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ESCAP statement on the care for children and adolescents with gender dysphoria: an urgent need for safeguarding clinical, scientific, and ethical standards

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According to the DSM-5-TR [1] gender dysphoria refers to “...the distress that may accompany the incongruence between one’s experienced or expressed gender and one’s assigned gender”, requiring also the presence of “...clinically significant distress or impairment in social, school, or other important areas of functioning”; the DSM-5-TR lists gender dysphoria among mental disorders. In contrast, the latest ICD-11 [2] describes gender incongruence as a condition “...characterized by a marked and persistent incongruence between an individual’s experienced gender and the assigned sex”. In order to avoid the stigma connected to mental disorders and the “double stigmatisation” of this historically highly stigmatised population, the ICD-11 decided

to remove the gender identity-related diagnoses from the section on mental disorders and include it in the section “Conditions Related to Sexual Health” [3]. As such, gender dysphoria is not a mental health disorder according to WHO definitions, but psychiatrists and other mental health professionals may be asked to be involved to address co-occurring mental health problems [4]. Even though not all people with gender incongruence experience distress or dysfunction, the condition can be accompanied by significant suffering and have a major psychosocial impact on the individual and the family, sometimes requiring medical and psychosocial interventions. Consequently, one of the major reasons for the decision to leave gender dysphoria diagnosis as a mental disorder in DSM-5-TR, was to enable funding for the provision

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of any medical and mental health treatments needed [3]. A proportion of people experiencing gender dysphoria (from here the term that calls for psychosocial and medical care will refer also to the more neutral term “gender incongruence” if not stated otherwise) pursue social, legal, and medical changes affirming their subjectively experienced gender. These may include presenting with the desired gender in their personal environments (e.g., family, friends, workplace, school, ...) by using different names and pronouns—referred to as *social transition*. It may also include formal changes of their name and/or gender on documents—referred to as *legal transition*. Finally, *medical transition* can be achieved by prescription of cross-sex hormones (estrogens or testosterone, depending on subjects’ biological characteristics) and/or gender-reassigning surgical procedures including genital (gynecological, urological) and other (mastectomy, plastic surgery, and ear, nose, and throat surgery procedures) [5, 6].

In the past century, gender dysphoria appeared to be a very rare phenomenon. When present, few people sought medical interventions, and specialized medical services available were rare or nonexistent in many countries until the last two decades. However, reliable data on past prevalence of gender dysphoria is lacking because the phenomenon was poorly investigated. When the specialised services were established, they were attended predominantly by small numbers of adults with assigned male sex (trans females), usually having a long-term history of gender dysphoria [5, 7]. The visits to specialized services by children and adolescents were much rarer events [8]. More recently, in the 2010s and thereafter, there was a substantial increase in referral rates of adolescents and young adults to specialized services for the assessment and treatment of gender dysphoria, with 6- to 19-fold increase between 2011 and 2017 [9–13]. At the same time, the characteristics of children and adolescents seeking support because of gender dysphoria have changed, so that most referrals now concern post-pubertal individuals with assigned female sex [10–14]. The specialized gender services also documented higher rates of psychiatric comorbidities of the children and adolescents referred [10, 14–17], highlighting the importance of psychiatric assessment. The most common conditions reported before the onset of the symptoms of gender dysphoria included neurodevelopmental disorders (especially autism), severe forms of depression and anxiety, and suicidality, as well as the experience of trauma (including sexual abuse) [10, 14–17].

The first protocol for the medical and psychological management of children and adolescents with gender dysphoria was published by Dutch researchers at the 4th Ferring Pharmaceuticals International Paediatric Endocrinology Symposium in Paris in 2006 [8]. Initial professional guidelines on the management of children and adolescents with gender dysphoria [8], have influenced the clinical practice in many countries over the subsequent two decades [6, 18–21]. The

emphasis in management of children and adolescents at the time was on psychological treatments, family counseling, and psychosocial care [21]. After the publication of a Dutch study on puberty suppression in adolescents with gender dysphoria in 2011 [22], puberty suppression (introduction of “puberty blockers”) and hormonal treatments for gender dysphoric youth after the start of puberty were also advised [6, 18, 20]. The time-limited use of puberty blockers (gonadotropin-releasing hormone analogs [GnRHa]) was advised to give youth with gender dysphoria additional time to develop and consolidate their sexual identity while preventing the development of sexualised physical characteristics. However, the original study [22] and subsequent observations showed that nearly all youth treated with puberty blockers later continued to receive hormonal gender-affirming therapy, which was instead only prescribed to less than a third of youth with gender dysphoria before the introduction of puberty blockers [6, 18, 20, 22, 23]. The findings questioned the supposed time-limited nature of puberty suppression interventions and raised concerns about the possible irreversible nature of decision-making when prescribing puberty blockers. Guidelines advised that the administration of cross-sex hormones (estrogens or testosterone) should begin after the age of 16 years, but could be started earlier in some instances if the incongruent experienced gender identity persisted, and youth wished to proceed with gender reassignment [6, 18–20]. Furthermore, guidelines advised that surgical procedures should be undertaken after the age of 18 years, although they have also occasionally been reported in minors [6, 9, 20].

