Cross-sex hormone therapy in Australia: the prescription patterns of clinicians experienced in adult transgender healthcare

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Short title: Transgender hormone therapy prescribing patterns

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INTRODUCTION

Cross-sex hormone therapies (otherwise known as hormone therapies or gender-affirming hormone therapies) are often prescribed to alleviate gender dysphoria - the distress many transgender individuals experience when their gender identity is markedly and persistently incongruent from their birth assigned sex. Aligning a person's physical characteristics with their gender identity may involve non-medical interventions such as binders and prostheses, as well as medical interventions such as masculinising or feminising hormone therapies and surgical interventions. The prescription and monitoring of hormone regimens, which may include testosterone or estradiol replacement as well as anti-androgen agents, is the focus of this study.

The consequences of delaying access to hormone therapies are significant. Australian studies demonstrate that over 70% of transgender people have medically diagnosed depression, and 48% have attempted suicide: numbers far higher than population prevalence rates, noting the potential for responder bias¹⁻³. Despite consensus between clinicians and individuals whose lived experience confirms the critical and often life-saving role of hormone treatment, research in the transgender field is in its infancy. Sound evidence suggests that hormonal treatment in transgender individuals decreases the risk of suicide^{4, 5}, alleviates gender dysphoria, and improves psychological functioning and overall quality of life^{6, 7}.

Although the World Professional Association for Transgender Health⁸ and the US Endocrine Society⁹ have published international guidelines on various regimens for hormonal treatment of transgender individuals, the evidence on which

recommendations are based is low-level- often citing expert opinion rather than clinical evidence. Randomised controlled trials to guide clinical choice and monitoring of hormonal therapy do not yet exist. Recommendations are therefore broad and open to interpretation. Additionally, there are differences internationally with availability, access, and cost of various medications, which significantly influences prescribing patterns. Australian and New Zealand Professional Association of Transgender Health (ANZPATH) promotes communication and collaboration amongst professionals involved in the healthcare of transgender individuals. ANZPATH membership signifies a level of interest and involvement in transgender healthcare above that of a regular healthcare practitioner. Amongst the ANZPATH electronic mailing list discussion groups, we observed wide ranging approaches and prescribing practices, reflecting the limitations of the currently available guidelines. Although prescribers may technically be working within the current guidelines, patients seeing more than one prescriber or health service may be exposed to differing or inconsistent advice. Developing guidelines relevant to the Australian context would therefore be beneficial, but first requires an understanding of current local practices.

The aim of our study was to determine hormone therapy prescribing patterns amongst medical practitioners experienced in providing adult transgender healthcare in Australia. Given the lack of evidence in the field, this would enable the development of a local consensus to inform Australian clinical guidelines for the management of transgender individuals. We hypothesised that due to the ambiguity of current international guidelines, opinion regarding choice of first-line hormonal therapy would vary significantly.

METHODS

This anonymous survey of hormone therapy prescribing patterns for adult transgender individuals was open to registered medical practitioners who were members of ANZPATH from September 30 to October 31, 2017. The survey was advertised at the ANZPATH Biennial Meeting in Sydney, Australia on October 1, 2017. Additionally, the forty-three hormone prescribers (general practitioners, endocrinologists, sexual health physicians and gynaecologists) – members of ANZPATH and listed as service providers in Australia (or known to be hormone prescribers) – were invited to participate via direct email in October 2017. Participants were invited to complete the survey to assess cross-sex hormone therapy prescribing patterns in adult transgender individuals via a link to an online survey platform provider (SurveyMonkey). The study was approved by the Austin Health Human Research Ethics Committee (HREC/17/Austin/372).

Inclusion criteria assessed via two screening questions were: a) Registered medical practitioners in Australia or New Zealand; and b) Prescribers of hormonal therapy to transgender individuals.

Demographics

Demographic data was obtained from respondents, including gender, age range, state or territory of practice, postcode of practice, type of healthcare provider (general practice, psychiatry, sexual health, endocrinology, gynaecology, paediatrics, surgical or other), case load (number of transgender patients treated per month), experience (number of years treating transgender individuals) and participation in teaching transgender medicine.

