Dr. Renzo Puccetti

Esame del disegno di legge C. 2575 Governo, recante "Disposizioni per l'appropriatezza prescrittiva e il corretto utilizzo dei farmaci per la disforia di genere"

25 novembre 2025

Audizione presso la Commissione «Affari Sociali» Camera dei Deputati

1

1

Dr. Renzo Puccetti

Blocco puberale in minori affetti da disforia di genere (2019)

11 giugno 2019
Audizione presso XII Commissione Permanente «Igiene e Sanità» Senato della Repubblica
Atto n.207
«Uso del medicinale Triptorelina»

https://www.senato.it/Leg18/webtv_comm_hq?video_evento=1315

2

2

Gli obiettivi (2019)

1. Ridurre la disforia di genere
2. Prendere tempo
3. Facilitare il risultato chirurgo estetico

Effetti psico-sociali (2019)

PSYCHOSOCIAL EFFECTS

All relevant results are shown in Table 3.

GnRHas

GnRHa treatment was associated with significant improvements in multiple psychological measures, including global functioning,[25–27] depression,[26,27] and overall behavioral and/or emotional problems.[26,27] The effects of GnRHas on anger and anxiety remain unclear with conflicting results.[26,27] Moreover, GnRHa treatment had no significant effect on symptoms of GD,[26,27] with researchers in 1 study observing a nonsignificant increase in GD and body image difficulties.[26]

TABLE 3 Psychosocial Effects of Hormonal Treatments in Transgender Youth

Study	Treatment	Outcome					
		Global Functioning	Depression	Anger and Anxiety	Behavioral and Emotional Problems		GD and Body Image
de Vries et al[27] (de Vries et al[29])[a]	GnRHa, GAH (not assessed)	Increase[b] (increase[b])	Decrease[b]	Decrease[c]	CBCL: decrease[b] in total and internalizing scores, decrease[b] (decrease[c]) in externalizing scores	YSR: decrease[b] in total and internalizing scores, decrease[b] (decrease[c]) in externalizing scores	No significant effect[d]
Costa et al[25]	GnRHa	Increase[e]	—	—	—	—	—

Although influential articles in this field, Cohen-Kettenis and Van Goozen[53] and Smith et al[54] were unable to be included in our study because of their focus on patients after sex reassignment surgery. CBCL, Child Behavior Checklist; YSR, Youth Self Report; —, not applicable.

[a] These 2 studies involved the same cohort and were therefore considered as 1 study. Parentheses are used to indicate the results of the earlier study[25] in which researchers examined a smaller subset of the cohort subsequently examined in the previous study.[27]

[b] Indicates significant change ($P < .05$).

[c] Indicates nonsignificant change ($P > .05$).

[d] It is important to note that the Utrecht Gender Dysphoria Scale that was used to measure GD in this study has various limitations, especially in relation to individuals who have already undergone social transition. Thus, the reported lack of improvement in GD here may reflect a lack of sensitivity in detecting psychological benefits. For example, it has been indicated in clinical experience that GnRHas help to satisfy the desire to prevent development of unwanted secondary sex characteristics (which is a criterion for GD under the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* in young adolescents), but the Utrecht Gender Dysphoria Scale does not have any items that address this issue.

[e] Indicates that a *P* value was not calculated.

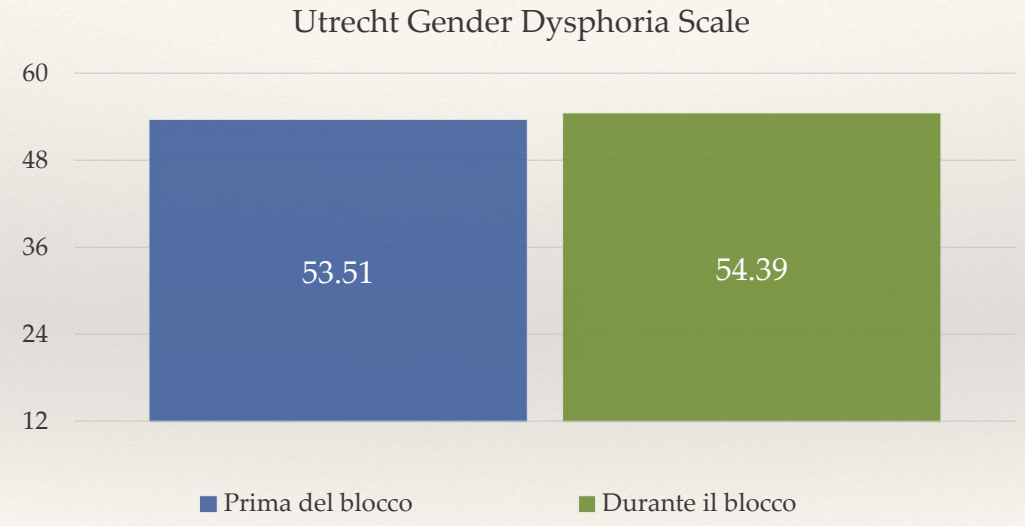
25. Costa R, Dunsford M, Skagerberg E, Holt V, Carmichael P, Colizzi M. Psychological support, puberty suppression, and psychosocial functioning in adolescents with gender dysphoria. *J Sex Med.* 2015;12(11):2206–2214
26. de Vries AL, McGuire JK, Steensma TD, Wagenaar EC, Doreleijers TA, Cohen-Kettenis PT. Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics.* 2014;134(4):696–704
27. de Vries AL, Steensma TD, Doreleijers TA, Cohen-Kettenis PT. Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. *J Sex Med.* 2011;8(8):2276–2283

