

SUPPLEMENTARY ONLINE MATERIALS IV

Table 1: Question 1. For children and adolescents with gender dysphoria, what is the clinical effectiveness of treatment with GnRH analogues compared with one or a combination of psychological support, social transitioning to the desired gender or no intervention? – mental health, body image

QUALITY					Summary of findings			IMPORTANCE	CERTAINTY
					No of events/No of patients (n/N%)	Effect			
Study	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Comparator	Result		
<i>Impact on neuronal activation patterns</i>									
<i>Mean ACC response to caregiver/peer angry/happy voices in gender dysphoria youth receiving gender affirming hormone treatment through testosterone administration (GAH+) vs. no gender dysphoria youth not receiving testosterone (GAH-)</i>									
1 study Morningstar et al 2023	Very serious limitations ¹	No serious indirectness	Not applicable	Not calculable	N=19	N=25	Significant 3-way-interaction (group x speaker x emotion): GAH+ loss less response to angry caregiver vs peer voice, GAH- showed less response to happy caregiver vs. peer voice	Low	LOW
<i>Impact on mental health</i>									
<i>Mean depression (CDI)-Score in gender dysphoria youth receiving gender affirming testosterone administration</i>									
1 study Grannis et al 2021	Very serious limitations ²	No serious indirectness	Not applicable	Not calculable	N=19	N=23	Sig. lower in Intervention Group $F(1,39) = 7.39, p = 0.01, \eta^2 = 0.16$	Critical	LOW
<i>Mean Suicidality (SBQ-R)-Score</i>									
1 study Grannis et al 2021	Very serious limitations ²	No serious indirectness	Not applicable	Not calculable	N=19	N=23	No sig. differences Past year: $F(1,39) = 3.85, p = 0.06, \eta^2 = 0.09$. Lifetime: $F(1,39) = 1.25, p = 0.27, \eta^2 = 0.03$	Critical	LOW
<i>Mean generalized anxiety (SCARED)-Score</i>									

1 study Grannis et al 2021	Very serious limitations ²	No serious indirectness	Not applicable	Not calculable	N=19	N=23	Sig. lower in Intervention Group $F(1,39) = 6.99, p = 0.01, \eta^2 = 0.16$	Critical	LOW
Mean social anxiety (LSAS)-Score									
1 study Grannis et al 2021	Very serious limitations ²	No serious indirectness	Not applicable	Not calculable	N=19	N=23	Sig. lower in Intervention Group $F(1,39) = 17.21, p < 0.001, \eta^2 = 0.32$	Critical	LOW
Impact on body image									
Mean body-image-scale (BSI)-Score									
1 study Grannis et al 2021	Very serious limitations ²	No serious indirectness	Not applicable	Not calculable	N=19	N=23	Sig. lower dissatisfaction in Intervention Group $F(1,39) = 10.47, p < 0.01, \eta^2 = 0.21$	Critical	LOW

¹Very high risk of bias (lack of randomization, lack of blinding, lack of reports of baseline-testosterone-level, highly skewed variations in exogenous hormone doses and administration duration).

²Very high risk of bias (lack of randomization, lack of blinding, possible bias due to self-reported outcome measures and knowledge about treatment).