IDEA Group Consensus Statement on Medical Management of Adult Gender Incongruent Individuals Seeking Gender Reaffirmation as Female

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Abstract

Cross sex hormone therapy (CSHT) is a strongly desired medical intervention for gender incongruent individuals. The goal is to change secondary sex characteristics to facilitate gender presentation that is consistent with the desired sex. When appropriately prescribed CSHT can greatly improve mental health and quality of life for gender incongruent individuals. Appropriate care for gender incongruent individuals in India is almost absent due to lack of country specific guideline and lack of training amongst the medical professionals. This document is intended to assist endocrinologists and physicians whose adult gender incongruent client is seeking gender reaffirmation as female (transfeminine). These individuals require a safe and effective CSHT regimen that will suppress endogenous male hormone secretion and maintain physiologic levels of female sex hormone. In this document, we offer suggestions based on an in-depth review of Guidelines of Endocrine Society, The World Professional Association for Transgender Health guidelines, the Sappho Good Practice Guide of India and collegial meetings with expert Indian clinicians working in this field. Clinicians represented in our expert panel are not gender specialists by training but have developed expertise due to the volume of gender incongruent individuals they manage. This consensus statement on medical management provides protocols for the prescribing clinician relating to diagnosis, baseline evaluation and counselling, prescription planning for feminizing hormone therapy and anti-androgen therapy, targets for monitoring hormone therapy, choice of therapy, clinical and biochemical monitoring, recommending sex reaffirmation surgery and peri-operative hormone therapy. The recommendations made in this document should not be perceived as a rigid set of guidelines and the treating clinicians are encouraged to modify our suggested protocols to address emerging issues.

Keywords: Cross sex hormone therapy, gender dysphoria, gender incongruence, Hijra, Indian consensus, transfeminine, transgender

Glossary

Cisgender: denoting to a person whose sense of personal gender identity corresponds with their assigned birth sex.

Gender identity: Internal sense of being male or female or identifying with both or neither.

Intersex or DSD (disorder of sexual differentiation): denoting to a person born with reproductive or sexual anatomy that does not fit typical definitions of female or male.

Transfeminine: denoting to a transgender person who were assigned male at birth, but identify with femininity to a greater extent than with masculinity.

Transmasculine: denoting to a transgender person who were assigned female at birth, but identify with masculinity to a greater extent than with femininity.

Transgender: denoting to a person whose sense of personal gender identity does not correspond with the assigned birth sex.

Access this article online

Quick Response Code:

Website: www.ijem.in

DOI: 10.4103/ijem.IJEM_593_19

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Submitted: 08-Nov-2019 **Revised:** 06-Feb-2020
Accepted: 19-Mar-2020 **Published:** 30-Apr-2020

How to cite this article: Majumder A, Chatterjee S, Maji D, Roychaudhuri S, Ghosh S, Selvan C, *et al.* IDEA group consensus statement on medical management of adult gender incongruent individuals seeking gender reaffirmation as female. Indian J Endocr Metab 2020;24:128-35.

Introduction

Gender incongruence (the incongruence between assigned gender and expressed/experienced gender) is a condition with limited public awareness and is associated with social stigma in our country.[1] It is not a disorder as per International Statistical Classification of Diseases 11 (ICD 11).[2] Gender Incongruence may be observed amongst apparently normal individuals, amongst individuals suffering from disorder of sexual differentiation (DSD) and also amongst some individuals known as "hijras". As per last census in 2011, there are 5 lakhs transgender individuals (mostly comprising hijras) in India which is most likely an underestimation. There is a general lack of awareness regarding gender incongruence in India. There also exists a lack of clarity regarding the medical procedures to be followed during gender reaffirmation in India.

Lack of awareness about potential benefits of endocrine treatment, distrust in modern medicine and a desire to preserve privacy are the reasons why transgender persons (TGP) often do not seek medical help.[1] Amongst those who seek medical help, it is often sought late. Most have inadequate family support, and sometimes undergo unplanned castration by untrained and unqualified individuals.[3,4] The lack of country specific guidelines and lack of training relating to the procedures to be followed for gender reaffirmation amongst the medical professionals are major hurdles for appropriate management in India.[1] This consensus statement has been developed to provide guidance to the medical professionals of this country, regarding hormone therapy in a resource limited setting, in individuals who are reared as males but are gender incongruent and wish to reaffirm their gender as females (transfeminine).

