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Medical care for children and adolescents with gender dysphoria and gender inconsistency in the light of current recommendations–how to implement the "primum non nocere" principle?[1]

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Abstract: Gender identity is one of the essential aspects of human functioning. The diagnosis of gender dysphoria or gender incongruence applies to people who do not have any developmental defects of the genital organs or sex hormone secretion disorders, while the problem is the lack of acceptance of functioning in their own body and the desire to become a person of the opposite sex. This phenomenon is increasingly observed in children and adolescents. In recent years there has been a trend towards earlier use of puberty blockers and sex steroids in minors with gender dysphoria or gender inconsistency in order to inhibit the development of sexual characteristics in the direction of their own sex (referred to as the sex assigned at birth) and to mimic them to the opposite sex, i.e. according to their gender identification. In addition, surgical procedures are performed to remove the gonads and change the appearance of the genitals (and/or breast) in the desired direction (these procedures are allowed in adults, although there are many advocates of performing them in adolescents). Such therapies have been described as "gender-affirming", as opposed to "conversion" therapies, i.e. interventions aimed at restoring the acceptance of one's own sex. The literature emphasizes the lack of evidence regarding the effectiveness and safety of these procedures, allowing for an unequivocal recommendation of their application in children and adolescents, as well as the possible relationship between the increase in the frequency of gender identity disorders and the influence of peer groups, in particular the media creating a climate of affirmation of transsexualism (and non-binary gender identification). Therefore some countries (e.g. Sweden) have tightened their legal regulations in this area. The most serious long-term consequence of gender-affirming therapies is infertility. This paper aims to present these problems based on current medical literature. Extremely important bioethical and legal aspect of these issues will only be indicated, although they undoubtedly require special attention and separate studies.
Keywords: gender identity, gender dysphoria, gender incongruence, gender-affirming therapy, children and adolescents

Introduction

Gender identification is one of the important aspects of human functioning. The diagnosis of dysphoria or gender incongruity concerns people who do not have any developmental defects in the sexual organs or disorders in the secretion of sex hormones, and the problem is the lack of acceptance of functioning in their own (otherwise physically healthy) body. The reasons for the differences (inconsistencies) between phenotypic sex (corresponding to the appearance of the genital organs, referred to in the current literature as sex assigned at birth) and gender identification are complex and not fully understood. The postulated mechanisms include differences in shaping the "brain sex" in a direction other than the gonadal sex (e.g. polymorphisms of genes encoding sex hormone receptors and proteins necessary for the proper functioning of sex hormones, epigenetic phenomena, the effect of excess androgens in fetal life). These issues–along with detailed source literature–were the subject of a separate study, published

1 Article in polish language: Opieka medyczna nad dziećmi i młodzieżą z dysforią płciową i niezgodnością płciową w świetle aktualnych rekomendacji – jak realizować zasadę „primum non nocere"? https://www.stowarzyszeniefidesetratio.pl/fer/2023-3Smy.pdf

in the Quarterly „Fides et Ratio" (Smyczyńska, 2020) and chapters in the book "Between a chromosome and a paragraph" (Smyczyńska 2,021; Zazula, 2021).

In recent years, the frequency of diagnosis of gender dysphoria/incongruence has been increasing, especially among young people (there is a particularly dramatic increase in the percentage of teenage girls declaring male gender identification and the need for transition, i.e. becoming similar to the male gender and functioning as a male person), which raises suspicions about the influence of additional factors (e.g. cultural) on the choice of transsexual gender identification (this phenomenon has not yet been fully explained). At the same time, in society, mainly through the activities of the media and social networking sites, a climate of acceptance or even affirmation of any gender identification (socio-cultural gender), including non-binary and undefined gender, is being created. Changes in this direction also included the nomenclature used in medical classifications and publications, which unfortunately translates into the use of less precise terms in relation to the essence of the described disorders and the actual nature of the medical procedures.

In addition to the undoubtedly beneficial aspects of these changes (cessation of discrimination or stigmatization of people based on their identification and sexual orientation), it seems important to draw attention to the fact that in reality it is not possible to change genetic sex (genetic information encoded in every cell of the human body) and gonadal sex (it is possible to deprive a person of the testicles or ovaries, but not to change them to gonads, which are an attribute of the opposite sex), while interventions regarding the appearance of the genital organs can bring good results, but often without achieving their full functionality and at the cost of a relatively high percentage of complications. Awareness of these limitations is important when making decisions about performing irreversible surgical procedures or using hormonal preparations. In relation to children and adolescents, one should bear in mind the risk resulting from incomplete awareness of the consequences of particular medical interventions and the possibility of changing the perception of these consequences in subsequent periods of life.

Medical aspects regarding the issue of gender incongruence and dysphoria (also called transsexualism) will be presented in the following parts of the article, with particular emphasis on minors. Extremely important legal and bioethical issues will be included only to the extent necessary to discuss medical issues. Also, issues related to disorders of sex development (genetic diseases, developmental defects and endocrine diseases affecting the development of sexual organs in fetal life) will not be included, because these disorders constitute separate disease entities and require separate diagnostic and therapeutic procedures.

1. Definitions, nomenclature and classifications of disorders

There are various classifications of conditions related to the discrepancies between the sex assigned at birth (*i.e.* determined after birth according to the appearance of the external genitalia) and gender identity. Moreover, the nomenclature used in subsequent versions of these classifications have been evolved in time.

In Poland, up to now, the International Classification of Diseases, version 10 (ICD-10), published by World Health Organization (WHO) in 1992, with the last update in 2019, should be used, however version 11 of this classification (ICD-11) was published in 2018 and is announced to be implemented in nearest few years.

In ICD-10 in there is a block of diagnoses (Chapter V) "Disorders of adult personality and behaviour" (F60-F69), which includes subsections related to gender identity and sexual orientation (see Table 1). It seems important to be familiar with the definitions and descriptions given in this classification.

Transsexualism (ICD-10, F64.0) is defined as "a desire to live and be accepted as a member of the opposite sex" with a distress and need for "surgery and hormonal treatment to make one's body as congruent as possible with one's preferred sex".

Table 1. Disorders of gender identity, sexual preferences and sexual orientation, according to the WHO Classification ICD-10[2]

Gender identity disorders (F64)	Psychological and behavioural disorders associated with sexual development and orientation (F66)*
Transsexualism (F64.0)	Sexual maturation disorder (F66.0)
Dual-role transvestism (F64.1)	Egodystonic sexual orientation (F66.1)
Gender identity disorder of childhood (F64.2)	Other psychosexual development disorders (F66.8)
Other gender identity disorders (F64.8)	Psychosexual development disorder, unspecified (F66.9)
Gender identity disorder, unspecified (F64.9)	

* Sexual orientation by itself is not to be regarded as a disorder

Gender identity disorder of childhood (ICD-10, F64.2) is placed in a block of disorders diagnosed in adults relates to symptoms that "usually first manifest during early childhood (and always well before puberty)", with "a persistent and intense distress about assigned sex" and "a desire to be of the other sex", with the proviso that "Gender identity disorders in individuals who have reached or are entering puberty should not be classified here but in F66".

Sexual maturation disorder (ICD-10, F66.2) relates to the situation when "the patient suffers from uncertainty about his or her gender identity or sexual orientation, which causes anxiety or depression" and should be diagnosed in adolescents who are uncertain of their sexual orientation, or in individuals who "find that their sexual orientation is changing".