Informed consent model

Questions were designed to gauge perspectives on the requirement for a formal mental health assessment prior to commencement of hormonal therapy – at times described as a potential barrier to healthcare¹. Current standards of care place a strong emphasis on involving a mental health professional to diagnose gender dysphoria and assess criteria for hormone therapy assessment for hormone therapy^{8, 9}. An informed consent model is an alternative approach¹⁰. While informed consent is integral before commencement of any treatment, the informed consent model is defined as a model of care in which, following appropriate education, a decision for hormone treatment is shared by the patient and a trained clinician (without a formal mental health assessment).

Cross-sex hormone therapy prescribing patterns

In addition, questions were designed to assess prescribing patterns and clinical treatment practices including the following: advice regarding fertility, reference to clinical practice guidelines, preferred testosterone and estrogen preparations, use of anti-androgen and progesterone treatments, frequency of monitoring after commencement of hormonal therapy, investigations used during monitoring, and treatment targets.

Practitioners were also asked for their views on priority areas for government funding, and their perspectives on the need for Australian-based clinical guidelines. The survey preamble and questions in full are included in Appendix 1.

Statistical analysis was performed using SPSS Statistics version 23 (IBM Corporation, NY, USA).

RESULTS

Of the 43 invitations to participate in the study sent to medical practitioners experienced in providing transgender healthcare, 35 responses were received. Demographic characteristics of the respondents are shown in Table 1.

Informed consent model

When asked whether the practitioner recommended a mental health assessment by a psychologist or psychiatrist before starting hormone treatment, 80% of practitioners responded ‘yes, always’ or ‘yes, usually’, and 20% responded ‘sometimes’. However, when asked whether practitioners followed an informed consent model, 48% responded ‘no, never’, 26% responded ‘sometimes’, 20% responded ‘yes, usually’, and 6% responded ‘yes, always’. All practitioners (100%) provided advice regarding fertility implications prior to starting hormone therapy.

Cross-sex hormone therapy prescribing patterns

Masculinising hormone therapy

Intramuscular testosterone undecanoate was the preferred first-line option for over 50% of practitioners prescribing masculinising hormone therapy (Table 2). Almost all practitioners (97%) targeted treatment to achieve total testosterone levels within the typical male reference range (total testosterone 10–30 nmol/L), and 3% targeted treatment to free testosterone 300–500 pmol/L rather than total testosterone levels. Investigations monitored regularly included total testosterone levels (76% of

respondents monitored this at most visits), estradiol levels (61%), full blood examination, electrolytes and renal function (61%) and liver function tests (73%). Occasional investigations (e.g. annually) included calcium, vitamin D, cancer screening, glucose and lipid profile. Mixed responses were received regarding bone mineral density with monitoring 'occasionally' in 33%, 'once-off' in 30%, and 'never' in 36%. Despite regular test monitoring, the majority of practitioners (52%) did not target serum estradiol levels in individuals receiving testosterone therapy.

Feminising hormone therapy

Oral estradiol valerate was the most preferred first-line treatment option for most practitioners (Table 2). In addition to estradiol, anti-androgen treatments were 'often' or 'almost always' used by 90% of practitioners, and both spironolactone and cyproterone acetate were frequently prescribed (Table 2). Progesterone for the purpose of breast development was infrequently prescribed: of the 29 respondents, 48.3% prescribed it 'sometimes', 44.8% 'never', and the remaining 6.9% 'other'.

The majority of practitioners (93%) targeted serum estradiol in the female reference range of approximately 200–799 pmol/L, with 3.5% aiming for higher levels at 700–1199 pmol/L and 3.5% assessing feminisation clinically, without measuring levels. Total testosterone targets used were in the female reference range < 2 nmol/L in 59% of practitioners, between 2–5 nmol/L in 14%, between 6 nmol/L and the lower limit of the male reference range in 7%, assessed clinically without measuring levels in 10%, and 'other' in 10%.

For individuals receiving feminising hormone therapy, investigations monitored regularly at most visits included total testosterone levels (83% of respondents), estradiol levels (86%), full blood examination (66%), electrolytes and renal function (69%), and liver function (69%). Occasional investigations (e.g. annually) included calcium, vitamin D, cancer screening, glucose and lipid profile. Similar to those on testosterone therapy, mixed responses were received regarding bone mineral density.

Monitoring

Most practitioners reviewed patients during the first year of hormone therapy every 2–3 months (71.4%) or every 4–6 months (17.1%).