GB

NL

Chew D, et al. Pediatrics 2018; 141(4): pii: e20173742. doi: 10.1542/peds.2017-3742. Epub 2018 Mar 7

Blocco puberale: effetto sulla disforia di genere (2019)

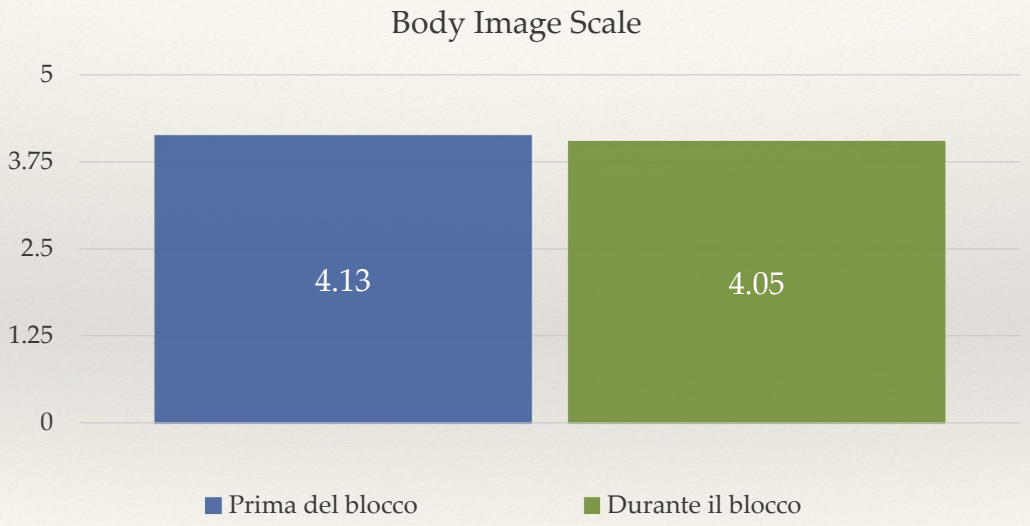


De Vries ALC, et al. Pediatrics 2014; 134(4): 696-704.

5

5

Blocco puberale: effetto sull'insoddisfazione dei caratteri sessuali primari (2019)



De Vries ALC, et al. Pediatrics 2014; 134(4): 696-704.

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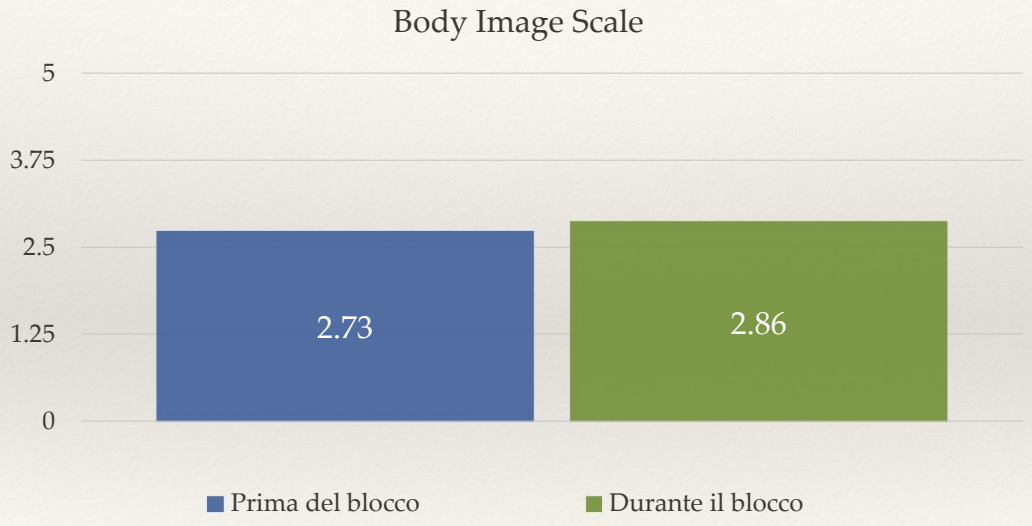
6

Blocco puberale: effetto sull'insoddisfazione dei caratteri sessuali secondari (2019)



De Vries ALC, et al. Pediatrics 2014; 134(4): 696-704.

