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Elie Vandenbussche

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Detransition-Related Needs and Support: A Cross-Sectional Online Survey

Elie Vandenbussche, BA

Faculty of Society and Economics, Rhine-Waal University of Applied Sciences, Kleve, Germany

ABSTRACT

The aim of this study is to analyze the specific needs of detransitioners from online detrans communities and discover to what extent they are being met. For this purpose, a cross-sectional online survey was conducted and gathered a sample of 237 male and female detransitioners. The results showed important psychological needs in relation to gender dysphoria, comorbid conditions, feelings of regret and internalized homophobic and sexist prejudices. It was also found that many detransitioners need medical support notably in relation to stopping/changing hormone therapy, surgery/treatment complications and reversal interventions. Additionally, the results indicated the need for hearing about other detransitioners' experiences and meeting each other. A major lack of support was reported by the respondents overall, with a lot of negative experiences coming from medical and mental health systems and from the LGBT+ community. The study highlights the importance of increasing awareness and support given to detransitioners.

KEYWORDS

Detransition; gender dysphoria; gender identity; cross-sex hormones; detransitioners; transgender; transition; support

Introduction

In recent years, there has been an increasing interest in the phenomenon of detransition. Many testimonies have been shared by self-identified detransitioners online and detrans communities have formed on social media. This phenomenon started to attract the attention of scholars, who have emphasized the need for research into the specific needs of this group (e.g., Butler & Hutchinson, 2020; Entwistle, 2020; Hildebrand-Chupp, 2020). A few case studies have been conducted in order to explore individual experiences of detransition (Pazos-Guerra et al., 2020; Turban & Keuroghlian, 2018). The latter studies highlighted the complexity of detransition experiences but did not provide sufficient data to assess the general needs and characteristics of detransitioners. The current study aims to explore this issue in more depth and to serve as a basis for future research on the phenomenon of detransition.

To date there has been little agreement on a definition of the word "detransition." As explained by Expósito-Campos (2021), this term has been used interchangeably to refer to what he perceives to be two distinctive situations: in

CONTACT Elie Vandenbussche el.vandenbussche@gmail.com Avenue des Lucioles 11, 1170 Bruxelles, Belgium.

the first, the detransitioning individual stops identifying as transgender; in the second, they do not. It is therefore necessary here to clarify exactly what is meant when writing about detransition.

In this paper, I will be using the following concepts: "medical detransition," "social detransition" and (male or female) "detransitioner." Medical detransition refers to the process of ceasing/reversing the medical aspects of one's medical transition. This might include stopping or changing hormone therapy and undergoing reversal surgeries, among others. Likewise, social detransition refers to the process of changing/undoing the social aspects of one's social transition. For example, it might include presenting oneself as one's birth sex again, changing one's post-transition name or going back to using the pronouns associated with one's birth sex.

The term "detransitioner" will be used here to refer to someone who possibly underwent some of these medical and/or social detransition steps and, more importantly, who identifies as a detransitioner. It is important to add this dimension, because the act of medical/social detransition can be performed by individuals who did not cease to identify as transgender and who do not identify as detransitioners or as members of the detrans community. Furthermore, some individuals might identify as detransitioners after having ceased to identify as trans, while not being in a position to medically or socially detransition due to medical or social concerns. As Hildebrand-Chupp (2020) puts it: "[B]ecoming a detransitioner involves a fundamental shift in one's subjective understanding of oneself, an understanding that is constructed within these communities." (p.802). More qualitative research should be conducted in order to better understand how members of the detrans community define themselves and make sense of their own detransition process. However, this goes beyond the scope of this study.

The creation of support and advocacy groups for detransitioners in recent years (e.g., DetransCanada, n.d., Detrans Voices, n.d., The Detransition Advocacy Network, n.d., Post Trans, n.d.) testifies to the formation of a detrans community whose members have specific needs. Scholars and clinicians have recently started raising concerns around the topic (e.g., Butler & Hutchinson, 2020; Entwistle, 2020; Hildebrand-Chupp, 2020; Marchiano, 2020). However, little research has been done specifically into the characteristics of this seemingly growing community.

Two informal surveys conducted by detransitioners (Hailey, 2017; Stella, 2016) have explored the demographics and (de)transition experiences of members of online female detrans communities. These will constitute interesting points of comparison in the discussion section of the current research.

The purpose of this exploratory study is to offer an overview of the current needs of detransitioners from online detrans communities, which will hopefully serve as a useful basis for further experimental studies around the topic of detransition. The current research primarily seeks to address the following

questions: What are the current needs of detransitioners? What support is given to detransitioners in order to fulfil these needs?

Methods

Procedure

A cross-sectional survey was conducted, using online social media to recruit detransitioners. Access to the questionnaire was open from the 16th of November until the 22nd of December 2019. Any detransitioner of any age or nationality was invited to take part in the study. The survey was shared by Post Trans (www.post-trans.com)—a platform for female detransitioners—via public posts on Facebook, Instagram and Twitter. Participants were also recruited through private Facebook groups and a Reddit forum for detransitioners (r/detrans). Some of the latter platforms were addressed exclusively to female detransitioners. The purpose of the study was presented as gaining a better understanding of detransitioners' current needs. Potential participants were asked to fill out the form and share it to fellow detransitioners. All participants have been fully anonymized.

Everyone who answered "yes" to the question "Did you transition medically and/or socially and then stopped?" was selected in the study. The individual questionnaires of the 9 respondents who answered "no" to this question were looked at closely, in order to assess whether they should be included in the study. Eight of them were added to the final sample, as their other answers indicated that their experiences lead them to identify as detransitioners.

This research was approved by the Ethics Committee for Noninvasive Research on Humans in the Faculty of Society and Economics of the Rhine-Waal University of Applied Sciences

Questionnaire design

The questionnaire consisted of 24 questions (see Appendix). The first series of questions was aimed at defining the profile of the respondent (age, sex, country, etc.), the second was asking about relevant aspects of transition and detransition experiences (transition type, gender dysphoria, therapy, medical interventions, reasons for detransitioning etc.), and the third focused on the needs encountered as well as the support (or lack of) received during the process of detransition (medical, psychological, legal and social needs and support).

Most of the items were multiple-choice questions. The conception of the multiple choices was based on observations drawn from several detransition online resources and forums. An open "other" category was available when relevant for the respondents to write in possibly lacking options. The survey

was designed to leave a lot of free space to add answers, since the detransition population is still very much under-researched and there is a lot to learn from each of its members. This is why a more qualitative approach was taken for the last question notably, leaving an open field for adding comments about the support—or lack of—received while detransitioning. This qualitative data was analyzed through the identification of recurrent themes, which will be presented in the results section.

Participants

A total of 237 participants were included in the final sample. The large majority was female; 217 female (92%) for 20 male respondents (8%). This was determined based on the answers to the question: "What sex were you assigned at birth?" The average age was 25.02 years (SD = 7.72), ranging from 13 to 64. The mean age of female detransitioners (M = 24.38; SD = 6.86) was lower than that of male detransitioners (M = 31.95; SD = 12.26).

Around half of the sample (51%) reported coming from the United States and close to a third from Europe (32%). Fifteen respondents are from Canada (6%), twelve from Australia (5%), and one from each of the following countries: Brazil, Kazakhstan, Mexico, Russia and South Africa.

Close to two thirds (65%) transitioned both socially and medically; 31% only socially. A few respondents rightly criticized the fact that the option of medically transitioning only was not available in the questionnaire. The absence of this option needs to be kept in mind when looking at the results.

Around half (51%) of the respondents started socially transitioning before the age of 18, and a quarter (25%) started medically transitioning before that age as well. The average age of social transition was 17.96 years (17.42 for females; 23,63 for males) (SD = 5.03) and that of medical transition was 20.70 years (20.09 for females; 26.19 for males) (SD = 5.36). Fourteen percent of the participants detransitioned before turning 18. The average age of detransition was 22.88 years (22.22 for females; 30.00 for males) (SD = 6.46). The average duration of transition of the respondents (including both social and medical transition) was 4.71 years (4.55 for females; 6.37 for males) (SD = 3.55).

Eighty percent of the male detransitioners underwent hormone therapy, compared to 62% for female detransitioners. Out of the respondents who medically transitioned, 46% underwent gender affirming surgeries.

Results

For sake of clarity, the results will be presented based on the three categories mentioned above in the methods section: profile of the respondents, relevant aspects of transition and detransition and, finally, detransition-related needs and support. The qualitative results will be displayed at the end of this section.

Profile of the respondents

Most of the information related to the profile of the respondents can be found in the methods section. The sample showed a high prevalence of comorbidities, considering that over half of the participants (54%) reported having had at least 3 diagnosed comorbid conditions (out of the 11 conditions listed in the survey—see Table 1). The most prevalent diagnosed comorbid conditions are depressive disorders (69%) and anxiety disorders (63%), including PTSD (33%) (see Table 1).

Relevant aspects of transition and detransition

A great majority of the sample (84%) reported having experienced both social and body dysphoria. (Social dysphoria being defined as a strong desire to be seen and treated as being of a different gender, and body dysphoria as a strong desire to have sex characteristics of the opposite sex/rejection of your own sex). Eight percent reported having experienced only body dysphoria, 6% only social dysphoria and 2% neither of them.

Forty-five percent of the whole sample reported not feeling properly informed about the health implications of the accessed treatments and interventions before undergoing them. A third (33%) answered that they felt partly informed, 18% reported feeling properly informed and 5% were not sure.

The most common reported reason for detransitioning was realized that my gender dysphoria was related to other issues (70%). The second one was health concerns (62%), followed by transition did not help my dysphoria (50%), found alternatives to deal with my dysphoria (45%), unhappy with the social changes (44%), and change in political views (43%). At the very bottom of the list are: lack of support from social surroundings (13%), financial concerns (12%) and discrimination (10%) (see Figure 1).

