraets et al., 2015). Additionally, the clinicians in this study said that, besides the adolescents and parents, they themselves took part in the decision-making process too. None of the adolescents and parents did not mention this. For patient-centred care shared decision-making (SDM) is considered essential and it is recommended by paediatric regulatory organizations (Barry & Edgman-Levitan, 2012; Harrison, Canadian Paediatric Society, & Bioethics Committee, 2004). The SDM approach in general care is evidence-based and promotes collaboration between patients, family members, and clinicians when making a decision regarding health care (Boland et al., 2019). Patients, family members, and clinicians can deliberately decide about the best treatment plan by exchanging information about the treatment's evidence (options, benefits, and risks) and the patient's and family's preferences (Légaré et al., 2011). In SDM the patient's expertise and values are considered along with empirical medical information, and the decision-making responsibilities of the patient, family members, and clinicians are balanced (Makoul & Clayman, 2006; Crickard, O'Brien, Rapp, & Holmes, 2010; Langer & Jensen-Doss, 2018).

Although little is known about SDM in the context of PS in transgender adolescents, research shows that SDM can support decisions about GAH treatment for transgender adolescents when integrating into practice the following five conditions: open communication, role agreement, supportive relationships, agreement about the decision, and sufficient time (Clark, Virani, Marshall, & Saewyc, 2021). Research shows that among other things the use of information-sharing techniques that are age-appropriate, breaking down a decision into smaller choices, and asking direct and simple questions all promote adolescents' ability to participate in medical discussion (Michaud, Blum, Benaroyo, Zermatten, & Baltag, 2015). Future research examining how transgender adolescents can best be involved in the decision-making process regarding PS is recommended.

Additionally, it is notable that most adolescents who proceeded to GAH after PS, and parents mentioned that they did not feel they had a choice whether or not to start the treatment with PS. By contrast, none of the adolescents who discontinued PS or their parents explicitly stated having no choice. It is noteworthy that, most adolescents, continuers and discontinuers, and their parents mentioned not really taking the treatment's possible negative consequences into consideration. This, even though most adolescents, parents, and clinicians stated that understanding the treatment and its consequences should be considered when assessing adolescents' MDC. Apparently, the possible negative consequences of the treatment do not outweigh the burden of the adolescents' gender incongruent feelings. One could therefore question whether

adolescents' MDC to start PS is at all 'required', when the adolescents might not even have a choice to make. This situation is not unique for the transgender adolescent care. For example, some patients undergoing deep brain stimulation do not have other treatment options left. Nevertheless, in the current medical model in the Netherlands, these patients still need to give their fully informed consent to the treatment (Schermer, 2011). In addition, it should be mentioned that one's feeling of not having a choice is different from having no choice; in fact, adolescents still have a choice to proceed to treatment or not, but for them one option is significantly preferable (i.e. to receive treatment).

Besides, the adolescents, both continuers and discontinuers, parents, and clinicians questioned what the term 'understanding' means regarding information about the treatment and its possible consequences in the context of adolescents' MDC to start PS; to what extent should an adolescent be able to understand the information regarding PS to be decision-making competent? Furthermore, most clinicians experienced challenges while assessing MDC and mentioned that they apply their own definition of MDC depending on the characteristics of the adolescent at hand. In addition, the results show MDC is generally assessed implicitly and not in a structured way in daily practice. This is in line with what earlier research in other contexts shows (Hein et al., 2015b). Except for one Dutch quantitative study, which shows that the vast majority (89%) of the examined transgender adolescents (aged 10-18 years) about to start PS treatment are competent to consent to this treatment, there is little evidence on transgender adolescents' MDC to start PS (Vrouenraets, de Vries, de Vries, van der Miesen, & Hein, 2021). Because clinicians indicate that they find it difficult to determine MDC, it would be desirable to develop a more uniform way to assess MDC and provide ethics support for the ethical dilemmas that are encountered when assessing MDC (Hartman, Metselaar, Molewijk, Edelbroek, & Widdershoven, 2018; Hartman et al., 2019; Hein & Hondius, 2017). Dissemination of knowledge about MDC to start PS would help to adequately support adolescents, parents, and clinicians in the decision-making process. Despite the fact that current transgender clinical guidelines state that adolescent's MDC is a prerequisite to start PS, the guidelines hardly clarify what 'adolescents having MDC' means in practice. Dutch researchers have, largely based on the information gained in the current study, developed an ethics support tool (in Dutch: 'wilsbekwaamheidswijzer') that provides clinicians information and direction on how to deal with adolescents' MDC. The tool provides clinical guidance on assessing adolescents' MDC, for example regarding what aspects the adolescents should understand about the treatment before they are considered competent (de Snoo-Trimp, de Vries, Molewijk, & Hein, 2022a; Molewijk, Abma, Stolper, & Widdershoven, 2008a). Making such an ethics support tool available to clinicians in other countries as well could be very helpful. Additionally, clinicians working in transgender treatment teams in the Netherlands rated moral case deliberation, a relatively well-established form of clinical

ethics support, as highly valuable in dealing with moral challenges in their clinical practice (Molewijk et al., 2008a; Vrouenraets, Hartman, Hein, de Vries, de Vries, & Molewijk, 2020). Moral case deliberation could also be used by the transgender treatment teams when, in clinical practice, they are confronted with moral challenges regarding adolescents' MDC to start PS and/or its assessment.

Aspects that are considered when assessing the adolescent's medical decision-making competence

Results further showed that the adolescents, parents, and clinicians mentioned several (contextual) aspects that, according to them, should be considered when assessing the adolescent's MDC to start PS. One aspect various adolescents, parents, and clinicians mentioned with regard to this, was the understanding of the treatment and its consequences. Various adolescents, both continuers and discontinuers, mentioned that before they started PS, they were not aware of some of the psychosocial consequences of delaying puberty while their peers underwent multifaceted developmental accomplishments. An example of a potentially negative consequence of keeping the adolescent in a prepubertal state is isolating the adolescent from peers (Rosenthal, 2014). On the other hand, research shows that the adolescents' psychological functioning improved or did not change after starting specialized transgender care involving PS (van der Miesen et al., 2020; Carmichael et al., 2021; Rew, Young, Monge, & Bogucka, 2021). Only a few of the adolescents and their parents stated that they fully understood what PS and its consequences entailed, but even so, the adolescents found themselves able to decide about whether or not to start the treatment. In both the beforementioned quantitative study regarding the assessment of MDC in transgender adolescents and the current qualitative study, the adolescents are judged competent and find themselves competent to decide on starting PS (Vrouenraets et al., 2021). Seemingly, fully understanding and appreciating the treatment are not requirements for MDC to start PS. This is in line with the statements of some clinicians and parents that not being able to understand and appreciate the impact of certain consequences of PS is inherent to the age, developmental stage and/or life experience of the adolescent, just as previous research in other contexts has shown (Hein et al., 2015b).

Age was another factor that most participants mentioned that may have a decisive impact on MDC, and should therefore be considered when assessing the adolescents' MDC. Age is often considered to be the best indicator of MDC (Hein et al., 2015c). Research shows that children aged ≥ 12 years may have MDC, provided they have favourable environmental factors (Grootens-Wiegers, Hein, van den Broek, & de Vries, 2017; Hein et al., 2014). On the other hand, the same research shows that there is no universal agreement regarding the age at which children can reasonably be expected to have MDC regarding every decision in every context. Early development of the reward system of the brain in combination with

late development of the control system reduces adolescents' MDC in certain challenging contexts which are not supportive (Grootens-Wiegers et al., 2017). Therefore, children and adolescents of the same age may have different levels of maturity and there is no general clear cut-off at which all children or adolescents have MDC (Grootens-Wiegers et al., 2017). Furthermore, some experts argue that children who have personal experiences with 'illness', may have greater understanding and insight compared to children who do not have this experience (Alderson, 2007; Bluebond-Langner, Belasco, & DeMesquita, 2010; Larcher & Hutchinson, 2010). This may specifically play a role in the case of gender non-conforming minors, where most adolescents seen at a gender identity clinic have long lasting or even life-long gender incongruent feelings. However, research does not confirm this hypothesis (Hein et al., 2015c; Vrouenraets et al., 2021). It is worthwhile considering to assess MDC and maturity on an individual basis rather than using a fixed age criterium, although the fact that most participants in the current study experienced age as an important aspect concerning MDC, may support that for certain more irreversible components of GAMT (by means of treatment with GAH and/or surgery), age criteria should remain existing (Coleman et al., 2012; Coleman et al., 2022; Hein et al., 2015a).

Relevance of medical decision-making competence

Finally, in our study clinicians pondered whether too much importance is placed on the adolescent's MDC. None of the adolescents and parents did mention this. So far, there is no direct correlation between having MDC and not having regrets about a decision later in life, something that some stakeholders seem to have in mind (Pang et al., 2021). Besides, respecting an individual's autonomy encompasses one's right to make a decision that is regretted later on in life (Glover, 1990). A balance that needs to be struck is between the risk of regret and the risk of not providing the treatment, since refraining from treatment might have harmful effects too (de Vries et al., 2021; Pang et al., 2021).

Strengths and weaknesses

There are some strengths and weaknesses to the present study. The qualitative nature of this study made it possible to find out, in depth, the ways in which transgender adolescents, their parents, and clinicians think about transgender adolescents' MDC to start treatment with PS. Another strength of this study is that adolescents who did continue with GAH after PS as well as adolescents who did not proceed to GAH were interviewed. This allowed us to compare their considerations. Nevertheless, the retrospective nature of this study raises the possibility of recall bias and hindsight bias of the informants. In addition, the informants were recruited from two Dutch treatment teams using the same protocol prescribing that PS was required for all adolescents before any further affirming treatment was provided. Adolescents recruited from other gender identity clinics in other contexts might report different considerations regarding MDC (Levine et al., 2022).

Therefore, we encourage prospective gathering of more qualitative data from adolescents who have not started PS yet, or receive PS but have not started treatment with GAH yet. Due to the small sample size, the non-participation rate and the skewed sex ratio, it is not completely certain if genuine saturation was reached. Non-participating adolescents who had discontinued treatment might have had other thoughts regarding the adolescents' MDC compared to the adolescents that have been interviewed. We, therefore, encourage gathering more qualitative data from a larger sample with a more balanced sex ratio.

CONCLUSION

In conclusion, this study shows that adolescents, their parents, and clinicians take various aspects into account regarding the adolescent's MDC. The four criteria one needs to fulfil to have MDC - understanding, appreciating, reasoning, and communicating a choice - were all, to a greater or lesser extent, mentioned as challenging by the participants, just as MDC being relative to a specific decision and context (Appelbaum & Grisso, 1988). Most adolescents, parents, and clinicians find understanding and appreciating what the treatment and its consequences entail, important for MDC. Nevertheless, even though most adolescents, both continuers and discontinuers, and parents felt they did not have a full understanding and appreciation of all consequences, they thought that they were able to make the decision to start PS. Parents' support of their child was considered essential in the decision-making process. However, several parents and clinicians wondered to what extent they themselves, and adults in general, are able to understand and appreciate certain consequences, let alone adolescents. The results of the current study show that clinicians find MDC challenging to assess in a uniform way. Dissemination of knowledge and support concerning the assessment of MDC and encountered ethical dilemmas about transgender adolescents' MDC is desirable in order for clinicians to support adolescents and parents in the decision-making process.

PART 3

**Significance of puberty suppression
and use of fertility preservation**

6

Trajectories of adolescents treated with gonadotropin-releasing hormone analogues for gender dysphoria

Tessa Brik

Lieke J. J. J. Vrouwenraets

Martine C. de Vries

Sabine E. Hannema

2020. *Archives of Sexual Behavior*, 49(7), 2611-2618

ABSTRACT

Gonadotropin-releasing hormone analogues (GnRHa) are recommended as initial treatment for adolescents diagnosed with gender dysphoria, providing time to follow gender identity development and consider further treatment wishes without distress caused by unwanted pubertal changes. This has been described as an extended diagnostic phase. However, there are also concerns about the physical, neurocognitive, and psychosocial effects of this treatment. In this retrospective study, we document trajectories after the initiation of GnRHa and explore reasons for extended use and discontinuation of GnRHa. Treatment was considered appropriate in 143 (67%) of the 214 adolescents eligible for treatment with GnRHa by virtue of their age/pubertal status, and all started GnRHa (38 transgirls, 105 transboys; median age, 15.0 years [range, 11.1-18.6] and 16.1 years [range, 10.1-17.9]). After a median duration of 0.8 years (0.3-3.8) on GnRHa, 125 (87%) started gender-affirming hormones (GAH). Nine (6%) discontinued GnRHa, five of whom no longer wished gender-affirming medical treatment (GAMT). Thirteen had used GnRHa for longer than required by protocol for reasons other than logistics and regularly met with a mental health professional during this time, supporting the use of treatment with GnRHa as an extended diagnostic phase. In conclusion, the vast majority who started GnRHa proceeded to GAH, possibly due to eligibility criteria that select those highly likely to pursue further GAMT. Due to the observational character of the study, it is not possible to say if treatment with GnRHa itself influenced the outcome. Few individuals discontinued GnRHa, and only 3.5% no longer wished GAMT.

INTRODUCTION

Increasing numbers of minors diagnosed with gender dysphoria are seen by paediatric endocrinologists. Gender dysphoria is the persistent feeling of incongruence between gender identity (sense of being a man, woman, or other) and the sex assigned at birth. The diagnosis gender dysphoria can be made if the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria are met (American Psychiatric Association, 2013). The prevalence of gender dysphoria among Dutch adolescents aged 12-18 years was recently estimated to be one in 6300 based on numbers of adolescents seeking medical treatment, with a ratio of transboys (assigned female at birth) to transgirls (assigned male at birth) of 1.9:1 (Wiepjes et al., 2018). Genetic, hormonal, psychological, and social factors may play a role, but the exact aetiology of gender dysphoria remains unknown (de Vries & Cohen-Kettenis, 2012; Hembree et al., 2017; Martinerie et al., 2018).

Gender dysphoria in prepubertal children can be expressed by dislike of their physical sex characteristics and gender incongruent behaviour. In many children, gender dysphoria will not persist, but if the gender dysphoric feelings intensify during puberty, they are thought to be unlikely to subside (de Vries & Cohen-Kettenis, 2012; Hembree et al., 2017; Zucker et al., 2011). When puberty starts (Tanner genital/breast stage 2) and gender dysphoria persists, adolescents are eligible to start with puberty suppression (PS) using gonadotropin-releasing hormone analogues (GnRHa) (Coleman et al., 2012; Hembree et al., 2017). Treatment with GnRHa aims to give the adolescent the opportunity to explore their gender identity and time to consider if they wish to pursue gender-affirming medical treatment (GAMT) while development of unwanted secondary sex characteristics is suppressed in order to reduce distress (Hembree et al., 2017; Zucker et al., 2011). Effects of GnRHa on pubertal development are reversible. This is in contrast to gender-affirming hormones (GAH) which have largely irreversible effects on secondary sex characteristics and may compromise fertility after prolonged use (de Roo, Tilleman, T'Sjoen, & de Sutter, 2016; Hembree et al., 2017).

Short-term adverse effects of GnRHa are hot flushes at the start of the treatment and sometimes mood alterations and fatigue (Delemarre-van de Waal & Cohen-Kettenis, 2006; Hembree et al., 2017; Schagen, Cohen-Kettenis, Delemarre-van de Waal, & Hannema, 2016). Few data are available on long-term adverse effects. Bone mineral density may be affected (Klink et al., 2015; Vlot et al., 2017), and since puberty is an important period for brain development (Sisk & Zehr, 2005), PS with GnRHa might also influence brain development. There is a lack of studies investigating effects of GnRHa on the brain. One study examined executive function and concluded that treatment with GnRHa had no detrimental effects on performance (Staphorsius et al., 2015). However, a longitudinal study among 25 adopted girls treated with GnRHa for early puberty reported a decrease in IQ from

100.2±12.7 to 93.1±10.5 with a significant decline of performance score during treatment, but it was concluded that the decrease in IQ was not clinically relevant (Mul et al., 2001). A limitation of the study was the lack of a control group. A second small cross-sectional study of girls treated with GnRHa because of precocious puberty found no significant difference in cognitive functioning, behavioural, and social problems compared to healthy age-matched controls, but the study did not have enough power to detect differences smaller than one standard deviation (Wojniusz et al., 2016). Wojniusz and colleagues did report that emotional reactivity was possibly higher in girls treated with GnRHa although these results were not conclusive. Girls with early or precocious puberty are treated at a younger age so it is unclear to what extent these results apply to adolescents treated with GnRHa for gender dysphoria. Further studies are needed to assess if and what effects GnRHa have on various aspects of brain development in adolescence.

Opinions about the use of GnRHa vary (Vrouenraets et al., 2015). Arguments for the use of GnRHa that have been brought forward are the benefit of early treatment with GnRHa for mental health and quality of life (de Vries et al., 2011a). Furthermore, it gives the adolescent and treatment team more time to explore the adolescent's gender identity and treatment wishes (Hembree et al., 2017). If the adolescent pursues GAMT, some surgeries may not be necessary or less invasive as secondary sex characteristics are less developed. Early treatment is correlated with better postsurgical outcomes, possibly because of a physical appearance more in line with the affirmed gender (Cohen-Kettenis & van Goozen, 1997; Leibowitz & de Vries, 2016). However, this may not be of equal importance to all adolescents and early PS also precludes certain surgeries such as penile inversion vaginoplasty by limiting penile growth. Some have argued that treatment with puberty suppression prevents devastating psychological and physical harms including suicide and that adolescents should therefore be able to access this treatment even without parental approval (Dembrof, 2019; Priest, 2019), but others have underscored that there is no evidence that PS prevents suicide and that the risk of suicide, although high, should not be overstated and should be seen in comparison with a clinical comparison group rather than the general population (Antommara, Shapiro, & Conard, 2019; Baker, 2019; Zucker, 2019).

Arguments against the use of GnRHa that have been raised include possible long-term adverse effects on health, psychological, and sexual functioning (Laidlaw, Cretella, & Donovan, 2019a; Richards, Maxwell, & McCune, 2019; Vrouenraets et al., 2015). Some state that adolescents may be unable to make far-reaching decisions at a young age, especially in the presence of comorbid psychiatric conditions, which are common among minors with gender dysphoria (Korte et al., 2008; Laidlaw et al., 2019a; Vrouenraets et al., 2015). Furthermore, gender identity develops and may change during adolescence. Concerns have been raised that the use of GnRHa may influence this process and might increase the likelihood of persistence of gender dysphoria (Korte et al., 2008; Laidlaw et al.,

2019a; Richards et al., 2019; Stein, 2012; Vrouenraets et al., 2015). It is unknown if the use of GnRHa prevents resolution of gender dysphoria (Korte et al., 2008). Many prepubertal children with gender dysphoria no longer experience gender dysphoria in adolescence, and the experience of romantic and sexual attraction is thought to play an important role in this process (Steensma, Biemond, de Boer, & Cohen-Kettenis, 2011). Some may come to understand themselves as homosexual or bisexual (Steensma et al., 2011). GnRHa, by suppressing sexual development, might interfere with this process (Korte et al., 2008). Another concern is that although treatment with GnRHa is to be used as an extended diagnostic phase, the start of it may lead the adolescents and parents to assume that transgender outcome is the only possible outcome which may prevent exploration of other possibilities (Leibowitz & de Vries, 2016).

To gain more insight into the use of GnRHa in adolescents with gender dysphoria, the current study aims to document trajectories after the initiation of GnRHa, i.e., discontinuation of GnRHa, prolonged use of GnRHa, and initiation of GAH; to investigate the duration of treatment with GnRHa; and to explore reasons for extended use and discontinuation of GnRHa.

6

METHOD

Participants

This is a single-centre retrospective study. Out of 269 children and adolescents registered at the Curium-Leiden University Medical Centre gender identity clinic in Leiden, the Netherlands, 214 were pubertal and within the appropriate age range for treatment at our paediatric clinic. Out of these, 143 (67%) had started treatment with GnRHa between November 2010 (when the clinic first started) and January 1, 2018. The study population consisted of these 143 adolescents (38 transgirls, 105 transboys). Not included in the study were children and adolescents in whom gender dysphoria was not diagnosed ($n = 39$), those who had coexisting problems that interfered with the diagnostic process and/or might interfere with successful treatment ($n = 9$), those that did not wish hormonal treatment ($n = 4$), those in whom the diagnostic evaluation was still ongoing ($n = 10$), and those who had stopped to attend appointments ($n = 9$).

Of adolescents who had started GnRHa, treatment status as of 1 July 2019 was reviewed. If they had used GnRHa monotherapy for more than three months longer than minimally required before the start of GAH according to the local protocol (see below for description of the treatment protocol), the reason for this was noted. The three months was chosen to select those who may have had a prolonged diagnostic phase rather than those in whom treatment with GAH started slightly later due to logistical issues such as rescheduling of

an appointment. Adolescents who had started treatment with GnRHa and had stopped this treatment were included in a detailed review. Baseline characteristics such as age and gender and data on the start, duration, and discontinuation of treatment were recorded from the medical files, as well as reasons given for the discontinuation of treatment with GnRHa and the adolescents' and parents' views on the treatment.

Procedure

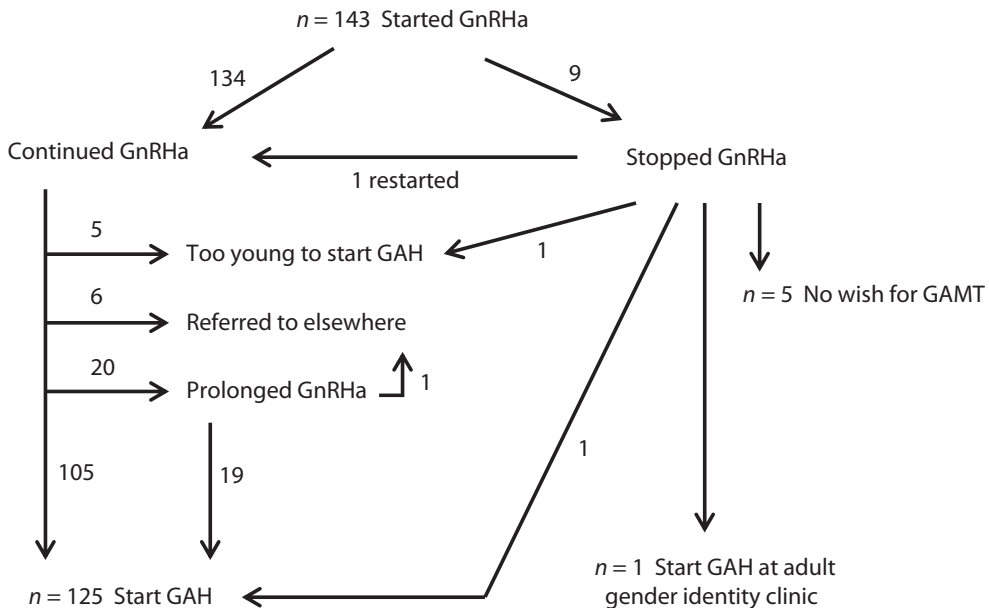
Before the start of treatment with GnRHa, all adolescents had a diagnostic evaluation by a paediatric endocrinologist and mental health professional (MHP) to confirm the diagnosis of gender dysphoria according to the DSM-5 criteria (American Psychiatric Association, 2013), to assess the presence of any medical, psychiatric, or psychosocial problems that might interfere with treatment, to assess if the adolescent was able to give informed consent for the treatment and to confirm that puberty had started, as recommended by current guidelines (Hembree et al., 2017). This evaluation usually consisted of approximately six visits (more if necessary) of the adolescent with an MHP in six to 12 months in addition to interviews with parents/guardians. All adolescents gave written informed consent for the treatment. Informed consent from parents/guardians was also required if the adolescent was <16 years old. After the start of treatment with GnRHa, follow-up visits were scheduled with the paediatric endocrinologist and MHP, usually every three months in the first year and every three to six months thereafter, to evaluate satisfaction with the treatment, adequacy of PS, and any side effects. In the case of mental health issues (psychiatric morbidity but also issues such as difficulty to express oneself and doubts about one's gender identity), adolescents were either seen more frequently by the psychologist of the gender team or referred to a local MHP for therapy.

According to the local protocol, adolescents were eligible for treatment with GAH from the age of 16 years and after at least six months of treatment with GnRHa. No maximum time of use of GnRHa was defined in the protocol. From 2016, adolescents who had already been treated with GnRHa for at least three years were eligible for treatment with GAH from the age of 15 years. From 2017, those who had been treated with GnRHa for at least two years and were 15 years old were eligible. Before the start of GAH, evaluation by a MHP and paediatric endocrinologist took place to assess the indication, any contraindications, and ability to give informed consent for this treatment. If adolescents had discontinued treatment with GnRHa, there was a follow-up appointment at which adolescents and parents were asked about current feelings regarding gender identity and how they looked back on the treatment.

RESULTS

During the study period, 143 adolescents started treatment with GnRHa (38 transgirls, 105 transboys). Median age at the start of treatment was 15.0 years (range, 11.1-18.6 years) in transgirls and 16.1 years (range, 10.1-17.9 years) in transboys. Of these adolescents, 125 (87%, 36 transgirls, 89 transboys) subsequently started treatment with GAH after 1.0 (0.5-3.8) and 0.8 (0.3-3.7) years of treatment with GnRHa (figure 3). Median age at the start of GAH was 16.2 years (range, 14.5-18.6 years) in transgirls and 17.1 years (range, 14.9-18.8 years) in transboys. Five adolescents who used GnRHa had not started GAH at the time of data collection, because they were not yet eligible for this treatment due to their age. At the time of data collection, they had used GnRHa for a median duration of 2.1 years (1.6-2.8). Six adolescents had been referred to a gender identity clinic elsewhere for further treatment. One of these was 17 years old and eligible for GAH but initially indicated he needed more time to decide about testosterone treatment and subsequently stated that he wished to delay the start of this treatment until after his school examinations. The other five were not eligible yet due to their age at the time of referral. Nine had discontinued treatment with GnRHa (see below), one of whom restarted GnRHa after five months. This individual and two others subsequently started treatment with GAH (figure 3).

Figure 3. Flow chart showing the trajectories of adolescents who started treatment with gonadotropin-releasing hormone analogues (GnRHa)



GAH refers to treatment with gender-affirming hormones; GAMT refers to gender-affirming medical treatment; GnRHa refers to treatment with gonadotropin-releasing hormone analogues.

Prolonged use of GnRHa

Twenty adolescents (three transgirls and 17 transboys) had used GnRHa for longer than minimally required by protocol. One was the transboy mentioned above who needed more time to decide about testosterone treatment. He had used GnRHa for 2.5 years when he was referred from the paediatric clinic to a clinic for adults elsewhere. The other 19 adolescents had subsequently started GAH. The median duration of GnRHa monotherapy in these 19 adolescents was 1.0 year (0.8-2.4). Reasons for prolonged use of GnRHa were (sometimes there was more than one reason): unstable situation due to family issues such as lack of parental support and/or acceptance of gender dysphoria ($n = 6$) or social problems such as lack of a safe home, excessive school absenteeism ($n = 5$); (psychiatric) comorbidity ($n = 8$) such as autism spectrum disorder or depression; more time needed for decision about treatment with GAH by the adolescent ($n = 1$) or for further diagnostics by the gender team ($n = 1$, because of non-binary aspects); and logistic issues such as missed/rescheduled appointments ($n = 8$; in seven this was the only reason). The 11 adolescents who received prolonged treatment with GnRHa because of mental health and/or psychosocial problems had regular (approximately monthly on average) appointments with a psychologist at the gender identity clinic ($n = 5$) and/or received support from a local MHP ($n = 9$) during this period.

Discontinuation of GnRHa treatment

From the 143 adolescents who started treatment with GnRHa, nine (6%; one transgirl, eight transboys) stopped this treatment after a median duration of 0.8 years (0.1-3.0), at a median age of 15.0 years (13.4-18.9). Four individuals discontinued although they did wish further endocrine treatment because for gender dysphoria. One stopped treatment because of an increase in mood problems and suicidal thoughts, and confusion attributed to treatment with GnRHa and restarted treatment (treatment with GAH) at an adult gender identity clinic elsewhere. He later indicated:

“I was already fully matured when I started GnRHa, menstruations were already suppressed by contraceptives. For me, it had no added value.” - Interview with a transboy, age 19 years

Another transboy experienced hot flushes, an increase in migraine, and had fear of injections in addition to stress due to problems at school and unrelated medical issues and therefore wished to temporarily discontinue treatment with GnRHa after four months. He restarted five months later and subsequently started testosterone treatment. A third transboy experienced mood swings starting four months after he had begun treatment with GnRHa. A year later, he started to frequently feel unwell and miss school. After 2.2 years, he developed severe nausea and rapid weight loss for which no cause was

identified. Because of this deterioration of his general condition, he wished to discontinue treatment with GnRHa after 2.4 years. He gradually recovered over the next two years. He subsequently started lynestrenol and testosterone treatment. The last adolescent had stopped GnRHa because his parents were unable to regularly collect medication from the pharmacy and take him to appointments for the injections. He subsequently started lynestrenol to suppress menses; he is not eligible yet for testosterone treatment.

The five others (3.5%) no longer wished gender-affirming medical treatment (GAMT). One adolescent had been very distressed about breast development at the start of GnRHa. She later thought that she might want to live as a woman without breasts. She did not want to live as a boy and did not wish testosterone treatment and decided to discontinue GnRHa although she dreaded breast development and menstruation. Another adolescent had concurrent psychosocial problems interfering with the exploration of gender identity and did not currently wish treatment. When looking back on treatment with GnRHa this individual said:

“The decision to stop GnRHa to my mind was made by the gender team, because they did not think gender dysphoria was the right diagnosis. I do still feel like a man, but for me it is okay to be just me instead of a he or a she, so for now I do not want any further treatment.” - Interview with an adolescent assigned female sex at birth, age 16 years

One adolescent felt more in between man and woman and therefore did not wish to continue treatment:

“At the moment, I feel more like ‘I am’ instead of ‘I am a woman’ or ‘I am a man’.”
- Interview with an adolescent assigned female sex at birth, age 16 years

Another individual made a social transition while using GnRHa and shortly afterward decided to discontinue treatment. He indicated that he had fallen in love with a girl and had never had such feelings, which made him question his gender identity. At subsequent visits, he indicated that he was happy living as a man.

The last adolescent stated:

“After using GnRHa for the first time, I could feel who I was without the female hormones, this gave me peace of mind to think about my future. It was an inner feeling that said I am a woman.” - Interview with an adolescent assigned female sex at birth, age 18 years

The adolescents and parents were also asked about their views on GnRHa in the treatment protocol for gender dysphoria. All of them saw it as the first step in treatment, but it was also clear that it was used as an extended diagnostic phase. They all felt free to stop GnRHa. They had varying visions on the role of GnRHa in the treatment for gender dysphoria. Some stated it gave them time to think and feel who they were and what they wanted in the future and felt that without treatment with GnRHa they would not have been able to make these decisions. Others stated that GnRHa should not be routinely offered before the start of GAH when adolescents are already fully matured, because of the lack of physical benefits. Instead, a consideration time of six months with psychological follow-up was suggested.

DISCUSSION

The great majority of adolescents who started GnRHa subsequently started GAH as soon as they were eligible for this treatment. Very few discontinued treatment, although slightly more than in previous studies in which cohorts of transgender adolescents were described. Out of 333 adolescents that had started PS at the VUmc gender identity clinic in the Netherlands up until December 2015, 1.9% stopped; reasons for discontinuation of GnRHa were not reported (Wiepjes et al., 2018). In the Canadian study by Khatchadourian and colleagues (2014), one of 27 individuals who started GnRHa stopped the treatment due to emotional lability, not because the wish to pursue transition had subsided. In the current study, 6% of those who started GnRHa discontinued and 3.5% no longer wished GAMT.

Several studies reviewed by Ristori and Steensma (2016) have found that much higher percentages (61-98%) of prepubertal children no longer experience gender dysphoria ('desist') as adolescents. The period between 10 and 13 years seems to be a crucial period in which social changes (for example starting secondary school), the physical changes of puberty, and first romantic and sexual experiences may lead to either an increase or a decrease/resolution of gender dysphoria (Steensma et al., 2011). The adolescents that start treatment with GnRHa have entered puberty and are mostly older than 13 years and may be past this critical period so that gender dysphoria may be more likely to persist. This may explain the lower percentage of resolution of gender dysphoria found in the studies of treated adolescents. In addition, the groups that started treatment in previous studies and in the current study consisted of selected adolescents that had had an extensive diagnostic process to establish if they met the eligibility criteria for treatment as well as the diagnostic criteria for gender dysphoria (Wiepjes et al., 2018). Alternatively, concerns have been raised that treatment with GnRHa itself may increase the chances of persistence of gender dysphoria (Korte et al., 2008; Richards et al., 2019; Stein, 2012;

Vrouenraets et al., 2015). Whether or not treatment with GnRHa influenced gender identity development cannot be concluded from the current study due to its observational nature. The study does show that gender identity development was not suppressed in all, as a few adolescents discontinued GnRHa because they no longer experienced gender dysphoria, but it is unknown if gender dysphoria would have subsided in more adolescents in the absence of treatment with GnRHa.

For one adolescent, the experience of falling in love made him doubt whether he was transgender. This is in line with previous findings that the first romantic experiences and the awareness of one's sexual attraction play an important role in the resolution of gender dysphoria in adolescents (Steensma et al., 2011). This emphasizes the importance of this topic in the diagnostic evaluation. However, some adolescents may not have had any romantic or sexual experiences, especially if they present at an early age. In addition, transgender adolescents were shown to be less experienced, both sexually and romantically, compared to peers from the general population (Bungerer, Steensma, Cohen-Kettenis, & de Vries, 2017). Treatment with GnRHa prevents the physical changes of puberty and is known to negatively affect sexual desire (Plosker & Brogden, 1994). PS might thus decrease the chances of adolescents having romantic and sexual experiences which might in turn influence gender identity development (Korte et al., 2008). This was not true for the adolescent in the current study who fell in love while using GnRHa and then decided to discontinue treatment, but it is uncertain if more adolescents would have had such experiences if they had not used GnRHa.

Two individuals who discontinued GnRHa indicated that they did not feel either male or female. A non-binary gender identity appears to be becoming more common among adolescents presenting at gender identity clinics (Butler, De Graaf, Wren, & Carmichael, 2018). For these adolescents, it may be more difficult to find out and understand their own gender identity and it is unclear what constitutes optimal care for this group.

Experienced side effects played a role in the decision to discontinue treatment with GnRHa in three adolescents. However, for none of the adolescents who stopped GnRHa in the current study, were potential long-term side effects a reason to decline or discontinue treatment with GnRHa. Lack of information about long-term effects of GnRHa use was not considered an important problem by interviewed adolescents with gender dysphoria in the study by Vrouenraets and colleagues (2016), but is seen as a major problem by many professionals (Vrouenraets et al., 2015).

In the current study, 13 adolescents who were eligible for treatment with GAH used GnRHa monotherapy for longer than the minimum time required by protocol for reasons other than logistics. During this time, they received mental health support from a local MHP

or from a psychologist from the gender team. This supports the idea that the time on GnRHa is used as an extended diagnostic phase where the adolescents can further explore their gender identity and treatment wishes and work on issues that might interfere with successful treatment. The great majority started GAH as soon as was possible within the treatment protocol, after a median duration of approximately one year. This does not mean that for them this time was not used as an extended diagnostic phase. Those who were youngest at the start of GnRHa were treated the longest, up to 3.8 years, with visits to the clinic every three to six months. In this period of growing up, becoming more independent, and discovering oneself, their development was followed by the team and discussed in relation to the treatment. Older adolescents, who presented after age 16 years, were often treated with GnRHa for the minimum period of six months. Generally, they were more mature than the younger adolescents at the start of the diagnostic process and many already had clear ideas about their treatment wishes. In adults, GAH are usually started directly after the diagnostic phase (Wiepjes et al., 2018).