Funding priorities and guidelines

When asked to select their top priority for government funding, 44.8% of respondents answered ‘better training for doctors in trans issues’, 24.1% selected ‘gender clinics’, 17.2% selected ‘psychology/psychiatry services’, and 10.3% selected ‘medical research’. The majority (79.3%) of practitioners supported the need for Australian-based clinical guidelines for the treatment of transgender individuals.

DISCUSSION

Amongst a cohort of Australian medical practitioners experienced in prescribing hormone therapy we found that the most preferred forms of masculinising and feminising hormones were, respectively, intramuscular testosterone undecanoate and oral estradiol valerate. Anti-androgen therapy with either spironolactone or cyproterone acetate was frequently prescribed. Australian prescribing patterns are influenced by availability, pharmaceutical benefits scheme (PBS) access and cost.

Since this survey concluded, there has been discontinuation of a transdermal testosterone solution formulation (Axiron), and the withdrawal from PBS of testosterone enantate (Primoteston), which will undoubtedly have an effect on future prescribing. Interestingly, cyproterone acetate is the anti-androgen agent used almost exclusively in Europe, whereas it has never been approved by the Food and Drug Administration in the United States, therefore Australia is in a unique position to have similar access to both agents. GnRH analogues are not PBS listed for transgender adults in Australia and are therefore rarely used due to prohibitively high costs.

Most cross-sex hormone therapy was delivered in primary care, in private clinics, which may well reflect a lack of public gender services around Australia and insufficient training of endocrinologists and sexual health physicians. The large majority of prescribers treated to achieve testosterone and estradiol levels in the reference range of the affirmed-gender and regularly monitored sex steroid levels, liver function tests, electrolytes and full blood count every 2–3 months in the first year of treatment.

Opinions regarding the use of an informed consent model of care were varying, however in almost all situations, mental health assessment and support prior to commencement of hormone treatment was recommended by prescribers. Notably, practice is likely dependent upon individual patient interactions and may well have been difficult to quantitate in a survey. Additionally, the recently released World Health Organisation's International Classification of Diseases 11th Revision (ICD-11) no longer classifies gender incongruence as a mental health disorder, which will influence the future provision of healthcare. As increasing numbers of physicians gain

experience in treating transgender individuals, it is likely that there will be a move away from the standard approach, to an informed consent model, which must still include mental health support. With an informed consent model, mental health practitioners remain an important part of the multidisciplinary team to manage mental health comorbidities and provide support during social and medical gender transition if required. Any holistic plan for care encompassing adequate mental health support (provided by GP's or mental health professionals) must be individualised, affirming and respectful of the patient.

Prescribing patterns observed are generally in keeping with recommendations of international guidelines^{8, 9}. With masculinising hormone therapy for transgender males, testosterone mono-therapy is effective at inducing masculinisation; however, there have been no randomised controlled trials to guide the optimal route or the optimal dose of therapy. Prescribers regularly monitor potential adverse effects of polycythaemia¹¹ and liver abnormalities¹² which are recommended in the product information for transdermal testosterone and testosterone undecanoate. Given the role of testosterone and estradiol in modulating lipid levels¹³ and insulin resistance¹⁴, and the fact that increased mortality in transgender individuals appears to be related to cardiovascular disease^{15, 16}, it is reasonable that cardiovascular risk factors are monitored periodically. Low estradiol levels often occur, particularly in trans male (female-to-male) individuals whose ovaries have been removed, potentially leading to adverse bone and metabolic effects. A recent animal model of cross-sex hormone therapy in female-to-male individuals suggests that the addition of low-dose estradiol to testosterone therapy in ovariectomised mice can improve atherosclerotic plaque¹⁷ and preserve bone architecture¹⁸; however, this requires further study in humans.

No clear consensus emerged on the monitoring of bone mineral density, and there is insufficient data to suggest that testosterone therapy or estradiol therapy in transgender adults causes adverse effects on bone density¹⁹. Current international guidelines recommend that clinicians obtain bone mineral density measurements only when risk factors for osteoporosis exist, specifically in those who cease sex hormone therapy after gonadectomy⁹.