In ICD-11, the terms "Gender identity disorders" and "transsexualism" have been replaced by "gender incongruence". This diagnosis is situated not in Chapter 06 "Mental, behavioural and neurodevelopmental disorders" (equivalent to Chapter V in ICD-10), but in a new Chapter 17 "Conditions related to sexual health" (HA00-HA8Z). According to ICD-11, the following detailed diagnoses (codes) are related to gender incongruence:

- "**Gender incongruence of adolescence and adulthood**" (ICD-11, H60), defined as "a marked and persistent incongruence between an individual ′s experienced gender and the assigned sex", with "a desire to 'transition', in order to live and be accepted as a person of the experienced gender"
- "**Gender incongruence of childhood**" (ICD-11, H61), related to "a marked incongruence between an individual's experienced/expressed gender and the assigned sex in pre-pubertal children", with "a strong desire to be a different gender than the assigned sex" that "must have persisted for about 2 years"
- **"Gender incongruence, unspecified"** (ICD-11, HA6Z), described as "residual category".

Moreover, the term the term "disorders" suggesting a kind of pathology concerning gender identity has been replaced by "incongruence" that is more neutral. Nevertheless, ICD-11 is still a classification "for Mortality and Morbidity Statistics".

In recommendations of World Professional Association for Transgender Health (WPATH) (Coleman, Radix, Bouman, Brown, de Vries et al. 2022), the term **gender diversity** is used and people with this condition are still referred to as **transgender** ones It is emphasized in recommendations and should not be questioned that transgender people should be treated with respecting their dignity. Moreover, similar terminology should be used in medical standards and in legal documents. This terminology is also suspected to further evolve in future (Coleman et al. 2022).

The nomenclature concerning discussed issues have also significantly evolved in in subsequent editions of classification "Diagnostic and Statistical Manual of Mental Disorders"(DSM), developed by American Psychiatric Association (APA). In DSM IV (2006) the term "gender identity disorder" was used, with subtypes based on sexual orientation. In version 5 (DSM-5), published in 2013, this term

2 https://icd.who.int/browse10/2019/en#/F60-F69

was replaced by "gender dysphoria" with no previously separated subtypes related to sexual orientation. Instead, separate criteria for children and for adults and adolescents were added. Nonetheless, gender dysphoria has not been removed from the classification of mental disorders. Apart from clearly defined criteria of gender dysphoria, DSM-5 (APA, 2013) includes additional specification if this condition exists with disorders of sex development or if it is post-transitional (i.e. in case of gender dysphoria in the person who has transitioned and lives in the desired gender).

The last DSM Text Revision in 2022 (DSM-5-TR) has introduced further updates in order to use "culturally-sensitive" language. Unfortunately, this generally positive tendency to refrain from the terms that could be considered to any degree pejorative, sometimes leads to the use of less precise terminology (see Table 2).

Table 2. Updates of the terminology related to gender dysphoria in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, text revision (DSM-5-TR), American Psychiatric Association (2022)

DSM-5	DSM-5-TR
Natal male	Individual assigned male at birth
Natal female	Individual assigned female at birth
Cross-sex medical procedure	Gender-affirming medical procedure
Cross-sex hormone treatment	Gender-affirming hormone treatment
Desired gender	Experienced gender
Disorders of sex development	Differences in sex development

With respect to these changes, it should be mentioned that the term "assigned sex" is in fact synonymous with somatic, gonadal and genetic sex, except for the relatively rare cases of disorders of sex development (DSD), which are classified separately as "Congenital malformations of genital organs" in ICD-10, while "Structural developmental anomalies of male genital system" or "Structural developmental anomalies of female genital system" in ICD-11. The change in nomenclature changing the nomenclature from "disorders" to "differences" of sexual development (DSD) should not obscure the fact that this category includes a number of developmental defects and diseases of the endocrine glands that have to be diagnosed and treated. This necessity is generally clear for disorders but not necessarily for differences. It should be also recalled that DSD relates to atypical genitalia or a discrepancy between genotypic and phenotypic sex (van Bever, Brüggenwirth, Wolffenbuttel, Dessens, Groenenberg *et al.* 2020).

Gender affirmation refers to affirming transgender people in their gender identity in different aspects of life (e.g. medical, behavioral, social or legal) and includes but is not limited to transition-related medical care (Coleman et al. 2022; Reisner, Poteat, Keatley, Cabral, Mothopeng et al. 2016). This means that the affirmation refers in fact to the interventions strengthening gender identity corresponding to the opposite sex (cross-sex) .

The persons with gender identity compatible with assigned (genital) sex are referred to as cisgender, while the persons with incongruence between gender identity and assigned (genital) sex – as transgender. It is also useful to differentiate between male-to-female (M/F) and female-to-male (F/M) persons, in older literature described as trans-women and trans-men. This nomenclature is useful to describe differences between these groups and gender-specific cross-sex medical interventions. However, some persons may define themselves as gender-ambivalent or non-binary.

2. Incidence of transgender experience

Due to different definitions used by the authors and different methods of estimation, there are significant differences in the reported incidence of transgenderism and gender dysphoria. It is also difficult to clearly compare the data from particular studies.

In a large administrative database, including 74 million of U.S. adults enrolled in commercial or Medicare Advantage plans, the overall incidence of gender diversity was 0.03%, with a tendency to higher

prevalence in younger age groups (Jasuja, de Groot, Quinn, Ameli, Hughto et al. 2020). As much as 43% of M/F and 45% of F/M transgender adults in this study were diagnosed with depression, however it has not been clarified if there is a relationship between the incidence of depression and the past gender-affirming medical interventions. In adult population of U.S., the prevalence of self-reported transgender status is estimated at 0.5 % (Crissman, Berger, Graham and Dalton 2017). In Sweden also 0.5% of asked adults declared the desire for cross-sex hormone administration or surgery, with higher proportion of those who felt or wanted to be perceived like a person of another sex (Åhs, Dhejne, Magnusson, Dal, Lundin et al. 2018). In the studies using 5-point Likert scale, the proportion of transgender M/F patients was 1.1% in Netherlands and 0.7% in Belgium, while of F/M it was 0.8% and 0.6%, respectively, with a relatively higher percent of those who declared gender ambivalence (van Caenegem, Wierckx, Elaut, Buysse, Dewaele et al. 2015; Kuyper and Wijsen 2014). In Canada, the proportion of transgender or non-binary people among the population aged at least 15 years was 0.33% and ranged from 0.12% in the oldest age group to 0,79% in the youngest one (Statistics Canada 2022).

It has been assessed that overall proportion of adults with transgender identity varies from 0.02-0.08% in health system databases to 0.3-0.5% in surveys. Moreover, in surveys performed among children and adolescents, transgender identity was assessed as 1.2-1.7%, while gender incongruence or ambivalence was reported by 2.5-8.4% respondents (Coleman et al. 2022). The observed age-related differences and temporal trends in the proportion of M/F and F/M persons in younger age groups, reported in the cited study, do not seem to confirm the persistent nature of gender dysphoria in children and adolescents at the population level. Moreover, in survey studies, similar or even higher percent of adolescents declared as not sure about their gender than as transgender ones, e.g.1.6% vs. 1.8% in the study of Johns, Lowry, Andrzejewski, Barrios, Demissie et al. (2019), while 2.5% vs. 1.2% in the study of Eisenberg, Gower, McMorris, Rider, Shea and Coleman (2017), respectively.