The period of PS used in adolescents is considered worthwhile by some of the adolescents, as the individual in the current study who indicated it gave peace of mind to think about the future. On the other hand, some post-pubertal adolescents perceived little benefit of the treatment, as stated by one transboy who discontinued GnRHa in the current study. A possible benefit of treatment with GnRHa for fully matured transgender boys may be the suppression of menstrual bleeding. Alternative methods may be used to achieve this, although GnRHa are more effective than progestins to immediately and fully suppress menstruation (Tack et al., 2016). Furthermore, many adolescents do not wish to use continuous oral contraceptives because of the fact that they contain 'female' hormones and because of fear that breast size may increase. Adolescents should be counselled on all available treatment options and their (side) effects so that they can make an informed choice.

The relatively small size of the cohort that was described is a limitation of the current study as well as its retrospective character. The duration of follow-up was limited, and in some of the adolescents who stopped treatment with GnRHa because they no longer experienced gender dysphoria, gender dysphoria might recur later in life. The observational design does not allow conclusions about any possible effect of treatment with GnRHa on gender identity development. A randomized controlled trial in adolescents presenting with gender dysphoria, comparing groups with and without treatment with GnRHa, could theoretically shed light on the effect of treatment with GnRHa on gender identity development. However, many would consider a trial where the control group is withheld treatment unethical, as the treatment has been used since the nineties and outcome studies although limited have been positive (de Vries et al., 2014; Smith, van Goozen, & Cohen-Kettenis, 2001). In addition, it is likely that adolescents will not want to participate

in such a trial if this means they will not receive treatment that is available at other centres. Mul and colleagues (2001) experienced this problem and were unable to include a control group in their study on treatment with GnRHa for adopted girls with early puberty because all that were randomized to the control group refused further participation. An alternative approach that has been suggested to gain more insight into the effect of treatment on gender identity development is to collect baseline data at the time of referral from adolescents who are on a long waiting list for diagnostic evaluation and treatment and compare the percentage of these adolescents in whom gender dysphoria is still present after a certain period of time to that in adolescents on treatment with GnRHa (Zucker, 2019).

In conclusion, this study shows that a small number of adolescents discontinued treatment with GnRHa because they no longer wished GAMT. This indicates that not all adolescents and parents assume that transgender outcome is the only possible outcome and shows that gender identity can still fluctuate when using GnRHa, at least in some adolescents. However, gender dysphoria subsided in a small number of adolescents and it is uncertain if this would have been different without treatment with GnRHa. Some adolescents used GnRHa for a prolonged period before starting GAH while regularly meeting with an MHP which is consistent with the use of treatment with GnRHa as an extended diagnostic phase. The great majority who had started treatment with GnRHa continued with GAH. It is important to take this into account when counselling adolescents who consider this treatment and their parents.

7

Perceptions on the function of puberty suppression of transgender adolescents who continued or discontinued treatment, their parents, and clinicians

Lieke J. J. J. Vrouwenraets

Martine C. de Vries

Irma M. Hein

Marijn Arnoldussen

Sabine E. Hannema

Annelou L. C. de Vries

2021. *International Journal of Transgender Health*, 23(4), 428-441

This study was funded by 'Fonds Wetenschappelijk Onderzoek Seksualiteit' (FWOS, projectnummer 18.008)

ABSTRACT

Purpose: Treatment for transgender adolescents with puberty suppression (PS) was developed to provide time for exploration before pursuing gender-affirming medical treatment (GAMT) with irreversible effects. It may also result in a more satisfactory physical outcome for those who continue with GAMT. Despite being the current first choice treatment, little research has examined the function of PS from the perspectives of transgender adolescents, their parents, and clinicians. Insight into the perceived functions of PS will help to adequately support adolescents in their decision-making process and give them the care they need.

Methods: Qualitative study using interviews with eight transgender adolescents who proceeded with GAMT after PS ('continuers'), six adolescents who discontinued PS ('discontinuers') and 12 parents, and focus groups with ten clinicians.

Results: All informants considered inhibition of development of secondary sex characteristics an important function of PS. Most continuers saw PS as the first step of GAMT. Nevertheless, some were glad that the effects were reversible even if they did not expect to change their minds. Some discontinuers did experience PS as an expanded diagnostic phase. One continuer used the time on PS to get used to living in the affirmed gender role, and several parents found the time helpful to adapt to their child's new gender role. PS provided clinicians more time for diagnostic assessment.

Conclusions: Adolescents, parents and clinicians do not all report the same functions of PS. Although international guidelines emphasize providing time for exploration of gender identity as an important reason for PS, many adolescents nowadays seem to have clear ideas about their gender identity and treatment wishes, and experience PS as the first step of GAMT. For some discontinuers however, PS offered a valued period of exploration. Guidelines could be modified to provide more customized care, taking adolescents' and parents' ideas about the functions of PS into account.

INTRODUCTION

International guidelines recommend treatment with puberty suppression (PS; using gonadotropin-releasing hormone analogues (GnRHa)) for transgender adolescents if certain criteria are fulfilled (Coleman et al., 2012; Hembree et al., 2017). It is recommended to start treatment after adolescents first exhibit physical changes of puberty (at least Tanner stage 2), in order to suppress further development of secondary sex characteristics in a reversible manner. According to these guidelines, one of the main reasons to start PS is to 'pause' puberty to expand the diagnostic phase so that adolescents have 'extra' time to explore their options and think about pursuing subsequent gender-affirming medical treatment (GAMT) with irreversible effects. A second reason to start PS in early puberty is that the physical outcome may be more satisfactory compared to PS in later stages of puberty and some surgeries such as mastectomy may not be necessary or less invasive because development of secondary sex characteristics is prevented (van de Grift et al., 2020). This may be a life-long advantage for adolescents (Cohen-Kettenis & van Goozen, 1997). In addition, PS can be used in adolescents in later stages of puberty to prevent facial hair growth in transgirls (assigned male at birth, with a female gender identity) and to stop menses in transboys (assigned female at birth, with a male gender identity) (Hembree et al., 2017). Treatment with PS has been shown to improve psychological functioning of adolescents in various domains (de Vries et al., 2011a; van der Miesen et al., 2020). Experiencing full endogenous puberty might impair well-being and healthy psychological functioning (Hembree et al., 2017). However, the positive effects of PS need to be weighed against possible drawbacks. Some of the long-term effects of PS are still unknown (Biggs, 2021; Giordano & Holm, 2020; Harris, Tishelman, Quinn, & Nahata, 2019). A potential negative impact on cognitive, physical and psychosocial development has been mentioned, for example the risk of impaired fertility (Chen et al., 2020; Harris, Kolaitis & Frader, 2020; Laidlaw et al, 2019b). Furthermore, concerns have been raised that preventing exposure to sex hormones and disrupting pubertal and sexual development may alter the course of gender identity development and may prevent spontaneous resolution of gender dysphoria or the recognition of oneself as homosexual rather than transgender (Korte et al., 2008; Vrouenraets et al., 2015). Furthermore, in a qualitative interview study, clinicians stated that they have concerns about the lack of long-term data on some possible side effects of treatment with PS (Vrouenraets et al., 2015). Additionally, certain options for genital surgery may not be available to those who started PS early in puberty necessitating the use of more invasive alternatives (van de Grift et al., 2020). Besides, there are worries about the risk of regret, since gender identity might fluctuate during adolescence (Vrouenraets et al., 2015). The results of a qualitative interview study with transgender adolescents showed that some adolescents themselves also had some hesitations regarding early medical treatment. They reported doubts, for example, about the ability of adolescents to make informed decisions with regard to medical treatment at the age of 12 or younger (Vrouenraets et al., 2016).

A study from the Netherlands showed that of all adolescents seen at the Amsterdam gender identity clinic, around 75% started with PS and the other 25% did not (Arnoldussen et al., 2020; Arnoldussen et al., 2022b). The vast majority of the adolescents who start PS subsequently start GAMT (e.g., Brik et al., 2020; de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2011b; Wiepjes et al., 2019). The follow-up studies that are available show that psychological functioning has significantly improved after PS, gender-affirming hormones (GAH) and surgeries (de Vries et al., 2011b; de Vries et al., 2014). Longer-term follow-up data on treatment satisfaction, psychological functioning and possible discontinuation of affirming treatment are currently being collected (no results yet).

Previous research has shown that many transgender adolescents seem to experience PS as the first necessary step of a seemingly clear trajectory towards further GAMT, rather than as an opportunity to consider further treatment wishes (Brik et al., 2020). This implies that PS may serve functions that are not mentioned in the guidelines. Little research has examined the motivation to apply for PS from the point of view of adolescents and their parents. Insight into the function of PS according to the adolescents, their parents, and their clinicians will help to adequately support the adolescents in their decision-making process and give them the care and information they need. In addition, functions of PS may vary among adolescents; for those who subsequently start with GAH the function of PS may be different than for those who discontinue PS. To gain more insight into this topic, we have performed a qualitative interview study focusing on the following questions: (1) what function did treatment with PS have for transgender adolescents, their parents, and their clinicians?; and (2) do transgender adolescents who continued to GAMT, adolescents who discontinued PS treatment, their parents, and clinicians have different ideas about the function of PS, and if so, in what sense?

METHODS

Participants

The study was approved by the institutional review board of the Amsterdam University Medical Centres, location VUmc, and the Leiden University Medical Centre (LUMC). Interviews and focus groups were conducted in the context of a larger study on transgender adolescents' competence to consent to PS and the function of this treatment. Transgender adolescents who proceeded to GAH after PS as well as adolescents who discontinued treatment with PS, and their parents were recruited from the gender identity clinics in Amsterdam and Leiden between January and September 2019. They were interviewed in order to explore their considerations and experiences regarding the function of PS. The same topics were discussed in focus groups with clinicians of the two treatment teams. The Amsterdam and Leiden gender identity clinics were the only two

academic gender identity clinics in the Netherlands that offered diagnostic assessment and treatment for adolescents at the time of the study. Both centres have multidisciplinary teams in which specialists in child and adolescent psychiatry and psychology, and paediatric endocrinology participate. The teams follow the same diagnostic procedures and treatment protocols.

Semi-structured individual interviews were held with 14 adolescents and 12 parents. The informants consisted of:

1. Six adolescents who had been treated with PS and had discontinued this treatment;
2. Eight transgender adolescents who were treated with PS and GAH;
3. Four parents of adolescents who had discontinued treatment with PS;
4. Eight parents of adolescents who were treated with PS and GAH.

Inclusion criteria for the adolescents who had discontinued treatment (group 1) were: a) diagnosis of gender dysphoria according to DSM-IV or DSM-5, depending on which version of the DSM was used at the time of diagnosis (American Psychiatric Association, 2013), b) had started PS at age 10-17 years, and c) had discontinued PS treatment. Out of 1015 adolescents diagnosed with gender dysphoria between 2000 and 2018 at the Amsterdam or Leiden gender identity clinic twenty adolescents in total were eligible. Eight adolescents could not be reached, mostly because their contact details were no longer up to date. One was not contacted because the adolescent had previously indicated that he did not want to be approached for research purposes. Two adolescents were not contacted because the involved clinician thought this was inappropriate due to, among others, comorbid mental health difficulties. Nine adolescents were asked to participate; initially the formerly involved clinician contacted the adolescent by telephone to explain what participation in the study implied and to ask if the researcher could contact the adolescent. If the adolescent agreed, the researcher contacted the adolescent to further explain the study and invite them to participate. Two adolescents declined without giving a reason, one parent did not want her child to participate because she did not think that was in the child's best interest, and six adolescents agreed to participate. All were interviewed face-to-face at a clinic visit or at their homes if preferred, between January 2019 and September 2019.

Inclusion criteria for the adolescents who had continued treatment (group 2) were: a) diagnosis of gender dysphoria according to DSM-IV or DSM-5, depending on which version of the DSM was used at the time of diagnosis (American Psychiatric Association, 2013), b) had started PS at age 10-15 years, c) had used PS for at least 12 months, d) had used GAH for at least six months, and e) age at the time of the interview between 15 and 20 years. The aim was to have at least as many adolescents in group 2 as in group 1. Therefore, thirteen consecutive adolescents were asked to participate when they attended their regular follow-up appointment in February and March 2019. These adolescents were not selected

in any way, in order to have a random selection of participants. Eight adolescents agreed to participate. Four adolescents could not participate because they had other appointments to attend on the day they visited the clinic and one adolescent declined without giving a reason. All adolescents were interviewed face-to-face. Characteristics of the two groups of adolescents are presented in table 9 (which can be found at page 81).

Four parents (three biological mothers and one adoptive mother) of adolescents who had discontinued treatment were asked to participate in the study and all agreed. The other parents were not asked because of logistic reasons. One parent was interviewed face-to-face and three via telephone because of traveling distance. The parents of all interviewed adolescents who continued treatment were asked to participate. Eight parents (seven biological mothers and one biological father) agreed. They were all interviewed face-to-face when their child attended their regular follow-up appointment at the Amsterdam University Medical Centres, location VUmc. All interviews with parents took place between February 2019 and September 2019.

In addition, two focus groups with clinicians from the two treatment teams were held. The informants were purposefully selected based on their discipline (all different disciplines working within both teams participated to assure representativeness for the complete treatment team; i.e., three child and adolescent psychiatrists, four child and adolescent psychologists and three paediatric endocrinologists). They had different levels of experience (ranging from one to 12.5 years) with care for transgender minors. Therefore, the participants of the focus groups can be considered representative of the larger group of members across the two teams in terms of the range of disciplines and level of experience. These focus groups took place in June and August 2019.

Procedure and measures

The interviews were conducted by two authors of this study, both had interview experience (MA and LV). They had not been involved in the diagnostic assessments of the adolescents they interviewed. Initial interview questions were formulated after review of the relevant literature and discussion within the research team involving all authors. The interview guide contained no close ended questions (see Appendix B, which can be found at page 223).

Two focus groups were conducted. One of the authors (MV) facilitated both focus groups. During the focus groups the questions asked in the interviews were presented along with several anonymous quotes from the interviews to get the conversation started. The participants were asked whether they agreed and/or identified with the quotes. Furthermore, the participants were invited to express possible other views they held on these topics.

All interviews and focus groups were audio-taped and transcribed verbatim. Before each interview and each focus group informed consent for participation and tape recording was obtained. The interview duration varied between the groups (adolescents who had stopped PS 41-73 minutes, their parents 15-48 minutes, adolescents who continued PS and had started with GAH 12-22 minutes, and their parents 13-38 minutes, focus groups 79-88 minutes).

Analysis

Data analysis was based on hermeneutic analysis (Miles & Huberman, 1994; Stake, 2005). After an initial open reading of the data, two of the authors presented some preliminary (sub)themes. Besides, one of these authors analysed the transcripts by selecting representative quotations for each of the defined themes, taking care to draw quotations from all data sources. Then, the same two authors conducted an additional round of analyses to assess whether the (sub)themes enabled them to accurately subdivide the outcome of the data. Besides, these two authors also re-analysed the transcripts by selecting representative quotations. Then, through a deliberative process, the authors redefined the initial (sub)themes until they reached a consensus.

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RESULTS

From the interviews and the focus groups, four themes regarding the function of treatment with PS emerged. Representative quotations are presented to illustrate the themes identified.

Theme 1: Reduction of suffering through inhibition of the development of secondary sex characteristics

All interviewed adolescents and all parents stated that inhibition of the development of secondary sex characteristics was one of the main reasons, and for several the most important reason, to start PS. Most stated that the fact that their bodies would not (continue to) develop in a way they did not want, was a great relief.

"It also gave me some peace of mind because I knew: okay, my body is not going to continue to develop, I will not become more masculine." - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

"Knowing that the treatment with puberty suppression would spare him breast-removal surgery was of course really good." - Interview with a parent of a transboy who continued PS; age at start PS: 12.9; age at interview: 15.5

The clinicians stated that almost all adolescents suffer from (the anticipation of) the development of secondary sex characteristics. For almost all clinicians, halting the development of the physical changes, and thereby reducing this suffering, were the main reasons to start PS. Clinicians hoped that the treatment would improve the adolescents' functioning now and later in life, and reduce the distress caused by the developing body to create time and rest for further exploration enabling a healthy psychological adolescent development.

"The main reasons [to start treatment with puberty suppression] are to reduce suffering and stress. An additional reason, to a variable degree [depending on the degree of development of secondary sex characteristics], is suppressing the development of physical changes." - Focus group with clinicians

"As far as I'm concerned, one of the reasons [to start treatment with puberty suppression] is to make the adolescent feel a little better at that moment, because you stop the puberty that the adolescent simply does not want." - Focus group with clinicians

Besides, most clinicians and one adolescent stated that the adolescents might be better able to decide whether or not to proceed with GAH when, through PS, they no longer suffer from the development of secondary sex characteristics and other physical developments that come with puberty.

"Once the adolescent is less stressed [about the development of the secondary sex characteristics] the adolescent is sometimes better able to judge if proceeding with gender-affirming hormones is really desired." - Focus group with clinicians

"The treatment with puberty suppression gave me more peace of mind, [...] it opened up my tunnel vision and helped me see more possibilities in terms of gender identity and everything. So, yes, it has helped me with the search for who I am." - Interview with an assigned female at birth who had discontinued PS; age at start PS: 15.5; age at discontinuation PS: 16.6; age at interview: 17.0

In addition, clinicians mentioned that the distress that adolescents and parents experience because of (the anticipation of) the development of secondary sex characteristics made them feel pressured to treat the adolescents.

"The treatment with puberty suppression gives [the adolescent] a kind of rest because the adolescent's agony [caused by the development of the secondary sex characteristics] is relieved. Additionally, the agony itself may put pressure on the decision-making for both the adolescent and the clinician involved." - Focus group with clinicians

"It sometimes happens that the parents are more stressed [than the adolescents themselves], [...] especially when it concerns younger adolescents [10/11 years old] [...] I sometimes find that difficult, when I feel the parents push very hard [to start treatment with puberty suppression]." - Focus group with clinicians

Theme 2: Providing more time to expand the diagnostic phase

Three out of the six adolescents who had discontinued PS (group 1), and all four of their parents, stated that they had primarily used PS to gain more time to think about whether or not to proceed with GAMT without having to worry about the physical changes of their body.

"It was a great relief; I did not have to worry about all that fuss [e.g., having my period and breast growth] but could simply think about who I am. To clarify things. [...] I became a woman, my breasts started to grow but I just did not want it. I simply needed a lot more time to think, because it was so unclear who I was and how I wanted to live my life." - Interview with an assigned female at birth who had discontinued PS; age at start PS: 12.1; age at discontinuation PS: 13.3; age at interview: 14.3

"When he was referred to the Amsterdam gender identity clinic he sometimes lived his life as a girl and sometimes as a boy; he was still searching and in doubt. In order to have more time, he started treatment with puberty suppression." - Interview with a parent of an assigned male at birth who had discontinued PS; age at start PS: 15.9; age at discontinuation PS: 16.7; age at interview: 22.9

One adolescent from group 1 stated that she initially did not think of PS as a way to gain extra time to think, but during PS she realised that she could use this time to explore her wishes regarding GAMT.

"When I started treatment with puberty suppression it really felt as the first step of the transition for me. After that, I would continue with testosterone treatment. [...] Only during the treatment with puberty suppression I realised, now I still have time to think [about whether I want to continue with the transition or not]." - Interview with an assigned female at birth who had discontinued PS; age at start PS: 16.7; age at discontinuation PS: 17.0; age at interview: 19.5

On the other hand, none of the eight interviewed adolescents who had proceeded with GAH, and none of their parents, stated that more time to explore and decide whether or not to pursue GAMT was a function of PS for them. They mentioned that they were/their child was already certain that they wanted to proceed with GAMT when starting PS. However, several of them stated that they could understand the rationale for other adolescents who might need this extra time to explore.

“For me, it was not a period of reflection. [...] I have never really had any doubts about wanting to be a man or not.” - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 15.5

“It was not as if she thought: good, now I have time to carefully think things over. She had already done that thinking before the puberty suppressing treatment.”
- Interview with a parent of a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

Additionally, one transgirl that continued PS and one parent stated that, even though extra time to explore and overthink whether or not to pursue GAMT was not a reason for them to start PS, they were both glad that if her (the child’s) thoughts had changed, no irreversible changes would have taken place.

“I liked the idea that the effects [of treatment with puberty suppression] were still reversible, even though I did not doubt her feelings, and did not think that it [stopping puberty suppressing treatment] would ever be necessary.” - Interview with a parent of a transgirl who continued PS; age at start PS: 12.0; age at interview: 18.1

Several clinicians stated that, at least in some situations, one of the reasons for them to let the adolescents start PS was to give the adolescents more time before deciding on GAMT. This time would allow them to further develop and become more autonomous.

“You use it [puberty suppressing treatment] as a period for delay and respite so that you make the step to a more irreversible treatment with gender-affirming hormones, surgery etc. at a later moment, when you believe the adolescent is able to oversee all consequences [of the treatment].” - Focus group with clinicians

“The adolescents become a bit more autonomous in that period between the ages of 13 and 16. During this period they become able to think a little more autonomously and [they] are a little less influenced by the environment. This happens very gradually, but it does make a difference.” - Focus group with clinicians

Besides, the clinicians mentioned that in some cases, another reason to start PS was to allow themselves more time for the diagnostic assessment. While observing the adolescent’s development over time, the indication for further treatment might become more clear. The clinicians explained that additional diagnostic evaluation did not only concern the diagnosis gender dysphoria itself, but other aspects of the adolescents’ life too.

“I think you also ‘buy’ time for the clinician to conduct a proper diagnostic evaluation.

In that period of time you [as the clinician] are able to follow the development of the adolescent. The information this provides may help create a better diagnostic image and arguments as to why you would or would not proceed to gender-affirming medical treatment. This [clarifying the diagnosis or these arguments] is often quite difficult when a child or adolescent is younger.” - Focus group with clinicians

“Sometimes adolescents believe that starting [puberty suppressing] treatment fixes everything, which is not a realistic idea. The adolescents have to work on a number of other things [problems in their lives] too. We [the adolescent and clinician] have to actively make a plan how to deal with and solve these problems, because not all problems will just disappear into thin air.” - Focus group with clinicians

Theme 3: Providing (more) time to get used to living in the affirmed gender role

Half of the adolescents who proceeded with GAH after PS stated that the period on PS provided their parents and others in their environment time to get used to them living in the affirmed gender role. Most parents confirmed this. Only one adolescent stated that she herself used this period to get used to living in the affirmed gender role too, but the other seven adolescents did not. None of the adolescents who had discontinued PS, stated that they considered having time to get used to living in the affirmed gender role a function of PS for them and/or people in their environment. However, some clinicians did mention giving the adolescents the opportunity to get used to living in their new gender role and evaluating this experience with the adolescents as a function of PS.

“The treatment with puberty suppression gave me and the people around me time to get used to me living as a girl. That was really essential, because if I had started with the female sex hormones straight away it might have been too much to get used to and my environment might not have understood [me living as a girl].” - Interview with a transgirl who continued PS; age at start PS: 12.9; age at interview: 17.8

“In the beginning, I found it quite difficult that I gave birth to a son who wanted to become a woman. We processed that in that period [when she was given treatment with puberty suppression].” - Interview with a parent of a transgirl who continued PS; age at start PS: 14.2; age at interview: 17.9

“They [the adolescents] have the opportunity to get used to living in the affirmed gender role and to find out for themselves what it is like.” - Focus group with clinicians

For the other half of the adolescents who proceeded with GAH, and their parents the period on PS was not a period to get used to living in the affirmed gender role. One parent even stated that the period on PS took too long for them.

"We never had to get used to anything because it had always been like this since his childhood; he looked like a boy since he was five years old, he played with other boys, and presented himself as a boy." - Interview with a parent of a transboy who continued PS; age at start PS: 12.9; age at interview: 15.5

"Of course it was a period in which we as parents could get used to it [our child presenting herself as a girl], but I did not need four years [to get used to it] [...] it could have been shorter because it was already clear to us and we had known for a long time [about the gender non-conforming feelings of our child]." - Interview with a parent of a transboy who continued PS; age at start PS: 11.9; age at interview: 18.5

Theme 4: The 'first step' of the gender-affirming medical treatment

All adolescents who proceeded with GAH stated that they viewed the start of PS as the first step in their trajectory of GAMT. Two adolescents who did not proceed with GAH stated this too. About half of the interviewed parents said they saw starting PS as the first step.

"For me it really was like the beginning of becoming a man because you need to have puberty suppression before you can start treatment with gender-affirming hormones." - Interview with a transboy who continued PS; age at start PS: 12.9; age at interview: 15.5

"The most important reason to start with puberty suppressing treatment was to subsequently start with male sex hormones." - Interview with an assigned female at birth who had discontinued PS; age at start PS: 17.0; age at discontinuation PS: 17.9; age at interview: 27.8

The clinicians acknowledged that most adolescents view the start with PS as the first step of the GAMT. Most clinicians stated that they had the feeling that some adolescents who presented at the gender identity clinic only had one goal in mind: GAMT. The metaphor of a train was used; some children and adolescents seem to be on a moving train with GAMT as their final destination from the moment of the first visit to the gender identity clinic. Some clinicians had the feeling that they needed to slow down some of these trains to make sure that each step was carefully considered.

"It is not as if we [clinicians] put them on some kind of train. Those children and adolescents are already on a train when they first visit the clinic and that makes steering the train more difficult." - Focus group with clinicians

DISCUSSION

Comparing the considerations of transgender adolescents who had continued with GAH after PS, adolescents who had discontinued treatment with PS, their parents, and clinicians reveals that they do not all have the same views on the functions of PS. Nevertheless, there was one reason to start PS which all informants agreed upon: inhibition of the development of secondary sex characteristics. In addition, some clinicians mentioned that PS reduced distress not only in adolescents but also in parents. This distress experienced by parents because of the physical changes their children undergo has been described in other studies as well (Butler et al., 2019; Field & Mattson, 2016). Additionally, especially clinicians considered it important that adolescents mature a little further during the years they receive PS, and that, while they experience less distress due to the undesired development of their bodies, they may be better able to decide on whether or not to proceed with GAMT and carefully consider the consequences of their decision. This is in line with the reason for considering PS mentioned in other studies; namely, that clinicians try to find a balance between the distress in transgender adolescents and the potential long-term risks of the treatment (Butler et al., 2019). Most adolescents who continued with GAH, however, stated that they already knew they wanted to start GAMT after PS.

The idea of PS as a way to 'buy' time to explore and decide whether or not to continue with GAMT was not endorsed by all informants. None of the adolescents who had started GAH after PS, nor their parents, saw this as a reason to start PS. Most stated that they did understand this rationale behind the treatment and that it might be relevant for other adolescents, but not for themselves, although several mentioned it was good that the effects of the treatment were reversible "just in case things would have changed." By contrast, most adolescents who had discontinued PS, and their parents, stated that they did, either initially or eventually, see PS as a way to buy time to explore their options and consider the subsequent trajectory. For clinicians, this extra time for exploration was a function of and a reason to start PS too, although this depended on the case. The finding that most adolescents did not use PS for further exploration of their gender identity is of note, but not an unexpected finding. For example, follow-up studies have already shown that the vast majority of adolescents who start PS subsequently start GAMT (e.g., Brik et al., 2020; de Vries et al., 2011b; Wiepjes et al., 2019). In the Netherlands, adolescents follow a careful assessment consisting of several appointments over a longer period of time to find out if they meet the criteria of the diagnosis gender dysphoria, if they understand

the consequences of medical intervention, and to explore if starting PS, and later on GAMT, is indicated (Cohen-Kettenis, Steensma, & de Vries, 2011). It is therefore important to keep in mind that adolescents never 'just' start PS. Hence it might not be surprising that most adolescents did not use PS to further explore their gender identity since they had already done so before the decision to start PS was made. The diagnostic trajectory that transgender adolescents followed in Amsterdam and Leiden might have selected those adolescents that were very likely to continue with GAMT. Nevertheless, clinicians and, to a lesser extent, parents of adolescents who had discontinued treatment, considered the possibility of further exploration important. So most adolescents who had continued PS and started GAH did not, in retrospect, see PS as a way to extend the diagnostic phase, in contrast to the fact that it is an important reason noted in the international guidelines (Coleman et al., 2012; Hembree et al., 2017). However, this does not mean that PS is not a valuable medical intervention. In our study, for those who discontinued PS, it was a valuable intervention proving the importance of having 'thinking time'. Furthermore, those who had continued PS and started GAH, acknowledged it had given their families time to adjust. Their clinicians reported the importance of having time to support further self-exploration and to prepare for treatment with irreversible effects. Additionally, the study of Brik and colleagues (2020) showed that several Dutch adolescents received mental health support from a local mental health professional or a psychologist of the treatment team of the gender identity clinic more frequently than minimally necessary by protocol during treatment with PS. This might support the idea that adolescents do use the period of PS as an extended diagnostic phase in which they further explore their gender identity and whether they want to continue with GAMT or not (Brik et al., 2020). If this results in a decision to pursue GAMT, adolescents might in hindsight not recognize that the period of PS was important in making this decision, even if in fact it was. The experiences of adolescents who had discontinued PS support this notion. Therefore, PS may expand the time of self-exploration even in those who feel certain about their gender trajectory and who will apply for further treatments later on.

About half of the adolescents who proceeded with GAMT used the time they received PS to get used to living in the affirmed gender role, as described in the international guidelines (Coleman et al., 2012; Hembree et al., 2017). Worth mentioning is that most adolescents stated that particularly their parents and other relatives had to get used to them living in the affirmed gender role, which was confirmed by most parents. This aspect is mentioned in other studies too (Alegría, 2018), but not in the international guidelines (Hembree et al., 2017).

All adolescents who proceeded with GAH, some of the adolescents who stopped PS, and about half of the parents stated that they saw the start with PS as the first step of the GAMT. Most clinicians recognize that many adolescents experience it as such. Sometimes

clinicians have the feeling they need to ‘slow down’ the adolescents who seem to have set GAMT as their final ‘goal’, in order to make sure that each step is carefully considered. Even though research shows mostly positive effects of PS, some of the long-term effects of the treatment are still unknown (Biggs, 2021; Giordano & Holm, 2020; Harris et al., 2019; Klaver et al., 2018; 2020; Klink et al., 2015; Schagen, Wouters, Cohen-Kettenis, Gooren, & Hannema, 2020). Concerns have been raised about adolescents regretting the treatment later in life, and about the effects of GnRHa on cognitive, physical and psychosocial development (Ashley, 2019; Chen & Simons, 2018; A. de Vries, 2020; Kaltiala-Heino, Bergman, Työljärvi, & Frisé, 2018; Laidlaw et al., 2019b; Vrouenraets et al., 2015; Wren, 2019). If PS is regarded as the first step of GAMT, children from the age of 10 make decisions with life-long consequences. One of the most pressing concerns is the possible loss of fertility due to adolescents ‘automatically’ proceeding to GAH and possibly gonadectomy and the fact that these adolescents will never undergo the puberty of their birth-assigned sex (Hudson et al., 2018). Loss of fertility, as well as concerns about (future) fertility may have a significant negative impact on quality of life and psychosocial well-being (Brik et al., 2019; Carter et al., 2010; Gorman, Su, Robert, Dominick, & Malcarne, 2015; Trent et al., 2003; Wenzel et al., 2005). On the other hand, one should keep in mind that even if treatment with PS might have harmful effects, refraining from intervention might have harmful effects as well (de Vries et al., 2021).

In conclusion, the reasons to start PS and the functions of this treatment for transgender adolescents described in the international guidelines are only partly in line with those reported by the adolescents themselves. They overlap to a larger extent with reasons and functions as mentioned by parents, and are largely in line with those reported by clinicians. The purpose with which children, adolescents and parents entered a gender identity clinic in the late 1990s and early 2000s, when the protocol for diagnostic assessment and treatment was drawn up, may be different from the purpose with which they enter a clinic nowadays and may also be different in other countries and contexts. Previously, families may have been ‘confused’ by the situation and the gender non-conforming feelings of the child. They may have wanted support in their search for a way to help the child. At that time, an extended diagnostic period through PS was an ideal option. At the present time, families who enter a clinic are much better informed through the internet, media and peers, and many will have a clear idea of the diagnosis and their treatment wishes. An extended diagnostic period to explore the possibility of pursuing GAMT might therefore not be appropriate for all those who currently enter a gender identity clinic. In that respect, the protocol could be modified to provide help that is more personalized and customized, taking into account someone’s purpose and thoughts. For example, one might consider following the treatment protocol for transgender adults, i.e., skipping PS and starting GAMT immediately after the diagnostic trajectory, in some cases such as older transgender adolescents who have experienced gender non-conforming feelings from an early age, if

this is in line with the adolescent's and parents' wishes. On the other hand, one adolescent who discontinued PS recounted that before she started PS she did not think of PS as a way to gain extra time to think. However, during PS she realised that she could use this time to explore her wishes regarding GAMT and she ultimately decided not to continue with PS and GAMT. This may be true for other adolescents as well and should be kept in mind. So even for adolescents who grow up in a supportive and affirming environment, a period of pause can turn out to be beneficial and give them time to become better informed and more realistic about the future. Additionally, the results of this study show that PS serves functions not only for the transgender adolescents themselves, but also for their parents and other relatives, and for clinicians. Family support plays an important role in shaping the transgender adolescents' health (Bouris et al., 2010). A review on this topic in sexual minorities found that, over time, parents generally become more accepting of their child (Rosario & Schrimshaw, 2013). Even though it is unknown whether these results may be generalized to transgender minors, giving parents and other relatives time to get used to their child's new gender role might increase their acceptance (Katz-Wise, Rosario, & Tsappis, 2016). PS might play a role in this regard by providing 'extra' time before GAMT is started. Nevertheless, one may wonder how much priority this function should be given, for example, if the adolescent could be harmed by staying on PS for a longer time, but the parents on the other hand need more time to get used to their child living in the affirmed gender role. From an ethical point of view, clinicians should balance the interests not only of the adolescents but also of the parents, and guidelines should recognize that PS might enable others to get used to the identity and gender role of the adolescent.

There are strengths and weaknesses to the present study. The qualitative nature of this study made it possible to find out, in depth, the ways in which transgender adolescents, their parents and clinicians think or feel about the function of PS. Another strength of this study is that adolescents who did continue with GAMT as well as adolescents who did not proceed with GAMT were interviewed. This allowed us to compare their considerations. Nevertheless, the retrospective nature of this study raises the possibility of recall bias and hindsight bias of the informants, and the first interview-question might appear to introduce bias, instead of being fully open-ended. In addition, it should be noted that the informants are recruited from two Dutch treatment teams which work according to the same treatment protocol where PS was required for all adolescents before any further affirming treatment was provided. Adolescents recruited from other gender identity clinics in other contexts might report a different function of PS. Therefore, we encourage prospective gathering of more qualitative data from adolescents who have not started PS yet or receive PS but have not started treatment with GAH yet, especially from other settings in other contexts, e.g., in clinics with a shorter history of providing care and in countries where less general knowledge on gender dysphoria/gender incongruence is available (e.g., Fortunato et al., 2020; Jokić-Begić et al., 2017; Shirdel-Havar, Steensma,

Cohen-Kettenis, & Kreukels, 2019). In addition, the ages when the adolescents visited the gender identity clinic for the first time, and the ages when they started PS differ between the group of adolescents who discontinued treatment and the group of adolescents who continued treatment. This possibly means that the adolescents in these two groups are different. Even though this is not a subject of this study, this is interesting to examine further in future research. Additionally, even though all adolescents who had discontinued treatment and agreed to participate were interviewed, and a slightly larger number of adolescents who continued treatment was interviewed, the sample size is small. Due to the small sample size, the non-participation rate and the skewed sex ratio, it is not completely certain if genuine saturation was reached. For non-participating adolescents who had discontinued treatment, PS might have fulfilled different functions compared to the adolescents that have been interviewed. We therefore encourage gathering more qualitative data of a larger sample with a more balanced sex ratio. In conclusion, this study shows that PS has various functions and is started for various reasons. This should be reflected by guidelines, leaving room for more customized care, taking the different functions and thoughts of the adolescents and parents regarding PS into account.

