**A Systematic Review of Psychosocial Functioning Changes after Gender-Affirming Hormone
Therapy among Transgender People**

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Abstract

Despite the large and growing prevalence of gender-affirming hormone therapy, there has been no systematic examination of potential psychosocial implications of such treatments. In this systematic review, we aimed to assess the current state and quality of evidence for effects of gender-affirming hormone therapy on psychosocial functioning (i.e., well-being, self-mastery and interpersonal functioning) in transgender people. We identified a total of 32 relevant papers, including 5 qualitative, 12 cross-sectional and 15 prospective cohort studies. The most consistent evidence is that gender-affirming hormone therapy reduces depressive symptoms and psychological distress while also potentially reducing general anxiety (indicators of well-being). Evidence for quality of life and affect is more mixed, but tends to point in the direction of improvements here too, especially for feminizing therapy. However, there was some evidence of affective dampening among transmasculine people and mood swings and emotional imbalances among transfeminine people. Self-mastery was the aspect of psychosocial functioning with the most ambiguous results, with early studies hinting at greater readiness to act on anger, confirmed in a more recent study with transgender men but not examined recently in transgender women. However, anger intensity does not seem to increase for those on either masculinizing or feminizing hormone therapy. Interpersonal functioning has received the least attention, with hints toward positive change for those on both feminizing and masculinizing hormone therapy (most commonly in the form of reduced social anxiety). Given the paramount importance of social relationships to health and well-being, high quality evidence for psychosocial effects of gender-affirming hormone therapy is vital to ensuring health equity for transgender people.

Keywords. Gender-affirming hormone therapy; transgender; psychosocial functioning; well-being; interpersonal functioning; mood

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1. Introduction

The most common form of medical intervention sought by transgender people, and sometimes the only form of medical treatment sought, is gender-affirming hormone therapy (Coleman, 2012; Hembree et al., 2017). For example, approximately 60%-70% of those who attended the most widely-used gender identity clinic in the Netherlands between 2010 and 2014 began hormone therapy within 5 years (Wiepjes et al., 2018). Once on gender-affirming hormone therapy, most transgender people continue to use some dosage of gender-affirming hormones throughout their lives. Transgender people tend to engage with these therapies to modify their physical presentation in line with their gender identity (Masumori et al., 2021; Sansfaçon et al., 2019), but hormones also affect psychological states and social interactions. However, despite the large and growing prevalence of gender-affirming hormone therapy across countries, no systematic review of research has been conducted in order to examine the state and quality of evidence for effects of gender-affirming hormone therapy on psychosocial functioning among transgender people. Given that decades of research in humans and non-human animals have confirmed that hormones strongly influence psychosocial functioning via biological pathways (Bos et al., 2012; McCall & Singer, 2012; Stanton, 2017; van Anders et al., 2011), this is a substantial oversight with critical implications for transgender health, limiting the ability of transgender people to provide fully informed consent for services (Cavanaugh et al., 2016).

Psychosocial functioning is a critical facet of human life that shapes how people relate to others and the quality of their social relationships. Psychosocial functioning refers to a variety of traits, characteristics and dispositions that have been broadly classified as (a) *well-being* (e.g., self-acceptance, positive mood, satisfaction with life), (b) *self-mastery* (e.g., self-control, low aggression and impulsivity) and (c) *interpersonal functioning* (e.g., trust, secure attachment, empathy; Ro & Clark, 2009). Better psychosocial functioning across these three domains has been shown to be associated with healthier experiences in social relationships, including higher quality romantic relationships (e.g., Joel et al., 2020) and friendships (e.g., Berry et al., 2000), potentially shaping

social isolation and loneliness throughout the life course (e.g., Vanhalst et al., 2013). Worryingly, accumulating evidence points toward impairments in psychosocial functioning and greater negative experiences in social relationships among transgender people relative to cisgender populations (Lewis et al., 2021). For example, transgender people report higher levels of social anxiety on average relative to cisgender people (Millet et al., 2017). Decades of research have shown that social relationships are vital to health and well-being (Berkman et al., 2000; Hawkey & Cacioppo, 2010), including longevity and mortality (Holt-Lunstad et al., 2010). In perhaps the starkest example of how poor psychosocial functioning and negative experiences in social relationships may affect transgender people, suicide rates are substantially elevated relative to cisgender people (with approximately one in three transgender people attempting suicide in their lifetimes; Adams et al., 2017), and past work has linked this risk in part to disruption in their social lives (Testa et al., 2017).

Transgender is used as an umbrella term to refer to anyone whose gender identity does not match their sex assigned at birth (e.g., including non-binary, gender fluid, and genderqueer people). Transgender people can seek hormone replacement therapies to affirm their gender identity. To aid with gender congruence and alleviate gender dysphoria, transgender people are commonly administered a regimen of gender-affirming hormones (generally involving exogenous administration of testosterone for transmasculine people and estradiol along with an anti-androgen for transfeminine people). Evidence suggests that gender-affirming hormone treatments reorganize brain structure and function (Kiyar et al., 2020), which is perhaps unsurprising given the general importance of sex steroids to neurobiology (Heany et al., 2016; McEwen & Milner, 2017). These fundamental neurobiological changes may in turn shape responses to social stimuli and general social functioning via biological processes/mechanisms (Kranz et al., 2020).

A growing body of research, principally from the field of social neuroendocrinology, has demonstrated that both endogenous and exogenous hormones influence psychosocial functioning via biological pathways (Bos et al., 2012; Stanton, 2017; van Anders et al., 2011). A relatively large number of studies have shown that exogenous administration of testosterone affects many aspects of psychosocial functioning in cisgender men and women, including increasing social aggression and decreasing emotion inference and trust (Eisenegger et al., 2011). For example, in one experiment

(Bos et al., 2010) cisgender women reported reduced trust in partners in a social exchange game after exogenous administration of testosterone relative to a placebo. Comparatively less research has been devoted to studying the psychosocial effects of exogenous administration of estrogen in humans, but some work suggests that it may improve mood in cisgender women, particularly for those diagnosed with depressive disorders (Wharton et al., 2012). Additionally, exogenous administration of progesterone has been shown to affect mood in cisgender women in both positive and negative ways, based upon dose and other factors, such as history of premenstrual syndrome (e.g., Björn et al., 2002).

Currently, transgender people are routinely prescribed such biological interventions without being made sufficiently aware of potential psychosocial implications (and available counselling options to support positive adjustment), potentially risking social disruption and, therefore, poorer health and well-being across the life course. At best, in addition to potential medical side-effects (e.g., increased risk of deep vein thrombosis for those on feminizing hormone therapies and increased risk of polycythaemia for those on masculinizing hormone therapies), clinical guidance may mention the possibility of some changes in mood or personality, such as increased aggression following commencement of testosterone (e.g., Coleman et al., 2012; Salas-Humara et al., 2019). A few reviews have been conducted on the effects of gender-affirming hormone therapy on mental health and quality of life (Baker et al., 2021; Costa & Colizzi, 2016; Hughto & Reisner, 2016; Nguyen et al., 2018), but these are all related to just one dimension of psychosocial functioning (i.e., well-being).