In the study summarizing 20 years of use of Dutch Protocol in Vrije University in Amsterdam (van der Loos, Klink, Hannema, Bruinsma, Steensma et al. 2023), a rapid, several time increase in the number of patients "assessed as female at birth" at age over 10 years was observed between 2012 and 2017, with only a slight increase in the number of patients "assessed as male at birth" in the same age group and a relatively small increase in the number of children under the age of 10. Very similar are the observations of Friesen, Söder and Rydelius (2017) in Sweden and of Butler, De Graaf, Wren and Carmichael (2018) in U.K. The occurrence of this phenomenon in different countries has quite recently been described in detail by Marianowicz-Szczygieł (2022).

The possible explanation of an increased number of adolescents with gender incongruence include: greater access to information on gender issues (on the internet and social media), a decrease of stigmatization together with an increase of acceptance in society, improved access to medical and increasing media interest in transgender issues (Indremo, Jodensvi, Arinell, Isaksson and Papadopoulos 2022). In support of the importance of this last circumstance, the authors have indicated the existence of a correlation between the increased interest in gender dysphoria on Google trends after media events concerning transgenderism in 2019.

It seems that the reasons for such situation cannot be associated only with greater incidence of true and permanent gender inconsistency (which increased during few years in one sex and only in teenagers), but this tendency may reflect current (and possibly temporal) trends emerging among young people.

Interestingly, in 7th version of WPATH Standards of Care (Coleman, Bockting, Botzer, Cohen-Kettenis, DeCuypere et al. 2012), there is a statement that gender dysphoria persisted into adulthood in only 2-4% girls and 1-2% boys. This data is, however, not recalled in more recent studies (possibly as it is not in line with current trends in "gender affirming" approach to minors).

These issues should be taken into account before starting any irreversible or potentially harmful medical procedures, as they indicate serious doubts as to

the true causes of feeling gender-related dysphoria and the real need for gender-affirming irreversible interventions in minors.

3. Available evidence and recommendations

In recent years there have been numerous recommendations on gender issues developed by various bodies in different countries. Some of them are signed by scientific societies and organizations, while others represent the views of their authors. The most important and the most up-to-date of them are discussed in next sections of the manuscript. The authors of particular guidelines have pointed at their limitations related to the scarcity of long-term data causing the necessity of relying mainly on expert opinions. Moreover, the content of the different guidelines varies to some extent and is mutable in subsequent versions of the same recommendations.

The Polish Society of Endocrinology published recommendations on the diagnosis and therapy of transsexualism several years ago (Mędraś and Józków, 2010). The Polish Sexological Society has issued recommendations on health care for transgender people (Grabski, Rachoń, Czernikiewicz, Dulko, Jakima et al. 2020), but they only apply to adults, without any reference to minors. Recently, the issue of transsexualism, taking into account the differences regarding minors, was discussed in the textbook "Andrology" (Robacha 2021) in the chapter "Psychological gender disorders".

4. Diagnosis of gender dysphoria in adolescents

According to current statements, gender identity disorders (also specified as gender dysphoria or gender incongruence) should be defined as a strong and persistent cross-gender identification that is associated with a remarkable distress related to living in an incongruent gender (Vita, Settineri, Liotta, Benvenga and Trimarchi 2018)

According to DSM-5-TR (American Psychiatric Association 2022), the diagnosis of gender dysphoria in adolescents requires fulfilling the following criteria:

A. marked incongruence between experienced/expressed gender and primary and/or secondary sex characteristics (also anticipated secondary sex characteristics in young adolescents), lasting for at least 6 months
B. a distress or impairment in functioning in different areas (social, occupational or others) of clinically significant severity

In this interpretation, gender incongruence alone does not meet the diagnostic criteria for gender dysphoria. However, in ICD-11 (WHO 2018), only the term "gender incongruence" was left, which allows a diagnosis to be made even if this incongruence is not the cause of suffering or functional impairment. This approach allows for qualifying for treatment also people who do not suffer or even feel discomfort only because they report the desire to transition.

5. Possible interventions

According to Dora, Grabski and Dobroczyński (2021), there are three main therapeutic approaches for children and adolescents with gender dysphoria:

- reduction of the experience of gender dysphoria by and strengthening identification with the assigned gender (i.e. with natal sex),
- supporting natural development of gender identification in childhood
- early affirmation of identification of a child with the experienced gender.

The authors of this relatively recent study have stated that literature concerning particular approaches is limited and each option is subject to criticism by supporters of the other approaches.

The main changes introduced in recent years are moving in the direction of gender-affirming procedures and supporting searching for gender identity, while against strengthening gender identification

consistent with. the sex assigned at birth. The basic scope of the intervention includes hormone administration, surgical procedures and psychotherapy.

5.1. Hormonal prescriptions

5.1.1. *Physiology of pubertal development*

The onset of puberty is related to activation of a pulsatile secretion of gonadoliberin (GnRH) in hypothalamus. GnRH stimulates synthesis of gonadotropins – luteinizing hormone (LH) and follicle stimulating hormone (FSH) – in pituitary gland. Gonadotropins induce secretion of sex steroids from gonads (estrogens and progesterone in ovaries, while testosterone in testes) and are important for ovulation and spermatogenesis. Estrogens induce development of female secondary sex characteristics; variability of pulsatile gonadotropin secretion is necessary for of cyclic changes in estradiol and progesterone secretion that is crucial for the proper course of menstrual cycle. Testosterone induces development of male secondary sex characteristics (virilization) and has some anabolic effects. Sex steroids inhibit gonadotropin secretion in the negative feedback mechanism. This description is, of course, very simplified, but may constitute the basis for understanding the mechanisms of action of particular interventions.

5.1.2. *Suppression of pubertal development*

Blocking puberty is achieved by using sustained-release GnRH agonists, i.e. synthetic peptides that bind to GnRH receptors in the pituitary, which inhibits the secretion of gonadotropins by the pituitary gland and, consequently, also the secretion of sex steroids by the gonads. These preparations are called puberty blockers. Such interventions suppress progression of puberty without affecting the development of sexual characteristics in the direction typical of the opposite sex. Effects of puberty blockers seem to be reversible, however with some reasonable concerns with respect to the future risk of osteoporosis and bone fractures, possible effects on final height and increase in body fat, while decrease in lean body mass. Long-term studies are available for children with premature puberty but not for transgender youths (Salas-Humara, Sequeira, Rossi, and Dhar 2019). Recommending administration of puberty blockers, the authors of the cited guidelines indicate that GnRH analogues have some positive effects on psychological and emotional problems but not for improvement of gender dysphoria.

In Poland, sustained-release GnRH analogues are approved for treatment of central (GnRH-dependent) premature puberty and selected forms of early puberty in children. In adults GnRH analogues are used in males with prostate cancers for androgen deprivation and in females with endometriosis, uterine fibroids or disorders of ovulation. According to the characteristics of medical product, therapy of transgender persons is not listed among the indications for the use of GnRH analogues in all age groups. In United States, GnRH analogues are also not approved by Food and Drug Administration (FDA) for the use in transgender youth (Salas-Humara et al. 2019).

5.1.3. *Gender- affirming (cross-sex) hormones*

This term relates to using estrogens in transgender M/F and testosterone in transgender F/M.

