



EVIDENCE SUMMARY

THE ASSOCIATION BETWEEN GENDER-AFFIRMING CARE AND YOUTH MENTAL HEALTH

ABSTRACT

INTRODUCTION:

Across the globe, recent years have seen an increase in the politicisation of gender-affirming healthcare for trans and gender diverse young people. In Australia, trans and gender diverse young people encounter many barriers to accessing gender-affirming medical care, including long wait times for specialist clinics, geographical isolation,

and financial cost. Health professionals in primary care settings are often a young person's first point of contact with the health system, and their understanding and support of evidence-based practice is important to improve the accessibility and quality of health care services for trans and gender diverse young people.

OBJECTIVES:

This literature review investigated the association between gender-related interventions in healthcare settings (i.e., puberty blockers, gender-affirming hormone therapy (GAHT) and gender-affirming surgery) and mental health and wellbeing outcomes for trans and gender diverse young people.

METHODS:

Three academic databases (Medline, PsycINFO, Embase) were systematically searched using a predefined search strategy, developed in collaboration with a team of academic, clinical, and lived experience experts, who were also consulted throughout the project. Studies involving gender-related care approaches or interventions in healthcare settings for trans and gender diverse young people under the age of 26 published before 25 September 2023 were included. A total of 14,690 abstracts were imported to Covidence software for screening. Once duplicates were removed, 10,180 were screened based on title and abstract, then narrowed to 637 full-text studies which were assessed for eligibility by at least one member of the research team.

RESULTS:

Forty-eight studies met inclusion criteria. Overall, puberty blockers were associated with improved general functioning and peer relations, and reduced depressive symptoms, suicidal ideation, and behavioural and emotional problems in trans and gender diverse young people. GAHT was associated with body image satisfaction and reduced psychological symptoms, including depression, anxiety, and suicidality. Gender-affirming surgery was associated with improved mental health outcomes, quality of life, and body image satisfaction.

CONCLUSION:

Gender-affirming medical care is associated with positive mental health, wellbeing, and quality of life outcomes in trans and gender diverse young people.

INTRODUCTION

Health professionals in primary care settings are often a young person's first point of contact with the health system. It is important that these health professionals are gender-affirming and build competency to provide high quality health care for trans and gender diverse young people. 'Trans and gender diverse' is an umbrella term used to describe people whose gender differs from the gender presumed for them at birth. This includes gender identities such as trans men or trans women, non-binary, gender questioning, agender, gender queer, Brotherboys and Sistergirls.

Trans and gender diverse young people have reported that health professionals' understanding of gender-affirming care and respect for their gender identity impacts on the accessibility of primary care services.⁽¹⁾ Australian and international guidelines for health professionals working with trans and gender diverse young people have been developed, in line with the latest evidence and in consultation with subject matter experts. These outline current best practice for primary health professionals in relation to assessment, intervention, safety, and other considerations for working with trans and gender diverse young people.

While there has been some progress in the visibility and acceptance of gender diversity in recent years, trans and gender diverse young people continue to experience discrimination and marginalisation in healthcare settings and the broader community, contributing to significantly higher rates of mental-ill health compared to their cisgender peers.⁽²⁻⁴⁾ It is essential to explore evidence-based approaches that enhance equitable access to healthcare and foster positive mental health and wellbeing outcomes for trans and gender diverse young people.

This literature review aims to investigate the association between gender care approaches and interventions delivered in health care settings and mental health and wellbeing outcomes for trans and gender diverse young people. Evidence-based gender-affirming medical interventions include medications (i.e., puberty blockers and gender-affirming hormone therapy) and gender-affirming surgeries. It is important to note that trans and gender diverse young people do not necessarily wish to engage in all types of gender-affirming interventions, and their pathways to gender affirmation are unique.

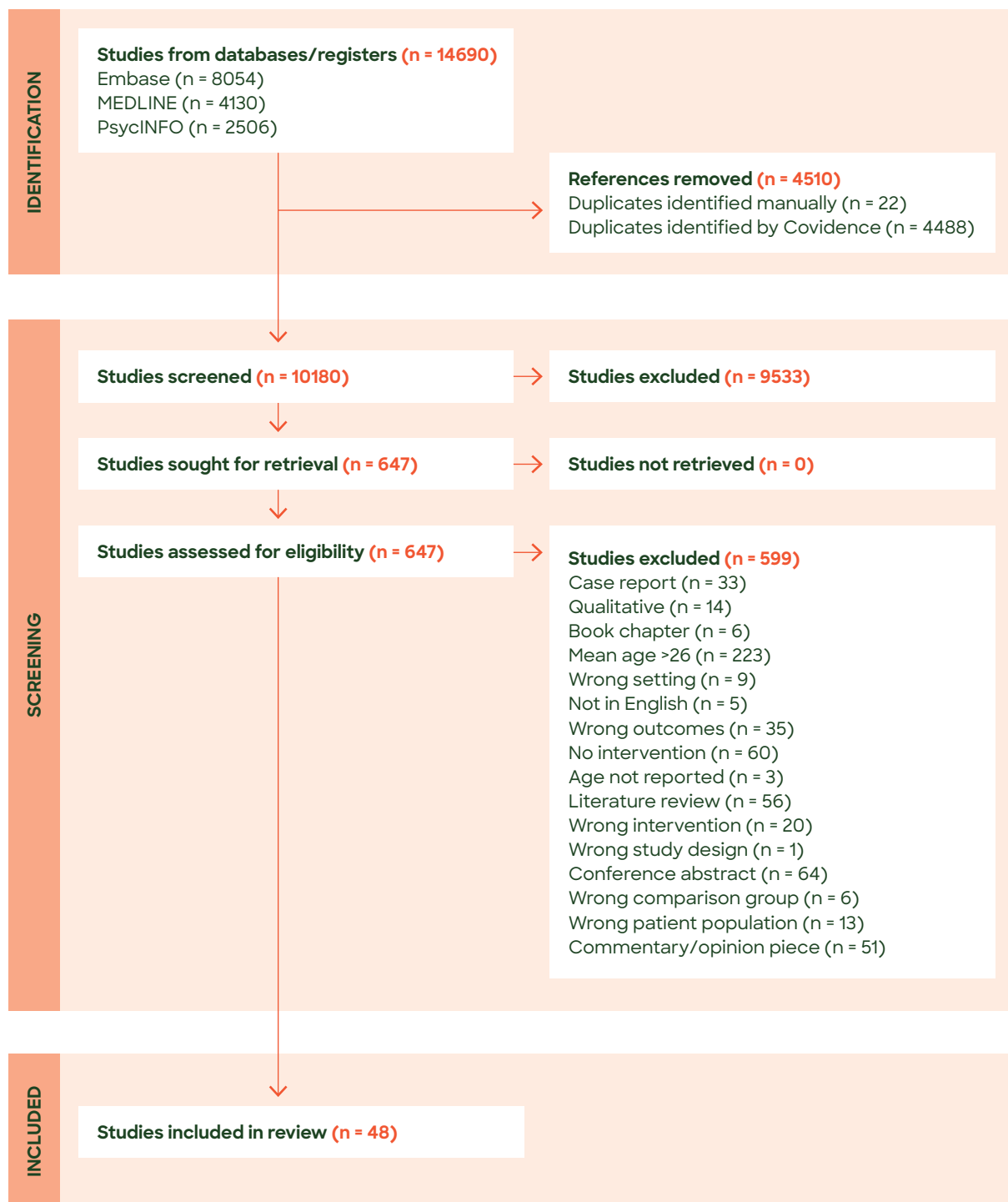


METHODS

Three academic databases were systematically searched using a predefined search strategy, developed in collaboration with a team of academic, clinical and lived experience experts (Appendix 1). Studies that focused gender care approaches or interventions in healthcare settings for trans and gender diverse young people under the age of 26 published before 25 September 2023 were included. A complete

list of inclusion and exclusion criteria is included in Appendix 2. Initially 14,690 abstracts were imported to Covidence software for screening. Once duplicates were removed, 10,180 records were screened based on title and abstract, then narrowed to 637 full-text studies which were assessed for eligibility by at least one member of the research team. A PRISMA flow diagram is displayed in Figure 1.

Figure 1:



RESULTS

A total of 48 studies met inclusion criteria for the review (Appendix 3). Despite the broad approach to exploring gender care approaches for trans and gender diverse young people, gender-affirming care was the only approach that was supported by peer-reviewed empirical research.

