

ESSM Position Statement

“Assessment and hormonal management in adolescent and adult trans people, with attention for sexual function and satisfaction”

Guy T’Sjoen, Department of Endocrinology and Center for Sexology and Gender, Ghent University and Ghent University Hospital, Belgium

Jon Arcelus, Institute of Mental Health, Faculty of Medicine and Health Sciences, University of Nottingham, Nottingham, UK

Annelou L.C. De Vries, Department of Child and Adolescent Psychiatry, Center of Expertise on Gender Dysphoria, VU University Medical Center, Amsterdam, The Netherlands

Alessandra D. Fisher, Andrology, Women’s Endocrinology, Gender Incongruence Unit, Careggi University Hospital, Italy

Timo O. Nieder, Institute for Sex Research, Sexual Medicine and Forensic Psychiatry, Interdisciplinary Transgender Health Care Center Hamburg, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Müjde Özer, Department of Plastic, Reconstructive and Hand Surgery, Amsterdam University Medical Center, Amsterdam, The Netherlands

Joz Motmans, Transgender Infopunt, Ghent University Hospital, Ghent, Belgium

Corresponding author: Guy T’Sjoen, Center for Sexology and Gender & Department of Endocrinology, Ghent University Hospital, Ghent University, C. Heymanslaan 10, 9000 Ghent, Belgium

Capsule: We present an ESSM position statement of trans health care, including an overview on up-to-date definitions and treatment options in both adolescent and adults, with attention for sexuality.

Abstract

Background: There is a general lack of recommendations for and basic information tailored at sexologists and other health care professionals for when they encounter trans people in their practice.

Aim: We present to clinicians an up-to-date overview of clinical consensus statements on trans health care with attention for sexual function and satisfaction.

Methods: The task force consisted of 7 clinicians experienced in trans health care, selected among ESSM scientific committee. Consensus was guided by clinical experience and a review of the available literature and by interactive discussions on trans health, with attention for sexual function and satisfaction where available.

Outcomes: The foci of the paper are assessment and hormonal aspects of trans health care.

Results: As the available literature for direct recommendations was limited, most of the literature was used as background or indirect evidence. Clinical consensus statements were developed based on clinical experiences and the available literature. The results are divided into 6 sections 1) general statements and statements on 2) assessment of children and adolescents, 2) assessment of adults, 3) hormone therapy in trans assigned female at birth and 4) assigned male at birth people and 5) sexual functioning and satisfaction in relation to surgical treatment.

Clinical Implications: With the multiple barriers to care that many trans people experience, basic care principles still need to be stressed. We recommend that health care professionals (HCPs) working with trans people recognise the diversity of genders, including male, female and non-binary individuals. Also, HCPs assessing gender diverse children and adolescents should take a developmental approach that acknowledges the difference between prepubescent gender diverse children and pubescent gender diverse adolescents and trans adults. Furthermore, trans people seeking gender affirming medical interventions should be assessed by HCPs with expertise in trans health care and gender affirming psychological practice. If masculinisation is desired, testosterone therapy with monitoring of serum sex steroid levels and signs of virilisation is recommended. Similar, if feminisation is desired, we recommend estrogens and/or anti-androgen therapy with monitoring of serum sex steroid levels and signs of feminisation. HCPs should be aware of the influence of hormonal therapy on sexual functioning and satisfaction. We recommend HCPs are aware of potential sexual problems during all surgical phases of treatment.

Strengths & Limitations: This is an up-to-date ESSM position statement. These statements are based upon the data that is currently available, however it is vital to recognise that this is a rapidly changing field and that the literature, particularly in the field of sexual functioning and satisfaction is limited.

Conclusion: This ESSM position statement provides relevant information and references to existing clinical guidelines with the aim of informing relevant healthcare professionals on best practices when working with transgender people.

Key words: transgender, non-binary, gender diverse, gender incongruence, feminisation, masculinisation, gender affirming surgery, sexual functioning, sexual satisfaction

Introduction

In view of the recent change in the clinical diagnosis use in transgender health in the new edition of the WHO International Classification of Disease (ICD-11)[1], this position statement aims to provide clinical advise to European sexologists and health care professionals (HCPs) who may encounter trans people in their clinical practice. Although international guidelines for the care of trans people exist, such as the Standards of Care developed by the World Professional Association for Transgender Health (WPATH)[2] or the Endocrine Society guidelines[3], they require updating due to the important change in the classification system that most European Health services will be using. The newly accepted diagnosis “Gender Incongruence” (GIC) has been moved out of the mental health chapter in the new edition of the ICD (ICD-11). This is an important change in the classification system that it hopes to depathologize trans people. The change in the ICD-11 questions the need of mental health professionals as part of the assessment of trans people wishing gender affirming medical interventions (GAMI). This paper is a Position Statement by the European Society for Sexual Medicine (ESSM) that provides clinicians working with trans people an up-to-date overview of trans health care in general and discuss the effect of GAMI in sexual function and satisfaction where evidence is available. There is an enormous variation of services working with trans people in Europe, from very well developed multi-disciplinary services to single individuals working independently. It is expected that by reading this document, European health care professionals and sexologists will increase the knowledge about trans health. This paper aims to provide information and up to date references to existing clinical guidelines that would make access to more specialised information easily available.

In this paper, the term “trans” is used as a short form, which is intended to take into account people whose gender identity does not (or not completely and/or permanently) match their sex assigned at birth. The adjective trans thus encompasses both trans binary people, who identify as women or men, as well as gender non-binary people who identify as neither (exclusively) male nor female. This latter group includes, but is not limited to, those who experience not having a gender identity (agender), or as having a gender identity that is changing and shifting over time (genderfluid or genderflux). Gender identity is defined as the psychological identification of oneself or the internal sense of being in relation to gender.[4] It is important to highlight that the term trans does not automatically imply a desire to gender affirming medical care (e.g., hormones or surgeries). Some

trans people undergo Gender Affirming Medical Intervention (GAMI), such as hormonal therapy, surgeries or other interventions but others do not desire these. Where necessary, the distinction is made between assigned male at birth (AMAB) and assigned female at birth (AFAB) trans people. When studies are cited, we will use ‘trans AFAB people’ and ‘trans AMAB people’ when these studies did not include information of the self-identified identity labels of the respondents. In most of these studies, respondents were classified by the authors themselves as trans men or trans women merely based on their assigned sex at birth, hereby ignoring the existence of gender non-binary trans people.

Methodology

The position statement is divided into six main sections (general statements, assessment of children and adolescents, assessment of adults, hormone treatment in both trans AFAB and AMAB people, and surgical interventions). The aim was not to undertake a systematic literature review in every single section. The authors of this position statement are ESSM members actively involved in the clinical care of adolescent and adult trans people in Europe. They were selected by the ESSM scientific committee based on their long standing clinical experience and scientific involvement in the specific areas of trans health. They had all published literatures reviews in their specific areas of expertise, or are/were part of the development of international guidelines. The disciplines involved are endocrinology, psychology, psychiatry, plastic/gender surgery, and sociology. The ESSM funded two face-to-face meetings but no further financial support was received for this work.

In 2018, a review of recent literature took place using the following words: for terms referring to transgender people (transsexualism, transgender, gender dysphoria, gender identity disorder, trans*, gender incongruence), for assessment (assessment, counselling, gender development, mental health, sexual function, sexual desire, sexual activity, sexual satisfaction), for hormonal treatment, (cross-sex hormones, testosterone, estrogen, blockers, GnRH agonist), for surgery (gender affirming surgery, gender confirming surgery, sex reassignment surgery, mastectomy, hysterectomy, ovariectomy, metoidioplasty, phalloplasty, erection prostheses, orchiectomy, vulvoplasty, vulvo-vaginoplasty, vaginoplasty, breast augmentation). Every term used for transgender people was combined using the “OR” and the “AND” operate with every term used

for hormonal treatment, surgical interventions. Literature research was conducted on PubMed, PsychINFO, Embase, and Scopus. from January 1, 1996 up to 2018 were included. It is important to acknowledge that the recommendations were consensus based and supported by the background literature. A literature search was carried out to determine whether there were any studies (published from January 1996 to April 2018) unknown to the authors that might be relevant to this position paper. The existing knowledge and selected literature was interactively discussed among the authors based on their clinical expertise and bringing in different disciplinary knowledge. The foci of the paper are assessment and hormonal aspects of trans health care, while the surgical options are only introduced. In addition, the selected literature of the impact of hormonal treatment and surgery on sexual functioning and sexual satisfaction was summarised. The literature as well as the clinical experience of the panel was used to develop the statements. The available literature for a direct recommendation was limited and most of the literature was used as background or indirect evidence. When a statement was not approved by all, it was re-written until consensus was reached. Each statement had to be approved by all the authors in order to be accepted. Furthermore, in view of the limitation on the amount of references allowed in this manuscript, each author selected the most relevant publications that will support the clinical consensus statements.