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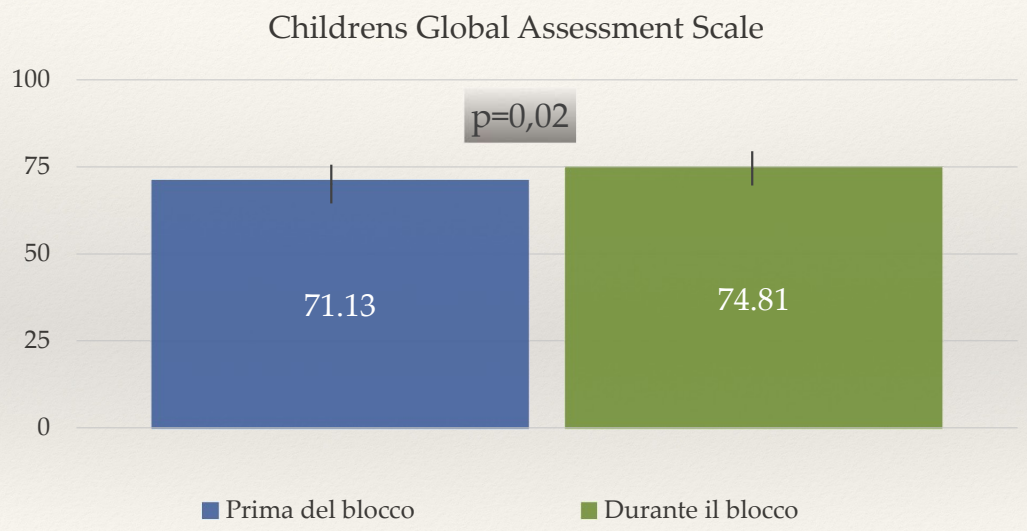
7

Blocco puberale: effetto sul funzionamento globale (2019)



De Vries ALC, et al. Pediatrics 2014; 134(4): 696-704.

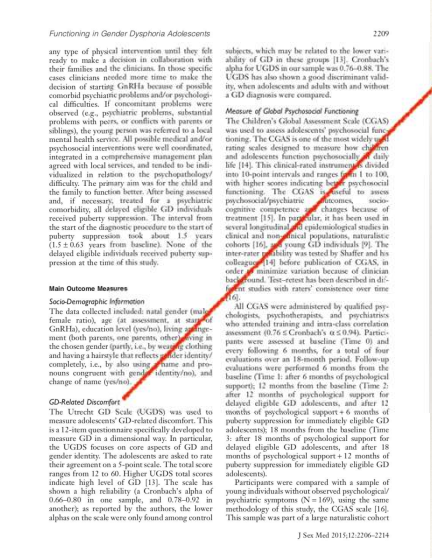
8

8

CGAS: Una variazione clinicamente non significativa (2019)

100-91	Superior functioning
90-81	Good functioning
80-71	No more than a slight impairment in functioning
70-61	Some difficulty in a single area, but generally functioning pretty well
60-51	Variable functioning with sporadic difficulties
50-41	Moderate degree of interference in functioning
40-31	Major impairment to functioning in several areas
30-21	Unable to function in almost all areas
20-11	Needs considerable supervision
10-1	Needs constant supervision

Che fine ha fatto la valutazione della disforia? (2019)



Functioning in Gender Dysphoria Adolescents 2209

any type of physical intervention until they felt ready to make a decision in collaboration with their families and the clinicians. In those specific cases clinicians needed more time to make the decision of starting GnRHa because of possible comorbid psychiatric problems and/or psychological difficulties. If concomitant problems were observed (e.g., psychiatric problems, substantial problems with peers, or conflicts with parents or siblings), the young person was referred to a local mental health service. All possible medical and/or psychosocial interventions were well coordinated, integrated in a comprehensive management plan agreed with local services, and tended to be individualized in relation to the psychopathology/difficulty. The primary aim was for the child and the family to function better. After being assessed and, if necessary, treated for a psychiatric comorbidity, all delayed eligible GD individuals received puberty suppression. The interval from the start of the diagnostic procedure to the start of puberty suppression took about 1.5 years (1.5 ± 0.63 years from baseline). None of the delayed eligible individuals received puberty suppression at the time of this study.

Main Outcome Measures

Socio-Demographic Information

The data collected included: natal gender (male/female ratio), age (at assessment, at start of GnRHa), education level (yes/no), living arrangement (both parents, one parents, others), living in the chosen gender (partly, i.e., by wearing clothing and having a hairstyle that reflects gender identity/completely, i.e., by also using a name and pronouns congruent with gender identity/no), and change of name (yes/no).