8

Use of fertility preservation among a cohort of transgirls in the Netherlands

Tessa Brik

Lieke J. J. J. Vrouwenraets

Sebastian E. E. Schagen

Andreas Meissner

Martine C. de Vries

Sabine E. Hannema

ABSTRACT

Purpose: The primary aims of the study are to examine the rate of attempted fertility preservation (FP) among a Dutch cohort of transgirls who started treatment with gonadotropin-releasing hormone analogues (GnRHa) and the reasons why adolescents did or did not choose to attempt FP.

Methods: The study was a single-centre retrospective review of medical records of 35 transgirls who started treatment with GnRHa between 2011 and 2017.

Results: Ninety-one percent of adolescents were counselled on the option of FP. Thirty-eight percent of counselled adolescents attempted FP, and 75% of them were able to cryopreserve sperm suitable for intrauterine insemination (IUI) or intracytoplasmic sperm injection (ICSI). Younger and Caucasian transgirls were less likely to attempt FP. No specific reason for declining FP was known in 33% adolescents, 32% of adolescents were not able to produce a semen sample because of early puberty, 17% felt uncomfortable with masturbation, 17% did not want to have children, and 13% wanted to adopt.

Conclusions: One third of adolescents attempted FP, which is much more than the percentage reported in previous studies from the United States. One third of the transgirls could not make use of FP because they were unable to produce a semen sample because of early pubertal stage. For these adolescents, alternatives need to be explored.

INTRODUCTION

Many transgender adolescents wish to undergo gender-affirming medical treatment (GAMT), which may initially consist of puberty suppression (PS) with gonadotropin-releasing hormone analogues (GnRHa), followed by gender-affirming hormones (GAH) and, in adulthood, gender-affirming surgery (Coleman et al., 2012; Hembree et al., 2017). Whereas the effects of GnRHa are reversible, long-term use of gender-affirming sex steroids may affect fertility, and if gonadectomy is performed, the transgender person will definitely be infertile (de Roo et al., 2016; Hembree et al., 2017; Olson, Forbes, & Belzer, 2011). Infertility may have a major impact on the lives of transgender minors. Previous studies showed that concerns about (future) fertility are associated with a significant reduction in quality of life (Carter et al., 2010; Trent et al., 2003; Wenzel et al., 2005). Research among adult transmen described significantly better self-perceived mental health status and vitality among those with children than those without children (Wierckx et al., 2012). This suggests that fertility preservation (FP) can influence quality of life in transgender adolescents.

A previous study showed that most transgender adolescents wanted to have children in the future (Strang et al., 2018). Another study, however, pointed out that transgender minors more often state “never wanting to have children” than has been reported in cisgender persons (Nahata, Tishelman, Caltabellotta, & Quinn, 2017). A survey revealed that 62% of adult transmen wanted to have children, and about 38% would have considered FP if it had been available at the time (Wierckx et al., 2012). Fifty-one percent of adult transwomen would have considered sperm cryopreservation if it had been offered (de Sutter, Verschoor, Hotimsky, & Kira, 2002). Nowadays, the World Professional Association for Transgender Health and Endocrine Society recommend counselling regarding FP options before initiating treatment with GnRHa (Coleman et al., 2012; Hembree et al., 2017). However, two recent studies from the United States indicate that transgender minors rarely use FP (Chen, Simons, Johnson, Lockart, & Finlayson, 2017; Nahata et al., 2017).

We aimed to investigate how many adolescents made use of FP in a Dutch cohort of transgirls who started treatment with GnRHa. In addition, we assessed if information about the risk of infertility had been given, if discussion of the option of FP was documented in the medical file, and what the given reason for declining FP was if the adolescent had not made use of FP. Furthermore, we explored what factors were associated with the use of FP.

METHODS

Study population

Transgirls who were referred to start treatment with GnRHa between June 2011 and August 2017 at the gender identity clinic Curium-Leiden University Medical Centre were eligible. Those who declined participation were excluded. The study population consisted of 35 transgirls. Before the start of treatment with GnRHa, all adolescents had a diagnostic evaluation to confirm the diagnosis gender dysphoria according to the DSM-5 criteria (Hembree et al., 2017) and to assess the presence of any psychiatric or psychosocial problems that might interfere with treatment. This evaluation included an IQ test and a psychiatric interview. Written informed consent for treatment with GnRHa was obtained from adolescents and for those aged younger than 16 years also from their parents/guardians. Informed consent forms contained information about the risk of infertility. The option of FP was discussed by the paediatric endocrinologist. If adolescents wished to cryopreserve sperm and thought they would be able to produce a semen sample via masturbation, they were referred to a fertility clinic where semen samples were preserved, on three occasions if indicated.

Data collection

Extracted data from the medical files were age, IQ, Tanner stage, testicular volume, ethnicity, sexual orientation, psychiatric comorbidity (depression, anxiety disorder, posttraumatic stress disorder, and autism spectrum disorder), family situation (i.e., raised in an intact family, divorced parents or other [including adopted, living in a foster-home]) and information about the desire to have children.

Ethics

The study is part of an observational study on the effects of hormonal treatment in adolescents with gender dysphoria, which was approved by the medical ethical committee of the Leiden University Medical Centre.

Statistics

Statistical analyses were performed with SPSS version 23 (IBM) using the t-test for continuous variables or Mann-Whitney U test if data were not normally distributed. Chi-square test or Fisher's exact test was used for categorical variables. No Bonferroni correction was applied when testing the association between several variables and the use of FP because this was meant to explore rather than confirm factors that may be of influence.

RESULTS

Study population characteristics are summarized in table 10.

Table 10. Characteristics of the 35 transgirls at the start of treatment with gonadotropin-releasing hormone analogues

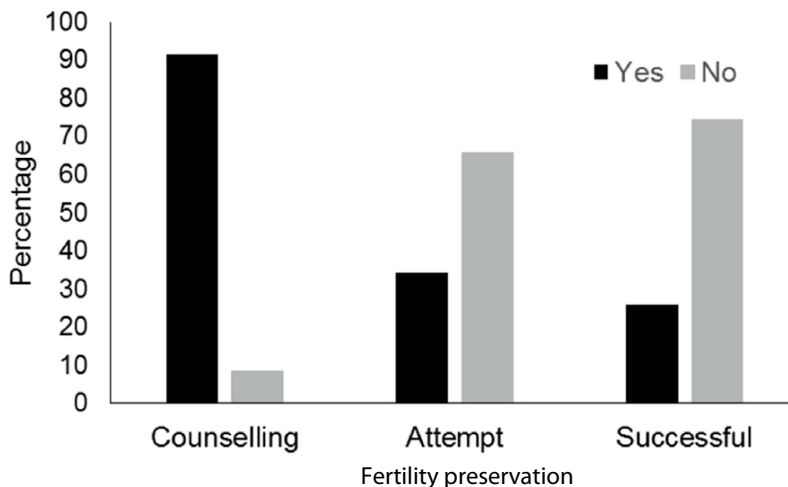
Characteristics	Mean \pm SD, median (range), or number (%)
Age (years)	14.8 \pm 1.9
IQ total	100 \pm 17
Testicular volume (mL)	15 \pm 6
Tanner genital stage	5 (2-5)
Ethnicity (<i>n</i> = 35)	
Caucasian	25 (71)
Other	10 (29)
Attracted to (<i>n</i> = 30)	
Men only	22 (63)
Other	8 (23)
Psychiatric comorbidity (<i>n</i> = 34)	
Yes	16 (46)
No	18 (51)
Interested in having children (<i>n</i> = 15)	
Yes	7 (20)
No	4 (11)
Maybe	4 (11)

Missing data are not shown.

SD refers to standard deviation.

All adolescents had been informed on the risk of infertility, and 91% (*n* = 32) had been counselled about the option of FP. In the other three cases, it was not clear from the medical notes if they had been counselled; two of them were early pubertal (testicular volume 5 mL) so that no FP options were actually available. Forty-one percent (*n* = 13) of the counselled transgirls were referred for sperm cryopreservation, and 38% (*n* = 12) had actually been to the fertility clinic to try to cryopreserve sperm (figure 4). One transgirl who had been referred had not been to the fertility clinic and had not started treatment with GnRH α yet at the time of the analysis because of psychosocial issues.

Figure 4. Counselling about fertility preservation, attempted fertility preservation, and successful fertility preservation (sperm suitable for IUI or ICSI preserved) among 35 transgirls

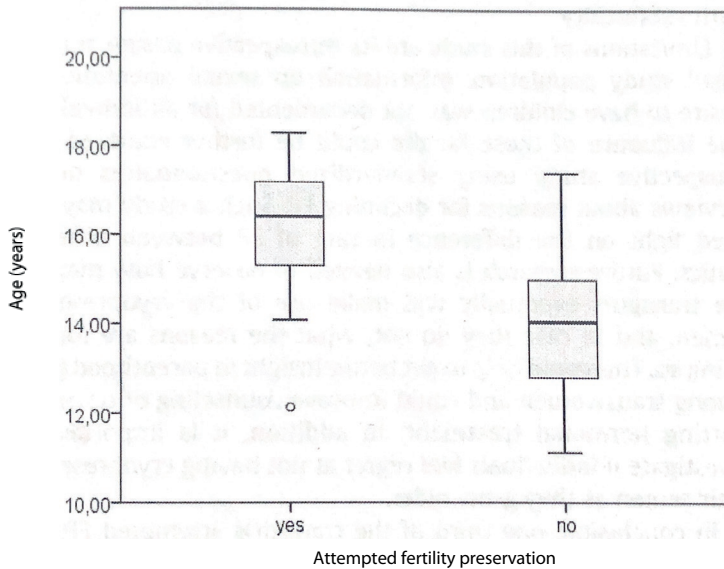


ICSI refers to intracytoplasmic sperm injection; IUI refers to intrauterine insemination.

Given reasons for not wanting to be referred for FP were (some of the transgirls gave more than one reason) not wanting to have children (17%, $n = 4$), wanting to adopt (13%, $n = 3$, one specifically said she did not want to have children who would be like her), feeling uncomfortable with masturbation or having an aversion of their penis (17%, $n = 4$), and feeling uncomfortable with the idea of being the biological father of the child (4%, $n = 1$). Eight persons (33%) did not give a specific reason for declining FP. Eight adolescents (33%) were not referred for FP because they were in early puberty and were not able to produce a semen sample through masturbation.

The mean age at the start of treatment with GnRHa in the group of transgirls who attempted FP was significantly higher (age 16.1 years \pm 1.7) than in the group that did not attempt FP (age 14.2 years \pm 1.7; $p = .003$; figure 5). Tanner stage and testicular volume were also higher in the group who attempted FP (Tanner stage G5, range 4-5; testicular volume 17.2 mL vs. G4, range 2-5; 13.4 mL), but these differences were not significant. The mean IQ in this population was 100 \pm 17. The mean IQ in the group who attempted FP was not significantly different from that in the group who did not (respectively 94 \pm 15 vs. 103 \pm 18; $p = .17$).

Figure 5. Age at the start of treatment with gonadotropin-releasing hormone analogues in transgirls who did and did not attempt fertility preservation. Mean age was significantly lower in the group who did not attempt ($n = 23$) than in the group who did attempt fertility preservation ($n = 12$, $p = .003$)



Because options to have children may depend on the sex of future partners, we investigated if sexual orientation was related to the use of FP. Transgirls who did not attempt FP were as likely to be attracted to men only (12 of 19) as transgirls who did attempt FP (10 of 11; $p = .2$), but only two transgirls were not attracted to men at all. No significant differences were seen in family situation (living together with both parents vs. separated parents/foster parents/adopted or other) between the two groups. However, fewer Caucasian girls attempted FP than girls with other ethnicities including Asian, African, and South American (20% vs. 70%; $p = .02$). Forty-seven percent of the transgirls suffered from psychiatric comorbidity (depression, anxiety disorder, posttraumatic stress disorder, or autism spectrum disorder). Those with psychiatric comorbidity were as likely to attempt FP as those without. Information about the desire to have children was present in medical files of 43% of the transgirls. All four transgirls who stated not wanting to have children declined FP, whereas 36% of those who were (potentially) interested in having children attempted FP.

Of the 12 adolescents who attempted FP, one was unable to ejaculate. She was 12 years old and at Tanner stage G4, with testicular volume 15 mL. One post-pubertal adolescent had azoospermia, whereas another had severe oligozoospermia with a few viable spermatozoa after thawing in only one sample, considered marginally usable for intracytoplasmic sperm

injection (ICSI) in the future, and no sperm was found when testicular sperm extraction was performed. The other nine adolescents, aged 14.1-18.5 years, one at Tanner stage G4, the others at Tanner stage G5, with testicular volume 15-25 mL, stored semen that was of sufficient quality to be used for intrauterine insemination ($n = 5$) or ICSI ($n = 4$).

DISCUSSION

This study shows that many transgirls have an interest in FP indicating this is an important topic to discuss before starting treatment with GnRHa. Tools are being developed to facilitate such discussions. Strang and colleagues (2018) have developed a Transgender Youth Fertility Attitudes Questionnaire, and Johnson and colleagues (2016) have indicated that they aim to develop a modular decision aid.

Most studies of FP by adolescents have been performed among cancer patients at risk for infertility and have shown that many decline FP because they do not want to delay the cancer treatment and because of severe illness and possibly costs (Burns, Boudreau, & Panepinto, 2006; Klosky et al., 2009). Two studies among transgender adolescents have also shown low uptake of FP (9%-14%) (Chen et al., 2017; Nahata et al., 2017). The use of FP in the present study is higher although still lower than the 51% of adult transgender women who stated that they would have made use of FP if it had been available (de Sutter et al., 2002). Thus, it will be important to see whether some of the transgirls who declined FP will regret their decision later in life. In the study of Strang and colleagues (2018), about half of 25 transgender adolescents who completed a questionnaire about fertility attitudes indicated they felt that their feelings about wanting biological children might change when they were older. On the other hand, to our knowledge, there are no data available yet on the actual use of cryopreserved semen by transgender adults apart from a report of one individual who used her cryopreserved semen for donor insemination of her partner (Wierckx et al., 2012).

The percentage of transgirls who did not wish to have children is similar to that reported by others (12%-37%) (Chen et al., 2018; Nahata et al., 2017; Strang et al., 2018). Previous studies in cisgender men showed a correlation between having a desire to have children and rate of sperm banking (Pacey et al., 2013). Such a correlation was not found in the present study, but in 57% of the medical files, information about the desire to have children was missing. In previous studies, more transgender adolescents stated they were interested in adopting children than in the present study, which raises the question if there might be a different view on adoption among adolescents in the United States compared with the Netherlands (Chen et al., 2018; Nahata et al., 2017).

Early pubertal phase precluded FP for a number of transgirls. Adolescents and physicians are faced with this dilemma between the wish for early treatment to avoid virilization on the one hand, and the wish for FP on the other hand, more often now that increasing numbers of adolescents are referred for hormonal treatment at younger ages. Research on *in vitro* maturation of spermatozoa might provide future solutions for these early pubertal adolescents (Wallace, Blough, & Kondapalli, 2014).

The need to masturbate was another reason to decline FP. Alternative options for extracting sperm such as testicular sperm extraction or electroejaculation stimulation could be used to facilitate FP. In the case report and literature review by Lau, Li and Soh (2014), electroejaculation appeared to be relatively safe. However, in the Netherlands, this procedure is currently only offered by some clinics to adolescents starting cancer treatment when it can be combined with a procedure that already requires anaesthesia such as placement of a central venous catheter.

Differences in costs of the procedure and health insurance coverage may explain some of the difference in use of FP between studies. Although costs were mentioned as a barrier by only 5% of transgirls in the retrospective study by Nahata and colleagues (2017), the reason for refusal of FP was unknown in 26%; therefore, costs may have been an important factor for more adolescents. In the present study, none of the patients had mentioned costs as a reason to decline FP probably because most insurance will cover most of the costs of FP.

When thinking of pregnancy/conception options, transgirls attracted to women might be more likely to cryopreserve their sperm than those attracted to men because this would allow them to conceive a child with their female partner. A previous study did indeed find that lesbian or bisexual transwomen were more likely to state that they would, if possible, have cryopreserved sperm than asexual or heterosexual transwomen (de Sutter et al., 2002). However, we did not find such a correlation, but this may have been because of the small group size and missing data, as only four transgirls stated they were attracted to women. Furthermore, sexual orientation is difficult to assess with certainty at a young age, so these results need to be interpreted with caution. In addition, transgirls who are attracted to men may also wish to use FP to allow them to have children with the help of a surrogate mother. Surrogacy (if not commercial) is legal in the Netherlands.

Caucasian transgirls were more likely to decline FP than adolescents with other ethnicities, but the latter were older than Caucasian transgirls (15.9 ± 1.5 years vs. 14.4 ± 1.9 years), so this association may be confounded by age. On the other hand, there may be a true association with ethnicity because of the differences in reproductive pressure and importance given to reproduction in different cultures. This is supported by a study by Schmid, Kirchengast, Vytiska-Binstorfer, and Huber (2004) where cisgender infertile women

from Islamic countries felt more distress because of infertility than Caucasian women. A survey among transgender adolescents also found that minors of colour expressed an interest in having biological children more often than white non-Hispanic/Latino minors (Chen et al., 2018). It is uncertain to what extent other relevant issues identified in previous studies, such as stigma towards sexual and gender minority parenting and pressure from one's family to have biological children or the feeling of disappointing one's family by not having biological children played a role in the population included in the present study (Chen et al., 2018; Strang et al., 2018).

Because of the lack of a control group, it is not possible to compare the outcome of FP among the transgirls to that in cis-gender adolescent males. In adults, poorer semen parameters and a higher incidence of oligozoospermia have been observed in transwomen compared with cisgender controls (Hamada et al., 2015; Li, Rodriguez, Gabrielsen, Centola, & Tanrikut, 2018). The cause of this difference is unclear, but psychological stress, self-induced high scrotal position of the testes, the use of tight underwear, and undisclosed hormone use were suggested as possible explanations as well as genetic causes (Hamada et al., 2015). Some of the adolescents in the present study also 'tucked away' their testes which may affect testicular function. One adolescent with severe oligozoospermia had one inguinal testis, which can be associated with subfertility.

Limitations of this study are its retrospective design and the small study population. Information on sexual orientation or desire to have children was not documented for all individuals. The influence of these factors could be further explored in a prospective study using standardized questionnaires or interviews about reasons for declining FP. Such a study may also shed light on the difference in rate of FP between different clinics. Future research is also needed to observe how many of the transgirls eventually will make use of the cryopreserved semen, and in case they do not, what the reasons are for not doing so. This could help to get better insight in parenthood goals among transwomen and could improve counselling of transgirls starting hormonal treatment. In addition, it is important to investigate if individuals feel regret at not having cryopreserved their semen as they grow older.

In conclusion, one third of the transgirls attempted FP, and most were able to store sperm suitable for future intrauterine insemination or ICSI. This stresses the need to discuss this topic before the start of treatment with GnRHa. Making different sperm extraction options available such as testicular sperm extraction or electroejaculation stimulation may make FP more accessible for transgirls for whom masturbation is a barrier. FP is currently not available for early pubertal adolescents, but research in this area might open up FP options for this group too. With future options on the way, an ethical and legal debate is essential, taking into account the right to equality and non-discrimination and the right to procreate of transgender people.

9

Dealing with moral challenges in treatment for transgender children and adolescents: evaluating the role of moral case deliberation

Lieke J. J. Vrouenraets
Laura A. Hartman
Irma M. Hein
Annelou L. C. de Vries
Martine C. de Vries
Bert A. C. Molewijk

2020. *Archives of Sexual Behavior*, 49(7), 2619-2634

This study was funded by the 'Netherlands Organization for Health Research and Development' (ZonMW, projectnumber 731010002)

ABSTRACT

Treatment teams providing affirmative medical care to transgender minors frequently face moral challenges arising from the care they provide. An adolescent's capacity to consent, for example, could raise several issues and challenges. To deal with these challenges more effectively, several Dutch treatment teams started using a relatively well-established form of clinical ethics support (CES) called moral case deliberation (MCD). MCD is a facilitator-led, collective moral inquiry based on a real case. This study's purpose is to describe the teams' perceived value and effectiveness of MCD. We conducted a mixed methods evaluation study using MCD session reports, individual interviews, focus groups, and MCD evaluation questionnaires. Our results show that Dutch transgender clinicians rated MCD as highly valuable in situations where participants were confronted with moral challenges. The clinicians reported that MCD increased mutual understanding and open communication among team members and strengthened their ability to make decisions and take action when managing ethically difficult circumstances. However, the clinicians also expressed criticisms of MCD: some felt that the amount of time spent discussing individual cases was excessive, that MCD should lead to more practical and concrete results, and that MCD needed better integration and follow-up in the regular work process. We recommend future research on three matters: studying how MCD contributes to the quality of care, involvement of transgender people themselves in MCD, and integration of CES into daily work processes.

INTRODUCTION

Transgender care is being offered to an increasing number of children and adolescents (Aitken et al., 2015; Chen et al., 2016; de Vries & Cohen-Kettenis, 2012; Wood et al., 2013). The incongruence they experience between assigned sex and identified gender is called gender dysphoria (GD) and may be diagnosed according to the DSM-5 when accompanied by distress (American Psychiatric Association, 2013). Children and adolescents with GD are usually treated by a team consisting of child and adolescent psychiatrists and psychologists, (paediatric) endocrinologists, gynaecologists (for fertility advice), and surgeons (for gender-affirmative surgery). In this article, the term 'adolescent' refers to children and adolescents in whom puberty has started. The start of puberty is defined as the appearance of Tanner stage 2-3 in boys (G2-3) and Tanner stage 2 in girls (M2). This article uses the term 'transgender adults/adolescents/children' to refer to persons diagnosed with GD.

Transgender teams base their treatment decisions on internationally recognized clinical guidelines set by professional transgender care associations. In practice, these guidelines are often adapted to local situations (Coleman et al., 2012; Hembree et al., 2017). A Dutch treatment protocol for transgender adolescents, sometimes referred to as 'the Dutch model', was the first in the world to explicitly describe medical transgender treatment for young adolescents (Cohen-Kettenis, Steensma, & de Vries, 2011). In the Dutch model, the eligibility criteria for such treatment are: a long history of GD, no psychosocial problems interfering with assessment or treatment, sufficient family or other social support, and the appearance of Tanner stages 2-3 indicating the onset of puberty (de Vries & Cohen-Kettenis, 2012; Delemarre-van de Waal & Cohen-Kettenis, 2006; Kreukels & Cohen-Kettenis, 2011; Shumer & Spack, 2015). Over the years, these eligibility criteria have not changed and are also part of the Standards of Care and Endocrine Society clinical practice guideline (Coleman et al., 2012; Hembree et al., 2017). Also, despite an enormous increase, main characteristics (with the exception of a shift in sex ratio with an overrepresentation of assigned females) of the referrals did not change over the years (Arnoldussen et al., 2020; Arnoldussen et al., 2022b). Mental health is an inseparable part of the clinical care of adolescents in the Netherlands. Besides the possible medical treatment, the clinical care requires an ongoing relationship with a psychologist and/or psychiatrist from the team. In many cases, it will also involve a local mental health specialist. In this article, we use the term 'gender-affirmative treatment' which includes the medical gender-affirmative part which is always preceded by assessment, and it is always accompanied by mental health counselling. This counselling consists of regular sessions in which information and advice is provided, and psychological and/or family support is given depending on the individual needs.

Professionals at gender identity clinics are frequently confronted with controversies and moral challenges arising from the care they provide for minors (Drescher & Pula, 2014; Vrouenraets et al., 2015). In general, moral challenges arise when professionals doubt as to the morally right course of action to take (Molewijk, Hem, & Pedersen, 2015). One type of moral challenge is a moral dilemma. In moral dilemmas, there are two mutually exclusive moral imperatives, neither of which is unambiguously desirable or acceptable (Stolper, Molewijk, & Widdershoven, 2016). Many clinical dilemmas fall into this category because they have a moral dimension. The moral dilemmas often faced by treatment teams working with transgender children and adolescents (and adults) include: (1) What should the professional do if the he/she is in doubt whether the adolescent fully comprehend the implications of gender-affirmative treatment?; (2) When is a psychiatric disorder so serious that we should not start gender-affirmative treatment?; and (3) Must we reach a multidisciplinary team consensus about the whole treatment before treatment commences, or is it justifiable for discipline X to start part Y of the whole gender-affirmative treatment before a consensus has been reached? (Byne et al., 2012; Gerritse et al., 2018; Milrod, 2014; Stein, 2012; Vrouenraets et al., 2015). Several reasons exist on why care for transgender adolescents entails a particularly large number of moral challenges. To begin with, care for transgender minors is a relatively new domain, on which there are many different normative views. These exist at both a professional and societal level (Byne et al., 2012). In addition, the normative views on the treatment for child and adolescent with GD are continuously evolving (Byne et al., 2012). Another common source of moral challenges in transgender care is the multidisciplinary nature of such care and the resulting divergence of professional views on the appropriate treatment criteria. Also, many of the long-term effects of administering medications or refraining from PS are as yet unknown, causing treatment uncertainty (Stein, 2012; Vrouenraets et al., 2015). Furthermore, medical treatment for transgender adolescents is seen as an intervention in a physically healthy and, in most cases, still developing body. Lastly, the adolescents undergoing such treatment are considered to be not yet fully developed in a psychological and cognitive sense (Byne et al., 2012; Crone, 2016; Moshman, 2017). These factors raise doubts about the potential risks of suppressing pubertal development in terms of physical development, brain growth, and the building of a consistent gender identity (Cohen-Kettenis et al., 2008).

In many clinical settings, clinicians are assisted in dealing with moral challenges and questions through structural clinical ethics support (CES) (Schildmann, Gordon, & Vollmann, 2010). Various CES methods are available, including individual consultations with an ethicist and ethics committee meetings. None of the current CES methods are versatile enough to cover the entire range of challenges and questions debated in the clinical context (Steinkamp & Gordijn, 2003). In the Netherlands, a relatively well-established type of CES is moral case deliberation (MCD) (Dauwerse, Weidema, Abma, Molewijk, & Widdershoven, 2014; Molewijk et al., 2008a). MCD is a facilitator-led, collective

moral inquiry by clinicians that focuses on a concrete moral question connected to a real clinical case (Dauwerse et al., 2014; Stolper et al., 2016). The aim of MCD is to create a dialogue that enables the treatment team to pursue a critical, yet constructive moral inquiry into the moral challenge at hand. The MCD facilitator uses a specific conversational method to structure multidisciplinary team meetings in which participants critically reflect on both current and past cases. Examples of such conversation methods are the Dilemma Method or the Socratic Dialogue (Molewijk et al., 2008a). The MCD method is designed to encourage clinicians to consider different viewpoints on the concrete moral challenges they experience in their everyday clinical work. MCD can stimulate reflection and deepen decision-making processes. It is not meant to substitute any aspect of the regular care or decision-making process, but rather as a supplement to these processes. MCD does not have any decision-making mandate and does not replace any decision-making mandate. However, various evaluative studies indicate that MCD can help improve a team's handling of moral challenges, increase the moral competency of clinicians, strengthen multidisciplinary cooperation, and facilitate the development, adjustment, and implementation of guidelines and policies (Hem, Pedersen, Norvoll, & Molewijk, 2015; Janssens, van Zadelhof, van Loo, Widdershoven, & Molewijk, 2014; Molewijk, Verkerk, Milius, & Widdershoven, 2008c; Weidema, Molewijk, Kamsteeg, & Widdershoven, 2015). In MCD sessions, a certified MCD facilitator supports a joint reasoning process, fostering a systematic and critical yet constructive dialogue while keeping the group's focus on the moral dimension of the case without giving advice (Stolper, Molewijk, & Widdershoven, 2015). Among the facts, the following can be included in the dialogue: protocols, existing policy and guidelines, legal regulations, and professionals' own practical experiences, and normative considerations. Preferably, an MCD session should take a multidisciplinary approach because this brings to light different viewpoints on the moral issue at hand. Conclusions and insights gained from MCD sessions may be used to develop or adjust multidisciplinary treatment policies in the future.

The obvious moral dimension of care for transgender adolescents creates a niche for specific CES services. Yet, it is not yet known which CES methods are most suitable for the particular moral dilemmas that arise in care for transgender minors. Vrouwenraets and colleagues (2015) conducted an interview study in which clinicians reported a need to structurally discuss moral challenges among their multidisciplinary transgender teams. This led to the initiative of using MCD as one of the CES methods for dealing with moral challenges in transgender care in the Netherlands.

The aim of this study is to describe how Dutch transgender clinicians evaluated the usefulness of MCD in dealing with moral challenges in the multidisciplinary clinical treatment for transgender adolescents. For this purpose, we have conducted a mixed methods evaluation study to answer the following questions:

1. How valuable do transgender care professionals evaluate MCD as CES, or in other words, what is their opinion of MCD?
2. What kind of change do MCD participants perceive after MCD sessions?
3. What recommendations can the interviewed professionals offer with respect to the future use of MCD?
4. Which MCD outcomes do the professionals hope to see when taking part in MCD sessions, and which MCD-related outcomes do they actually experience during MCD sessions and afterward in their daily work?

METHOD

Participants and procedure

During the period when the data for this study were collected, from February 1, 2014, until April 13, 2015, there were two gender identity clinics offering gender-affirming medical treatment (GAMT) in the Netherlands. These were (1) the Centre of Expertise for Gender Dysphoria at the Amsterdam University Medical Centres, location VU University Medical Centre (VUmc) in Amsterdam, which offered care for children, adolescents, and adults; and (2) the clinical treatment for transgender adolescents clinic at Curium-Leiden University Medical Centre in Leiden, which offered care for children and adolescents. At both locations, specialists in child and adolescent psychiatry and psychology, endocrinology, and paediatric endocrinology worked in multidisciplinary teams. The two teams followed the same diagnostic and treatment procedures, had similar protocols, and regularly held joint meetings. In 2013, the board overseeing transgender clinical care in the Netherlands introduced MCD to complement the two teams' regular care and decision-making processes. The aim was to create opportunities for the clinicians to thoroughly reflect on the moral dilemmas they faced in difficult cases. Therefore, MCD was only intermittently used by the transgender teams.

In the period from October 2013 until January 2015, the two teams convened for nine joint meetings during which a total of 17 MCD sessions were held. During six of these joint meetings, two or three parallel MCD sessions were held, depending on the number of participants. In each of these parallel MCD sessions, a different case was discussed. We analysed six of these MCD sessions for this study. The sessions were led by trained and certified MCD facilitators employed by the Department of Medical Humanities of the Amsterdam University Medical Centres, location VUmc, which is responsible for all CES services at that institution. The sessions analysed in this study used the MCD dilemma method, which consists of the 10 steps listed in Appendix C (which can be found at page 224) of this study (for a detailed example of an MCD dilemma method see the paper of Stolper et al., 2016). Furthermore, clinicians from both teams completed a validated

questionnaire on perceived MCD outcomes (Euro-MCD; Svantesson et al., 2014) and participated in individual interviews and focus groups.

The participants in this study were members of the Amsterdam and Leiden transgender teams. Both teams included endocrinologists and specialists in child and adolescent psychiatry and psychology. The Amsterdam team also included surgeons and gynaecologists. The gender identity clinic in Amsterdam had approximately 30 team members when this study was conducted. The team in Leiden had seven members in the same period. Ten to fifteen team members participated in each MCD session. We individually interviewed three specifically selected team members from each team. The interviewees were two child and adolescent psychiatrists, two child and adolescent psychologists, and two endocrinologists. The interviewees had different levels of experience with care for transgender minors. Therefore, the six interviews can be considered representative of the larger group of participants across the two teams in terms of their range of disciplines and experience level.

In addition to the interviews, we conducted two focus groups: one with nine members of the Amsterdam team, and one with six members of the Leiden team. Each focus group consisted of a representative part of the multidisciplinary team from which it was derived. In order to make the groups representative, we included members with different disciplines and levels of experience in the field of transgender child and adolescent care. No more information about the participants can be provided here because this could compromise the anonymity of some participants, since certain functions are performed by only one or two members of a given team. The focus groups were used to refine and validate the findings from the interviews. As part of the mixed method design, we conducted a small cross-sectional survey using the Euro-MCD questionnaire at two joint meetings of the Amsterdam and Leiden teams (T0 and T1). Twenty-eight professionals from the Amsterdam team and six from Leiden completed the Euro-MCD questionnaire at T0 ($n=34$). Twenty professionals on the Amsterdam team and two from Leiden completed the questionnaire at T1 ($n=22$). To protect the privacy of the respondents, their names were not collected. Therefore, it was not possible to match those who participated in this survey twice and no longitudinal data were collected (table 11).

Table 11. Overview number of participants

Team	Team members (n)	Participants (n)				
		In each MCD session	Individual interviews	Focus groups	Euro-MCD questionnaire at T0	Euro-MCD questionnaire at T1
Amsterdam	30	-	3	9	28	20
Leiden	7	-	3	6	6	2
Total	37	10 to 15	6	15	34	22

MCD refers to moral case deliberation; '-' refers to no data available.

Design

We used a mixed method research design consisting of a qualitative and a quantitative component. In each of these, the stakeholders evaluated the MCD sessions (Morse, Niehaus, Wolfe, & Wilkins, 2006). We collected data in four different ways (table 12). To answer the first, second, and third research questions, we used the qualitative data recorded on audiotapes of the MCD sessions and collected during the individual interviews and focus groups. In order to answer the fourth research question, we used data obtained from the Euro-MCD questionnaires, the individual interviews, and the focus groups.

Table 12. Overview of the dataset

Data collection method	Moment in time	n	Type of data	Amount
Audiotapes of MCD sessions		6	Transcript	4
			Summary for member check	6
Individual interviews		6	Transcript	6
			Summary for member check	6
			Observational note	4
Focus groups		2	Transcript	2
			Summary for member check	2
			Observational note	2
Euro-MCD questionnaire	T0; prior to the MCD sessions	34	Questionnaire	34
	T1; after participating in two to four MCD sessions	22	Questionnaire	22

MCD refers to moral case deliberation.

Audiotapes of moral case deliberation sessions

From October 2013 until January 2015, the transgender teams for children and adolescents organized six MCD sessions which were incorporated into this research project. The MCD sessions were structured according to the dilemma method (Stolper et al., 2016), lasted

from 50 to 116 minutes and were audiotaped. We transcribed verbatim four MCD sessions. The MCD facilitators wrote a summary of all six MCD sessions and sent this back to the MCD participants to verify its accuracy.

Moral case deliberation evaluation in individual interviews

We conducted semi-structured individual interviews with six members of both the Amsterdam and Leiden transgender teams in February 2015. We formulated our initial interview topics after reviewing the relevant literature and then examining how the teams had experienced the MCD sessions (Janssens et al., 2014). The interviews contained general topics and no closed-ended questions. In the interviews, we asked the participants to elaborate on their personal experiences with MCD and the method's effects, or lack thereof, at the patient level or protocol level.

One of the researchers conducted the interviews, and a participating intern took notes during the four interviews. The interviews lasted from 60 to 90 minutes and were audiotaped and transcribed verbatim. A summary of each individual interview was sent to the participant to verify its accuracy.

Evaluation of moral case deliberation by focus groups

We conducted two focus groups in March 2015. During these focus groups, we presented several anonymous quotes from the individual interviews to trigger the conversation. We asked the group participants whether they could identify and/or agree with the quotes and invited the participants to express any other views they held on the use of MCD. Our goal was to establish a dialogue among the team members rather than maintaining a strict question-and-answer format.

Two of the researchers facilitated each focus group. During one focus group, a second researcher made observatory notes, while in the other focus group the observatory notes were taken by a participating intern. The focus groups lasted from 100 to 120 minutes and were audiotaped and transcribed verbatim. A summary of each focus group discussion was sent to the transgender team to verify their accuracy.