Methods

This consensus statement with guidance on diagnosis, hormone therapy, follow up and recommendation for sex reaffirmation surgery was based on guidelines published by globally recognised professional bodies as well as those published from India, namely guidelines of The Endocrine Society, The World Professional Association for Transgender Health (WPATH) guidelines and the Sappho Good Practice Guide, India.[5-7] The expert group after discussion has made the following recommendations:

Recommendation 1: Diagnosis

Evidence: The Diagnostic and Statistical Manual of Mental Disorders (DSM-5 302.85 (F64.9)) diagnostic criteria has been endorsed by The Endocrine Society guidelines of 2017[5] and this was also upheld by the WPATH for diagnosis of gender incongruence/dysphoria.[6] The Sappho Good Practice Guide published from the expert group meeting in Kolkata 2017[7] also acknowledged the DSM 5 criteria.[8] It may be noted ICD 11 no longer classifies gender incongruence as a mental disease. It is now included as a disorder of sexual health.

Consensus: The expert group recommends usage of DSM 5 as diagnostic criteria for the diagnosis of gender incongruent individuals and the treating endocrinologist should seek help from mental health professionals (MHP) to confirm the diagnosis [Annexure 1: Table 1].[8] Diagnosis of gender incongruence particularly in a pre-pubertal child or adolescent may be difficult to make. The current document is meant for adults with gender incongruence and the management of children and adolescents is beyond the scope of this document.

Evidence: Although evaluation and care for a person with gender incongruence is a multi-disciplinary effort, the diagnosis is usually best made by a MHP. This is in keeping with the WPATH and The Endocrine Society guideline. The group recognizes and supports the current trend that diagnosis is patient initiated and treatment can be started by any interested clinician with appropriate knowledge.[9]

Endocrine Society recommends that it is necessary to make a distinction between gender incongruence/dysphoria and conditions that have similar presentations, e.g. body dysmorphic disorder, and also to exclude other underlying psychiatric co-morbidities.

Consensus: The expert group recommends diagnosis of gender incongruence should be made with the help of at least one MHP or clinical psychologist.

Recommendation 2: Baseline evaluation and counselling

Evidence: The Indian legal system recognises the age of consent as 18 years. Hence, the age of 16 as mentioned in the Endocrine Society guidelines and also in that of WPATH is not appropriate in India. Instead the Sappho Good Practice Guide[7] to gender transition has been adapted by the expert group. CSHT is not recommended for individuals below age of 18 as per the Endocrine Society guidelines (only use of Gonadotropin Releasing Hormone (GnRH) analogs to block pubertal hormones is suggested). The other items of the checklist for baseline evaluation and counselling are congruent for the three guidelines and have been unanimously adopted. It is important to appraise the patient regarding the irreversibility of the effects of gonadectomy and also to discuss prospects of gamete conservation.[10] The potential cost implications and resource constraints of gamete preservation in India, needs to be discussed before starting feminizing hormone therapy.

Consensus: The expert group recommends the following check list prior to initiation of CSHT:

1. Confirmation of attainment of age of consent (above age 18 years)
2. Confirmation preferably from one MHP [Annexure 2] or from one psychologist [Annexure 3] to exclude other confounding illnesses or mental disorders and also to prove persistent gender incongruence
3. Affidavit affirming name and preferred gender (optional)
4. It is suggested that the individual should have experienced documented cross dressing (Real Life Experience) for at least 3 months duration. This may not be possible in all situations as many subjects dress in a sex neutral manner

5. Physical examination: height, weight, blood pressure and examination of breasts, genitalia and digital rectal examination (DRE) for prostate
6. Laboratory investigation: HbA1c, potassium, urea, creatinine, lipid profile, thyroid function test, liver function tests, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone, estradiol, hepatitis B surface antigen (HbsAg), anti-Hepatitis C Antibody, VDRL and tests for human immunodeficiency virus (HIV)
   Karyotype testing is optional as is evaluation of prostate-specific antigen (PSA) and screening and surveillance of bone health[11-18]
7. Informed consent for CSHT [Annexure 4]
8. Counselling regarding the possible effects along with risks and benefits of long term feminisation therapy and confirm that the patient has the capacity to understand the consequences and is capable of taking hormones in a responsible manner
9. Counselling for adoption of healthy lifestyle with regards to body weight and substance abuse. Control of hypertension and diabetes if coexisting[19-22]
10. Counselling for the option of gamete preservation[10]
11. Counselling for the option of voice therapy and laryngeal surgery.