34 participants (14%) added a variety of other reasons such as absence or desistance of gender dysphoria, fear of surgery, mental health concerns related

Table 1. Number of participants with comorbid conditions.

Comorbid condition	Diagnosed	Suspected
Depressive disorder	163 (70%)	32 (14%)
Anxiety disorder	149 (63%)	43 (18%)
Post-traumatic stress disorder	79 (33%)	63 (27%)
Attention deficit disorder	57 (24%)	50 (21%)
Autism spectrum condition	47 (20%)	61 (26%)
Eating disorder	46 (19%)	58 (25%)
Personality disorder	40 (17%)	26 (11%)
Obsessive compulsive disorder	35 (15%)	44 (19%)
Polycystic ovary syndrome (only females)	22 (10%)	13 (6%)
Dissociative identity disorder	14 (6%)	23 (10%)
Schizo-spectrum disorder	5 (2%)	9 (4%)

"Diagnosed" and "Suspected" were mutually exclusive categories.

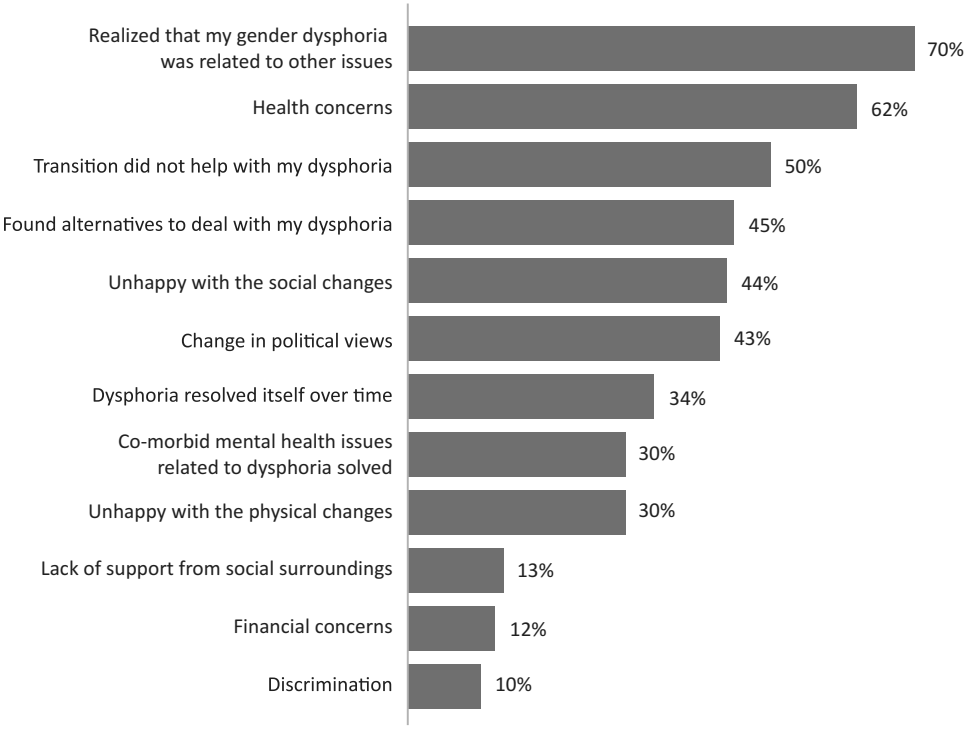

Figure 1. Reasons for detransitioning.

to treatment, shift in gender identity, lack of medical support, dangerosity of being trans, acceptance of homosexuality and gender non-conformity, realization of being pressured to transition by social surroundings, fear of surgery complications, worsening of gender dysphoria, discovery of radical feminism, changes in religious beliefs, need to reassess one's decision to transition, and realization of the impossibility of changing sex.

Detransition-related needs and support

The different types of needs were divided into four categories in the questionnaire: medical, psychological, legal and social needs.

Medical needs

The most commonly chosen answer was the need for receiving accurate information on stopping/changing hormonal treatment (49%), followed by receiving help for complications related to surgeries or hormonal treatment (24%) and receiving information and access to reversal surgeries/procedures (15%). Forty-six percent of the participants reported not having any detransition-related medical need. Sixteen respondents (7%) added another non-listed answer, such as tests to determine current reproductive health, information

about long-term effects of hormone therapy, about the health consequences of having had a full hysterectomy and about pain related to chest binding.

Psychological needs

Psychological needs appeared to be the most prevalent of all, with only 4% of the respondents reporting not having any. The answers working on comorbid mental issues related to gender dysphoria and learning to cope with gender dysphoria; finding alternatives to medical transition are at the top of the list, both with 65%. Below that, learning to cope with feelings of regret (60%), followed by learning to cope with the new physical and/or social changes related to detransitioning (53%) and learning to cope with internalized homophobia (52%). Thirty-four respondents (14%) added another non-listed answer, such as trauma therapy, learning how to deal with shame and internalized misogyny, how to cope with rejection from the LGBT and trans communities and how to deal with the aftermath of leaving a manipulative group. Other answers disclosed the need for help recovering from addictive sexual behavior related to gender dysphoria, psychosexual counseling and peer support.

Legal needs

More than half of the sample (55%) reported not having any detransition-related legal need. The main legal need expressed was changing back legal gender/sex marker and/or name (40%), followed by legal advice and support to take legal action over medical malpractice (13%). Five respondents (2%) added another non-listed answer, such as employment legal aid and support to take legal action for having been forced to go through a sterilization.

Social needs

The big majority of the respondents reported a need for hearing about other detransition stories (87%). The second most common answer was getting in contact with other detransitioners (76%), followed by receiving support to come out and deal with negative reactions (57%). Thirty-three respondents (14%) added another non-listed answer such as being accepted as female while looking male, help navigating social changes at the workplace, building a new social network, more representation of butch lesbians, real life support and finding a community.

When looking at from whom the respondents received support while transitioning and detransitioning, it appears that the biggest source of help comes from online groups/forums/social media for both transition and detransition (65%). The support received from friends, partner(s) and family is a little higher for detransition (64%) than for transition (56%).

Only 8% of the respondents reported having received help from an LGBT+ organization while detransitioning, compared to 35% while transitioning.

Similarly, 5% reported having received help from a trans-specific organization while detransitioning, compared to 17% while transitioning.

A total of 29% reported having received support for their detransition from the medical professionals that helped them during their transition. In contrast, 38% sought support from a new therapist/doctor. A part of the sample reported not receiving help from anybody for transitioning (8%) and for detransitioning (11%) (see Figure 2).

Around half of the respondents (51%) reported having the feeling of not having been supported enough throughout their detransition, 31% said they did not know and 18% answered that they had received enough support.

Qualitative results

Two open-ended questions allowed participants to write more extensively about their needs and support in the questionnaire. The first one enabled the respondents to write about any additional need that they encountered while detransitioning, while the second asked about the support—or lack of—that they had received.

Additional comments about needs

Thirty-seven participants (16%) left various comments about specific needs that they experienced during their transition and detransition.

Several respondents expressed the need for different types of therapy and counseling for dealing with issues of dissociation, childhood sexual trauma, anorexia, relationship issues and body issues caused by irreversible gender affirming surgeries. A participant also mentioned the importance of help revolving around suicide prevention for those who need it.

Additionally, someone emphasized the need for therapists to validate the feelings of being harmed by transition that some detransitioners experience, rather than dismissing or opposing them. Similarly, another respondent expressed the need for non-judgmental medical practitioners. Someone else described the need for as much medical autonomy as possible and a total freedom from psychology and psychiatry. A participant also explained that she would have needed to know the health risks of chest binding before experiencing them.

Furthermore, two respondents highlighted the need to look into individual experiences and needs without forcing them into a rigid model of transition. Others wrote about the need for more information about detransition and a better general understanding of this phenomenon.

Lastly, a few female detransitioners expressed the need for being valued as a woman, for learning about feminist theories and for more gender-nonconforming role models.

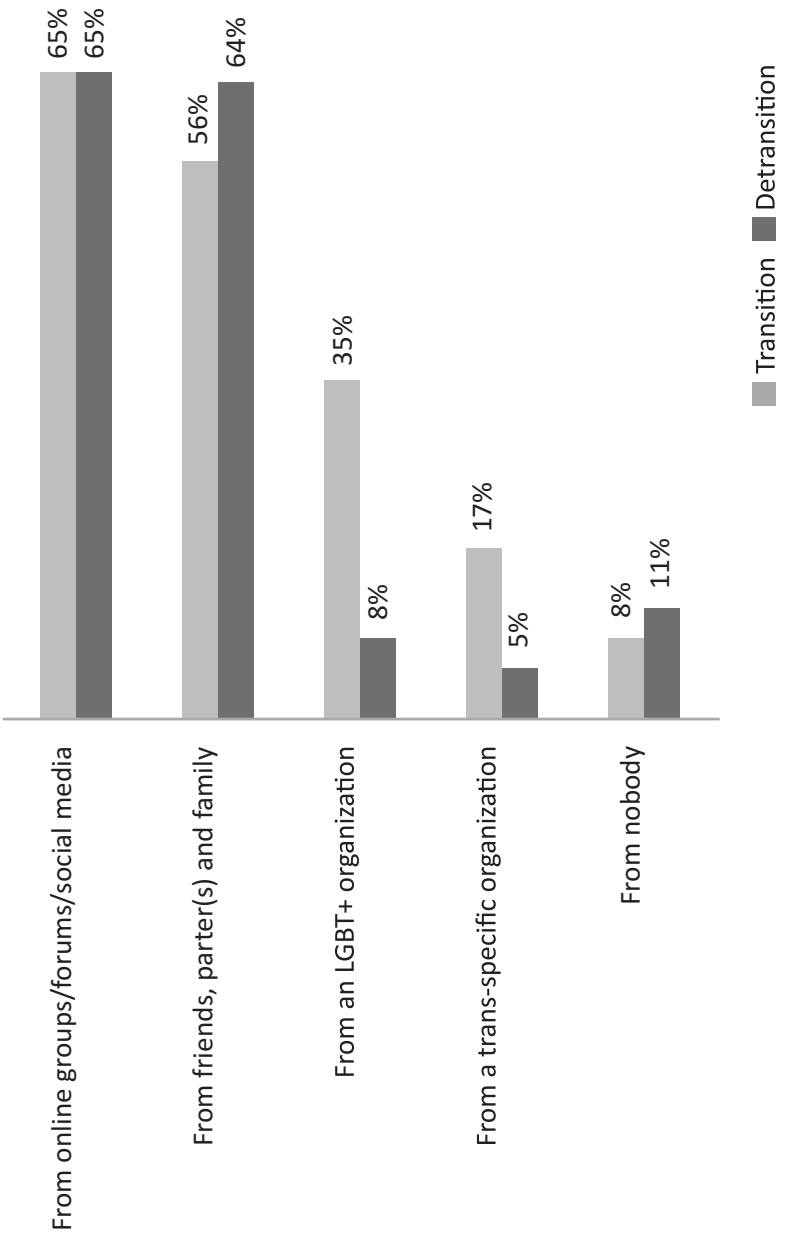

Figure 2. Comparison between transition and detransition support.