The aim of the current review was to evaluate the state of evidence for effects of gender-affirming hormone therapy on a wider range of dimensions of psychosocial functioning among transgender people. We sought to include studies with as many different research methodologies as possible, but our key interest was in seeking to understand any potential causal effects in psychosocial functioning resulting from gender-affirming hormone therapy. That is, we aimed to understand not only what effects hormone therapy might have on psychosocial functioning, but also whether these could be unambiguously and directly related to the hormonal changes, or whether existing evidence does not separate this from the various other changes that are associated with gender identity transition.

2. Methods

2.1 Eligibility Criteria

All empirical research published or in press by March 2021 was considered for inclusion in the current systematic review. To be deemed eligible, research needed to 1) include transgender participants who had previously used or were currently using gender-affirming hormone therapy; 2) evaluate at least one psychosocial outcome as broadly defined in the introduction (when multiple relevant outcomes were presented, all were included, but we chose to include total scale scores over subscales when both were presented separately in one paper); 3) encompass normal levels of functioning/symptomatology and not focus exclusively on clinical diagnoses/thresholds; 4) for quantitative research, provide a relevant comparison either within-person before and after gender-affirming hormone therapy, or between-person comparing transgender people who had previously or were currently using gender-affirming hormone therapy to transgender people who had not yet used gender-affirming hormone therapy, or who were on a waitlist to receive gender-affirming hormone therapy; 5) for quantitative research, include psychometrically validated quantitative measures rather than ad hoc self-reports of symptoms or review of medical chart notes; and 6) for qualitative research, include a formal and systematic thematic analysis rather than a cursory description of observations from text.

2.2 Search Strategy and Study Selection

We followed PRISMA guidelines when they carried out the search strategy for this review (Moher et al., 2009). Key terms were identified from a number of articles on the topic (Baker et al., 2021; Hughto & Reisner, 2016; Nguyen et al., 2018; Nobili et al., 2018, Spivey & Edwards-Leeper, 2019) along with MeSH terms. PubMed, PsycNet and Web of Science databases were searched between the years 1980 to 2021. This time period was selected due to the relative recency of papers that explore this topic as highlighted in similar prior reviews, where the dates of individual papers did not stretch past 40 years prior to the search despite the wider date range employed (Blanchard et al., 1983; Nobili et al., 2018). Terms for transgender people (e.g., transgender, non-binary, gender diverse, gender fluid, transmasculine, transfeminine, transsexual and gender dysphoria) were searched using the OR function and were combined with terms related to psychosocial outcomes (e.g., mood, anxiety, depression, self-esteem), as well as hormone usage (e.g., hormones, cross sex hormone

therapy, testosterone replacement therapy, feminizing, masculinizing). Additionally, the reference lists of selected articles as well as the ‘similar readings’ function in PubMed were searched to identify any further possible relevant papers (Figure 1 & Table 1).

3. Results

3.1 Qualitative Review

We identified only five (16%) qualitative studies, including four semi-structured interviews and one mixed-methods report (for the mixed-methods study, Mohamed & Hunter, 2018, only the qualitative element was pertinent to the objectives of this review). The qualitative research identified ($k = 5$) predominantly involved transfeminine (i.e., transitioning to a female gender identity) experiences (Araya et al., 2021; Giovanardi, 2019; Mohamed & Hunter, 2018; Riggs et al., 2020; Rosenberg et al., 2019), with only two studies (Araya et al., 2021; Riggs et al., 2020) including transmasculine (i.e., transitioning to a male gender identity) participants. In the following sections we briefly summarize results related to changes in psychosocial functioning from the qualitative literature, organized by the experiences of transfeminine and transmasculine people.

3.1.1 Transfeminine Experiences

Overall, the qualitative literature tended to support positive changes in well-being among transfeminine people after starting gender-affirming hormone therapy, although often with the qualification that improvements in well-being were attributed to satisfaction with changes in appearance rather than to direct effects of hormones on psychosocial states (Giovanardi, 2019; Mohamed & Hunter, 2018; Rosenberg et al., 2019). More specifically, in addition to reductions in distress (Rosenberg et al., 2019), participants reported improvements in self-image and self-acceptance (Araya et al., 2021; Mohamed & Hunter, 2018; Riggs et al., 2020) and less self-monitoring (Rosenberg et al., 2019) after beginning gender-affirming hormone therapy. There were also indications of changes in emotional functioning, generally experienced as positive and related to greater emotional range and freedom-of-expression (Mohamed & Hunter, 2018; Rosenberg et al., 2019), but sometimes noted as negative and related to mood swings and emotional imbalance (Giovanardi, 2019; Mohamed & Hunter, 2018). Finally, improvements in interpersonal functioning and the quality of relationships were commonly reported after beginning gender-affirming hormone

therapy (Araya et al., 2021; Giovanardi, 2019; Mohamed & Hunter, 2018), but again these were also largely attributed to changes in satisfaction with appearance rather than direct effects of hormones (Giovanardi, 2019; Mohamed & Hunter, 2018). While a desire for changes to appearance is a core aspect of seeking gender-affirming hormone therapy for many transgender people (Sansfaçon et al., 2019), understanding this as a separate pathway (i.e., a psychological one) can help to isolate any potential biological pathway through which hormones might affect psychosocial functioning.

3.1.2 Transmasculine Experiences

Qualitative evidence for changes in psychosocial functioning among transmasculine people came from only one study (Araya et al., 2021). In this study, transmasculine participants described increased confidence and assertiveness, but also concern over increased difficulty controlling anger and reduced emotional openness. A second study (Riggs et al., 2020) included transmasculine participants in the overall sample, but no quotes from transmasculine participants were included in the subtheme related to gender-affirming hormone therapy and sense of self, therefore it was not clear if the reported experiences (which are summarized in the previous section) were exclusive to transfeminine participants or not.

3.2 Quantitative Review

3.2.1 Cross-Sectional Studies

Twelve cross-sectional studies (38%) met the inclusion criteria for our review. The total number of transgender participants across the cross-sectional studies was 3,666, with individual sample sizes ranging from 49 to 868 transgender participants. The most common method of recruitment in the cross-sectional studies was general online convenience sampling ($k = 7$), while four studies used hospital-based sampling and one used convenience sampling from universities. Most studies ($k = 9$) compared transgender people who were on, or had undergone, gender-affirming hormone therapy to those who had never done so, but three studies compared transgender people on gender-affirming hormone therapy to either those planning to undergo gender-affirming hormone therapy or those currently waitlisted. While 11 of these studies included assessments of well-being (the majority of studies focused on depressive symptoms and anxiety), only 1 included a measure relevant to self-mastery and 4 included measures relevant to interpersonal functioning.