SOCIAL AFFIRMATION

Social affirmation of one's gender refers to changes that a trans or gender diverse young person can make in their social life to express their gender.⁽⁵⁾ Studies related to social affirmation are not included in the main results of this review due to their focus on young people in the community, rather than in health services. Nonetheless, these studies suggest social affirmation is important and primary care practitioners clearly have a role to play in socially affirming their patients' gender identity (e.g., using their identified name and pronouns). Some research has shown socially transitioned young people have levels of depression, anxiety, and self-worth comparable to cisgender siblings (and cisgender controls), according to both self- and parent-reports.⁽⁵⁻⁷⁾ In other research with trans and gender diverse young people, chosen name use in multiple contexts (school, home, work, with friends) was associated with lower depression, suicidal ideation, suicidal behaviour, and greater self-esteem.^(8, 9) Another study with a subset of trans and gender diverse children who had a diagnosis of gender dysphoria, found no association between social transition or chosen name use with mood, anxiety and past suicidal behaviour.⁽¹⁰⁾ Longitudinal research is needed to better understand how social affirmation may impact on youth mental health over time. Overall, most evidence suggests that when trans and gender diverse young people are supported to socially transition or when their gender identity is affirmed, they experience mental health outcomes similar to their cisgender siblings and peers.

GENDER-AFFIRMING MEDICAL TREATMENT

PUBERTY BLOCKERS

Puberty blockers are an informal name for Gonadotropin-releasing hormone analogues (GnRHa), such as Goserelin (Zoladex), Leuprorelin (Lucrin), or Triptorelin (Diphereline). They are recommended as an initial treatment for early adolescents experiencing gender-related distress. They are effective treatments for suppressing puberty and menses.⁽¹¹⁾ This allows additional time for gender identity development while preventing further distress caused by changes to the body during puberty.⁽¹²⁾

Three longitudinal studies,^(11, 13, 14) and two cross-sectional studies,^(15, 16) have investigated the youth mental health outcomes associated with GnRHa treatment. 'Gold standard' research designs that usually apply within a medical model, such as randomised controlled trials (RCTs), may not be appropriate for investigating gender-affirming care interventions, which seek to operate beyond a clinical, medical, or deficit model. Also, RCTs are rare in this field of research, given ethical issues associated with delaying access to treatment for a control group.⁽¹⁷⁾ A longitudinal study of 70 trans and gender diverse adolescents found that from the start of GnRHa to the start of gender-affirming hormone therapy (GAHT; i.e. estrogen or testosterone), general functioning improved, while depressive symptoms and behavioural and emotional problems decreased significantly. There was no change in anxiety, anger, gender dysphoria or body satisfaction.⁽¹⁴⁾ Similarly, another study of 121 adolescents receiving GnRHa found psychosocial function increased steadily over the 18 month study, to within normal range for cis-gendered peers. Half of the participants experienced delayed eligibility for GnRHa and had poorer psychosocial outcomes, despite also receiving psychological support.⁽¹³⁾ A smaller study found no significant changes in psychological distress nor self-harm during GnRHa treatment, although there were a number of study limitations including short-term follow up with a high rate of drop out, and the majority of participants commenced GnRHa in the late stages of puberty, which may have influenced the findings.^(11, 18) Half of participants reported positive mood changes, while a quarter reported negative mood changes or reduced energy.

A survey of over 20,000 trans and gender diverse young adults found that 16.9 per cent reported that they wanted to receive GnRHa as part of their gender care during early adolescence, while only 2.5 per cent had actually received it.⁽¹⁵⁾ After adjusting for other variables, those who received GnRHa treatment had significantly lower odds of lifetime suicidal ideation compared to those who wanted puberty suppression but did not receive GnRHa treatment. Finally, a Dutch study found that trans and gender diverse young people who had received gender-affirming care including GnRHa (n=178) reported fewer

internalising problems, self-harm/suicidality, and stronger peer relationships than trans and gender diverse young people who had not yet received gender-affirming care (n=272). The group receiving treatment reported similar psychosocial functioning compared to 651 of their same-age cisgender peers.(16) Overall, the peer-reviewed literature suggests that GnRHa is correlated with improved general functioning and peer relations, and reduce depressive symptoms, suicidal ideation, and behavioural and emotional problems in trans and gender diverse young people.

TRAJECTORY OF CHILDREN AND YOUNG PEOPLE ACCESSING GENDER-AFFIRMING MEDICAL TREATMENT

Most young people who access gender-affirming care, continue to access gender-affirming interventions over time, and most children who access GnRHa treatment go on to access GAHT in adolescence.(11) While discontinuation of treatment is not necessarily a negative outcome, the rate of discontinuation of gender-affirming medical treatment among adolescents is consistently low across studies, varying from zero to 10 per cent.(12, 19–22). Variability across studies may be related to differing eligibility criteria, developmental stages, quality of service provision, and sociocultural contexts. When gender dysphoria continues for young people during puberty, it is unlikely to subside.(12)

Trans and gender diverse adolescents taking GnRHa have reported better psychosocial function and life satisfaction, along with lower rates of depression and lifetime suicidality than those who accessed gender-affirming medical treatment at a later stage.(23) Those accessing GnRHa,(23) reported comparable rates of mental health and wellbeing to the population average, which may reflect the benefits of early access to gender-affirming care. Early access to GAHT (during adolescence) is also associated with lower odds of suicidal ideation.(24)

GENDER AFFIRMING HORMONE THERAPY (GAHT)

Gender-affirming hormone therapy (GAHT) involves administering sex hormones or hormonal medications to align secondary sex characteristics more closely with gender identity. For the vast majority of trans and gender diverse young people, GAHT is their first introduction to gender-affirming medical treatment. For example, in a study of 316 youth receiving GAHT, 93 per cent did not previously receive GnRHa treatment.(23)

Access to GAHT remains limited. A large survey found the percentage of trans and gender diverse young people who want GAHT but do not receive it (approximately 50 per cent) far outweighs those who receive it (14 per cent).(25). Those receiving GAHT were significantly more likely to have parental support and lower odds of recent depression and suicidality compared to those who wanted GAHT but did not have access to it.(25) Similarly, a large cross-sectional study of over 27,000 trans and gender diverse adults in the U.S. found that access to GAHT during adolescence and early adulthood was associated with better mental health outcomes compared to desiring but not accessing GAHT.(24) Overall, this correlational research found a positive association between access to GAHT for trans and gender diverse young people and positive mental health outcomes.

Research trials and longitudinal studies have further supported this association. A three-month RCT was recently undertaken with 64 trans and gender diverse young adults seeking testosterone therapy. At three months, the immediate testosterone treatment group experienced significantly reduced gender dysphoria, depression, and suicidality compared to those who were placed on the three-month waitlist.(26) Another study found trans and gender diverse young people receiving GAHT (testosterone) experienced significantly less depression, anxiety, and distress related to body image when compared to same age trans and gender diverse people not receiving testosterone.(27) Many longitudinal studies, with and without control groups, have also investigated the mental health and wellbeing outcomes of GAHT for trans and gender diverse young people. Over time, GAHT appears to reduce gender dysphoria,(28) body uneasiness/dissatisfaction,(29–32) and psychiatric symptoms.(29, 30) For example, GAHT has been associated with reduced rates of depression,(33–35) suicidality,(31, 35, 36) and anxiety.(31, 34, 35) One study with a brief follow up period found no significant changes to depression and anxiety, which suggested that improvements may occur gradually.(37) GAHT has also been associated with increased general wellbeing,(36) and life satisfaction.(34) Appearance congruence also increased over time and was associated with improved psychological outcomes.(34) One study focused specifically on facial appearance found that both



trans men and women experienced increased satisfaction after receiving GAHT.(38) One study showed significant improvement in quality of life,(39) whereas another found no change.(30) Although not the aim of GAHT treatment, it does not appear to influence self-esteem,(30, 38) disordered eating attitudes and behaviours,(29, 40) or aggression.(41, 42)

In a small number of studies related to GAHT, only the trans-masculine cohort met the age criteria for inclusion in this review.(28, 41, 43) One study found that trans-masculine young people receiving testosterone experienced a clinically significant improvement in emotional well-being and social functioning.(28) Another study found trans-masculine young people who received testosterone experienced significantly lower rates of social anxiety, depression, and suicidality compared to the cohort who did not receive GAHT. Although there were no significant relationships between estrogen and depression and anxiety symptoms for trans-feminine participants, longer duration of estrogen was associated with less suicidality.(32)

Altogether, the evidence suggests that GAHT is associated with body image satisfaction and reduced psychological symptoms, including depression, anxiety, and suicidality.

SURGICAL INTERVENTIONS

Top surgery involves removing or augmenting chest tissue to create a more masculine or feminine appearance and is the most common gender-affirming surgical procedure accessed by trans and gender diverse young people.(44) Bottom surgery involves changing the look and function of genitals to align with gender identity. For those who desire it, bottom surgery remains inaccessible to most trans people in Australia due to significant barriers including the prohibitive cost and very limited number of skilled surgeons.