Recommendation 3: Feminizing hormone therapy

Evidence: The hormone therapy in gender incongruent males is complex as initiation of estrogen therapy is itself not enough to suppress endogenous testosterone production. Hence, there is a need for concomitant anti-androgen therapy or GnRH analogues in most individuals. The initiation of therapy should be preceded by a detailed discussion about the treatment regimen, the possible physical changes expected, duration taken for the changes to appear and discussion regarding the medical risks for that individual person related to hormone therapy. Estrogen, the cornerstone for feminization of transfeminine individual typically requires supraphysiological doses, and estrogen requirement is more in those who are not receiving GnRH therapy and in those with preserved testes. The dose is gradually up-titrated to keep in balance the clinical response on one hand and risk of side effect on the other.[23]

The most serious adverse effect of estrogen therapy is VenousThromboembolism (VTE). Increasing age and bodyweight are two important factors that increase the risk of VTE with estrogen use.[24] Tobacco cessation should be discussed and appropriate help should be sought. However, there has been no benefit found in screening the prospective estrogen users to identify the population at risk of VTE with currently available tools.

Other common side effects of estrogen therapy is mild in nature and often does not require any change in medication.

a. Breast pain or tenderness
b. Vomiting and loss of appetite
c. Weight gain or loss
d. Nervousness, depression and irritability
   Leg cramps and joint pain.

Drug therapy for feminisation was recommended in line with the Endocrine Society and the WPATH guidelines. However, due to economic constraints, oral formulations of estrogen have been recommended by the expert committee despite increased risk of VTE. Transdermal estradiol, especially reservoir patch, which has lower systemic side effects, are not much successful in tropical climate.[25]

Consensus: The expert group recommends the use of available estrogen preparations, keeping in mind the doses, advantages and limitations of each preparation [Annexure 5: Table 2].[26-28]

The expert group discourages estrogen therapy in the following concomitant medical conditions:

1. Previous history of VTE
2. History of estrogen sensitive neoplasm
3. Advanced stages of chronic liver disease
4. Hypertriglyecridemia (relative contraindication).

As different preparations of oral estrogens are available in India, a table [Annexure 6: Table 3] elucidating available dose equivalence is included.

Recommendation 4: Progestin therapy

Evidence: Use of progestins is controversial because of its proliferative effect on breast tissue. It does not lower the serum testosterone levels and associated with many side effects. Estradiol therapy achieve gonadal steroid level equivalent to those of cis-women and Endocrine Society Guideline recommends estradiol only.[5] However, some evidence suggests that progesterone may help in feminization process, optimisation of breast maturation, increase in bone formation and have possible cardiovascular health benefits.[29] A typical dose is Drospirenone 3 mg daily used along with cyproterone. Adverse effects include - increased potassium level, depression, weight gain, lipid changes, increase in breast cancer risk and possible suppression of the pituitary adrenal axis. The micronized form of progesterone is ideal and preferred.

Consensus: The expert group discourages the routine use of progestin therapy.

Recommendation 5: Therapy to minimize androgen effect

Evidence: Suppression of testosterone production and/or blocking its effects contributes to the suppression/minimization of male secondary sexual characters (i.e., those which are reversible after completion of puberty). This also allows the use of lower estradiol dosing with its antecedent benefits. They are thus as a class of drugs recommended by all the major available guidelines and publications[5,6,17] and is also endorsed by the indigenous Sappho Good Practice Guide.[7] Anti androgenic drugs used are spironolactone,[30] 5-alfa reductase inhibitors,[31] GnRH agonists[32] and Cyproterone acetate[33] and have been placed in the hierarchy of choice by the expert committee. Androgen-reducing medications are the first line therapy,

as it reduces endogenous testosterone levels or activity, and thus diminishes masculine characteristics including body hair. They also minimize the dosage of estrogen needed; thereby reducing the risks associated with high-dose exogenous estrogen therapy. GnRH analogues as anti-androgens are the preferred first line therapy. However, in a resource limited setting, spironolactone with/without finasteride is a reasonable alternative. Alpha reductase inhibitors will not cause a fall in serum testosterone levels and spironolactone may or may not cause a fall, because of their modes of action. As discussed in the previous section, the consensus was not to advise progestins; hence cyproterone acetate is not recommended.