Moral case deliberation evaluation by means of the Euro-MCD questionnaire

The Euro-MCD questionnaire is a qualitatively validated questionnaire (Svantesson et al., 2014). This instrument was developed to measure: (1) the perceived importance of MCD outcomes prior to MCD sessions (T0); (2) the experienced MCD outcomes during the MCD sessions (T1); and (3) the experienced MCD outcomes within daily work after a series of two to four MCD sessions (T1). The 26 outcomes cover six domains: enhanced emotional support; enhanced collaboration; improved moral reflexivity; improved moral attitude; improvement at organizational level; concrete results concerning the care or treatment

(see Appendix D, which can be found at page 225, for an example). Participants were asked at T0 how important they found these 26 outcomes (on a 4-point Likert scale: very important; important; somewhat important; not important); and at T1 whether they experienced these outcomes (on a 4-point Likert scale: experienced to a great extent; experienced to a reasonable extent; experienced to some extent; did not experience). The Euro-MCD questionnaire also contains some open-ended questions asking, for instance, what outcome the respondent expected (without reading the 26 outcomes) and how the respondent prioritized the five most important outcomes. Finally, the Euro-MCD questionnaire also collects some of the participants' general characteristics (e.g., age, sex, specialty, institution). We obtained these empirical data between April 2014 and October 2014, during two joint meetings of the Amsterdam and Leiden teams.

Data analysis

Moral case deliberation sessions, individual interviews, and focus groups

Following an initial open reading of the qualitative data, the authors independently identified some preliminary sub-themes. Then, through a deliberative process, the authors redefined the initial sub-themes into main themes until they reached a consensus. This hermeneutic analysis (Miles & Huberman, 1994; Stake, 2005), partly inspired by the interview guide, resulted in four main themes: (1) Positive experiences with MCD; (2) Critical remarks about MCD; (3) Changes in daily work processes after MCD; (4) Recommendations for the future use of MCD or MCD elements in daily work processes.

Two authors conducted an additional round of analyses to assess whether the themes or sub-themes enabled them to accurately subdivide the outcome of qualitative data. Following this assessment, they kept the four initially defined main themes unchanged. We then re-analysed the transcripts of the MCD sessions, the focus groups, and the individual interviews and selected representative quotations for each of the defined themes, taking equal care to draw quotations from all data sources.

Integration of moral case deliberation sessions, individual interviews, focus groups, and Euro-MCD questionnaires

In the present study, the results obtained from each of the four methods to produce four sets of findings were collected and analysed separately. Subsequently, these data were combined in a process called 'triangulation' (O'Cathain et al., 2010). Combining the data of all four methods consisted of comparing the qualitative and quantitative data and reflecting upon the similarities and differences found.

Research ethics

Prior to the individual interviews, focus groups, and MCD sessions, we gave all participants oral instructions to inform them of the voluntary nature of their participation; they were told that they could withdraw from the interview, focus group or MCD session at any time with no explanation required. Furthermore, we emphasized that the data we were about to collect would remain anonymous. Upon each interview, focus group, and MCD session, we obtained the participants' oral informed consent for their participation and tape recording. No clinician refused to take part in an interview or MCD sessions. Due to the small size of the teams, we cannot provide more details about the participants in this paper without potentially compromising our commitment to confidentiality.

RESULTS

Below, we describe the data obtained from MCD sessions, individual interviews, focus groups, and Euro-MCD questionnaires. We largely answered the first three research questions based on the qualitative data, and the last research question based on the quantitative data.

How valuable do transgender care clinicians evaluate moral case deliberation as clinical ethics support, or in other words, what is their opinion of moral case deliberation?

First, we will present the positive experiences team members reported having with MCD. This will be followed by an outline of their critical remarks about MCD.

Positive experiences with moral case deliberation

Becoming aware of others' perspectives and interests

Nearly all interviewed participants reported that they had gained more insight into the perspectives and interests of the other stakeholders in the case discussed. Some found it valuable to hear how professionals from other disciplines viewed the case.

"You always look at a situation from a certain perspective. Since people from different disciplines take part in moral case deliberation sessions, you learn to view a situation from another perspective." - Individual interview with a clinician

"Sometimes patients and clinicians look at a certain situation in a similar way, but there are also times when they view things differently. Moral case deliberation brings that to the surface." - Individual interview with a clinician

Dialogue among all instead of discussion among some

Participants often voiced appreciation of the fact that all MCD participants were encouraged to contribute and that disagreements were discussed in a less polarizing way than is customary. Due to the structure of the dilemma method and the MCD facilitator's role, participants have to take the time to listen to others instead of attempting to convince others of their own point of view. This enabled the participants to structure the relevant arguments and take a more open attitude towards other perspectives. The dilemma method encourages the participants to incorporate the arguments and merits of 'the other side' of the dilemma rather than to try to discredit a colleague's opinion.

"Sometimes our disagreements are expressed with so much emotion, that you can get the impression that the one [team member] who expresses the strongest emotion has the truth on their side. Moral case deliberation is good at neutralizing the emotions and returning participants to the crux of the matter. Moral case deliberation encourages you to acknowledge the merits of both sides of a dilemma." - Individual interview with a clinician

"I like the fact that you do not have to persuade anyone else of your point of view [in a moral case deliberation session], and that it is possible for several opinions to coexist. This does not happen in regular meetings, because in those meetings decisions have to be made and all you want is to get your own point of view across." - Focus group with clinicians

Paying closer attention to your own arguments and contextual factors, rather than blindly following protocol

Another frequently mentioned positive experience with MCD was that it enabled the teams to explore in great detail how they had handled a given protocol and why they had done so, which gave them deeper insight. Furthermore, the teams often used MCD sessions to discuss cases or requests not covered by the existing protocol. During the MCD sessions, the participants exchanged ideas on the question, 'Which rules do we view as absolute and which can be handled with greater flexibility, and when it comes to the latter, under what conditions may we do so?'

"Certain decisions can be found in our protocol, but in moral case deliberation, you are encouraged to ask questions like: 'Why do we do things that way?' and 'What, precisely, is the risk if we take this step?'" - Individual interview with a clinician

"In the collaboration between Amsterdam and Leiden, we also look at the boundaries of the protocol and how we handle these boundaries in practice." - Individual interview with a clinician

Extra time for reflection is important and useful

The participants appreciated the time MCD offers for talking about problematic cases. They said this was particularly important because of the current cultural emphasis on efficiency; in general meetings, for instance, less time is available for exchanging viewpoints or discussing difficult cases.

“Nowadays, with all the pressure to work as efficiently as possible, it is becoming even more important to set aside moments to discuss a difficult situation.” - Individual interview with a clinician

“After all, transgender care is a subject surrounded by many controversies and one in which a lot of pressure is applied by parents, children, and interest groups. The topic is sometimes so fraught that it is helpful to put on the brakes now and then so we can discuss matters calmly first.” - Focus group with clinicians

One participant reported having gotten a fresh perspective thanks to MCD. This individual remarked that professionals with more experience tend to work faster, but by applying previous experience to new situations, they run the risk of being blind to potentially different characteristics in these new situations. MCD sessions helped restore this participant’s sensitivity to the particularity of the case at hand.

“Over time, you sort of put blinkers on, because similar cases appear and you do not have the time to really consider the case because of your busy schedule. You do not have time to think. That really is a problem.” - Individual interview with a clinician

Critical remarks about moral case deliberation

The tempo is sometimes too slow and the sessions last too long

In MCD sessions, every participant is actively encouraged to contribute. A couple of participants characterized themselves as goal-oriented and said they were frustrated by the length of the deliberations, especially when they felt that participants were repeating a certain point that had already been discussed.

“Sometimes I get the feeling that we know what our goal is, and we could get there faster. Maybe it is necessary to involve the whole group in a deliberation, but sometimes I find it frustrating that it takes so long.” - Individual interview with a clinician

Discussing several similar cases in succession gives less insight

MCD requires an organization to invest a certain amount of time, so some participants questioned whether MCD was worth the time investment. Some participants said they

considered the nature of the cases themselves to be an important criterion to determine whether MCD was worth the time it takes. Some noted that team members felt a certain 'fatigue', especially when the case under discussion was not recognizable to everyone or when it had the same characteristics as a previously discussed case.

"Here we go again, another patient who has characteristic X." - Individual interview with a clinician

Others who had not experienced this themselves could imagine it might happen to them in the future.

"You cannot organize a moral case deliberation for every patient, so you need to constantly weigh whether it is a worthwhile time investment. So far, we have only discussed cases that offered us new insights, but I can imagine that sooner or later we will reach a saturation point." - Individual interview with a clinician

These different experiences show that what participants see as 'the same' or 'similar' was often ambiguous and unclear.

Insufficient follow-up

Some participants mentioned that there was insufficient follow-up after MCD. The MCD sessions frequently produced new insights and signals, but it was unclear what follow-up actions were being taken if any and who should be responsible for following up. For instance, one difficult request which had long been expressed was discussed in an MCD session, but subsequently kept coming up in regular team meetings and yet no action was taken.

"And more in general, when we do reach some kind of conclusion, there's often no concrete follow-up. And that's a shame." - Individual interview with a clinician

"This caused some irritation. We talked about this case in a moral case deliberation, so we knew we should see some kind of an outcome, but we still did not know what the outcome would be." - Individual interview with a clinician

Perhaps taking time to deliberate is all that really counts, and not this particular method?

Most participants said taking more time to deliberate a case was worthwhile and that it helped them deal with moral challenges in their work. Some asserted that it was not the particular method (in this case, MCD) that had made the difference, but merely the fact that the team was taking ample time to deliberate a case.

"I wonder whether this [giving more thought to a case and asking more constructive questions regarding the case] is due to the [method] moral case deliberation or due to the fact that we have taken time for each case. The fact that we talked about one patient for an hour and a half is in itself enormously valuable. That is independent of the method used. Normally, we would never do that." - Focus group with clinicians

What kind of change do moral case deliberation participants perceive after moral case deliberation sessions?

Changes in treatment decisions

Some participants reported that they changed treatment plans because of a discussion in an MCD session. After the MCD session in question, some team members who were treating a particular patient held a small meeting about the MCD's results and its implications for the individual treatment plan. They subsequently called the patient in and elaborated on their new treatment plan.

"After the moral case deliberation session, we made another decision [...] a different policy was applied [...] instead of prescribing puberty suppression treatment [in accordance with the adolescent protocol] to an adolescent aged 17.5 years, we decided to not prescribe any medical treatment at that moment. But instead, we let the adolescent start treatment with gender-affirming hormones when he turned 18, following the adult protocol [...] we are talking about a concrete change, with concrete conditions. Furthermore, a concrete policy has emerged from it. Different from what our local protocol suggests and different from what was discussed earlier with the patient." - Individual interview with a clinician

Learning effects in moral case deliberation sessions and outside

Participants attributed several learning effects to MCD. The teams grew more experienced with the specific method which helped them get to the heart of a case sooner.

"The repetition of the dilemma method enables you to get to the heart of the case and its policy more quickly. We are internalizing the method more and more, now that we have used it several times." - Focus group with clinicians

Thorough analysis of a particular case helped team members deal with similar cases. Some participants reported having become more aware of certain issues after they were discussed in an MCD session. They reported reacting more adequately to similar situations thanks to the discussion they had held in MCD.

"Within [a] moral case deliberation [session], you take the content and that particular patient into account. What are the criteria and arguments on which we base a decision? And what are the advantages and disadvantages? This also has a learning effect for cases that are similar." - Individual interview with a clinician

"I notice that you internalize what has been talked about [during a moral case deliberation session] and that you bear that in mind during subsequent contact with patients [...] In my opinion, that is an important added value of a moral case deliberation session: that you learn to break through the standard pathways and ideas." - Focus group with clinicians

Participants became aware of the normative dimension of a problem.

"Due to moral case deliberation, I realised that our care is full of moral dilemmas. I first had the impression that it was all more or less determined. This realisation is sometimes unsettling, but also a good thing." - Individual interview with a clinician

Improved decision-making process

Most participants stated that the quality of treatment decisions improved in different ways.

"You're forced to think about it [the case at hand] systematically and not to make decisions too quickly. It helps you to carefully consider things, and this improves the quality of the decision." - Individual interview with a clinician

The MCD method structured the conversation. All pro and con arguments are given a place, creating coherence. The MCD framework contributed to more nuanced judgments in which the separate and sometimes conflicting values and norms are considered and weighed.

Some participants said they had learned to give a better explanation and justification for certain decisions. They reported being able to explain more precisely why they had made a certain decision and had learned to give substantiated arguments to the patient, family, and colleagues.

"The decisions we make are very impactful [...] you do have the responsibility to the patient to explain why you are starting treatment, or why not. [...] [Therefore] it is important to make the underlying idea explicit. [...] So I think that, especially in this population, it is good to have some sort of mini moral case deliberation on very difficult cases." - Individual interview with a clinician

What recommendations can the interviewed professionals offer with respect to the future use of moral case deliberation?

Structurally embedding moral case deliberation sessions

Most participants recommended that MCD sessions be structurally embedded into regular interdisciplinary meetings. Most expressed a belief that structurally embedding MCD sessions would increase the successful use of MCD. Furthermore, some participants said they would appreciate the opportunity to hold ad hoc MCD sessions on urgent cases in their regular clinical work. However, others argued that it would be too difficult in practical terms to schedule such an ad hoc MCD session.

"I wonder whether there will be a moral case deliberation session if you do not structurally embed it in your organization. Especially when it is with a large group, it is difficult to find a date for an ad hoc moral case deliberation session. I think that moral case deliberation is therefore more likely to succeed if we do it structurally, in regular interdisciplinary meetings." - Individual interview with a clinician

Training team members as moral case deliberation session facilitators

Some participants said it would be of great value to have a colleague trained as an MCD session facilitator because this would make it easier to organize ad hoc MCD meetings. Others doubted whether this colleague could show the neutrality required of an MCD facilitator, because he or she would also be a member of the treatment team.

"It would be good to have the expertise in-house. That would lower the threshold for an ad hoc moral case deliberation session." - Focus group with clinicians

"I wonder whether a member of the team can achieve the neutrality needed to be a facilitator of moral case deliberation sessions." - Focus group with clinicians

Using elements of moral case deliberation in other meetings

Some participants saw the potential value of using elements of MCD to structure discussions in other meetings. The participants mentioned various steps of the dilemma method that they wanted to introduce as part of regular team meetings (such as brainstorming on alternatives and the table with norms and values for the various treatment or decision options).

"One of the great things I find are the questions: 'What are your alternatives?' [and] 'Are there alternatives?' These are questions that could also be considered during regular meetings. What is the broad range of available options? Our discussions are often just yes or no." - Individual interview with a clinician

Better follow-up

The interviews and focus groups led to some concrete recommendations for improving the use of MCD in the daily work of transgender teams. These recommendations were: to better monitor the to-do lists and other conclusions agreed upon in MCD sessions; to better coordinate team members' tasks and responsibilities after these sessions; to discuss the results and actions agreed upon in MCD sessions during regular treatment team meetings and to ensure that current guidelines and policies reflect these results.

"After conducting a moral case deliberation session, how can we ensure that we get a fixed moment to reflect on the question: 'How do we proceed with what has been discussed in relation to our final decision-making?' Maybe we could do that during a moment of feedback to the team." - Individual interview with a clinician

Which moral case deliberation outcomes do the professionals hope to see when taking part in moral case deliberation sessions, and which moral case deliberation-related outcomes do they actually experience during moral case deliberation sessions and afterwards in their daily work?

Prior to starting their MCD sessions, 34 team members completed the Euro-MCD questionnaire. This survey asked these professionals what outcomes they expected MCD to have, and how important these specific outcomes were to them. The questionnaire was based on 26 pre-defined MCD-related outcomes (T0) (Svantesson et al., 2014). After the team members had attended two to four MCD sessions, they were asked once again to complete the Euro-MCD questionnaire (T1), but this time regarding, (1) which MCD-related outcomes they had actually observed during the MCD sessions overall; and (2) which MCD-related outcomes they had observed in their daily work after the MCD sessions ($n = 22$).

Table 13 provides an overview of the most important results of the Euro-MCD questionnaire at T0 and T1, by means of the outcomes as described in the fixed-choice questions.

Table 13. Outcomes of Euro-MCD questionnaire at T0 and T1; outcomes as described in the fixed-choice questions of Euro-MCD questionnaire (including the corresponding number)

Outcomes described most often as ‘important’ or ‘very important’ before starting with MCD sessions (T0, n = 34)	Percentage assessed as ‘important’ or ‘very important’
8. Better mutual understanding of each other’s reasoning and acting	97%
2. More open communication among co-workers	91%
13. Enables me and my co-workers to decide on concrete actions in order to manage the ethical difficult situations	89%
Outcomes described most often as ‘not important’ or ‘a little important’ before starting with MCD sessions (T0, n = 34)	Percentage assessed as ‘not important’ or ‘somewhat important’
12. Enhances my understanding of ethical theories (ethical principles, values and norms)	66%
4. Enables me to better manage the stress caused by ethical difficult situations	63%
17. I listen more seriously to others’ opinions	61%
Most often experienced outcomes during the MCD sessions (T1, n = 22)	Percentage assessed as ‘reasonably experienced’ or ‘highly experienced’
10. I and my co-workers become more aware of recurring ethical difficult situations	85%
8. Better mutual understanding of each other’s reasoning and acting	84%
2. More open communication among co-workers	82%
Least often experienced outcomes during the MCD sessions (T1, n = 22)	Percentage assessed as ‘not experienced’ or ‘experienced to some extent’
19. Strengthens my self-confidence when managing ethical difficult situations	67%
12. Enhances my understanding of ethical theories (ethical principles, values and norms)	65%
4. Enables me to better manage the stress caused by ethical difficult situations	63%
Most often experienced outcomes after the MCD sessions in their daily work (T1, n = 22)	Percentage assessed as ‘reasonably experienced’ or ‘highly experienced’
9. I see the ethical difficult situations from different perspectives	55%
10. I and my co-workers become more aware of recurring ethical difficult situations	55%
24. Enhances mutual respect amongst co-workers	55%
Least often experienced outcomes after the MCD sessions in their daily work (T1, n = 22)	Percentage assessed as ‘not experienced’ or ‘experienced to some extent’
4. Enables me to better manage the stress caused by ethical difficult situations	85%
13. Enables me and my co-workers to decide on concrete actions in order to manage the ethical difficult situations	75%
12. Enhances my understanding of ethical theories (ethical principles, values and norms)	75%

MCD refers to moral case deliberation.

When completing the questionnaire at T0, prior to participating in the MCD sessions, almost all respondents rated improvement in the areas of 'open communication among co-workers' and 'mutual understanding of reasoning and behaviour' as 'important' or 'very important'. When they completed the questionnaire at T1, most participants reported having experienced more open communication and mutual understanding during the MCD sessions. Furthermore, most team members experienced an improvement in 'becoming aware of recurring, ethically difficult situations' both during the MCD sessions and in their daily work after these sessions.

The results from T0 showed that respondents rated the MCD-related outcomes 'to enhance my own understanding of ethical theories' and 'to manage stress related to the cases better' as 'not important' or 'somewhat important'. In line with these results, the respondents reported at T1 that they had either not experienced these two outcomes, or only experienced them to some extent, during the MCD sessions and afterward in their daily work.

A large majority of respondents initially rated an improvement in 'enabling team members to decide on concrete actions in order to manage ethically difficult situations' as 'important' or 'very important'. At T1, however, most respondents reported that they had not experienced this outcome in their daily work subsequent to the MCD sessions, or only to some extent.

Most participants experienced an increase in mutual respect among team members in their daily work after the sessions. During the individual interviews and focus groups, several participants mentioned that participating in an MCD session enhanced mutual trust on the team. They attributed this to having learned more about the thinking behind their colleagues' actions at work because the MCD sessions encouraged individuals to express their own opinions rather than team opinions. Furthermore, the results of the Euro-MCD questionnaire revealed that the majority of clinicians experienced an 'enhancement in mutual respect among the team members' after participating in the MCD sessions, and that they 'became more aware of the stakeholders' different perspectives' and of 'recurring, ethically difficult situations'.

"I think that moral case deliberation is a very good way of bringing about greater mutual trust. You usually get closer [...] during moral case deliberation sessions there are no team opinions, but all individual opinions, that strengthens your sense of connection." - Focus group with clinicians

Some participants stated that mutual trust is especially crucial in transgender care because several treatment steps are deeply interwoven, requiring close cooperation between the various disciplines involved in the transgender care trajectory.

“The amount of cooperation [between different disciplines] in transgender care is uncommon in the medical world. A doctor normally makes his or her own diagnosis and then starts treatment. Even when a patient is referred by someone else, the doctor will always take their own look. [...] I do not think there is any other field of care in which the clinician takes care of the diagnostics and the physician then carries out the medical treatment. This requires trust in each other’s expertise.” - Individual interview with a clinician

DISCUSSION

This project described Dutch transgender clinicians’ assessment of MCD sessions effectiveness in their clinical work with adolescents. A representative group of 34 team members from two teams in different cities participated in this mixed methods evaluation study, enabling us to acquire a broad, but nuanced understanding of their experiences with six MCD sessions.

Our results showed that the clinicians considered MCD a useful method that has helped them deal with care situations where they were uncertain which step was morally right or where they could not agree on a what was the best possible care. In the individual interviews and focus groups, team members indicated that the need for thorough reflection on work challenges is particularly critical now because the current focus on efficiency has cut into contemplation time. The team members indicated a need to devote time, structure (in the shape of a facilitator and a conversation method), and dialogue (instead of a polemical debate) to a thorough reflection on difficult cases. Yet, not all team members valued the various aspects of MCD in the same way. They disagreed on how much time should be spent on an MCD session and how MCD sessions should be structured. Their criticisms of the MCD process focused on: the length of time dedicated to discussing individual cases, the need for more practical and concrete results after MCD sessions and the lack of follow-up and integration of MCD into regular work process. These results are in line with other studies on MCD, which show that the follow-up, organization, and implementation of CES can be challenging in clinical practice (Finder & Bliton, 2011; Hartman, Inguaggiato, Widdershoven, Wensing-Kruger, & Molewijk, 2020; Hartman et al., 2019; Hem et al., 2015; Weidema, van Dartel, & Molewijk, 2016).

Team members were critical about whether or not the MCD’s dialogue, including the specific conversation method used, was a determining factor leading to the perceived results. They wondered whether these same results could be achieved simply by taking the time to deliberate on a case. The data obtained in this study do not allow us to draw any conclusions about whether time or MCD as such was a more determinant factor. Nevertheless, we can say that MCD probably adds value in highlighting the moral

aspects of a case. Such elements do not necessarily emerge in regular case discussions but result from the MCD method, structure, and facilitator-led form. As a result, MCD helps participants to increase their moral reflection skills (Dauwerse, 2013). Most regular case discussions take just as much time, but seldom get beyond the clinical aspect of the case and seldom take into account the values and norms behind the clinical reasoning. In addition, the structure and focus of MCD sessions allows focusing on dialogue rather than on debate and gives participants room to constructively discuss differences of opinion and to reflect on morally complex or problematic cases (Molewijk, van Zadelhof, Lendemeijer, & Widdershoven, 2008b). This contrasts with most regular case discussions, in which participants typically try to convince others of their own opinion in a heated debate. Such a setting tempts participants to repeat the same argument time and time again. A recent Dutch study showed that MCD sessions offer more of the hallmarks of good moral deliberation than regular case discussions, as a greater proportion of the participants' statements were categorized as examples of moral focus, variety of argumentation, and open interaction (de Snoo-Trimpp, Kremer, Jellema, & Molewijk, 2022b).

The MCD sessions analysed in this study led to changes for the gender identity clinics at both the treatment plan and general policy levels. The sessions resulted in concrete changes of treatment plans and contributed to several adjustments of the general transgender care policy (Hartman et al., 2019; Hartman et al., 2020). For example, changes were made as to how strictly clinics apply the age criterion for starting puberty suppressing treatment. Dutch gender identity clinics strictly maintained a minimum age of 12 years for eligibility to start this treatment. Partly due to the outcomes of several MCD sessions focusing on cases of young children and puberty suppressing treatment, the clinics now apply the minimum age criterion more flexibly. This result is in line with other studies which show that MCD promotes the development, improvement, and implementation of guidelines and policies (Molewijk et al., 2008b). It should be noted that describing other changes in clinical policy resulting from the MCD sessions analysed in this study is beyond the scope of the current study. Nevertheless, for more information about the integration of CES into the daily work processes at a Dutch gender identity clinic see Hartman and colleagues (2019; 2020).

The individual interviews and focus groups in this study led to concrete recommendations on improving the use and implementation of MCD. The recommendations were: to ensure the lessons learned from MCD sessions are followed up; to boost the sense of ownership and responsibility regarding actions to be taken; and to ensure the lessons learned are reflected in guidelines and policies. To put these recommendations into action, in our local situation a steering group was created with members from the management team of the Centre of Expertise for Gender Dysphoria at the Amsterdam University Medical Centres, location VUmc in Amsterdam. Two of the researchers discussed the recommendations

with the steering group. Together, they decided to make adjustments to the MCD sessions themselves (e.g., focusing more on 'who will do what' at the closure of each session) and to see to a deeper embedding of MCD in the work processes of the Centre of Expertise for Gender Dysphoria at the Amsterdam University Medical Centres, location VUmc in Amsterdam (Hartman et al., 2019; Hartman et al., 2020).

The quantitative results from the Euro-MCD questionnaire, in which 26 possible outcomes of MCD are described (Svantesson et al., 2014), showed participants' preferences for MCD outcomes and which MCD-related outcomes the participants actually observed during and after the MCD sessions. The results confirmed that the clinicians expressed a particularly strong wish to see 'mutual understanding', 'more open communication', and a greater ability to 'decide on concrete actions' as MCD outcomes. Most participants indeed noted an improvement in 'mutual understanding' and 'open communication' after participating in the MCD sessions. Furthermore, after participating in the MCD sessions, a majority of the team members experienced an 'enhancement in mutual respect among the team members' and 'became more aware of the stakeholders' different perspectives' and of 'recurring, ethically difficult situations'. Participants reported that spending more time reflecting on other team members' thinking gave them a greater awareness of other stakeholders' perspectives on the MCD case in question, which enhanced the trust within the team. These results are in line with other studies, which show that MCD can help teams more effectively deal with moral challenges and enhance collaboration and mutual trust (Hem et al., 2015; Janssens et al., 2014; Molewijk et al., 2008c; Weidema et al., 2015).

Besides the developments in the field of MCD, research also focuses on developing other new and innovative forms of CES. For example, forms of CES which can be used by sole practitioners. Such as ethics consultation (Aulisio, Arnold, & Youngner, 2000; Molewijk, Slowther, & Aulisio, 2015) and a moral compass which can be used individually (Hartman et al., 2018).

Ever since the research for this study was conducted, CES has become a standard part of transgender care and MCD has been added to the CES toolbox. MCD is now part of policy days, in ad hoc situations, and occasionally in educational settings such as one-day professional courses on decision-making competence. In addition to MCD, several other methods have been added to the CES toolbox as well (Hartman et al., 2019; Hartman et al., 2020). Moreover, since this research was conducted one member of each team has been trained as an MCD facilitator, which enables the teams to use MCD in an ad hoc fashion whenever so desired. As such, this evaluation study enabled the professionals at the Amsterdam and Leiden teams to shape and embed CES as they themselves saw fit. This can be seen as part of an 'integrative approach' to CES (Hartman et al., 2019).

Till now, at the gender identity clinic, it is not standard to involve patients in MCD sessions. However, participation of patients themselves in MCD sessions might bring to light new viewpoints on the moral issue at hand. The participation of transgender people's own practical experiences and normative considerations can then be taken into account and might stimulate reflection and deepen decision-making processes even more. This could also enlarge the understanding of each other's perspectives on good care. Therefore, participation of transgender people seen in the clinic and/or from the community at large in MCD sessions would be a great next step.

The current study showed that most team members at the gender identity clinics in the Netherlands have positive experiences with MCD. Other studies show that MCD is also considered valuable by professionals in other branches of care, both in the Netherlands and internationally (de Snoo-Trimpp et al., 2020). However, we cannot assume that MCD is appreciated by transgender clinicians outside the Netherlands. Therefore, we would encourage the collection of more qualitative and quantitative data on how gender identity clinics in other countries experience CES and MCD. It would be worthwhile to explore what kind of support CES in general and MCD in particular can offer in other countries. A European study on the experiences of MCD and their outcomes highlights considerable differences in Europe, regarding the experiences with MCD outcomes and the rating of various MCD outcomes in terms of their importance to clinicians (Svantesson et al., 2019). An international study focusing specifically on the relevance of CES in transgender care would show us whether there are cultural differences regarding: (1) the types of moral challenges transgender teams from other countries are confronted with; (2) how these challenges are framed; and (3) how the teams deal with these moral challenges.

STRENGTHS AND LIMITATIONS

The present study had strengths and weaknesses. The mixed methods nature of this study enabled us to find out, in depth, how professionals who provide care for transgender adolescents in the Netherlands evaluated MCD. The qualitative data and quantitative data were mutually supportive. Furthermore, the diversity of the MCD participants enabled us to record a wide variety of clinicians' experiences and considerations. Nevertheless, the participants in this study were solely from gender identity clinics in the Netherlands. Besides, only six members of the Amsterdam and Leiden teams were interviewed individually, in order to reduce the burden on the clinicians. Despite the small number of interviewees, we believe that due to our careful selection of participants our study results reflect the views of a representative group.

CONCLUSION

In this mixed method study, Dutch transgender clinicians evaluated the use of MCD as a form of ethics support. Although respondents were critical of the length of time spent on MCD, the lack of follow-up on insights gained from MCD sessions, and of the determining factors of the MCD sessions, they widely felt that it helped them to more effectively deal with moral challenges and that it contributed to improved mutual understanding, respect, and communication among their team members. Given the inherent ethical dimension of transgender care, especially in the care for children and adolescents in which the treatment can have life-long consequences, and where treatment decisions are often surrounded by complex moral controversies and uncertainties, MCD appears to be a valuable addition to current treatment models in transgender care. MCD offers a trained facilitator, who is neutral, and a specific conversation method that make it easier and more profound to reflect upon the moral dimension of specific complex decisions. During MCD, the professionals' reasoning and knowledge are included, yet MCD makes (possible conflicts of) underlying norms and values explicit and gives suggestions how to handle the uncertainty or disagreement within a team. As such, MCD can be seen as an additional tool that can be used in complex cases. For future research, it would be worthwhile to compare the usual decision-making process by transgender teams with decision-making processes that include the use of MCD more systematically. Finally, more research is needed which focuses on the actual contribution of MCD to the improvement of care quality (including its determining factors), the involvement of transgender people in MCD, and on how to integrate CES more into daily work processes.

General discussion

INTRODUCTION

This thesis describes the ethical dilemmas surrounding the use of early medical treatment for transgender minors, one specific being competence to give informed consent. The various studies in this thesis cover almost a decade, a time in which significant changes have occurred regarding how transgender minors are perceived, and regarding the care that is provided to them. In 2013, at the start of the first study included in this thesis, the possibility of treatment with puberty suppression (PS) had generated a relatively new dimension to the clinical management of transgender adolescents. It has been an approach of which ethical challenges have been acknowledged since the introduction of it (e.g. Cohen-Kettenis et al., 2008; Kreukels & Cohen-Kettenis, 2011). Even though the use of PS in the care of adolescents was adopted by a rapidly increasing number of gender identity clinics, and the World Professional Association for Transgender Health (WPATH) and the Endocrine Society included this treatment option in their guidelines on care for transgender children and adolescents, many clinicians working with transgender minors remained critical (e.g. Coleman et al., 2012; Coleman et al., 2022; Hembree et al., 2017; Rew et al., 2021; Vrouenraets et al., 2015). Since the introduction of PS, the debate has never been quiet and moved between extremes, and the discussions were at times emotion-laden. At that time, it was not fully clear what the underlying thoughts and considerations were of the people who criticize PS treatment, and of those who support the use of PS. In particular, advocates of PS, openly stated their considerations, ideas, and clinical research data regarding PS in, among others, scientific journals (e.g. Hembree, 2011; Olson et al., 2011), while people who criticized the treatment mostly stated their considerations and ideas via social media, and barely in scientific journals (e.g. An interview with Dr. Joseph Nicolosi Part 1/3, 2010; Chemical castration - not the best for children, 2011). Over time, the people who criticize the treatment, and the ones who support the use of early medical treatment do not seem to have come closer to each other; in fact, the debate seems to have become only harsher (e.g. Lament, 2014; Osserman & Wallerstein, 2022). Currently there hardly seems to be little room for a 'nuanced middle-ground' anymore (e.g. Bazelon, 2022).

In the last decade, people criticizing early medical treatment for transgender minors have also increasingly begun to publish their research data and outlining their critical views in internationally peer-reviewed journals, just as providers supporting early medical treatment already did. They state that PS in transgender adolescents should occur in the context of research since the treatment is, according to them, largely experimental (Biggs, 2019; Heneghan & Jefferson, 2019). They stress that there are still too many unanswered questions regarding the treatment; questions that include the treatment's reversibility, the age at start, its psychosocial effect and impact, the role of physiological puberty in developing gender identity, medical decision-making competence (MDC), transition regret

later in life, and long-term effects on mental health, bone mineral density, cardiovascular health, quality of life and, a worry of many, fertility (Heneghan & Jefferson, 2019; Laidlaw et al., 2019b; Malone, Hruz, Mason, & Beck, 2021; Naezer et al., 2021; Richards et al., 2019). Of note, many advocates of the use of early medical treatment share having worries about these topics (Olson-Kennedy et al., 2016; Vrouenraets et al., 2015). Furthermore, critics of the use of PS in transgender adolescents emphasize that it regards a medical intervention with major bodily consequences used for adolescents who are not physically ill (Sadjadi, 2013). Some claim that treatment with PS for transgender adolescents should be curtailed until one is able to apply the same scientific rigor that is required for other medical treatments (Richards et al., 2019). Some however are concerned that bias and politicization will prevent a truthful scientific debate about the interventions for these adolescents (Malone et al., 2021).

On the other hand, advocates of the treatment stress the positive results of providing PS to adolescents in the early stages of puberty, provided that the adolescents are eligible for starting this treatment based on the criteria mentioned in two established international transgender guidelines (Coleman et al., 2022; Hembree et al., 2017; see also table 3 which can be found at page 14). Although, according to those criticizing treatment, they may not meet the golden evidence-base standard, various long-term and shorter-term follow-up studies in different parts of the world show positive results regarding the effectiveness of PS, improving the adolescent's psychological functioning and appearance congruence, and decreasing emotional and behavioural problems (e.g. Chen et al., 2023; Costa et al., 2015; van der Miesen et al., 2020; de Vries et al., 2011a; de Vries et al., 2014). Other relatively large scale prospective longitudinal studies in different parts of the world are in progress (Olson-Kennedy et al., 2019; Reardon, 2016; Tollit et al., 2019).

In addition, there is debate about whether every transgender adolescent could profit from treatment in early puberty, or that there is a not earlier recognized developmental pathway of post-puberty onset gender dysphoria. Whether these adolescent profit similarly from early treatment is unclear since still little is known about for example challenges that transgender adolescents who present at an older age with gender dysphoria might face and what effects that might have on, for example, eventually detransitioning (Chen et al., 2020; A. de Vries, 2020; Sevlever & Meyer-Bahlburg, 2019; Turban, Carswell, & Keuroghlian, 2018a).

Furthermore, it is stressed that withholding adolescents from PS is not a neutral option and might cause life-long harm (Coleman et al., 2022; Cohen & Gomez-Lobo, 2021; de Vries et al., 2021; Vrouenraets et al., 2015). Providing this treatment in the early stages of puberty ensures that, among others, transgirls do not have to deal with a deepened voice, and masculinization of their face, and transboys do not have to deal with breast development,

reducing their distress and the associated dysphoria (Kreukels & Cohen-Kettenis, 2011). However, of note, research shows that even though more and more treatment teams provide treatment with PS, they do that with a feeling of unease because of the relatively little data regarding long-term psychological and physical outcome available (Vrouenraets et al., 2015; Vrouenraets et al., 2022a).

A challenge regarding the lack of evidence-base is that the golden standard of a randomized controlled trial is neither feasible nor ethical, leaving clinicians with unanswered questions and inherent ethical challenges about what is best practice in care for transgender minors.