For trans-masculine youth (n=136) undergoing top surgery, chest dysphoria was significantly reduced post-surgery.(45) A qualitative study of 30 trans-masculine youth aged 13-21 found that chest dysphoria triggered strong negative emotions, suicidal ideation, and functional limitations, that were not adequately relieved by GAHT.(46) All post-surgery youth reported resolution of chest dysphoria, improved quality of life and functioning, and lack of regret.(46) Similarly, quantitative studies have supported that top surgery improves chest dysphoria, gender congruence, and body image satisfaction post-surgery for trans and nonbinary young people.(47-49) Two surveys of young people found that most were very satisfied with the overall experience of top surgery and its result including cosmetic appearance.(20, 50) Most people strongly agreed that surgery improved their mental health (77 per cent) and overall quality of life (82 per cent).(20) Another study found that pre-operative depression was associated with poor health-related quality of life six months post-mastectomy (masculinising

chest surgery), which suggests it is important to screen patients for depression and provide additional psychological support as needed.(44) Recent advances in top surgery procedures may further improve body satisfaction, quality of life, and psychosocial wellbeing.(51)

There is relatively little research focused on the mental health and wellbeing outcomes associated with other types of gender-affirming surgery, including bottom surgery, in young adults. One survey of young adults found that following intestinal vaginoplasty (a specific type of bottom surgery), trans women reported a good quality of life.(52) An Iranian study similarly found that gender reassignment surgery was significantly correlated with higher quality of life scores.(53) Overall, the evidence suggests that gender-affirming surgery is associated with improved mental health outcomes, quality of life, and body image satisfaction in trans and gender diverse young people.

HOW COMMON ARE FEELINGS OF REGRET?

For trans and gender diverse people who pursue gender-affirming surgery, feelings of regret after surgery are rare. Across the included studies, the number of participants who reported feelings of regret was near zero.(20, 21, 45, 46, 50, 54) Another study of nearly 7,000 trans and gender diverse people in the Netherlands found that only 0.6 per cent of transwomen and 0.3 per cent of transmen expressed regret after gonadectomy (surgical removal of testes or ovaries).(55) As with any type of surgery, regret may be related to outcomes, pre-operative expectations, or complications.(56) Also, external factors such as social pressure or repercussions such as family rejection, harassment, and social stigma commonly influence feelings of regret related to gender-affirming medical care.(57)



COMBINATIONS OF GENDER-AFFIRMING MEDICAL TREATMENT

Longitudinal research has found young people initiating GnRHa and/or GAHT experienced improved depression symptoms,(39, 58) suicidal ideation,(39, 58) quality of life,(39) and global self-worth,(59) over time. Cross-sectional research has also found an association between gender-affirming hormonal interventions (GnRHa and GAHT) and fewer anxiety symptoms.(60) In one study, young people who received GAHT and/or gender-affirming surgery reported less emotional and behavioural problems than prior to commencing treatment, similar to the national norm.(61) GAHT and surgery combined were associated with a better body image than the absence of treatment or where only GnRHa or GAHT were applied.(62) Young people who received GnRHa followed by GAHT treatment along with psychosocial support experienced significantly improved gender dysphoria.(63)

One study followed 55 trans young people (mean age 13.6 at baseline) through commencing GnRHa, GAHT, and gender-affirming surgery. One year post-surgery (primarily vaginoplasty for transwomen and mastectomy and hysterectomy with ovariectomy for transmen), gender dysphoria was alleviated and psychological functioning and wellbeing improved to be similar to same-age cisgender peers.(54) In a survey of 350 Brazilian trans and gender diverse youth, having completed multiple steps of gender affirmation (social, legal, and medical/surgical) was associated with decreased depression and anxiety symptoms. Furthermore, engaging in gender affirmation processes helped trans young people to feel more socially accepted and positive about their gender identity.(64) This evidence suggests that gender-affirming interventions may have a cumulative effect for improving body image, mental health and wellbeing.

RE-AFFIRMATION

A small number of trans and gender diverse people may identify as gender fluid or align with a different gender identity over time or in different contexts. A recent Australian study found that of 196 children and adolescents who commenced GnRHa or GAHT, only two (one per cent) reidentified with their birth-registered sex.(65) In another study of nearly 2,000 youth and young adults who underwent gender-affirming surgery (mean age 24.5), only six (0.3 per cent) either requested reversal surgery or re-affirmed their gender to align with their sex assigned at birth.(56) It is important to note that re-affirmation of gender is not synonymous with regret or adverse outcomes, and these should not be conflated.(57)

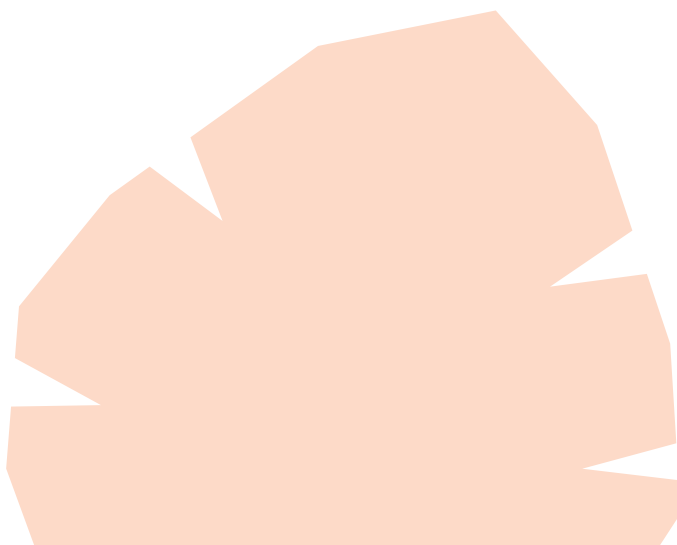
A survey in the US found that over 80 per cent of trans and gender diverse people who re-affirmed their gender were driven by at least one external factor.(57) Young people in this survey were most likely to report feeling pressure to re-affirm their gender presumed at birth from a parent, friends, the community, or societal stigma.

DISCUSSION

The evidence that gender-affirming care is correlated with enhanced youth mental health and wellbeing outcomes is consistently and overwhelmingly positive. Despite ethical barriers to conducting high quality RCTs, there is also emerging evidence to support that gender-affirming care has a direct impact on these improved outcomes. Augmenting gender-affirming medical interventions with multi-disciplinary psychosocial support may further enhance outcomes.(60, 61, 66)

Gender-affirming care is the only therapeutic gender-care approach supported by peer-reviewed literature and endorsed by peak medical bodies in Australia, the United States, and many other countries.(67) Furthermore, it aligns with key clinical care principles including person-centred care. This means treating people with dignity and respect, communicating about treatment options, and encouraging participation in decision-making. This promotes autonomy, sense of agency and self-determination, and upholds basic human rights. Person-centred care is foundational to safe, high-quality healthcare and is embedded in clinical care standards including the National Safety and Quality Health Service (NSQHS) Standards and the Primary and Community Healthcare Standards.

Conversely, withholding gender-affirming care is known to be harmful. Young people may feel their identity has been invalidated and avoid accessing health care in the future, leading to poorer health outcomes.(1) Legislation banning gender-affirming care implemented in some parts of the United States has had a negative impact on mental health including gender dysphoria, depression, anxiety, and risk of suicide, as well as increased stigma and decreased safety and access to medical care, according to both young people and their parents.(68) Discriminatory policies and the rhetoric surrounding them are harmful to trans and gender diverse young people and their families, and health professionals play an important role in correcting misinformation perpetuated by such policies(69). Advocacy for accessible, gender-affirming health care is clearly needed for trans and gender diverse young people internationally.



GENDER-AFFIRMING CARE IS THE ONLY EVIDENCE-BASED APPROACH

The current review did not find any empirical research of alternative approaches to gender-affirming care that yielded positive mental health or wellbeing outcomes, despite the broad search strategy encompassing all approaches to gender-related distress in young people. Only one peer-reviewed paper investigating an alternative approach met the inclusion criteria. This study found that for transgender adolescents, gender identity change efforts were associated with a 55 per cent increase in attempted suicide and doubled the risk of running away compared to those who had not been exposed, with worse outcomes for people exposed at a younger age of 11-14.(67) Additional research has confirmed that interventions with the intent to change gender identity are detrimental to mental health, including increasing suicidality and self-harm.(70, 71) Conversion practices are also unlawful across several Australian states and territories.

Gender Exploratory Therapy (GET) has been proposed as another alternative to gender-affirming care, in which gender affirmation in young people is discouraged, while first using talk therapy to explore the meaning and potential pathological roots of their gender identity or gender questioning. The approach and its parameters are not yet clearly defined and there is a lack of peer-reviewed evidence investigating the outcomes of this approach. Proponents of GET argue that it is a “neutral” approach which has no predetermined outcome.(72) However, some academics have likened it to conversion therapy in its aims, in that there is no clear endpoint for “exploration” unless the young person has accepted their gender as the gender presumed for them at birth.(17) The approach is also at odds with expert consensus that being trans is not pathological.