Estrogens are used in order to achieve the development of female secondary sex characteristics in the patients with genetic and phenotypic male sex (assigned at birth as boys). Due to the risk of thromboembolic events, it is suggested to prefer 17β-estradiol rather than ethinyl estradiol and to choose the route of administration which avoid hepatic first pass metabolism, preferably transdermal (however with no sufficient support for this recommendation for transgender M/F in published studies) (Salas-Humara et al. 2019). Gradual increasing the doses of estrogens is advised due to their potential impact on final height, as higher doses or their rapid escalation may decrease final height (this might be expected by M/F patient but is completely irreversible). Personal and family history should be taken before estrogens administration and other risk factors of thromboembolism (obesity and smoking) should be discussed. There is also some concern related to inconclusive data on the risk of hyperprolactinemia and hypertriglicerydemia during estrogen use

(Salas-Humara et al. 2019). The effects of estrogens administration may develop during few years, e.g. maximal breast development is expected after 2 years. The patient should be able to understand both the possible side effects and the irreversibility of the effects of estrogen therapy. The decrease of depressive symptoms during feminizing hormone therapy has been reported, however there are no prospective studies in this aspect (Salas-Humara et al. 2019). Potential adverse effects include an increase of body fat and BMI that was observed in adults, with no such effect in one published study on transgender youths (Jarin, Pine-Twaddell, Trotman, Stevens, Conard et al. 2017). Salas-Humara et al. (2019) have stated that the data concerning blood pressure in adult transgender M/F is inconclusive, while in adolescents it is limited to one study with 6-months follow-up (Jarin et al. 2017). With respect to the risk of malignancy in M/F patients, Salas Humara et al. (2019) have pointed at insufficient evidence to draw conclusions concerning breast cancers and prostate cancers, nevertheless with no data on increased risk of these tumors. Other effect of increased estrogen levels may be hyperprolactinemia and development of pituitary tumors (*prolactinoma*), however its risk in M/F adolescents on estrogen therapy has not been definitely assessed (Jarin et al. 2017). International Endocrine Society, bringing together members from over 100 countries, has recommended monitoring prolactin concentrations in such patients and implement appropriate management in case of hyperprolactinemia (Hembree, W. C., Cohen-Kettenis, P. T., Gooren, L., Hannema, S. E., Meyer et al, 2017).

As estrogens alone not always fully suppress testosterone production in transgender M/F, they are commonly prescribed together with GnRH blockers or antiandrogens (Spironolactone, Cyproterone acetate) (Coleman et al. 2022). However, the lack of data on the use of Spironolactone in monotherapy makes impossible to assess the effects of this drug in transgender M/F patients, while the health risks of Cyproterone acetate are debated and randomized protocols with anti-androgen drugs are requested (Glintborg, T'Sjoen, Ravn and Andersen 2021; Hembree et al. 2017; Salas-Humara et al, 2019). There is a clear recommendation of Endocrine Society (Hembree et al. 2017) against use progesterone in transgender M/F due to the increased risk of breast cancers and cardiovascular diseases, however the evidence is from the study on postmenopausal women (Chlebowski, Manson, Anderson, Cauley, Aragaki et al. 2013), not on transgender adolescents. Similar is the statement of Glintborg et al. (2021).

In Poland, in accordance with the characteristics of available estradiol-containing medicinal products (Estrofem, Systen 50), indications to estradiol administration in monotherapy include only estrogens deficiency in post-menopausal women after histerecotmy, who do not require standard hormonal replacement therapy with estrogens and progesterone. A study by the Agency for Health Technology Assessment and Tariff System (2023) was recently published confirming the validity of using cyproterone and estradiol in transsexuals (M/F), based on the results of studies using these drugs in transgender adults or people over 16 years of age. Estrogens are also used in adolescent girls with hypogonadism in the initial phase of sex steroids substitution (Nordenström, Ahmed, van den Akker, Blair, Bonomi et al. 2022).

Testosterone is used due to its anti-estrogen, virilizing and anabolic effects that enable promoting development of male secondary sex characteristics in genetic and phenotypic female persons (assigned at birth as girls). This include change of voice (irreversible after 6 months of treatment), skin hair growth (irreversible after 1 year) that may be connected with androgenic alopecia, possible increase of final height (depending on many factors and with no certainty about its improvement), induction of amenorrhea and changes in body shape (that may be to some extend irreversible). The effect of high testosterone levels in women is also enlargement (hypertrophy) of the clitoris, atrophic changes in the vaginal epithelium and the appearance or intensification of acne lesions. In the case of F/M people, the discussed effects of testosterone use may be at least partially accepted and even expected, but a serious problem is their irreversible nature in the event of an erroneous, hasty diagnosis of transsexualism in a girl with temporary gender identity disorders who wants to return to functioning as a female person.

With respect to mental health outcomes of testosterone administration in transgender youth, there are the reports on reduction of depression rates and anxiety, as well as on the increase on anger, especially in the initial phase of treatment (Salas-Humara et al. 2019). According to the cited statement, there are no common contraindications to testosterone administration, however, the same authors are not entirely consistent in drawing attention to concerns about complications of testosterone therapy started in adolescence, with respect to the possibility of increased risk of cardiovascular hypertension, diseases, polycythemia-related thromboembolism and cancers. The patients should be aware of the risk of breast, uterine and ovarian cancers, if they have these organs left (Salas-Humara et al. 2019).

It should be borne in mind that in Poland, the only approved indication for testosterone administration is male hypogonadism, including delayed puberty in boys (approved for use over 15 years). However, according to the characteristics, particular drugs for intramuscular (e.g. *Testosteronum prolongatum*) or subcutaneous (e.g. *Androtop*) administration are not recommended for use before the age of 18 years, as their safety and efficacy in children and adolescents have not been established. Similarly, testosterone products are approved by U.S. Food and Drug Administration (FDA) only for men with testosterone deficiency, *i.e.* with failure of the testicles to produce testosterone due to associated medical conditions (*e.g.* genetic defects, chemotherapy, hypothalamic or pituitary insufficiency). According to the Safety Announcement of U.S. FDA (2014) testosterone therapy turned out to be associated with an increased risk of cardiovascular events (heart attacks and strokes, or even death), however further clinical studies should be conducted to assess the real scale of such risk. Polish characteristics of testosterone products list breast cancers, prostate cancers (diagnosed or suspected), benign prostatic hypertrophy, nephrotic syndrome and hepatic neoplasms as contraindications to the use of testosterone, and advise caution in the patients with cardiac, renal or hepatic failure, epilepsy, migraine, as well as in obese subjects with chronic diseases of respiratory system.

Other intervention in F/M adolescents may be temporal (reversible) menstrual suppression, obtained by administration of oral contraceptives (or other methods of contraception), progesterone or puberty blockers (Coleman et al. 2022; Roden, 2023). Interestingly, there is also evidence that some patients may not desire testosterone therapy and only need appropriate menstrual underwear (i.e. special underwear tailored to individual needs with increased absorbency, not requiring the use of disposable menstrual hygiene products, providing greater freedom during bleeding, increasing the sense of security and maintaining discretion) and improved hygiene (Coleman et al. 2022; Roden, 2023). In WPATH recommendations there is also an important suggestion to use only GnRH agonists but not sex steroids in the patients who are unsure that they desire steroid hormones (Coleman et al. 2022).