Additional comments about support

At the end of the questionnaire, a second open-ended question invited the participants to give further comments about the support—or lack of—that they had received during their detransition process.

A third of the participants (34%) answered this question, often with long and detailed accounts of their personal experiences with regard to this aspect. The most common themes identified were: loss of support from the LGBT community and friends (see Table 2), negative experiences with medical professionals (see Table 3), difficulty to find a detrans-friendly therapist and lack of offered alternatives to transitioning (see Table 4), as well as isolation and lack of overall support. Some gave more positive accounts of the support that they had received from their family, partners and friends and emphasized their important role.

A recurrent theme in the answers was a sense amongst respondents that it was very difficult to talk about detransition within LGBT+ spaces and with trans friends. Many expressed a feeling of rejection and loss of support in relation to their decision to detransition, which lead them to step away from LGBT+ groups and communities (see Table 2).

Whilst a minority reported positive experiences with medical professionals during their detransition, most participants expressed strong difficulties finding the help that they needed during their detransition process. Participants' own descriptions of the nature of these difficulties can be found in Table 3.

Another reported issue was the difficulty of finding a therapist willing and able to look at the factors behind gender dysphoria and to offer alternatives to transitioning. Some respondents highlighted the fact that they were

Table 2. Extracts about experiences of exclusion from LGBT+ communities.

"The LGBT+ community doesn't support detransitioners and I lost all LGBT+ friends I had because they deemed me transphobic/terfy, only non-LGBT+ friends supported me."
"Where I live detransitioners are seen bad for most of the LGBT community, so it's hard to talk about it with freedom."
"It is unacceptable that, at least in my experience, detransition is not something allowed to be talked about in LGBT spaces."
"Only lesbians and feminists helped me. The trans and queer community demonized me and ostracized me for my reidentification."
"I lost a lot of support and attracted a lot of hostility from trans people when I detransitioned socially. I also deal with a lot of people assuming that my dysphoria is gone entirely/cured because I have detransitioned socially, and decided not to go through with medical transition."
"Lgbt organizations don't want to talk about detransition. I did not feel welcome at lgbt events after I detransitioned."
"Telling my trans friends that I'm desisting is nearly impossible. The community is too toxic to allow any kind of discussion about alternatives to transition, sources of dysphoria beyond 'that's just who you are', or stories about detransitioners."
"I've been shunned by most of my trans identifying friends. I had to leave my old doctor, therapist and LGBT group out of shame and embarrassment."
"I have several de-trans friends whom had permanent body alterations they regretted that led to more dysphoria and eventually their suicides. Biggest factors were a lack of medical support and outright rejection from LGBT organisations/communities."
"I still have transgender friends who don't want me to talk about detransition. They're okay with me being detransitioned, but they don't want me to criticize transition or discuss the negative side effects of HRT."

Table 3. Extracts about negative medical experiences during detransition.

"I needed gender and transition experienced providers to assist with my medical detransition, but none of them seemed to understand or provide the type of care I needed, despite my self-advocacy. I got better care from providers outside of the LGBT and transgender specialty clinics."
"I still struggle to find a doctor who has knowledge of detransition and the effects HRT had on me/my best course of action since stopping."
"When I first brought up wanting to stop T to my doctor, they were very dismissive and condescending about it."
"My experience with transition left me with greatly diminished faith in medicine and zero faith in the mental health profession. I now avoid all doctors most of the time (unless I am convinced they are the only way to access a strongly evidence-based treatment or diagnostic tool for a condition which causes more suffering than doctors themselves- many do not) and totally avoid any contact with mental health professionals, and am much better off for it."
"As soon as I 'detransed' I was discharged from all gender services, despite asking for help in dealing with sex dysphoria should it arise again."
"I had no medical help from the doctor who prescribed me T, she wanted nothing to do with me."
"The team that transitioned you is not willing to help you detransition. You need new doctors."
"The medical team that helped me transition is helpful, but they are also causing a lot of hassle, which is very frustrating for me. Like for example they keep me stuck with my male sex marker for I don't know how long, and they don't believe I'm sure enough that I want to detransition, because they think I should have consistent 'reverse dysphoria' and mine kinda isn't so consistent."
"My hormone blocker implant is several years old and is only barely still functioning but they will not remove it. It's in my arm and I have no contact with the doctor because he shut down his business apparently."

Table 4. Extracts about the difficulty of finding a detrans-friendly therapist.

"It is very hard to find a therapist who won't tell you it's 'internalized transphobia' or that dealing with dysphoria in other ways is 'conversion therapy'."
"The only thing that comes to mind is one of the therapists I had, who pushed me not to detransition."
"Therapists are unprepared to handle the detrans narrative and some that I have seen since detransitioning have pushed the trans narrative. Some therapists couldn't tell the difference between being transgender and having internalized misogyny and homophobia."
"I could have benefitted from counseling but don't trust psychologists ideological bias."
"I struggled to find a therapist who supported questioning my trans identity and considering alternatives to transitioning; most only knew how to encourage transitioning and reinforced the harmful ideas that led to my wrongly identifying as FtM in the first place."
"I was doubtful that transition would help my dysphoria before beginning and was assured by multiple professionals that transition was The Solution and proven to work for everyone with dysphoria. A 'gender specialist' therapist flat-out told me that transitioning was the only method of reducing dysphoria that worked when I expressed my desperation for an alternate solution."
"The gender clinic I went to basically told me that the only way to deal with gender dysphoria was transitioning even when I told them I wanted to detransition."
"I struggled to find a therapist who supported questioning my trans identity and considering alternatives to transitioning; most only knew how to encourage transitioning and reinforced the harmful ideas that led to my wrongly identifying as FtM in the first place."
"The biggest issue for me was that when I did try to get support from a therapist or psychologist on entangling the actual reasons behind my dysphoria and how to deal with it, and deal with detransitioning, nobody had any clue or any experience, so they couldn't help me. Which made me even feel more lonely, and made detransitioning so much harder mentally than transitioning was."

cautious regarding the possible ideological bias or lack of knowledge of therapists.

Overall, most respondents explained that their detransition was a very isolating experience, during which they did not receive enough support. However, some participants emphasized the fact that the support that they received from their family, partners and friends, as well as online detrans groups and lesbian and feminist communities was extremely important and valuable to them.

Discussion

The present study was designed to better understand the needs of detransitioners, as well as the support—or lack of—that they are currently receiving. In order to do so, members of online detrans communities were recruited to answer a survey, in which questions were asked about their demographics, their transition and detransition experiences and the needs that they faced as well as the support that they received while detransitioning. In this section, I will discuss the results in relation to the main research question of the current study: What are the needs of detransitioners?

The sample surveyed appeared to be mostly female, young, from Western countries, with an experience of both social and medical transition and a high prevalence of certain comorbid conditions. The current study found that most detransitioners stopped transitioning before their mid-twenties, after an average of 4 years of transition. This observation is consistent with that made by Stella (2016) in her informal study on female detransitioners. The average transition age of the 203 respondents of her survey was 17.09 years, compared to 17.42 years in female detransitioners of the current study. The average detransition age of her sample was 21.09 years, compared to 22.22 years here.

Another finding of the current study was that a majority of the sample underwent hormone therapy (62% for females; 80% for males) and 45% of those who medically transitioned underwent gender affirming surgeries. This is likely to have implications in terms of the medical needs faced by this population. Close to half of the sample (49%) reported a need for receiving accurate information on stopping or changing hormone therapy, and almost a quarter (24%) reported the need for receiving help for complications related to surgeries or hormone therapy. The latter finding is concerning when looking at the negative medical experiences described by respondents in Table 3. Participants recounted situations in which their doctors either did not believe them, did not listen to them, refused them services, or simply did not have the required knowledge to help them during their detransition process. These experiences had a negative impact on some of the participants' trust in healthcare providers.

Similarly, the current study suggested that detransitioners have important psychological needs. This was made visible on the one hand through the fact that a majority of respondents (65%) reported the need for help in working on comorbid mental conditions related to gender dysphoria and in finding alternatives to medical transition. Other needs were reported by a majority of participants, such as learning to cope with feelings of regret (60%), learning to cope with the new physical and/or social changes related to detransitioning (53%) and learning to cope with internalized homophobia (52%). On the other hand, the high prevalence of comorbid conditions described in Table 1 might also be an indicator of important psychological needs. These results are similar

to that found by Hailey (2017) in her informal survey of comorbid mental health in detransitioned females. In her study, 77% reported a diagnosis of a depressive disorder (compared to 70% here), 74% of the sample reported a diagnosis of an anxiety disorder (compared to 63% here), 32% reported a diagnosis of PTSD (compared to 33% here) and 22% reported a diagnosis of an eating disorder (compared to 19% here). This is also very concerning information considering the descriptions made by detransitioners about the difficulty of finding a therapist willing or able to help them, and of finding alternative ways to deal with gender dysphoria after detransitioning (see Table 4).