‘Wait-and-see’ approaches also have a negative impact on young people’s mental health and wellbeing, as studies have shown that unmet needs for gender-affirming care contribute to mental health inequities including higher rates of suicide and self-harm.(73) Distress associated with gender dysphoria also tends to increase as young people go through stages of puberty.(15) Young people presenting for gender-affirming treatment at an older age and later pubertal stage have greater rates of depression, anxiety, and use of psychoactive medication than those presenting earlier.(74) Greater perceived gender affirmation progress and gender congruence are associated with fewer mental health symptoms in trans adolescents.(75) Interventions designed to reduce wait times appear to improve mental health and wellbeing. For example, the innovative First Assessment Single-Session Triage (FASST) clinic that provided information and support to young people and their families and triaged them onto a secondary waitlist for subsequent multidisciplinary care improved depression, anxiety, quality of life, and sense of agency.(76)

STRENGTHS AND LIMITATIONS OF THIS LITERATURE REVIEW

This review used a comprehensive and systematic literature search strategy, which adds to its strength. However, it is possible that a small number of relevant studies may have been missed. Grey literature and anecdotal evidence were also excluded from this evidence review. Most studies included in this review were uncontrolled observational studies with small to moderate sample sizes and limited follow up. While it would be ideal to be able to draw from more high-quality evidence, such as randomised controlled trials, this is often unfeasible as it would be unethical to withhold interventions which are known to improve the health and wellbeing of participants. Nonetheless, the quantity and quality of research related to care for trans and gender diverse young people is increasing over time, so it will be important to review the best available evidence as more data becomes available in the future. This review also focused on mental health and wellbeing outcomes, so it is important to consider this information in conjunction with research exploring physical and sexual health outcomes associated with gender care interventions.

CONCLUSION

- Overall, the peer-reviewed evidence supports gender-affirming care as the best available approach to improve mental health, wellbeing, and quality of life outcomes for trans and gender diverse children and young people.
- Earlier access to gender-affirming care and accessing multiple types of gender-affirming interventions are both associated with better body image, mental health, and wellbeing outcomes.
- Augmenting medical care with multi-disciplinary, gender-affirming psychosocial support may further enhance outcomes.(60, 61, 66)
- Limiting access to gender-affirming care, using a ‘wait and see’ approach or interventions with an aim to change a young person’s gender identity are not evidence-based and are detrimental to youth mental health and wellbeing.
- There is clearly a positive correlation between gender-affirming care and youth mental health and wellbeing outcomes. Further high quality longitudinal studies, such as the Trans20 study currently underway in Australia,(77) will be useful to investigate the impact of gender-affirming care on youth mental health and wellbeing outcomes.
- Further research about the mental health outcomes associated with gender-affirming care is also needed in non-Western countries and focusing on First Nations and culturally and linguistically diverse young people in Australia.

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APPENDIX 1

Literature Search Strategy (Medline, PsycINFO, Embase)

Please note: Some of the terms included in the search are outdated, but were included to be inclusive of relevant historical research.

POPULATION		MENTAL HEALTH AND WELLBEING OUTCOMES
Youth*	Gender dysphori*	Mental health
Young adj2 adult*	Gender-related distress	Psychosocial function*
Adolescen*	Gender incongruen*	Psychological distress
Young adj2 person*	Transgender*	Depressi*
Young adj2 people*	Trans-gender*	Anxiety
Teen*	Non-binary	Well-being
Emerging adult*	Nonbinary	Wellbeing
Young adj2 female*	Trans	Quality of life
Young adj2 male*	Genderqueer	Mental illness
Young adj2 wom#n	Gender queer	Mental ill-health
Young adj2 m#n	Agender	Mental disorder*
P?ediatric*	Gender divers*	Psychosocial impairment*
Underage	Gender-divers*	Life adj2 satisfaction
Minors	Gender varian*	School adj2 attendance
	Gender-varian*	Academic achievement
	Gender atypical	Vocational outcome*
	Transm#n	Employment outcome*
	Transwom#n	Body image
	Trans-m#n	Eating disorder*
	Trans-wom#n	Suicid*
	Gender-nonconform*	Self harm*
	Gender questioning	“Substance use”
	Gender fluid	Alcohol adj3 drug
	Gender minority	Substance abuse
	Intergender	
	Gender identity disorder	
	Trans-male	
	Bigender	
	Trans-fem*	
	Trans-masculin*	
	Brotherboy	
	Sistergirl	

Subject Headings – e.g. MeSH in Medline

POPULATION		MENTAL HEALTH AND WELLBEING OUTCOMES
Adolescent/ Sexual and Gender Minorities/ Intersex persons Transgender persons		Mental Health/
Young Adult/ Transexualism/		Quality of Life/
Pediatrics/ Gender dysphoria/		Mental Disorders/
		Personal satisfaction/
		Psychological well-being/
		Depression/
		Anxiety/ or Anxiety Disorders/
		Body Dysmorphic Disorders/ or Body Image/



APPENDIX 2

Inclusion and Exclusion Criteria

	INCLUSION CRITERIA	EXCLUSION CRITERIA
Population	<ul style="list-style-type: none"> • Trans and gender diverse young people (mean age <25.9 years old or ‘youth’ descriptors if age not reported). • Studies where the sample was aged 26 or over if the mean age at time of receiving treatment was below 26. • Studies where the mean age of one group was aged under 26 if results were reported separately. (e.g., if the mean age of trans men was below 26.0 but the mean age of trans women was above this would be included if the results for trans men were reported separately. Only this group’s results would be used for this current review). 	<ul style="list-style-type: none"> • Mean age 26 or over • Differences of Sex Development (DSD): congenital condition in which development of chromosomal, gonadal or anatomical sex is atypical (e.g., people who are intersex), unless the participants identify as trans.
Intervention/exposure	<ul style="list-style-type: none"> • Gender care intervention or approach delivered by a health professional (e.g. GP, allied health professional). Gender care refers to health care to support trans and gender diverse people with their gender identity and/or gender dysphoria. • Legislative bans or other restrictions to the delivery of gender care interventions (e.g. Covid pandemic). 	<ul style="list-style-type: none"> • Interventions with a primary aim of treating mental health disorders in trans and gender diverse people (eg. prevention or treatment of eating disorders, substance use, major depression etc.).
Context	<ul style="list-style-type: none"> • In a health care setting 	<ul style="list-style-type: none"> • All non-health care settings, such as schools or community centres
Outcomes	<ul style="list-style-type: none"> • Mental health • Mental ill-health/symptoms • Wellbeing and related concepts (e.g. Quality of life, resilience, coping, self-esteem) • Psychosocial function/impairment • Minority stress • Gender-related distress/gender dysphoria • Body image/satisfaction 	<ul style="list-style-type: none"> • Physical health • Sexual function/satisfaction
Study characteristics	<ul style="list-style-type: none"> • Peer reviewed original research, including controlled trials, cohort studies and cross-sectional studies 	<ul style="list-style-type: none"> • Editorials • Commentary • Conference abstracts • Dissertations • Secondary research (i.e., literature reviews) • Case studies and case series • Qualitative studies
Comparison	<ul style="list-style-type: none"> • Between groups <ul style="list-style-type: none"> - No treatment control - Active treatment control • Within participants <ul style="list-style-type: none"> - Before and after 	<ul style="list-style-type: none"> • Cisgender youth • No comparison