General statements

Statements

1. We advise that HCPs when working with trans people recognise the diversity of genders, including male, female and non-binary individuals.
2. We advise that HCPs when working with trans people openly ask for the individual gender experience of the person seeking treatment, including which pronouns and name they like to be addressed with, and recognise this may change in the future.
3. We advise that HCPs when working with trans people critically reflect upon discriminatory factors influencing both access to and outcomes of gender-related health care services, and make the necessary changes to accommodate all trans individuals.
4. We advise that HCPs when working with trans people should critically reflect on their own possible prejudices, ethics and power positions.

5. We advise that HCPs when working with adults trans people should explain the result of the clinical assessment with the aim of a shared understanding and shared responsibility.

Evidence

The traditional notion of the gender binary has been shaken due to empirical findings of the last 10 years. Large-scale online surveys provide information on the extent to which trans people either find themselves identifying with a gender within or beyond the binary. In an online study in the USA with 6,436 trans participants, only 67% of the participants stated identifying within the gender binary, 33% stated having another gender identity.[5] In a recent European large-scale survey, similar results of 20% up to 36% of trans people identifying beyond a binary gender (e.g., agender, gender non-binary, genderflux, ...) were found.[6] Modern gender theories are based on these recent empirical findings and assume a variety of gender identities, with people identifying as male or female, to people who have a gender which is neither male nor female and may identify as both male and female at one time, as different genders at different times, as no gender at all, or dispute the very idea of any or only two genders.[7] A professional attitude should be characterised by respect and acceptance for this variety of gender identities, based on the knowledge that gender identity is very personal and only the individual knows this.

Trans people should be addressed with their desired pronouns and names. The request to use diverse pronouns (e. g., they) or the rejection of pronouns (e. g., for persons who identify gender-neutral or agender) should be taken just as seriously as the request of pronouns for women or men (e. g., for persons who identify as female or male). Since names and preferred pronouns, as well as gender experiences, may change in the course of a treatment, such changes should be taken into account.[8] Using the person's chosen name is associated with lower depression, suicidal ideation, and suicidal behaviour.[9]

In their everyday lives trans people often share the experience of social exclusion, lack of (legal) gender recognition, discrimination and stigmatisation, similar to members of other sexual or gender minorities. Rejection, non-affirmation, and victimization are strongly related to suicidal ideation through experiences of internalized transphobia and negative expectations.[10] The risk of minority stress and its severe implications is increased if further disadvantageous features are present such as a low socioeconomic status, physical and/or mental health issues, physical or mental disability, poor education, and migration.[11] These socioeconomic factors largely determine their possible

access to, and experiences with, trans health care services.[12] Furthermore, the increasing social protection of sexual and gender minorities against discrimination and exclusion plays an important role on the way to a better health of trans people.

The way in which relationships are formed in the health care of trans people is of central importance. In order to ensure a needs-based, flexible and individualised health care for sexual and gender minorities, HCPs should reflect on their own understandings of sex and gender.

Values

The evidence regarding the prevalence of and diversity in trans populations is consistent but limited, possibly implying care services are currently insufficient. Being respectful to trans people is paramount for any health care professional working with this population. In addition, understanding the vulnerabilities of some trans people may help when developing a client-centred treatment plan.

Remarks

Until recently, most evidence found is based on binary conceptions of transgender experiences, overlooking the gender diversity within the trans population. A European approach in the acquisition of inclusive prevalence data is timely, stressing the responsibility of European institutions and national governments to support this research. The organisation of trans health care will largely benefit from and be affected by this information.

Assessment of gender diverse children and adolescents

Statements

6. We advise that HCPs assessing gender diverse children and adolescents support the exploration and expression of the youth's experienced gender and help to reduce experienced barriers for those seeking care.
7. We advise that HCPs assessing gender diverse children and adolescents take a developmental approach that includes that gender related developmental pathways may be

more open to change in prepubescent gender diverse children compared to pubescent gender diverse adolescents and adults.

8. We advise that HCPs assessing gender diverse children and adolescents assess resilience and vulnerabilities, and treat (or refer for treatment) possible mental health problems.
9. We advise that HCPs assessing gender diverse children and adolescents support parents and/or legal guardian and school and other important social networks (when possible) to provide a safe and accepting home and school environment.
10. For prepubescent gender diverse children who desire to live in a role consistent with their experienced gender identity, we advise the HCPs advise that parents and the social environment consider social transitioning of the child after discussing the pros and the cons and while providing continuous psychological support.
11. For pubertal gender diverse adolescents, we advise that HCPs inform and explore all non-medical and medical options, including the effect that GAMIs (puberty blockers, hormones as well as surgical) may have on sexuality and fertility and if indicated, facilitate GAMIs.
12. In countries requiring an assessment process including a clinical diagnosis in order to access Gender Affirming Medical Intervention (GAMI), we advise that HCPs assessing trans adolescents for GAMI have the expertise in reaching the required diagnosis for their health service.

Evidence

Trans care clinics for youth have seen a sharp increase in referrals and interest over the last decades, reflecting the recognition that young children and adolescents can experience gender diversity and that children and families seek support.[13] Access to this sort of care is a serious concern in large parts of the world where there is still much stigma around gender diversity.

An important distinction between the age groups is that in many prepubescent gender diverse children the incongruence between birth assigned gender and experienced gender will remit before puberty although some criticise the follow-up studies with this finding.[14] Especially for prepubescent children who are not yet in need of medical interventions, it is therefore argued that a diagnosis of GIC should be removed from the classification systems.[15] However, at present, many health services globally require a diagnostic term to receive refunds from insurance.[16]

With regard to psychological functioning, gender diverse children and adolescents show higher rates of emotional and behavioural problems (depression, anxiety, suicidality, autism) than norm populations.[17-19] There is some evidence that youth who grow up in supportive environments that allow social transitioning and provide access to GAMI, may experience less distress.[20, 21] Other studies show a link between peer acceptance/poor peer relations, victimisation and mental health problems.[22, 23] Acceptance at home and at school is therefore important for the well-being of gender diverse children and adolescents.[23] Acceptance entails that the child is provided with enough space to explore gender diverse feelings on a continuous basis, without the expectations of a singular developmental pathway. This also includes exploring sexuality, and sexual relationships, as they in turn might shape gender identity processes.[24, 25]

For pubescent gender diverse adolescents, GAMI including puberty suppression as part of a broader approach with mental health support is helpful to reduce the distress accompanying the incongruence between physical (growing) sex characteristics and experienced gender.[21] Evidence for the effectiveness of this approach comes from studies that initiated pubertal suppression in trans adolescents after a careful assessment regarding the following; a) the adolescents shows a persistent and long lasting GIC that usually intensified or began around the start of puberty (and did not remit), b) the adolescents' co-occurring psycho-social difficulties should not interfere or hamper assessment or treatment, c) the adolescent understands the pros and cons of GAMI and has sufficient capacity to give informed consent, d) the adolescent has sufficient family or other social support to pursue GAMI, and e) the adolescent has actually experienced of the first physical pubertal changes (Tanner stage G2) since blocking is not necessary before that time and the experience of puberty is deemed important for gender identity development.[21]

It has been argued that as many health services globally require a diagnostic term to have access to health services, a diagnosis has been left in both classifications. Both the revisions of the diagnostic criteria of 'gender dysphoria' (GD) in the DSM-5 and of 'gender incongruence' (GIC) in the ICD-11 aim at extending the scope to include non-binary trans people.[1, 26] Gender identities or experiences that are outside the gender binary (men and women) are explicitly recognised for the first time ("alternative gender different from one's assigned gender"), without conceptualising an inherent degree of psychopathology.[26] Additionally, chromosomal variations and/or diverse sex developments (DSD) are no longer listed as exclusion criteria of GIC/GD.[26] Furthermore, both the ICD-11 and the DSM 5 have separate diagnostic criteria sets for a diagnosis in children and in

adolescents/adults respectively.[1, 26] Therefore, HCPs should know about the current diagnostic criteria and their implications (e. g., inclusion of genders that are beyond the gender binary, focus on GIC/GD, not on the identity of the person concerned), especially in countries where a referral from a mental health professional is needed for access to hormonal and/or surgical treatment.