Consensus: The expert group recommend the use of following agents to minimize androgen effect:

1. GnRH agonists[28,32]:
    a. Triptorelin depot 3.75 mg monthly or 11.25 mg 3 monthly (IM or SC)/Leuprolide3.75 mg monthly or 11.25 mg 3 monthly (IM or SC)/Goserelin3.6 mg monthly or 10.8 mg every 3 monthly (SC upper abdominal wall)
    b. Action – decrease the release of gonadotropins and thereby production of sex hormones by the gonads
    c. Adverse effect - decreased libido, headache and decreased bone mineral density
    d. Limitation - Expensive and need to be injected.
2. Spironolactone:
    a. Dose - 100-400 mg per day[27,30]
    b. Action - a diuretic used as an antihypertensive agent and directly inhibits testosterone secretion and androgen binding to the androgen receptor
    c. Adverse effect - fall in blood pressure and electrolyte imbalance.
3. 5-alpha reductase inhibitors (finasteride 5 mg per day or dutasteride 0.5 mg per day)[28,31]:
    a. Action - block the conversion of testosterone to 5-alpha dihydrotestosterone and is used when there is residual testosterone
    b. Effect - reduce scalp hair loss, body hair growth, sebaceous glands secretion
    c. Adverse effect - Erectile dysfunction (not an issue in transfaminine individual).

Recommendation 6: Other Ancillary therapy (Laser, Eflornithine, Vitamin D and Calcium supplementation)

Evidence: Transfeminine individuals always face unique dermatologic needs in addition to routine care. Decrease in male-pattern hair growth is a desired cutaneous change with CSHT but hormone therapy alone may not eliminate facial hair growth sufficiently. The use of eflornithine and laser is often used as ancillary therapy for removal of body hair.[34] Eflornithine is an inhibitor of ornithine decarboxylase with proven eficacy in reducing unwanted facial hair when applied twice daily in the area of skin under the chin. Objective improvement may not be observed before 8 weeks' treatment and the hair growth may returns to pre-treatment level within 8 weeks of stopping treatment. Laser, on the other hand, may reduce hair growth permanently and can address a larger surface area in little time but costly. Little is known about the use of calcium and vitamin D in transgender men and the published data does not show definitive evidence in favour of universal usage of this among gender incongruent individuals.[35]

Consensus: The expert group recommend that the Laser therapy and Eflornithine may be used as ancillary therapy for removal of body hair but does not support the routine use of vitamin D and calcium supplementation.

Recommendation 7: Targets for monitoring hormone therapy

Evidence: The biochemical cut offs or targets for testosterone and estradiol in an individual undergoing hormone therapy have been chosen in line with the values laid down by the Endocrine Society,[5] WPATH[6] and the indigenous Sappho Good Practice Guide[7] and have been further strengthened by the evidence presented by Gardner.[36] The University of California UCSF Medical Center, which houses a Center of Excellence for Transgender Medicine, also recommends along the same lines[17] and adds to the strength of this consensus. The patient should be offered the choice of being tested for hormones levels every 6 months to monitor adequacy of therapy and to avoid overtreatment. In most low resource settings in India, testing may be less frequently performed.

Consensus: The expert committee recommends the following targets for hormone therapy:

A. Serum testosterone levels should be <55 ng/dl
B. Serum estradiol should be 100- 200 pg/ml.

Recommendation 8: Choice of therapy

Evidence: GnRH agonists suppress testosterone levels and are the commonly prescribed therapy in many guidelines including The Endocrine Society guideline[5] and WPATH guideline. [6] However, GnRH may be considered as second-line therapy in resource poor setting owing to their high cost[9]. Replacement dose is individualised and up-titrated gradually from low dose, depending on clinical response and adverse effects.

Consensus: The expert committee recommends the sequence of feminizing therapy depending on the financial status of the individual [Annexure 7: Table 4].

Recommendation 9: Clinical and biochemical monitoring

Evidence: Prolactin level may be affected by CSHT[37] and may be measured every 3-6 months as per recommendations of major guidelines.[5,6,7,17] Hepato-toxicity and acute liver injury needs to be assessed heralding the need for evaluation of liver function tests at regular intervals.[15,38]

VTE is a major complication of estrogen therapy although the extent of risk varies according to the route of administration.[24,39,40] The incidence has increased up to 20-fold owing to the use of CSHT, particularly estrogen.[41] Treatment of VTE entails active treatment to suppress the episode of acute thrombosis, and secondary prevention.[41]

The presence of estrogen receptors in breast and prostate cancer tissue[42] necessitate the need for breast and prostate cancer screening in individuals receiving feminisation therapy but the modalities for screening and the frequency of screening has not been laid down by the existing guidelines. There is an increased risk of breast cancer in trans-women compared to cisgender men, and a lower risk in trans-men compared with cisgender women. In trans-women, the risk of breast cancer was shown to be increased during a relatively short duration of hormone treatment and the characteristics of the breast cancer resembled a more female pattern. These results suggested that breast cancer screening guidelines for cisgender people are sufficient for transgender people using hormone treatment.[43]