The majority (84%) of the respondents reported having experienced both body and social gender dysphoria. Half of the sample (50%) later reported having decided to detransition due to the fact that their transition did not alleviate their gender dysphoria. Others (45%) reported having found alternative ways to deal with their gender dysphoria (see Figure 1). These results highlight the necessity to start looking into alternative solutions for treating gender dysphoria, in order to help those who did not find medical and/or social transition fulfilling.

In addition to that, 70% of the sample reported having realized that their gender dysphoria was related to other issues. Further research should be conducted in order to identify the ways in which other issues such as comorbid mental health conditions, trauma or internalized misogyny and homophobia possibly interact with gender dysphoria, and what can be done to alleviate them.

Furthermore, the high prevalence of autism spectrum condition (ASC) (20%) found in detransitioners in the current study, which is supported by Hailey (2017) findings (15%), also constitutes an interesting avenue for future research. Previous studies have provided evidence suggesting a co-occurrence of gender dysphoria and ASC (e.g., De Vries, Noens, Cohen-Kettenis, Van Berckelaer- Onnes, & Doreleijers, 2010; Glidden, Bouman, Jones, & Arcelus, 2016; VanderLaan et al., 2014; Van Der Miesen, Hurley, & De Vries, 2016; Zucker et al., 2017), which might explain the high number of detransitioners with an ASC diagnosis found in the current study.

In general, support given to detransitioners seems to be very poor at the moment, considering the fact that only 18% of the participants in the current study reported having received enough support during their detransition.

Based on the results of the current study, it appears that detransitioning is often accompanied by a break with LGBT+ communities. Only 13% of the participants reported having received support from an LGBT+ or trans-specific organization while detransitioning, compared to 51% while transitioning (see Figure 2). In addition to that, many respondents described experiences of outright rejection from LGBT+ spaces due to their decision to detransition (see Table 2). Looking at studies showing the positive role

of peer support and trans community connectedness on the mental health of its members (Johnson & Rogers, 2019; Pflum, Testa, Balsam, Goldblum, & Bongar, 2015; Sherman, Clark, Robinson, Noorani, & Poteat, 2020), it seems reasonable to suspect that this loss of support experienced by detransitioners must have serious implications on their psychological well-being.

Fortunately, the current study shows that detransitioners have access to other sources of support, online (groups, forums, social media) and in their social surroundings (family, partners and friends) (see Figure 2). Online groups and websites for detransitioners seem to be particularly important in light of the social needs expressed by the respondents of the current study. An overwhelming majority of respondents reported the need for hearing about other detransition stories (87%) and for getting in contact with other detransitioners (76%). Detransitioners need platforms and spaces where they can connect with each other and build a community. This point is best illustrated by the following account of one participant: "I found the peer support I received through other detransitioned women to be totally adequate and feel I benefited substantially from learning how to exist without institutional validation."

Conclusion

The aim of the present research was to examine detransitioners' needs and support. The four categories of needs (psychological, medical, legal and social) that were created for sake of clarity in the survey were a simplification of the real complexity of the experiences made by detransitioners and they have their limitations. Nonetheless, these categories enabled the current study to uncover the fact that most detransitioners could benefit from some form of counseling and in particular when it comes to psychological support on matters such as gender dysphoria, comorbid conditions, feelings of regret, social/physical changes and internalized homophobic or sexist prejudices. Medical support was also found to be needed by many, in order to address concerns related to stopping/changing hormone therapy, surgery/treatment complications and access to reversal interventions. Furthermore, the current study has shown that detransitioners need spaces to hear about other detransition stories and to exchange with each other.

Unfortunately, the support that detransitioners are receiving in order to fulfill these needs appears to be very poor at the moment. Participants described strong difficulties with medical and mental health systems, as well as experiences of outright rejection from the LGBT+ community. Many respondents have expressed the wish to find alternative treatments to deal with their gender dysphoria but reported that it was impossible to talk about it within LGBT+ spaces and in the medical sphere.

These accounts are concerning and they show the urgency to increase awareness and reduce hostility around the topic of detransition among healthcare providers and members of the LGBT+ community in order to address the specific needs of detransitioners.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Appendix.

Full Questionnaire

(1) How old are you?
(2) What country are you living in?
(3) What sex were you assigned at birth?
- Female
- Male
- Other:

(4) How do you see yourself now? (Tick all that apply)
- Woman
- Man
- Trans man
- Trans woman
- Female detransitioner
- Male detransitioner
- Non binary
- Other:

(5) Did you transition socially and/or medically and then stopped?
- Yes, both
- Only socially
- No

(6) Did you experience body dysphoria and/or social dysphoria? (Body dysphoria = strong desire to have sex characteristics of the opposite sex/rejection of your own sex; Social dysphoria = strong desire to be seen and treated as being of a different gender)
- Yes, both
- Only body dysphoria
- Only social dysphoria
- No

(7) Who helped you starting your social/medical transition? (Tick all that apply)
- A medical team specialized in transition
- An LGBT+ organization
- A trans-specific organization
- A therapist/doctor
- Online groups/forums/social media
- Friends, partner(s) and family
- Nobody
- Other:

(8) If you transitioned medically, how long were you in therapy before getting any hormones or surgeries? (in months; write 0 if none)

(9) During your transition, did you undergo some of the following interventions/treatments? (Tick all that apply)
- Hormone blockers
- Feminizing hormone treatment
- Masculinizing hormone treatment
- Gender affirming surgery(ies)
- No

(10) Do you feel like you were properly informed about the health implications of these treatments/interventions before undergoing them?
- Yes
- Partly
- No
- I am not sure

(11) What were the reasons that made you stop transitioning/detransition? (Tick all that apply)
- Health concerns
- Change in political views
- Transition did not help with my dysphoria
- Lack of support from social surroundings
- Discrimination
- Financial concerns
- Dysphoria resolved itself over time
- Unhappy with the physical changes
- Unhappy with the social changes
- Comorbid mental health issues related to dysphoria solved
- Realized that my gender dysphoria was related to other issues
- Found alternatives to deal with dysphoria
- Other:

(12) Were you diagnosed with or do you suspect having any of the following conditions?

	Diagnosed	Suspected	No
Attention Deficit (Hyperactive) Disorder			
Autism Spectrum Condition			
Anxiety Disorders			
Depressive Disorders			
Dissociative Identity Disorder			
Eating Disorders			
Obsessive Compulsive Disorder			
Polycystic Ovary Syndrome			
Post Traumatic Stress Disorder			
Personality Disorders			
Schyzo-spectrum Disorder			

(13) If you transitioned socially, at what age did you start?
(14) If you transitioned medically, at what age did you start?
(15) At what age did you start detransitioning/stop transitioning?
(16) What are the medical needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Receiving accurate information on stopping/changing hormonal treatment
- Receiving information and access to reversal surgeries/procedures
- Receiving help for complications related to surgeries or hormonal treatment
- None
- Other:

(17) What are the psychological needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Learning to cope with gender dysphoria; finding alternatives to medical transition
- Learning to cope with the new physical and/or social changes related to detransitioning
- Learning to cope with feelings of regret
- Learning to cope with internalized homophobia
- Working on comorbid mental issues related to gender dysphoria
- None
- Other:

(18) What are the legal needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Changing back legal gender/sex marker and/or name
- Legal advice and support to take legal action over medical malpractice
- None
- Other:

(19) What are the social needs that you had while detransitioning/stopping your transition? (Tick all that apply)
- Getting in contact with other detransitioners
- Receiving support to come out and deal with negative reactions
- Hearing about other detransition stories
- None
- Other:

(20) Is there any other need that you would like to mention?

(21) Which of these needs did you get support for?

	Full support	Partly	Not at all	Not needed
Medical needs				
Psychological needs				
Legal needs				
Social needs				

(22) From whom? (Tick all that apply)
- The medical team that helped me transition
- An LGBT+ organization
- A trans specific organization
- The therapist/doctor who supported me through my transition
- A new therapist/doctor
- Online groups/forums/social media
- Friends, partner(s) and family
- Nobody
- Other:

(23) Do you feel like you have received enough support throughout your detransition process overall?
- Yes
- No
- I don't know

(24) If you have any comment concerning the support/lack of support you received during your detransition, you can write it here.

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ORIGINAL PAPER

Individuals Treated for Gender Dysphoria with Medical and/or Surgical Transition Who Subsequently Detransitioned: A Survey of 100 Detransitioners

Lisa Littman[1]

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Abstract

The study's purpose was to describe a population of individuals who experienced gender dysphoria, chose to undergo medical and/or surgical transition and then detransitioned by discontinuing medications, having surgery to reverse the effects of transition, or both. Recruitment information with a link to an anonymous survey was shared on social media, professional listservs, and via snowball sampling. Sixty-nine percent of the 100 participants were natal female and 31.0% were natal male. Reasons for detransitioning were varied and included: experiencing discrimination (23.0%); becoming more comfortable identifying as their natal sex (60.0%); having concerns about potential medical complications from transitioning (49.0%); and coming to the view that their gender dysphoria was caused by something specific such as trauma, abuse, or a mental health condition (38.0%). Homophobia or difficulty accepting themselves as lesbian, gay, or bisexual was expressed by 23.0% as a reason for transition and subsequent detransition. The majority (55.0%) felt that they did not receive an adequate evaluation from a doctor or mental health professional before starting transition and only 24.0% of respondents informed their clinicians that they had detransitioned. There are many different reasons and experiences leading to detransition. More research is needed to understand this population, determine the prevalence of detransition as an outcome of transition, meet the medical and psychological needs of this population, and better inform the process of evaluation and counseling prior to transition.

