

# **A randomised controlled trial of spironolactone versus cyproterone in trans people commencing estradiol**

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## **Background**

Spironolactone and cyproterone are commonly used as anti-androgens with estradiol in trans people seeking feminisation. While use of cyproterone results in greater suppression of testosterone than spironolactone due to its mechanisms of action, it is unclear whether this results in meaningful differences in feminisation.

## **Methods**

We conducted a randomised controlled trial of spironolactone 100mg daily or cyproterone 12.5mg daily in trans people commencing estradiol. The primary outcome was breast chest distance at six months. Secondary outcomes included changes in body fat assessed via dual x-ray absorptiometry and serum testosterone. Statistical analysis was performed using a linear mixed effects model and  $p < 0.05$  deemed statistically significant.

## **Results**

Of 62 participants enrolled, 56 participants completed and were included in final analysis (cyproterone group  $n=28$ , spironolactone group  $n=28$ ). At six months, there was no between-group difference in breast chest distance (9.2 cm (3.0) vs 8.2cm (2.7),  $p=0.27$ ). Cyproterone use was associated with a greater increase in percentage body fat and gynoid fat, greater suppression of serum total testosterone (1.48 nmol/L (3.45) vs 4.15 nmol/L (5.38),  $p < 0.0001$ ) and hyperprolactinaemia (610 mIU/L (201) vs 292 mIU/L (135),  $p < 0.0001$ ). There was no between-group difference in Patient Health Questionnaire 9 total score, blood pressure, serum urea, creatinine or alanine transferase.

## **Conclusions**

There was no between-group difference in the breast chest distance at six months. Cyproterone use was associated with a greater increase in percentage fat and gynoid fat, greater suppression of testosterone and hyperprolactinaemia. Choice of anti-androgen should be individualised based on patient and clinician preference.