Values

The evidence regarding the best assessment process for gender diverse children and adolescents is limited. Evidence regarding the prevalence of mental health problems in this population and the positive impact of GAMIs on mental health, quality of life and fertility is convincing. In case GAMIs are indicated, adolescents and their parents should be informed on the effect on their future sexual and reproductive health so they can reach an informed decision. Legally, in many European countries, adolescents cannot provide informed consent before age of majority and they need their parents for medical decision making.[27] However, in some member states, minors are capable of giving their consent and make their independent medical decisions at a certain age, or there is no fixed minimum age requirement for consent to medical treatments and each situation is treated individually depending on the maturity of the child.[27] From a psychological perspective we advise that trans adolescents are capable of making an independent informed medical decision while weighting the pros and cons of GAMI. As long as the adolescent lives in a family constellation, supporting the parents or other caretakers in providing a safe and supporting living situation is another preferred prerequisite.

Remarks

Clinicians working with gender diverse children and adolescents should have adequate knowledge and training or access to appropriate supervision. Assessment should take into consideration the evidence of a positive effect on mental health following social and psychological support and/or puberty suppression and/or hormonal treatment, and the effect on well-being of withdrawing these treatments.

Assessment of trans adults

Statements

13. We advise that HCPs working with trans people should inform trans adults seeking GAMI of its effect and assess the capacity of the individual to reach an informed consent regarding GAMI.
14. We advise that, in view of the strong evidence regarding the high levels of mental health problems in adults presenting at trans health services, particularly in those not on hormone treatment, HCPs whose role is informing and assessing the capacity to consent for GAMI in trans people wishing these interventions should have expertise in mental health in order to be able to identify those requiring further support from mental health professionals to allow for the best possible outcome of GAMI.
15. We advise that HCPs whose role is informing and assessing the capacity to consent for GAMI in trans people wishing these interventions, should explore resilience and social support, in view of its association with health-related quality of life and psychological wellbeing.
16. We advise that HCPs whose role is informing and assessing the capacity to consent for GAMI in trans people wishing these interventions, should inform clients about the effect that GAMIs (hormones as well as surgical) may have on sexual health and fertility.
17. In countries requiring an assessment process including a clinical diagnosis in order to access Gender Affirming Medical Intervention (GAMI), we advise that HCPs assessing trans adults for GAMI have the expertise in reaching the required diagnosis for their health service.

Evidence

HCPs working with trans adults should assess the individual's capacity to consent to GAMI.[28] In spite of the lack of evidence as to the best assessment process to follow, professionals working with the trans population should avoid being seen as gatekeepers.[29, 30] The role of the HCP will be to inform about GAMI and explain that the role of this intervention is to reduce GIC.[2]

Along with the increasing prevalence of non-binary trans adults, the clinical characteristics of GIC can be very different from individual to individual.[2] Additionally, differences with regard to their treatment wishes across trans people identifying as male or female and non-binary trans people (identifying as genderqueer, agender, non-binary, etc.) seem to be important.[31, 32]

In addition, professionals should be able to identify those who may present with mental health problems, not in order to stop the initiation of GAMI, but with the aim of increasing resilience and support achieving the best possible outcome of GAMI. The HCP may not be a mental health professional but they should have expertise in mental health in order to identify those who may require the input of a mental health professional.[2, 33] This is due to the evidence regarding the existence of higher levels of mental health problems, particularly depression,[34, 35] anxiety,[35, 36] suicidality and self-harm,[37] among people attending trans health services (pre-hormone treatment) when compared to the cisgender population.[38] Mental health problems are predicted by not being on hormone treatment,[38, 39] having poor social support,[39, 40] and lack of resilience.[41]

An important discussion to have with those seeking GAMI is the effect of treatment on sexual health and fertility. Few studies have explored the quality of sexual life in the trans population post GAMI. Sexual function, sexual desire and frequency of sexual activity, but also sexual satisfaction and pleasure can change after GAMI.[42, 43] Although the quality of sexual life improves post GAMI, research has demonstrated that it does not reach the levels of cisgender people.[44] But even if sexual function is impaired, the majority of participants report that they are more satisfied with their sexual life post-operatively.[45] This is particularly the case for trans AFAB people.[44, 46] There are significant gaps in the literature regarding sexual satisfaction and sexual health, with most studies using small convenience samples that do not allow for generalisation. In addition, most substantial literature focusses on sexual functioning only, and not on sexual satisfaction. Lastly, many studies are limited by the lack of validated measures.[42, 43] Similarly, GAMI will also affect fertility.[47] Therefore, as part of the assessment process HCPs whose role is informing and assessing the capacity to consent for GAMI in trans people wishing these interventions should inform trans people about the effects that GAMI may have on their sexual function and fertility.

Today's trans health care is coordinated best in a multimodal concept between community-based self-help, mental health counselling and/or treatment and various transition-related somatic interventions (e. g., hormone treatment, hair removal, speech therapy, surgeries).

As gender identity is very personal and only the individual knows this, it can be argued as to whether a professional is able to assess it.[4, 48] As a consequence, HCPs working in trans health services may not assess the individual's gender identity but their ability to understand the role of GAMI and their capacity to consent to treatment. Decisions on the necessity and sequence of interventions should be made in a participatory manner in the sense of agreement between treatment seekers and HCPs. In order to ensure individual trans health care in the long term, the therapeutic relationship should take into account both the body knowledge and self-determination of trans persons as well as the clinical expertise of HCPs.

As for gender diverse children and adolescents (see above), HCPs should know about the current diagnostic criteria and their implications (e. g., inclusion of genders that are beyond the gender binary, focus on GIC/GD, not on the identity of the person concerned), especially in countries where a referral from a mental health professional is needed for access to hormonal and/or surgical treatment.

Values

The evidence regarding the best assessment process is limited. However, evidence regarding the positive effect of GAMI on mental health, quality of life, suggests that professionals involved in the assessment of adults with a trans identity should have experience in trans health and be able to recognise those requiring further input of mental health professionals. The existence of a mental health problem should not be a reason not to commence of GAMI, unless the capacity to consent for this treatment is affected. The process for the initiation of GAMI should primarily include providing information to the person as to the effect of GAMI in their life, and to assess the capacity for decision making of the individual. The assessor should also explore factors affecting quality of life such as mental health problems, support systems and resilience as this may affect the outcome of GAMI.

Remarks

Previous findings on the outcome of multimodal treatment date from the classic treatment paradigm of binary transgender people, which excluded non-binary trans people.[49-51] Therefore, follow-up studies need to empirically examine the extent to which the paradigm shift in both assessment

and treatment reflected by the changes in diagnostic criteria from ICD-10 to ICD-11 actually leads to an improved health care for trans people. Standards regarding the assessment of trans people seeking GAMI that are evidence based are needed. Clinicians working in this field should have adequate knowledge, training and access to appropriate supervision. Assessment should take into consideration the evidence of a positive effect on wellbeing and mental health following hormonal treatment and the effect of withdrawing treatment in suicidality.