3.2.1.1 Feminizing Hormone Therapy

3.2.1.1.1 Well-Being

For those on feminizing hormone therapy, five cross-sectional studies (Blanchard et al., 1983, Davis & Colton Meier, 2014; Gomez-Gil et al., 2012; Hughto et al., 2020; Tomita et al., 2019) demonstrated lower levels of depressive symptoms relative to controls while one study with a moderately sized sample composed of United States Armed Forces veterans (Tucker et al., 2018) found no significant difference. Although one study (Gorin-Lazard et al., 2012) recruiting via psychiatric departments of public teaching hospitals in the south of France found better quality of life for those on feminizing hormone therapy, two other studies (Gooren et al., 2015; Jellestad et al., 2018) in Switzerland and Thailand, using relatively small convenience samples, failed to confirm this effect using the same outcome measure, the Short Form (36) Health Survey (SF-36). Note, however, that the study from Thailand (Gooren et al., 2015) included participants who were primarily acquiring hormones from friends rather than medical professionals. Similarly, while two studies (Davis & Colton Meier, 2014; Gomez-Gil et al., 2012) showed lower levels of anxiety in those on feminizing hormone therapy relative to controls, three other studies (Blanchard et al., 1983; Hughto et al., 2020; Tomita et al., 2019) showed no significant differences, although each of these studies utilized different measures of anxiety making comparisons between studies somewhat unclear. One study (Gooren et al., 2015) reported no significant difference in optimism, but this study may have been underpowered to detect such an effect.

3.2.1.1.2 Self-Mastery

One study (Davis & Colton Meier, 2014) demonstrated less anger for those on feminizing hormone therapy.

3.2.1.1.3 Interpersonal Functioning

Two studies (Butler et al., 2019; Gomez-Gil et al., 2012) reported lower levels of social anxiety for those on feminizing hormone therapy relative to controls, while one study (Tomita et al., 2019) found no difference in social anxiety using the same measure as Butler et al., 2019, the 3-item Social Phobia Inventory (Mini-SPIN), in a large online convenience sample. One other study

(Gooren et al., 2015) suggested no significant difference in terms of social functioning, although this study may have been underpowered to detect such an effect.

3.2.1.1.4 Summary of Cross-Sectional Evidence for Feminizing Hormone Therapy

Taken together, the most consistent evidence is for lower levels of depressive symptoms for those on feminizing hormone therapy relative to controls (an indicator of improvements in well-being). While less general and social anxiety as well as greater quality of life are also possible, evidence is less consistent for these outcomes. This may be due to differences in measures used to assess anxiety and the source from which participants in a given study were acquiring hormones (medical professional versus “black market”). Furthermore, evidence for outcomes such as optimism, anger and social functioning is limited by the fact that only single studies have examined these traits in transgender people undergoing feminizing hormone therapy, and statistical power in these studies was also somewhat limited.

3.2.1.2 Masculinizing Hormone Therapy

3.2.1.2.1 Well-Being

For those on masculinizing hormone therapy, four cross-sectional studies (Colton Meier et al., 2011; Gomez-Gil et al., 2012; Hughto et al., 2020; Tomita et al., 2019) demonstrated lower levels of depressive symptoms relative to controls while one study (Tucker et al., 2018) with a moderately sized sample composed of United States Armed Forces veterans found no significant differences using the Patient Health Questionnaire-9 (PHQ-9). Results for quality of life were very mixed, with two studies (Gorin-Lazard et al., 2012; Newfield et al., 2006) suggesting higher scores for those on masculinizing hormone therapy relative to controls, one relatively small study (Jellestad et al., 2018) finding no significant difference, and one study (Gooren et al., 2015) showing evidence for lower quality of life (albeit again in a relatively small convenience sample of participants who were primarily acquiring hormones from friends rather than a medical professional). More consistently, three studies (Colton Meier et al., 2011; Gomez-Gil et al., 2012; Tomita et al., 2019) demonstrated lower levels of anxiety, but one study (Hughto et al., 2020) with a relatively large online convenience sample in the United States found no significant difference using the Depression, Anxiety and Stress

Scale (DASS-21). One study (Gooren et al., 2015) reported no significant difference in optimism, although this study may have been underpowered to detect such an effect.

3.2.1.2.2 Self-Mastery

No cross-sectional studies focusing on masculinizing hormone therapy included measures relevant to self-mastery.

3.2.1.2.3 Interpersonal Functioning

Consistently, three studies (Butler et al., 2019; Gomez-Gil et al., 2012; Tomita et al., 2019) demonstrated lower levels of social anxiety for those on masculinizing hormone therapy relative to controls. One other study (Gooren et al., 2015) suggested no significant difference in terms of social functioning, although once again this study used a small convenience sample.

3.2.1.2.4 Summary of Cross-Sectional Evidence for Masculinizing Hormone Therapy

Taken together, the most consistent evidence is for lower levels of depressive symptoms as well as general and social anxiety for those on masculinizing hormone therapy relative to controls (indicators of improvements in well-being and interpersonal functioning). Results for quality of life were mixed, with one study even demonstrating lower levels for those on masculinizing hormone therapy relative to controls (one of the few cases of lesser well-being for those on gender-affirming hormone therapy), although this may have been due to the fact that participants in this study were primarily acquiring hormones from friends and other “black market” sources without appropriate medical guidance and supervision. While there were no cross-sectional studies assessing constructs related to self-mastery, evidence for outcomes such as optimism and social functioning is limited by the fact that only a single study has examined these traits in transgender people undergoing masculinizing hormone therapy.

3.2.2 Prospective Cohort Studies

Fifteen prospective cohort studies (47%) met the inclusion criteria for our review. The total number of participants across these studies was 3,165. Sample sizes in the studies ranged from 47 to 898 participants. The cohorts were recruited from gender identity clinics or medical centers in Italy ($k = 4$), the Netherlands ($k = 3$), the UK ($k = 2$), the USA ($k = 1$), and Turkey ($k = 1$). Two papers used the ENIGI cohort (Dekker et al., 2016), a collaborative international study sampled from cooperating

gender identity clinics in Belgium, the Netherlands, Italy, and Norway. Additionally, two papers used convenience sampling in the USA and Germany/Switzerland (including online sampling). Three studies included cisgender control groups, two studies included transgender people not undergoing gender-affirming hormone therapy as controls, and one study included both types of control groups. While 14 of these studies included indicators of well-being (the majority of studies focused on depression, anxiety and psychological distress), only 4 included measures relevant to self-mastery (typically measures of anger), and only 2 included measures relevant to interpersonal functioning.