Keywords Gender dysphoria · Detransition · Transgender

Introduction

Detransition is the act of stopping or reversing a gender transition. The visibility of individuals who have detransitioned is new and may be rapidly growing. As recently as 2014, it was challenging for an individual who detransitioned to find another person who similarly detransitioned (Callahan, 2018). Between 2015 and 2017, a handful of blogs written by individual detransitioners started to appear online, private support groups for detransitioners formed, and interviews with detransitioners began to appear in news articles, magazines, and blogs (Anonymous, 2017; 4thwavenow, 2016; Herzog, 2017; McCann, 2017). Although few YouTube videos about detransition existed prior to 2016, multiple detransitioners started to post videos documenting their experiences in 2016 and the numbers of these videos continues to increase.[1] In late 2017, the subreddit r/detrans (r/detrans, 2020) was revitalized and in four years has grown from 100 members to more than 21,000 members. A member poll of r/detrans conducted in 2019 estimated that approximately one-third of the members responding to the survey were desisters or detransitioners (r/detrans, 2019). The Pique Resilience Project, a group of four detransitioned or desisted young women, was founded in 2018 as a way to share the experiences of detransitioners with the public (Pique Resilience Project, 2019). In late 2019, the Detransition Advocacy Network, a nonprofit organization to "improve the well-being of detransitioned people everywhere" was launched (The

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✉ Lisa Littman
Lisa.Littman@gmail.com

[1] The Institute for Comprehensive Gender Dysphoria Research, 489 Main Street, Warren, RI 02885, USA

[1] A search of the word "detransition" in YouTube can be filtered by date of upload. https://www.youtube.com/results?search_query=%22detransition%22&sp=CAI%253D22.

Detransition Advocacy Network, 2020) and the first formal, in-person conference for detransitioned people was held (Bridge, 2020). In the face of this massive change, clinicians have called for more research into the experiences of detransitioners (Butler & Hutchinson, 2020; Entwistle, 2021; Marchiano, 2020).

Although there were rare published reports about detransitioners prior to 2016, most of the published literature about detransition is recent (Callahan, 2018; D'Angelo, 2018; Djordjevic et al., 2016; Kuiper & Cohen-Kettenis, 1998; Levine, 2018; Marchiano, 2017; Pazos Guerra et al., 2020; Stella, 2016; Turban & Keuroghlian, 2018; Turban et al., 2021; Vandenbussche, 2021). The prevailing cultural narratives about detransition are that most individuals who detransition will retransition and that the reasons for detransition are discrimination, pressures from others, and nonbinary identification (Turban et al., 2021). However, case reports are shedding light on a broader and more complex range of experiences that include trauma, worsened mental health with transition, re-identification with natal sex, and difficulty separating sexual orientation from gender identity (D'Angelo, 2018; Levine, 2018; Pazos Guerra et al., 2020).[2] Detransitioners and desisters, in their own words, have provided additional depth to the discussion, describing that:

(1) Trauma (including sexual trauma) and mental health conditions contributed to their transgender identification and transition (Callahan, 2018; Herzog, 2017; twitter.com/ftmdetransed & twitter.com/radfemjourney, 2019)
(2) Their dysphoria and transition were due to homophobia and difficulty accepting themselves as homosexual (Bridge, 2020; Callahan, 2018; upperhandMARS, 2020)
(3) Peers, social media, and online communities were influential in the development of transgender identification and desire to transition (Pique Resilience Project, 2019; Tracey, 2020; upperhandMARS, 2020)
(4) Their dysphoria was rooted in misogyny (Herzog, 2017)

Two recently published convenience sample reports provide additional context about the topic of detransition. First, Turban et al. (2021) analyzed data from the United States Trans Survey (USTS) (James et al., 2016). The USTS contains data from 27,715 transgender and gender diverse adults from the U.S. who were recruited through lesbian, gay, bisexual, transgender, queer (LGBTQ), and allied organization outreach. The USTS included the question, "Have you ever detransitioned? In other words, have you ever gone back to living as your sex assigned at birth, at least for a while?" with the multiple choice options of "yes," "no," and "I have never transitioned." For the 2,242 participants who answered "yes," Turban et al. analyzed the responses to the multiple choice question, "Why did you detransition? In other words, why did you go back to living as your sex assigned at birth? (Mark all that apply)." Although most of the offered answer options were about external pressures to detransition (pressure from spouse or partner, pressure from family, pressure from friends, pressure from employer, discrimination, etc.), participants could write in additional reasons that were not listed. Turban et al.'s sample included more natal males (55.1%) than natal females (44.9%). Roughly half (50.2%) had taken cross-sex hormones and 16.5% had obtained surgery. The findings revealed that most (82.5%) of the sample expressed at least one external factor for detransitioning and 15.9% expressed at least one internal factor (factors originating from self).

The second study by Vandenbussche (2021) recruited detransitioners from online communities of detransitioners and analyzed data for the participants who answered affirmatively to the question, "Did you transition medically and/or socially and then stopped?" The sample of 237 participants was predominantly natal female (92%), and from the U.S. (51%) and Europe (32%). Most (65%) had transitioned both medically and socially. Participants selected from multiple choice options to indicate why they detransitioned with options covering a range of experiences. Respondents also had the option to write in additional reasons. Frequently endorsed reasons for detransition included realizing that their gender dysphoria was related to other issues (70%); health concerns (62%); observing that transition did not help their dysphoria (50%); and that they found alternatives to deal with their dysphoria (45%). In contrast to Turban et al. (2021), external factors such as lack of support, financial concerns, and discrimination were less common (13%, 12%, and 10%, respectively). Many in the sample described that when they detransitioned they lost support or were ostracized from lesbian, gay, bisexual, and transgender (LGBT) communities, suggesting that many of the participants in Vandenbussche (2021) would not have been reached by the recruitment efforts of the USTS (James et al., 2016).

The objective of the current study was to describe a population of individuals who experienced gender dysphoria, chose to undergo medical and/or surgical transition and then detransitioned by discontinuing medications, having surgery to reverse the effects of transition, or both. In contrast to Turban et al. (2021) and Vandenbussche (2021), this study focused only on

[2] The debate about the terminologies used to describe an individual's sex (including "assigned sex at birth," "biological sex," "natal sex," "birth sex," "sex," etc.) is far from settled. Although some professionals have argued for the use of "assigned sex at birth," others argue that this terminology is misleading and not consistent with the events that occur at birth and prior to birth (Bouman et al., 2017; Byng et al., 2018; Dahlen, 2020; Griffin et al., 2020). Supporting the unsettled nature of the discussion, I received conflicting comments from the reviewers of this manuscript about my selection of natal sex terms–one reviewer asked that I justify my preference for natal sex over the other terminologies; another reviewer expressed support for my use of natal sex. I prefer to use "natal sex" and "birth sex" because they are accurate and objective. Further, I propose that "natal sex" and "birth sex" might be seen as reasonable, polite compromise terms between "biological sex" and "assigned sex at birth."

individuals who transitioned and detransitioned medically, surgically, or both. For the purpose of this study, medical transition refers to the use of puberty blockers, cross-sex hormones, or anti-androgens and surgical transition refers to any of a variety of surgical procedures (common surgical procedures include mastectomy, genital surgery, and breast augmentation). This study does not describe the population of individuals who undergo medical or surgical transition without issue nor is it designed to assess the prevalence of detransition as an outcome of transition. Instead, the goal was to identify detransition reasons and narratives in order to inform clinical care and future research.

Method

Participants and Procedure

During the recruitment period, 101 individuals who met the study criteria completed online surveys. Inclusion criteria were (1) completion of a survey via Survey Monkey; (2) answering that they had taken or had one or more of the following for the purpose of gender transition: cross-sex hormones, anti-androgens, puberty blockers, breast surgery, genital surgery, other surgery; and (3) answering that they had done any of the following for the purpose of detransitioning: stopped taking cross-sex hormones, stopped taking anti-androgens, stopped taking puberty blockers, had any surgery to reverse transition. One survey was excluded for nonsense answers leaving 100 surveys for analysis. The sample included more natal females (69.0%) than natal males (31.0%) with respondents who were predominantly White (90.0%), non-Hispanic (98.0%), resided in the U.S. (66.0%); had no religious affiliation (63.0%), and support the rights of gay and lesbian couples to marry legally (92.9%) (see Table 1). At the time of survey completion, the mean age of respondents was 29.2 years (SD = 9.1) though natal females were significantly younger ($M = 25.8$; SD = 5.0) than natal males ($M = 36.7$; SD = 11.4), $t(98) = -6.56$, $p < .001$. Prior to transitioning, natal females were more likely to report an exclusively homosexual sexual orientation and natal males were more likely to report an exclusively heterosexual sexual orientation.

A 115-question survey instrument with multiple choice, Likert-type, and open-ended questions was created by the author and two individuals who had personally detransitioned. The author had met both detransitioners by way of introductions from colleagues. The author and both individuals who had detransitioned created questions for the survey, provided feedback, and revised the survey questions collaboratively with a focus on content, clarity, and relevance to a variety of transition and detransition experiences. The survey instrument included two questions that were adapted from an online survey of female detransitioners (Stella, 2016). Once completed, the survey was uploaded onto Survey Monkey (SurveyMonkey, Palo Alto, CA) via an account that was HIPAA-enabled.

Recruitment information with a link to the survey was posted on blogs that covered detransition topics and shared in a private online detransition forum, in a closed detransition Facebook group, and on Tumblr, Twitter, and Reddit. Recruitment information was also shared on the professional listservs for the World Professional Association for Transgender Health, the American Psychological Association Section 44, and the SEXNET listserv (which is a listserv of sex researchers and clinicians) and the professionals on the listservs were asked to share recruitment information with anyone they knew who might be eligible. Efforts were made to reach out to communities with varied views about the use of medical and surgical transition and recruitment information stated that participation was sought from individuals regardless of whether their transition experiences were positive, negative or neutral. Potential participants were invited to share recruitment information with any potentially eligible person or community with potentially eligible people. The survey was active from December 15, 2016 to April 30, 2017 (4.5 months). The median time to complete a survey was 49 min; 50% of the surveys were completed between 32 and 71 min. There were no incentives offered for participating. Data were collected anonymously, without IP addresses, and stored securely with Survey Monkey.