GD-Related Discomfort

The Utrecht GD Scale (UGDS) was used to measure adolescents' GD-related discomfort. This is a 12-item questionnaire specifically developed to measure GD in a dimensional way. In particular, the UGDS focuses on core aspects of GD and gender identity. The adolescents are asked to rate their agreement on a 5-point scale. The total score ranges from 12 to 60. Higher UGDS total scores indicate high level of GD [13]. The scale has shown a high reliability (a Cronbach's alpha of 0.66–0.80 in one sample, and 0.78–0.92 in another); as reported by the authors, the lower alphas on the scale were only found among control subjects, which may be related to the lower variability of GD in these groups [13]. Cronbach's alpha for UGDS in our sample was 0.76–0.88. The UGDS has also shown a good discriminant validity, when adolescents and adults with and without a GD diagnosis were compared.

Measure of Global Psychosocial Functioning

The Children's Global Assessment Scale (CGAS) was used to assess adolescents' psychosocial functioning. The CGAS is one of the most widely used rating scales designed to measure how children and adolescents function psychosocially in daily life [14]. This clinical-rated instrument is divided into 10-point intervals and ranges from 1 to 100, with higher scores indicating better psychosocial functioning. The CGAS is useful to assess psychosocial/psychiatric outcomes, socio-cognitive competence and changes because of treatment [15]. In particular, it has been used in several longitudinal and epidemiological studies in clinical and nonclinical populations, naturalistic cohorts [16], and young GD individuals [9]. The inter-rater reliability was tested by Shaffer and his colleagues [14] before publication of CGAS, in order to minimize variation because of clinician background. Test–retest has been described in different studies with raters' consistence over time [16].

All CGAS were administered by qualified psychologists, psychotherapists, and psychiatrists who attended training and intra-class correlation assessment (0.76 ≤ Cronbach's α ≤ 0.94). Participants were assessed at baseline (Time 0) and every following 6 months, for a total of four evaluations over an 18-month period. Follow-up evaluations were performed 6 months from the baseline (Time 1: after 6 months of psychological support); 12 months from the baseline (Time 2: after 12 months of psychological support for delayed eligible GD adolescents, and after 12 months of psychological support + 6 months of puberty suppression for immediately eligible GD adolescents); 18 months from the baseline (Time 3: after 18 months of psychological support for delayed eligible GD adolescents, and after 18 months of psychological support + 12 months of puberty suppression for immediately eligible GD adolescents).

Participants were compared with a sample of young individuals without observed psychological/psychiatric symptoms (N = 169), using the same methodology of this study, the CGAS scale [16]. This sample was part of a large naturalistic cohort

J Sex Med 2015;12:2206–2214

GD-Related Discomfort

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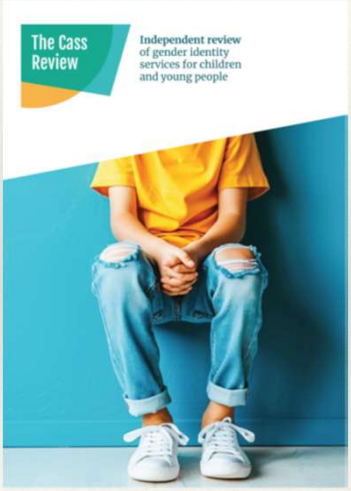
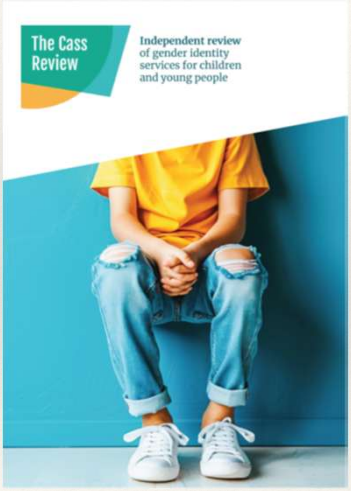
Che c'è di nuovo dal 2019?

Rapporto Cass: 10 aprile 2024



- Commissionato dal SSN inglese nel 2020 con favore politico bipartisan
- Presieduto dalla prof.ssa Hillary Cass (già presidente del Royal College of Paediatrics)
- Marzo 2022: Rapporto ad interim
- 10 Aprile 2024 Rapporto finale

Rapporto Cass: 10 aprile 2024



- 386 pagine
- 912 referenze bibliografiche
- 8 revisioni della letteratura (condotte dal Centre for Review and Dissemination dell'Università di York di cui uno sul blocco puberale
- 92 ricercatori

13

13

Rapporto Cass: blocco puberale (dà tempo?)