3.2.2.1 Feminizing Hormone Therapy

3.2.2.1.1 Well-Being

The most consistent evidence for changes in psychosocial functioning after feminizing hormone therapy included reductions in psychological distress in three studies (Colizzi et al., 2014; Fisher et al., 2016; Heylens et al., 2014) and reductions in depressive symptoms in three studies (Aldridge et al., 2020; Colizzi et al., 2014; Fisher et al., 2016). One study (Achille et al., 2020) with a relatively small sample of transgender youth in the USA and follow-up at 6 and 12 months found no statistically significant effect of masculinizing hormone therapy on change in depressive symptoms from 0 to 12 months on the Center for Epidemiologic Studies Depression Scale (CESD-R) or the PHQ-9 Modified for Teens (although the authors noted that both effect sizes were “notably large” in the direction of reduced depressive symptoms). For anxiety, results were more mixed, with two studies (Aldridge et al., 2020; Nobili et al., 2020) in the UK with relatively large samples showing no significant evidence of differences after 12 (Nobili et al., 2020) and 18 months (Aldridge et al., 2020) on the Hospital Anxiety and Depression Scale (HADS-A), but one study (Colizzi et al., 2014) in Italy finding significant reductions in anxiety after 12 months on the Zung Self-Rating Anxiety Scale (SAS). Quality of life was found to be greater after feminizing hormone therapy in two studies (Allen et al., 2019; Manieri et al., 2014), but another study (Achille et al., 2020) with a relatively small sample of transgender youth in the USA and follow-up at 6 and 12 months showed no statistically significant difference on the Pediatric Quality of Life and Enjoyment Scale (PQLES-SF), with the different measures across studies making comparisons difficult. For affect, one study (Matthys et al., 2021) from the ENIGI cohort found no difference in negative affect but a decrease in positive affect

after feminizing hormone therapy in a 3-year follow-up. The difference reported in this study emerged in the first 3 months and then stayed stable over repeated follow-ups over 3 years, only returning to levels statistically non-significantly different from baseline at the final time point. Another study (Slabbekoorn et al., 2001) conducted in the Netherlands with a small sample and follow-up after about 3 months found evidence of increased affect intensity.

3.2.2.1.2 Self-Mastery

For self-mastery, two studies (Defreyne et al., 2019; Slabbekoorn et al., 2001) found no significant differences in anger intensity (with the more recent study, utilizing the ENIGI cohort and a 3-year follow-up, much larger and of higher quality). However, one study (Slabbekoorn et al., 2001) with a small sample and follow-up after about 3 months showed increased anger readiness. Similarly, another study (Van Goozen et al., 1995) also conducted in the Netherlands in the early 1990's, with a very small sample and follow-up after about 3 months, showed increased anger proneness on the Anger Expression Scale (AX) and Anger Situation Questionnaire (ASQ) after feminizing hormone therapy.

3.2.2.1.3 Interpersonal Functioning

Finally, one study (Slabbekoorn et al., 2001) with a small sample and follow-up after about 3 months showed increased emotional expressiveness.

3.2.2.1.4 Summary of Longitudinal Evidence for Feminizing Hormone Therapy

Taken together, these prospective cohort studies tended to show that feminizing hormone therapy reduced psychological distress and depressive symptoms as well as potentially improving quality of life (all indicators of improvements in well-being). Effects on anxiety and affect were less consistent, with one high quality study potentially showing reductions in positive affect over the course of a 3-year follow-up but no differences in negative affect. In terms of self-mastery, effects on anger were mixed, with the highest quality study finding no differences but smaller and less recent studies finding increased anger readiness and proneness after 3 months (suggesting that perhaps time course does matter to an extent, with changes evident earlier, i.e., with the first 3 months of hormone therapy). Evidence from a single study suggested improved emotional expressiveness (an indicator of improvements in interpersonal functioning).

3.2.2.2 Masculinizing Hormone Therapy

3.2.2.2.1 Well-Being

As with feminizing hormone therapy, the most consistent evidence for changes in psychosocial functioning after masculinizing hormone therapy involved reductions in psychological distress in four studies (Colizzi et al., 2014; Fisher et al., 2016; Heylens et al., 2014; Turan et al., 2018) and depressive symptoms in three (Aldridge et al., 2020; Colizzi et al., 2014; Fisher et al., 2016). Similar to feminizing hormone therapy, the same study (Achille et al., 2020) found no statistically significant effect of masculinizing hormone therapy on depressive symptoms in a relatively small sample of transgender youth from 0 to 12 months follow-up on the CESD-R or PHQ-9 Modified for Teens (with the same caveat that both effect sizes were “notably large” in the direction of reduced depressive symptoms). Also similar to feminizing hormone therapy, two studies (Aldridge et al., 2020; Nobili et al., 2020) showed no significant evidence of differences in anxiety 18 and 12 months after masculinizing hormone therapy on the HADS-A, but one study (Colizzi et al., 2014) found significant reductions in anxiety after 12 months on the SAS. Quality of life was not found to be significantly different after masculinizing hormone therapy in two studies (Achille et al., 2020; Manieri et al., 2014) with limited sample sizes and different measures, although one study (Allen et al., 2019) with a small sample of transgender youth did find an increase on the General Well-Being Scale (GWBS) of the Pediatric Quality of Life Inventory after 3 months. Interestingly, measures of affect generally showed evidence of affective dampening after masculinizing hormone therapy, including less positive and negative affect in the ENIGI cohort (Matthys et al., 2021) as well as less affect intensity in a smaller sample (Slabbekoorn et al., 2001). One study (Metzger & Boettger, 2019) conducted in Germany with a very small sample also found reductions in neuroticism.

3.2.2.2.2 Self-Mastery

As with feminizing hormone therapy, the same two studies (Defreyne et al., 2019; Slabbekoorn et al., 2001) found no significant differences in anger intensity after masculinizing hormone therapy, including in the ENIGI cohort (Defreyne et al., 2019). However, three studies with relatively small samples did show increases in anger expression (Motta et al., 2018), anger readiness

(Slabbekoorn et al., 2001) and anger proneness (Van Goozen et al., 1995), all within 3-7 months of commencing masculinizing hormone therapy.

3.2.2.2.3 Interpersonal Functioning

For interpersonal functioning, although once again research was limited, one study (Metzger & Boettger, 2019) with a very small sample found increases in extraversion and agreeableness after 3 and 6 months of follow-up. Another study (Slabbekoorn et al., 2001), with a small sample and follow-up after about 3 months, found no significant difference in emotional expressiveness on the Affective Communication Test (ACT) after masculinizing hormone therapy.