Hormone therapy in trans AFAB people

Statements

18. We advise initiating pubertal hormone suppression in trans adolescents, when gender incongruence or nonconformity is assessed, interfering psycho-social difficulties are addressed if possible, and after they show their first pubertal changes (Tanner stage G2) and when they have sufficient capacity to give informed consent.
19. We advise in adolescents desiring masculinising hormone treatment, when they have sufficient capacity to give informed consent, puberty induction with testosterone, often using a gradually increasing dose schedule.
20. We advise that before initiation of Gonadotropin-releasing hormone analogs (GnRHa) or progestogen and/or testosterone the hormone-prescribing physician should screen for conditions that may worsen with the start of treatment.
21. If masculinisation is desired, we advise testosterone therapy with monitoring of serum sex steroid levels and signs of virilisation.
22. We advise the hormone-prescribing physician discusses the effects and possible adverse health effects of GnRHa, progestogen and/or testosterone treatment, including fertility preservation options, based on the person's goals prior to any hormonal intervention.
23. We advise informing trans subjects on the expected changes upon GnRHa, progestogen and/or testosterone initiation on its effect on body satisfaction, on sexual function (desire and activity), and considering the role that factors such as relationship status and possible surgical interventions will play.

Evidence

Table 2:

	Mode of administration		Type	Dosage	Frequency
Testosterone	Parenteral	Intramuscular	Testosterone esters	200-250 mg	Every 2-3 weeks
			Testosterone undecanoate	1000 mg	Every 10-12 weeks
		Subcutaneous	Testosterone esters	75-125 mg	Every week
	Transdermal		Androgen gel	25-100 mg	Once daily
	Oral		Testosterone undecanoate	160 mg	Once or twice daily
Progestational agents	Oral		Lynesterol	5 – 10 mg	Once daily
			Medroxyprogesterone	5 – 10 mg	Once daily
	Parenteral		Medroxyprogesterone	150 mg	Once every three months

If desired, trans adolescents usually start with GnRH α to inhibit female pubertal development, such as breast formation and menses, after they show their first pubertal changes (Tanner stage G2) and when they have sufficient capacity to give informed consent and interfering psycho-social difficulties are addressed, acknowledging that in many occasions they may not be resolved which should not affect the decision to initiate GnRH α .^[52] A male pubertal induction is obtained using an increasing dose of testosterone.^[3] Late adolescents often start testosterone ester at 75 mg intramuscular every two weeks, followed by the maintenance dosage after 6 months. If started,

GnRHa are advised to be continued at least until the maintenance dosage of testosterone is reached and to be continued until gonadectomy. In late-pubertal trans AFAB people menses can be suppressed using a progestational agent. GnRHa treatment may induce adverse effects on fertility and bone mineralisation, and effects on brain development remain unknown.[3]

Trans men and non-binary AFAB people desiring masculinisation often opt for testosterone therapy with the aim to change their physical appearance to better match their gender identity. This may range from a more androgynous presentation to maximal virilisation.[3] Testosterone therapy that is initiated and monitored by a medical professional rarely leads to adverse events.[53] Before initiation of testosterone the hormone-prescribing physician needs to screen for conditions that may worsen with the start of virilising treatment, such as polycythaemia, sleep apnoea, deep vein thrombosis, pulmonary embolism, or untreated arterial hypertension. Absolute contraindications for testosterone therapy are (desired) pregnancy or lactation. If hormone therapy is contraindicated due to serious health conditions, access to non-hormonal medical interventions should be considered.[3]

The preferred options for GAMI and monitoring in trans AFAB people have been summarised recently.[3] Often, the principles of hormone replacement therapy in hypogonadism with the aim to reach cisgender male testosterone levels are followed. If oophorectomy was performed, testosterone treatment is usually continued lifelong to avoid symptoms of hypogonadism, such as vasomotor symptoms and osteoporosis. If induction of amenorrhea is desired and does not occur with testosterone treatment alone, the addition of a progestational agent or GnRHa may be considered.[54] If hysterio-oophorectomy was performed, this additional medication can be stopped. Laboratory monitoring of sex steroid levels and haematocrit is advised every three months in the first year, and once or twice yearly thereafter.[3] As many trans people have a desire for parenthood, reproductive options should be addressed by the health care providers at each stage of the gender affirming process. It is advised to preserve oocytes, ovarian tissue, or embryos before the initiation of gender affirmation therapies, if a genetically related parental desire exists, to avoid emotional difficulties when interrupting testosterone therapy in order to preserve germ cells.[55]

Masculinising effects of testosterone treatment may include lowering of the voice, interruption of menses (if still present), appearance of male-pattern facial and body hair or male pattern baldness, increased prevalence and severity of acne, clitoral enlargement, increased muscle mass and strength and decreased fat mass. Height and bone structure will remain unchanged, as will the degree of

subcutaneous fat, unless physical activity is increased. Clitoral growth has been described up to 3.19 +/- 0.54 cm (+ 60%) after 3 months of testosterone treatment, and to 3.83 +/- 0.42 cm after two years of testosterone treatment.[56] Longer follow-up data are currently not available. Vaginal and cervical atrophy may lead to vaginal dryness, itching and painful penetration, for which over-the-counter lubricants may be helpful. If cervical tissue is present, and if mastectomy was not performed, monitoring is recommended as in cisgender females.

The literature on sexual functioning in the trans people desiring masculinisation is scarce and cannot be generalised, given the diversity within this group.[43] Therefore they should need to be evaluated in this domain according to many variables, such as e.g. the use of testosterone treatment, and modalities of genital surgery. The role of having a partner or presence of mental health symptomatology on sexual function should also not be underestimated.[57] A higher sexual desire in trans AFAB people who had recently started testosterone therapy was described.[46] Other studies noted an increase in sexual desire, fantasies, arousal and frequency of masturbation after one year of testosterone therapy.[58] Also, more sexual satisfaction, more sexual excitement, more easily reaching orgasm[45], and mostly (70%) an increase in sexual desire have been described in longer-term follow-up.[42, 46, 59]

Safety

Currently, there is no evidence for an increase in short and midterm cardiovascular adverse outcomes in trans people on testosterone treatment.[60-62] Data on older trans AFAB people are scarce but statements based on clinical experience are in favour of continuing testosterone.[60] As for independent cardiac risk factors, the decrease in high-density lipoprotein cholesterol, and increase in triglycerides and low-density lipoprotein cholesterol have been shown.[61] Haematocrit increases in the first year (+ 4.4 – 17.6% range), stabilising afterwards, within the reference range for cisgender men and rarely inducing clinically significant erythrocytosis.[63] Thromboembolic events are also reported to be rare.[64] Increase in insulin resistance or hepatotoxicity are not anticipated with parenteral or transdermal testosterone.[3] There is also no decrease in bone density to be expected,[65] even though there are very limited data on the risk of osteoporotic fractures. Osteoporosis screening should be performed especially in those who stop testosterone treatment after gonadectomy, or in those with limited compliance with therapy or with other risks for bone loss.[3] Oncological data in trans AFAB people are limited to few case-reports, recently

summarised: one vaginal, one cervical, seven breast, three ovarian and one endometrial cancers have been described to date.[66]

Updated legislation in many European countries have omitted the need for gonadectomy for legal gender affirmation, so that the number of trans AFAB people who do not choose hysterectomy is expected to increase.[67] Cervical smears are reported to be less frequently performed in trans AFAB people compared to cisgender women.[68] Large-scale prospective studies will be needed to evaluate the risk of trans AFAB people on testosterone treatment who did not undergo mastectomy or hysterectomy. Professionals should adhere to the established screening protocols based on the anatomical situation.

Values

In adolescent transgender care, puberty suppression has become an important element, even if long-term success is not well-documented so far. However, denying medical intervention is potentially harmful.

Knowledge of the short and midterm effects of testosterone in trans AFAB people shows rarely serious adverse events leading to interruption of treatment. In addition, serious adverse events leading to interruption of treatment are rarely encountered, if guided by a hormone-prescribing physician.

Remarks

The information on sexual function and satisfaction in trans AFAB people is quite limited, but most of the available literature points towards an improvement in sexual desire, activity, and satisfaction with testosterone treatment.

This information is based on convenience samples of trans AFAB people who underwent genital surgery. There is a lack of literature on the effect of hormonal therapy in non-binary population or on trans men who did not undergo genital surgery.