Information available on cancer outcomes for transgender people is scant as there are no large long term prospective studies investigating cancer incidence and mortality in lesbian, gay, bisexual, and transgenders. Also, general population cancer statistics do not usually collect details of sexual orientation or status, so the relevant information is unavailable. Transgender individuals who have undergone sex reaffirmation surgery may need to be aware of the possibility of cancer due to residual reproductive tissue that may have been left behind after surgery. They may also opt out of cancer screening and examinations because of emotional or physical distress associated with the gender-genital organ discordance. As reported for lesbians, gay men and bisexual individuals, transgender individuals are also likely to consume alcohol and abuse tobacco, and may also be at high risk of contracting HIV and Human Papilloma Virus infection, further increasing the risk of developing malignancies. Studies suggest that the transgender population is less likely to receive recommended cancer screening compared to cisgender population, putting the onus on specialists to increase awareness, disseminate information and provide guidance to the primary health care providers.[44]

Breast cancer screening: Hormone replacement therapy (HRT) has been well established as a risk factor for breast cancer. Although breast cancer is rare among men, the effect of exposure to exogenous estrogen among male-to-female (MTF) transgender population has not been studied. The fact that estrogen receptors are expressed in breast tissue[43] and that these patients receive supra-physiological doses of estrogen and for a longer duration (beyond the average menopausal age) puts them at a possible higher risk of development of cancer. These factors make screening for breast cancer necessary but currently available data is based on isolated case reports only. A large Dutch registry including 1800 individuals reported only one case of breast cancer when followed up for a period of 15 years (range 1 to 30 years). Estrogen therapy alone without progesterone among females with Turner's syndrome and from Women's Health Initiative study did not actually find increase risk of breast cancer. However, we need data from larger cohorts and longer periods of follow up before the actual risk can be ascertained. Current guidelines suggest screening for breast cancer as in cisgender individuals as per the prevalent guidelines.[45]

Prostate cancer screening: Although the prostate is biologically a male organ, prostatectomy is not usually performed as part of reaffirmation surgery. As prostatic cancer has been traditionally been thought to be androgen dependent, one would expected that these individuals may be protected from developing prostatic cancer.[46] However, rare cases of prostate cancer have been reported in transgender females.[46] It is possible that these cancers existed before the start of hormone manipulation or factors other than androgen (but including estrogen) could drive the development of prostate cancer. An increased estrogen to dihydrotestosterone ratio has been shown to have the highest effect on stromal cell growth. As these individuals are likely to have elevated estrogen to dihydrotestosterone ratio, this could be one possible mechanism that increases their susceptibility to develop prostate cancer. It is important not to miss screening for prostatic cancer in these individuals. The current evidence suggests that transgender women should be screened for carcinoma prostate similar to cisgender men.[44,46]

Bone mineral density: Bone health and sex hormones are intimately inter-related. Puberty is associated with significant bone accruement in both genders, and boys develop wider bones with greater cortical size due to periosteal apposition occurring in and around puberty.[47] Hypogonadism in both genders have been associated with accelerated bone loss and osteoporosis. Hence, gender reaffirmation therapies in these individuals could have deleterious effects on bone if they are rendered hypogonadal without estrogen replacement therapy following orchidectomy.[35,47] Though data are scarce, the evidence from a meta-analysis suggests that the bone mineral density (BMD) increases in individuals receiving feminisation therapy.[48] Long-term CSHT seemed to affect only lumbar spine BMD in transgender women and had a neutral effect on BMD in transgender men. This evidence is of low to moderate quality due the observational study design, small sample sizes, and variations in hormone therapy protocols.[49]

A recent 10-year follow-up data of transgender individuals receiving CSHT revealed that sex hormone replacement therapy did not have any deleterious effects on bone health or BMD.[50] Hence, regular assessment of BMD is not necessary in patients undergoing gender reaffirming hormonal therapy appropriately. However, proportion of subjects with low BMD at baseline amongst individuals planning CSHT was reported to be 21.9%, indicating that 1 in 5 patients may be vulnerable to developing bone health problems. It may be advisable to screen all patients planning to undergo CSHT with a baseline BMD and follow up the ones that have low Z scores (T scores are inappropriate in this setting). Male-specific control data is used to determine the Z score. If a subject has frequent breaks in hormone replacement therapy, it renders her vulnerable to developing osteoporosis. Such subjects need screening with BMD. As CSHT *per se* does not increase the risk of osteoporosis, most guidelines recommend screening patterns to be followed as applicable in the general population.[5] The UCSF guidelines clearly state that there is insufficient evidence to recommend BMD as a routine follow-up investigation.[17]