More insight in the core of the ethical dilemmas that play a role in the care of transgender minors, and more empirical data that could give direction in some of the ethical dilemmas are needed in order to give clinicians direction to deal with these issues, and to inform and guide minors referred to the gender identity clinic. Therefore, the first overall aim of this research was to gain more insight in the core of the ethical dilemmas that play a role in the care of transgender minors, and the underlying intuitions and considerations of stakeholders in the field regarding early medical treatment. The stakeholders are transgender adolescents who proceeded with gender-affirming medical treatment (GAMT) after PS, adolescents who were diagnosed with gender dysphoria but who did not proceed with GAMT after starting treatment with PS, their parents, clinicians working in gender treatment teams, and people who are critical about the use of early medical treatment for transgender minors. The second, subsequent aim is to provide empirical data regarding these ethical dilemmas.

The starting point of this thesis was a broad interview study we conducted which gave insight into the ethical dilemmas that play a role in the use of early medical treatment for transgender minors according to the stakeholders (Vrouenraets et al., 2015; Vrouenraets et al., 2016). Clinicians working with transgender minors and people criticizing the use of early medical treatment for transgender minors from around Europe and North-America, transgender minors themselves, and their parents were interviewed. Multiple themes, described in chapter 2 and 3, emerged which gave rise to different, and sometimes even opposing, views on the treatment for transgender minors. In the subsequent chapters we examined several of these themes to gain deeper understanding of the controversies and possible solutions.

In this general discussion we reflect on the meaning of our study outcomes to the broader context of the political and public discussions. We will do this by means of five themes that consistently emerged in these discussions: the minors' MDC, considerations regarding starting or refraining from PS, co-occurring psychosocial challenges, the social context, and clinical ethics support. One by one, these themes will be discussed. For each theme, it

will be described how the considerations, ideas and newly obtained scientific data, when applicable, have changed and developed over the years. Furthermore, suggestions for future studies, and implications for clinical practice are given.

1. MINORS' MEDICAL DECISION-MAKING COMPETENCE

Transgender minors' MDC to start PS is an issue which is given increasingly attention and importance over the years, and which is mentioned in almost all debates and discussions regarding the use of medical treatment for transgender minors (e.g. Downs, & Whittle, 2018; Ouliaris, 2022; Wren 2019; Levine et al., 2022). It is not only mentioned by those directly involved in the care of these minors, but also by influences not directly involved in clinical care, like society and the media (e.g. Cook, 2022; Robbins, 2022; Tampier, 2022). Furthermore, adolescents' MDC appears to be a recurring and increasingly important issue in case law (e.g. Hughes, Kidd, Gamarel, Operario, & Dowshen, 2021; Kidd et al., 2021; Ouliaris, 2022). The lawsuit regarding Keira Bell, and the large-scale and profound consequences of the response to the verdict of this lawsuit show why it was so important to further research this topic (Barbi & Tornese, 2022; see the general introduction for more details about this lawsuit).

From the start of this study project providers supporting the use of early medical treatment stated that research showed that relatively young children can meaningfully participate in the consent process, whereas people criticizing the use of early medical treatment raised doubts about what minors can understand (e.g. Abel, 2014; Giordano, 2008a; Giordano et al., 2021; Mann et al., 1989; Sadjadi, 2013). Some questioned whether the adolescents, at the time they decide on PS, actually have the mental competence to decide on starting that treatment (Vrouenraets et al., 2015). Of note, several clinicians, working in minors treatment teams of gender identity clinics, also questioned to what extent adolescents who are eligible to start PS are actually competent to make that decision (Vrouenraets et al., 2015). Furthermore, transgender adolescents themselves and their parents had doubts about the minors' competence to make these decisions too (Vrouenraets et al., 2016; Vrouenraets et al., 2022a).

Therefore, we conducted a study that aimed to determine whether the adolescents who were eligible to start PS were competent to make that decision. The Dutch version of the MacArthur Competence Assessment Tool for Treatment (MacCAT-T), a validated semi-structured interview, modified for minors was used (Grisso et al., 1997; Vrouenraets et al., 2021). The results of this study are reassuring, showing that the majority (about 90%) of the adolescents participating in this study have thoroughly thought about PS, understand what the treatment involves, and are deemed competent to decide (Vrouenraets et al., 2021).

Furthermore, even though age is often considered to be the best determinant for having MDC, the results of this study did not show a relation between age and level of MDC regarding starting PS (Dorn et al., 1995; Vrouenraets et al., 2021). One remark in this context is that the sample included few participants aged younger than 12, although research in other medical contexts shows that children under the age of 11 were not always deemed to be competent to consent (Hein et al., 2014; Vrouenraets et al., 2021).

The study revealed that, in line with the expectations of the transgender adolescents, their parents, and the clinicians, and other studies, minors with a higher intelligence were assessed as better decision-making competent (Hein et al., 2015c; Miller et al., 2014; Vrouenraets et al., 2021; Vrouenraets et al., 2022a). Sex (birth-assigned girls) was also related to MDC in this sample. A hypothesis for the association between sex and MDC found in our study is that the birth-assigned girls participating in our study might have had a more advanced puberty compared with the participating birth-assigned boys, which might be related to a better understanding of the treatment's consequences (Koerselman & Pekkarinen, 2017). This would be in line with the thoughts of the transgender adolescents, their parents, and the clinicians that developmental stage is related to MDC. Finally, psychological difficulties seemed to be of little relevance for MDC in our sample as we did not find an association between MDC and the duration of the adolescent's diagnostic trajectory, and behavioural and/or emotional difficulties (Vrouenraets et al., 2021).

2. CONSIDERATIONS REGARDING STARTING OR REFRAINING FROM PUBERTY SUPPRESSION

The current state of science regarding the medical aspects of care for transgender minors is promising. Several review studies show reassuring results regarding the use of PS (e.g. Ramos et al., 2021; Rew et al., 2021; Turban & Ehrensaft, 2018). Even though PS may have an effect on bone mineral density, results show that kidney function, liver function, and liver profiles seem to be unaffected (Marantz & Coates, 1991; Schagen et al., 2016; Steensma et al., 2013). Due to these effects of PS, the established international transgender guidelines recommend careful monitoring of the minors' physical development while receiving PS, by means of, among others, bone density assessments and blood monitoring, to ensure that testosterone and oestrogen are adequately suppressed (Coleman et al., 2022; Hembree et al., 2017; Klink et al., 2015; Vlot et al., 2017). Furthermore, even though concerns are raised about a decreased height velocity of the minors receiving PS, multiple studies show that although growth decelerated while minors received PS, there is an acceleration in growth while they subsequently received gender-affirming hormones (GAH) (e.g. Boogers et al., 2022; Korkmaz et al., 2019; Willemsen et al., 2022). Results show that adult height is not negatively affected by PS and GAH in transboys (Willemsen et al., 2022). The study of

Boogers and colleagues shows that adult height in transgirls was slightly lower than the height predicted at start of PS, but there was no significant difference from target height (2022).

Furthermore, with regard to the psychological aspects of PS in care for transgender minors, several studies show that the use of PS is associated with improvement of affect, psychological functioning, and internalising psychopathology by improving depression and anxiety symptoms, controlling self-mutilation episodes, and reducing suicidal thoughts and suicidality in adulthood (e.g. Costa et al., 2015; de Vries et al., 2011a; Khatchadourian et al., 2014; Rew et al., 2021; Tucker et al., 2018). In addition, PS is associated with improvement of quality of life and social life (e.g. Schneider et al., 2017; White Hughto & Reisner, 2016).

One of our early studies found that clinicians should take the possible physical and/or psychological harmful consequences of treatment with PS into account when considering starting treatment with PS for transgender adolescents (Vrouenraets et al., 2015). Concerns were mentioned regarding, among others, consequences for cognitive and brain development, and fertility (Vrouenraets et al., 2015). These concerns still exist. Despite increasing research into the possible consequences of PS for, among others, neurodevelopment, bone mineral density, and fertility, the full consequences (both adverse and beneficial) of the use of PS are not yet known (e.g. Arnoldussen, Hooijman, Kreukels, & de Vries, 2022a; Chen et al., 2020; Cheng et al., 2019; Schagen et al., 2020; Vlot et al., 2017). This lack of large long-term studies causes many stakeholders to worry and speculate about harmful long-term consequences (Giordano & Holm, 2020; Kimberly et al., 2018). In fact, these concerns have led some countries, for example England and Sweden, to limit access to care and allow treatment with PS for transgender minors only in research settings (Cass, 2022; Socialstyrelsen (National Board of Health and Welfare), 2022). Important to realise is the fact that most transgender adolescents who participated in our 2016 study stated that the lack of long-term physical and psychological outcomes did not, and would not stop them from wanting treatment with PS (Vrouenraets et al., 2016). Furthermore, many adolescents, both adolescents who proceeded to GAH after PS, and adolescents who discontinued treatment with PS, and their parents stated that they simply accepted possible negative consequences of the treatment with PS and mentioned that they did not really take them into consideration (Vrouenraets et al., 2022a).

The role of physiological puberty in developing a consistent gender identity

One possible consequence of PS that causes worries in some, regards the idea that interrupting the development of secondary sex characteristics, by means of PS, may disrupt the development of a gender identity that is congruent with the assigned gender

(Korte et al., 2008; Vrouenraets et al., 2015). Most people who participated in our 2015 study, the ones who criticize the use of early medical treatment and the ones who claim its benefits, agreed on the fact that the use of PS might change the way adolescents think about themselves (Vrouenraets et al., 2015). However, most of them thought that the use of PS did not inhibit the spontaneous development of a gender identity that would become congruent with the assigned gender after many years of having an incongruent gender identity.

One research study shows that the period between 10 to 13 years of age, the time in which onset of puberty is common, may be a key period for retransition, and that gender identity may be more stable after these years for minors who have gender incongruent experiences before these ages (Steensma et al., 2011; Steensma et al., 2013). After these ages, gender identity changes in only a few. For instance, research shows that only 1.9% to 3.5% of the transgender minors who started GAMT during or after their puberty, discontinued their treatment and no longer desired GAMT (e.g. Brik et al., 2020; Carmichael et al., 2021; de Vries et al., 2011b; Hembree et al., 2017). Although numbers are low, these findings endorse that one's gender identity *can* change in the period one is receiving treatment with PS.

Some informants participating in our 2015 study stated that although PS may disrupt the development of a consistent gender identity, in some cases, the very real risks of the present (e.g. possible risk for suicide because of gender incongruent experiences) override the possible risks for the future (e.g. the individuals' uncertainty) (Vrouenraets et al., 2015). This consideration is also mentioned in other studies (e.g. Turban & Keuroghlian, 2018). Furthermore, some adolescents who as young adults experienced a change in gender identity, and subsequently stopped GAMT, did not regret undergoing the treatment (Turban et al., 2018s; Turban & Keuroghlian, 2018; Turban, Loo, Almazan, & Keuroghlian, 2021). One young adult who stopped GAMT even stated that undergoing the treatment with GAH was essential for the consolidation of their gender identity (Turban et al., 2018a).

Of current interest, in recent years the hypothesis of 'rapid-onset gender dysphoria' has been suggested (e.g. Littman, 2019; Hutchinson, Midgen, & Spiliadis, 2020). There is some controversy about what is described as rapid-onset gender dysphoria (Littman, 2019). Some describe rapid-onset gender dysphoria as the phenomenon where the development of gender dysphoria begins suddenly during puberty or after completion of puberty in adolescents or young adults who did not meet criteria for gender dysphoria in childhood (Littman, 2019). Some wonder whether there are new aetiologies leading to gender dysphoria, whether rapid-onset gender dysphoria has the same desistence and persistence rates, and outcomes as the previously studied gender dysphorias, and whether it responds the same to treatment (Littman, 2019). A hypothesis on this rapid-onset phenomenon is that the transgender identification and gender dysphoria of rapid-

onset gender dysphoria may be more temporary (Littman, 2019). While others state that the term rapid-onset gender dysphoria was coined to describe a supposedly epidemic of adolescents and young adults coming out as transgender people 'out of the blue' due to mental illness and social contagion (Ashley, 2020). The phenomenon of rapid-onset gender dysphoria is receiving increasing attention in lay media and scientific research (e.g. Ashley, 2020; Hutchinson et al., 2020). Further research regarding this phenomenon is needed in order to further substantiate these hypotheses on additional scientific data.

Consequences for fertility

An area of concern that in more recent years has become increasingly evident for many involved in early medical treatment for transgender minors are the consequences of early medical treatment for fertility (e.g. Laidlaw et al., 2019b; Vrouenraets et al., 2015). Therefore, we have explored this issue in more detail in several of our studies. The effects of PS on gonadal function and the development of secondary sex characteristics are reversible when PS is discontinued (Hembree et al., 2017). However, if adolescents subsequently undergo treatment with GAH and gonadectomy this will result in loss of fertility (de Roo et al., 2016; Hembree et al., 2017; Olson et al., 2011). If minors start treatment with PS at a young age by which they never undergo their endogenous puberty, they will also not be able to pursue fertility preservation (Brik et al., 2019; Hudson et al., 2018). In addition, fertility outcomes may vary depending on birth-assigned sex, and on the type of treatment individuals choose to undergo. For example, not all adolescents pursue gonadectomy (Cheng et al., 2019). Nevertheless, the vast majority of the adolescents who start treatment with PS subsequently proceed to treatment with GAH, with loss of fertility as a possible result (Brik et al., 2020). Nonetheless, preliminary results of a longitudinal study suggest that the negative impact of treatment with GAH on spermatogenesis can be reversed in transwomen. This raises the question whether the previous claims that treatment with GAH for transwomen inevitably leads to permanent loss of fertility are correct (de Nie et al., 2023). Further and larger research is needed to confirm these findings (de Nie et al., 2023).

Infertility and concerns about (future) fertility may have a major negative impact on someone's mental health and quality of life (Carter et al., 2010; Trent et al., 2003). This is in line with the finding that possible loss of fertility as a consequence of PS evoked concerns in several interviewed adolescents, their parents, and all interviewed clinicians (Vrouenraets et al., 2015; Vrouenraets et al., 2022a). On the other hand, a questionnaire study conducted in Canada shows that for the majority of the transgender adolescents fertility is a low current and future life priority (Chiniara, Viner, Palmert, & Bonifacio, 2019). The majority of the transgender adolescents in this and some other studies conducted in the United States, have a wish to become a parent, but are open to alternatives for building a family, like adopting children (Chen et al., 2018; Chiniara et al., 2019). In contrast, one of our studies conducted in the Netherlands shows that only 13% of the 22 participating

transgender adolescents who did not want to be referred for fertility preservation, say they are interested in adopting children (Brik et al., 2019). This difference raises the question if there might be a different view on adopting children in the United States and Canada compared with the Netherlands (Brik et al., 2019).

Additionally, of interest in this regard, research on survivors of paediatric cancer show that the wish for future children may change over time, which is in line with the observation that some of the transgender adolescents we interviewed say that only during the period they got treatment with PS, they started to realise what the impact of some consequences could be (Armuaud et al., 2014; Stein et al., 2014; Vrouenraets et al., 2022a). Furthermore, transgender adolescents, their parents, and clinicians stated that not being able to understand and appreciate the impact of certain consequences of treatment with PS, for example possible loss of fertility for one's future life, is inherent to the adolescent's developmental stage and/or age (Vrouenraets et al., 2022a).

The WPATH Standards of Care (7th and 8th version) and Endocrine Society clinical practice guideline on care for transgender children and adolescents recommend counselling regarding fertility preservation options before initiating treatment with PS (Coleman et al., 2012; Coleman et al., 2022; Hembree et al., 2017). Our study shows that all 35 participating adolescents who were referred to start treatment with PS, had been informed about the risks of infertility, and 32 (91%) of them had been counselled about the option of fertility preservation (Brik et al., 2019). Counselling does not always lead to proceeding to actual fertility preservation however. Two studies from the United States indicate that transgender adolescents rarely use fertility preservation, respectively three and five percent (Nahata et al., 2017; Chen et al., 2017). Our study with transgirls in the Netherlands shows a much higher percentage (38%) of transgirls attempting fertility preservation, of which 75% was able to cryopreserve sperm (Brik et al., 2019). However, the same study shows that one-third of the transgirls who attempted fertility preservation, could not make use of it because they were not able to produce a semen sample because of early pubertal stage. This is in line with the results of other studies (de Sutter et al., 2002; Persky et al., 2020). Besides the physical limitations to producing a semen sample, several adolescents and their parents also mentioned barriers from a psychological perspective (Brik et al., 2019; Cheng et al., 2019; Vrouenraets et al., 2022a). Discomfort with reproductive anatomy, for example not feeling comfortable with masturbation or having an aversion of their penis, is a major influencing factor for some transgender adolescents in deciding about fertility preservation (Brik et al., 2019; Perksky et al., 2020; Nahata et al., 2017; Vrouenraets et al., 2022a).

In sum, several aspects make it all the more important that transgender adolescents deciding on starting PS are adequately informed about the possible impact of GAMT on fertility, and about fertility preservation (Vrouenraets et al., 2022a). Guidance on best

practices for engaging in fertility preservation counselling with transgender adolescents and their parents is recommended in order to give them adequate information and support in considering fertility preservation (Tishelman et al., 2019). Future research on alternatives for fertility preservation options which are less psychologically burdensome for the transgender adolescents and their parents, which could be used to facilitate fertility preservation, is recommended (Brik et al., 2019). One such option that is currently investigated, is the provision of TESE (Testicular Sperm Extraction) for transgirls in early stages of puberty (e.g. Adeleye, Stark, Jalalian, Mok-Lin, & Smith, 2021). Finally, further research regarding the possible positive and harmful psychological impact of the fertility preservation procedures would also be valuable (Baram et al., 2019; Chen & Simons, 2018).

Perceived functions of treatment with puberty suppression

In addition to the possible harmful consequences of starting or refraining from treatment with PS, the functions treatment with PS has for the adolescents, their parents, and their clinicians should also be taken into account when considering starting or refraining from PS. Treatment for transgender adolescents with PS was developed for two main reasons: first, to 'pause' the development of sexual sex characteristics in order to expand the exploration and assessment phase (Delemarre-van de Waal & Cohen-Kettenis, 2006). In that way adolescents have 'extra' time to explore their options, and experience living in the affirmed gender role, before pursuing GAMT by means of treatment with GAH and/or surgery, with (partially) irreversible effects. Secondly, the physical appearance will be more satisfactory and congruent to the experienced gender when starting PS in the early stages of puberty compared to PS in later puberty. Furthermore, in that way, some surgery such as mastectomy may not be necessary or less invasive because development of secondary sex characteristics is prevented (Coleman et al., 2022; Hembree et al., 2017; van de Griff et al., 2020). Even though the two established international transgender guidelines describe these and other reasons to use treatment with PS for transgender adolescents, little is known about the functions of PS as reported by the transgender adolescents themselves, their parents, and their clinicians. Two of our studies show that many transgender adolescents experience the function of treatment with PS as the first necessary step of a seemingly clear trajectory towards further gender-affirming interventions, rather than as an opportunity to explore and consider further treatment wishes (Brik et al., 2020; Vrouenraets et al., 2022b). This suggests that treatment with PS may serve other functions than the ones mentioned in the established international transgender guidelines (Vrouenraets et al., 2022b). Insight into the perceived functions of PS would help to adequately support adolescents in their decision-making process and give them the care they need.

In line with one of the reasons to start PS mentioned in the established international transgender guidelines, the findings of one of our interview studies and other studies

show that inhibition of the development of secondary sex characteristics was an important function of the treatment for all participating transgender adolescents who proceeded with GAH after treatment with PS, the adolescents who discontinued treatment with PS, their parents, and clinicians (Coleman et al., 2022; Hembree et al., 2017; Vrouenraets et al., 2022b). Inhibition of the development of secondary sex characteristics will result in a more satisfactory physical appearance and congruent to the experienced gender for those who continue with GAMT. The second main reason to use PS mentioned in the established international transgender guidelines is to provide adolescents 'extra' time for exploration and considerations (Coleman et al., 2022; Hembree et al., 2017). In this regard, contrasting results emerged; on the one hand, most adolescents who proceeded with treatment with GAH did not experience the time on PS as an extended exploration phase (Vrouenraets et al., 2022b). Most of them saw PS as the first step of GAMT, even though some were glad that the effects of PS were reversible even if they did not expect to change their minds. This is in line with the results of one of our other studies (Brik et al., 2020). On the other hand, these same two studies also show results that endorse the use of PS to provide adolescents 'extra' time for exploration and considerations. As it turned out, most adolescents who discontinued treatment with PS did experience the time on PS as an extended exploration phase (Vrouenraets et al., 2022b). Furthermore, some transgender adolescents used the time on PS in order to get used to living in the affirmed gender role themselves, or used that time to let their parents get used to the situation and/or to accept the gender dysphoria (Brik et al., 2020; Vrouenraets et al., 2022b). Several parents endorse that they found the time their child was on PS helpful to adapt to their child's new gender role (Vrouenraets et al., 2022b). Of note, the results of one of our studies show that about 10 percent of the adolescents who started GAH had used PS for longer (at least three months more) than required by protocol for reasons other than logistics and regularly met with a mental health professional during this time (Brik et al., 2020). Examples of reasons for this prolonged use of PS were more time to decide about treatment with GAH, lack of parental support or acceptance of gender dysphoria, comorbidity such as depression or autism spectrum disorder, and further diagnostics by the clinicians of the treatment team (Brik et al., 2020). This supports the idea that the time on PS is used as an extended diagnostic phase where adolescents can further explore their gender identity and treatment wishes, and work on issues that might interfere with successful treatment. In addition, the period the adolescents were on PS also proved useful for several clinicians, providing them more time for diagnostic assessment (Brik et al., 2020; Vrouenraets et al., 2022b).

The functions mentioned by the transgender adolescents, their parents, and clinicians are not all in line with the reasons to use PS as mentioned in the two established international transgender guidelines (Coleman et al., 2022; Hembree et al., 2017; Vrouenraets et al., 2022b). Results of our studies could be implemented in the guidelines, taking the different perceived functions and thoughts of the adolescents and their parents regarding PS into

account, and therefore leaving room for more customized care. In doing so, clinicians will be able to provide the transgender adolescents and their parents information about PS that is relevant for the adolescents and parents, and is more in line with the adolescents' and parents' considerations and ideas. This in turn will lead to better mutual understanding, and therefore will lead to better grounded informed consent of these adolescents and parents, preventing the risk of eroding into a merely legal and formalistic form of protection (Vrouenraets et al., 2022b).

Consequences when refraining from treatment with puberty suppression

Furthermore, besides the possible harmful consequences of the early medical interventions, informants of our 2015 study also mentioned the possible harmful consequences of refraining from interventions (Vrouenraets et al., 2015). Refraining from intervening is not a neutral option; not permitting transgender adolescents access to medical interventions may be accompanied with the risk of poor mental health outcomes, for example suicidal ideations, suicidality and/or harassment (e.g. Bauer, Scheim, Pyne, Travers, Hammond, 2015; Olson-Kennedy, Rosenthal, Hastings, & Wesp, 2016; Tucker et al., 2018; Turban, King, Carswell, & Keuroghlian, 2020). Therefore, for each individual person the right balance needs to be struck between the possible, partly still unknown consequences of treatment with PS, and the possible unknown consequences of refraining from this treatment, and take into account what is best for that individual person.

3. CO-OCCURRING PSYCHOSOCIAL CHALLENGES

Gender dysphoria in minors is associated with a range of co-occurring psychosocial challenges, and the risk of co-occurring psychiatric difficulties in these minors is high. This is a finding that reveals ethical and clinical challenges as to how to perceive and address these vulnerabilities when transgender adolescents apply for GAMT (Bechard, VanderLaan, Wood, Wasserman, & Zucker, 2017; Holt, Skagerberg, & Dunsford, 2016; Spack et al., 2012). A recent review study, including 32 studies, shows that adolescents presenting for an intervention regarding their gender dysphoria, experience high rates of mental health problems (Thompson, Sarovic, Wilson, Säm fjord, & Gillberg, 2022). The most frequent co-occurring psychopathologies are depression, anxiety, and attention deficit disorders. Furthermore, the prevalence of autism spectrum disorders, schizophrenia spectrum disorders, self-harm, psychoses, and suicidal ideations is higher in transgender adolescents compared to the cis population (Thompson et al., 2022).

To date, the precise association between gender dysphoria and co-occurring psychopathology is unknown. However, a review study Paz-Otero, Becerra-Fernández,

Pérez-López, and Ly-Pen conducted describes that experienced minority stress is one factor that justifies this association (2021). The interview and questionnaire study we conducted shows that several professionals share this view (Vrouenraets et al., 2015). They think that the negative impact of society can be a mediating factor, stating that society marginalizes minority groups. Indeed, various studies show that high rates of perceived stress and lack of support appear to be facilitators of psychopathology in the transgender population (Hoy-Ellis & Fredriksen-Goldsen, 2017; Witcomb et al., 2018). This perceived stress may lead to significant internalized transphobia, which appear to increase the depression and anxiety in the transgender population (Chodzen, Hidalgo, Chen, & Garofalo, 2019).

Specifically, the suggested overlap between autism spectrum disorder and gender dysphoria/gender incongruence has been much disputed (Kallitsounaki & Williams, 2022). A recent review study shows that the prevalence of an autism spectrum disorder diagnosis in transgender individuals is 11%, compared to approximately one percent in the worldwide population (Kallitsounaki & Williams, 2022; Lai, Lombardo, & Baron-Cohen, 2014). Some suggest that a great part of the increased number of referrals to gender identity clinics involves transgender individuals who are on the autism spectrum, which may create additional challenges for clinicians regarding the assessment for GAMT and medical decision-making regarding the medical treatment (e.g. Lehmann, Rosato, McKenna, & Leavey, 2020). The aforementioned review study confirms a link between autism spectrum disorder and gender dysphoria/gender incongruence (Kallitsounaki & Williams, 2022). However, it does not provide tools regarding its consequences for care (Kallitsounaki & Williams, 2022).

Several people claiming the risks of the use of early medical treatment for transgender minors, as well as people stressing the benefits of it, think that whether gender dysphoria and co-occurring psychopathology are merely interrelated or coexisting, depends on the individual and the co-occurring psychopathology (Vrouenraets et al., 2015). In our research, some stress that severe coexisting psychopathology should be addressed before GAMT in minors is started. Others state that, even though coexisting psychopathology may interact with gender dysphoria and related medical treatments, those two aspects may be the result of completely different underlying processes and should therefore have separate treatment plans, strategies, and goals (Vrouenraets et al., 2015). In line with this consideration, one could state that instead of focusing on only the transgender individuals, one should start 'depathologizing' gender dysphoria, and realise that these coexisting psychopathologies are not the result of gender variability in itself or that the gender variance is not a consequence of psychopathology (Littman, 2019; Paz-Otero et al., 2021). However, in order to gain more information about this association, further research is needed, while in clinical practice, co-occurring psychological difficulties may lead to ethical dilemmas when providing GAMT.

4. THE SOCIAL CONTEXT

The visibility of transgender minors and attention to their care has increased over the years. At the start of this study project, in 2013, professionals already mentioned the role of the social context in the way gender dysphoria is perceived. One of the issues regarding the role of the social context brought up by the informants of the 2015 study, was the increasing media attention (Vrouenraets et al., 2015). At the time that study was conducted, several professionals wondered in what way the increasing media attention affects the way minors' gender incongruent experiences were perceived by the minors and by the society the minors live in (Vrouenraets et al., 2015). Since 2013, the media coverage of minors with gender incongruent experiences has continued to increase enormously. Newspapers, television programs, magazines, movies, and the internet pay increasing attention to transgender children and adolescents (Pang et al., 2020; Sadjadi, 2013; Zucker et al., 2008).

Since the media have an increasingly important influence on the development of adolescents' identity, especially in western communities, one could wonder what role the media plays in adolescents' gender identity development (Alper et al., 2016; Henrich et al., 2010). Even though research shows an association between the increased media attention and the increase of minors referred to gender identity clinics, this study does not tell us anything about causation (Pang et al., 2020). On the one hand, the positive media attention may foster minors' self-esteem, help them cope with discrimination, and mediate negative experiences (Craig, McInroy, McCready, & Alaggia, 2015). On the other hand, one could speculate whether the media attention might have a negative effect by, for example, leading to medicalization of gender incongruent experiences, or unintentionally causing more minors to reach out for care regarding their gender incongruent experiences which potentially might cause some of them to be wrongly diagnosed with gender dysphoria (Bechard et al., 2017; Littman, 2019). However, a study focusing on adolescents referred to one of our Dutch gender identity clinics during recent years does not provide any indications for evidence of this last hypothesis; the study shows that even though there is an exponential increase of referrals between 2000 and 2016, and more assigned females were referred, no time trends were observed regarding the intensity of dysphoria and in demographics (Arnoldussen et al., 2020; Arnoldussen et al., 2022b). Furthermore, the percentage of referred adolescents diagnosed with gender dysphoria after a diagnostic trajectory, remained the same (Arnoldussen et al., 2020; Arnoldussen et al., 2022b).

Another study aimed to investigate whether positive and/or negative media attention regarding transgender and gender diverse matters is associated with the number of minors referred to gender identity clinics (Indremo, Jodensvi, Arinell, Isaksson, & Papadopoulos, 2022). These study results show that negative media attention was associated with a decrease of the number of referrals, while a positive media event was associated with no

alterations of referrals (Indremo et al., 2022). In this regard, one should keep in mind that a decrease of referrals does not necessarily mean that there are less children and adolescents with gender incongruent experiences. Therefore, a decrease of referrals might even lead to worse mental health among a group of minors not seeking care because of the risk and barriers in accessing the care they actually need (Pang, Hoq, & Steensma, 2022).

Changes in the social context, such as the increased media coverage of transgender children and adolescents, therefore entail ethical challenges to clinical practice. People criticizing the use of early medical treatment and advocates of it speculate about the positive and/or negative influence the increased media attention might have, and how to cope with it in clinical practice (e.g. Indremo et al., 2022; Pang et al., 2020; Vrouenraets et al., 2015). More research on the role and influence of the increased media attention is needed to better understand its impact.

5. CLINICAL ETHICS SUPPORT

The studies included in this thesis address several ethical dilemmas surrounding early medical treatment for transgender minors. In the studies described in this thesis we sought to further explore various themes that play a role in the care of transgender minors, and provide more substantiation regarding these ethical dilemmas. This, in order to ensure that the debate is scientifically knowledge-based instead of primarily assumption-based. However, our studies show that ethics is an inherent dimension of transgender care, especially in the care for children and adolescents in which the treatment can have life-long consequences, and where treatment decisions made in minors are often surrounded by complex ethical controversies and uncertainties (Vrouenraets et al., 2020).

Several clinicians who were interviewed in the context of the interview study described in chapter 2, mentioned that participation in that interview study made them think more explicitly about various ethical themes related to the care of transgender minors (Vrouenraets et al., 2015). It encouraged them to discuss the issues in their multidisciplinary treatment teams. Furthermore, they reported a need to structurally discuss ethical challenges among their teams. Something which is mentioned in another study regarding moral challenges in transgender care as well (Gerritse et al., 2018). This led to the initiative of using moral case deliberation (MCD) as one of the clinical ethics support methods for dealing with ethical and moral challenges in transgender care in the Netherlands.

Moral case deliberation

Moral case deliberation (MCD) is a relatively well-established form of clinical ethics support and may help clinicians deal with ethical and moral challenges more effectively

(Dauwerse et al., 2014; Molewijk et al., 2008a). MCD is a facilitator-led, collective moral inquiry by clinicians that focuses on a concrete moral question connected to a real clinical case (Dauwerse et al., 2014; Stolper et al., 2016). In order to evaluate the usefulness of MCD in dealing with ethical and moral challenges in the multidisciplinary clinical treatment for transgender minors we conducted a mixed methods evaluation study (Vrouenraets et al., 2020). The results of this study showed that the participants of this study widely felt that MCD helped them to more effectively deal with ethical and moral challenges. They reported that MCD improved the mutual understanding, respect, and communication among their team members. They also stated that MCD strengthened their ability to make decisions and take action when managing ethically difficult circumstances. However, the participants were critical of the length of time spent discussing individual cases was excessive, some felt that MCD should lead to more practical and concrete results, and that MCD needed better integration and follow-up in the regular work process (Vrouenraets et al., 2020). Some of these limitations were also mentioned in another study regarding the use of MCD in transgender care (Hartman et al., 2018).

During MCD, the professionals' knowledge and reasoning are included, yet MCD makes (possible conflicts of) underlying norms and values explicit. Furthermore, it gives suggestions how to deal with possible uncertainty or disagreement within a team. As such, MCD can be seen as an additional tool that can be used in complex cases. This finding is in line with results of other studies describing the use of MCD in transgender care (e.g. Gerritse et al., 2018; Hartman et al., 2018). However, future research focussing on the actual contribution of MCD to the improvement of quality of care of transgender minors is recommended. Finally, it would be worthwhile studying the involvement of transgender people themselves in MCD, and the integration of clinical ethics support into daily work processes (Vrouenraets et al., 2020).

CONCLUDING CONSIDERATIONS

Ethical and moral challenges and dilemmas are inextricably linked to transgender care, especially when it concerns children and adolescents, and the possible life-long consequences of providing them with or refraining from early medical treatment. This is because it is a relatively new field, in which developments are rapid, there is still relatively little empirical data available on long-term outcomes, and it is a subject of a polarized debate. The challenges and dilemmas regarding early medical treatment for transgender minors, which were already expressed by clinicians about a decade ago, as described in our first article from 2015, only seem to have enlarged and sharpened since then (Vrouenraets et al., 2015). Initially, these dilemmas appeared to be an issue only for those directly involved in this care. However, today, a much broader group of people is expressing their

opinions and thoughts regarding this subject. Additionally, the role of the media and case law are increasing. With this, the debate seems to have become harsher, the controversy appears to have increased, and the people criticizing the use of early medical treatment and the people supporting it seem to be driven apart even further.

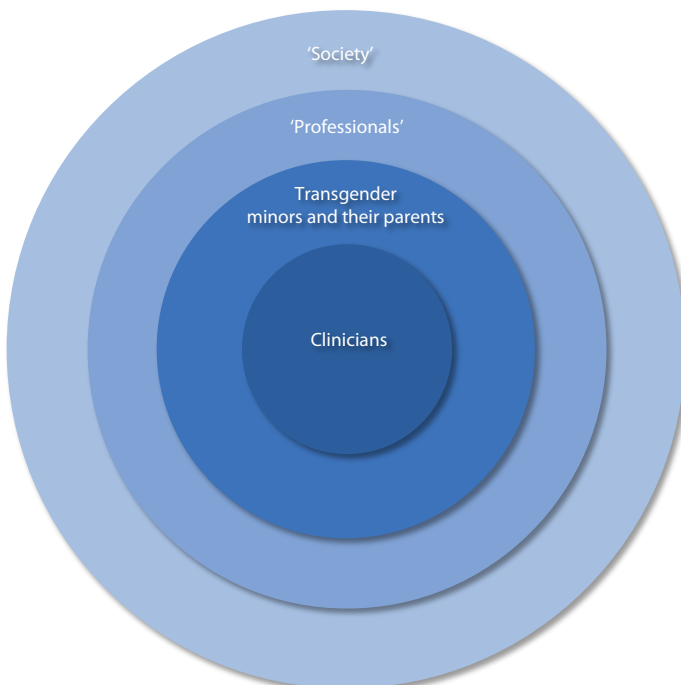
These changes and the associated ethical dilemmas, require the clinician to take an adjusted role with regard to (medical) treatment for transgender minors. Previously, the clinician needed to take into account predominantly the minors', the minors' parents', and their own professional standards, perspectives, thoughts, and wishes. Today, the voices of other influences, such as professional associations, the media, and case law seem to have become louder. Nowadays, clinicians should be aware of these increased 'societal forces'. Therefore, clinicians in treatment teams providing care to transgender minors can be seen as balance artists; they need to balance the treatment wishes, demands, and voices from different influences which exert their influence on the clinicians' work at different levels (M. de Vries, 2020).