Feminising hormone therapy is more complex, as estradiol alone is usually insufficient to lower endogenous testosterone levels to the female reference range and anti-androgens are almost always required (typically cyproterone acetate or spironolactone). As transdermal estradiol avoids the first pass liver effect, there is a theoretical benefit of decreased arterial and venous thromboembolism. However, there have been no prospective, randomised controlled trials evaluating oral versus transdermal estradiol in any population (transgender or postmenopausal women), and any observational case-control studies have been in relatively high-risk populations in postmenopausal women^{20, 21}. One large population-based study of postmenopausal women has shown a similar increased risk of stroke when comparing oral estradiol and high dose (>50 mcg/day) transdermal estradiol – those typically used in trans females²²; however in contrast, meta-analyses suggest that transdermal estrogens carry minimal or no thrombotic risk²³ with minimal effects on haemostatic variables²⁴. Without data for the transgender population specifically, we must extrapolate based on studies of postmenopausal women. These suggest that while absolute risks of thromboembolism are low, there does appear to be a dose-response relationship, and a higher probability in those with cardiovascular risk factors²⁵. As

such, the lowest dose necessary to induce feminisation should be used, and transdermal routes may be more appropriate for those at high risk of thromboembolism; however, the data to support this is scant. From a practical perspective, the preference for oral routes as first-line may reflect the fact that adherence of the patch is an issue, particularly if there is excessive hair or sweat on the skin.

Monitoring practices for individuals on feminising hormone therapy is similar to those on masculinising hormone therapy; however, in addition, those receiving spironolactone should have their electrolytes and renal function measured periodically⁹.

Providers considered education of health professionals to be a priority for government funding, and careful consideration should be given to evaluating the best methods of delivering such education, not only at undergraduate and postgraduate levels, but also to clinicians. Given the increasing visibility of transgender individuals and rising demand for transgender health services seen worldwide, it is likely that all clinicians will need awareness of gender-affirming care. Although Australian data is lacking, only 30% of North American medical schools had provided any training relating to transgender healthcare²⁶. Participants in our survey expressed widespread support for the development of Australian clinical guidelines on the treatment of transgender individuals, and this may well be an effective means of educating and supporting health professionals in prescribing hormone therapy.

There were a number of key limitations to this survey. The study was small; however, practitioners experienced in transgender healthcare are few in Australia, and we had a high response rate – likely capturing a representative sample of clinicians of varying ages and clinical experience. We advertised the study to ANZPATH members only, and as such may not have captured all relevant hormone prescribers in Australia. However, this was so that only those with a certain level of interest and involvement in transgender healthcare would be surveyed. Responder bias may have impacted results. There was a predominance of Victorian respondents which may have skewed practices; however a previous Australian transgender community survey has similarly demonstrated greatest number of respondents reside in Victoria². No responses were received from South Australian, Northern Territory or New Zealand prescribers.

CONCLUSION

A greater evidence base is required to guide best treatment and clinical care practices in transgender health, particularly as the majority of individuals will require treatment lifelong. Realistically, it will be many years before such evidence is available and until then, clinical decisions will be based on expert opinion only. Experienced hormone prescribers in Australia largely use medication regimens and monitor sex steroid levels and potential adverse effects of sex hormone therapy in accordance with broad recommendations listed in international guidelines. Further education on transgender healthcare is needed. The development of guidelines adapted for the Australian context would be a valuable resource for clinicians initiating and monitoring hormone therapy in adult transgender individuals. This study provides the first insight into the current Australian hormone prescribing practices amongst experienced medical practitioners in adult transgender medicine.

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TABLES AND FIGURES

Table 1. Participant characteristics of 35 respondents.