Consensus: This expert committee suggests clinical and biochemical monitoring at 3-6 months interval to evaluate efficacy and safety of treatment regimen:

1. Physical monitoring:
   a. Breast growth
   b. Growth of body and facial hair
   c. Libido and erectile function
   d. Testicular size
   e. Softening of skin.
2. Biochemical monitoring:[15,37,38,51]
   a. Testosterone
   b. Estradiol
   c. Prolactin
   d. Liver function test.
3. Reaffirmation of awareness and importance of VTE[24,39,40] - A protocol to screen for VTE in Indian setting may be developed in future. The use of transdermal estrogen will help but is yet to be successfully used in India. Clinical evaluation, till date, remains the procedure of choice for the detection of VTE
4. Routine cancer screening for breast and prostate:
   a. Breast: Screening to be done as per recommendation from NCCN[45]
      Between 25 to 39 years of age - clinical breast examination
      After 40 years of age - mammography ideally to be done every year
      High risk subjects with family history or known genetic mutation should be screened earlier (individualized)
   b. Prostate: Screening to be done as per recommendation from NCCN[46]
      Between 45 to 75 years of age - PSA and DRE (optional)
      PSA <1 ng/ml - repeat every 2 to 4 years
      PSA 1 to 3 ng/ml - repeat every 1 to 2 years
      PSA >3 ng/ml - evaluate further
      Beyond 75 years - screening to be considered if subject is well and life expectancy is more than 10 years.
5. BMD testing should be done at baseline along with serum calcium and 25(OH) vitamin D
   a. If high risk for osteoporotic fracture at baseline: follow up and monitoring every 3 year
   b. If low risk for osteoporotic fracture at baseline: follow up at age 60 and then every 3 year.[47,49]

Recommendation 10: Recommending sex reaffirmation surgery

Evidence: Although surgery on different body structures can be considered for sex reaffirmation surgery, genital surgery is the most important. Genital sex reaffirmation surgery, though not universally demanded by individuals, is a necessary step towards transition. The guideline for recommending the sex reaffirmation surgery is laid down in the WPATH (version 7) standards of care,[6] the Endocrine Society guidelines[5] and the Sappho Good Practice Guide.[7] The surgical techniques have improved remarkably in recent years and comprises a combination of gonadectomy, penectomy, and creation of a pseudovagina. The person must be both eligible and ready for sex reaffirmation surgery.[5] Estrogen should be stopped four weeks before surgery to reduce risk of VTE and patient may receive a single dose of GnRH for the interim period. Estrogen could be resumed four weeks post-operatively if there are no complications.[52] Sex reaffirmation surgery or hormone therapy are not necessary for legal recognition of gender change after the NALSA (National Legal Services Authority of India) verdict from Supreme court of India in April 2014. Despite this verdict, the Ministry of External Affairs still requires medical verification in the form of certificate of sex change by a board of doctors of a hospital, in order to change gender markers on a previously existing passport.

Consensus: The expert committee recommends to use of an eligibility and readiness criteria for sex reassignment surgery [Annexure 8: Table 5]. MHP should be involved to exclude conditions resembling gender incongruence and to ascertain competence in decision making.

Recommendation 11: Pre and post-operative hormone therapy

Evidence: The major perioperative concerns include VTE and pulmonary embolism. These events are related to immobility during surgery and also to the thrombotic effects of hormone therapy. Hence, many experts advocate discontinuance of hormones 2-4 weeks prior to surgery.[53] However, complete withdrawal of hormone treatment can have a profound and distressing impact on the patient. The surgeon and endocrinologist should discuss with the individual in reaching a informed decision regarding the withdrawal of hormones during perioperative period and reinitiation after surgery.[53]

Consensus:

1. Stop estrogen four weeks before surgery
2. Restart four weeks post-operative when the patient is completely ambulatory and there are no complications
3. Re-evaluate the need of hormones:
   GnRH and spironolactone may be stopped after orchidectomy
   Estrogen dose may be reduced after breast augmentation surgery
   Transdermal estrogen only to be allowed if VTE is encountered during perioperative period.

Conclusion

Adult gender incongruent individuals seeking gender reaffirmation as female with hormone therapy require a safe and effective hormone regimen that will suppress endogenous androgen production and maintain feminising hormone levels within the normal range for healthy young women with minimal side effects. A MHP should provide inputs in the ongoing care during the endocrine transition and decision for surgical sex reaffirmation. Regular monitoring for adverse drug reactions and monitoring for

known physical risks is the key to the successful endocrine therapy.