Hormone therapy in trans AMAB people

Statements

24. We advise initiating pubertal hormone suppression in trans adolescents, when gender incongruence or nonconformity is assessed, interfering psycho-social difficulties are addressed if possible, and after they show their first pubertal changes (Tanner stage G2) and when they have sufficient capacity to give informed consent.
25. We advise in adolescents desiring feminising hormone treatment, when they have sufficient capacity to give informed consent, puberty induction with 17beta-estradiol, often using a gradually increasing dose schedule.
26. We advise that before initiation of GnRHa or anti-androgens and/or estrogens treatment the hormone-prescribing physician needs to screen for conditions that may worsen with the start of treatment.
27. If feminisation is desired, we advise estrogens and/or anti-androgen therapy with monitoring of serum sex steroid levels and signs of feminisation.
28. We advise the hormone-prescribing physician discusses the effects and possible adverse health effects of GnRHa, anti-androgens, and/or estrogen treatment, including fertility preservation options and consequences for genital surgery, based on the person's goals prior to any hormonal intervention.
29. We advise informing trans clients on the expected changes upon GnRHa, estrogen and/or anti-androgen initiation and its effect on body satisfaction, sexual desire and activity, and considering the role factors such as relationship status and possible surgical interventions can play.

Evidence

Table 2

	Mode of Administration	Type	Total Dose	Frequency
--	------------------------	------	------------	-----------

Estrogen	Oral	Estradiol (17 beta-estradiol valerate)	2-6 mg	Once or twice daily
	Parenteral (intramuscular)	Estradiol valerate	5-30mg	Every 1-2 weeks
		Estradiol cypionate	2-10 mg	Every week
	Transdermal	Estradiol patch	25-100 µg/ 24h	New patch every 3days
		Estradiol gel	1,5 mg	Once or twice daily
Antiandrogens	Oral	Spironolactone Cyproterone acetate	100mg 10-50mg	Once or twice daily
GnRH agonists	Intramuscular	Triptorelin	11.23 mg	3-Monthly
	Intramuscular or subcutaneous	Triptorelin	3.75 mg	Monthly

If desired, trans adolescents can start GnRHa when Tanner stage is over G2 to inhibit male pubertal development and when they have sufficient capacity to give informed consent and interfering psycho-social difficulties are addressed, acknowledging that in many occasions they may not be resolved which should not affect the decision to initiate GnRHa.[56] A female pubertal induction is obtained using increasing dose of estrogens (usually 17-beta estradiol).[56] GnRHa should be continued at least until the maintenance dosage of estradiol is reached, and is advised to be continued until gonadectomy. In late-pubertal trans AMAB people endogenous androgen production can be suppressed using antiandrogens such as cyproterone acetate (CPA).[3]

Some trans women and non-binary individuals AMAB may seek hormonal treatment in order to make their body more congruent with their gender identity. Antiandrogen and/or estrogen treatment initiated and monitored by an experienced medical professional rarely leads to adverse events.[54]

Before starting treatment, the treating clinician should evaluate and address conditions that can be exacerbated by this treatment, such as thromboembolic diseases, breast cancer, macroprolactinoma, coronary artery disease, cerebrovascular disease, cholelithiasis, and hypertriglyceridemia.[3] If hormone therapy is contraindicated due to serious health conditions, access to non-hormonal interventions should be considered according to the wish of the person.

In order to induce (more) feminine secondary sex characteristics and/or to reduce the masculine ones, estrogens and/or anti-androgens can be used. The debate on the use of progesterone is ongoing, caused by a lack of data.[3] A wide range of estrogenic compounds exists, of which 17beta-estradiol (oral 2-6 mg/d or transdermal) represents the treatment of choice. Estrogen dosage should be adjusted in order to maintain serum estradiol at the level for premenopausal females (100-200 pg/ml), although timing of treatment intake may affect blood concentrations. The most commonly antiandrogen used drug in Europe is CPA (oral 10 to 50 mg, once daily), a progestin with antiandrogenic properties. GnRHa are also effective in reducing testosterone levels with a low risk of adverse effects.[3]

Cessation of tobacco use should be strongly recommended to avoid increased risk of thromboembolism and cardiovascular complications.[3] Traditionally, physicians advise estrogens should be stopped some weeks before any elective surgical intervention (including gender-affirming surgery), and can be resumed once the person is fully mobilised.[3] However, practices are changing based on emerging literature.[69] After gonadectomy, estrogen treatment should be continued, in order to avoid the signs and symptoms associated with hypogonadism and to avoid osteoporosis. There is no consensus on whether hormonal treatment has to be stopped when trans women and non-binary individuals AMAB get older, mirroring the post-menopausal milieu.

Many persons seeking feminisation are interested in using their own cryopreserved sperm to fulfil a future child wish[70]; thus fertility preservation techniques should be discussed and offered before starting hormone treatment.[55] Indeed, sperm cryopreservation, surgical sperm extraction and testicular tissue cryopreservation can be proposed.

The most studied effect of feminising hormonal treatment is represented by breast development, which seems to be the only physical modification significantly correlated with the reduction of body dissatisfaction in trans AMAB people.[71] However, less than 20% of trans AMAB people reach a Tanner breast stage 4-5 after 2 years of treatment,[71] explaining why 50-60% seek augmentation mammoplasty.[72] Testis volume decreases by 40% after one year of therapy, making it easier to hide genitals and, thus, alleviating the perceived psychological distress.[71] Changes in fat distribution have been reported, with a decrease of lean body mass and an increase of subcutaneous body fat.[63] Hormonal treatment also induces a reduction in facial and body hair, as well as a decreased oiliness of skin.[71, 73] Complete removal of male sexual hair requires electrolysis or laser treatment or both. No voice changes are to be expected.[74]

A decrease in sexual desire, spontaneous erections and male sexual dysfunction, often desired, are usually observed within 1-3 months after starting hormonal treatment.[3] According to a recent study, having a partner, being on hormone treatment, and having undergone some breast surgery have been associated with a better subjective perception of sexuality.[57] However, despite high rates of trans people declaring that they are dissatisfied with their sexual life before GAMIs,[57] only few studies have investigated sexual functioning and satisfaction in trans AMAB people and are mostly focused on genital surgery outcomes.[2, 42, 45, 57, 59, 75, 76] Indeed, studies evaluating the effect of hormonal intervention on sexual health, desire and arousability, and satisfaction are few and show contradictory results.[46, 59, 77, 78]

Safety

Among the possible adverse outcomes of hormonal treatment in trans AMAB people, a specific area of concern is represented by cardiovascular disease. According to a recent meta-analysis including 3231 trans AMAB people with a follow-up range from 3 months to 41 years, only a significant increase in triglycerides was observed during hormonal treatment.[61] Regarding the incidence of acute cardiovascular events, the largest available cohort study showed higher rates of venous thromboembolism and, to a lesser extent, ischemic stroke in trans AMAB people compared to cisgender men and women.[64] In addition, myocardial infarction rates were greater among trans AMAB people than in matched cisgender women, but similar to those observed among cisgender men. However, given the low quality of evidence due to the methodological limitations of the included studies, and heterogeneity of treatment, further research is needed to better clarify the cardiovascular effects of hormone therapy in trans AMAB people.

An increase in lumbar spine bone mineral density has been reported with hormonal treatment in trans AMAB people, with a low rate of fractures.[65, 79] The prevalence of hormone sensitive cancers seems to be low among trans AMAB people during hormonal treatment.[66]

Values

Even if so far long-term success is not well-documented in adolescent transgender care, puberty suppression has become an important element. Denying medical intervention may be potentially harmful. Short and midterm effects of feminising are largely beneficial, and the possible side

effects of not receiving treatment when requested outweigh the potential risks of this treatment. In addition, serious adverse events leading to interruption of treatment are rarely encountered, if guided by a hormone-prescribing physician.

Remarks

To date, only a limited number of studies have investigated sexual satisfaction in trans AMAB persons and are mostly focused only on sexual function and satisfaction after genital affirming surgery. Studies specifically focused on non-binary individuals or on trans women who did not undergo genital surgery are missing.

Sexual functioning and satisfaction in relation to surgical treatment in trans people

Statements

30. We advise HCPs should be aware of potential sexual problems during all surgical phases of treatment.
31. We advise that regardless of surgical pathways, HCPs should be aware of diversity in sexual practices in trans people.
32. We advise that surgeons performing Gender Affirming Surgery (GAS) collaborate with sexologists with knowledge and experience with trans people, if available.