Buying time to think/explore

14.23 The University of York's systematic review of care pathways (Taylor et al: Care pathways) reported that 0-8% of young people discontinued puberty suppression. Compared

- «La revisione sistematica dei percorsi di cura dell'Università di York ha riportato che lo 0-8% dei giovani interrompevano la soppressione puberale» (p.176)

14.25 These data suggest that puberty blockers are not buying time to think, given that the vast majority of those who start puberty suppression continue to masculinising/feminising hormones, particularly if they start earlier in puberty. It was

- «Questi dati suggeriscono che i bloccanti puberali non fanno guadagnare tempo per pensare, dato che la grande maggioranza di coloro che iniziano la soppressione della pubertà continuano verso gli ormoni mascolinizzanti o femminizzanti» (p.176)

14

14

Rapporto Cass: il blocco puberale NON dimostra di ridurre la disforia

Reducing gender dysphoria/improving body satisfaction

14.26 Only two moderate quality studies looked at gender dysphoria and body satisfaction; the original Dutch protocol (de Vries et al., 2011b) and the UK early intervention study (Carmichael et al., 2021). Neither reported any change before or after receiving puberty suppression.

- «Solo due studi di qualità moderata hanno verificato la disforia e la soddisfazione corporea […] Nessuno ha riportato alcun cambiamento prima o dopo avere ricevuto la soppressione puberale». (p.176)

15

15

Rapporto Cass: il blocco puberale migliora la salute mentale?

Psychological and mental health improvements

14.27 As outlined in Chapter 2, the original Dutch protocol (de Vries et al., 2011b) found improvements in mental health in a pre-post study without a comparison group, but the GIDS early intervention study (Carmichael et al., 2021) did not replicate this finding. The systematic review on interventions to suppress puberty (Taylor et al: Puberty suppression) identified one other good quality study (van der Miesen et al., 2020), which produced an intermediate result with improvements in some mental health measures but not others.

- «Il protocollo originale olandese ha rilevato miglioramenti nella salute mentale in uno studio prima-dopo senza gruppo di confronto, ma il GIDS early intervention study non ha confermato questo risultato. La revisione sistematica sugli interventi per sopprimere la pubertà ha individuato un altro studio di buona qualità che ha prodotto un risultato intermedio con miglioramenti in alcune misure di salute mentale, ma non in altre». (p.176)

16

16

Rapporto Cass: evidenza INSUFFICIENTE sulla salute mentale

14.28 The University of York concluded that there is insufficient and/or inconsistent evidence about the effects of puberty suppression on psychological or psychosocial health. This is in line with the finding of the NICE review (2020) and other systematic reviews, apart from the systematic review commissioned by WPATH (Baker et al., 2021), which reported some benefit. However, in the latter systematic review, eight of the 12 studies reporting psychological outcomes were rated as low quality, which may explain the difference.

- «L'Università di York ha concluso che c'è un'evidenza insufficiente e/o incoerente circa gli effetti della soppressione della pubertà sulla salute psicologica o psicosociale. Questo è in linea con i risultati della revisione NICE e altre revisioni sistematiche, con l'eccezione della revisione sistematica commissionata dalla WPATH che ha riportato qualche beneficio. Tuttavia in quest'ultima revisione, 8 dei 12 studi che hanno riportato gli effetti psicologici erano valutati di bassa qualità, il che può spiegare la differenza» (pp. 176-7)

17

17

Rapporto Cass: il blocco puberale NON ha dimostrato di ridurre il suicidio

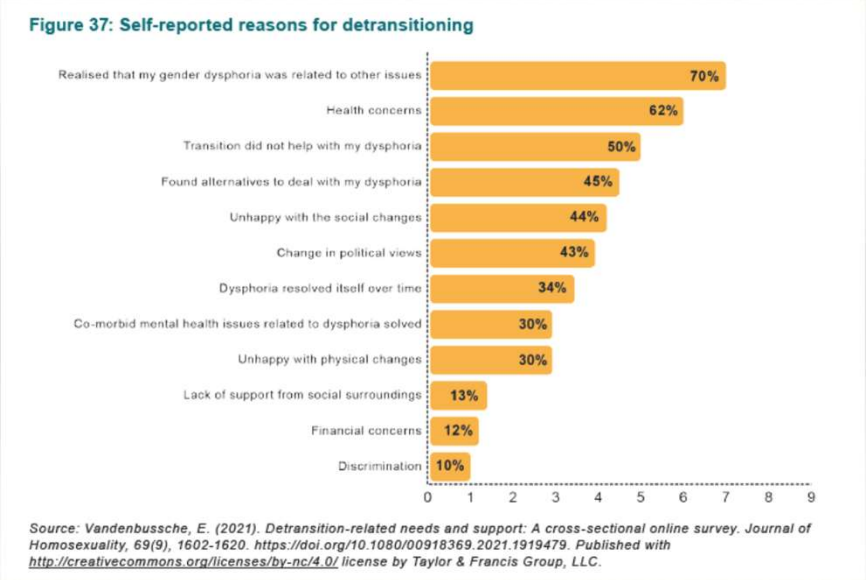
15.43 In summary, the evidence does not adequately support the claim that gender-affirming treatment reduces suicide risk.