More recently, clinicians, scientists, and the general public have been increasingly questioning some of the existing practices and standards of care for children and adolescents presenting with gender dysphoria [6, 18, 20, 24–26]. Research found some serious health consequences of puberty blockers and cross-sex hormones, particularly when treatments are started in minors [27–33]. There have also been several examples of non-adherence to the core professional and medico-ethical principles when providing care for gender dysphoric children and adolescents in some countries [25, 34–45]. Therefore, it is important to emphasise again here the key principles that must be guaranteed in the work with minors with gender dysphoria [46, 47]:

- the *principle of non-maleficence*: do not use outside the research environment any experimental interventions with potentially irreversible effects, or interventions with unknown long-term consequences; do not adopt new practices prematurely without sufficient evidence; do not continue with outdated practices that might not be in the best interest of the patient.
- the *principle of beneficence*: adopt medical interventions with favorable benefits-to-harms ratio; consider benefits-

- to-harms ratio of not providing medical interventions; ensure adequate diagnosis and treatment of co-existing psychiatric disorders; ensure comprehensive diagnostic assessment of gender dysphoria instead of only relying on the self-assessment of children and adolescents.
- the *principle of autonomy*: involve minors in the decision-making processes around their care in an age- and development-appropriate manner, assessing their capacity to consent; adopt an adequate informed consent process for possibly lifelong and irreversible decisions, securing that children and adolescents fully understand the potential risks, benefits, and irreversible nature of the treatments; consider the rights of their parents and guardians to consent to any major intervention or for participation of their children in research on experimental treatments; consider the rights of their parents and guardians to be fully informed about the current care for their children; offer adequate support and resources to those who decide to de-transition to their assigned sex, and respect their decision to do so.
- the *principle of justice*: ensure access to reliable and up-to-date information, assessment, and treatment for gender dysphoria, and during transition or de-transition; adopt equal precautionary measures for all; and protect the rights of children and young people as a group in a particularly vulnerable developmental phase.

Several independent reviews were performed assessing the evidence for the benefits and harms of the recommended treatments [33, 48–53]. In particular, two National Institute for Health and Care Excellence (NICE) evidence reviews focused on the use of GnRHa [49] and cross-sex hormones [50] in minors, evaluating clinical effectiveness, short- and long-term safety, and cost-effectiveness of the two interventions compared with alternative conditions (psychological support, social transitioning to the desired gender, or no intervention). The NICE reviews also examined whether there were any different outcomes in specific subgroups, across the diagnostic criteria used, or based on the age at commencement or the duration of treatment [49, 50]. NICE defined “critical outcomes” for both interventions as effects on gender dysphoria, mental health (depression, anger and anxiety), and quality of life; “important outcomes” as effects on body image, psychosocial impact (global and psychosocial functioning), engagement with health care services, extent of and satisfaction with surgery, and stopping treatment [49, 50]. NICE defined additional “important outcomes” as changes in bone mineral density for the GnRHa interventions, and de-transition, as short- and long-term safety outcomes, and adverse effects for cross-sex hormones interventions [49, 50]. For cross-sex hormones interventions, an additional “critical outcome” was suicidality [50]. Additionally, a recent review of animal mammal