3.2.2.2.4 Summary of Longitudinal Evidence for Masculinizing Hormone Therapy

Taken together, these prospective cohort studies tended to show that masculinizing hormone therapy reduced psychological distress and depressive symptoms (indicators of improvements in well-being). Effects on quality of life and anxiety were less consistent. Notably, some studies suggested a dampening in affective experiences after masculinizing hormone therapy, although it is unclear whether this might indicate improvements or decrements in well-being given that this encompassed dampening of indicators of both positive and negative affect. For self-mastery, some studies indicated increased anger readiness and expression as well as proneness to anger (potential indicators of decrements in self-mastery), although this was not confirmed by increased anger intensity, suggesting that the emotion itself might not be affected, but rather the willingness to show/express it. Limited evidence on interpersonal functioning was inconclusive.

3.2.3 Bias and Adjustment for Potential Confounders

Cross-sectional studies provide limited evidence for changes in psychosocial functioning after gender-affirming hormone therapy due to a lack of comparison of outcomes across time (required to reflect change). Prospective cohort studies are the gold-standard in terms of evidence for change, however, these studies are also vulnerable to risk of bias due to confounding factors. This is particularly important in this case because as people undergo gender identity transition, many physical and social changes occur that can, by themselves, explain the results discussed in this review. Despite pre-/post-hormone therapy designs, prospective cohort studies showed substantial risk of bias related to confounding. For example, gender identity transition can significantly improve body image, which

by itself can improve psychosocial functioning (e.g., Davison & McCabe, 2006). At the same time, for some people transitioning is accompanied by a significant amount of exposure to stigma, thereby negatively affecting at least some indicators of well-being (e.g., anxiety) or interpersonal functioning (e.g., social phobia).

Table 2 lists the various potential confounders adjusted for across the included studies. Notably, measures of body image and gender-affirming surgeries were most commonly included, but these critical confounders were still only adjusted for in about one third of quantitative studies. Other potentially critical confounders, such as gender affirmation by others and social stigma (Doyle et al., 2021), were only adjusted for in two studies each. Given these limited attempts to adjust quantitative estimates for plausible (or even known) confounders, the extant quantitative literature cannot be conclusive in terms of biological versus psychological or sociocultural pathways by which gender-affirming hormone therapy might influence psychosocial outcomes. This remains a substantial limitation of this body of work.

4. Discussion

The current systematic review highlights the state of the art concerning the potential effects of gender-affirming hormone therapy on psychosocial functioning for transgender people. The most consistent evidence across qualitative and quantitative studies (both cross-sectional and prospective cohorts) is that gender-affirming hormone therapy reduces depressive symptoms and psychological distress while also potentially reducing general anxiety (consistent with results of previous systematic reviews; Baker et al., 2021; Costa & Colizzi, 2016; Hughto & Reisner, 2016; Nguyen et al., 2018). Interestingly, this happens irrespective of whether the treatment is feminizing or masculinizing, which might be taken to suggest that these well-being improvements are not necessarily directly due to hormonal changes, but to the positive effects of transition on body image (or other confounders), which in turn improves well-being (or even simply a reflection of the positive sense that having control and autonomy over one's body and gender expression brings).

Existing evidence for effects of hormone therapy on quality of life and affect is more mixed, but tends to point in the direction of improvements here too, especially for feminizing therapy. However, there was some quantitative evidence of affective dampening among transgender men,

which may be related to the restricted range of emotions described by transmasculine participants in qualitative work. Relatedly, transfeminine people sometimes described mood swings and emotional imbalances that might be time- and context-sensitive and potentially not caught by previously employed quantitative methods (e.g., day-to-day fluctuations in emotions may require daily diary or ecological momentary assessment methodologies, which have not yet been employed in this literature).

Self-mastery was the aspect of psychosocial functioning with the most ambiguous results. Earlier studies (conducted in the 1990's and early 2000's) hinted at decreased self-mastery in the form of greater readiness to act on anger, both for those on masculinizing and feminizing hormone therapy. This was also confirmed in a more recent study with transgender men but not examined recently in transgender women. However, anger intensity does not seem to increase for those on either masculinizing or feminizing hormone therapy. These results are consistent with a recent systematic review of effects of testosterone therapy on aggression in transgender men (Kristensen et al., 2021). Importantly, while self-mastery is a broader construct than just anger, no studies have examined related elements of self-mastery, such as self-control or impulsivity. This remains an important avenue for future investigation.

Interpersonal functioning, however, has received the least attention in the scientific literature. Evidence for improvements in this domain is limited and inconclusive, but hints toward positive change, once again for those on both feminizing and masculinizing hormone therapy (most commonly in the form of reduced social anxiety). Given the dearth of research on interpersonal functioning, future studies on gender-affirming hormone therapy should aim to include relevant measures, such as loneliness, trust, attachment styles, empathy, relationship satisfaction and other forms of social functioning.

It is interesting to note that in the domains of well-being and self-mastery, some potential differences identified in both qualitative and quantitative work could reflect gendered stereotypes of psychosocial functioning. For example, the affective dampening reported in some studies among transmasculine participants is in line with gender role expectations that men should not experience or express “too much” emotion, while greater readiness to act on anger/aggression among

transmasculine participants could be related to the fact that this specific emotion is an exception to (and reversal of) this norm (Plant et al., 2000). Among transfeminine participants, reports of mood swings and emotional imbalances may be in line with core stereotypes of women (Shields, 2002). Both qualitative and quantitative studies may be at risk of self-report bias, suggesting that other types of tasks that do not rely on self-report exclusively (e.g., behavioral tasks) may prove useful in unpacking these preliminary findings.

Across all outcomes, consideration of study quality, measures, sample size and other factors is necessary. Generally, studies were at risk of bias due to confounding and many included small samples with consequent low statistical power to detect changes in psychosocial functioning. Furthermore, while the variety of measures used in the literature is in some ways a strength (i.e., in terms of generalizability of effects), it is difficult to compare inconsistent results across studies when they may be a product of the specific measures (or operationalizations) used in each study.

In quantitative studies, including cross-sectional and prospective cohort studies, there is a need for research with adequate control groups, potentially composed of matched cisgender people as well as transgender people not wishing to undergo gender-affirming hormone therapy as well as those waitlisted for treatment (Streed et al., 2017). Identifying appropriate control groups is no easy task, given that these might differ depending on the outcome examined. For example, transgender people waiting for hormone therapy might be particularly distressed because they feel that what they need is still far away. So, with regard to well-being, perhaps people who “are where they want to be” (e.g., transgender people who do not want hormone therapy) are a better comparison.

One important consideration that is not systematically considered in the literature is the importance of timing. When it comes to biological changes, time is key: Sometimes time can make things better, sometimes it makes things worse. For some, hormone therapy might induce initial effects that are distressing, which subsequently disappear to reveal its positive effects in their full glory. Or it might provide an initial boost that raises expectations and fails to fulfil its promise. Research examining the effects of hormone therapy on psychosocial outcomes needs to explicitly take time into account to ensure this becomes more fully understood.