Roughly speaking, these forces can be classified into three 'shells' (figure 6). The outer layer that influences and impacts the work of the clinician, and therefore needs to be taken into account by the clinician nowadays, is broadly speaking: 'society'; for example, the media and all people who are not directly linked to the care of individual transgender children and adolescents, but who nonetheless express their opinions and ideas regarding the treatment approaches (M. de Vries, 2020). The middle layer consists of 'professionals'; for example professional associations, parent support groups, adult activists, clinicians who used to work in the field of transgender care, and case law (e.g. Gilligan, 2019a; Gilligan, 2019b). For most of them, the most important aspect is that the care provided to the minors is as much evidence-based and legally justified as possible. However, since the (medical) treatment for transgender children and adolescents is relatively new and some outcome concerns may only evolve many years after initiation of treatment in late adulthood (e.g. regret about infertility, low bone density), some of this care is not yet examined using large, long-term follow-up study designs, and therefore not (yet) evidence-based. The 'forces' of this layer can result in ethical dilemmas with which the clinician needs to deal. The last layer, in the specialized gender identity clinics, consists of the transgender children or adolescents themselves, and their parents. Despite that the clinician has always had to deal with the children, adolescents, and their parents, the way of dealing with the people in this central layer has changed over the years. The children, adolescents, and their parents referred to the gender identity clinic in the late 1990s and early 2000s, when the protocol for diagnostic assessment and treatment was drawn up, were mainly overwhelmed and 'confused' by the gender non-conforming feelings of the child and the situation. They mostly wanted support in their search for a way to help the child. Most of them saw the clinician working at the gender identity clinic as someone

who could help and support them with this. The children, adolescents, and parents who enter a gender identity clinic nowadays, are generally much better informed through the media, the internet, and peers. In which it is important to mention that this information sometimes leads to children, adolescents, and parents having misconceptions about for example treatment options, with which the clinician must adequately deal. Unlike some decades ago, most who are referred to a gender identity clinic at the present time, have a clear idea of the diagnosis and their treatment wishes. This has an impact on the role expected of clinicians. As a result, a clinician needs to deal with this inner layer differently nowadays compared to one or two decades ago.

The clinician needs to find an adequate balance in the force fields between these different layers, of which some are relatively 'new', and of which all are continuously in motion concerning their perspective on the ethical dilemmas that play an important role in early medical treatment for transgender minors (M. de Vries, 2020). The ongoing collection of - both qualitative and quantitative - data related to the care and treatment for transgender children and adolescents, and the personalization of care, have important functions in continually evaluating and optimizing the care so that an adequate balance can be found in dealing with these various 'forces'.

Figure 6. The three 'shells' that exert their influences on the clinicians' work at different levels



LIMITATIONS AND DIRECTIONS FOR FUTURE RESEARCH

Outlining the various challenging themes involved in the care of transgender minors, and providing empirical data regarding the ethical dilemmas that are of concern in the care of transgender minors, gives clinicians direction to deal with these dilemmas, and informs and guides minors referred to the gender identity clinic. Some of the studies included in this thesis are largely focused on transgender minors receiving care as it is provided in the Netherlands. Therefore, the findings of these studies might not be similar for all other contexts, especially because the minors participating in our studies had extensive and thorough diagnostic evaluation before they were assessed eligible for treatment with PS. Transgender adolescents and their parents in other contexts, for example without this support, might have other considerations and thoughts about early medical treatment. Similar research with transgender minors and their parents in other contexts would therefore be a great addition.

In order to bring the ethical debate further, additional systematic interdisciplinary and (worldwide) multicentre *long-term* data regarding the themes outlined in this thesis are needed, as it provides evidence-based data as a foundation for optimization of the care given. Furthermore, these research data are essential in order to bring some empirical answers into the debate regarding early medical treatment.

CLINICAL IMPLICATIONS

Although PS is not a risk-free medication and additional (worldwide) multicentre long-term quantitative and qualitative data are called for to better understand the possible adverse reactions and benefits of the treatment, treatment with PS still seems promising for transgender minors when given in a context of sufficient psychological support (e.g. Rafferty et al., 2018; Ramos et al., 2021; Turban & Ehrensaft, 2018). However, despite the promising current state of science regarding the medical and psychological aspects of care for transgender minors, many transgender minors, their parents, their clinicians, and others still express concerns and face ethical dilemmas regarding the use of early medical treatment for these minors. Apparently, promising results regarding the medical and psychological aspects of the treatment are not sufficient, and an ethical justification for the treatment seems to be required in addition. Therefore, data is needed from an ethical perspective to fill in this gap in this ongoing debate regarding the use of early medical treatment for transgender minors. The findings outlined in this thesis seem to justify the use of early medical treatment for transgender minors from this ethical point of view, as proposed in the two established international transgender guidelines (Coleman et al., 2022; Hembree et al., 2017). However, an appropriate individual treatment plan should be drawn

up for each individual minor who enters a gender identity clinic. Despite the justification of the use of early medical treatment, various concerns as described in this thesis still need to be weighed with each individual minor. The results of this thesis show that, among others, the minors' medical decision-making competence (MDC), the possible physical and/or psychological harmful effects of early medical interventions and of refraining from interventions, the consequences for fertility, the co-occurring psychosocial challenges, physiological puberty in developing a consistent gender identity, and the social context play an important role regarding early medical treatment and therefore should be taken into account when determining the most appropriate care for the minor in question.

Additionally, dissemination of knowledge and support concerning the assessment of MDC and encountered ethical dilemmas is desirable in order for clinicians to adequately support minors and their parents in the decision-making process regarding early medical treatment. A good step to do so has been taken by some Dutch researchers; they have, largely based on the findings gained in several of the studies included in this thesis, developed an ethics support tool, the so called 'Competence Consultant' (De Snoo-Trimp et al., 2022a). This tool provides clinicians with information and direction on how to deal with minors' MDC. The tool provides clinical guidance on assessing minors' MDC, for example regarding what aspects the minors should understand about the treatment before they are considered competent (De Snoo-Trimp et al., 2022a). It would be very helpful if such an ethics support tool could be made available to clinicians in other countries as well. However, despite the grip these developments offer, ethical challenges and complex cases will be indistinguishably linked to care for transgender minors (Vrouenraets et al., 2021). The use of moral case deliberation (MCD), a relatively well-established form of clinical ethics support, shows to help clinicians to more effectively deal with these ethical dilemmas and complex cases (Dauwerse et al., 2014; Molewijk et al., 2008a; Vrouenraets et al., 2020).

This thesis shows that care for transgender children and adolescents inherently involves ethical dilemmas, even if more clinical research data will be provided to underpin the evidence-base. Evidence alone will likely not be able to provide answers to all raised uncertainties concerning adolescent gender-affirming medical care. Ethical dilemmas will therefore probably remain part of this sensitive field of care. This thesis illuminates some of these ethical dilemmas and proposes ways of dealing with them in clinical practice.

11

Summary

Chapter 1

In the last decades, in various parts of the world, the number of minors seeking care regarding their gender incongruent experiences has increased tremendously throughout the Western world, and transgender minors have increasingly become a subject of discussion (e.g. Aitken et al., 2015; Arnoldussen et al. 2020; Arnoldussen et al., 2022b; Chen et al., 2016; Handler et al., 2019; Kaltiala et al., 2020; Pang et al., 2020; Wood et al., 2013; Wiepjes et al., 2018). Additionally, over the years, the term used to address this condition changed, there has been an increase of media attention regarding transgender children and adolescents worldwide, and case law also plays an increasing role in the care and rights of transgender individuals nowadays (e.g. Dyer, 2020a; Pang et al., 2020; Stolberg, 2017; GLAD LGBTQ Legal Advocates & Defenders, 2017; Walch et al., 2021). Herewith, the question of how to best organize care for these children and adolescents has become very prominent. However, determining what constitutes the best care for these transgender minors brings ethical issues and dilemmas along.

The recommendations regarding the (medical) treatment for these children and adolescents have been in development as well. Over the last few decades, the possibility of treatment with puberty suppression (PS) has generated a relatively new, but controversial dimension to the clinical management of transgender adolescents. Even though the use of PS in the care of these minors was adopted by a rapidly increasing number of gender identity clinics, and two established international transgender guidelines included this treatment option, many clinicians working with transgender minors remain critical (Coleman et al., 2022; Hembree et al., 2017; Rew et al., 2021; Vrouenraets et al., 2015).

Another issue in the care of transgender adolescents about which there is no consensus is the minors' MDC when starting PS. According to two established international transgender guidelines, an important prerequisite to start treatment with PS is that transgender adolescents are competent to give informed consent (Coleman et al., 2022; Hembree et al., 2017). However, there is increasing public discussion whether adolescents are actually competent to make a decision regarding PS treatment, especially because the treatment has far-reaching long-term consequences (e.g. Baron & Dierckxsens, 2021; D'Abbrera et al., 2020; Giordano et al., 2021; Levine, 2022; Pang et al., 2021; Siddique, 2021; Tampier, 2022). To date, little empirical research exists regarding minors' MDC to decide on starting PS, and little is known about the perceptions of the transgender adolescents, their parents, and clinicians on the minors' MDC to decide on starting PS. Research regarding these aspects is needed to underpin both the ethical debate and clinical practices.

Debate about care for transgender minors moves between extremes, and discussions are at times emotion-laden. People claiming the risks of the use of early medical treatment, and the ones who stress its benefits seem to have different underlying ideas about,

among others, minors' MDC, decision-making authority, and the role of concurrent psychological, social, and/or medical issues, often without openly stating them (e.g. Dubin et al., 2020; Baron & Dierckxsens, 2021; Lemma, 2018). What was missing in the discussions is an elucidation of the underlying ideas and theories. Additionally, insight into the considerations and ideas of transgender adolescents themselves, their parents, and experienced professionals remains limited.

The overall aims of this study were therefore twofold. First, we aimed to gain more insight in the core of the ethical dilemmas that play a role in the care of transgender minors, and the underlying intuitions and considerations of stakeholders in the field regarding early medical treatment. The second, subsequent aim was to provide empirical data regarding these ethical dilemmas that play a role in the care of transgender minors. Herewith to make sure that treatment for transgender minors is not only clinically, but also ethically appropriate. Second, to find common ground between various clinicians around the world regarding early medical treatment. Third, to provide the stakeholders in the field direction to deal with these ethical dilemmas in clinical practice. And fourth, to allow clinicians to safely exercise the clinical judgment to undertake the course of action which is in the child's best interests, based on objective, scientific data and not (largely) on subjective opinions.

Chapter 2

Chapter 2 explicates the considerations, underlying ideas, assumptions, and theories of those who criticize and those who support the use of early medical treatment regarding treatment with PS for transgender minors. Our goal was to get a clearer picture of the similarities and differences between their viewpoints in order to move forward the ethical debate. In total, 36 professionals, working in 17 different treatment teams in 10 different countries from around Europe and North-America, participated in this interview and open-ended questionnaire study.

The results show that the considerations of people claiming the risks of the use of early medical treatment, and people supporting it touch on fundamental ethical concepts in paediatrics; concepts such as best interest, autonomy, and the role of the social context. From the literature, interviews, and questionnaires, seven themes emerged which gave rise to different, and sometimes even opposing, views on early medical treatment for transgender adolescents. The first theme is the availability or nonavailability of an explanatory model for gender dysphoria (GD). Even though most informants agree that a combination of factors, such as genetic, hormonal, neurodevelopmental, and psychosocial factors play a role, opinions differ as to whether, and if so, which factor(s) prevail in the aetiology (De Vries & Cohen-Kettenis, 2012; Meyer-Bahlburg, 2010). The second theme regards the nature of GD; most informants find it difficult to articulate their thoughts

about this aspect. Many see GD as neither a medical disease nor a social construct, but as a normal, but less frequent variation of gender expression. However, some state that the need for medical treatment in itself, to relieve the suffering, implies that GD is not merely a normal variation, and that that is what defines GD as a disorder. The role of physiological puberty in developing a consistent gender identity is the third theme that emerged. Most informants agreed on the fact that treatment with PS indeed may change the way adolescents think about themselves. However, most of them did not think that PS inhibits the spontaneous formation of a gender identity that is congruent with the assigned gender after many years of having an incongruent gender identity. Additionally, several endocrinologists mentioned that PS has been used for many years in precocious puberty, and no cases of GD have been described in that context, as far as they know. Also, most emphasized that they deliberately start PS only when the adolescents have reached Tanner stage 2 or 3, in order to give them at least some kind of 'feeling' with puberty before starting to suppress puberty. The fourth theme is the role of comorbidity. The prevalence of co-occurring psychiatric problems in transgender minors is high (de Vries et al., 2011; Meyenburg, 2014; Wallien, Swaab, & Cohen-Kettenis, 2007). The precise mechanisms that link GD and coexisting psychopathology are unknown. Most informants state that it differs between individuals, and depends on the comorbid problem whether GD and the co-occurring problem(s) are merely coexisting or interrelated. Some professionals stress the importance of addressing treatment of severe coexisting psychopathology before addressing GD-related medical interventions, while others state that it depends on the individual and specific comorbid problem. The fifth theme regards the possible physical or psychological harmful effects of early medical interventions for transgender minors, and of refraining from interventions. Although (the sparse) research until now mostly shows no negative, and even positive results regarding the consequences of PS, advocates of the treatment remain cautious and people criticizing the treatment sceptical because of the fact that (long-term) risks and benefits of available treatments have not been fully established. Possible harmful effects of refraining from interventions are mentioned too. The sixth theme regards medical decision-making competence (MDC) and the decision-making authority, which is an important point of disagreement in the discussion regarding early medical treatment for transgender minors. Most informants agreed on the thought that adolescents' competence should be determined on an individual case by case basis. They did not agree on how to actually do this, for example regarding who should have final authority to make decisions regarding early medical treatment; the adolescents themselves, and/or the parent(s) and/or treatment team were mentioned. The last theme regards the role of the social context in the way gender dysphoria is perceived. Some think that the way gender incongruent behaviour of minors is perceived in a specific culture, largely influences whether it is pathologized or not. Furthermore, some speculate that the increasing attention in the media might lead to medicalization of gender incongruent behaviour.

The discussion regarding the use of PS is in full swing. Some consider the established international transgender guidelines too liberal, while others find them too conservative. Additionally, more and more treatment teams embrace the Dutch protocol, but still retain a feeling of unease. Discussion of the diverse themes needs to continue based on research data as an addition to merely opinions. Otherwise ideas, assumptions and theories on GD treatment will diverge even more, which might lead to (even more) inconsistencies between approaches recommended by clinicians across different sites/countries. Moreover, participation in the study encouraged several clinicians in thinking more explicitly about the various themes and to discuss the ethical issues in their teams.

Chapter 3

In chapter 2 we described the considerations regarding early medical treatment of 36 professionals from 17 treatment teams worldwide. Nevertheless, little is known about the way transgender adolescents themselves think about early medical treatment. The third chapter therefore describes a study on the considerations and opinions of transgender adolescents concerning the concepts of 'sex' and 'gender', and the use of PS in GD. Furthermore, we compared the considerations on the use of PS of the adolescents with those of professionals, using the data collected in chapter 2.

Informants were 13 adolescents, between the ages of 13 and 18, diagnosed with GD recruited from the gender identity clinic in Leiden, the Netherlands. All adolescents, except for one, were treated with PS. The adolescent who was not treated with PS immediately started treatment with gender-affirming hormones (GAH) because she was above the age of 18 when treatment was indicated, which is in line with the Dutch protocol. The mean age at which the participating adolescents started PS was 15 years and 10 months. Individual semi-structured interviews, containing general topics and no close-ended questions, were conducted (30-40 minutes). After no new content was found in the interviews, subject enrolment was stopped, this is called data saturation (Guest et al., 2006).

Three themes emerged from the interviews; the first theme regards the difficulty of determining what is an appropriate lower age limit for starting PS. Most adolescents found it difficult to define an appropriate age limit and saw it as a dilemma. The adolescents seemed to be more cautious than some professionals, for example regarding the minors' MDC in this context; most adolescents had doubts about whether minors are capable of making decisions regarding medical treatment at the age of 12 or younger, while some treatment teams are exploring the possibility of lowering the current age limit for PS. The second theme regards the lack of data on the long-term effects of PS; this lack is not a reason to not start PS in most adolescents. However, this was a big issue for the professionals. The third theme, the role of the social context, consisted of two subthemes: the first one was the increased media-attention, on television and on the internet, the

second one was an imposed stereotype. Both adolescents and professionals had diverging viewpoints regarding the increasing media-attention; some thought positively about this, while others raised doubts.

Comparing the interviews of the adolescents with those of the professionals reveals that the adolescents and professionals do not agree about all topics. It is striking that, compared to the professionals, adolescents were often more cautious in their treatment views. It is important to give voice to the transgender adolescents themselves in order to prevent professionals acting upon (possibly incorrect) assumptions about the adolescents' views instead of the adolescents' actual considerations and opinions. Gathering more qualitative research data from transgender adolescents in other sites/countries is encouraged.

Chapter 4

Chapter 4 reports on the examination of transgender adolescents' medical decision-making competence (MDC) to give informed consent for starting treatment with PS. Transgender adolescents' competence to give informed consent is an important prerequisite for PS (Coleman et al., 2012; Hembree et al., 2017). However, in society, there is doubt whether they are capable of this, which in some countries has even led to limited access to this intervention. There is no empirical evidence on transgender adolescents' MDC to decide on PS. Therefore we assessed in a structured, replicable way, the MDC of Dutch transgender adolescents who were assessed eligible to start PS. The participants were 74 adolescents between the ages of 10 and 18. All attended the gender identity clinic in Amsterdam or Leiden, the Netherlands. All participants underwent the usual diagnostic trajectory, including a psycho-diagnostic assessment and several monthly sessions with a mental health provider over a longer period of time (usually about six months), before being assessed eligible for PS. The MacArthur Competence Assessment Tool for Treatment (MacCAT-T) was used. This is a quantitative semi-structured interview used to assess the four criteria a person needs to fulfil in order to reach MDC, being: understanding the information relevant to one's condition and the proposed treatment, appreciation of the nature of one's circumstances, reasoning about benefits and potential risks of the options, and being able to express a choice (Appelbaum & Grisso, 1988). The study aimed not only to assess the adolescents' MDC, but also to investigate potential associated variables (e.g. full scale IQ, sex, age, behavioural and emotional difficulties). The parent-reported Child Behaviour Checklist (CBCL) was used to assess behavioural and emotional difficulties (Achenbach & Rescorla, 2001; Verhulst & van der Ende, 2013).

The diagnostic trajectory concludes with a session for signing an informed consent (IC) statement by the adolescent and parents. This standard IC session was videotaped and used to establish the reference standard for MDC. After the IC session, the MacCAT-T interview was administered, which was also videotaped, to provide the MacCAT-T based

judgements of MDC. A panel of 12 experts - including child psychiatrists and psychologists, paediatric endocrinologists, and master thesis medical students - was trained in judging MDC. The adolescent's MDC in each IC video was judged by two expert and the clinician involved in the adolescent's diagnostic trajectory. The MDC in each MacCAT-T video was judged by three experts.

We found that 93.2% and 89.2% of the transgender adolescents who were about to start PS and were participating in this study, were assessed competent to give IC on the basis of the standard clinical assessment and when using the MacCAT-T interview, respectively. The intermethod agreement was 87.8%. The interrater agreements of the reference standard and MacCAT-T-based judgements were 89.2%, and 86.5%, respectively. Furthermore, full scale IQ-score and sex were both significantly related to MacCAT-T total score; birth-assigned girls showed a higher total MacCAT-T score, as did adolescents with a higher full scale IQ-score. Age at the IC session, level of emotional and behavioural challenges, and the duration of the diagnostic trajectory were not significant related to the MacCAT-T total score.

It is reassuring that the majority of the transgender adolescents participating in this study seem to have thoroughly thought about PS, understand what PS involves, and are deemed competent to decide. However, this might not be similar for all other contexts, particularly because our study cohort had extensive and thorough diagnostic evaluation before the MDC assessment, as opposed to adolescents without this support. Additionally, the study results indicate feasibility and validity of the MacCAT-T in clinical practice. However, these results do not answer questions on how to respect the developing autonomy of incompetent adolescents ethically. We conclude that as long as there are only limited data on transgender adolescents' MDC regarding starting PS, an individualized approach is highly important for this group.

Chapter 5

Chapter 5 reports on the perceptions on medical decision-making competence (MDC) to start PS of transgender adolescents who proceeded with gender-affirming medical treatment (GAMT) after PS, adolescents who discontinued treatment with PS, their parents, and clinicians. According to international transgender guidelines, one of the prerequisites for PS is that adolescents have MDC (Coleman et al., 2012; Hembree et al., 2017). As described earlier, chapter 4 describes an assessment of 74 transgender adolescents' MDC regarding starting PS, showing that the vast majority (about 89%) of these adolescents is competent to consent to this treatment. Nevertheless, little is known about the considerations and ideas of transgender adolescents themselves, their parents, and clinicians regarding adolescents' MDC to start PS.

In order to obtain insight into these considerations and ideas, semi-structured interviews were conducted with eight transgender adolescents (10-15 years old) who proceeded with GAMT after PS ('continuers'), six adolescents (10-17 years old) who discontinued treatment with PS ('discontinuers'), and 12 of their parents. In addition, two focus groups with in total 10 clinicians from the gender identity clinics in Amsterdam and Leiden, the Netherlands, were held.

The four criteria one needs to fulfil in order to have MDC - understanding, appreciating, reasoning, communicating a choice - were all, to a greater or lesser extent, mentioned by most participants, just as the relatedness to a specific decision and context (Appelbaum & Grisso, 1988). Most adolescents, parents, and clinicians find understanding and appreciating PS and its impact important for MDC. Most informants, including most adolescents themselves, stated that they thought that they themselves/ the adolescents did not fully understand and appreciate the treatment and its consequences. However, most of them estimated that they/the adolescents were nonetheless able to decide about the treatment. Most adolescents, parents, and clinicians stated that not being able to understand and appreciate the impact of certain consequences of PS is inherent to the adolescents' age and/or developmental stage. Parents' support was considered essential in the decision-making process. The fact that PS has effects that are largely medical reversible was a reassuring idea for some adolescents and parents, while other adolescents did not take this aspect into account when deciding about PS. Certain consequences of PS and uncertainty about long-term effects (e.g. potential loss of fertility when proceeding to GAH and gonadectomy) causes doubts for some. Most clinicians encounter difficulties defining MDC. Some mentioned that they assess MDC differently depending on the adolescents' developmental age. Some adolescents, parents, and clinicians mentioned the role of age, intelligence, and mental health problems as possible variables associated with MDC. Some clinicians pondered whether too much importance is placed on the adolescents' MDC. Although some stakeholders have in mind that there is an association between having MDC and not having regrets about a decision later in life, this is not endorsed by literature (Pang et al., 2021).

We concluded that clinicians find it difficult to assess adolescents' MDC regarding starting PS, and to put into practice in a uniform way. Dissemination of knowledge and support concerning assessment of MDC and encountered ethical dilemmas about transgender adolescents' MDC is desirable in order for clinicians to adequately support adolescents and parents in the decision-making process.

Chapter 6

Treatment with PS aims to give the transgender minors the opportunity to explore their gender identity, and time to consider if they wish to pursue GAMT while development of

unwanted secondary sex characteristics is suppressed in order to reduce distress. Even though the effects of PS on pubertal development are reversible, the treatment may bring short-term adverse effects along. Additionally, few clinical research data are available on long-term adverse effects. Furthermore, opinions about the use of PS vary. To gain more insight into the use of PS in transgender adolescents, chapter 6 documents adolescents' trajectories after the initiation of treatment with PS. The chapter reports on discontinuation of treatment with PS, prolonged use of PS, and initiation of GAH in order to investigate the duration of treatment with PS. Additionally, it explores reasons for extended use and discontinuation of PS in a retrospective way.

The study population consisted of 143 (67%) of the 214 adolescents registered at the Curium-Leiden University Medical Centre gender identity clinic in Leiden, the Netherlands, who were eligible for treatment with PS by virtue of their age/pubertal status, and all started treatment with PS. The adolescents were between the ages of 11 and 18, and 38 of them were transgirls, and 105 were transboys. Of these adolescents who started treatment with PS, treatment status was reviewed. If they had used PS monotherapy for more than three months longer than minimally required before the start of GAH according to the local protocol, the reason for this was noted. Adolescents who had started treatment with PS and had stopped this treatment were included in a detailed review. Baseline characteristics such as age and gender, and data on the start, duration, and discontinuation of treatment were recorded from the medical files, as well as reasons given for the discontinuation of the treatment with PS and the adolescents' and parents' views on the treatment.

According to the local protocol, before the start of treatment with PS, all adolescents had a diagnostic evaluation by a paediatric endocrinologist and mental health professional to confirm the diagnosis of gender dysphoria according to the DSM-5 criteria, to assess the presence of any medical, psychiatric, or psychosocial problems that might interfere with treatment, to assess if the adolescent was able to give informed consent for the treatment, and to confirm that puberty had started, as recommended by current established international transgender guidelines.

We found that after a median duration of 0.8 years (0.3-3.8) on PS, 125 (87%) adolescents started GAH. Nine (6%) adolescents discontinued treatment with PS, five of whom no longer wished GAMT. Several reasons were given for the discontinuation of PS, being among others, the experience of falling in love, the feeling of being either male or female, experiencing side effects of the treatment, and experiencing of concurrent psychosocial problems interfering with the exploration of gender identity. Thirteen adolescents had used PS for longer than required by protocol for reasons other than logistics and regularly met with a mental health professional during this time. This supports the idea that the time on PS is used as an extended diagnostic phase where adolescents can further explore

their gender identity and treatment wishes, and work on issues that might interfere with successful treatment.

In conclusion, the vast majority of adolescents who started treatment with PS proceeded to GAH, possibly due to eligibility criteria that select those highly likely to pursue further GAMT. A small number of adolescents discontinued treatment with PS because they no longer wished GAMT. This indicates that not all adolescents and parents assume that the outcome of identification as transgender is the only possible outcome and shows that gender identity can still fluctuate when using PS, at least in some adolescents. However, gender dysphoria subsided in a small number of adolescents and it is uncertain if this would have been different without treatment with PS. Due to the observational character of the study, it is not possible to say if treatment with PS itself influenced the outcome. Some adolescents used PS for a prolonged period before starting GAH while regularly meeting with a mental health professional which is consistent with the use of treatment with PS as an extended diagnostic phase. The great majority who had started treatment with PS continued with GAH. It is important to take this into account when counselling adolescents who consider this treatment and their parents.

Chapter 7

Chapter 7 describes the perceptions of transgender adolescents, their parents, and clinicians on the function of treatment with PS for transgender adolescents. It is not known whether the functions of PS as described in established international transgender guidelines correspond to the perceived functions of PS according to the aforementioned stakeholders (Coleman et al., 2012; Hembree et al., 2017). For this study the same sample and method as described in chapter 5 were used.

The results show that the continuers, discontinuers, their parents, and clinicians do not all have the same views on the functions of PS. Primarily, all informants considered inhibition of (further) development of secondary sex characteristics an important, and for some the most important, function of PS. Some discontinuers did experience PS as an expanded diagnostic phase, providing them 'extra' time before deciding on GAMT, while most continuers saw PS as the first step of GAMT. Nevertheless, some continuers and some of their parents were glad that the effects of PS were reversible even if they did not expect to change their minds. One continuer and several parents used the time (their child was) on PS, to get used to (their child) living in the affirmed gender role. Some clinicians considered it important that adolescents mature a little further during the years they receive PS, and that, while they experience less distress due to the undesired development of their bodies, they may be better able to decide on whether or not to proceed with GAMT and carefully consider the consequences of their decision. One of the discontinuers mentioned this

function as well. Some clinicians mentioned that the extra time provided them time for additional assessment.

Although international transgender guidelines emphasize providing time for exploration of gender identity as an important reason for PS, many adolescents nowadays seem to have clear ideas about their gender identity and treatment wishes, and experience PS as the first step of GAMT (Coleman et al., 2012; Hembree et al., 2017). For some discontinuers however, PS offered a valued period of exploration. The extra time served a function for some parents and clinicians in some cases as well. Guidelines could be modified to provide more customized care, taking adolescents', parents', and clinicians' ideas about the functions of PS into account.

Chapter 8

Whereas the effects of PS are reversible, long-term use of gender-affirming sex steroids may affect fertility, and if gonadectomy is performed, the transgender person will definitely be infertile. Infertility may have a major impact on the lives of transgender minors, and previous studies suggest that fertility preservation can influence quality of life in transgender adolescents. Nowadays, the World Professional Association for Transgender Health (WPATH) and Endocrine Society recommend counselling regarding fertility preservation options before initiating treatment with PS. However, two recent studies from the United States indicate that transgender minors rarely use fertility preservation. In order to get insight into the use of fertility preservation among Dutch transgirls, chapter 8 describes how many adolescents made use of fertility preservation in a Dutch cohort of transgirls who started treatment with PS. In addition, we assessed if information about the risk of infertility had been given, if discussion of the option of fertility preservation was documented in the medical file, and what the given reason for declining fertility preservation was if the adolescent had not made use of fertility preservation. Furthermore, we explored what factors were associated with the use of fertility preservation.

The study was a retrospective review of medical records of 35 transgirls who started treatment with PS between 2011 and 2017 at the Curium-Leiden University Medical Centre gender identity clinic in Leiden, the Netherlands. Extracted data from the medical files were age, intelligence quotient (IQ), Tanner stage, testicular volume, ethnicity, sexual orientation, psychiatric comorbidity, family situation, and information about the desire to have children.

All adolescents had been informed on the risk of infertility, and 32 (91%) of them were counselled about the option of fertility preservation. Thirteen (41%) of the counselled transgirls were referred for sperm cryopreservation, and twelve (38%) of them had actually

been to the fertility clinic to try to cryopreserve sperm. One transgirl who had been referred had not been to the fertility clinic and had not started treatment with PS yet at the time of the analysis because of psychosocial issues. Nine (75%) of the transgirls who had been to the fertility clinic to try to cryopreserve sperm, were able to cryopreserve sperm suitable for intrauterine insemination ((IUI) or intracytoplasmic sperm injection (ICSI).

Given reasons for not wanting to be referred for fertility preservation were (some of the transgirls gave more than one reason) not wanting to have children (17%, $n = 4$), wanting to adopt (13%, $n = 3$), feeling uncomfortable with masturbation or having an aversion of their penis (17%, $n = 4$), and feeling uncomfortable with the idea of being the biological father of the child (4%, $n = 1$). No specific reason for declining fertility preservation was known in eight (33%) adolescents, and eight (33%) of the adolescents were not referred for fertility preservation because they were in early puberty and were not able to produce a semen sample through masturbation.

The mean age at the start of treatment with PS in the group of transgirls who attempted fertility preservation was significantly higher than in the group that did not attempt fertility preservation. Tanner stage, testicular volume, and mean IQ in the group who attempted fertility preservation was not significantly different from that in the group who did not. Neither were family situation and psychiatric comorbidity (depression, anxiety disorder, posttraumatic stress disorder, or autism spectrum disorder). Furthermore, fewer Caucasian transgirls (20%) attempted fertility preservation than transgirls (70%) with other ethnicities including Asian, African, and South American.

In conclusion, one third of the transgirls attempted fertility preservation, and most were able to store sperm suitable for future intrauterine insemination (IUI) or intracytoplasmic sperm injection (ICSI). This stresses the need to discuss this topic before the start of treatment with PS. Making different sperm extraction options available such as testicular sperm extraction or electroejaculation stimulation may make fertility preservation more accessible for transgirls for whom masturbation is a barrier. Fertility preservation is currently not available for early pubertal adolescents, but research in this area might open up fertility preservation options for this group too. With future options on the way, an ethical and legal debate is essential, taking into account the right to equality and non-discrimination and the right to procreate of transgender people.

Chapter 9

Chapter 9 describes the evaluation of the usefulness of moral case deliberation (MCD) in dealing with moral challenges and dilemmas in the care for transgender minors. MCD is a facilitator-led, collective moral inquiry based on a real case (Dauwerse et al., 2014; Molewijk et al., 2008a; Stolper et al., 2016). It is a relatively well-established form of clinical

ethics support. MCD sessions were introduced in two Dutch treatment teams of gender identity clinics where specialists in child and adolescents psychiatry and psychology, and (paediatric) endocrinology worked in multidisciplinary teams. Between October 2013 and January 2015 the two teams participated in a total of 17 MCD sessions. The treatment team members evaluated the use of MCD. Data was collected using six individual interviews, two focus groups with in total 15 clinicians, a cross-sectional survey using an MCD evaluation questionnaire at two moments (T0, $n = 34$; T1, $n = 22$), and audiotapes of six MCD sessions.

The clinicians rated MCD as highly valuable in situations when confronted with moral challenges. They reported that MCD helped them to more effectively deal with moral challenges, and that it contributed to improved mutual understanding and open communication among team members. Additionally, according to them, it made them pay closer attention to their own arguments and contextual factors, rather than blindly following the clinical protocol. Furthermore, it strengthened their ability to make decisions and take action when managing ethically difficult circumstances. However, the clinicians also made critical remarks about MCD: some felt that the amount of time spent discussing an individual case was excessive, that MCD should lead to more practical and concrete results, and that MCD and the insights gained during the MCD sessions needed better integration and follow-up in the regular work process.

Especially in the care for transgender minors, treatment decisions are often surrounded by complex moral controversies and uncertainties. During MCD sessions, the professionals' reasoning and knowledge are included, yet MCD makes (possible conflicts of) underlying norms and values explicit and gives suggestions how to handle the uncertainty or disagreement within a team. As such, MCD can be seen as an additional tool that can be used in complex cases. More research focusing on the actual contribution of MCD to the improvement of care quality (including its determining factors), the involvement of transgender people in MCD sessions, and on how to integrate clinical ethics support more into daily work processes, is needed.

Chapter 10

Ethical challenges and dilemmas are inextricably linked to transgender care, especially regarding the care of children and adolescents, and the possible life-long consequences of providing them with or refraining from early medical treatment. This is because it is a relatively new field, in which developments are rapid, there is still relatively little empirical data available on long-term outcomes, and it is a subject of a polarized debate. The challenges and dilemmas regarding early medical treatment for transgender minors, which were already expressed by clinicians about a decade ago, as described in our first article from 2015, only seem to have been enlarged and sharpened since then (Vrouenraets et al., 2015). Initially, these dilemmas seemed to be an issue only for those directly involved

in this care. However, today, a much broader group of people is expressing their opinions and thoughts regarding this subject. Additionally, the role of the media and case law are increasing. With this, the debate seems to have become only harsher. Additionally, the controversy seems to have become greater, and people claiming the risks of early medical treatment, and the ones claiming its benefits appear to be driven apart even further (e.g. Lament, 2014; Osserman & Wallerstein, 2022). Currently there hardly seems to be much little room for a 'nuanced middle-ground' anymore (e.g. Bazelon, 2022).

More insight in the core of the ethical dilemmas that play a role in the care of transgender minors, and more empirical data that could give direction in some of the ethical dilemmas are needed in order to give clinicians direction to deal with these issues, and to inform and guide minors referred to the gender identity clinic. Therefore, the first overall aim of this research was to gain more insight in the core of the ethical dilemmas that play a role in the care of transgender minors, and the underlying intuitions and considerations of stakeholders in the field regarding early medical treatment. The stakeholders are transgender adolescents who proceeded with GAMT after PS, adolescents who were diagnosed with gender dysphoria but who did not proceed with GAMT after starting treatment with PS, their parents, clinicians working in gender treatment teams, and people who are critical about the use of early medical treatment for transgender minors. The second, subsequent aim is to provide empirical data regarding these ethical dilemmas.