According to the recent report of Gawlik, Antosz, Kasparek, Nowak and Grabski (2022), in Poland over 90% of transgender patients did not start hormonal treatment before the age of 18 years, and the most commonly used drugs were testosterone or estradiol and cyproterone, while the use of puberty blockers was not reported.

5.2. Gender-affirming (cross-sex) surgical interventions

5.2.1. *Gonadectomy and hysterectomy*

This procedures are – in fact – irreversible removal of otherwise healthy gonads (ovaries or testicles), making the person undergoing this procedure definitely infertile. Nevertheless, people who decide to have a gonadectomy as one of steps of gender-affirming therapy may want to have biological offspring in the future (Rodriguez-Wallberg, Obedin-Maliver, Taylor, Van Mello, Tilleman and Nahata 2023), even if they deny such a need when they are still children or teenagers.

It is technically possible and recommended to preserve ovarian or testicular tissue, or mature gametes (oocytes or sperm), that is referred to as "fertility preservation" (Coleman et al. 2022; Rodriguez-Wallberg et al. 2023; Salas-Humara et al. 2019;

Wang, Hengel, Ren, Tong, and Bach 2020). As both gender-affirming therapy hormonal and especially surgical procedures performed in transgender persons have irreversible negative effect on fertility, the only chance of having biological offspring is fertility preservation(Wang et al. 2020). Due to the adverse effects of gender-affirming therapies on fertility (including definitely irreversible infertility after gonadectomy), such procedures are recommended prior to administering hormones. However, cryopreservation of mature gametes requires an appropriate stage of maturation which may be a limitation in the case of adolescents, especially as the initiation of hormonal interventions is recommended at as early stage of puberty as Tanner 2.

Currently, the only option for prepubertal children is storing ovarian or testicular tissue for autotransplantation (i.e. for re-implantation of the gonads previously removed during the gender-affirming treatment), as there is no technique of maturation oocytes or sperm from cryopreserved pre-pubertal ovaries or testes *in vitro* of proven effectiveness (Coleman et al. 2022; Rodriguez-Wallberg et al, 2023). Moreovever, there are only single case reports of re-transplantation of ovarian tissue concerning early pubertal adolescents, while no cases of re-transplantation of testicular tissue in humans in the literature (Rodriguez-Wallberg et al. 2023); current evidence about the possibility of re-transplanting testicular tissue taken in the prepubertal period comes only from animal studies (Wang et al. 2020). It is postulated to discuss the possibility of cryopreservation gonadal tissue, however with the awareness of the lack of data on the actual possibilities of their use in the future (Rodriguez-Wallberg et al. 2023). It should also be commented here that "preserved fertility" related to cryopreservation of gametes is limited to in vitro fertilization procedures, while not allows fertilization during sexual intercourse. Hysterectomy performed in transgender F/M makes them impossible to get pregnant in future.

It seems that the details of these limitations are not widely known even among people interested in gender reassignment and are not taken into account by the bodies proposing hormone therapies in younger and younger children, in whom the use of methods of fertility preservation available for adults and post-pubertal adolescents may be impossible. It is also important to consider the age at which the minor is fully capable of assessing the long-term consequences of the such interventions and about the right of parents/guardians to consent to the performance of irreversible procedures which may result in infertility, even if the minor is fully convinced of the rightness of his/her decision (and finds gender-affirmative support from specialists).

5.2.2. *Genital surgery*

In transgender M/F patients, gender reassignment surgery includes removal of the penis (usually together with testes) and creation of neovagina, i.e. a structure designed to resemble a vagina, most often using the skin of the penis and scrotum, but it is possible to use flaps of skin and mucous membranes from other areas. It is not possible to create or recreate the vaginal epithelium and its physiological hydration, and the multitude of surgical techniques indicates that none of them is optimal. Post-operatively such patients often require calibration (dilation) of neovagina to enable sexual intercourse. There is also a risk of recto-vaginal fistula (Colebunders, Brondeel, D'Arpa, Hoebeke and Monstrey 2017; Salas-Humara et al. 2019).

U osób transpłciowych K/M operacja rekonstrukcji narządów płciowych obejmuje falloplastykę i metoidoplastykę różniące się szczegółami wykonywanych zabiegów oraz uzyskiwanymi efektami – falloplastyka wiąże się z większą długością *neophallusa*, natomiast metoidoplastyka pozwala na lepsze doznania erogenne (Robinson, Blasdel, Cohen, Zhao i Bluebond-Langner, 2021); szczegółowy opis tych operacji wykracza poza zakres niniejszego artykułu. Autorzy cytowanej pracy podają wysoki odsetek powikłań, w tym 40% ryzyko wystąpienia przetok cewkowo-skórnych, zwężeń cewki moczowej (ponad 30%) i prawie 20% ryzyko pogorszenia stanu zdrowia psychicznego. To ostatnie stwierdzenie należy traktować jako poważne ostrzeżenie, gdyż u osób z dysforią płciową nie występuje wcześniej choroba somatyczna gonad ani narządów płciowych, a celem interwencji jest poprawa zdrowia psychicznego. Według

niedawnej publikacji (Gottlieb i Cripps, 2023) nie określono żadnego standardu opieki w odniesieniu do rekonstrukcji prącia. Nie ma również zgody co do stosowania protez prącia, które według jednych autorów (Colebunders i in.,(2017) nie mają żadnej funkcjonalności, natomiast według innych autorów (Barnard, Cakir, Ralpha i Yafi, 2021) wskazania do operacji protezowania prącia mogą być poszerzone i obejmować osoby transpłciowe.

In transgender F/M patients genital reconstruction (cross-sex) surgery includes phalloplasty (a procedure involving the creation of a structure resembling the shape of a penis from tissue taken from other parts of the body) and metoidoplasty (a more limited procedure using only tissues from the genital area) that differ in the details of the performed procedures and with the obtained effects – phalloplasty is related to a longer length of neophallus (newly created structure resembling a penis), while metoidoplasty allows for better erogenous sensations (Robinson, Blasdel, Cohen, Zhao and Bluebond-Langner 2021); the detailed description of these operations goes beyond the scope of present paper. The authors of cited manuscript have reported a high complication rate, including 40% risk of urethro-cutaneous fistulae, urethral strictures (over 30%) and almost 20% risk of worsening mental health. The latter finding should be taken into account as a serious warning, as in the patients with gender dysphoria there is no previous somatic disease of gonads or genitals and the aim of the interventions is to improve mental health. According to a very recent paper of Gottlieb and Cripps (2023), no standard of care has been identified with respect to penile reconstruction. There is also no agreement according to penile prosthesis, as according to Colebunders et al. (2017) they have no functionality, while according to Barnard, Cakir, Ralph and Yafi (2021) the indications for penile prosthetic surgery may be broaden and include transgender persons.

Despite the previously mentioned concerns regarding the potential increased risk of ovarian and uterine cancer in F/M people using testosterone preparations in which these organs are left (Salas-Humara et al., 2019), currently there a recommendation against oophorectomy (surgical removal of ovaries) and hysterectomy (uterine resection), as there is insufficient evidence (lack of prospective data) that such procedures should be performed in order to decrease the risk of ovarian and endometrial cancers, instead, appropriate cervical cancer screening should be offered to F/M patients (Coleman et al. 2022). Such recommendations reduce the scope of mutilating procedures that F/M people undergo, but on the other hand, the possibility of underestimating the oncological risk should be taken into account.