- «L'evidenza non supporta adeguatamente l'affermazione che il trattamento affermativo di genere riduce il rischio di suicidio». (p.187)

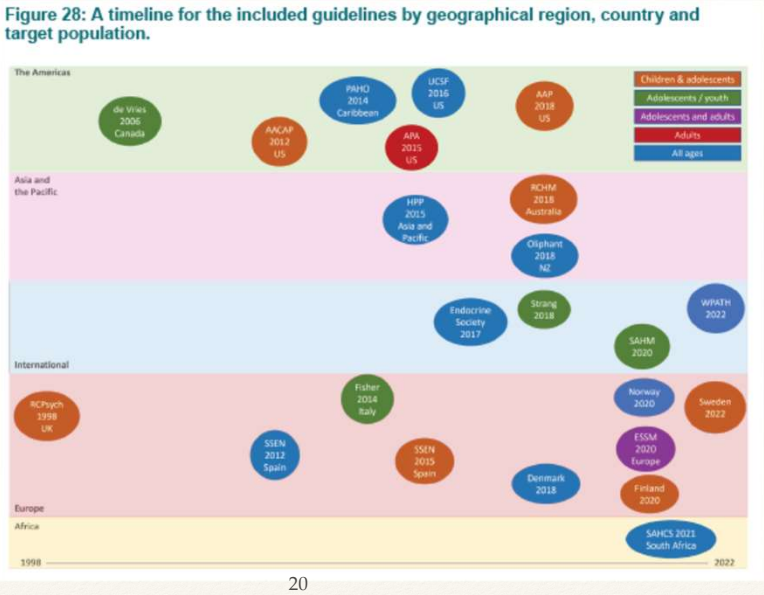
18

18

Rapporto Cass: perché la «detransizione»



Rapporto CASS: linee guida



(p. 127)

Rapporto CASS: qualità linee guida (sec. AGREE II)

Table 6: Critical appraisal domain scores

Guideline ID	Scope and Purpose	Stakeholder involvement	Rigour of development	Clarity of presentation	Applicability	Editorial Independence
AACAP 2012	65	39	44	63	7	31
American Academy of Paediatrics 2018	70	26	12	30	6	69
American Psychological Association 2015	74	74	24	50	18	14
Council for Choices in Healthcare Finland 2020	91	69	51	72	56	0
de Vries 2006	63	31	10	74	17	6
Endocrine Society 2009	65	33	44	70	22	31
Endocrine Society 2017	63	33	42	72	21	92
European Society for Sexual Medicine 2020	63	52	39	70	7	58
Fisher 2014	65	20	12	35	17	44
Health Policy Project 2015	63	63	16	24	33	6
Norwegian Directorate of Health 2020	76	81	30	57	47	17
Oliphant 2018	44	39	12	33	21	0
Pan American Health Organisation 2014	52	44	13	31	21	0
Royal Children's Hospital Melbourne 2018	81	59	19	41	19	14
Society for Adolescent Health and Medicine 2020	41	24	17	41	7	0
South African HIV Clinicians Society 2021	59	59	21	43	24	69
Strang 2018	87	31	18	37	15	19
Swedish National Board of Health & Welfare 2022	91	87	71	83	25	36
UCSF 2016	70	41	23	37	26	0
WPATH 2012	85	61	26	56	17	17
WPATH 2022	83	63	35	56	24	39

≥70%, 31%-69%, ≤30%

AACAP, American Academy of Child &Adolescent Psychiatry; UCSF, University of California, San Francisco; WPATH, World Professional Association for Transgender Health

(p. 129)

Rapporto CASS: qualità linee guida (sec. AGREE II)

- «La maggioranza delle linee guida descrivevano insufficiente l'evidenza sui rischi e i benefici del trattamento medico negli adolescenti, particolarmente in relazione agli effetti a lungo termine. Nonostante questo, molte poi proseguivano citando questa stessa evidenza per raccomandare i trattamenti medici» (p. 130)

Rapporto CASS: qualità linee guida (sec. AGREE II)

- «In alternativa facevano riferimento ad altre linee guida, che raccomandavano i trattamenti medici, come base per fare le stesse raccomandazioni» (p. 130)