and human studies reported possible effects of puberty blockade on neurodevelopment [33]. The NICE reviews and other independent reviews from UK, Sweden, Finland, and recently Germany (which updated the original NICE reviews by examining all studies published until August 2023) were consistently critical of the current evidence base [33, 48–52]. The reviews highlighted that research on treatment benefits and harms of gonadal suppression and cross-sex hormones for children and adolescents with gender dysphoria has significant conceptual and methodological flaws, that the evidence for the benefits of these treatments is very limited, and that adequate and meaningful long-term studies are lacking. The reviews, therefore, recommend extreme caution in using these interventions. The German review also pointed out the poor reliability and instability of a gender dysphoria diagnosis in a specific child over time, but also the possible effects of the decisions to block puberty or preventing medical transitioning on a child's psychosocial development and mental health. They further recommend that “Children and adolescents with gender dysphoria should therefore primarily receive psychotherapeutic interventions that address and reduce their experienced burden. Any decision to use puberty blockers and/or cross-sex hormones should be made on a case-by-case basis after judicious risk benefit evaluation and, if possible, within clinical studies. Beforehand, psychiatric/psychotherapeutic diagnosis and treatment of concomitant mental disorders should be undertaken.” (Electronic Supplementary Online Materials I: Adapted abbreviated English version, Page 3) [52]. Additionally, the World Health Organization (WHO) has recently indicated that the evidence base for commencing medical gender reassignment interventions during developmental years is weak and insufficient, and therefore the forthcoming WHO guidelines will not concern minors [54]. In parallel with the reviews, there have been changes in medical (and legal) practices in many countries [24, 55, 56]. Despite the current paucity of evidence, and the difficulties that clinicians and families may experience when faced with an adolescent with severe and persistent gender dysphoria, hormonal and surgical treatments may be justifiable decisions in certain cases, because of the associated distress and mental health risk.

In the light of recent scientific developments in understanding, the European Society of Child and Adolescent Psychiatry (ESCAP) urges *all professionals* (e.g., those working in health care, social care, education) working with children and adolescents with gender dysphoria to:

- Insist on continuing an open professional debate on gender dysphoria in children and adolescents including performing and sharing high-quality research on aetiology, comorbidity, and treatment, and openly reporting the resulting research findings.

- Deliver professional management of gender dysphoria addressing the specific individual needs and wishes of children or adolescents, provide adequate baseline and follow-up diagnostic assessment for gender dysphoria, cognition and any comorbidities, and provide empathic and safe care.
- Insist that novel and experimental interventions related to gender dysphoria are differentiated from routine clinical treatment and are performed exclusively as part of documented observational intervention protocols or research trials, safeguarding standards for research on pediatric participants and vulnerable populations (e.g., respecting standard of minimal harm; ensuring adequate informed consent process depending not only on the subject's age, but also on their cognitive, emotional, and social development; ensuring previous research on animal models and adult population when using experimental interventions; respecting precautionary principle when using experimental interventions).
- Report and remind on the need for long-term follow-up studies. ESCAP calls on the EU to build a framework or study register which should include the patients presently treated, patients not receiving treatment, and the ones who discontinued the treatments, to better understand the outcomes of different treatment paths, including cognitive, psychological and physiological effects.
- Promote active learning from any potential past flaws in the management of children and adolescents with gender dysphoria, to prevent violations of existing clinical, scientific, and ethical standards.
- Insist on delivering explicit attention to individuals who seek de-transition or regret their transition, to address, respect and understand their experiences, provide appropriate care and support, and consider how these narratives can be integrated into clinical practice.
- Foster open, inclusive, and evidence-based professional debate on the development of standards for the best care for children and adolescents with gender dysphoria. Such debate and any decision-making processes should include experts with lived experience of gender incongruence with various outcomes (transition, de-transition, resolution without interventions and any other possible outcomes).
- Insist that the professional management of children and adolescents with gender dysphoria should be based on due diligence. Ensuring that healthcare providers are adequately trained and knowledgeable about gender dysphoria, its treatment, and the unique needs of this population.
- Insist that the research findings are published solely on the grounds of quality criteria and not based on their findings.

ESCAP firmly believes that there is an urgent need to apply widely endorsed clinical, scientific, and ethical standards to the care of children and adolescents with gender dysphoria. It is important to base decisions for possible medical transitions on a rigorous assessment of individual needs and their capacity to consent regarding the serious long-term consequences of these treatments. Long-term follow-up studies are urgently needed to better understand both the natural course of gender dysphoria in the absence of medical treatment and the consequences of medical transition. A clinical research framework with patient and public involvement should be established and promoted at the European level to facilitate relevant research. The standards of evidence-based medicine must ensure the best and safest possible care for each individual in this highly vulnerable group of children and adolescents. As such, ESCAP calls for healthcare providers not to promote experimental and unnecessarily invasive treatments with unproven psychosocial effects and, therefore, to adhere to the "primum-ni-nocere" (first, do no harm) principle. Finally, ESCAP insists that respect for all kinds of different views and attitudes is an essential part of an ongoing open professional debate that we wish to stimulate.

Declarations

Conflict of interest The authors report no conflict of interest with regards to this publication.

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