The starting point of this thesis was a broad interview study we conducted which gave insight into the ethical dilemmas that play a role in the use of early medical treatment for transgender minors according to the stakeholders (Vrouenraets et al., 2015; Vrouenraets et al., 2016). In this context, we interviewed clinicians working with transgender minors, and people criticizing the use of early medical treatment for transgender minors from around Europe and North-America, transgender minors themselves, and their parents. Multiple themes, described in chapter 2 and 3, emerged which gave rise to different, and sometimes even opposing, views on the treatment for transgender minors. In subsequent chapters, we examined several of these themes to gain deeper understanding of the controversies and possible solutions. In the general discussion we reflect on the meaning of our study outcomes to the broader context of the political and public discussions. We will do this by means of five themes that consistently emerged in these discussions: the minors' medical decision-making competence (MDC), considerations regarding starting or refraining from PS, co-occurring psychosocial challenges, the social context, and clinical ethics support. One by one, these themes are discussed. For each theme, it is described how the considerations, ideas and newly obtained scientific data, when applicable, have changed and developed over the years.

The field of the care of transgender children and adolescents has been, and still is, in motion, and the associated ethical challenges and dilemmas, require the clinician to take an adjusted role with regard to (medical) treatment for transgender minors. They can be seen as balance artists; initially they had to balance between the treatment wishes, demands, and voices from predominantly the transgender minors, their parents, and their own (M. de Vries, 2020). Nowadays, the voices of other influences, such as professional associations, the media, and case law seem to have become louder. Therefore, clinicians need to find an adequate balance in the force fields between these different 'layers', of which some are relatively 'new', and of which all are continuously in motion concerning their perspective on the ethical dilemmas that play an important role in early medical treatment for transgender minors, as outlined in this thesis, into account (M. de Vries, 2020).

Although PS is not a risk-free medication and additional (worldwide) multicentre long-term quantitative and qualitative data are called for to better understand the possible adverse reactions and benefits of the treatment, treatment with PS still seems promising for transgender minors when given in a context of sufficient psychological support (e.g. Rafferty et al., 2018; Ramos et al., 2021; Turban & Ehrensaft, 2018). However, despite the promising current state of science regarding the medical and psychological aspects of care for transgender minors, an ethical justification for the treatment seems to be required in addition. Therefore, data is needed from an ethical perspective to fill in this gap in this ongoing debate regarding the use of early medical treatment for transgender minors. The findings outlined in this thesis seem to justify the use of early medical treatment for transgender minors from this ethical point of view, as proposed in the two established international transgender guidelines (Coleman et al., 2022; Hembree et al., 2017). Despite this justification, various concerns as described in this thesis still need to be weighed with each individual minor. The results of this thesis show that, among others, the minors' MDC, the possible physical and/or psychological harmful effects of early medical interventions and of refraining from interventions, the consequences for fertility, the co-occurring psychosocial challenges, physiological puberty in developing a consistent gender identity, and the social context play an important role regarding early medical treatment and therefore should be taken into account when determining the most appropriate care for the minor in question.

Additionally, dissemination of knowledge and support concerning the assessment of MDC and encountered ethical dilemmas is desirable in order for clinicians to adequately support minors and their parents in the decision-making process regarding early medical treatment. A good step to do so has been taken by some Dutch researchers; they have,

largely based on the findings gained in several of the studies included in this thesis, developed an ethics support tool, the so called 'Competence Consultant' (De Snoo-Trimp et al., 2022a). This tool provides clinicians with information and direction on how to deal with minors' MDC (De Snoo-Trimp et al., 2022a). It would be very helpful if such an ethics support tool could be made available to clinicians in other countries as well. However, despite the grip these developments offer, ethical challenges and complex cases will be indistinguishably linked to care for transgender minors (Vrouenraets et al., 2021). The use of moral case deliberation (MCD), a relatively well-established form of clinical ethics support, shows to help clinicians to more effectively deal with these ethical challenges and complex cases (Dauwerse et al., 2014; Molewijk et al., 2008a; Vrouenraets et al., 2020).

This thesis shows that care for transgender children and adolescents inherently involves ethical dilemmas, even if more clinical research data will be provided to underpin the evidence-base. Evidence alone will likely not be able to provide answers to all raised uncertainties concerning adolescent gender-affirming medical care. Ethical dilemmas will therefore probably remain part of this sensitive field of care. This thesis illuminates some of these ethical dilemmas and proposes ways of dealing with them in clinical practice.

A

Addendum

APPENDIX A

Data analysis

All interviews were audio-taped and transcribed verbatim. Before each interview informed consent for participation and tape recording was obtained. The interviews took between 50 and 90 minutes to administer. Data analysis was based on the constant comparative method (Corbin & Strauss, 2014; Malterud, 2001). We used an iterative process wherein we continually went back to the field and interviewed new participants to collect more data. The following processes of data gathering and analyses were used: (1) interviews; (2) questionnaires; (3) transcription of the interview data; (4) open coding, which involved identifying relevant concepts in the text; (5) constant comparison of open codes, looking for conceptual similarities and differences; (6) identification of emerging themes and a theoretical framework; (7) continued sampling and interviewing as theoretical categories emerged and novel questions arose; and (8) continued coding and comparison of codes until nothing new was added to the theoretical categories. Data collection continued as long as new information came up. After no new content was found in the interviews and questionnaires, subject enrolment was stopped. This process, called thematic saturation, is a well-described qualitative method to avoid unnecessarily large and repetitive data sets (Guest et al., 2006).

APPENDIX B

Initial interview questions

1. For you, was the treatment to suppress puberty time to consider and decide on irreversible treatment or was the treatment important to you for other reasons?
2. How thoughtful was the decision to start puberty suppression at the time?
3. Have there been any consequences, or has there been any impact of the treatment with puberty suppression that you had not foreseen, that you were not aware of, that were better or worse than you had expected?
4. To what extent did you make your decision to start puberty suppression in a different way from your decision to start with treatment with gender-affirming hormones?
5. Is there anything that has not been discussed in this interview but that you think is relevant in relation to the topic, anything that you would like to add?

APPENDIX C

List of steps in the dilemma method *

1. Moral case is presented
2. [Formulation of a general moral question]
3. Short formulation of the case presenter's dilemma: Should I do A or B?
4. Opportunity for clarification & questions
5. Scheme with 'perspectives', 'values' and 'norms'
6. Brainstorm on possible alternatives
7. Round of individual answers to the dilemma question
8. Discuss possible group consensus, disagreement or decision ('weigh' values & norms)
9. Make practical appointments and plan date to evaluate these appointments
10. Evaluation of MCD content and process, also considering the facilitator's role

* Molewijk et al., 2008a; Molewijk & Ahlzen, 2011; Stolper et al., 2016

APPENDIX D

Impression of the Euro-MCD questionnaire *

Instructions: Below is a list of possible outcomes from a moral case deliberation (MCD) session. Please indicate how important you consider each outcome in terms of how much it would strengthen you and your co-workers' ability to manage ethically difficult situations. The list includes outcomes that may occur during MCD sessions and/or afterward in everyday clinical practice.

1. Develops my skills in analysing ethically difficult situations
2. More open communication among co-workers
3. Co-workers reach a consensus on how to manage ethically difficult situations
4. Enables me to better manage the stress caused by ethically difficult situations
5. Contributes to the development of practice/policies in the workplace
6. Gives me more courage to express my ethical views
7. I feel more secure to express doubts or uncertainty regarding ethically difficult situations
8. Better mutual understanding of reasoning and behaviour
9. I see ethically difficult situations from different perspectives
10. My co-workers and I become more aware of recurring, ethically difficult situations
11. Increases my awareness of the complexity of ethically difficult situations
12. Enhances my understanding of ethical theories (ethical principles, values and norms)
13. Enables me and my co-workers to decide on concrete steps to manage ethically difficult situations
14. Greater opportunity for everyone to have their say
15. Creates more opportunity to share difficult emotions and thoughts with co-workers
16. I can see more courses of action to manage ethically difficult situations
17. I listen more seriously to others' opinions
18. Increases awareness of my own emotions regarding ethically difficult situations
19. Boosts my self-confidence when managing ethically difficult situations
20. Develops my ability to identify the core ethical question in difficult situations
21. My co-workers and I examine existing practice/policies in the workplace/organization more critically
22. My co-workers and I manage disagreements more constructively
23. I have a better understanding of my own responsibility in ethically difficult situations
24. Enhances mutual respect among co-workers
25. I become more aware of my preconceived notions
26. I understand better what it means to be a good professional

* Svantesson et al., 2014

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LIST OF ABBREVIATIONS

CBCL	Child Behaviour Checklist
DSM	Diagnostic and Statistical Manual of Mental Disorders
FP	Fertility preservation
GAH	Gender-affirming hormones
GAMT	Gender-affirming medical treatment
GD	Gender dysphoria
GnRHa	Gonadotropin-releasing hormone analogues
IC	Informed consent
ICD	International Classification of Diseases
ICSI	Intracytoplasmic sperm injection
IQ	Intelligence quotient
IUI	Intrauterine insemination
MacCAT-T	MacArthur Competence Assessment Tool for Treatment
MCD	Moral case deliberation
MDC	Medical decision-making competence
MHP	Mental health professional
PS	Puberty suppression
SDM	Shared decision-making
WPATH	World Professional Association for Transgender Health

NEDERLANDSE SAMENVATTING

Hoofdstuk 1. Inleiding

Mensen met genderincongruente gevoelens ervaren een discrepantie tussen hun genderidentiteit en het geslacht dat hen bij de geboorte is toegewezen. Men spreekt van genderdysforie (GD) als er sprake is van genderincongruente gevoelens die langdurig aanwezig en diepgeworteld zijn, gepaard gaan met gevoelens van onbehagen, en er een sterke wens is om van het 'andere' gender (of een alternatief gender dat anders is dan het geslacht waarmee ze geboren zijn) te zijn (American Psychiatric Association, 2022). De term genderdysforie wordt gebruikt in de vijfde versie van het psychiatrisch handboek 'Diagnostic and Statistical Manual of Mental Disorders', kortweg DSM-5-TR (American Psychiatric Association, 2022). Genderincongruentie is de term die wordt gebruikt in het internationale ziekte-classificatiesysteem van de World Health Organization (WHO), de elfde revisie van het 'International Classification of Diseases', kortweg de ICD-11 (World Health Organization, 2022). In de afgelopen decennia is in verschillende delen van de wereld het aantal kinderen en jongeren dat zorg zoekt voor de genderincongruente gevoelens die zij ervaren enorm toegenomen en zijn transgender jongeren steeds vaker onderwerp van gesprek en discussie geworden (bv. Aitken et al., 2015; Arnoldussen et al. 2020; Arnoldussen et al., 2022b; Chen et al., 2016; Handler et al., 2019; Kaltiala et al., 2020; Pang et al., 2020; Wood et al., 2013; Wiepjes et al., 2018). Daarnaast is er wereldwijd een toename van media-aandacht voor transgender kinderen en jongeren, en speelt ook de rechtspraak een steeds grotere rol in de zorg en rechten van transgender personen (o.a. Dyer, 2020a; Pang et al., 2020; Stolberg, 2017; GLAD GLBTQ Legal Advocates & Defenders, 2017; Walch et al., 2021). Hiermee is de vraag hoe de zorg voor deze kinderen en jongeren het beste georganiseerd kan worden zeer prominent geworden.

Het bepalen van wat de beste zorg voor transgender jongeren is, brengt ethische vraagstukken en dilemma's met zich mee. In de afgelopen decennia heeft de mogelijkheid van behandeling met puberteitsremmers (PR) een relatief nieuwe, maar controversiële dimensie toegevoegd aan de klinische behandeling van transgender jongeren. Puberteitsremmers remmen de ontwikkeling van de secundaire geslachtskenmerken. Zo worden door deze behandeling bij transjongens - zij identificeren zich als jongen maar hebben bij de geboorte het geslacht meisje toegewezen gekregen - onder andere de borstgroei, het breder worden van de heupen en (de start van) de menstruatie geremd. Bij transmeisjes - zij identificeren zich als meisje maar hebben bij de geboorte het geslacht jongen toegewezen gekregen - worden door deze behandeling onder andere de stemverlaging en ontwikkeling van overige uiterlijke kenmerken van een man (zoals verbrede schouders, kaaklijn, en haargroei) geremd. De behandeling met PR heeft tot doel de transgender jongeren de gelegenheid te geven hun genderidentiteit te verkennen en hen tijd te geven om te overwegen of zij een genderbevestigende behandeling middels

genderbevestigende hormonen (voor transjongens is dit testosteron, voor transmeisjes zijn dit oestrogenen) en/of chirurgie willen starten, terwijl de ontwikkeling van - voor hen - ongewenste secundaire geslachtskenmerken wordt onderdrukt om het leed dat zij hierdoor ervaren te verminderen. Volgens het Nederlandse protocol ('the Dutch protocol') komen jongeren vanaf 12 jaar in aanmerking voor deze behandeling mits bij hen de diagnose GD is gesteld en zij aan diverse aanvullende voorwaarden voldoen. In sommige gevallen komen kinderen al voor hun twaalfde hiervoor in aanmerking, bijvoorbeeld wanneer onder andere de diagnose GD bij hen reeds op de kinderleeftijd is gesteld en zij voor het twaalfde jaar reeds in de puberteit komen (tenminste Tanner stadium 2 of 3; Tanner stadia beschrijven de fases van de lichamelijke ontwikkeling). Hoewel de effecten van PR op de lichamelijke puberteitsontwikkeling omkeerbaar zijn, kan de behandeling op korte termijn nadelige effecten met zich meebrengen. Bovendien zijn er weinig klinische onderzoeksgegevens beschikbaar over de bijwerkingen op de lange termijn. Ondanks dat een snel toenemend aantal genderidentiteitsklinieken PR gebruikt in de zorg voor deze jongeren, en deze behandeloptie is opgenomen in internationale transgender zorgrichtlijnen, blijven sommige zorgverleners die met transgender jongeren werken kritisch en lopen de meningen over het gebruik ervan uiteen (Coleman et al., 2022; Hembree et al., 2017; Rew et al., 2021; Vrouwenraets et al., 2015).

Een andere kwestie in de zorg voor transgender jongeren waarover discussie bestaat is de wilsbekwaamheid van de jongeren wat betreft het starten met de behandeling met PR. Volgens de internationale transgender zorgrichtlijnen is een belangrijke voorwaarde om een behandeling met PR te starten dat transgender jongeren in staat zijn om geïnformeerde toestemming ('informed consent') te geven (Coleman et al., 2022; Hembree et al., 2017). Er is echter steeds meer maatschappelijke discussie of jongeren daadwerkelijk in staat zijn om een beslissing te nemen om al dan niet te starten met de behandeling met PR, vooral omdat de behandeling ingrijpende gevolgen heeft op de lange termijn (o.a. Baron & Dierckxsens, 2021; D'Abbrera et al., 2020; Giordano et al., 2021; Levine, 2022; Pang et al., 2021; Siddique, 2021; Tampier, 2022). Tot op heden bestaat er weinig empirisch onderzoek naar de wilsbekwaamheid van jongeren om te beslissen over het starten met PR. Ook is er weinig bekend over de opvattingen van de transgender jongeren, hun ouders en zorgverleners over de wilsbekwaamheid van de jongeren. Onderzoek hiernaar is nodig ter onderbouwing van zowel het ethische debat als de klinische praktijk.

Het debat over de medische zorg voor transgender jongeren beweegt zich tussen twee uitersten: voorstanders van vroegtijdige medische behandeling vinden het een mensenrecht, tegenstanders vinden het een ongeoorloofd experiment op minderjarigen. De discussies hierover zijn vaak beladen met emoties. Mensen die de voordelen van het gebruik van vroegtijdige medische behandeling benadrukken, en degenen die vooral wijzen op de risico's ervan, lijken verschillende onderliggende ideeën te hebben

over onder andere de wilsbekwaamheid van de jongeren en de rol van comorbide psychologische, sociale en/of medische kwesties, vaak zonder deze openlijk te benoemen (bv. Dubin et al., 2020; Baron & Dierckxsens, 2021; Lemma, 2018). Wat ontbrak in de discussies is een verheldering van de onderliggende ideeën en theorieën. Daarnaast blijft inzicht in de overwegingen en ideeën van transgender jongeren zelf, hun ouders en ervaren professionals beperkt.

De overkoepelende doelstellingen van de studies die zijn opgenomen in dit proefschrift waren dan ook tweeledig; ten eerste wilden we meer inzicht krijgen in de kern van de ethische dilemma's die spelen in de zorg voor transgender jongeren, en in de onderliggende intuïties en overwegingen van betrokkenen in het veld ten aanzien van vroegtijdige medische behandeling. Het tweede, daaropvolgende doel was het verkrijgen van empirische onderzoeksgegevens over deze ethische dilemma's, om de discussies verder te brengen en de betrokkenen in het veld richting te geven hoe met deze ethische dilemma's in de klinische praktijk om te gaan.

Deel 1. Opvattingen van de verschillende betrokkenen over ethische kwesties in kaart gebracht

Hoofdstuk 2. Vroegtijdige medische behandeling van transgender kinderen en jongeren: een empirisch ethische studie

Hoofdstuk 2 beschrijft de overwegingen, onderliggende ideeën, aannames en theorieën van degenen die kritiek hebben op en degenen die voorstander zijn van het gebruik van vroegtijdige medische behandeling met PR bij transgender jongeren. Ons doel was om een duidelijker beeld te krijgen van de overeenkomsten en de verschillen tussen hun standpunten om het ethische debat vooruit te helpen. In totaal namen 36 professionals deel aan dit onderzoek waarbij gebruik is gemaakt van interviews en vragenlijsten. De professionals waren zorgverleners werkzaam in 17 verschillende behandelteams in 10 verschillende landen in Europa en Noord-Amerika, ethici en politici.

De resultaten laten zien dat de overwegingen van mensen die de risico's van het gebruik van vroegtijdige medische behandeling benadrukken, en van mensen die deze behandeling juist ondersteunen, veelal betrekking hebben op dezelfde fundamentele ethische concepten in de (kinder)geneeskunde; concepten zoals het belang van het kind of de jongere, autonomie, en de rol van de sociale context. Uit de literatuur, de interviews en de vragenlijsten kwamen zeven thema's naar voren die leiden tot verschillende en soms zelfs tegengestelde opvattingen over vroegtijdige medische behandeling. Het eerste thema is het al dan niet beschikbaar zijn van een verklarend model voor GD. Hoewel de meeste informanten het erover eens zijn dat een combinatie van factoren, zoals genetische, hormonale, neurologische en/of psychosociale factoren een rol speelt,

verschillen de meningen over de vraag of, en zo ja, welke factor(en) de overhand heeft/hebben in de etiologie (De Vries & Cohen-Kettenis, 2012; Meyer-Bahlburg, 2010). Het tweede thema betreft de aard van GD; de meeste informanten vinden het moeilijk om hun gedachten hierover te verwoorden. Velen zien GD niet als een medische ziekte of als een sociaal construct, maar als een normale, maar minder frequente variant van gender expressie. Sommigen stellen echter dat de behoefte aan medische behandeling op zich, om het lijden te verlichten, impliceert dat GD niet louter een variatie is, en dat dat maakt dat GD als een stoornis dient te worden gedefinieerd. De rol van de fysiologische puberteit in het ontwikkelen van een consistente genderidentiteit is het derde thema dat naar voren kwam. De meeste informanten waren het erover eens dat behandeling met PR de manier waarop jongeren over zichzelf denken kan beïnvloeden. De meesten van hen dachten echter dat PR de vorming van een genderidentiteit die congruent is met het bij de geboorte toegewezen geslacht niet belemmeren, wanneer er al vele jaren sprake is van een incongruente genderidentiteit. Bovendien noemen verscheidene endocrinologen dat PR al vele jaren worden gebruikt bij kinderen en jongeren met 'Pubertas Praecox' (vroegtijdige puberteit), en dat er voor zover zij weten geen gevallen van het 'ontstaan' van incongruente genderidentiteiten in die context zijn beschreven. Ook benadrukten de meesten endocrinologen dat zij bewust pas beginnen met de behandeling met PR wanneer de jongeren een soort 'eerste ervaring' met de puberteit hebben gehad (tenminste Tanner stadium 2 of 3) voordat zij starten met het remmen van de puberteit. Het vierde thema is de rol van comorbiditeit. De prevalentie van co-existente psychiatrische problemen bij transgender jongeren is hoog (de Vries et al., 2011; Meyenburg, 2014; Thompson et al., 2022). De precieze mechanismen die GD en co-existente psychopathologie met elkaar verbinden zijn vooralsnog onbekend. De meeste informanten stellen dat het per individu verschilt, en dat het afhankelijk is van de comorbide problematiek of GD en de co-existente problematiek(en) slechts naast elkaar bestaan of dat deze met elkaar samenhangen. Sommige professionals benadrukken het belang van het behandelen van ernstige co-existente psychopathologie voordat er medische behandeling wat betreft de GD wordt gestart. Anderen stellen daarentegen dat dit af dient te hangen van het individu en de specifieke co-existente problematiek(en). Het vijfde thema betreft de mogelijke lichamelijk en/of psychisch schadelijke gevolgen van vroegtijdige medische, maar ook juist van het onthouden van vroegtijdige medische behandeling. Hoewel (het schaarse) onderzoek tot nu toe nauwelijks negatieve, en zelfs positieve resultaten laat zien wat betreft de gevolgen van PR, blijven voorstanders van de behandeling voorzichtig en mensen die de behandeling bekritisieren sceptisch omdat de (lange termijn) risico's en voordelen van de beschikbare behandelingen nog niet volledig zijn vastgesteld. Voorts worden mogelijke schadelijke effecten van juist het afzien van vroegtijdige medische behandelingen genoemd door sommige informanten. Het zesde thema betreft de wilsbekwaamheid en de beslissingsbevoegdheid. Dit is een belangrijk punt van onenigheid in de discussie over vroegtijdige medische behandeling.

De meeste informanten waren het erover eens dat de wilsbekwaamheid van jongeren per individu dient te worden beoordeeld. Zij waren het echter niet eens over de vraag wie de uiteindelijke bevoegdheid moet hebben om beslissingen te nemen over vroegtijdige medische behandeling: de jongeren zelf, en/of de ouder(s) en/of het behandelteam. Het zevende en laatste thema betreft de rol van de sociale context in hoe GD wordt gezien en ervaren. Sommigen dachten dat de manier waarop genderincongruent gedrag van jongeren in een bepaalde cultuur wordt ervaren en benaderd, van grote invloed is op het al dan niet pathologiseren ervan. Verder speculeren sommigen dat de toenemende aandacht in de media kan leiden tot medicalisering van genderincongruent gedrag.

De discussie over het gebruik van PR is in volle gang. Sommigen vinden de vastgestelde internationale transgender zorgrichtlijnen te liberaal, terwijl anderen ze te conservatief vinden. Daarnaast omarmen steeds meer behandelteams het Nederlandse protocol ('the Dutch protocol') waarin het gebruik van PR wordt beschreven als behandelmogelijkheid, maar blijft er bij hen een gevoel van onbehagen bestaan. De discussie over de eerder beschreven thema's moet worden voortgezet op basis van wetenschappelijke onderzoeksgegevens als aanvulling op louter meningen. Anders zullen ideeën, veronderstellingen en theorieën over de behandeling van GD nog verder uiteenlopen, wat zou kunnen leiden tot (nog meer) inconsistenties tussen benaderingen die door zorgverleners op verschillende locaties en in verschillende landen worden aanbevolen.

Hoofdstuk 3. Een kwalitatief onderzoek naar de opvattingen van transgender jongeren over sekse, gender en puberteitsremmers

In hoofdstuk 2 beschreven we de overwegingen met betrekking tot vroegtijdige medische behandeling van verschillende professionals uit verschillende landen. Er is echter weinig bekend over hoe transgender jongeren zelf denken over vroegtijdige medische behandeling. Het derde hoofdstuk beschrijft daarom een onderzoek naar de overwegingen en opvattingen van transgender jongeren over de begrippen 'sekse' en 'gender', en over het gebruik van PR bij GD. Verder hebben we de overwegingen over het gebruik van PR van de transgender jongeren vergeleken met die van professionals aan de hand van de in hoofdstuk 2 verzamelde onderzoeksgegevens.

De informanten waren 13 jongeren (13-18 jaar ten tijde van de start van dit onderzoek) die allen de diagnose GD hadden en in behandeling waren bij de genderidentiteitskliniek in Leiden. Alle jongeren, op één na, werden behandeld met PR. De jongere die niet werd behandeld met PR startte niet in eerste instantie met PR, maar startte direct met een behandeling met genderbevestigende hormonen omdat zij ouder dan 18 jaar was toen behandeling geïndiceerd werd, zoals beschreven in het in Nederland gehanteerde protocol. De gemiddelde leeftijd waarop de deelnemende jongeren met PR begonnen was 15 jaar en 10 maanden. Voor dit onderzoek werden individuele semi-gestructureerde

interviews met open vragen over diverse onderwerpen afgenomen (30-40 minuten). Op het moment dat er geen nieuwe informatie tijdens de interviews naar voren kwam, werden er geen nieuwe informanten meer geïnccludeerd. Dit wordt 'datasaturatie' genoemd (Guest et al., 2006).

Uit de interviews zijn drie thema's naar voren gekomen; het eerste thema betreft de moeilijkheid om te bepalen wat een geschikte minimum leeftijd is om met PR te beginnen. De meeste jongeren vonden het moeilijk om een geschikte leeftijdsgrens te bepalen. Het viel hierbij op dat sommige jongeren voorzichtiger leken dan sommige professionals, bijvoorbeeld wat betreft de wilsbekwaamheid van de jongeren in deze context; de meeste jongeren betwijfelden of jongeren in staat zijn beslissingen te nemen over medische behandeling op de leeftijd van 12 jaar of jonger, terwijl sommige behandelteams de mogelijkheid onderzoeken om de huidige leeftijdsgrens voor behandeling met PR te verlagen. Het tweede thema betreft het gebrek aan onderzoeksgegevens over de lange termijn effecten van PR; dit gebrek is voor de meeste jongeren geen reden om niet met PR te beginnen. Voor de professionals was dit echter wel een groot probleem. Het derde thema, de rol van de sociale context, bestond uit twee subthema's: het eerste was de toegenomen media-aandacht, op televisie en internet, het tweede was een 'opgelegd' stereotype. Zowel jongeren als professionals hadden uiteenlopende zienswijzen over de toegenomen media-aandacht; sommigen dachten hier positief over, terwijl anderen hun twijfels uitten.

Vergelijking van de interviews van de jongeren met die van de professionals laat zien dat de jongeren en de professionals het niet over alle onderwerpen eens zijn. Opvallend is dat jongeren, in vergelijking met de professionals, soms terughoudender waren in hun opvattingen over behandeling bijvoorbeeld met betrekking tot de wilsbekwaamheid van jongeren. Op andere vlakken waren ze juist voortvarender, bijvoorbeeld wat betreft het accepteren van mogelijke lange termijn effecten. Het is belangrijk om de transgender jongeren zelf een stem te geven om te voorkomen dat professionals handelen vanuit (mogelijk onjuiste) veronderstellingen over de opvattingen van de jongeren in plaats van hun werkelijke overwegingen en meningen. Voorts wordt het verzamelen van meer kwalitatieve onderzoeksgegevens van transgender jongeren op andere locaties en in andere landen aangemoedigd.

Deel 2. Wilsbekwaamheid ten aanzien van beslissingen over puberteitsremmers

Hoofdstuk 4. De beoordeling van de wilsbekwaamheid van transgender jongeren met betrekking tot behandeling met puberteitsremmers

Hoofdstuk 4 doet verslag van het onderzoek naar de wilsbekwaamheid van transgender

jongeren om informed consent te geven voor het starten met een behandeling met PR. De competentie van transgender jongeren om informed consent te geven is een belangrijke voorwaarde voor behandeling met PR (Coleman et al., 2012; Hembree et al., 2017). In de samenleving wordt echter getwijfeld of de jongeren hiertoe in staat zijn. In sommige landen heeft dit zelfs geleid tot beperkte toegang tot deze behandeling. Er is geen empirisch bewijs over de wilsbekwaamheid van transgender jongeren om te beslissen over behandeling met PR. Daarom onderzochten wij op een gestructureerde, repliceerbare manier de wilsbekwaamheid van transgender jongeren in Nederland van wie was vastgesteld dat ze in aanmerking kwamen voor PR. De participanten waren 74 jongeren (10-18 jaar) die in zorg waren bij de genderidentiteitskliniek in Amsterdam of Leiden. Alle participanten ondergingen het 'reguliere' diagnostisch traject, bestaande uit onder andere een psychodiagnostisch onderzoek en een aantal maandelijkse afspraken met een zorgverlener van het transgender behandelteam gedurende een langere periode (meestal ongeveer zes maanden), voordat ze in aanmerking kwamen voor behandeling met PR. Voor ons onderzoek werd de 'MacArthur Competence Assessment Tool for Treatment' (MacCAT-T) gebruikt. Dit is een kwantitatief semi-gestructureerd interview dat wordt gebruikt om de vier criteria te beoordelen waaraan een persoon dient te voldoen om medisch wilsbekwaam te zijn, namelijk: de informatie die relevant is voor de aandoening en de voorgestelde medische behandeling begrijpen, de betekenis van de informatie voor de eigen situatie op waarde inschatten, redeneren over voordelen en potentiële risico's van de verschillende opties, en in staat zijn een keuze te uiten (Appelbaum & Grisso, 1988). Dit onderzoek had niet alleen tot doel de wilsbekwaamheid van de jongeren te beoordelen, maar ook te onderzoeken welke variabelen mogelijk gerelateerd zijn aan wilsbekwaamheid (zoals intelligentie, geslacht, leeftijd, en gedrags- en emotionele problemen).

Indien na afloop van het 'reguliere' diagnostisch traject de diagnose GD wordt gesteld wordt dit traject afgesloten met een afspraak waarin een informed consent verklaring wordt ondertekend⁶. Bij iedere aan dit onderzoek deelnemende jongere werd deze reguliere informed consent-afspraken opgenomen op video om de 'referentiestandaard' voor wilsbekwaamheid vast te stellen. Vervolgens werd het MacCAT-T-interview bij iedere jongere afgenomen en opgenomen op video. Een panel van 12 deskundigen - waaronder kind- en jeugdpsychiaters en -psychologen, kinder-endocrinologen en masterstudenten geneeskunde - werd getraind in het beoordelen van wilsbekwaamheid. Van iedere deelnemende jongere werd de wilsbekwaamheid beoordeeld door twee

6 Deze verklaring wordt getekend door de jongere en diens gezagdragende ouder(s) wanneer de jongere tussen de 12 en 15 jaar oud is. Wettelijk gezien hoeft deze alleen door de jongere ondertekend te worden wanneer de jongere 16 jaar of ouder is, en alleen door de gezagdragende ouder(s) wanneer het een kind onder de 12 jaar betreft.

deskundigen uit het panel aan de hand van de informed consent-video. Daarnaast werd de wilsbekwaamheid van iedere jongere beoordeeld door de zorgverlener van het genderteam die betrokken was bij het reguliere diagnostisch traject van de desbetreffende jongere. Tot slot werd de wilsbekwaamheid in elke MacCAT-T video beoordeeld door drie deskundigen uit het panel.

In dit onderzoek vonden wij dat 93,2% van de transgender jongeren die op het punt stonden te beginnen met behandeling met PR en deelnamen aan deze studie, competent werden bevonden om informed consent te geven op basis van de reguliere klinische beoordeling ('referentiestandaard'), en 89,2% van hen bij gebruik van het MacCAT-T interview. De overeenkomst tussen de twee gebruikte methoden om wilsbekwaamheid te beoordelen (de zogenoemde 'intermethod agreement') was hoog, namelijk 87,8%. De overeenkomsten tussen de beoordelingen van de verschillende beoordelaars per jongere (de zogenoemde 'intrater agreement') op basis van de referentiestandaard en de MacCAT-T waren ook hoog, namelijk respectievelijk 89,2% en 86,5%.

Voorts bleken zowel de totaal intelligentiequotiënt (IQ) score als het geslacht significant gerelateerd te zijn aan de MacCAT-T totaalscore; dit houdt in dat jongeren waarbij bij de geboorte het geslacht meisje was toegeschreven, en jongeren met een hogere totaal IQ score over het algemeen een hogere totale MacCAT-T score hadden en dus dat zij als 'meer' wilsbekwaam beoordeeld werden. Leeftijd ten tijde van de informed consent-afspraken, de mate van gedrags- en emotionele moeilijkheden, en de duur van het reguliere diagnostisch traject waren daarentegen niet significant gerelateerd aan de MacCAT-T totaalscore.

Het is geruststellend dat de meerderheid van de transgender jongeren die aan deze studie deelnam, grondig lijkt te hebben nagedacht over de behandeling met PR, begrijpt wat behandeling met PR inhoudt, en competent wordt geacht om een beslissing te nemen al dan niet met deze behandeling te starten. Het is echter mogelijk dat deze bevinding niet voor alle andere contexten geldt. De participanten in deze studie hebben namelijk een uitgebreide en grondige diagnostische evaluatie gehad voorafgaand aan de beoordeling van hun wilsbekwaamheid, terwijl jongeren in andere contexten deze ondersteuning soms niet hebben.

Voorts wijzen de huidige onderzoeksresultaten erop dat de MacCAT-T in de klinische praktijk bruikbaar en valide is. De huidige resultaten geven echter geen antwoord op de vraag hoe de zich ontwikkelende autonomie van wilsbekwame jongeren ethisch gerespecteerd dient te worden. Wij concluderen dat zolang er slechts beperkte wetenschappelijke onderzoeksgegevens zijn over de wilsbekwaamheid van transgender jongeren wat betreft het starten met behandeling met PR, een geïndividualiseerde aanpak voor deze groep van groot belang is.

Hoofdstuk 5. Wilsbekwaamheid ten aanzien van starten met puberteitsremmers: de opvattingen van transgender jongeren, hun ouders en zorgverleners

Hoofdstuk 5 rapporteert over de opvattingen over wilsbekwaamheid om behandeling met PR te starten. Het gaat om de opvattingen van transgender jongeren die na PR startten met genderbevestigende medische behandeling, jongeren die de behandeling met PR staakten, hun ouders en zorgverleners. Zoals hierboven beschreven, rapporteert hoofdstuk 4 over de beoordeling van de wilsbekwaamheid van 74 transgender jongeren wat betreft het starten met PR. Daaruit blijkt dat de overgrote meerderheid (ongeveer 89%) van deze jongeren competent wordt bevonden om toestemming te geven voor deze behandeling. Toch is er weinig bekend over de opvattingen en overwegingen van transgender jongeren zelf, hun ouders en zorgverleners met betrekking tot de wilsbekwaamheid van jongeren ten aanzien van het starten met PR.

Om inzicht te krijgen in deze opvattingen en overwegingen hebben we semi-gestructureerde interviews afgenomen met acht transgender jongeren (10-15 jaar) die na behandeling met PR zijn doorgegaan met genderbevestigende medische behandeling ('continuërs'), zes jongeren (10-17 jaar) die de behandeling met PR hebben gestaakt ('discontinuërs'), en 12 van hun ouders. Daarnaast werden twee focusgroepen gehouden met in totaal 10 zorgverleners van de genderidentiteitsklinieken in Amsterdam en Leiden.

De meeste informanten noemden in meer of mindere mate alle vier de criteria waaraan iemand dient te voldoen om wilsbekwaam te zijn - begrijpen, waarderen, redeneren, en een keuze communiceren - als aspecten die van belang zijn voor wilsbekwaamheid ten aanzien van het starten met behandeling met PR, net als de samenhang ervan met een specifieke beslissing en context (Appelbaum & Grisso, 1988). Desalniettemin verklaarden de meeste informanten, waaronder de meeste jongeren zelf, dat zij dachten dat zichzelf/de jongeren de behandeling en de gevolgen ervan niet volledig begrepen en waardeerden. De meesten van hen meenden echter dat zij/de jongeren desondanks in staat waren over het starten met de behandeling te beslissen.

Wij concludeerden dat zorgverleners het moeilijk vinden om de wilsbekwaamheid van jongeren voor het starten met behandeling met PR te beoordelen en om dit op een uniforme manier in praktijk te brengen. Verspreiding van kennis en ondersteuning met betrekking tot de beoordeling van wilsbekwaamheid en de ervaren ethische dilemma's over de wilsbekwaamheid van transgender jongeren is wenselijk, zodat zorgverleners jongeren en ouders adequaat kunnen begeleiden in het besluitvormingsproces.