Participation in this study was voluntary. Electronic consent was obtained from all participants in the following manner. The first page of the online survey informed respondents about the research purpose, potential risks and benefits, that participation was voluntary, and provided contact information for the researcher. Survey questions were only displayed if the participant clicked "agree" which indicated that they read the information, voluntarily agreed to participate and were at least 18 years of age.

Measures

Demographic and Baseline Characteristics

Information was collected about participant age, natal sex, race/ethnicity, country of residence, educational attainment, socioeconomic status, religion, attitudes about legal marriage for gay and lesbian couples, and where they first heard about the study. The term sexual orientation in this article is intended to refer to the natal sex of the participant and the natal sex of the individuals with whom they are sexually attracted. Participants were asked to select one or more labels for how they identified their sexual orientation prior to transition with options inclusive of participant sex (e.g., asexual female, bisexual female, heterosexual female, etc.). These responses were coded to be consistent with participant natal sex and were categorized into homosexual, heterosexual, bisexual, pansexual, asexual, and multiple. The multiple category included respondents who

Table 1 Demographic and baseline characteristics

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Race/ethnicity**		
White	62 (89.9%)	28 (90.3%)
Multiracial	6 (8.7%)	3 (9.7%)
Other	4 (5.8%)	0 (0%)
Asian	1 (1.4%)	1 (3.2%)
Hispanic	1 (1.4%)	1 (3.2%)
Black	0 (0%)	0 (0%)
Country of residence		
USA	46 (66.7%)	20 (64.5%)
UK	8 (11.6%)	1 (3.2%)
Canada	5 (7.2%)	4 (12.9%)
Australia	2 (2.9%)	2 (6.5%)
Other	8 (11.6%)	4 (12.9%)
Education		
Bachelor's or graduate degree	29 (42.0%)	18 (58.1%)
Associates degree	3 (4.3%)	1 (3.2%)
Some college but no degree	28 (40.6%)	9 (29.0%)
High school graduate or GED	8 (11.6%)	2 (6.5%)
< High school	1 (1.4%)	0 (0%)
Other	0 (0%)	1 (3.2%)
Socioeconomic status compared to others in country of residence		
Above average (somewhat or very much)	19 (27.5%)	12 (38.7%)
About average	20 (29.0%)	7 (22.6%)
Below average (somewhat or very much)	27 (39.1%)	12 (38.7%)
Prefer not to say	3 (4.3%)	0 (0%)
Categorized sexual orientation (by natal sex) prior to transition[a]		
Homosexual	18 (26.1%)	2 (6.5%)
Heterosexual	6 (8.7%)	12 (38.7%)
Bisexual	15 (21.7%)	8 (25.8%)
Pansexual	4 (5.8%)	1 (3.2%)
Multiple	20 (29.0%)	5 (16.1%)
Asexual	6 (8.7%)	3 (9.7%)
Religious affiliation		
No religious affiliation	41 (59.4%)	22 (73.3%)
Liberal Christian	5 (7.2%)	3 (10.0%)
Liberal Jewish	5 (7.2%)	0 (0%)
Conservative Christian	1 (1.4%)	2 (6.7%)
Liberal Muslim	1 (1.4%)	0 (0%)
Conservative Jewish	0 (0%)	0 (0%)
Conservative Muslim	0 (0%)	0 (0%)
Other	16 (23.2%)	3 (10.0%)
Legal marriage for gay and lesbian couples		
Favor	65 (97.0%)	26 (83.9%)
Oppose	1 (1.5%)	5 (16.1%)
Don't know	1 (1.5%)	0 (0%)
Source where participant first heard about study		
Detransition blogs	26 (37.7%)	15 (48.4%)
Other social media	37 (53.6%)	11 (35.5%)
A person they know	3 (4.3%)	3 (9.7%)
Other	3 (4.3%)	2 (6.5%)

*May select more than one answer

[a]Natal females were more likely to express an exclusively homosexual sexual orientation prior to transition ($\chi^2 = 5.15$. The *p*-value is .023). Natal males were more likely to express an exclusively heterosexual sexual

Table 1 (continued)

orientation prior to transition ($\chi^2 = 13.05$. The p value is $< .001$). Natal sex differences were not significant for individuals expressing pre-transition sexual orientations of bisexual, pansexual, multiple, and asexual. For bisexual sexual orientation, $\chi^2 = 0.20$. For pansexual sexual orientation, $\chi^2 = 0.29$. For multiple sexual orientations reported, $\chi^2 = 1.88$. For asexual sexual orientation, $\chi^2 = 0.02$

selected more than one response where responses indicated more than one pattern of sexual attraction (e.g., lesbian female and heterosexual female). Other questions about baseline characteristics included questions about diagnosed psychiatric disorders and neurodevelopmental disabilities, trauma, and non-suicidal self-injury (NSSI) before the onset of gender dysphoria.

Gender Dysphoria Onset and Typologies

Participants were asked how old they were when they first experienced gender dysphoria and whether this was during childhood, at the onset of puberty, during puberty, or later. Respondents were categorized as having early-onset gender dysphoria if they indicated that their gender dysphoria began "during childhood" and late-onset gender dysphoria if their gender dysphoria began "at the onset of puberty" or later. To evaluate typologies, participants were characterized by Blanchard's (1985, 1989) typology as homosexual (if the sexual orientations listed prior to transition were exclusively homosexual) or non-homosexual which includes heterosexual, asexual, bisexual, pansexual, and multiple responses.

Transition

Participants were asked for their age and the year that they first sought care to transition, sources that encouraged them to believe that transition would be helpful to them, and whether they felt pressured to transition. The friendship group dynamics that were identified in previous work were assessed by asking respondents whether their friendship group mocked people who were not transgender, whether people in their pre-existing friend group transitioned before the participant decided to transition, and how participant popularity changed after announcing that they would transition (Littman, 2018). Questions were asked about participant experiences with clinicians, the social, medical, and surgical steps they took to transition, and the duration of time spent taking each medication.

Detransition

Participants were asked for their age and the year that they decided to detransition, how long they were transitioned before deciding to detransition, their reasons for wanting to detransition, what sources encouraged them to believe that detransition would be helpful to them, and whether they felt pressured to detransition. Participants were also asked which social, medical, and surgical steps they took to detransition and whether they contacted the doctor or clinic that they used for their transition to tell them that they detransitioned.

Transition and Detransition Narratives

In this article, "narratives" denote participant interpretations of their experiences and rationales surrounding their decisions to transition and detransition. To associate each participant survey with a set of relevant narratives, the data were reviewed with horizontal (beginning to end) passes and vertical passes for selected questions (these questions are listed in the supplemental materials). Surveys were coded as belonging to zero or more of the following narrative categories: discrimination, nonbinary, retransition, trauma and mental health, internalized homophobia, social influence, and misogyny. Each narrative and the responses that were associated with them are detailed below. Example quotes were selected with care taken to avoid quoting a participant more than once per narrative. Narratives are ordered and reported with the more commonly accepted narratives first and the newer narratives next.

The *discrimination* narrative was defined as when someone detransitioned due to experiencing discrimination or external social pressures. The *nonbinary* narrative consisted of answering that their current identification was "nonbinary/genderqueer" or providing open-text responses that described aspects of discovering or maintaining a nonbinary identification. Although there were no questions in the survey specifically asking about retransition, the *retransition* narrative was identified if participants expressed that they had retransitioned or resumed transition in any of the open-text responses in the survey. The *gender dysphoria was caused by trauma or a mental health condition* narrative was identified by selection for the answers, "what I thought were feelings of being transgender were actually the result of trauma," "what I thought were feelings of being transgender were actually the result of a mental health condition," "I discovered that my gender dysphoria was caused by something specific (ex. trauma, abuse, mental health condition)" or open-text responses consistent with these reasons. The *internalized homophobia/difficulty accepting oneself as a lesbian female, gay male, or bisexual person* narrative consisted of descriptions that the respondents' discomfort and distress about being lesbian, gay, or bisexual was related to their gender dysphoria, transition, or detransition, or that they assumed they were transgender because they did not yet understand themselves to be lesbian, gay or bisexual. The *social pressure to transition* narrative was identified with an affirmative

answer to whether they felt pressured to transition with an open-text response indicating that the pressure came from a person or group of people. The *misogyny* narrative was identified for natal female respondents with open-text responses using the word "misogyny" or expressing a hatred of femaleness.

Gender Identification at Start of Transition and at Survey Completion

Participants were asked how they identified their gender when they started their transition and at the time of survey completion. They were given options of female, male, nonbinary/genderqueer, trans man/FTM, trans woman/MTF, none of the above, and other. Responses were coded by natal sex and categorized as transgender, birth sex, nonbinary, and other. Answers that were combinations of the above categories were reported as combinations such as "birth sex and nonbinary."

Self-Appraisal of Transition and Detransition

One question asked if participants believe they were helped and another if they were harmed by their transition with options of "very much," "a little," or "not at all." These results were categorized into exclusively helped, exclusively harmed, and both helped and harmed. Participants were asked which of the following reflected their feelings about their transition: "I am glad that I transitioned," "I wish I had never transitioned," "Transitioning distracted me from what I should have been doing," "Transition was a necessary part of my journey." Participants were asked to rate their regret about their transition ("no regrets," "mild regrets," "strong regrets," and "very strong regrets") and were asked to indicate their satisfaction with their decisions to transition and detransition ("extremely satisfied," "very satisfied," "somewhat satisfied," "somewhat dissatisfied," "very dissatisfied," and "extremely dissatisfied"). Satisfaction options were collapsed into "satisfied" and "dissatisfied." In addition, participants were asked if they knew then what they know now, would they have chosen to transition.