Characteristic	N (%) – Total n=35
Gender	
Female	19 (54.3%)
Male	14 (40.0%)
Trans and gender diverse*	2 (5.7%)
Age (years)	
20 – 29	1 (2.9%)
30 – 39	8 (22.9%)
40 – 49	12 (34.3%)
50 – 59	10 (28.6%)
60 – 69	3 (8.6%)
>70	0 (0%)
No response	1
State or Territory	
Victoria	20 (57.1%)
Queensland	5 (14.3%)
Western Australia	4 (11.4%)
New South Wales	3 (8.6%)
Australian Capital Territory	1 (2.9%)
Tasmania	1 (2.9%)
South Australia	0 (0%)
Northern Territory	0 (0%)
No response	1
Practice location	
Metropolitan	31 (88.6%)
Rural/Remote	3 (8.6%)
No response	1
Sub-specialty	
General Practice	22 (62.9%)
Endocrinology	7 (20.0%)
Sexual Health	6 (17.1%)
Type of practice	
Private clinic	28 (80.0%)
Public hospital-based gender clinic	3 (8.6%)
Public sexual health clinic	3 (8.6%)
No response	1
Number of years treating transgender individuals (years)	
<5	13 (37.1%)
6 – 10	12 (34.3%)
11 – 20	4 (11.4%)
>20	6 (17.1%)
Average number of transgender patients seen per month	
<5	7 (20.0%)
6 – 10	9 (25.7%)
11 – 20	8 (22.9%)
>20	11 (31.4%)

Involvement in teaching or training in transgender medicine	
Yes	19 (54.3%)
No	13 (37.1%)
No response	3

*As not all individuals with non-binary gender identities identify with the term transgender, the term trans and gender diverse was used in the survey as an inclusive umbrella term to describe all those whose gender identity is incongruent with their birth-assigned sex.

Table 2. Preferred cross-sex hormone therapy medications.

	N (%) – Total n=35
<i>Preferred first-line masculinising testosterone preparations</i>	
Testosterone undecanoate (intramuscular)	17 (48.6%)
Testosterone enantate (intramuscular)*	11 (31.4%)
Testosterone gel/cream	5 (14.3%)
Transdermal testosterone patch	0 (0%)
Oral testosterone undecanoate	0 (0%)
Other	0 (0%)
No response	2 (5.7%)
<i>Preferred first-line feminising estradiol preparations</i>	
Estradiol valerate (oral)	25 (71.4%)
Oral combined contraceptive pill containing ethinyl estradiol	0 (0%)
Transdermal estradiol patch	3 (8.6%)
Estrogen implants	0 (0%)
Estradiol intramuscular injections	0 (0%)
Other [#]	1 (2.9%)
No response	6 (17.1%)
<i>Do you use anti-androgen treatments in addition to estradiol therapy?</i>	
Almost always	20 (57.1%)
Often	6 (17.1%)
Sometimes	2 (5.7%)
Only if I can't suppress the testosterone on estradiol alone	1 (2.9%)
No response	6 (17.1%)
<i>Anti-androgen medications used (more than one option could be selected)</i>	
Spironolactone	27 (93.1%)
Cyproterone acetate	28 (96.6%)
5-alpha reductase inhibitors (finasteride, dutasteride)	10 (34.5%)
Bicalutamide	1 (3.5%)
No response	6 (17.1%)
<i>Do you prescribe progesterone for breast development?</i>	
Almost always	0
Often	0
Sometimes	14 (40.0%)
Never	13 (37.1%)
Other	2 (5.7%)
No response	6 (17.1%)

*At the time of the survey, testosterone enantate was still available on the PBS,

however this was removed from the PBS in February 2018. [#]Other response was

“depends on age of patient; transdermal in older, oral in younger”

APPENDIX 1 – PREAMBLE AND SURVEY QUESTIONS

Cross-sex hormone therapy prescribing patterns in Australia

We invite you to have your say on hormone therapy for trans and gender diverse individuals.

The purpose of this study

This survey is intended for medical practitioners who currently prescribe hormonal therapy for gender transition in trans and gender diverse individuals. As there is a lack of research in this area, there is no right or wrong answer and we are interested in the breadth of opinions and prescribing patterns of cross-sex hormone therapy throughout Australia and New Zealand. The results will assist in developing consensus guidelines and research directions studying optimal methods to deliver and monitor the effects of hormone therapy.

This survey is to help us understand more about transgender healthcare and is part a series of surveys aimed at trans and gender diverse individuals, Endocrinologists and trainees, and doctors that work in transgender healthcare.

Taking part in this study

You must be aged over 18 to take part in this survey. You do not need to complete a formal consent form to take part in this study. By completing this survey, you are consenting that your answers will be used in this study. All responses are anonymous. This study has been approved by the Austin Health Human Research Ethics Committee (Reference number HREC/17/Austin/372)

Risks of this project

If you feel uncomfortable answering any questions you may choose not answer a particular question or choose not to complete the survey.