5.2.3. *Chest surgery*

This term relates to removal of breast tissue (mastectomy) in transgender F/M and breast augmentation in M/F ones.

According to recent recommendations, mastectomy is permitted in minors below 18 years of age, when recommended by mental health providers, if testosterone therapy alone does not provide sufficient reduction of breast size (Salas-Humara et al. 2019). It should be noted that there is only limited data that such irreversible removal of mammary glands improves quality of life of persons with gender dysphoria (Poudrier, Nolan, Cook, Saia, Motosko et al. 2019; Salas-Humara et al. 2019; Alcon, Kennedy, Wang, Piper, Loeliger et al. 2021), nevertheless the patients' satisfaction outcomes are generally positive (Day, Klit, Lang, Mejdahl and Holmgaard 2023). In the latter study of Day et al. (2023) the response rate was as high as 93%, while in the study of Alcon et al. (2021) it was only 43% (22 out of 51 F/M patients completed the dedicated Gender Quality of Life survey 1 year after mastectomy).

In M/F patients, surgical enlargement of breast (with implants or fat grafting) is recommended after at least 12 months of feminizing hormones administration. The risk of breast cancers in the transgender M/F patients taking estradiol after breast augmentation surgery has not been evaluated (Salas-Humara et al. 2019). Despite the fact that – conversely to mastectomy – breast augmentation may be reversible (by re-operation), the Endocrine Society requires reaching 18 years of age to consent for chest augmentation (Hembree et al. 2017).

5.2.4. *Other procedures*

It is also possible to perform minor interventions that do not influence hormonal function and fertility, as facial masculinization or feminization, or voice surgery (Pasternak and Francis, 2019; Salas-Humara et al. 2019). Different nonmedical interventions, like chest padding or genital tucking, have also been proposed, however with the attention paid at their potential negative health effects (especially with respect to increase of scrotal temperature that might affect spermatogenesis and fertility) (Coleman et al. 2022). It seems somewhat puzzling that the same authors have allowed orchidectomy as one of the methods of gender-affirming therapy.

5.3. Psychological and psychosocial interventions

It seems that psychological interventions should have crucial role in management of minors with gender dysphoria. Unfortunately, in a very recent systematic review of Lehmann and Leavey (2023), concerning psychological and psychosocial interventions for gender diverse minors and their families, only four papers published between 2001 and 2021 met the inclusion criteria, and the main conclusion from the study is the need for further research in this area.

On the other hand, in WPATH SOC-8 (Coleman et al., 2022) there is no acceptance for reparative and conversion therapies undertaken to change person's gender identity or gender expression, due to their inefficiency and an increased risk of worsening mental health. The authors have emphasized that "efforts undertaken a priori to change a person's identity are clinically and ethically unsound" (Coleman et al. 2022, p.S53). Similar has been the statement of Turban, Beckwith, Reisner and Keuroghlian (2020), concerning psychotherapy that should be only gender-affirming, while not focused on regaining identification with the sex assigned at birth. In other part of WPATH recommendations there is a statement supporting psychological interventions as effective tools that may be helpful for "exploring gender identity and its expression, enhancing self-acceptance and hope" (Coleman et al. 2022, p. S175), referring to the work of Matsuno and Israel (2018).

Such approach may be considered with respect to persons with clearly defined gender identity, while – as can be seen from the previously quoted reports on frequency of gender incongruence – a large proportion of youths is ambivalent, non-binary or searching for their identity. It seems questionable to recommend that only gender reassignment solutions be offered in such cases. There is no doubt that all the activities must be undertaken with respect for human dignity and identity.

American Academy of Child & Adolescent Psychiatry (2018) in the Policy Statement concerning conversion therapy stated that interventions that intend to promote a particular gender and/or sexual orientation may be harmful and have no scientific credibility. The authors have proposed implementation of treatment focused on exploration of different aspects of identity to help the youth understand it, with no predetermined outcome. However, they have considered justified only gender-affirming (i.e. targeted towards transition) medical interventions, while not conversion (i.e. targeted to regain an identity consistent with one's biological sex) therapies. It should be noted that, in fact, the term "affirmation" is used in this context for the interventions that cause significant and often irreversible changes in the functioning of the body, while "conversion" relates to the attempts to regain gender integrity without irreversible interventions in the somatic integrity.

There are also other views regarding the psychotherapy of people with gender incongruence. The methodology of the previously cited study of Turban et al. (2020) has been criticized by D'Angelo, Syrulnik, Ayad, Marchiano, Kenny and Clarke (2021). The latter authors have also stressed the need for the least invasive treatment options, as psychological treatment focused on the relief from gender dysphoria, before progressing to irreversible medical interventions.

6. Timing of interventions, legal aspects and informed consent

According to recent recommendations (Coleman et al. 2022), the diagnosis of gender incongruence should be established according to ICD-11 classification (WHO 2018) or other taxonomy (in Poland the currently used version is ICD-10). Differences between various classifications have been described in dedicated part of the manuscript.

There is no approval for medical interventions in prepubertal children with gender dysphoria (Salas-Humara et al. 2019). The Endocrine Society (Hembree et al. 2017) recommends against using puberty blockers before the onset of puberty. The patients should be evaluated by experienced mental health professionals and ensured that their gender identity is accepted.

Medical interventions offered to transgender people include suppression of puberty, hormonal therapies and surgical operations, which should be chosen individually, according to the patient's needs and desires (Coleman et al. 2022). According to Dutch Protocol (van der Loos et al. 2023), suppression of puberty can be offered to children at least 12 years of age, at Tanner stage of breast or genital of 2 or more (i.e. after the onset of puberty). Gender-affirming hormones for puberty induction (testosterone in F/M adolescents, while estrogens for M/F ones) can be started at the age at least 15-16 years. Such procedures are in line with the guidelines of the Endocrine Society (Hembree et al. 2017). After at least 1 year of hormone administration, people "become eligible for gender-affirming surgery" after which they must continue to use hormones (van der Loos et al. 2023); unfortunately, the authors have not referred to a single item of literature to support their position in this aspect. The protocol presented by van der Loos et al. (2023) introduced an additional requirement of at least one year of observation before using puberty blockers, intended for a diagnostic evaluation.

Criteria for hormonal therapy for adolescents, provided by the Endocrine Society (Hembree et al. 2017) and WPATH (Coleman et al. 2022), include:

- gender dysphoria diagnosed by mental health professional,
- the ability of adolescent to give informed consent for the proposed interventions (it an adolescent have not reached the age necessary for legal medical consent, the consent must be obtained from the parents).

Risks and side effects of treatment should be discussed, including the potential compromise of fertility (infertility) and the possibilities to preserve fertility before the administration of gender-affirming hormones. The latter issue is of special importance in persons subjected to gonadectomy, that is in general not accepted in minors.

Pubertal blockers are proposed for suppression of puberty from the onset of breast development or testicular enlargement in order to delay development of potentially irreversible secondary sex characteristics (e.g. breast development, change of voice) and getting amenorrhea. The indication for such intervention is gender dysphoria diagnosed by mental health professional, worsening from the onset of puberty. According to WPATH (Coleman et al. 2022), in concordance with Dutch Protocol (van der Loos et al. 2023), the therapy should be initiated at Tanner stage 2, however, blockers of puberty may also be started at later stages of pubertal development, together with gender-affirming (cross-sex) hormones (estrogens, testosterone) that allows to use lower doses of sex steroids. Blocking puberty has been considered reversible but the authors have admitted that there is a lack of long-term studies on associated risks and also no consensus on the duration of such treatment, except for its discontinuation after gonadectomy (Salas-Humara et al. 2019).