Furthermore, in all of these studies, participants were transgender people who volunteered to participate in a study, so results might depend on how the study's aims were introduced to them in interaction with the agenda they might have wanted to push forward. For example, studies stating their goals were to examine effects of hormone therapy might have attracted participants who wanted to demonstrate its benefits, whereas studies claiming their aim was on understanding well-being among transgender people might have attracted more participants who wanted to voice negative experiences. These details might in fact explain some of the contradictions found and point to the need to consider these more psychosocial aspects of transition with greater care when conducting this kind of research.

In addition, without a better understanding of what transgender people wish to achieve with their transition, it is hard to know exactly whether a particular change is positive or negative. For example, increases in anger in transgender men might at first seem negative, but they might be experienced positively if the person in question sees this as confirming their masculinity (to themselves and perhaps also to others). At the same time, outcomes need to be understood by reference to what transgender people think medical providers wish to achieve, or even what medical providers tell them about desirable or expected effects. Given the asymmetric dependency transgender people often feel from their doctors, some might wish to report effects that are in line with what is expected, so as to ensure the continuation of treatment. Alternatively, people might have been given expectations that are thwarted and low well-being might refer more to disappointment than to hormonal effects.

An important starting point in understanding potential psychosocial implications of gender-affirming hormone therapy is indeed to listen to the voices and experiences of transgender people. There have been calls among scholars to prioritize empowerment of transgender people and communities in relevant research, especially by including their voices throughout the research process (Tebbe & Budge, 2016). Despite the importance of this area of research and the logic of querying transgender people's lived experiences as they relate to gender-affirming hormone usage, very few studies have been conducted on this topic. Furthermore, only one of the five studies identified here

explicitly included transmasculine people in the sample. Therefore, the voices of transgender men, as well as experiences on masculinizing hormones, are almost entirely absent from the literature.

5. Conclusion

There is some evidence that gender-affirming hormone therapy may be related to improved psychosocial functioning for transgender people, but this is primarily increased well-being, rather than self-mastery or interpersonal functioning—with patterns across these dimensions that may diverge for those on masculinizing versus feminizing hormone therapies. Given the paramount importance of social relationships to health (Berkman et al., 2000; Hawkey & Cacioppo, 2010), high quality evidence for psychosocial effects of gender-affirming hormone therapy is vital to ensuring health equity for transgender people. Further carefully conducted and executed research on this topic will be essential to promoting transgender health in future, with increasing numbers of people accessing these services over time.

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Table 1. Studies included in systematic review by study type ($K = 32$)

Author	Aim	Design	Measures	No of participants	Participant demographics	Results	Location
Blanchard et al (1983)	Examined the relationship between psychological and social adjustment, and gender transition.	Cross-sectional	Tension (TSC-VII) Depression (TSC-IV) MMPI lie scale Involvement Cohabitation	55	Transgender women	Social feminisation (accessing GAHT) led to significantly reduced feelings of tension and depression.	Canada
Butler et al (2019)	Examined whether gender-affirming medical interventions were associated with lower social anxiety among transgender individuals.	Cross-sectional	Mini-Social Phobia Inventory (social anxiety) (Mini-SPIN) Gender affirming medical interventions (GAMI)	715	Transgender people who complete the Trans Health Survey (291 Transfeminine, 424 Transmasculine)	Individuals who had completed a course of hormones reported significant lower MINI-SPIN (social anxiety) scores compared to those who were planning on using hormones.	USA
Colton Meier et al (2011)	Examined the relationship of hormone replacement therapy, specifically testosterone, with various mental health outcomes	Cross-sectional	Depression, Anxiety, and Stress Scale (DASS) Multidimensional Scale of Perceived Social Support (MSPSS) Short Form 36-item Questionnaire version 2 (SF-36v2)	369	Transgender men	Results of the study indicate that female-to-male transsexuals who receive testosterone have lower levels of depression, anxiety, and stress, and higher levels of social support and health related quality of life.	USA
Davis & Colton Meier (2014)	Examined the effects of testosterone treatment with or without chest reconstruction surgery (CRS) on mental health in transgender women.	Cross-sectional	Beck Anxiety Index (BAI) Beck Depression Inventory (BDI) Snell Clinical Anger Scale (CAS)	208	Transgender women	Participants on TRT reported reductions in anxiety, anger, and depression when compared to the untreated group.	USA

			Mood and sexuality (open-ended measures)			Moreover, there were open-ended reports of increased happiness in the TRT group.	
Gomez- Gil et al (2012)	Sought to evaluate the presence of social distress, anxiety and depression in transgender people. There was an emphasis on hormone usage vs non-hormone usage in the sample.	Cross- sectional	Social anxiety and distress scale (SADs) Hospital anxiety and depression scale (HADs)	187	120 transgender people who had undergone hormone therapy. 67 transgender people who had NOT undergone hormone therapy.	Depression, anxiety and distress scores were significantly higher in those who had NOT undergone hormone therapy indicating that transgender people undergoing hormone therapy had better psychosocial outcomes.	Spain
					(113 transgender women, 74 transgender men)		
Gooren et al (2015)	Compared 60 transgender men (toms) with 60 transgender women (kathoeys) regarding their use of cross-sex hormones, mental wellbeing and acceptance by their family	Cross- sectional	Life Orientation Test Revised (LOT-R) The Social Functioning Questionnaire (SFQ) The Short Form Health Survey 36 (SF-36)	120	60 transgender men 60 transgender women	There were no differences in mental well-being among transgender men and transgender women However, transgender men currently using cross-sex hormones scored on average poorer on mental health measures when compared to non-users. Those undergoing cross- sex hormone treatment were 5-8 times more likely to be associated	Thaila nd

						with poor scores on interpersonal relationships with their parents. Self-acceptance was not significantly different between transgender men and women using cross-sex hormone therapy vs those who were not but they were approaching statistical significance (.057).	
Gorin-Lazard et al (2012)	Assessed the relationship between hormone therapy and self-reported quality of life scores in transgender people while exploring the confounding factors that may influence this relationship.	Cross-sectional	Beck Depression Inventory (BDI) Short form 36 (SF-36)	61	44 Transgender people who had undergone hormone therapy 16 Transgender people who had NOT undergone hormone therapy. (31 transgender women, 30 transgender men)	Hormone therapy has a positive effect on the overall mental and physical health of transgender people. Depression in an independent context was found to be predictive of poorer quality of life regardless of hormone therapy.	France
Hughto et al (2020)	Examined changes in self-reported suicidal ideation, suicide attempts, and non-suicidal self-injury (NSSI) before and after initiating the gender affirmation process, and linear regression analyses to examine	Cross-sectional	Transgender related discrimination (adapted from Rood et al 2015) Gender affirmation Investigator created NSSI scale Depression, anxiety,	288	Transgender Adults 234 transmasculine (49 non-binary people) 54 transfeminine	Results showed that overall participants reported lower levels of anxiety, depression and stress post HRT.	USA