Further information and who to contact

The person you may need to contact will depend on the nature of your query.

Clinical contact person

Dr Ingrid Bretherton

Position: PhD Candidate

Telephone: 9496 2486

Email: ibretherton@student.unimelb.edu.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Complaints contact person

Position: Complaints Officer

Telephone: (03) 9496 4090 or (03) 9496 3248

Email: ethics@austin.org.au

Questions (select one response unless otherwise stated)

1. Are you currently a registered medical practitioner working in Australia or New Zealand?

- ☐ Yes
- ☐ No

2. Where is your main place of practice?

- ☐ Western Australia
- ☐ Northern Territory
- ☐ Queensland
- ☐ New South Wales
- ☐ Australian Capital Territory
- ☐ Victoria
- ☐ Tasmania
- ☐ South Australia
- ☐ Other (please specify)

3. Do you currently prescribe medical therapy to trans and gender diverse individuals?

- ☐ Yes
- ☐ No

4. What is your gender?

- ☐ Male
- ☐ Female
- ☐ Trans masculine
- ☐ Trans feminine
- ☐ Gender non-binary/ gender queer/ gender neutral
- ☐ Other (please specify)

5. What is your age range?

- ☐ 20-29
- ☐ 30-39
- ☐ 40-49
- ☐ 50-59
- ☐ 60-69
- ☐ >70

6. What type of healthcare provider are you?

- ☐ GP or GP registrar
- ☐ Psychiatrist or Psychiatry Registrar
- ☐ Sexual health physician or Registrar
- ☐ Endocrinologist or Endocrinology Registrar
- ☐ Gynaecologist or Gynaecology Registrar
- ☐ Paediatrician or Paediatrics Registrar
- ☐ Other (please specify)

7. Where do you mainly practice?

- ☐ Private clinic
- ☐ Hospital based gender clinic

- Other (please specify)

8. What is the postcode of your main place of practice?

9. Do you teach or train other health professionals in transgender health?

- Yes
- No
- Unsure

10. On average, how many trans or gender diverse patients do you see per month?

- <5
- 6-10
- 11-20
- >20

11. How many years have you been treating trans individuals?

- <5
- 6-10
- 11-20
- >20

12. For individuals identifying as trans or gender diverse, who desire hormonal therapy, do you usually recommend a mental health assessment by a psychologist or psychiatrist before starting treatment?

- No, never
- Sometimes
- Yes, usually
- Yes, always

13. Do you ever follow an "informed consent model" in which, following appropriate education, the ultimate decision regarding treatment rests with the patient alone (rather than requiring a mental health assessment for readiness)?

- No, never
- Sometimes
- Yes, usually
- Yes, always

14. Do you provide advice about fertility implications before starting hormone treatment?

- No, never
- Sometimes
- Yes, usually
- Yes, always

15. On average how often would you review a patient during the first year of hormone therapy?

- Every 1-2 weeks
- Monthly

- Every 2-3 months
- Every 4-6 months
- Every 7-12 months
- Other (please specify)

16. Do you refer to any clinical practice guidelines when managing transgender patients? (you may select more than one)

- Endocrine Society Clinical Practice Guidelines
- WPATH standards of care
- None
- Other (please specify)

17. Which testosterone preparation do you prefer to prescribe most often (your first-line option if a patient asks you for your opinion)?

- IM testosterone undecanoate (such as Reandron 1000)
- IM testosterone enanthate (such as Primoteston Depot)
- Transdermal testosterone gel/cream (such as Testogel, Axiron, Androforte 5)
- Transdermal testosterone Patch (such as Androderm)
- Oral testosterone undecanoate (such as Andriol, Tesocaps)
- Other (please specify)

18. How often do you monitor (or ensure another doctor has monitored) the following, if at all?

For each test select Never/Once off/Regularly (e.g. most visits)/Occasionally (e.g. annually)

Total testosterone

Estradiol

Full blood examination

Electrolytes/renal function

Liver function test

Calcium

Vitamin D

Bone mineral density

Malignancy screening

Metabolic screen (glucose, lipids)

19. In transmales, what serum total testosterone target do you generally aim for?

- I don't check, I assess clinically
- Below the male reference range (i.e. <10nmol/L)
- Within the male reference range (i.e. 10-30nmol/L)
- Above the male reference range (i.e. >30nmol/L)
- Other (please specify)

20. In transmales, what serum estradiol level do you generally target?

- I don't check, I assess clinically
- Within the male reference range
- Below the female reference range
- Other (please specify)

21. Regarding feminising hormone therapy, which oestrogen preparation do you prefer to prescribe most often (your first-line option if a patient asks you for your opinion)?