APPENDIX 3

Included studies

Table 1. Studies investigating GnRHa and mental health outcomes

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	SUMMARY OF MENTAL HEALTH FINDINGS
Carmichael, Butler, Masic, Cole, De Stavola, Davidson, et al., 2021 (11) McPherson & Freedman, 2023 (18)	Uncontrolled before and after study	44 young people with severe and persistent gender dysphoria attending a specialist gender service (AMAB=25; AFAB=19) aged 12–15 years, (Tanner ≥III for AMAB; Tanner ≥II for AFAB), on GnRHa treatment.	<u>GnRHa (24-month of treatment vs baseline):</u> No changes from baseline to 12 or 24 months in CBCL or YSR total t-scores or for CBCL or YSR self-harm indices, nor for CBCL total t-score or self-harm index at 36 months. NS change in gender dysphoria or body image. For both self-report (YSR) and parent report (CBCL), most participants experienced no reliable change in distress across all time points. Between 15% and 34% reliably deteriorate and between 9% and 29% reliably improve. Rates of reliable recovery range from 0% to 35% depending on the scale and time point. Reliable recovery fell to zero percent on all subscales at the final time point except for CBCL Externalizing scale which shows 1 out of 5 participants (20%) had moved into the normal range at 36 months.
Costa, Dunsford, Skagerberg, Holt, Carmichael & Colizzi, 2015 (13)	Controlled before and after study	201 adolescents aged 12–17 years (AMAB:AFAB ratio 1:1.6) attending the London Gender Identity Development Service	<u>Puberty suppression (12 months GnRHa + psychological support vs 12 months psychological support only):</u>
de Vries, Steensma, Doreleijers & Cohen-Kettenis, 2011 (14)	Uncontrolled before and after study	70 adolescents (33 AMAB; 37 AFAB) aged 11–17 years (M=13.6) receiving GnRHa and preparing for GAHT.	<u>GnRHa (vs pre-GnRHa):</u> Less impairment to psychological functioning (CBCL: M(SD) 54.46(11.23) vs 60.70(12.76), F(df, errdf) 26.17(1,52), p<.001); YSR: M(SD) 50.00 (10.56) vs 55.46 (11.56), F(df, errdf) 16.24 (1,52), p<.001). NS differences in gender dysphoria or body image dissatisfaction.
Turban, King, Carswell & Keuroghlian, 2020 (15)	Cross-sectional survey	N = 20,619 trans and gender diverse people aged 18–35 years (M = 23.4 years). 45.2% AMAB.	<u>Puberty suppression (vs wanting and not receiving puberty suppression):</u> Lower prevalence of lifetime suicidal ideation (aOR = 0.3, P = 0.001, 95% CI: 0.2–0.6), controlling for demographic variables.
van der Miesen, Steensma, de Vries, Bos & Popma, 2020 (16)	Cross-sectional survey	<u>Pre-treatment:</u> 272 adolescents referred to a gender clinic (AMAB=116; AFAB=156; age M=14.5) who had not yet received GAC. <u>Mid-treatment:</u> 178 adolescents (AMAB=68; AFAB=110; age M=16.8) receiving puberty suppression treatment.	<u>Puberty suppression (vs pre-treatment):</u> Less suicidality (M(SD) .17(.52) vs .41(.78), F=44.26, p<.001, d=.36), internalising behaviours (M(SD) 7.76(6.67) vs 11.67(8.38), F=14.16, p<.001, d=.52), and peer relationship issues (M(SD) .70(1.06) vs 1.08(1.31), F=12.58, p<.001, d=.32).

Note: AFAB = assigned female at birth, AMAB = Assigned male at birth, aOR = adjusted odds ratio, CBCL = Child Behavior Checklist, M = mean, GAHT = gender affirming hormone therapy, GnRHa = gonadotropin-releasing hormone agonist, NS = not significant, SD = standard deviation, YSR = Youth Self Report.

Table 2. Studies investigating GAHT and mental health outcomes

SUMMARY OF MENTAL HEALTH FINDINGS			
AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	SUMMARY OF MENTAL HEALTH FINDINGS
Aldridge, Patel, Guo, Nixon, Pierre Bouman, Witcomb, et al., 2021 (33)	Study design Uncontrolled before and after study	Sample characteristics N=178 (95 AMAB; 83 AFAB) young people (mean age = 23 years)	Summary of mental health findings GAHT (18 months treatment vs baseline): Decreased depression (M change = -2.05 (95%CI -2.72 to -1.38), p<.001). NS change in anxiety.
Allen, Watson, Egan & Moser, 2019 (36)	Uncontrolled before and after study	N=47 young people (33 AFAB; 14 AMAB) aged 12-20 years (M=16.59; SD=1.19) receiving GAHT	GAHT (≥3 months vs pre-treatment): Less suicidality (F(1, 44) 15.09, p<.001, partial η ² =.26), higher wellbeing (F(1, 44) 11.39, p=.002, partial η ² =.21, respectively).
Chen, Abrams, Clark, Ehrensaft, Tishelman, Chan, et al., 2021 (23)	Cross-sectional	<u>GnRHα Group:</u> N=95 youth (mean age = 11.22 years (SD= 1.46)). 51.6% AMAB. <u>GAHT Group:</u> N=316 youth (mean age = 16.0 years (SD=1.88)) 62% AFAB. 93% had not received prior gender affirming care.	<u>GnRHα access in early puberty (vs GAHT in later puberty):</u> Less depression (28.6% vs 51.6%), anxiety (22.1% vs 57.3%), and lifetime suicidality (23.6% vs 66.6%).
Chen, Berona, Chan, Ehrensaft, Garofalo, Hidalgo, et al., 2023 (34)	Uncontrolled before and after study	N=315 transgender and nonbinary young people (60.3% transmasculine) aged 12-20 years (M=16; SD=1.9) receiving testosterone or estradiol	GAHT (change over time from baseline to 24 months treatment): Improvements over time for all psychosocial outcomes (Wilk's lambda, 0.32; F (20,122) = 12.86; p<.0001). Significant increases in appearance congruence (annual increase on a 5-point scale, 0.48; 95%CI, 0.42 to 0.54; sβ=1.48), positive affect (annual increase on a 5-point scale, 0.48; 95%CI, 0.42 to 0.54; sβ=1.48), and life satisfaction (annual increase on a 100-point scale, 2.31; 95%CI, 1.65 to 2.99; β=0.52). Significant decrease in depression (annual change on a 63-point scale, -1.27; 95% CI, -1.98 to -0.57; sβ=-0.29) and anxiety (annual change on a 100-point scale, -1.47; 95% CI, -2.15 to -0.80; β=-0.35).
Defreyne, T'Sjoen, Bouman, Brewin & Arcelus, 2018 (41)	Uncontrolled before and after study	64 transmen aged 18-26 (M=20.0) years.	Testosterone HRT (pre-post): Depression decreased (-1.42, 95% CI 2.61-0.24, p =.019). NS changes to aggression or anxiety.
Filipov, Kavla, Sahin, Gokler & Turan, 2023 (30)	Cross-sectional	No GAC: N=37 FtM gender diverse adults (M age 24.38±4.55) GAHT: N=35 FtM gender diverse adults who received GAHT for >6 months (M age 24.20±4.71)	Testosterone (vs no GAC): Better body satisfaction (116.00 (IQR 111.00-142.00) vs 143.00 (IQR133.00-157.00), p<.0001). Less psychoticism (0.70 (IQR .40-1.10) vs 0.40 (IQR .2--8), p=0.0003). No other significant QoL or psychological health differences.

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	SUMMARY OF MENTAL HEALTH FINDINGS
Foster Skewis, Bretherton, Leemaqz, Zajac & Cheung, 2021 (28)	Controlled before and after study	<p><u>Masculinising GAHT:</u> N=42 (35 = trans; 7 =NB) adults newly commencing GAHT. M age = 24.0</p>	<p>Full-dose masculinising GAHT (baseline → 6-month treatment): Reduced gender dysphoria (aMD -6.80 (95%CI -8.68, -4.91), $p < 0.001$). Improved emotional well-being (aMD 7.48 (95%CI 1.32, 13.64), $p = 0.018$) and social functioning (aMD 12.50 (95%CI 2.84, 22.15), $p = 0.011$).</p>
Grannis, Leibowitz, Gahn, Nahata, Morningstar, Mattson, et al., 2021 (27)	Cross-sectional	<p><u>Testosterone:</u> N=19 transboys and men aged 9-21 (M=17.03±1.24) year <u>No treatment:</u> N=23 transboys and men aged 9-21 (M=15.75±1.47)</p>	<p><u>Testosterone (vs no treatment):</u> Lower generalised anxiety (F(1, 39) = 6.99, $p = 0.01$, $\eta^2 = 0.16$), social anxiety, (F(1, 39) = 17.21, $p < 0.001$, $\eta^2 = 0.32$), depression (F(1, 39) = 7.39, $p = 0.01$, $\eta^2 = 0.16$), and body image dissatisfaction (M(SD) = 91.16 (19.67) vs M(SD) = 108.09 (13.32), F(1, 39) = 10.47, $p < 0.01$, $\eta^2 = 0.21$). NS difference in suicidality or non-suicidal self-injury.</p>
Grannis, Mattson, Leibowitz, Nahata, Chen, Strang, et al., 2023 (32)	Cross-sectional	<p><u>AFAB GAHT:</u> N=21 trans and non-binary AFAB young people aged 9-21 (M=17.04±1.18) years, receiving testosterone. <u>AFAB no GAHT:</u> N=29 trans and non-binary AFAB young people aged 9-21 (M= 15.24±1.72) years not receiving GAHT (N=3 receiving puberty blockers) <u>AMAB GAHT:</u> N=15 trans and non-binary AMAB young people aged 9-21 (M= 17.64±0.86) years receiving estrogen <u>AMAB no GAHT:</u> N=15 trans and non-binary AMAB young people aged 9-21 (M= 16.27±1.49) not receiving GAHT (N=10 receiving puberty blockers)</p>	<p><u>Testosterone (vs AFAB no GAHT):</u> Lower generalised anxiety (M(SD) 38.75(17.41) vs 50.25(14.12), F(df1,df2) 7.76(1,45), $p < .01$), depressive symptoms (M(SD) 13.38(7.81) vs 18.34(7.02), F(df1,df2) 5.62(1,47), $p < .05$), social anxiety (M(SD) 50.21(22.34) vs 78.62(31.41), F(df1,df2) 14.80(1,42), $p < .001$), body image dissatisfaction (M(SD) 92.29(19.74) vs 103.14(18.99), F(df1,df2) 7.46(1,47), $p < .01$). NS difference in suicidality. <u>Estrogen (vs AMAB no GAHT):</u> Lower body image dissatisfaction (M(SD) 85.33(16.21) vs 88.53(29.01), F(df1,df2) 4.88(1,29), $p < .05$). NS difference in generalised anxiety, depressive symptoms, social anxiety, or suicidality.</p>
Green, DeChants, Price & Davis, 2022 (25)	Cross-sectional	<p><u>GAHT</u> 1216 trans and non-binary young people aged 13-24 (M=19.95(±2.80)) years who accessed GAHT. <u>No GAHT</u> 4537 transgender or nonbinary youth aged 13-24 (M=16.91(±2.97)) years who wanted but did not receive GAHT.</p>	<p><u>GAHT access (vs wanting but not receiving GAHT)</u> Lower rates of depression (60.8% vs 75%, $\chi^2(1)=95.38$, $p < .001$), serious consideration of suicide (43.9% vs 57.1%, $\chi^2(1)=65.89$, $p < .001$), and suicide attempt (14.6% vs 23.2%, $\chi^2(1)=40.24$, $p < .001$).</p>