Financial support and sponsorship

We would like to express our deep and sincere gratitude to the Integrated Diabetes and Endocrine Academy (IDEA) for taking this initiative. We also acknowledge the logistical support and would like to express our sincere appreciation for the continuous learning opportunities that extended by the academy.

Conflicts of interest

There are no conflicts of interest.

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Annexure 1

Table 1: Diagnostic criteria for Gender Incongruent Adults based on DSM5

Criteria	Description
A.	A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested by at least two of the following:
	1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics.
	2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender.
	3. A strong desire for the primary and/or secondary sex characteristics of the other gender.
	4. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender).
	5. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).
	6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender)
B.	The condition is associated with clinically significant distress or impairment in social occupational, or other important areas of functioning.
Specify if	With a disorder of sex development (Congenital adrenal hyperplasia or Partial androgen insensitivity syndrome)
Specify if	Post-transition: The individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one cross-sex medical procedure or treatment regimen- namely, regular cross-sex hormone treatment or gender reassignment surgery confirming the desired gender (e.g, penectomy, vaginoplasty in a natal male; mastectomy or phalloplasty in a natal female).

ANNEXURE-2

TO WHOM IT MAY CONCERN

This is to certify that (Name)....., born on..... (Date), resides at (Address)
.....

(identification -VOTER ID CARD NO / PASSPORT NO / AADHAR NO / PAN NO: .....) identifies himself/herself as FTM or FTM transgender person.

..... (Name)'s preferred pronoun is he/she. (Name) is examined by me today (Date).....

..... (Name) meet the DSM5 criteria for Gender Dysphoria / Gender Incongruence. A thorough history of his/her development of Gender Dysphoria / Gender Incongruence has been obtained.

..... (Name) has been living as MTF/FTM transperson since last.....(Years). He/She has adequate understanding on mental health and challenges consequent to the non-confirming gender identity and also has a good / little social support system. There is no evidence of any major psychiatric disorder at present.

..... (Name) appears well adjusted to his/her preferred gender (male/female) and is presently psychologically fit to give consent and start gender reaffirmation treatment. His/Her Signature is attached herewith.

Signature of the subject

Signature of psychiatrist

Date:

Registration No:

ANNEXURE-3

TO WHOMSOEVER IT MAY CONCERN

(Name) is a (Age) year old male who has an established longstanding and strong identity as a female and is now seeking Hormone Therapy / Sex Reassignment Surgery to aid in the medical transition.

I met (Name) on (Date) for evaluation. My evaluation is summarized in this letter. The client refers to himself in feminine gender and to respect the feelings, I will be using female pronouns throughout the letter.

(Name), a (age) old individual, educated up to (Educational Qualification) and is currently formally employed in (Name of City). She has described a desire to be treated like a member of the female sex since her childhood. She reports to have been interested in games played by girls and has been cross dressing since (duration). Since her childhood/adolescence/ adulthood, she seems to have significant progress in her transitioning and seems very happy in her decision. She also reports of being attracted to males. Her gender and sexual attraction appear tied. She tends to have a strong / poor support system that includes her other family members.

My clinical evaluation of (Name) suggests average/good intelligence and the capacity for informed & stable decisions and she has strong desire to belong to female biological gender. Her judgment appears to be stable and good. I have no hesitation in recommending her for Hormone Therapy / Sex Reassignment Surgery as per standard protocol. Her Signature is attached herewith.

Signature of the subject

Signature of psychologist
Date:

Address of psychologist

ANNEXURE-4

CONSENT FORM FOR FEMINIZING MEDICATIONS

Name: …… ID No. …….

Biological Sex: M / F / Other DOB:……

Address:……..... Pincode: ……

Contact Number:…… P.S:..……

I……do hereby give consent for administering feminising medications. I understand that estrogen, androgen antagonists, or combination of the two may be prescribed to reduce male physical features and feminise my body. I understand that if I am taking estrogen, I will probably develop breasts and as soon as breasts start growing, it is recommended to start doing breast self-examination and to have an annual breast examination by a doctor or nurse.

I understand that the feminizing changes are generally not permanent (that is they will likely reverse if I stop taking feminizing medications) and I also understand that taking feminizing medications will make my testicles to produce less testosterone, which can affect my overall sexual function and reproductive capacity in future; hence the concept of sperm preservation is discussed for potential usage.

I understand that there are some aspects of my body that may not significantly changed by feminizing medications specially beard/moustache hair.

I understand that the medical effects and safety of feminizing medications are not fully understood and that there may be long-term risks that are not yet known.