Data Analysis

After data were cleaned, statistical analyses were performed using google sheets. Results are presented as frequencies, percentages, medians, means and standard deviations. *t* tests and chi-square tests were performed for selected variables and were considered significant for $p < .05$. Qualitative data were obtained from the open-text answers to questions that allowed participants to provide additional information. Selected open-text responses were categorized, tallied, and reported numerically. Salient respondent quotes and summaries from the qualitative data were selected to illustrate the quantitative results and to provide relevant examples.

Results

Before Transition

Mental health diagnoses and traumatic experiences before the onset of gender dysphoria. Table 2 shows data about psychiatric disorders, neurodevelopmental disabilities, NSSI, and trauma that were reported as occurring prior to the onset of gender dysphoria. Because these conditions and events occurred before participants began to feel gender dysphoric, they cannot be considered to be secondary to gender incongruence or transphobia.

Gender dysphoria onset and typology. Most participants (82.0%) were living with one or both parents when they first experienced gender dysphoria at a mean age of 11.2 years (SD = 5.6). The mean age of gender dysphoria onset was not statistically different between natal females ($M = 11.3$; SD = 5.4) and natal males ($M = 11.0$; SD = 5.9), $t(96) = 0.25$. By Blanchard typologies, 26.1% of natal females were exclusively homosexual and 73.9% non-homosexual while 6.5% of natal males were exclusively homosexual and 93.5% non-homosexual (Blanchard, 1985, 1989). Slightly more than half of the respondents (56.0%) experienced early-onset gender dysphoria and slightly less than half (44.0%) experienced late-onset gender dysphoria. Although late-onset gender dysphoria in natal females was largely absent from the scientific literature prior to 2012 (Steensma et al., 2013; Zucker & Bradley, 1995; Zucker et al., 2012a), 55.1% of the natal female participants reported that their gender dysphoria began with puberty or later. Because the information about the timing of gender dysphoria onset was obtained from participants reporting on their own experiences, it can be assumed that these cases were indeed late-onset rather than early-onset gender dysphoria that was concealed from parents and other people.

Transition reasons. Table 3 shows data about the reasons that individuals wanted to transition and the most frequently endorsed were: wanting to be perceived as the target gender (77.0%); believing that transitioning was their only option to feel better (71.0%); the sensation that their body felt wrong the way it was (71.0%), and not wanting to be associated with their natal sex (70.0%). Most participants believed that transitioning would eliminate (65.0%) or decrease (63.0%) their gender dysphoria and that with transitioning they would become their true selves (64.0%).

Sources of transition encouragement and friend group dynamics. Participants identified sources that encouraged them to believe transitioning would help them. Social media and online communities were the most frequently reported, including YouTube transition videos (48.0%), blogs (46.0%), Tumblr (45.0%), and online communities (43.0%) (see supplemental materials). Also common were people who the respondents knew offline such as therapists (37.0%); someone (28.0%) or a group of friends (27.0%) that they knew in-person. A subset of

Table 2 Mental health diagnoses and traumatic experiences prior to the onset of gender dysphoria

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Diagnosed with a mental illness or neurodevelopmental disability**[a]		
Depression	27 (39.1%)	5 (16.1%)
Anxiety	22 (31.9%)	5 (16.1%)
Attention deficit hyperactivity disorder (ADHD)	10 (14.5%)	2 (6.5%)
Post-traumatic stress disorder (PTSD)	10 (14.5%)	1 (3.2%)
Eating disorders	10 (14.5%)	0 (0%)
Autism spectrum disorders	9 (13.0%)	1 (3.2%)
Bipolar disorder	9 (13.0%)	0 (0%)
Obsessive compulsive disorder	6 (8.7%)	3 (9.7%)
Borderline personality disorder	5 (7.2%)	0 (0%)
Schizophrenia or other psychotic disorders	1 (1.4%)	0 (0%)
None of the above	28 (40.6%)	17 (54.8%)
Other	7 (10.1%)	2 (6.5%)
Non-suicidal self-injury (NSSI)[b]		
Engaged in NSSI before the onset of gender dysphoria	19 (27.5%)	5 (16.1%)
Trauma[c]		
Experienced a trauma less than one year before the start of gender dysphoria	33 (47.8%)	4 (12.9%)

*May select more than one answer

[a]Natal sex difference for one or more pre-existing diagnoses (100-none of the above) was not significant [$\chi^2(1, 100) = 1.76$]

[b]Natal sex differences for NSSI before the onset of gender dysphoria was not significant ($\chi^2 = 1.52$)

[c]Experiencing a trauma less than one year before the start of gender dysphoria was statistically different [$\chi^2(1, 100) = 11.19$, $p < .001$] with natal females > natal males

Table 3 Transition reasons

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Reasons for transition**		
I wanted others to perceive me as the target gender	53 (76.8%)	24 (77.4%)
I thought transitioning was my only option to feel better	50 (72.5%)	21 (67.7%)
My body felt wrong to me the way it was	50 (72.5%)	21 (67.7%)
I didn't want to be associated with my natal sex/natal gender	51 (73.9%)	19 (61.3%)
It made me uncomfortable to be perceived romantically/sexually as a member of my natal sex/natal gender	49 (71.0%)	18 (58.1%)
I thought transitioning would eliminate my gender dysphoria	43 (62.3%)	22 (71.0%)
I felt I would become my true self	42 (60.9%)	22 (71.0%)
I identified with the target gender	40 (58.0%)	24 (77.4%)
I thought transitioning would lessen my gender dysphoria	45 (65.2%)	18 (58.1%)
I felt I would fit in better with the target gender	36 (56.5%)	20 (64.5%)
I felt I would be more socially acceptable as a member of the target gender	38 (55.1%)	11 (35.5%)
I felt I would be treated better if I was perceived as the target gender	35 (50.7%)	14 (45.2%)
I saw myself as a member of the target gender	31 (44.9%)	18 (58.1%)
I thought transitioning would reduce gender-related harassment or trauma I was experiencing	35 (50.7%)	5 (16.1%)
I had erotic reasons for wanting to transition	9 (13.0)	12 (38.7%)
Other	9 (13.0%)	3 (9.7%)

*May select more than one answer

participants experienced the friendship group dynamics identified in previous work, including belonging to a friendship group that mocked people who were not transgender (22.2%), having one or more friend from the pre-existing friend group transition before the participant decided to transition (36.4%), and experiencing an increase in popularity after announcing plans to transition (19.6%) (Littman, 2018). Most did not have this experience (68.7%, 61.6%, and 62.9%, respectively).

Pressure to transition. More than a third of the participants (37.4%) felt pressured to transition. Natal sex differences in feeling pressured to transition were significant by chi-square test with natal females > natal males $\chi^2(1, 99) = 4.22$, $p = .04$. Twenty-eight participants provided open-text responses of which 24 described sources of pressure (17 described social pressures and 7 described sources that were not associated with other people). Clinicians, partners, friends, and society were named as sources that applied pressure to transition, as seen in the following quotes: "My gender therapist acted like it [transition] was a panacea for everything;" "[My] [d]octor pushed drugs and surgery at every visit;" "I was dating a trans woman and she framed our relationship in a way that was contingent on my being trans;" "A couple of later trans friends kept insisting that I needed to stop delaying things;" "[My] best friend told me repeatedly that it [transition] was best for me;" "The forums and communities and internet friends;" "By the whole of society telling me I was wrong as a lesbian;" and "Everyone says that if you feel like a different gender…then you just are that gender and you should transition." Participants also felt pressure to transition that did not involve other people as illustrated by the following: "I felt pressured by my inability to function with dysphoria" and "Not by people. By my life circumstances."

Experiences with clinicians. When participants first sought care for their gender dysphoria or desire to transition, more than half of the participants (53.0%) saw a psychiatrist or psychologist; about a third saw a primary care doctor (34.0%) or a counselor (including licensed clinician social worker, licensed professional counselor, or marriage and family therapist) (32.0%); and 17.0% saw an endocrinologist. For transition, 45.0% of participants went to a gender clinic (44.4% of those attending a gender clinic specified that the gender clinic used the informed consent model of care); 28.0% went to a private doctor's office; 26.0% went to a group practice; and 13.0% went to a mental health clinic (see supplemental materials).

The majority (56.7%) of participants felt that the evaluation they received by a doctor or mental health professional prior to transition was not adequate and 65.3% reported that their clinicians did not evaluate whether their desire to transition was secondary to trauma or a mental health condition. Although 27.0% believed that the counseling and information they received prior to transition was accurate about benefits and risks, nearly half reported that the counseling was overly positive about the benefits of transition (46.0%) and not negative enough about the risks (26.0%). In contrast, only a small minority found the counseling not positive enough about benefits (5.0%) or too negative about risks (6.0%) suggesting a bias toward encouraging transition.

Transition

Participants were on average 21.9 years old (SD = 6.1) when they sought medical care to transition with natal females seeking care at younger ages ($M = 20.0$; SD = 4.2) than natal males ($M = 26.0$; SD = 7.5), $t(97) = -5.07$, $p < .001$. Given that the majority of natal males were categorized as Blanchard typology non-homosexual, the finding that natal males sought medical care to transition at older ages than natal females is concordant with previous research (Blanchard et al., 1987). The average year for seeking care was more recent for natal females ($M = 2011$; SD = 3.8) than natal males ($M = 2007$; SD = 6.9), $t(96) = 2.78$, $p = .007$, and thus, there may have been differences in the care they received due to differences in the culture surrounding transition and the prevailing medical approaches to gender dysphoria for the time.

