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

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 & Ehresnaff, 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 met 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 responses 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 (Armuand 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 Grift 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-OCCURING 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, Sämfjord, & 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 medicate 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

- Society
- Professionals
- Transgender minors and their parents
- Clinicians
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.