It should be recalled here that in Poland the use of GnRH analogs in transgender minors is off-label therapy. Moreover, despite the pressure to use puberty blockers, it is uncertain whether such treatment does not reinforce the experienced dysphoria, due to the lack of data confirming the lack of effect of such treatment on gender identity (Robacha 2021). The concerns with respect to the use of puberty blockers in minors have also been discussed in the paper of Poleszak, Szabat P, Szabat M, Wójcik, Boreński

et al. (2019). The same caveat seems to apply even more to the early use of sex steroids for (trans)gender affirmation.

Even more far-reaching concerns about the use of puberty blockers have been presented by Richards, Maxwell and Mccune (2019) who pointed at loss of positive effect of sex steroids on consolidation gender identity, threatening the maturation of adolescent brain and limited experience with respect to causes of rapid increase of incidence of gender dysphoria and to safety profile of suppressing otherwise normal puberty. There is also a concern that the use of puberty blockers may be a factor that makes identification of adolescents with their own gender more difficult.

Previously, initiating gender-affirming hormones was recommended no earlier than at the age of 16 years, however, recent guidelines of Endocrine Society are more "flexible" in this aspect (Hembree et al. 2017).

American authors (Salas-Humara et al. 2019) are aware of the risks related to hormonal therapy with sex steroids, as venous thromboembolism or cardiovascular disease, as well as of an increased risk of depression and anxiety or even suicide (however, the reason for gender-affirming therapies is defined by them in the same document as improvement of mental health and life saving), so they suggest "to consider a risk/benefit analysis discussion with the patient and/or guardians about the medical interventions which may potentiate the patients' baseline risk of certain side effects".

In WPATH SOC-8 (Coleman et al. 2022) there is a clear recommendation that transgender or gender diverse adolescents should be informed about effects of gender-affirming medical interventions on reproductive capacity, especially the loss of fertility. The authors have also pointed out that future needs of minors with regard to having their biological offspring might change over time. Moreover, they have stressed that, up to now, only preliminary studies, concerning evaluation of decisions made in youth by transgender adults, are available (without providing proper citations, while drawing the evidence from studies on childhood cancer survivors that is in fact quite a different group).

Before initiating gender-affirming interventions, there is necessary to concern possible peer and social media influence on adolescents' perceptions of their own gender and needs for treatment. Parents or caregivers may provide important information, especially concerning the sudden change of gender identity, related to specific situations (Coleman et al. 2022).

As mentioned before, Endocrine Society recommends not to perform surgical interventions until the age of 18 (Hembree et al. 2017). However, there are also suggestions that certain procedures (e.g. chest masculinization) may be acceptable at a younger age (Salas-Humara et al. 2019). The term "chest masculinization" should be understood here as mastectomy (surgical removal of breast tissue).

It is also generally required to document at least 12 months of gender-affirming hormones administration due to gender dysphoria before surgical interventions and to discuss the long-term outcomes of such procedures with the patient (Hembree et al. 2017; Salas-Humara et al. 2019), however WPATH requires only 6 months period of hormonal treatment before gonadectomy or "gender affirming" genital surgery (Coleman et al. 2022).

With respect to the age when the patient would be able to give an informed consent, both the age of legal informed consent and sufficient mental capacity of the patient should be taken into account (Coleman et al. 2022; Hembree et al. 2017; Salas-Humara et al. 2019). Physicians of various specialties and other professionals dealing with transgender youth should be aware of the applicable legal regulation, in particular those related to minors.

Coleman et al. (2022), have stated that in some of young people the experience of gender diversity might result neither in embodying an opposite gender than assigned at birth nor in the need for medical interventions. Moreover, they have noted that any decisions on starting gender-affirming interventions without detailed and multidisciplinary diagnostics might be associated with the risk of non-optimal interventions with respect to the best long-term interest of young persons. The evidence of positive impact of acceptance and affirmation on mental

health improvement (regardless of whether medical interventions were undertaken) has also been stressed in the cited paper.

Despite the publication of subsequent recommendations, in the case of children and young adolescents with gender dysphoria, basic bioethical dilemmas remain unresolved: first–regarding the choice of course of action ("careful observation" carrying the risk of intensifying dysphoria, or "gender affirmation" with all its medical consequences) and the second one–regarding the discrepancy between the requirement to obtain the patient's informed consent for irreversible medical interventions related to the potential loss of fertility and the recommendation to implement these procedures at the onset of puberty (which usually occurs before reaching the age of understanding the consequences of decisions made and required for the legal capacity to give informed consent to medical procedures) (Baron and Dierckxsens, 2022).

The last issue concerning management of patients with gender dysphoria is uncertainty about their long-term effects. The need for further studies assessing the effects of gender-affirming hormone administration on physical and mental health of transgender patients is underlined even by advocates of these therapies (Coleman et al. 2022; Salas-Humara et al., 2019). In a very recent paper, Conflitti, Spaziani, Pallotti, Tarsitano, Di Nisio at al. (2023) have pointed at the risk of unsatisfaction with the results of changes and future regrets related to gender-affirming hormone treatment and surgery, especially in the context of the lost fertility.

After period of expanding indications for gender-affirming treatment and the tendency to start it at an increasingly younger age, the opposite trends have appeared in recent years, and this is the case in countries where quite extensive use of medical interventions has been allowed so far. In Sweden, the National Board of Health and Welfare (Socialstyrelsen 2022), central *national* authority for social and health services under the Ministry of *Health* and Social Affairs, has stated that the risks of puberty blockers and gender-affirming hormones "currently outweigh the possible benefits" for minors and "the treatment should be offered only in exceptional cases", despite previous approval for such interventions in 2015. This change of approach is supported by three factors: the continued lack of scientific evidence concerning both efficacy and safety of hormonal treatments offered to adolescents with gender incongruence, the new knowledge about the phenomenon of detransition of young adults who underwent gender-affirming therapy (Littman 2021) and unexplained increase in the number of adolescents (especially registered as girls) seeking care for gender incongruence. Moreover, Swedish authorities (Socialstyrelsen 2022) recommend following recommendations of psychiatrists from more than 20 years ago: Cohen-Kettenis and van Goozen (1997), and Smith, van Goozen and Cohen-Kettenis (2001). Similar tendencies in other countries are reported in a recent paper of Black (2023).

At this point, it is worth recalling once again that the sole purpose of affirmative therapies is to improve mental health by changing the phenotype (secondary and tertiary sex characteristics). Hormonal therapies and irreversible surgical interventions are undertaken in people with normal structure and function of genital organs and gonads, and restoring the state before they were carried out is extremely difficult, and in most cases even impossible.

With regard to children and adolescents with gender dysphoria or incongruence, the aspect of the broadly understood body dissatisfaction that may appear in due to different reasons seems to be insufficiently taken into account. In general population, body dissatisfaction may be related to psychological problems (depressive mood, eating disorders, low self-esteem). It has been documented that among children with gender incongruence, greater body dissatisfaction with the genital area correlated with psychological problems (Verveen, van der Miesen, de Graaf, Kreukels, de Vries, A and Steensma 2023).