Evidence

Gender Affirming Surgery (GAS) is an umbrella term for a variety of surgical procedures.[80] It is important to know that trans people may or may not follow a standard linear progression to hormones and then surgical procedures.[81] They may not choose surgical interventions for several reasons, including sexual motivations.[32] Surgeons interested in GAS are recommended in anticipation of a probably more liberal approach for the upcoming SOC8, to get acquainted with the surgical chapters in the Standards of Care for transgender and gender non-conforming people,

version 7 (SOC7) from the World Professional Association for Transgender Health (WPATH) where all details can be found about the multidisciplinary aspect of care and timing of surgery.[2] Medical contraindications are assessed by the responsible surgeon and anaesthesiologist who should maintain safety criteria according to American Surgical Association (ASA). The trans person should be well informed on the negative effects of smoking and/or a body mass index (BMI) of less than 18 and more than 30 kg/m². [82-84]

Surgical procedures for feminising GAS are orchiectomy, vulvoplasty (no vaginal cavity is made), vulvo-vaginoplasty, breast augmentation, voice surgery, chondrolaryngoplasty and facial feminisation. In vulvo-vaginoplasty the inner lining is made with penile skin, skin grafts, penile skin combined with skin grafts or a bowel segment.[85, 86] The base of the penis and the perineoscrotal region that will form vaginal inner lining or will be placed around the clitoris should be depilated permanently. Otherwise hair growth within the neo-vagina can cause discharge or odour.

Surgical procedures for masculinising GAS are mastectomy, removal of female sexual organs, metoidioplasty and phalloplasty. Urethral lengthening, optional in both metoidioplasty and phalloplasty, entails a higher complication risk. Urethral lengthening is often done with skin of the forearm. To prevent hair growth inside the urethra, depilation is advised, because discharge and voiding problems can occur. If desired, a colectomy may need to precede in some centres.[87] Removal of female sexual organs can be done individually or all at once (hysterectomy, ovariectomy and colectomy). If a colectomy will be performed, a hysterectomy must also be performed. The ovaries may remain in situ, upon request.

Voiding problems can occur in genital GAS, implying it is advisable to co-operate with a urologist when offering care for trans individuals, so consultation is possible when needed before, during surgery and after surgery. In an ideal setting, collaboration with pelvic physiotherapists is advisable for voiding problems after GAS and accessibility problems of the vagina after a vaginoplasty, during dilation or sexual contact.

The potential sexual problems trans people encounter may occur in all phases of surgical treatment. Collaboration with a sexologist with knowledge and experience with trans people is recommended. Overall results lean towards favourable sexual outcomes after genital surgeries in trans people, although research into the quality of sexual life in the trans population post GAMI is limited.[44]

The majority of post-surgical AMAB people report satisfaction with their sexual life post-operatively.[45]

In the majority of trans AFAB people with metoidioplasty, voiding while standing as well as penetrative sexual intercourse is not reached.[88] However, regarding sexual satisfaction, patient-reported satisfaction with sexual function and aesthetic outcome is very high (up to 100%), and no problems with sexual arousal, masturbation, or orgasms were reported.[89, 90]

In trans AFAB people with phalloplasty, sexual activity was higher (masturbation and with partner), and they used their genitals more frequently during sex compared with before surgery (31-78%).[91] Sexual expectations were more frequently met in the group with an erection prosthesis (compared to those without), but pain during intercourse was more often reported.[45] However, in most of the studies that were selected in the review period, the overall data were limited, heterogeneous, of very low quality, and validated measurement tools were missing. There is a strong need for future research, which should focus on the development of validated tools to assess postsurgical sexual outcomes.

Because of the lack of psychosexual education or guidance during the hormonal and post-operative phase, combined with low sexual experience, most trans people lack knowledge of the new anatomy, ways of sexual stimulation and getting aroused and what changes can be expected. Pain with penetration can occur after genital feminisation and masculinisation, and it is important to explore the right cause of the pain before planning a hastily surgical correction.[92-94] Phantom pain after vaginoplasty is one of the lesser known problems and should be taken seriously.[95]

Values

The ESSM emphasises the importance to share the responsibility in the decision making process towards surgery together with all involved HCPs and to keep well written documentation of the met criteria for a specific surgical treatment.

Remarks

To date, validated tools helping the choice for interventions for trans people are lacking. Sexual outcomes are mostly postsurgical while other phases are underexposed. There is need for future research, to focus on the development of validated tools to assess sexuality in trans people.

Conclusion

We presented with this document an up-to-date ESSM position statement on trans health care, with attention for sexual functioning and satisfaction. The data on trans health care are rapidly emerging, and all suggestions and statements are based on the currently available data, acknowledging this is a rapidly changing field.

Limitations

The primary aim of the position statement was to formulate clinical consensus statements for European clinicians working in the field of transgender health in view of the recent change in the clinical diagnosis use in transgender health in the ICD-11.[1] The paper also aims to provide recommendations regarding sexual health care of trans people, although due to the limited amount of publications the recommendations that can be provided in this area are minimal. Furthermore, this position paper does not aim to provide detailed clinical guidelines for professionals such as those from the WPATH or the Endocrine Society.[2, 3]

Acknowledgements

The authors wish to thank Mario Maggi, Marieke Dewitte, Cobi Reisman, and Giovanni Corona for their constructive remarks and feedback. The final draft was accepted by the ESSM Executive Committee and the ESSM affiliated societies, except for the DGSMTW (Deutsche Gesellschaft für Sexualmedizin, Sexualtherapie und Sexualwissenschaft).

References

1. World Health Organisation. *International Classification of Diseases 11th Revision*. Genf: World Health Organisation. 2018; Available from: <https://icd.who.int/>.
2. Coleman, E., et al., *Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People, Version 7*. International Journal of Transgenderism, 2012. **13**(4): p. 165-232.
3. Hembree, W.C., et al., *Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline*. Endocr Pract, 2017. **23**(12): p. 1437.
4. Arcelus, J. and W.P. Bouman, *Language and terminology*, in *The Transgender Handbook: A guide for transgender people, their families and professionals* W.P. Bouman and J. Arcelus, Editors. 2017, Nova: New York.
5. Grant, J.M., et al., *Injustice at every turn: A report of the National Transgender Discrimination Survey*. 2011, National Center for Transgender Equality and National Gay and Lesbian Task Force: Washington, DC.
6. European Union Agency for Fundamental Rights, *Being trans in the European Union. Comparative analysis of EU LGBT survey data*. 2014, Publications Office of the European Union: Luxembourg.
7. Richards, C., et al., *Non-binary or genderqueer genders*. International Review of Psychiatry, 2016. **28**(1): p. 95-102.
8. Auer, M.K., et al., *Transgender transitioning and change of self-reported sexual orientation*. PLoS One, 2014. **9**(10): p. e110016.
9. Russell, S.T., et al., *Chosen Name Use Is Linked to Reduced Depressive Symptoms, Suicidal Ideation, and Suicidal Behavior Among Transgender Youth*. Journal of Adolescent Health, 2018. **63**(4): p. 503-505.
10. Testa, R.J., et al., *Suicidal ideation in transgender people: Gender minority stress and interpersonal theory factors*. Journal of abnormal psychology, 2017. **126**(1): p. 125-136.
11. Thorne, N., et al., *A comparison of mental health symptomatology and levels of social support in young treatment seeking transgender individuals who identify as binary and non-binary*. International Journal of Transgenderism, 2018: p. 1-10.
12. Loos, F.K., et al., *[Subjective indicators of treatment success and experiences of discrimination in interdisciplinary trans* healthcare. Qualitative results from an online survey]*. Zeitschr Sexualforsch, 2016. **29**(03): p. 205-223.
13. Turban, J.L., et al., *Transgender and gender non-conforming youth*, in *IACAPAP e-Textbook of Child and Adolescent Mental Health*, J.M. Rey, Editor. 2018, International Association for Child and Adolescent Psychiatry and Allied Professions Geneva.
14. Steensma, T.D. and P.T. Cohen-Kettenis, *A critical commentary on "A critical commentary on follow-up studies and "desistence" theories about transgender and gender non-conforming children"*. International Journal of Transgenderism, 2018. **19**(2): p. 225-230.
15. Winter, S., et al., *The Proposed ICD-11 Gender Incongruence of Childhood Diagnosis: A World Professional Association for Transgender Health Membership Survey*. Archives of Sexual Behavior, 2016. **45**(7): p. 1605-1614.