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	SUMMARY OF MENTAL HEALTH FINDINGS
Kaltiala, Heino, Tylöjärvi & Suomalainen, 2020 (35)	Uncontrolled before and after study	52 adolescents who had taken GAHT (11 transfemales; 41 transmales). Mean age at diagnosis= 18.1 years (SD=1.1; range 15.2–19.9).	<u>GAHT (12 months treatment vs baseline):</u> Less depression (54% vs 15%, $p < .001$), anxiety (48% vs 15%, $p < .001$), and suicidality/self-harm (35% vs 4%, $p < .001$).
Kuper, Stewart, Preston, Lau & Lopez, 2020 (31)	Uncontrolled before and after study	N= 148 young people aged 9–18 years (M=14.9) receiving gender affirming hormone therapy (N = 25 puberty suppression only; N = 123 feminizing or masculinizing hormone therapy).	<u>GnRHα and/or GAHT (one year treatment vs pre-treatment)</u> Lower body image dissatisfaction (M(SD) 69.9(15.6) vs 51.7(18.4), $p < .001$), self-reported depressive symptoms (M(SD) 9.4(5.2) vs 7.3(4.6), $p < .001$), anxiety symptoms (M(SD) 32.4(16.3) vs 28.6(16.1), $p < .01$). NS difference reported to any other mental health outcome.
Matthys, Defreyne, Elaut, Fisher, Kreukels, Staphorsius, DenHeijer & T'sjoen 2021 (43)	Uncontrolled before and after study	422 transmen, aged 20–28 (mean age = 22.00).	<u>Testosterone (36 months treatments vs baseline):</u> NS differences in positive or negative affect.
Nolan, Zwickl, Locke, Zajac & Cheung, 2023 (26)	Randomised Controlled Trial	N=62 trans and gender diverse adults aged 20–28 (Median=22.5) seeking initiation of testosterone therapy.	<u>Testosterone (3-month treatment vs waitlist control):</u> Decreased gender dysphoria (M difference, -7.2; 95% CI, -8.3 to -6.1; $p < .001$), suicidality (mean difference, -6.5; 95% CI, -8.2 to -4.8 points; $p < .001$), and depression (PHQ-9 M difference, -5.6; 95% CI, -6.8 to -4.4; $p < .001$), greater cessation of suicidal ideation (52% vs 5%, $p = .002$).
Oda & Kinoshita, 2017 (66)	Cross-sectional survey, controlled before and after study	N=155 female-to-male individuals aged 15–43 (M age = 25.6) who consulted a gender identity clinic, diagnosed with gender dysphoria	<u>GAHT (vs no GAHT) at initial consultation:</u> NS difference on any MMPi scales. <u>Commencing GAHT + Psychotherapy (vs no treatment at baseline):</u> Significant improvements in depression, hysteria, psychiatric disease qualitative deviation, and psychasthenia MMPi scale scores. <u>GAHT + Psychotherapy (vs GAHT) at follow up:</u> Significantly lower psychiatric disease qualitative deviation score on MMPi.
Pham, Eadeh, Garrison & Ahrens, 2023 (29)	Uncontrolled before and after study	91 transgender and non-binary adolescents with a new visit to a multidisciplinary gender clinic, not already taking medications (estrogen, testosterone or puberty blockers). Mean age = 15.2 years. 61% transmasculine, 32% transfeminine, 7% non-binary or gender fluid.	<u>Gender affirming medical care (after 3, 6 and 12 months vs baseline):</u> NS changes in disordered eating. NS difference in disordered eating by gender identity or gender affirming medications or time spent receiving gender affirming care.

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	SUMMARY OF MENTAL HEALTH FINDINGS
Tebbens, Nota, Liberton, Meijer, Kreukels, Forouzanfar, et al., 2019 (38)	Uncontrolled before and after study	14 transmen, aged 21–25, mean age 22.	GAHT at 3 or 12 months (vs baseline): NS difference in self-esteem. Increase in satisfaction with facial appearance overall at 3–months [59.9, 95% CI 53.2–66.5, $p < .05$] and 12–months [59.9, 95% CI 54.1–65.6, $p < .05$] compared to baseline [52.4, 95% CI 44.2–60.6].
Turan, Aksoy Poyraz, Usta Saglam, Demirel, Haliloglu, Kadioglu, et al., 2018 (40)	Uncontrolled before and after study	37 with female-to-male gender dysphoria.	GAHT after 6 months (vs baseline): Body uneasiness BUT*A-Global Severity Index ($t(37) = 3.42, p = .002$), BUT*A-Body Image Concern ($t(37) = 3.70, p = .001$), and BUT*A-Depersonalization ($t(37) = 3.27, p = .002$) scores decreased significantly. NS change on any BUT*B subscales (the focus of attention of a specific body part or function). General psychopathological symptoms of interpersonal sensitivity [$t(37)$]=3.35, $p = .002$] and psychoticism [$t(37)$]=3.90, $p < .001$] decreased. NS on other SCL-90-R subscales. NS difference in eating attitudes and behaviours.
Turban, King, Kobe, Reisner & Keuroghlian, 2022 (24)	Cross-sectional	21,598 transgender adults who had ever wanted GAHT. One group had received GAHT in adolescence.	GAHT (vs wanting and not receiving GAHT): Lower past-year suicidal ideation for those who accessed GAHT in early adolescence (aOR = 0.4, 95% CI = 0.2–0.6, $p < .0001$), late adolescence (aOR = 0.5, 95% CI = 0.4–0.7, $p < .0001$), or adulthood (aOR = 0.8, 95% CI = 0.7–0.8, $p < .0001$) compared to no access. GAHT access at age 14–17 years (vs as an adult): Lower odds of past-month severe psychological distress (aOR = 0.6, 95% CI = 0.5–0.8, $p < .0001$), past-year suicidal ideation (aOR = 0.7, 95% CI = 0.6–0.9, $p = .0007$), past-month binge drinking (aOR = 0.7, 95% CI = 0.5–0.9, $p = .001$), and lifetime illicit drug use (aOR = 0.7, 95% CI = 0.5–0.8, $p = .0003$).
van Kemenade, Cohen-Kettenis, Cohen & Gooren, 1989 (42)	Uncontrolled before and after study	14 trans females, mean age 25.7 (SD = 4.4) years.	Antiandrogen treatment at 8 weeks (vs at week 1): Increased VAMS energy (M(SD) = 40 (12.2) vs 45.3(8.3) $p < .05$) and relaxation (M(SD) = 39.0(12.5) vs 45.3(11.5)). Decreased feelings of irritation (M(SD) = 22.9(12.1) vs 16.8(13.2)), fatigue (M(SD)=34.7(15.0) vs 17.5(11.4)) and tension/anxiety (M(SD)=23.2(15.8) vs 18.3(13.0)). Significance tests conducted at 8 weeks for energy only. NS difference in VAMS fatigue, cheerfulness, sociability, unhappiness, aggression, depression and feelings of change. NS difference in anxiety, depression or aggression.