23

23

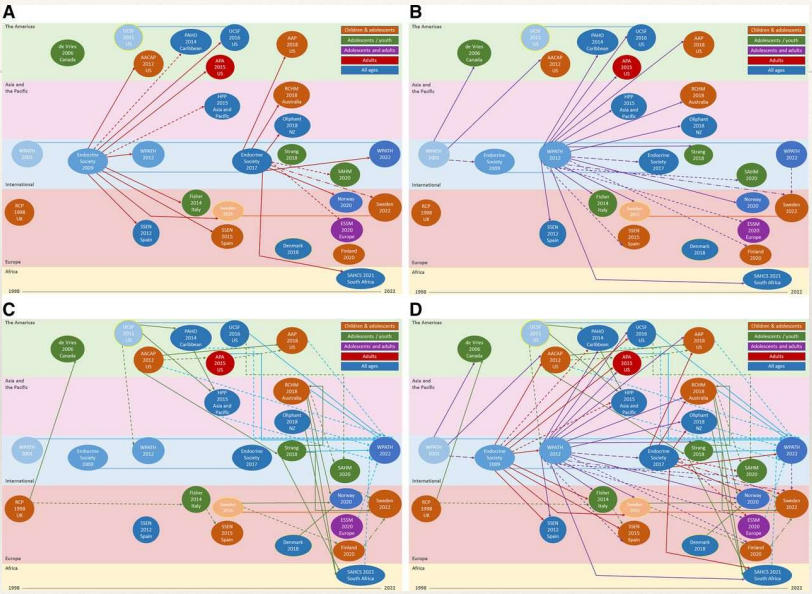
Rapporto CASS: qualità linee guida (sec. AGREE II)

- «Le prime versioni di due linee guida internazionali, l'Endocrine Society 2009 e la World Professional Association for Transgender Healthcare (WPATH) 7, hanno influenzato quasi tutte le altre linee guida.
- Queste due linee guida sono inoltre strettamente interconnesse, con la WPATH che ha adottato le raccomandazioni dell'Endocrine Society e ha agito come co-sponsor e ha fornito contributi alle bozze delle linee guida dell'Endocrine Society.
- La WPATH 8 ha citato molte delle altre linee guida nazionali e regionali a supporto di alcune delle sue raccomandazioni, nonostante queste siano state notevolmente influenzate dalla WPATH 7» (p. 130)

24

24

Links between guidelines.



Jo Taylor et al. Arch Dis Child 2024;109:s65-s72

ADC

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25

Rapporto CASS: qualità linee guida (sec. AGREE II)

- «La circolarità di questo approccio può spiegare il motivo per cui c'è stato un apparente consenso in aree chiave della pratica nonostante l'evidenza fosse scarsa». (p. 130)
- «La valutazione delle linee guida solleva seri dubbi sull'affidabilità delle attuali linee guida. La maggior parte di esse non ha seguito gli standard internazionali per lo sviluppo delle linee guida (AGREE Next Steps Consortium, 2017)» (p. 130)

26

26

2024: revisione tedesca

Übersichtsarbeit

Beyond NICE: Aktualisierte systematische Übersicht zur Evidenzlage der Pubertätsblockade und Hormongabe bei Minderjährigen mit Geschlechtsdysphorie

Florian D. Zepf[1,2], Laura König[1,2], Anna Kaiser[3], Carolin Ligges[1,2], Marc Ligges[1,2], Veit Roessner[4,5], Tobias Banaschewski[3,6] und Martin Holtmann[7]

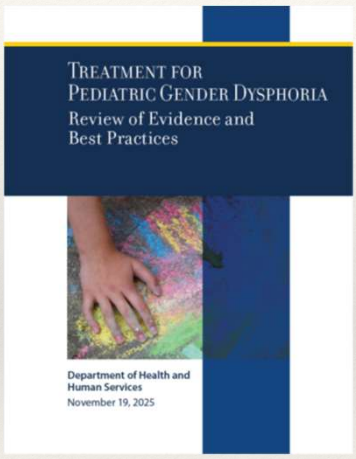
[1] Department of Child and Adolescent Psychiatry, Psychosomatic Medicine and Psychotherapy, Jena University Hospital, Friedrich Schiller University Jena, Jena, Germany
[2] German Center for Mental Health (DZPG), Site Jena-Magdeburg-Halle, Jena, Germany
[3] Central Institute of Mental Health, Medical Faculty Mannheim/Heidelberg University, Mannheim, Germany
[4] Department of Child and Adolescent Psychiatry, TU Dresden, Dresden, Germany
[5] German Center for Child and Adolescent Health (DZJK), partner site Leipzig-Dresden, Germany
[6] German Center for Mental Health (DZPG), partner site Mannheim-Heidelberg-Ulm, Germany
[7] LWL-Universitätsklinik Hamm der Ruhr-Universität Bochum, Hamm, Germany