16. Beek, T.F., et al., *Gender Incongruence of Adolescence and Adulthood: Acceptability and Clinical Utility of the World Health Organization's Proposed ICD-11 Criteria*. PloS one, 2016. **11**(10): p. e0160066.
17. Leibowitz, S. and A.L. de Vries, *Gender dysphoria in adolescence*. Int Rev Psychiatry, 2016. **28**(1): p. 21-35.
18. Ristori, J. and T.D. Steensma, *Gender dysphoria in childhood*. Int Rev Psychiatry, 2016. **28**(1): p. 13-20.
19. Van Der Miesen, A.I., H. Hurley, and A.L. De Vries, *Gender dysphoria and autism spectrum disorder: A narrative review*. Int Rev Psychiatry, 2016. **28**(1): p. 70-80.
20. Olson, K.R., et al., *Mental health of transgender children who are supported in their identities*. Pediatrics, 2016. **137**(3): p. peds. 2015-3223.
21. de Vries, A.L., et al., *Young adult psychological outcome after puberty suppression and gender reassignment*. Pediatrics, 2014. **134**(4): p. 696-704.
22. de Vries, A.L., et al., *Poor peer relations predict parent- and self-reported behavioral and emotional problems of adolescents with gender dysphoria: a cross-national, cross-clinic comparative analysis*. Eur Child Adolesc Psychiatry, 2016. **25**(6): p. 579-88.
23. Ryan, C., et al., *Family acceptance in adolescence and the health of LGBT young adults*. Journal of Child and Adolescent Psychiatric Nursing, 2010. **23**(4): p. 205-213.
24. Bungener, S.L., et al., *Sexual and romantic experiences of transgender youth before gender-affirmative treatment*. Pediatrics, 2017. **139**(3): p. e20162283.
25. Steensma, T.D., et al., *Desisting and persisting gender dysphoria after childhood: A qualitative follow-up study*. Clinical child psychology and psychiatry, 2011. **16**(4): p. 499-516.
26. American Psychiatric Association, *Diagnostic and Statistical manual of mental disorders. 5th edition*. 2013, Washington, DC: American Psychiatric Association.
27. European Union Agency for Fundamental Rights, *Minimum age requirements concerning children's rights in the EU - Specific data on Marriage and sexual consent; Citizenship; Political Participation; Religion; Health*. 2017, European Union Agency for Fundamental Rights.
28. Radix, A. and J. Eisfeld, *[Informend Consent in Transgender Care. Perspectives from a US-based Community Health Center]*. Zeitschr Sexualforsch, 2014. **27**(01): p. 31-43.
29. Keo-Meier, C.L. and K.M. Fitzgerald, *Affirmative Psychological Testing and Neurocognitive Assessment with Transgender Adults*. Psychiatric Clinics of North America, 2017. **40**(1): p. 51-64.
30. Eyssel, J., et al., *Needs and concerns of transgender individuals regarding interdisciplinary transgender healthcare: A non-clinical online survey*. PLoS ONE, 2017. **12**(8): p. e0183014.
31. Koehler, A., J. Eyssel, and T.O. Nieder, *Genders and Individual Treatment Progress in (Non-)Binary Trans Individuals*. The Journal of Sexual Medicine, 2018. **15**(1): p. 102-113.
32. Beek, T.F., et al., *Partial Treatment Requests and Underlying Motives of Applicants for Gender Affirming Interventions*. The Journal of Sexual Medicine, 2015. **12**(11): p. 2201-2205.
33. Nieder, T.O., et al., *[Trans healthcare : Between depsychopathologization and a needs-based treatment of accompanying mental disorders]*. Nervenarzt, 2017. **88**(5): p. 466-471.

34. Witcomb, G.L., et al., *Levels of depression in transgender people and its predictors: Results of a large matched control study with transgender people accessing clinical services*. Journal of Affective Disorders, 2018. **235**: p. 308-315.
35. Heylens, G., et al., *Psychiatric characteristics in transsexual individuals: multicentre study in four European countries*. Br J Psychiatry, 2014. **204**(2): p. 151-6.
36. Millet, N., J. Longworth, and J. Arcelus, *Prevalence of anxiety symptoms and disorders in the transgender population: A systematic review of the literature*. International Journal of Transgenderism, 2017. **18**(1): p. 27-38.
37. Arcelus, J., et al., *Risk factors for non-suicidal self-injury among trans youth*. The journal of sexual medicine, 2016. **13**(3): p. 402-412.
38. Dhejne, C., et al., *Mental health and gender dysphoria: A review of the literature*. International Review of Psychiatry, 2016. **28**(1): p. 44-57.
39. Davey, A., et al., *Social Support and Psychological Well-Being in Gender Dysphoria: A Comparison of Patients With Matched Controls*. The Journal of Sexual Medicine, 2014. **11**(12): p. 2976-2985.
40. Köhler, A., et al., *[Treatment Experiences and Social Support in Individuals with Gender Incongruence/Gender Dysphoria - A ENIGI 5 Year Follow-Up Study in Three European Countries]*. Psychother Psychosom Med Psychol, 2019.
41. Bockting, W.O., et al., *Stigma, Mental Health, and Resilience in an Online Sample of the US Transgender Population*. American Journal of Public Health, 2013. **103**(5): p. 943-951.
42. Klein, C. and B.B. Gorzalka, *Sexual Functioning in Transsexuals Following Hormone Therapy and Genital Surgery: A Review (CME)*. Journal of Sexual Medicine, 2009. **6**(11): p. 2922-2939.
43. Stephenson, R., et al., *The Sexual Health of Transgender Men: A Scoping Review*. Journal of sex research, 2017. **54**(4-5): p. 424-445.
44. Nobili, A., C. Glazebrook, and J. Arcelus, *Quality of life of treatment-seeking transgender adults: A systematic review and meta-analysis*. Reviews in Endocrine and Metabolic Disorders, 2018.
45. De Cuypere, G., et al., *Sexual and physical health after sex reassignment surgery*. Archives of Sexual Behavior, 2005. **34**(6): p. 679-90.
46. Wierckx, K., et al., *Sexual desire in female-to-male transsexual persons: exploration of the role of testosterone administration*. European journal of endocrinology, 2011. **165**(2): p. 331-7.
47. Chen, D., et al., *Attitudes Toward Fertility and Reproductive Health Among Transgender and Gender-Nonconforming Adolescents*. Journal of Adolescent Health, 2018. **63**(1): p. 62-68.
48. Güldenring, A.-K., *A critical view of transgender health care in Germany: Psychopathologizing gender identity – Symptom of ‘disordered’ psychiatric/psychological diagnostics?* Int Rev Psychiat, 2015. **27**(5): p. 427–434.
49. White Hughto, J.M. and S.L. Reisner, *A Systematic Review of the Effects of Hormone Therapy on Psychological Functioning and Quality of Life in Transgender Individuals*. Transgend Health, 2016. **1**(1): p. 21-31.
50. Murad, M.H., et al., *Hormonal therapy and sex reassignment: A systematic review and meta-analysis of quality of life and psychosocial outcomes*. Clinical Endocrinology, 2010(72): p. 214–231.

