Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes


CRD summary
The authors concluded that very low quality evidence suggested that hormonal interventions in individuals undergoing sex reassignment were likely to improve gender dysphoria, psychological functioning and comorbidities, sexual function and overall quality of life. This conclusion reflects the evidence but methodological limitations related to individual studies and the review synthesis suggest that it should not be considered reliable.

Authors' objectives
To evaluate the effects of hormonal therapy on quality of life and other psychosocial outcomes in individuals undergoing sex reassignment.

Searching
Five databases (including MEDLINE, EMBASE and PsycINFO) were searched from 1966 to February 2008. No language restrictions were imposed. Search terms were reported. Further studies were identified through reference lists of included articles and content experts.

Study selection
All studies (except single case reports) that investigated the use of endocrine interventions as part of sex reassignment in male-to-female or female-to-male individuals with gender identity disorder were eligible for inclusion. The outcomes of interest were quality of life and other psychosocial outcomes (as defined in the review). Studies with a follow-up period of less than three months were excluded.

The included studies were published between 1971 and 2007. The mean age of male-to-female participants was 38 years. The mean age of female-to-male participants was 31 years. Most studies were reportedly performed in Europe; single studies were performed in Canada and Singapore. Where reported, hormone therapies and treatment durations varied across the studies. Exposure to hormone therapy was self-reported in most studies. Outcomes were measured using structured interviews, clinical exams, questionnaires and a website.

Two reviewers independently selected the studies for inclusion; any disagreements were resolved by discussion, with involvement of a third reviewer where necessary.

Assessment of study quality
The strength of the evidence was assessed using the GRADE approach. Multiple reviewers undertook the GRADE assessments; any disagreements were resolved through consensus or arbitration.

Data extraction
Data on the outcomes were extracted by two independent reviewers to enable calculation of odds ratios with 95% confidence intervals (controlled studies only) or proportions (uncontrolled studies).

Methods of synthesis
Odds ratios (with 95% confidence intervals) and proportions from individual studies were pooled using random-effects meta-analysis. Statistical heterogeneity was assessed using the $I^2$ statistic. Subgroup analyses were performed for male-to-female and female-to-male populations.

Results of the review
Twenty-eight observational studies were included in the review (1,833 participants). It was unclear whether three or four studies included a control group; the other studies did not. Across the studies (where reported), length of follow-up (or time between sex reassignment and study with cross-sectional studies) ranged from two months to 16 years. None of the studies were randomised. Drop-out rates (where reported) ranged from zero to 75%. The overall quality of the
evidence was very low.

Following sex reassignment, most participants reported statistically significant improvements in gender dysphoria (80%, 95% CI 68 to 89; eight studies; $I^2=82\%$), psychological symptoms (78%, 95% CI 56 to 94; seven studies; $I^2=86\%$), quality of life (80%, 95% CI 72 to 88; six studies; $I^2=78\%$) and sexual function (72%, 95% CI 60 to 81; 15 studies; $I^2=78\%$).

Further results were reported in the paper.

**Authors' conclusions**

Very low quality evidence suggested that hormonal interventions in individuals undergoing sex reassignment were likely to improve gender dysphoria, psychological functioning and comorbidities, sexual function and overall quality of life.

**CRD commentary**

The review question was clear and supported by broad inclusion criteria. Relevant databases were searched and no language restrictions were imposed. Efforts were made throughout the review process to minimise reviewer error and bias. The overall strength of the evidence was assessed using a suitable well-known tool; results showed that the evidence was of very low quality. Study details were presented.

The statistical methods of synthesis did not seem appropriate given the substantial heterogeneity shown between the studies. The authors acknowledged the risk of reporting bias within the studies. They stated that inferences regarding hormonal therapy were weak and confounded because the therapy was co-administered with surgery and psychotherapy, and data were reported for the sex reassignment process as a whole. The authors also stated that cultural differences should be considered as the findings were mostly derived from European countries and their generalisability to other populations was unknown.

The authors' conclusion reflects the evidence presented but methodological limitations related to the individual studies and the review synthesis suggest that this conclusion should not be considered reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that prior to treatment clinicians should inform individuals of the uncertain balance between the benefits and harms of hormonal therapy in the sex reassignment context.

**Research:** The authors stated that further research was required to investigate the benefits and harms associated with hormonal therapy in individuals undergoing sex reassignment. It was also suggested that standardised scales be validated and consistently used to facilitate inference and subgroup comparisons. Cross-cultural studies were suggested as a way of assessing the impact that cultural stigma and victimisation might have on treatment outcomes.

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