2024: revisione tedesca

- «L'evidenza disponibile sull'uso dei bloccanti della pubertà e degli ormoni per la transizione nei minori è limitatissima a pochi studi con piccoli numeri e questi studi hanno una metodologia e una qualità problematiche.
- Mancano anche studi a lungo termine adeguati e significativi. L'evidenza attuale non suggerisce che i sintomi di disforia di genere e di salute mentale migliorino significativamente quando i bloccanti della pubertà o gli ormoni per la transizione sono usati sui minori con disforia di genere.
- Gli interventi terapeutici per gestire e ridurre la sofferenza percepita possono diventare rilevanti nei bambini e negli adolescent con disforia di genere»

Z Kinder Jugendpsychiatr Psychother. 2024;52(3):167-187.

Rapporto HHS-USA: 19 novembre 2025



- 406 pagine di rapporto peer review
- 114 pagine di bibliografia
- 182 pagine di appendice condotta sulle revisioni sistematiche
- 42 pagine di bibliografia
- Migliaia di studi vagliati

29

29

Rapporto HHS-USA: blocco puberale

Overall, the absence of long-term, high-certainty evidence on these critical outcomes (including suicides, fractures, fertility, growth, and neurocognitive development) leaves substantial uncertainty about the effects of PBs.

- «Nell'insieme l'assenza di evidenze certe nel lungo termine riguardo questi effetti critici (inclusi i suicidi, le fratture, la fertilità, la crescita, lo sviluppo neurocognitivo) lasciano un'incertezza sostanziale circa gli effetti dei bloccanti della pubertà» (p. 91)

30

30

Rapporto HHS-USA: blocco puberale

Although PBs are frequently described as a "pause button,"[30] no studies have systematically examined their role in the decision-making process or the outcomes of those who discontinue treatment.

- «Sebbene i bloccanti della pubertà siano di frequente descritti come un bottone PAUSA, nessuno studio ha esaminato in maniera sistematica il loro ruolo nel processo decisionale o negli effetti per coloro che interrompono il trattamento». (p.90)

31

31

Rapporto HHS-USA: detransizione

7.6.2 Detransition and regret

This serious issue has been minimized with the claim that detransition and regret rates are vanishingly low. In fact, the detransition rate is unknown.[99] The ubiquitous claim that the detransition and regret rates are vanishingly low is unsupported by the evidence.[100] A U.K. population-based study not focused on minors found that about one-fifth of patients discontinued hormonal interventions within five years, with more than half of them reporting experiences of detransition and/or regret.[101] Reasons for detransition are complex[102] and can be related to external[103] or internal[104] factors. With respect to

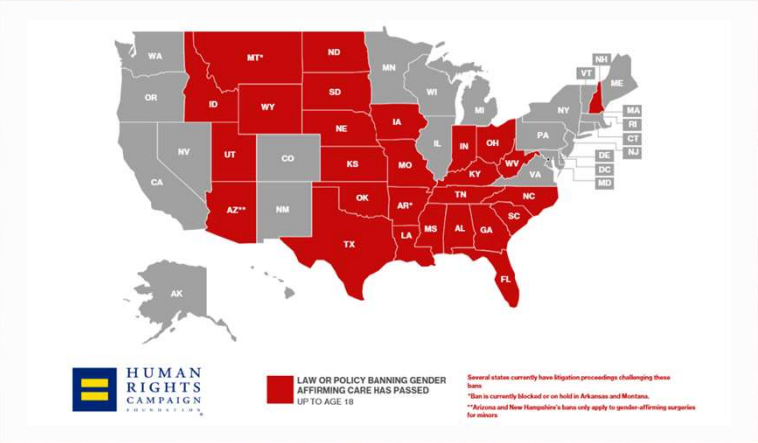
- «L'affermazione ubiquitaria che la detransizione e il pentimento sono incredibilmente rare non è supportata dall'evidenza». (p. 123)
- Uno studio di popolazione nel Regno Unito non focalizzato sui minori ha rilevato che un quinto dei pazienti interrompeva gli interventi ormonali entro 5 anni con più della metà di questi che riferivano esperienze di detransizione o pentimento». (p.132)

32

32

Stati USA

Leggi o regolamenti approvati per il divieto di BP o ormoni Cross-Sex



Comitato Nazionale per la Bioetica

2018

- Trattamento giustificabile se condotto da una équipe multidisciplinare e specialistica.

2024

- il CNB auspica che le prescrizioni avvengano solo nell'ambito delle sperimentazioni promosse dal Ministero della Salute.

Proposte

1. Revocare la rimborsabilità della triptorelina a carico del SSN, stante l'assenza di prove di appropriatezza.
2. Avviare uno studio nazionale sotto l'egida ministeriale controllato con placebo con verifica degli outcomes.

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