- Oral oestradiol valerate (such as Progynova)
- Oral combined OCP containing ethinyloestradiol (such as Microgynon)
- Transdermal oestradiol (such as Estradot or Estraderm)
- Oestrogen implants
- Oestradiol intramuscular injections
- Other (please specify)

22. How often do you monitor (or ensure another doctor has monitored) the following in a transfemale patient?

For each test select Never/Once off/Regularly (e.g. most visits)/Occasionally (e.g. annually)

Total testosterone

Estradiol

Full blood examination

Electrolytes/renal function

Liver function test

Calcium

Vitamin D

Bone mineral density

Malignancy screening

Metabolic screen (glucose, lipids)

23. In transfemales, which oestradiol level do you generally target?

- I don't check, I assess clinically
- 0-199 pmol/L
- 200-699 pmol/L
- 700-1199 pmol/L
- 1200-1700 pmol/L
- Other (please specify)

24. In transfemales, which serum total testosterone level do you generally target?

- I don't check, I assess clinically
- Within the female reference range (i.e. <2 nmol/L)
- Between 2-5 mol/l
- Between 6 mol/L and the lower limit of the male reference range
- Other (please specify)

25. Do you use anti-androgen treatments in addition to oestrogen therapy?

- Only if I can't suppress the testosterone on oestrogen alone
- Almost always
- Often
- Sometimes
- Rarely
- Never

26. Which anti-androgen treatments do you use (select all that apply)

- ☐ Spironolactone
- ☐ Cyproterone acetate
- ☐ 5-alpha reductase inhibitors (finasteride, dutasteride)
- ☐ Bicalutamide
- ☐ Other (please specify)

27. Do you prescribe progesterone (i.e. medroxyprogesterone or Provera) for breast development?

- ☐ Almost always
- ☐ Often
- ☐ Sometimes
- ☐ Never
- ☐ Other

28. If you had to choose one, where do you think government funding should be directed?

- ☐ Gender clinics
- ☐ Support groups
- ☐ Trans advocacy groups
- ☐ Legal assistance
- ☐ Better training for doctors in trans issues
- ☐ Transgender medical research
- ☐ Psychology/psychiatry services
- ☐ Other (please specify)

29. Do you think there should be Australian-based clinical guidelines for treatment of trans and gender diverse individuals?

- ☐ Yes
- ☐ No
- ☐ Unsure

ABSTRACT (250 words)

Background: Despite increasing demand for transgender healthcare, guidelines for cross-sex hormone therapy are based on low-level evidence only. As most data are based on international expert opinions, interpretations and practices vary significantly.

Aims: To aid the development of Australian clinical guidelines, we aimed to identify cross-sex hormone therapy prescribing patterns amongst medical practitioners experienced in adult transgender healthcare.

Methods: We conducted an anonymous online survey of experienced hormone prescribers who were members of the Australian and New Zealand Professional Association for Transgender Health.

Results: We received 35 responses from 43 individuals listed with ANZPATH. Mental health assessments prior to commencement of hormonal therapy were recommended by 80% of prescribers. The preferred first-line masculinising hormone therapy was intramuscular testosterone undecanoate (46% of respondents). The most commonly prescribed feminising agents were oral estradiol valerate (first-line in 71.4%) with either spironolactone or cyproterone acetate. Most respondents (>90%) targeted sex steroid reference ranges of the affirmed gender and 71.4% reviewed individuals every 2–3 months in the first year. Better training for doctors was seen as the most pressing priority for government funding, and 79.3% supported the development of local Australian-based guidelines.

Conclusions: Experienced hormone prescribers in Australia largely use medication regimens and monitor sex steroid levels and potential adverse effects of sex hormone therapy in accordance with broad, subjective recommendations listed in international guidelines. Additional practitioner training is necessary, and local Australian-based guidelines would offer specific, relevant guidance to clinicians in the initiation and monitoring of cross-sex hormone therapy for adult transgender individuals.

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