Deel 3. De betekenis van behandeling met puberteitsremmers en het gebruik van fertiliteitspreservatie

Hoofdstuk 6. Het beloop van medische trajecten bij transgender jongeren na het starten met puberteitsremmers

Hoofdstuk 6 gaat over het traject van jongeren na de start met de behandeling met PR. Na start met PR zijn er verschillende routes mogelijk: volgens protocol starten met genderbevestigende hormonen, de behandeling met PR staken, en langer dan volgens protocol PR gebruiken.

We onderzochten de trajecten van 143 (67%) van de 214 jongeren die waren ingeschreven bij de genderidentiteitskliniek van Curium-Leids Universitair Medisch Centrum in Leiden, in Nederland, die op grond van hun leeftijd of stadium van de puberteit in aanmerking kwamen voor behandeling met PR, en die allen begonnen met de behandeling met PR. De jongeren waren tussen de 11 en 18 jaar oud. Achtendertig van hen waren transmeisjes en 105 transjongens. Van deze jongeren die met de behandeling met PR begonnen, werd de behandelstatus bekeken. Als zij meer dan drie maanden langer dan minimaal vereist volgens het Nederlandse protocol enkel behandeling met PR kregen voorafgaand aan de start van genderbevestigende hormonen, werd de reden van dit 'verlengd' gebruik genoteerd (in de tekstbox hieronder wordt dit protocol nader toegelicht). Jongeren die met PR waren begonnen en deze behandeling staakten, werden opgenomen in een gedetailleerde beschrijving. Uit de medische dossiers werden basiskenmerken zoals leeftijd, geslacht en gegevens over de start, duur en staking van de behandeling met PR verkregen, evenals de redenen voor het staken van de behandeling, en de mening van de jongeren en de ouders over de behandeling.

Alle jongeren ondergingen voorafgaand aan de behandeling met PR het reguliere diagnostische traject onder begeleiding van een kinder-endocrinoloog en een kind- en jeugdpsycholoog en/of -psychiater. Dit, om de diagnose GD volgens de DSM-5-criteria te bevestigen, om de aanwezigheid van medische, psychiatrische en/of psychosociale problemen te beoordelen die de behandeling zouden kunnen belemmeren, om te beoordelen of de jongere in staat was informed consent voor de behandeling te geven, en om te bevestigen dat de puberteit was begonnen, zoals aanbevolen in de huidige internationale transgender zorgrichtlijnen.

Volgens het gehanteerde protocol kwamen jongeren in aanmerking voor behandeling met genderbevestigende hormonen vanaf de leeftijd van 16 jaar en na minimaal zes maanden behandeling met PR. In het protocol was geen maximum duur voor het gebruik van PR vastgelegd. Vanaf 2016 kwamen jongeren die al minstens drie jaar behandeling met PR hadden ondergaan, in aanmerking voor behandeling met genderbevestigende

hormonen vanaf de leeftijd van 15 jaar. Vanaf 2017 kwamen jongeren die ten minste twee jaar met PR waren behandeld en 15 jaar oud waren voor de genderbevestigende hormoonbehandeling in aanmerking.

Wij vonden dat na een mediane duur van 0.8 jaar (0.3-3.8 jaar) enkel behandeling met PR, 125 van de 143 (87%) jongeren startten met behandeling met genderbevestigende hormonen. Negen (6%) jongeren stakten de behandeling met PR, van wie er vijf geen genderbevestigende behandeling meer wensten. Er werden verschillende redenen opgegeven voor het staken van de behandeling met PR, onder andere de ervaring van verliefdheid, de ervaring zich tussen man en vrouw in te voelen, het ervaren van bijwerkingen van de behandeling, en het ervaren van co-existente psychosociale problemen die de exploratie van de genderidentiteit in de weg stonden. Dertien jongeren gebruikten PR langer dan het protocol als minimum voorschrijft (maximaal gedurende in totaal 2.5 jaar) om andere dan logistieke redenen en hadden gedurende die tijd regelmatig een afspraak met een psycholoog of psychiater. Dit ondersteunt het idee dat de tijd dat jongeren behandeling met PR krijgen wordt gebruikt als een 'verlengde diagnostische fase' waarin jongeren hun genderidentiteit en behandelingswensen verder kunnen verkennen, en kunnen werken aan problemen die een succesvolle behandeling in de weg zouden kunnen staan.

Geconcludeerd kan worden dat de overgrote meerderheid van de jongeren die een behandeling met PR begonnen, overging op behandeling met genderbevestigende hormonen. Dit is mogelijk het gevolg van de toelatingscriteria die de jongeren 'selecteren' waardoor de kans groot is dat zij verder zullen gaan met genderbevestigende behandeling. Een klein aantal jongeren stopte met de behandeling met PR omdat zij geen genderbevestigende behandeling meer wensten. Dit wijst erop dat niet alle jongeren en ouders ervan uitgaan dat het resultaat van identificatie als transgender de enige mogelijke 'uitkomst' van behandeling met PR is. Daarnaast laat het zien dat de genderidentiteit nog steeds kan fluctueren tijdens de behandeling met PR, althans, bij sommige jongeren.

Hoofdstuk 7. Hoe jongeren zelf, hun ouders en zorgverleners denken over de functie van puberteitsremmers; zowel bij stoppen als bij doorgaan met deze behandeling

Het is niet bekend of de functies van behandeling met PR zoals beschreven in de internationale transgender zorgrichtlijnen overeenkomen met de functies van PR zoals ervaren door transgender jongeren, hun ouders en zorgverleners (Coleman et al., 2012; Hembree et al., 2017). Hoofdstuk 7 beschrijft de opvattingen van de hierboven genoemde belanghebbenden met betrekking tot de functie van behandeling met PR bij transgender jongeren. Voor het onderzoek beschreven in dit hoofdstuk zijn hetzelfde studie-cohort en dezelfde methode gebruikt als beschreven in hoofdstuk 5.

Uit de resultaten blijkt dat de 'continuërs', de 'discontinuërs', hun ouders en zorgverleners niet allemaal dezelfde opvattingen hebben over de functies van PR. Ten eerste, alle informanten vonden remming van de (verdere) ontwikkeling van secundaire geslachtskenmerken een belangrijke, en voor sommigen zelfs de belangrijkste, functie van PR. Sommige 'discontinuërs' ervoeren PR als een 'verlengde' diagnostische fase, waardoor zij 'extra' tijd kregen voordat zij besloten al dan niet te starten met de behandeling met genderbevestigende hormonen. De meeste 'continuërs' zagen PR daarentegen als de eerste stap van de genderbevestigende behandeling. Desalniettemin waren sommige 'continuërs' en sommige van hun ouders blij dat de effecten van PR op de lichamelijke puberteitsontwikkeling omkeerbaar waren, ook al verwachtten zij niet dat ze of hun kind van gedachten zou(den) veranderen. Eén 'continuer' en verscheidene ouders gebruikten de tijd die zij PR kregen, om te wennen aan het leven in de bevestigde geslachtsrol. Sommige zorgverleners vonden het belangrijk dat jongeren wat verder rijpen in de jaren dat zij PR krijgen, en dat zij, terwijl zij minder leed ervaren door de ongewenste puberteitsontwikkeling van hun lichaam, wellicht beter in staat zijn om te beslissen of zij al dan niet doorgaan met behandeling met genderbevestigende hormonen en om de gevolgen van hun beslissing zorgvuldig te overwegen. Eén van de 'discontinuërs' noemde deze functie ook. Voorts vermeldden sommige zorgverleners dat de 'extra' tijd henzelf tijd bood voor aanvullende beoordeling.

Concluderend, hoewel de internationale transgender zorgrichtlijnen benadrukken dat het bieden van tijd voor exploratie van de genderidentiteit een belangrijke reden is voor behandeling met PR, lijken veel jongeren tegenwoordig duidelijke ideeën te hebben over hun genderidentiteit en behandelwensen, en ervaren ze PR als de eerste stap van genderbevestigende behandeling (Coleman et al., 2012; Hembree et al., 2017). Voor sommige 'discontinuërs' bood PR echter een waardevolle periode van exploratie. Ook voor sommige ouders en zorgverleners had de extra tijd in sommige gevallen een functie. Zorgrichtlijnen zouden kunnen worden aangepast om zorg meer op maat te bieden, rekening houdend met de ideeën van de jongeren, de ouders en de zorgverleners over de functies van PR.

Hoofdstuk 8. Fertiliteitspreservatie bij transmeisjes

Terwijl de effecten van PR op de lichamelijke puberteitsontwikkeling omkeerbaar zijn, kan langdurig gebruik van genderbevestigende hormonen de vruchtbaarheid beïnvloeden. Voorts zal de transgender persoon zeker onvruchtbaar zijn als gonadectomie (verwijdering van de geslachtsklieren) wordt uitgevoerd. Onvruchtbaarheid kan grote gevolgen hebben voor het leven van transgender jongeren, en eerdere studies suggereren dat het behoud van de vruchtbaarheid de levenskwaliteit van transgender jongeren positief kan beïnvloeden. Tegenwoordig benadrukken de 'World Professional Association for Transgender Health' (WPATH) en de 'Endocrine Society' het belang van het geven van

toelichting over de opties voor fertiliteitspreservatie alvorens een behandeling met PR te starten. Uit twee recente studies uit de Verenigde Staten blijkt echter dat transgender jongeren zelden gebruik maken van fertiliteitspreservatie. Om inzicht te krijgen in het gebruik van fertiliteitspreservatie onder transmeisjes in Nederland, wordt in hoofdstuk 8 beschreven hoeveel jongeren gebruik maakten van fertiliteitspreservatie in een Nederlands cohort van transmeisjes die een behandeling met PR startten. Daarnaast gingen we na of er door de betrokken zorgverlener informatie was gegeven over het risico op onvruchtbaarheid, of het bespreken van de optie van fertiliteitspreservatie was gedocumenteerd in het medisch dossier, en wat de opgegeven reden(en) was/waren om af te zien van fertiliteitspreservatie als de jongere hier geen gebruik van had gemaakt. Voorts onderzochten wij welke factoren samenhangen met het gebruik van fertiliteitspreservatie.

Dit onderzoek was een retrospectieve review van medische dossiers van 35 transmeisjes die tussen 2011 en 2017 een behandeling met PR startten in de genderidentiteitskliniek van Curium-Leids Universitair Medisch Centrum in Leiden, in Nederland. Gegevens die uit de medische dossiers verkregen zijn waren leeftijd, intelligentiequotiënt (IQ), Tanner stadium, testiculaire volume, etniciteit, seksuele oriëntatie, psychiatrische comorbiditeit, gezinssituatie en informatie over de kinderwens.

Uit de analyse bleek dat alle jongeren ($n = 35$) geïnformeerd waren over het risico van onvruchtbaarheid, en dat 32 (91%) van hen de mogelijkheid van fertiliteitspreservatie werd geadviseerd. Dertien (41%) van de geadviseerde transmeisjes werden doorverwezen voor cryopreservatie van sperma, en twaalf (38%) van hen zijn daadwerkelijk naar de fertiliteitskliniek gegaan om te proberen sperma te laten cryopreserveren. Eén doorverwezen transmeisje is niet naar de fertiliteitskliniek geweest en was op het moment van de analyse in het kader van dit onderzoek nog niet begonnen met een behandeling met PR vanwege psychosociale problemen. Negen (75%) van de 12 transmeisjes die naar de fertiliteitskliniek zijn geweest om te proberen sperma te cryopreserveren, konden sperma cryopreserveren dat geschikt was voor intra-uteriene inseminatie (IUI) of intracytoplasmatische sperma injectie (ICSI).

Voorts werden de volgende redenen opgegeven om niet te willen worden doorverwezen voor fertiliteitspreservatie (sommige jongeren gaven meer dan één reden): geen kinderwens hebben (17%, $n = 4$), willen adopteren (13%, $n = 3$), zich ongemakkelijk voelen bij masturbatie of een afkeer hebben van hun penis (17%, $n = 4$), en zich ongemakkelijk voelen bij het idee de biologische vader van het kind te zijn (4%, $n = 1$). Bij acht (33%) jongeren was geen specifieke reden bekend om af te zien van fertiliteitspreservatie, en acht (33%) van de jongeren werden niet doorverwezen voor fertiliteitspreservatie omdat zij in de vroege puberteit verkeerden en niet in staat waren om via masturbatie een spermamonster te produceren.

De gemiddelde leeftijd bij het begin van de behandeling met PR in de groep transmeisjes die fertiliteitspreservatie probeerden, was significant hoger dan in de groep die geen fertiliteitspreservatie probeerde. Het Tanner stadium, het testiculaire volume, en het gemiddelde IQ in de groep die fertiliteitspreservatie probeerde, verschilden niet significant van die in de groep die dat niet deed. Dat gold ook voor de gezinssituatie en psychiatrische comorbiditeit (depressie, angststoornis, posttraumatische stressstoornis, of autisme spectrum stoornis).

De conclusie is dat één derde van de transmeisjes fertiliteitspreservatie heeft geprobeerd, en dat de meesten in staat waren sperma op te slaan dat geschikt is voor toekomstige intra-uteriene inseminatie (IUI) of intracytoplasmatische sperma injectie (ICSI). Dit benadrukt de noodzaak om dit onderwerp te bespreken voordat de behandeling met PR begint. Het beschikbaar stellen van verschillende mogelijkheden voor sperma-extractie, zoals testiculaire sperma-extractie of stimulatie door middel van elektro-ejaculatie, kan fertiliteitspreservatie toegankelijker maken voor transmeisjes voor wie masturbatie een belemmering vormt. Fertiliteitspreservatie is momenteel niet beschikbaar voor jongeren die zich nog in de vroege puberteit bevinden. Onderzoek op dit gebied zou echter ook voor deze groep mogelijkheden voor fertiliteitspreservatie kunnen bieden. Met het oog op toekomstige mogelijkheden is een ethisch en juridisch debat essentieel, waarbij rekening wordt gehouden met het recht op gelijkheid en non-discriminatie, en het recht op voortplanting van transgender personen.

Deel 4. Ethiekondersteuning

Hoofdstuk 9. Omgaan met ethische uitdagingen in de behandeling van transgender kinderen en jongeren: een evaluatie van de rol die moreel beraad kan spelen

Hoofdstuk 9 beschrijft de evaluatie van de bruikbaarheid van moreel beraad bij het omgaan met ethische uitdagingen en dilemma's in de zorg voor transgender jongeren. Moreel beraad is een gesprek waarin participanten gezamenlijk een ethische kwestie bespreken aan de hand van een casus uit hun werk (Dauwerse et al., 2014; Molewijk et al., 2008a; Stolper et al., 2016). Het is een veel gebruikte vorm van ethiekondersteuning.

Bij twee Nederlandse behandelteams binnen de genderidentiteitsklinieken van Leiden en Amsterdam werden moreel beraad sessies ingevoerd. In deze teams werkten specialisten in kinder- en jeugdpsychiatrie, -psychologie, en (kinder)endocrinologie in multidisciplinaire teams. Tussen oktober 2013 en januari 2015 namen de twee behandelteams deel aan in totaal 17 moreel beraad sessies. De leden van de behandelteams evalueerden het gebruik van moreel beraad. De onderzoeksgegevens werden verzameld met behulp van zes individuele interviews, twee focusgroepen waaraan in totaal 15 zorgverleners deelnamen,

een cross-sectionele moreel beraad-evaluatievragenlijst op twee momenten (T0, $n = 34$; T1, $n = 22$), en audio-opnamen van zes moreel beraad sessies.

De zorgverleners beoordeelden moreel beraad als zeer waardevol in situaties waarin zij geconfronteerd werden met ethische uitdagingen en dilemma's. Zij meldden dat moreel beraad hen hielp effectiever om te gaan met ethische uitdagingen, en dat het bijdroeg tot meer wederzijds begrip en open communicatie tussen teamleden. Bovendien zorgde het er volgens hen voor dat zij meer aandacht besteedden aan hun eigen argumenten en aan contextuele factoren, in plaats van blindelings het gehanteerde klinisch protocol te volgen. Voorts versterkte het hun vermogen om beslissingen te nemen en actie te ondernemen in ethisch moeilijke omstandigheden. De zorgverleners maakten echter ook kritische opmerkingen over moreel beraad: sommigen vonden dat er te veel tijd werd besteed aan het bespreken van één individuele casus, dat moreel beraad tot meer praktische en concrete resultaten moest leiden, en dat moreel beraad en de tijdens de moreel beraad sessies verworven inzichten beter moesten worden geïntegreerd en opgevolgd in het reguliere werkproces.

Vooral in de zorg voor transgender kinderen en jongeren zijn behandelbeslissingen vaak omringd door complexe ethische controverses en onzekerheden. Tijdens moreel beraad sessies worden de redeneringen en de kennis van de zorgverleners meegenomen, maar moreel beraad maakt ook (mogelijke conflicten van) onderliggende normen en waarden expliciet en geeft suggesties hoe met de onzekerheid of onenigheid binnen een team om te gaan. Als zodanig kan moreel beraad worden gezien als een instrument dat aanvullend kan worden gebruikt in 'complexe' gevallen. Er is meer onderzoek nodig naar de daadwerkelijke bijdrage van moreel beraad aan de verbetering van de zorgkwaliteit (inclusief de bepalende factoren), de betrokkenheid van transgender personen bij moreel beraad sessies, en naar hoe ethiekondersteuning meer kan worden geïntegreerd in de dagelijkse werkprocessen.

Hoofdstuk 10. Discussie

Ethische uitdagingen en dilemma's zijn onlosmakelijk verbonden met transgenderzorg, met name als het gaat om de zorg voor kinderen en jongeren en de mogelijke levenslange gevolgen van het al dan niet verlenen van medische behandeling in een vroeg stadium. Dit komt omdat het een relatief nieuw gebied betreft, waarin de ontwikkelingen snel gaan, er nog relatief weinig empirische onderzoeksgegevens beschikbaar zijn over de resultaten op de lange termijn, en het onderwerp is van een gepolariseerd debat. De uitdagingen en dilemma's rond vroegtijdige medische behandeling, die zo'n tien jaar geleden al door zorgverleners werden geuit, zoals beschreven in ons eerste artikel uit 2015, lijken sindsdien alleen maar groter en nijpender te zijn geworden (Vrouenraets et al., 2015). Aanvankelijk leken deze dilemma's alleen aan de orde voor degenen die direct bij

deze zorg betrokken waren. Tegenwoordig spreekt echter een veel bredere groep mensen zich uit over dit onderwerp. Voorts spelen de media en de rechtspraak een steeds grotere rol. Daarmee lijkt het debat alleen maar harder te zijn geworden. Ook lijkt de controverse groter te zijn geworden, waarbij mensen die vooral wijzen op de risico's van vroegtijdige medische behandeling en degenen die de voordelen ervan benadrukken steeds verder uit elkaar lijken te drijven (bv. Lament, 2014; Osserman & Wallerstein, 2022). Momenteel lijkt er nauwelijks nog ruimte te zijn voor een 'genuanceerde middenweg' (bv. Bazelon, 2022).

Meer inzicht in de kern van de ethische dilemma's die een rol spelen in de zorg voor transgender kinderen en jongeren, en meer empirische onderzoeksgegevens wat betreft deze ethische dilemma's zijn nodig om zorgverleners richting te geven aan hun handelen, en om kinderen en jongeren die naar genderidentiteitsklinieken worden verwezen adequaat te informeren en begeleiden. Daarom was het eerste doel van ons onderzoek om meer inzicht te krijgen in de kern van de ethische dilemma's die een rol spelen in de zorg voor transgender kinderen en jongeren, en in de onderliggende opvattingen en overwegingen van belanghebbenden in het veld met betrekking tot vroegtijdige medische behandeling. Het tweede, doel was empirische onderzoeksgegevens te verschaffen die gedachtevorming over deze ethische dilemma's verder zou kunnen brengen.

Dit proefschrift beschrijft de thema's die aanleiding gaven tot verschillende en soms zelfs tegenstrijdige opvattingen over de behandeling voor transgender jongeren. Vijf thema's kwamen consequent naar voren in de context van de politieke en publieke discussies: de wilsbekwaamheid van de jongeren, overwegingen met betrekking tot het al dan niet starten met de behandeling met PR, co-existente psychosociale problematiek, de sociale context, en ethiekondersteuning. Deze thema's worden in de discussie één voor één uitgewerkt om meer inzicht te krijgen in de controverses en mogelijke oplossingen. Per thema wordt beschreven hoe de opvattingen, overwegingen en nieuw verkregen onderzoeksgegevens, indien van toepassing, in de loop der jaren zijn veranderd en ontwikkeld. Voorts staan we stil bij de betekenis van onze onderzoeksresultaten voor de bredere context van de politieke en publieke discussies.

Het veld van de zorg voor transgender kinderen en jongeren is en blijft in beweging, en de bijbehorende ethische uitdagingen en dilemma's nopen de zorgverlener tot een aangepaste rol ten aanzien van de (medische) behandeling. De zorgverleners kunnen gezien worden als evenwichtskunstenaars; aanvankelijk moesten zij balanceren tussen de behandelwensen, eisen en behoeften van met name de transgender jongeren, van hun ouders, en van die van henzelf (M. de Vries, 2020). Tegenwoordig lijken de wensen en behoeften van andere 'partijen', zoals beroepsverenigingen, de media en de rechtspraak echter ook meer een rol te spelen. Zorgverleners dienen dan ook een adequaat evenwicht te vinden in het krachtenveld tussen deze verschillende 'partijen', waarvan sommige relatief 'nieuw' zijn en die allemaal voortdurend in beweging zijn wat betreft hun

perspectief op de ethische dilemma's die een belangrijke rol spelen in een vroegtijdige medische behandeling, zoals geschetst in dit proefschrift (M. de Vries, 2020).

Hoewel PR geen risicoloze medische behandeling is en aanvullende (wereldwijde) multicentra kwantitatieve en kwalitatieve onderzoeksgegevens nodig zijn om de mogelijke bijwerkingen en voordelen van de behandeling beter te begrijpen, lijkt behandeling met PR nog steeds veelbelovend voor transgender jongeren wanneer deze wordt gegeven in een context van voldoende psychologische ondersteuning (o.a. Rafferty et al., 2018; Ramos et al., 2021; Turban & Ehrensaft, 2018). Echter, ondanks de veelbelovende huidige stand van de wetenschap met betrekking tot de medische en psychologische aspecten van de zorg voor transgender jongeren, lijkt daarnaast een ethische rechtvaardiging van de behandeling nodig. Onderzoeksgegevens vanuit ethisch perspectief zijn dan ook nodig om dit gemis in dit debat over vroegtijdige medische behandeling op te vullen. De in dit proefschrift geschetste bevindingen lijken vanuit dit ethische oogpunt het gebruik van vroegtijdige medische behandeling volgens de internationale zorgrichtlijnen te rechtvaardigen. Daarbij dienen verschillende bezwaren zoals beschreven in dit proefschrift echter wel bij iedere jongere afgewogen te worden. Zo laten de resultaten van dit proefschrift zien dat onder andere de wilsbekwaamheid van de jongere, de mogelijke fysieke en/of psychische schadelijke effecten van het al dan niet toepassen van vroegtijdige medische behandelingen, de gevolgen voor de vruchtbaarheid, de co-existente psychosociale problematiek en de sociale context een belangrijke rol spelen in het al dan niet toepassen van vroegtijdige medische behandeling en dienen daarom meegewogen te worden bij het bepalen wat de meest geschikte zorg voor de jongere in kwestie is.

Daarnaast is verspreiding van kennis en ondersteuning met betrekking tot de beoordeling van wilsbekwaamheid en de ondervonden ethische dilemma's wenselijk om zorgverleners in staat te stellen jongeren en hun ouders adequaat te begeleiden in het besluitvormingsproces betreffende vroegtijdige medische behandeling. Een goede stap hiertoe is gezet door enkele Nederlandse onderzoekers; zij hebben, grotendeels op basis van de bevindingen uit verschillende van de studies die in dit proefschrift zijn opgenomen, een ethisch ondersteuningsinstrument ontwikkeld, de zogenaamde 'Wilsbekwaamheidswijzer' (De Snoo-Trimp et al., 2022a). Dit instrument geeft zorgverleners informatie en richting over hoe om te gaan met de wilsbekwaamheid van jongeren (De Snoo-Trimp et al., 2022a). Het zou behulpzaam zijn als een dergelijk ethisch ondersteuningsinstrument ook voor zorgverleners in andere landen beschikbaar wordt. Desalniettemin zullen, ondanks de houvast die een ontwikkeling zoals deze biedt, ethische uitdagingen en complexe casussen onlosmakelijk verbonden zijn aan de zorg voor transgender jongeren (Vrouenraets et al., 2021). Het gebruik van moreel beraad, een veel gebruikte vorm van ethiekondersteuning, kan zorgverleners helpen effectiever

om te gaan met deze ethische uitdagingen en complexe casussen (Dauwerse et al., 2014; Molewijk et al., 2008a; Vrouwenraets et al., 2020).

Dit proefschrift laat zien dat zorg voor transgender kinderen en jongeren inherent ethische dilemma's met zich meebrengt, zelfs wanneer er meer klinische onderzoeksgegevens zullen komen om de 'evidence-base' ervan te onderbouwen. Wetenschappelijke onderbouwing alleen zal geen antwoord kunnen geven op alle opgeworpen onzekerheden betreffende de genderbevestigende medische zorg voor jongeren. De ethiek kan hierbij ondersteuning bieden. Ethische dilemma's zullen immers deel blijven uitmaken van de transgender zorg. Dit proefschrift geeft inzicht in deze ethische dilemma's en geeft manieren en richting hoe hier in de genderzorg mee om te gaan.

CURRICULUM VITAE

Lieke Vrouwenraets was born on July 24th, 1989 in Veldhoven, the Netherlands. After graduating from the Stedelijk Gymnasium in 's-Hertogenbosch in 2007, she moved to Leiden to study at Leiden University. During her bachelor's degree Psychology (propedeuse cum laude) she attended the Honours Class 'Human aging: from brain to society'. Subsequently she started her master in Child & Adolescent Psychology at the same university. During this master's degree program she did a research and clinical internship at LUMC-Curium, the Department of Child and Adolescent Psychiatry of the Leiden University Medical Centre (LUMC). Throughout this clinical internship she gained experience in the healthcare for transgender children and adolescents and children and adolescents with psychiatric problems. During her studies she worked among others as a counsellor for children and adolescents with developmental disabilities (Inzowijs).

Despite that her initial interest after graduating was in clinical work, she 'succumbed' to the inspiring words of Prof. Dr. Martine de Vries, Prof. Dr. Henriëtte Delemarre-van de Waalt, and Dr. Miranda Fredriks to start doing scientific research. This led in 2013 to the combination of clinical work in the gender treatment team at LUMC-Curium, with doing qualitative research regarding the controversies surrounding the treatment with puberty suppression for transgender minors at the LUMC. This period, which lasted a year and a half, further fuelled her interest in combining clinical- and research work regarding the healthcare for transgender children and adolescents. She expanded the research project by undertaking a parttime PhD at the LUMC, focusing on the ethical dilemmas & decision-making in the healthcare for transgender minors under the supervision of Prof. Dr. Martine de Vries, Dr. Annelou de Vries (Amsterdam UMC), and Dr. Irma Hein (Amsterdam UMC). To obtain the data for the studies described in this thesis, she also worked as a researcher within the gender treatment team of Department of Child and Adolescent Psychiatry, Amsterdam University Medical Centres, Location VUmc. Besides the PhD she continued doing clinical work at the gender treatment team at LUMC-Curium.

In 2018 she received a research grant from the 'Fonds Wetenschappelijk Onderzoek Seksualiteit' (FWOS) to continue her PhD project. Besides the clinical work she did at the gender treatment team between 2014 and 2022, she also worked with children and adolescents with psychiatric problems. She did this at Curium-LUMC and the neighbourhood health centre for minors and their families. In addition, during this period she also contributed to research regarding the effectiveness of a blended cognitive behavioural therapy program for children and adolescents with an anxiety disorder ('Dappere Kat'), in collaboration with among others the University of Groningen, the Netherlands. Besides

she was trained to be a moderator moral case deliberation, and as a 'MYmind' teacher, a mindfulness training for children and adolescents with (characteristics of) attention deficit hyperactivity disorder (ADHD) and/or autism spectrum disorders (ASD) and their parents.

In the beginning of 2022 she started the postmaster's program to become a health care psychologist (GZ-psycholoog BIG), with a specialization in child and adolescent psychology, at the Medical Psychology department of the Willem-Alexander Children's Hospital at LUMC where she works with paediatric patients. She is planning to finish her training as a health care psychologist in May 2024.

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DANKWOORD

Wat voel ik me bevoorrecht dat ik onderzoek heb mogen doen naar de ethische controverses die heersen op het gebied van de vroegtijdige medische behandeling van transgender kinderen en jongeren; een gebied dat, toen ik in 2013 met dit onderzoek begon, in de kinderschoenen stond, dat in het afgelopen decennium zo in ontwikkeling is geweest en nog steeds is, waarin nog zo veel te onderzoeken is, en waarover zo veel uiteenlopende ideeën en opvattingen bestaan die door steeds meer partijen geuit worden. Voorts ben ik dankbaar dat ik de mogelijkheid heb gekregen het (kwalitatieve) onderzoekswerk te combineren met het klinische werk in het genderteam; mijns inziens heeft dat tot een voor mij ontzettend leerzame periode & waardevolle kruisbestuiving geleid. Ik heb ongelooflijk veel geleerd van de verhalen, kennis en ervaringen van zo veel betrokkenen. Dit proefschrift had dan ook niet tot stand kunnen komen zonder de vele verschillende vormen van ondersteuning. Daarvoor wil ik dan ook graag iedereen bedanken die hier een steentje aan heeft bijgedragen, en in het bijzonder de hieronder genoemde mensen.

Graag wil ik alle kinderen, jongeren, hun ouders, zorgverleners en andere professionals enorm bedanken voor het delen van hun tijd & verhalen met mij. Zonder jullie had dit proefschrift niet tot stand kunnen komen. I would like to thank the clinicians working in gender treatment teams abroad for sharing their time & stories with me. Without your contributions I could not have completed this thesis.

Prof. dr. M.C. de Vries, beste Martine, al voordat duidelijk was dat het ZonMw onderzoek zou uitmonden in een proefschrift was jij al 'on board'. Vanaf het eerste moment gaf je mij het vertrouwen om de onderzoeken uit te voeren, de artikelen te schrijven en lezingen op allerlei plekken te geven. Veel dank daarvoor, voor de mogelijkheden die je mij hebt geboden en voor jouw altijd aanwezige enthousiasme en daadkracht, ze inspireren me.

Dr. A.L.C. de Vries, beste Annelou, dankzij jou heb ik een kijkje in de wereld van het Amsterdamse genderteam kunnen nemen en kon ik zo dichtbij de 'kern' van 'the Dutch protocol' komen. Wat een unieke ervaring heb je mij daarmee geboden. Ik heb veel van jouw kennis en ervaring op onder andere het gebied van de zorg voor transgender kinderen en jongeren en het doen van wetenschappelijk onderzoek geleerd; veel dank daarvoor.

Dr. I.M. Hein, beste Irma, tijdens het traject gaf je me het gevoel geregeld spreekwoordelijk naast me te staan om met me mee te kijken naar mogelijkheden en me te behoeden voor eventuele valkuilen die ik vanuit mijn enthousiasme soms over het hoofd dreigde te zien. Wat geweldig dat ik zo veel heb mogen leren van al jouw kennis en ervaring op onder

andere het gebied van wilsbekwaamheid. Veel dank daarvoor en voor het gevoel van rust en kalmte dat jij uitstraalt.

Collega's van het (voormalig) genderteam van Curium & het LUMC, wat voel ik me bevoorrecht dat ik naast mijn onderzoekswerk ook klinisch werk binnen ons genderteam mocht doen samen met jullie. In het bijzonder wil ik jullie, Gudrun & Corine, bedanken voor het bieden van de 'veilige haven' waar ik altijd op terug kon vallen dankzij jullie kennis, ervaring en luisterend oor. En natuurlijk Sabine, ik ben blij dat ik, sinds onze kennismaking in Thailand, zowel wat betreft het klinische- als het onderzoekswerk veel van jouw benijdenswaardige kennis, ervaring en oneindige drive heb mogen leren. Ik hoop dat onze paden elkaar zullen blijven kruisen.

Collega's in het LUMC op de afdeling Ethiek en Recht van de Gezondheidszorg, collega's van de Medische Psychologie van het WAKZ, en voormalig collega's van het genderteam in het AMC, bedankt voor jullie steun en prettige werkomgevingen de afgelopen jaren. In het bijzonder Anna en Marijn. Dank voor de plezierige tijd tijdens het verkrijgen en verwerken van de data, het schrijven van de (gezamenlijke) artikelen, het geven van lezingen tijdens congressen, en de nodige afleiding daaromheen. En Marleen, dank voor jouw luisterend oor en het sparren over (werk)uitdagingen. Ook wil ik graag Prof. dr. Henriëtte Delemarre-van de Waal, die helaas veel te jong in 2014 is overleden, bedanken voor het mij enthousiast maken om dit onderzoek uit te voeren.

Mijn paranimfen, Anne & Nikki, ik ben ongelooflijk dankbaar & trots dat jullie vandaag naast me staan. Lieve Anne, niemand begrijpt zo goed als jij hoe de afgelopen jaren waren, niet alleen wat betreft het onderzoekswerk, maar ook op persoonlijk vlak. Tijdens de diverse 'highs & lows' kon ik op jouw steun & hulp rekenen. Dank daarvoor Anne, maar vooral voor het er zijn. Lieve Nikki, sinds onze gezamenlijke masterstage bij LUMC-Curium kan ik altijd op jouw steun en meedenken rekenen, en als dat niet op de werkvloer is, dan op de dansvloer. Dank je Nikki voor de sprankelende, leergierige & altijd optimistische (met het beste asymmetrische tintje) vriendin die je bent.

Vriendinnen, vrienden, Bonbon, de Erikjes, mijn hockeyteam, dank voor al die fijne momenten die voor de nodige ontspanning zorgen. In het bijzonder wil ik jullie, Gisèle & Michèle bedanken. Lieve Gies, dank voor het - in allerlei vormen - fijne samen zijn wanneer er dingen gevierd kunnen worden, maar ook wanneer het even wat minder soepel gaat. Lieve Mies, wat ontzettend fijn dat ik bijna twee decennia nadat we samen op het hockeyveld stonden, meer dan ooit te voren kan genieten van jou. Je staat altijd voor me klaar. Ik ben ongelooflijk blij met de gezelligheid & warmte van jullie beide zo dichtbij!

Liefste broers. Chiel, dank voor jouw hulp met de vertalingen van de vele citaten in dit boek, of er nu haast achter zat of niet, je maakte er zonder meer tijd voor. Joen, dank voor de fijne diner- & spelletjesavonden, en het samen trainen voor de twee Ironman70.3 races als 'ontspanning' en manier om de gedachten in mijn hoofd op een rijtje te krijgen. Op naar weer een volgende opnieuw samen met Maart? Maart, zo ver weg daar in Indonesië, maar altijd daar voor mij. Dank voor alle 'spar-skype-sessies' over de meest uiteenlopende onderwerpen, met zo veel tranen van het lachen, en soms ook van verdriet. Dank voor het samen wegdromen, maar ook voor het relativeren. Dank voor het meedenken met de grote lijnen & het invullen van de details. Ik ben het meest trotse zusje als ik tussen jullie drie in sta. Ik hou van jullie.

Lieve pap en mam, dank voor jullie onvoorwaardelijke liefde, steun en vertrouwen in mij. Pap, het maakt niet uit hoe laat het is, waar het om gaat, hoe klein of groot het is, ik kan altijd op jouw meedenken en hulp rekenen. Lieve mam, engel op aarde, dank voor het altijd bieden van een luisterend oor en voor het áltijd klaarstaan. Zonder jullie had ik hier niet gestaan. Dit boekje draag ik met heel veel liefde op aan jullie. Ik weet niet wat ik zonder jullie zou moeten, ik hou van jullie.