	associations between gender affirmation experiences and self-reported depressive, anxiety, and stress symptoms.					and stress scale (DASS-21)	(4 non-binary people)	
Jellestad et al (2018)	Examined the associations between gender affirming interventions, depression and quality of life scores in transgender people.	Cross-sectional	Short Form (36) Health Survey questionnaire (SF-36). Short Form of the Center for Epidemiologic Studies-Depression Scale (ADS-K)	143	Transgender people (77 transfeminine, 41 transmasculine, 25 non-binary people).		Both transfeminine and transmasculine individuals reported a lower QoL compared to the general population. Within the trans group, nonbinary individuals showed the lowest QoL scores and significantly more depressive symptoms. Medical hormone interventions were associated with better mental wellbeing but even after successful medical transition, transgender people remain a population at risk for low QoL and mental health, and the nonbinary group showed the greatest vulnerability	Switzerland
Newfield et al (2006)	Evaluated health related quality of life in transgender men on the full SF-36 measurement domains. Of particular note are the depression, anxiety, and role	Cross-sectional	Short form 36-Question Health survey V2 (SF-36v2)	446	Transgender men		Transgender men who had received hormone therapy reported improvements in their mental health, depression and anxiety on the SF-36 when	USA

	emotional (social functioning) scales.					compared to those who had not received hormone therapy. This was also true for their role emotional score (social functioning) which improved following GAHT. Better depression, anxiety, PTSD, and mental health scores were associated with those who had undergone GAMIs such as hormone therapy and/or surgery.	
Tomita, Testa, & Balsan (2019)	Explored relationships between three stages of gender affirming medical interventions (GAMIs) and scores on 6 behavioural health symptom measures.	Cross-sectional	10-item Suicidal ideation scale (SIS-10) 10-item Center for Epidemiologic Studies Depression Scale-10th edition (CES-D-10) Social phobia inventory (Mini-SPIN) Generalised anxiety disorder (GAD-7) 17-item PTSD Check List–Civilian Version (PCL-C)	868	Transgender people (363 Transfeminine, 505 transmasculine)		USA
Tucker et al (2018)	Investigated whether undergoing hormone or surgical transition intervention(s) relates to the frequency of recent suicidal ideation (SI) and symptoms of depression in transgender veterans.	Cross-sectional	Suicidal behaviors Questionnaire (SBQ-R) Patient Health Questionnaire-9 (PHQ-9)	206	Transgender veterans (178 transgender women, 28 transgender men)	Veterans who had undergone hormone therapy and other surgical intervention to affirm their gender reported significantly lower levels depression.	USA

Mohamed and Hunter (2018)	Investigated transgender women's experiences and attitudes to hormone therapy.	Mixed methods	Beliefs about medicines questionnaire (BMQ) Inductive thematic analysis	67	Transgender women	Improvements in depression were highlighted by participants as well as overall wellbeing and feelings of gender dysphoria.	UK
Achille et al (2020)	Examined the associations of endocrine intervention (puberty suppression and/or cross sex hormone therapy) with depression and quality of life scores over time in transgender youths (6-month intervals between 2013-2018).	Prospective cohort	The Center for Epidemiologic Studies Depression Scale (CESD-R) [8], The Patient Health Questionnaire Modified for Teens (PHQ-9_Modified for Teens) [9], Quality of Life Enjoyment and Satisfaction Questionnaire (QLES-Q-SF) [10]	50	Transgender youths (33 transgender men, 17 transgender women)	Mean depression and suicidal ideation scores decreased over time from baseline (no hormones) to study endpoint (substantial hormone intervention)	USA

Aldridge et al (2020)	investigated the effect of 18-month gender affirming hormone therapy (GAHT) on depression and anxiety symptomatology and the predictors on mental health outcomes in a large population of transgender people	Prospective cohort	baseline and at 18 months Hospital Anxiety and Depression Scale (HADS), the Multidimensional Scale of Perceived Social Support (MSPSS) and the Autism Spectrum Quotient—Short Version (AQ-Short)	178	Transgender people (adults and youths) (95 assigned male at birth, 83 Assigned female at birth)	symptomatology was significantly decreased for depression ($P < .001$) and non-significantly reduced for anxiety ($P = .37$). Scores on the MSPSS predicted reduction in depression, while scores on the AQ-Short predicted reduction in anxiety.	UK
Allen et al (2019)	A longitudinal evaluation of the effectiveness of gender affirming hormones for improving psychological well-being and decreasing suicidality among transgender youth referred to a transgender health specialty clinic at a large Midwest children's hospital.	Prospective cohort	The Ask Suicide-Screening Questions (ASQ) The General Well-Being Scale (GWBS) of the Pediatric Quality of Life Inventory	47	Transgender youths (33 assigned female at birth, 14 assigned male at birth)	After gender-affirming hormones, a significant increase in levels of general well-being and a significant decrease in levels of suicidality were observed.	USA

Colizzi et al (2014)	Evaluated the presence of psychiatric conditions in transgender patients and compared psychiatric conditions related to the hormonal intervention in a one year follow-up assessment.	Prospective cohort	Zung Self-Rating Anxiety Scale (SAS) Zung Self-Rating Depression Scale (SDS) Symptom Checklist 90-R (SCL-90-R)	118	Transgender patients 78 transgender women 29 transgender men	Anxiety, depression and psychological distress reduced significantly following GAHT at the 12 month marker for the transgender patients.	Italy
Defreyne et al (2019)	Assessed whether anger intensity increases in transgender men undergoing hormone therapy to identify the predictors for anger intensity. Also transgender women were assessed to see if anger intensity decreases following hormone therapy.	Prospective cohort	Hormone usage over 3 years (baseline, 3 months, 12 months, and 36 months follow ups). STAXI-2 (State-Trait Anger Expression Inventory-2) State Anger (S-Anger)	898	440 Transgender men 468 Transgender women	State anger levels are more dependent on psychological vulnerability as opposed to hormone usage.	Belgium
Fisher et al (2016)	Assessed whether cross sex hormone therapy related body changes affected psychobiological well-being in people with gender dysphoria.	Prospective cohort	Body Uneasiness Test (BUT) Symptom Checklist 90 revised (SCL-90-R) Gender Identity/Gender Dysphoria questionnaire (GIDYQ-AA) Beck Depression Inventory (BDI) II	413	125 transgender women 42 transgender men	Beck depression inventory scores significantly reduced over the course of gender affirming hormone therapy over the two years.	Italy