51. Sutcliffe, P.A., et al., *Evaluation of surgical procedures for sex reassignment: a systematic review*. J Plast Reconstr Aesthet Surg, 2009. **62**(3): p. 294-306.
52. Cohen-Kettenis, P.T., H.A. Delemarre-van de Waal, and L.J.G. Gooren, *The Treatment of Adolescent Transsexuals: Changing Insights*. The Journal of Sexual Medicine, 2008. **5**(8): p. 1892-1897.
53. Wierckx, K., et al., *Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the European network for the investigation of gender incongruence*. The journal of sexual medicine, 2014. **11**(8): p. 1999-2011.
54. Wierckx, K., et al., *Long-term evaluation of cross-sex hormone treatment in transsexual persons*. J Sex Med, 2012. **9**(10): p. 2641-51.
55. De Roo, C., et al., *Fertility options in transgender people*. Int Rev Psychiatry, 2016. **28**(1): p. 112-9.
56. Fisher, A.D., et al., *Medical treatment in gender dysphoric adolescents endorsed by SIAMS-SIE-SIEDP-ONIG*. J Endocrinol Invest, 2014. **37**(7): p. 675-87.
57. Bartolucci, C., et al., *Sexual quality of life in gender-dysphoric adults before genital sex reassignment surgery*. J Sex Med, 2015. **12**(1): p. 180-8.
58. Costantino, A., et al., *A prospective study on sexual function and mood in female-to-male transsexuals during testosterone administration and after sex reassignment surgery*. Journal of sex & marital therapy, 2013. **39**(4): p. 321-35.
59. Wierckx, K., et al., *Sexual Desire in Trans Persons: Associations with Sex Reassignment Treatment*. Journal of Sexual Medicine, 2014. **11**(1): p. 107-118.
60. Gooren, L.J. and G. T'Sjoen, *Endocrine treatment of aging transgender people*. Reviews in endocrine & metabolic disorders, 2018.
61. Maraka, S., et al., *Sex Steroids and Cardiovascular Outcomes in Transgender Individuals: A Systematic Review and Meta-Analysis*. J Clin Endocrinol Metab, 2017. **102**(11): p. 3914-3923.
62. van Kesteren, P.J., et al., *Mortality and morbidity in transsexual subjects treated with cross-sex hormones*. Clinical endocrinology, 1997. **47**(3): p. 337-42.
63. Defreyne, J., et al., *Prospective evaluation of hematocrit in gender-affirming hormone treatment: results from European Network for the Investigation of Gender Incongruence*. Andrology, 2018. **6**(3): p. 446-454.
64. Getahun, D., et al., *Cross-sex Hormones and Acute Cardiovascular Events in Transgender Persons A Cohort Study*. Annals of Internal Medicine, 2018. **169**(4): p. 205-+.
65. Singh-Ospina, N., et al., *Effect of Sex Steroids on the Bone Health of Transgender Individuals: A Systematic Review and Meta-Analysis*. J Clin Endocrinol Metab, 2017. **102**(11): p. 3904-3913.
66. Braun, H., et al., *Cancer in Transgender People: Evidence and Methodological Considerations*. Epidemiol Rev, 2017. **39**(1): p. 93-107.
67. Motmans, J., J. Defreyne, and E. Wyverkens, *Being transgender in Belgium. Ten years later*. 2018, Brussels: Institute for the equality of women and men.
68. Peitzmeier, S.M., et al., *Pap test use is lower among female-to-male patients than non-transgender women*. American journal of preventive medicine, 2014. **47**(6): p. 808-12.
69. Gaither, T.W., et al., *Postoperative Complications following Primary Penile Inversion Vaginoplasty among 330 Male-to-Female Transgender Patients*. The Journal of urology, 2018. **199**(3): p. 760-765.

70. Wierckx, K., et al., *Sperm freezing in transsexual women*. Arch Sex Behav, 2012. **41**(5): p. 1069-71.
71. Fisher, A.D., et al., *Cross-Sex Hormone Treatment and Psychobiological Changes in Transsexual Persons: Two-Year Follow-Up Data*. J Clin Endocrinol Metab, 2016. **101**(11): p. 4260-4269.
72. Wierckx, K., L. Gooren, and G. T'Sjoen, *Clinical review: Breast development in trans women receiving cross-sex hormones*. J Sex Med, 2014. **11**(5): p. 1240-7.
73. Giltay, E.J. and L.J. Gooren, *Effects of sex steroid deprivation/administration on hair growth and skin sebum production in transsexual males and females*. J Clin Endocrinol Metab, 2000. **85**(8): p. 2913-21.
74. Van Damme, S., et al., *The Effectiveness of Pitch-raising Surgery in Male-to-Female Transsexuals: A Systematic Review*. J Voice, 2017. **31**(2): p. 244.e1-244.e5.
75. Cerwenka, S., et al., *Sexual behavior of gender-dysphoric individuals before gender-confirming interventions: a European multicenter study*. J Sex Marital Ther, 2014. **40**(5): p. 457-71.
76. Selvaggi, G., et al., *Genital sensitivity after sex reassignment surgery in transsexual patients*. Ann Plast Surg, 2007. **58**(4): p. 427-33.
77. Elaut, E., et al., *Hypoactive sexual desire in transsexual women: prevalence and association with testosterone levels*. Eur J Endocrinol, 2008. **158**(3): p. 393-9.
78. Wierckx, K., et al., *Quality of Life and Sexual Health after Sex Reassignment Surgery in Transsexual Men*. Journal of Sexual Medicine, 2011.
79. Wiepjes, C.M., et al., *Bone Mineral Density Increases in Trans Persons After 1 Year of Hormonal Treatment: A Multicenter Prospective Observational Study*. J Bone Miner Res, 2017. **32**(6): p. 1252-1260.
80. Colebunders, B., et al., *An Update on the Surgical Treatment for Transgender Patients*. Sexual Medicine Review, 2017. **5**(1): p. 103-109.
81. Wiepjes, C.M., et al., *The Amsterdam Cohort of Gender Dysphoria Study (1972-2015): Trends in Prevalence, Treatment, and Regrets*. The Journal of Sexual Medicine, 2018. **15**(4): p. 582-590.
82. Hoogendoorn, J.M., et al., *Rauchen ist nachteilig für die Heilung von Knochen und Weichteilen*. Unfallchirurg, 2002. **105**(1): p. 76-81.
83. Bamgbade, O.A., et al., *Postoperative complications in obese and nonobese patients*. World Journal of Surgery, 2007. **31**(3): p. 556-561.
84. Berrington de Gonzalez, A., et al., *Body-mass index and mortality among 1.46 million white adults*. New England Journal of Medicine, 2010. **363**(23): p. 2211-9.
85. Horbach, S.E., et al., *Outcome of Vaginoplasty in Male-to-Female Transgenders: A Systematic Review of Surgical Techniques*. The Journal of Sexual Medicine, 2015. **12**(6): p. 1499-512.
86. Jiang, D., et al., *Does Depth Matter? Factors Affecting Choice of Vulvoplasty Over Vaginoplasty as Gender-Affirming Genital Surgery for Transgender Women*. The Journal of Sexual Medicine, 2018. **15**(6): p. 902-906.
87. Frey, J.D., et al., *A Systematic Review of Metoidioplasty and Radial Forearm Flap Phalloplasty in Female-to-male Transgender Genital Reconstruction: Is the "Ideal" Neophallus an Achievable Goal?* Plastic and Reconstructive Surgery - Global Open, 2016. **4**(12): p. e1131.

88. Hage, J.J., *Metoidioplasty: An alternative phalloplasty technique in transsexuals*. Plastic and Reconstructive Surgery, 1996. **97**(1): p. 161-167.
89. Perovic, S.V. and M.L. Djordjevic, *Metoidioplasty: a variant of phalloplasty in female transsexuals*. BJU International Journal, 2003. **92**(9): p. 981-985.
90. Vukadinovic, V., et al., *The role of clitoral anatomy in female to male sex reassignment surgery*. Scientific World Journal, 2014. **2014**: p. 437378.
91. van de Grift, T.C., et al., *A Longitudinal Study of Motivations Before and Psychosexual Outcomes After Genital Gender-Confirming Surgery in Transmen*. The Journal of Sexual Medicine, 2017. **14**(12): p. 1621-1628.
92. Djordjevic, M.L., D.S. Stanojevic, and M.R. Bizic, *Rectosigmoid vaginoplasty: clinical experience and outcomes in 86 cases*. J Sex Med, 2011. **8**(12): p. 3487-94.
93. Lawrence, A.A., *Patient-reported complications and functional outcomes of male-to-female sex reassignment surgery*. Archives of Sexual Behavior, 2006. **35**(6): p. 717-27.
94. Leriche, A., et al., *Long-term outcome of forearm free-flap phalloplasty in the treatment of transsexualism*. BJU Int, 2008. **101**(10): p. 1297-300.
95. Ramachandran, V.S. and P.D. McGeoch, *Occurrence of phantom genitalia after gender reassignment surgery*. Med Hypotheses, 2007. **69**(5): p. 1001-3.