7. Special problems in caring for children and adolescents with gender dysphoria

"Gender-affirming" therapy is used in people with gender dysphoria, i.e. those who feel discomfort related to their own sexual characteristics, whose

registered gender, gonadal and phenotypic sex are consistent and there is no somatic disease affecting the sex glands and genital organs. Hormonal interventions, and especially irreversible surgical procedures, involve the deprivation of the patient's normal gonads (ovaries, testicles) and/or sexual organs, which may have a significant negative impact on the mental state in the event of the desire to return to the original sex or even just the finding that gender change did not meet expectations regarding the solution of mental problems, and additionally had negative consequences for reproductive health. Taking into account the possible mental lability of teenagers, also in terms of their own gender identification, it seems necessary to be very careful when undertaking this type of medical procedures in minors.

This statement seems of special importance in the context of dramatically increasing number of adolescents (especially girls) who declare gender incongruence. There is some evidence that the explanation of this trend should include the influence of media and culture (Marianowicz-Szczygieł, 2022). As documented in a recent survey, Polish young transgender persons get information about hormone therapy or surgical procedures mainly from the Internet The relationship between the occurrence of dysphoria and functioning in a peer group in which there are other transgender-identifying persons has been conformed in a survey study on U.S. adolescents published by Littman (2018).

Young people entering the phrase "transition" may be the first to go to, for example, the portal. TRANZYCJA.PL, where they will find information clearly indicating that "after gender reconciliation during medical and/or social transition, gender inconsistency is cured", which may encourage taking such actions without realizing their real consequences. In this situation, it is necessary to provide all people with the problem of gender nonconformity with reliable information about the possibilities and limitations of modern medicine in all aspects of therapy, even before is onset.

Apart from the very important legal, bioethical and religious aspects (beyond the scope of this study) related to undertaking irreversible medical interventions in people with gender dysphoria, and to collecting and freezing gonad tissue or gametes in order to obtain biological offspring in the future through assisted reproductive techniques, while taking into account only "technical" limitations at the current stage of development of medical techniques, it should be emphasized that in the case of children and adolescents (especially in the initial stages of puberty), maintaining fertility and reproductive health requires at least postponing (and, if possible, avoiding) the use of hormonal therapies and surgical procedures, in particular those involving the removal of the gonads and genitals.

Summary

People with gender dysphoria and gender incongruence problems require individual (personalized) treatment in each case, with respecting their dignity and the way they perceive their own gender. Providing real help to such people requires comprehensive expertise (and therefore should be carried out in a multidisciplinary team) and awareness of not only the possibilities, but above all the limitations of the therapies offered and the irreversible nature of some medical interventions.

This is particularly important in relation to children and adolescents, in whom, before starting treatment, on the one hand, developmental defects, genetic and hormonal disorders must be excluded, and on the other hand, the search for their own gender identity during puberty, temporary identification with a gender different from their own biological sex and finally the influence of the peer group and/or social should be taken into account. It seems that the scale of potential and documented complications of hormonal therapies and surgical interventions (see Table 3) offered to patients for the purpose of "gender affirmation" justifies postponing their implementation until after adulthood, when their actual nature can be discussed in detail and fully informed consent. This approach can also protect minors from the consequences of medical procedures of which they were not fully aware, even if they thought they un-

Table 3. Complications of hormone therapies and "gender-affirming" surgeries

Persons K/M	**Persons M/K**
Hormonal therapies	
Puberty blockers	
Blocking normal sexual maturation in somatically healthy people Slowing down the rate of growth (reducing the pubertal growth spurt) Adverse effect on bone mineral density and body composition	
Primary or secondary amenorrhea Poor development or atrophy of the mammary glands	Inhibition of testicular development Impaired testosterone secretion Inhibition of spermatogenesis
Sex steroids	
Testosterone	Estrogens
Usually acceleration of growth rate, but possible shortening of growth period with early administration of high doses of testosterone (lower final height)	Shortening of the growth period with early administration of high doses of estrogen (lower final height)
Clitoral hypertrophy Atrophy of the vaginal epithelium Acne severity Androgenetic alopecia Lowering the voice Changes in body shape	Hypogonadotropic hypogonadism (testosterone deficiency) Hyperprolactinemia Gynecomastia Eunuchoid silhouette Increase of fat tissue
Increased risk of thromboembolism / cardiovascular disease	
Potentially increased risk of breast cancer, uterine cancer and ovarian cancer	Potentially increased risk of breast cancer and prostate cancer
Surgery	
Ovariectomy	Removal of the testicles
Permanent and irreversible infertility (cryopreservation options limited to mature gonads) Permanent and irreversible estrogen deficiency	Permanent and irreversible infertility (cryopreservation options limited to mature gonads and sperm) Permanent and irreversible testosterone deficiency
Hysterectomy	Removal of the penis
Loss of ability to get pregnant (except donor uterus transplant)	Permanent change in the appearance and the loss of function of the male external genitalia
"Reconstructive" procedures of the genital organs	
Urethrocutaneous fistulas and urethral strictures	Rectovaginal fistulas

derstood the information received, and additionally have "knowledge" from peers or from websites run by "transition" propagators.

The basic condition for undertaking any medical interventions should be to discuss with the patient and parents the consequences of using hormonal preparations, including those that are distant and insufficiently assessed, taking into account infertility and oncological aspects. It is not allowed to refrain from excluding other causes of lack of acceptance of one's gender, which requires conducting a reliable and in-depth psychological or even psychiatric assessment. The patients with problems with gender identification should receive appropriate psychological help, with full respect for their dignity and understanding of the suffering they experience. It is necessary to individualize and optimize the procedures in each case. Education in the field of dealing with children and adolescents with gender dysphoria should be taken into account by the staff of medical and educational facilities (family doctors and pediatricians, teachers, school counselors and psychologists, catechists). Lack of substantive knowledge or relying on media information can cause a lot of harm, and in turn, lack of empathy can lead to the loss of trust of an already wounded young person. On the other hand, one must not avoid precisely presenting to a minor the actual nature of the medical actions to be taken against him

or her. It is necessary to consider the terminology used, where de facto mutilating procedures and the use of drugs leading to significant and sometimes irreversible changes in the functioning of the body, including infertility, are euphemistically referred to as "affirming". Additionally, society lacks reliable knowledge about the scale of temporary gender identity disorders among children and adolescents, and such information is not provided by supporters of the so-called early adoption of "affirmation therapies".

In a systemic approach to the difficulties experienced by children and adolescents with problems related to gender dysphoria, it would certainly be helpful to develop national standards of psychological and medical care based on documented knowledge, with particular emphasis on the distinct stages of development (childhood, adolescence, adults) and complications or lack of sufficient evidence of the safety of medical procedures proposed by some bodies that consider themselves experts in the field in question. Improving the situation in the field of care for children and adolescents with gender dysphoria and gender nonconformity disorders certainly requires substantive discussion on the issues discussed, both among scientific authorities and people directly caring for children and adolescents, as well as appropriate legislative and organizational actions, taking into account, first of all, the protection of minors against the too easy adoption of irreversible or potentially irreversible medical interventions or procedures with not fully documented safety and effectiveness. It seems that it is necessary to use the experience not only of countries developing "gender-affirming" therapies, but also–and perhaps even primarily–of countries and expert teams that withdraw consent to carry out such procedures in favor of more conservative treatment and psychological care.

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