Note: AFAB = assigned female at birth, AMAB = assigned male at birth, aMD = adjusted mean difference, aOR = adjusted odds ratio, BUT = Body Uneasiness Test, CI = confidence interval, GAC = gender affirming care, GAHT = gender affirming hormone treatment, GnRHα = gonadotropin-releasing hormone agonists, QR = interquartile range, M = mean, MMPI = Minnesota Multiphasic Personality Inventory, NS = not significant, PHQ-9 = Patient Health Questionnaire, SCL-90-R = Symptom Checklist-90 Revised, SD = standard deviation, QoL = quality of life, VAMS = Visual Analogue Mood Scale

Table 3. Studies investigating gender-affirming surgery and mental health outcomes in trans young people

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	SUMMARY OF MENTAL HEALTH FINDINGS
Arianmehr, Cheraghi & Ahmadpanah, Mohammadi, 2022 (53)	Cross-sectional survey	N=235 transgender people (189 transmen; 46 transwomen; mean age = 24.16 years, SD=4.81) from provinces around Iran	<u>Gender Affirming Surgery (vs no surgery):</u> higher vitality (M(SD), 60.76(18.35) vs 38.64(21.88), p<.001), emotional role (M(SD) 9.23(41.85) vs 37.38(40.59), p=.011), and mental health (M(SD)59.07(18.55) vs 41.22(21.02), p=.001). Lower social functioning (M(SD) 31.73(29.58) vs 61.65(25.91), p=.001).
Ascha, Sasson, Sood, Cornelius, Schauer, Runge, et al., 2022 (47)	Controlled before and after study	N=70 trans and non-binary AFAB people aged 13 to 24 years (M=18.6; SD=2.7) seeking gender-affirming top surgery (N=36 received surgery; N=34 did not receive surgery).	<u>Top surgery (3-month post-op vs no surgery):</u> Significant improvement in chest dysphoria (relative decrease -25.48 (95% CI, -32.85 to -18.11), gender congruence (relative increase 7.78 (95% CI, 6.06-9.50), and body dissatisfaction (relative decrease -7.20 (95% CI -11.68 to -2.72).
Boskey, Jolly, Kant & Ganor, 2023 (48)	Uncontrolled before and after study	N=153 transmasculine and non-binary young people aged 15-35 (M=20.1 (SD=4.2)) seeking gender affirming top surgery.	<u>Gender affirming top surgery (6-month, 12-month post-op vs baseline):</u> improved gender congruence (M(SD) 4.2(95%CI 4.0-4.4), 4.2(95%CI 4.1-4.4) vs 3.1(95%CI 3.0-3.3), p<.001), appearance congruence (M(S) 4.2(95%CI 4.0-4.4), 4.2(95%CI 4.0-4.3) vs 2.8(95%CI 2.6-3.0), p<.001), and reduced chest dysphoria (M(SD) 3.6(95%CI 2.3-4.6), 3.5(95%CI 2.5-4.4) vs 27.7(95%CI 26.1-29.0), p<.001). NS difference in gender identity acceptance.
Cohen-Kettenis & Goozen, 1997 (19)	Uncontrolled before and after study	N=19 young people undergoing gender-affirming surgery (14 transmen; 5 transwomen). M age= 17.5 at pretest, 22.0 at follow-up.	<u>Gender affirming top surgery (one-year post-surgery vs pre-surgery):</u> Lower gender dysphoria (M(SD) 14.8(3.2) vs 51.7(6.3), p<.001). Higher self-esteem (M(SD) 27.9(7.1) vs 24.3(6.8), p=.05) and significantly less feelings of inadequacy (M(SD) 12.0(6.7) vs 16.2(10.2); p=.04)
Kaur, Gallo, Wang, Rae, McEvenue, Semple, et al., 2023 (44)	Uncontrolled before and after study	N=115 people aged 16-61 (M = 25.7±6.9) years undergoing masculinising chest surgery.	<u>Gender affirming top surgery (mastectomy; six month follow up vs pre-operatively):</u> Lower rates of anxiety/depression problems (52.18% vs 73% reporting “some” or “a lot” of problems).
Olson-Kennedy, Warus, Okonta, Belzer & Clark, 2018 (45)	Cross-sectional	Transmasculine youth. 68 postsurgical, M age = 19 (SD = 2.5) years. 68 non surgical M age = 17 (2.5) years.	<u>Gender affirming top surgery (vs no gender affirming top surgery):</u> Lower chest dysphoria M(SD)= 3.3 [3.8] vs 29.6 (10.0), p < .001.
Romano, Bouaoud, Schmidt, Rausky, Stivala, Atlan, et al., 2023 (51)	Uncontrolled before and after study	25 transgender patients who had undergone masculinising torsoplasty. M age 25.84 (SD = 9.17)	<u>Gender affirming top surgery (vs pre-operatively):</u> Paired data responses for preoperative and postoperative were available for only five patients. Postoperative BREAST-Q scores showed higher rates of chest satisfaction (mean score of 18.40 vs. 39.71), sexual well-being (mean score of 6.40 vs. 17.48), and psychosocial well-being (mean score of 30.40 vs. 41.29) after masculinising torsoplasty compared to before surgery. Significance tests not performed.
van de Griff, Elfering, Grejdanus, Smit, Bouman, Klassen & Mullender, 2018 (49)	Cross-sectional	N=101 transmen seeking or having received gender affirming top surgery (50 pre-operative, mean age 24.5 ± 9.6 years; 52 post-operative, mean age 26.4 ± 7.7 years)	<u>Mastectomy (>6 months post-surgery vs pre-surgery):</u> Improved satisfaction with appearance (chest t98 = -11.4, p < 0.001, d = 2.3; nipples t97 = -5.2, p < 0.001, d = 1.0; body t97 = -5.2, p < 0.001, d = 1.0) and psychological outcome (p=0.05). NS change to social outcomes.

Note: CI = confidence interval, M = mean, NS = not significant

Table 4. Studies investigating combinations of gender-affirming treatment and mental health outcomes in trans young people

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	INTERVENTION/EXPOSURE	SUMMARY OF MENTAL HEALTH FINDINGS
Achille, Taggart, Eaton, Osipoff, Tafuri, Lane, et al., 2020 (39)	Uncontrolled before and after study	N=50 endosex trans young people (mean age = 16.2 years; SD=2.2; range = 9-25) referred to an endocrinology clinic	Puberty suppression (GnRHa and/or antiandrogens for transfemales, GnRHa and/or Medroxyprogesterone for transmales); GAHT (testosterone for transmales, estrogen for transfemales)	<u>Endocrine interventions (pre-post):</u> Improved depression on CESD-R (21.4 vs 13.9 (t(48) = 3.996, p< 0.001)). PHQ-9 decreased (t(49) = 3.753, p< 0.001), QoL NS.
Allen, Tollit, McDougall, Eade, Hoq & Pang, 2021 (76)	Uncontrolled before and after study, controlled before and after study	<u>FASST group:</u> 142 children's gender clinic patients (80 trans males, 29 trans females, 16 non-binary, 16 unsure, 1 response declined). Median age 15.0 years (IQR 13.7 -16.2). <u>Control group:</u> 120 historical patients, median age 14.9 years (IQR 12.4 - 16.7) and 50.8% AFAB.	FASST single intake and information session at a children's gender clinic	<u>FASST (pre-post):</u> Improved GoL (SMD 0.39, 95% CI: 0.23 to 0.56; p < .001), reduced depression (SMD 0.24; 95% CI: 0.36 to 0.11; p <.001) anxiety (SMD 0.14, 95% CI: 0.26 to 0.02; p = .025, respectively), and family dysfunction (55.8% vs 44.9%; 95% CI: 21.4 to 0.6; p = .039). NS change to high-risk suicidality. <u>FASST (vs no FASST):</u> Less anxiety (SMD 0.31; 95% CI: 0.57 to 0.05; p= .021).
Arnoldussen, van der Miesen, Elizinga, Alberse, Popma, Steensma, et al., 2022 (59)	Uncontrolled before and after study	N=70 adolescents (49 transmen and 21 transwomen) with mean age = 14.65 years (SD=2.08) at T0 and mean age = 20.70 years (SD=1.49) at T1.	GnRHa, GAHT, and gender affirmation surgery	<u>Medical transition (≥6 months treatment vs pre-medical transition):</u> improved self-perceived physical appearance (M(SD) 12.81(95%CI 11.92-13.70) vs 10.16(95%CI 9.37-10.95), p<.001), and global self-worth (M(SD) 14.19(95%CI 13.32-15.06) vs 12.02(95%CI 11.13-12.90), p<.001). Transmen saw improved self-perceived behavioural conduct (M(SD) 16.88(95%CI 16.11-17.64) vs 15.37(95%CI 14.53-16.20), p=.003).
Becker, Auer, Barkmann, Fuss, Moller, Nieder, et al., 2018 (62)	Cross-sectional	N=82 adolescents (62 transmen; 20 transwomen) aged 14-21 years with diagnosed gender dysphoria	No medical intervention VS GnRHa and/or GAHT only VS GAHT and surgery	<u>Medical transition (surgery + GAHT, GAHT vs no medical intervention):</u> Improved feelings of attractiveness/self-confidence (M(SD) 41.70(11.05), 33.01(10.91), vs 29.29(7.93), F=4.77, p<.010, 2p=.048) and accentuation of body appearance (M(SD) 55.59(10.25), 51.50(9.56) vs 46.20(11.26), F=6.0, p=.003, 2p.060).