Heylens et al (2014)	Investigated how gender reassignment therapy affects psychopathology and other psychosocial factors.	Prospective cohort	Symptom Checklist-90 (SCL-90)	57	Individuals with gender dysphoria (46 transgender women, 11 transgender men)	Significant decreases were found in the subscales such as anxiety, depression, interpersonal sensitivity, and hostility.	Belgium
Manieri et al (2014)	Described the care and treatment of subjects, highlighting both the endocrinometabolic effects of the hormonal therapy and the quality of life (including interpersonal relationships) during the first year of cross-sex therapy.	Prospective cohort	WHO QoL questionnaire (WHOQOL-100)	83	56 Transgender women 27 Transgender men	Most transgender women reported higher emotional lability (exaggerated changes in mood) and sensitivity in interpersonal relationships. Also reported a higher emotional intensity in alignment with life events. Transgender men reported an increase in impulsiveness and aggressiveness.	Italy

Matthys et al (2021)	Assessed the impact of gender affirming hormone treatment on affect among transgender people.	Prospective cohort	Positive and negative affect schedule (PANAS) 3 year tracking (Baseline, 12 months, 18 months and 36 months).	873	451 transwomen 422 Transmen	Negative affect scores significantly decreased after one year and remained consistent across the remaining 24 months.	The Netherlands
Metzger & Boettger (2019)	Aimed to analyse the effect of testosterone therapy on transgender men's personalities.	Prospective cohort	NEO-Personality inventory (NEO-PI-R)	50	23 Transgender men 27 Cisgender matched controls	The first three months yielded the biggest changes in personality with neuroticism decreasing along with depression. Conversely, extraversion, assertiveness, and warmth all significantly increased. Interpersonal stress decreased, social interaction traits all increased, and personal wellbeing also increased.	Sweden

Motta et al (2018)	Assessed the effect of testosterone treatment on anger expression in transgender men.	Prospective cohort	Spielberger's State-Trait Anger Expression Inventory (STAXI-2)	52	Transgender men	Anger expression was found to be significantly higher following testosterone usage.	Italy
Nobili et al (2020)	Explored the impact of Cross-sex Hormone Treatment (CHT) on autistic traits, independent of changes in anxiety longitudinally.	Prospective cohort	Hospital Anxiety and Depression scale (HADs) AQ Short (Autistic trait scale)	118	Transgender people (59 AMAB, 59 AFAB)	There were no significant changes in anxiety scores over the four year period.	UK
Slabbekorn et al (2001)	Investigated whether cross-sex hormone treatment in transsexuals affected the intensity of negative and positive emotions in general, and aggressive and sexual feelings in particular.	Prospective cohort	Expectancy list of mood and sexual interest The Dutch Sex Role Questionnaire (NSV) The Affect Intensity Measure (AIM) The Short Anger Situation Questionnaire (ASQ) The Affective Communication Test (ACT)	101	47 Transgender women 54 Transgender men	Depression, tiredness, tenseness and changeable mood all improved following hormone therapy. However, aspects of negative emotions related to powerlessness, disappointment, and sadness were equal following transgender women's hormone usage. Positive	The Netherlands

						emotions improved for transgender women on measures of happiness and liveliness. Transgender men reported higher levels of anger following GAHT.	
Turan et al (2018)	Examined the alteration of body uneasiness, eating attitudes/behaviors, and psychological symptoms in transgender men after Cross sex Hormone Therapy.	Prospective cohort	Body Uneasiness Test (BUT) Eating Attitudes Test (EAT-40) Symptom Checklist-90-Revised (SCL-90-R)	77	Transgender men (& 40 cisgender women as controls)	SCL-90-R scores decreased at 6 months following cross sex hormone therapy i.e., Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety etc.	Turkey
Van Goozen et al (1995)	Sought to understand the activating effects of sex hormones on behavioural measures in transgender people.	Prospective cohort	Instruments Aggression and anger proneness questionnaires. Buss-Durkee Hostility inventory The Anger Expression (AX) scale	50	35 Transgender men 15 Transgender women	The administration of androgens to females was associated with an increase in aggression proneness, sexual arousability and spatial ability performance. The effects of cross-sex hormones were just as pronounced in the male-to-female group upon androgen deprivation: anger and aggression	The Netherlands

						proneness, sexual arousability and spatial ability decreased.	
Araya et al (2021)	Aimed to describe adolescents' history and experiences with romantic partners and found aspects of hormone usage that influenced these factors.	Qualitative	Semi-structured interviews	30	Transgender adolescents (18 transgender men and 12 transgender women)	Participants reported increases in their confidence and assertiveness following hormone therapy. Transmasculine individuals also reported undesired outcomes such as a feeling of difficulty controlling anger and feeling emotionally distant.	USA

Giovanardi et al (2019)	Explored the psychological aspects of hormonal treatments for gender non-conforming adults, including the controversial use of puberty suppression treatments.	Qualitative	Semi-structured interviews	10	Adult transgender women	Overall, the participants were satisfied with treatment as it prevented the severe body dysphoria and social phobia trans-people experience with puberty. It seems that the risk of social isolation and psychological suffering is increased by the general lack of acceptance and stigma toward trans-identities in the Italian society. However, during gender transitions, they highlight the need to focus more on internal and psychological aspects, rather than over-emphasize physical appearance.	Italy
Riggs et al (2020)	Explored the views of transgender youth and their parents on medical affirming interventions.	Qualitative	Semi-structured interviews	21	10 Transgender youth (5 male, 4 female, 1 non-binary) 11 Parents (9 female, 1 male, 1 non-binary)	Hormone blockers were seen to improve aspects of happiness but there was an important distinction made between their mental health affirming effects and the fact that they "just stop puberty"	Australia

Rosenberg et al (2019)	This study aimed to provide an exploration of trans women's negotiation of the psycho and physiosexual shifts which result from GAHT.	Qualitative	Semi-structured interviews	12	Transgender women	Participants reported a greater sense of liberation following GAHT. One participant talked about how their depression and anxiety had decreased.	Australia
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Table 2. Adjustment for potential confounding by study

Confounder	<i>k</i>
Body image	10
Gender-affirming surgeries	8
Sexuality	5
Suicidal ideation	5
Non-binary participants included	3
Alcohol and substance use	2
Cognitive functioning and reasoning (e.g., visual and verbal tasks)	2
Gender affirmation from others	2
Personal views on hormone therapy	2
Puberty blockers	2
Self-harm	2
Social stigma	2
Social support	2
Assertiveness	1
Autism	1
Body mass index	1
Communication style	1
Eating disorders	1
Gender identity disclosure	1
Honest responding	1
Negative life events	1
Paranoid ideation	1
Psychiatric hospitalisation	1
Psychopharmacological treatments (e.g., anti-depressants, anti-anxiety medication, etc.)	1
Relationship status	1
Ruminating disorders	1
Social transition	1
Subjective dysphoria	1

Figure 1. Flow Diagram of Selected Literature