I understand that feminizing medications can damage the liver, possibly leading to liver disease, increases the risk of blood clots (which may cause permanent damage or death) increases the risk for diabetes and heart disease, increases blood pressure, increases the risk of gallstones, can cause nausea and vomiting, can cause headaches or migraines, and increases the risk of non-cancerous tumors of the pituitary gland (prolactinoma). I have been informed that I am more likely to have dangerous side effects from estrogen if I smoke, am overweight, am over 40 years old, or have a history of blood clots, high blood pressure, or a family history of breast cancer.

I understand that physical examinations and blood tests are needed on a regular basis to check for negative side effects of feminizing medications. I understand that feminizing medications can interact with other medication (including other sources of hormones), dietary supplements, herbs, alcohol, and street drugs.

I understand about the benefits and risks of feminizing medications, the possible or likely consequences of hormone therapy, and potential alternative treatment options and I understand the risks that may be involved. I understand that this form covers known effects and risks and that there may be long-term effects or risks that are not yet known.

I have had sufficient opportunity to discuss treatment options with the health care provider and all of my questions have been answered to my satisfaction.

Signature of Next of Kin / Guardian (witness) Signature of patient

Name: Date:

Address:

Date:

Signature of the health care provider

Name:

Date:

Annexure-5

Table 2: Available estrogen preparations in India

Estrogen preparations	Dose	Advantages	Limitations
Oral Estradiol Valerate	2 to 8 mg per day	Estradiol levels can be monitored, Risk of VTE is slightly less than with Ethinyl Estradiol or Conjugated Equine Estrogen	High risk of VTE
Oral *17-beta* Estradiol	1-6 mg daily	Inexpensive and estradiol levels can be monitored	High risk of VTE specially in older patients (>40 yrs)
Oral Ethinyl Estradiol	50-100 ug per day	Inexpensive	Cannot be monitored by measurement of serum levels and high risk of VTE
Conjugated Equine Estrogen	1.25 to 5 mg per day	Widely available	Cannot be monitored by measurement of serum levels, high risk of VTE, expensive and contains impurities
Parenteral Estradiol Valerate	10-20 mg IM every 1-2 week	Estradiol levels can be monitored, Risk of VTE is slightly less than with Ethinyl Estradiol or Conjugated Equine Estrogen	Injectable preparation
Transdermal *17-beta* Estradiol gel (0.06%) for application	1.25 gm gel per day (0.75 mg estradiol) to 5 gm gel per day (3 mg estradiol) (Application in the arms or in the upper half of the body)	Low risk of venous thromboembolism	Not easily available in India May not be successful in a tropical country like India

Annexure-6

Table 3: Approximate equivalents of estrogen preparations

Estrogen preparations	Equivalent dose
Oral Estradiol Valerate	1mg
17-Beta estradiol	1 mg
Ethinyl estradiol	10ug
Conjugated equine estrogens	0.625 mg
Transdermal 17-beta Estradiol gel (0.06%)	0.75mg
Transdermal estradiol patch	25ug twice weekly application

Annexure-7

Table 4: Choice of feminizing therapy

	Anti-androgen therapy	Feminizing hormone therapy	Ancillary therapy
Resource poor setting	Spironolactone + finasteride or dutasteride	Oral Estrogen or Parenteral Estradiol valerate	Laser + Eflornithine + Vitamin D and Calcium
Resource rich setting	GnRH agonists + Spironolactone + finasteride or dutasteride	Oral Estrogen or Parenteral Estradiol valerate	Laser + Eflornithine + Vitamin D and Calcium

Annexure-8

Table 5: Eligibility and readiness criteria for sex reaffirmation surgery

Serial No	Criteria description
1.	Must be a major (attained the age of 18 years)
2.	Had a successful continuous full-time Real Life Experience (cross dressing) during last 12 months.
3.	Have used cross-sex hormones continuously and responsibly for past 12 months (if they have no medical contraindication)
4.	Have (if required by the MHP) regularly participated in psychotherapy throughout the Real Life Experience at a frequency determined jointly by the patient and the MHP.
5.	Have shown demonstrable knowledge of all practical aspects of surgery (e.g., cost, required lengths of hospitalizations, likely complications, postsurgical rehabilitation, etc.)
6.	Have shown demonstrable progress in consolidating one's gender identity with CSHT without periods of return to his original gender
7.	Have shown demonstrable progress in dealing with work, family, and interpersonal issues resulting in a significantly better state of mental health with CSHT
8.	Had clearance certificates for sex reassignment surgery from two mental health professionals. Two separate letters or one letter with two signatures is acceptable. If one of the psychiatry opinions is conflicting then the matter shall be referred to a third psychiatrist and the majority opinion shall prevail.