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	INTERVENTION/EXPOSURE	SUMMARY OF MENTAL HEALTH FINDINGS
<p>Becker-Hebly, Fahrenkrug, Campion, Richter-Appelt, Schulte-Markwort & Barkmann, 2021 (61)</p>	<p>Controlled before and after study</p>	<p>N=75 young people seeking or receiving gender affirming care (64 transmen; 11 transwomen; mean age 15.6 years at baseline (SD=1.2), 17.4 years (SD=1.7) at follow-up.)</p>	<p>Psychosocial intervention; GnRHa; GAHT; GAHT and gender affirming surgery (mostly mastectomy)</p>	<p>No medical intervention (2-year follow-up vs baseline): More externalising problems (56.38(95%CI 59.19-62.57) vs 57.81(95%CI 53.67-61.95)). NS change to internalising problems or global functioning. <u>GnRHa (2 years treatment vs baseline):</u> Improved global functioning (81.82 (95%CI 76.77-86.86) vs 57.73 (95%CI 50.98-64.48)). NS change to internalising or externalising problems. <u>GAHT + GnRHa (2 years treatment vs baseline):</u> Less internalising problems (59.56(95%CI55.83-63.29) vs 64.94(95%CI 60.91-68.97)). Significantly higher global functioning (85.63(95%CI 82.33-88.92) vs 73.13(95%CI 69.19-77.06)). NS change to externalising problems. <u>Gender affirming surgery + GAHT (vs baseline):</u> Less internalising problems (55.36(95%CI 49.49-61.24) vs 65.73(95%CI 59.31-72.14)) and externalising problems (45.27(95%CI 37.97-52.58) vs 54.09(95%CI 48.85-59.33)). Significantly improved global functioning (83.64(95%CI 78.20-89.07) vs 66.36(95%CI 52.42-64.13)).</p>
<p>Cantu, Moyer, Connelly & Holley, 2020 (37)</p>	<p>Controlled before and after study</p>	<p>77 trans and gender non-conforming young people aged 11-18 years seeking gender-affirming care.</p>	<p>GnRHa and/or GAHT</p>	<p><u>Commencing GAHT (vs not commencing GAHT):</u> NS difference to depression or anxiety.</p>
<p>de Vries, McGuire, Steensma, Wagenaar, Doreleijers & Cohen-Kettenis, 2014 (54)</p>	<p>Uncontrolled before and after study</p>	<p>N=55 transgender young adults (22 transwomen and 33 transmen) who had received puberty suppression during adolescence. Mean age 13.6 years at T0 (intake), 16.7 years at T1 (on puberty suppression), 20.7 years at T2 (after gender affirming surgery).</p>	<p>GnRHa + surgery (vaginoplasty for transwomen; mastectomy and hysterectomy with ovariectomy for transmen)</p>	<p><u>Gender Affirming Surgery and GAHT combination (>1 year post surgery vs intake):</u> Higher global functioning (M(SD) 79.94(11.56) vs 71.13(10.46), p<.001). Lower internalising symptoms (CBCL: M(SD) 50.45(10.04) vs 60.83(12.36), p<.001; YSR: 50.06(11.15) vs 55.47(13.08), p=.005), externalising symptoms (CBCL: M(SD) 47.85(8.59) vs 57.85(13.73), p<.001), gender dysphoria (M(SD) 15.81(2.78) vs 53.51(8.29), p<.001), primary sex characteristic dissatisfaction (M(SD) 2.59(.82) vs 4.13(.59), p<.001), secondary sex characteristic dissatisfaction (M(SD)1.93(.63) vs 2.63(.6), p<.001)</p>
<p>Fontanari, Vilanova, Schneider, Chinazzo, Soli, Schwarz, et al., 2020 (64)</p>	<p>Cross-sectional</p>	<p>N=350 young people (42.64% transboys, 24.28% transgirls, 33.14% non-binary) aged 16 to 24 (M=18.61) years old.</p>	<p>Hormonal and/or surgical intervention</p>	<p><u>Hormonal and/or surgical gender affirmation (vs no hormonal or surgical affirmation):</u> Less anxiety and impairment (8.03 (95%CI 6.59-9.49) vs 10.84 (95%CI 9.97-11.71) p=.001), depression 15.61 (95%CI 14.06-16.27) vs 18.21 (95%CI 17.52-18.90), p<.001).</p>

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	INTERVENTION/EXPOSURE	SUMMARY OF MENTAL HEALTH FINDINGS
Lavender, Shaw, Maninger, Butler, Carruthers, Carmichael, et al., 2023 (63)	Uncontrolled before and after study	N=38 young people (28 AFAB; 10 AMAB), <15 years old when at Tanner stage II or above.	>1 year GnRHa + GAHT	<u>GAHT</u> (one year of GAHT vs Baseline): Lower rates of suicidality and self-harm (9% vs 64% thoughts of suicide and/or deliberate self-harm actions). Less externalising problems (49.38 (95%CI 44.96-53.79) vs 52.91 (95%CI 48.26-59.56), p=.04), primary sex characteristic dissatisfaction (4.11 (95%CI 3.75-4.48) vs 4.71 (95%CI 4.39-5.02), p=.02), gender dysphoria (3.97 (95%CI 3.49-3.63) vs 4.70 (95%CI 4.45-4.94), p=.02).
Olsavsky, Grannis, Bricker, Chelvakumar, Indyk, Leibowitz, et al., 2023 (60)	Cross-sectional	75 trans and non-binary adolescents, mean age = 16.39. 52% were receiving gender-affirming hormonal interventions.	GnRHa or GAHT	Receiving gender-affirming hormonal interventions were associated with fewer anxiety symptoms (b = -0.23; p <.05) and marginally associated with less depression symptoms (b = -0.21; p <.05) compared to young people not receiving gender-affirming hormonal interventions. NS for non-suicidal self-injury and suicidality.
Tordoff, Wanta, Collin, Stepney, Inwards-Breland & Ahrens, 2022 (58)	Uncontrolled before and after study.	Trans and non-binary adolescents and young adults, mean age 15.8 (SD=1.6) years	GnRHa, GAHT or both.	After 12 months, 60% lower odds of depression (adjusted odds ratio [aOR], 0.40; 95% CI, 0.17-0.95) and 73% lower odds of suicidality (aOR, 0.27; 95% CI, 0.11-0.65) among youths who had initiated GnRHa or GAHT compared with youths who had not. NS association between GnRHa or GAHT and anxiety.

Note: AFAB= assigned female at birth, AMAB = assigned male at birth, aOR = adjusted odds ratio, CBCL = Child Behaviour Checklist, CESD-R= Center for Epidemiological Studies Depression Scale - Revised, CI = confidence interval, FASST= First Assessment Single Session Triage, GAHs = gender affirming hormones, GAHT = gender affirming hormone therapy, GnRHa = gonadotropin-releasing hormone agonist, M = mean, N = number, PHQ-9 = Patient Health Questionnaire, GoL = quality of life

Table 6. Other interventions

AUTHORS, YEAR	STUDY DESIGN	SAMPLE CHARACTERISTICS	INTERVENTION/EXPOSURE	SUMMARY OF MENTAL HEALTH FINDINGS
Brandtsma, Visser, Volk, Rijn & Dekker, 2022 (78)	Uncontrolled before and after study	Young people aged 12–23 years (M=17.8; 56.1% AMAB; 43.9% AFAB) with co-occurring autism spectrum disorder and gender dysphoria	Peer support group and parent support sessions	Peer support (vs no peer support at baseline): improved parent-reported psychological wellbeing ($t(16) = -2.39, p = .029, d = 0.58$) and self-reported psychological complaints ($t(23) = 2.63, p = 0.015, d = 0.54$). Increased feelings of gender dysphoria ($z(25) = 3.05, p = .002, r = -.61$). NS effect on self-reported psychological wellbeing, self-esteem or social responsiveness.
Campbell & Rodgers 2023 (67)	Cross-sectional survey	27,715 trans adults. Results reported as “transgender youth exposed to conversion therapy”	Conversion therapy	<u>Conversion therapy (vs no conversion therapy):</u> Associated with an immediate 13.8%, and lifetime 55% increase in risk of suicide attempt ($p < .001$), and immediate 47.5%, and lifetime 128% increase in risk of running away from home ($p < .01$). NS difference in risk of suicide attempt or absconding prior to exposure to conversion therapy. Younger age at time of conversion therapy (11–14) associated with greater increases in suicidality and absconding risk.
Moussaoui, O’Connell, Elder, Grover, & Pang, 2023 (79)	Cross-sectional	530 trans and gender diverse adolescents AFAB attending their first appointment at a specialist paediatric gender service. M age = 15.2 (SD=1.3)	Menstrual suppression via combined oral contraceptive pill or one of several different progestin-only methods	<u>Menstrual suppression via combined oral contraceptive pill (vs no menstrual suppression):</u> NS differences in depression, anxiety, or gender dysphoria.

Note: AFAB = assigned female at birth, AMAB = assigned male at birth, M = mean, SD = standard deviation, SMD = standard mean difference, IQR = interquartile range.



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