At the start of transitioning, nearly all (98.0%) of the participants identified as either transgender (80.0%), nonbinary (15.0%), or both transgender and nonbinary (3.0%). Participants identified which social, medical, and surgical steps they had taken to transition. Table 4 shows these steps, separated by natal sex where appropriate. Most respondents adopted new pronouns (91.0%) and names (88.0%), and the vast majority (97.1%) of natal females wore a binder. Most participants took cross-sex hormones (96.0%) and most natal males took anti-androgens (87.1%). The most frequent transition surgery was breast or chest surgery for natal females (33.3%). Genital surgery was less common (1.4% of natal females and 16.1% of natal males). Natal females took testosterone for a mean duration of 2.0 years (SD = 1.6). Natal males took estrogen for a mean duration of 5.1 years (SD = 5.9) and anti-androgens for 2.8 years (SD = 2.6). The minority of patients who took puberty blockers took them for a mean duration of less than a year ($M = 0.9$ years; SD = 0.6).

Detransition

Before deciding to detransition, participants remained transitioned for a mean duration of 3.9 years (SD = 4.1) with natal females remaining transitioned for a shorter period of time ($M = 3.2$ years; SD = 2.7) than natal males ($M = 5.4$ years; SD = 6.1), $t(96) = -2.40$, $p = .018$. When participants decided to detransition they were a mean age of 26.4 years old (SD = 7.4) though natal females were significantly younger ($M = 23.6$; SD = 4.5) than natal males ($M = 32.7$; SD = 8.8), $t(97) = -6.75$, $p < .001$. The mean calendar year when participants decided to detransition was 2014 ($M = 2014$; SD = 3.3), but the difference

Table 4 Steps taken for social, medical, and surgical transition

	N (%)
*Social transition**	
Pronouns	91 (91.0%)
Different name	88 (88.0%)
Clothes/hair/makeup	90 (90.0%)
Legal name change	49 (49.0%)
Gender/sex changed on government documents	36 (36.0%)
Voice training	20 (20.0%)
Natal female	
Wore a binder	67 (97.1%)
*Medical transition**	
Cross-sex hormones	96 (96.0%)
Puberty blockers	7 (7.0%)
Natal male	
Anti-androgens	27 (87.1%)
*Surgical transition**	
Face/neck surgery	5 (5.0%)
Natal female	
Breast/chest surgery	23 (33.3%)
Genital surgery (to create a penis)	1 (1.4%)
Natal male	
Breast implants	5 (16.1%)
Genital surgery (to create a vagina)	5 (16.1%)

*May select more than one answer

between natal females and natal males was not significant ($M = 2014$, SD = 3.3; $M = 2014$, SD = 3.5), $t(95) = 0.52$.

Respondents detransitioned for a variety of reasons and most (87.0%) selected more than one reason. The most frequently endorsed reason for detransitioning was that the respondent's personal definition of male and female changed and they became comfortable identifying with their natal sex (60.0%) (see Table 5). Other commonly endorsed reasons were concerns about potential medical complications (49.0%); transition did not improve their mental health (42.0%); dissatisfaction with the physical results of transition (40.0%); and discovering that something specific like trauma or a mental health condition caused their gender dysphoria (38.0%). External pressures to detransition such as experiencing discrimination (23.0%) or worrying about paying for treatments (17.0%) were less common.

Encouragement and pressure to detransition. Participants were asked to select sources that encouraged them to believe that detransitioning would help them. These included blogs (37.0%), Tumblr (35.0%), and YouTube detransition videos (23.0%) (see supplemental materials). At some point in their process, 23.2% felt pressured to detransition. There was no significant difference between natal females and natal males for feeling pressured to detransition, $\chi^2(1, 99) = 1.11$. Of the 21 open-text responses provided, 14 respondents expressed social pressure to detransition; three expressed internal pressure to detransition and four provided responses that were neither

Table 5 Reasons for detransitioning

	Natal female *N* (%) $N = 69$	Natal male *N* (%) $N = 31$
*Reasons for detransitioning**		
My personal definition of female or male changed and I became more comfortable identifying as my natal sex	45 (65.2%)	15 (48.4%)
I was concerned about potential medical complications from transitioning	40 (58.0%)	9 (29.0%)
My mental health did not improve while transitioning	31 (44.9%)	11 (35.5%)
I was dissatisfied by the physical results of the transition/felt the change was too much	35 (50.7%)	5 (16.1%)
I discovered that my gender dysphoria was caused by something specific (ex, trauma, abuse, mental health condition)	28 (40.6%)	10 (32.3%)
My mental health was worse while transitioning	27 (39.1%)	9 (29.0%)
I was dissatisfied by the physical results of the transition/felt the change was not enough	22 (31.9%)	11 (35.5%)
I found more effective ways to help my gender dysphoria	25 (36.2%)	7 (22.6%)
My physical health was worse while transitioning	21 (30.4%)	11 (35.5%)
I felt discriminated against	12 (17.4%)	11 (35.5%)
I had medical complications from transitioning	12 (17.4%)	7 (22.6%)
Financial concerns about paying for transition care	11 (15.9%)	6 (19.4%)
My gender dysphoria resolved	10 (14.5%)	5 (16.1%)
My physical health did not improve while transitioning	9 (13.0%)	2 (6.5%)
I resolved the specific issue that was the cause of my gender dysphoria	6 (8.7%)	4 (12.9%)
I realized that my desire to transition was erotically motivated	1 (1.4%)	5(16.1%)
Other	19 (27.5%)	6 (19.4%)

*May select more than one answer

or unclear. Regarding social pressure to detransition, seven participants expressed that the pressure came from partners, parents, or other family members as shown in the following example quotes: "I was threatened that if I did not immediately detransition I would NEVER see my […] children again," "My father very much wanted me to desist," and "Parents constantly encouraging me to detransition." Five participants expressed societal pressure to detransition as expressed in the following quotes: "I did not pass, I was mocked in public, I could not get a job. It was not ok to be trans" and "Well, I mean basically the entire world was against me transitioning, so yeah." One participant felt pressured by doctors and another one from a blog.

Detransition steps. Table 6 shows data about the social, medical, and surgical steps participants took to detransition. Nearly all participants medically detransitioned by ceasing cross-sex hormones (95.0%). Social detransition steps were also common and included returning to the use of previously used pronouns (63.0%) and birth names (33.0%) and changing one's clothes and hair presentations (48.0%). Surgical detransition steps were less common (9.0%).

Finding better ways of coping with gender dysphoria**.** Participants were asked to select responses that that they considered to have been better ways for them to cope with their gender dysphoria. Responses included community (44.0%), mindfulness/meditation (41.0%), exercise (39.0%), therapy (24.0%), trauma work (24.0%), medication to treat a mental health condition (18.0%), and yoga (14.0%).

Table 6 Social, medical, and surgical detransition steps

	N (%)
*Social detransition**	
Previous pronouns	63 (63.0%)
Clothes/hair/makeup	48 (48.0%)
Birth name	33 (33.0%)
New name (not birth name)	24 (24.0%)
None of the above	2 (2.0%)
*Medical detransition**	
Stopped cross-sex hormones	95 (95.0%)
Stopped puberty blockers	4 (4.0%)
Started hormones consistent with natal sex	14 (14.0%)
Natal male	
Stopped anti-androgens	17 (54.8%)
*Surgical detransition**	
Surgery to reverse changes from transition	9 (9.0%)

*May select more than one answer

Transition and Detransition Narratives

Several transition and detransition narratives emerged from the data. A sizable minority of participants (41.0%) expressed more than one narrative in their responses.

The *discrimination and external pressures to detransition* narrative was described by 29.0% of participants. Examples include: "I had to detransition in order to get a job"; "I was afraid of being homeless and unable to support myself"; "I felt much happier with myself but I couldn't go anywhere without being afraid. I passed okay but not perfectly. I was stared down and sneered at in the women's clothes section, I wouldn't dare use a public toilet because I'd find either violent men or women who wished an encounter with a violent man on me."

A *nonbinary* narrative was expressed by 16.0% of participants. Some described that they discovered their nonbinary gender identity during their transition, as in the following quotes: "I still was uncomfortable with my body and figured I should stop and make sure I really wanted to keep going. I didn't and I decided I must be nonbinary, not FTM"; "Transitioning didn't do what I thought I wanted it to. I had transitioned to the wrong gender. I still felt wrong. Then, I realized I was not male, but genderqueer. I detransitioned to suit my true identity." And others described a consistent nonbinary identification, as in the following quote, "I identified the same way that I did before. I had gotten what I wanted out of HRT and was ready to stop taking it." (Cross-sex hormones are sometimes referred to as "hormone replacement therapy" and abbreviated as HRT).

Three participants (3.0%) expressed the *retransition* narrative in open-text answers indicating that they had retransitioned, including the following quotes: "I am now transitioning for a second time"; I retransitioned after 5 years of detransitioning"; and "Anyway, I retransitioned over 10 years after detransitioning."

Most participants (58.0%) expressed the *gender dysphoria was caused by trauma or a mental health condition* narrative which included endorsing the response options indicating that their gender dysphoria was caused by something specific, such as a trauma or a mental health condition. More than half of the participants (51.2%) responded that they believe that the process of transitioning delayed or prevented them from dealing with or being treated for trauma or a mental health condition. The following are example quotes that were in response to why participants chose to detransition: "I slowly began addressing the mental health conditions and traumatic experiences that caused such a severe disconnect between myself and my body…"; "I was starting to become critical of transition because I felt that many people were doing it out of self-hatred and started to realize that applied to me as well"; "I was deeply uncomfortable with my secondary sex characteristics, which I now understand was a result of childhood trauma and associating my secondary sex characteristics with those events."

Despite the absence of any questions about this topic in the survey, nearly a quarter (23.0%) of the participants expressed the *internalized homophobia and difficulty accepting oneself as lesbian, gay, or bisexual* narrative by spontaneously describing that these experiences were instrumental to their gender dysphoria, their desire to transition, and their detransition. All

of the participants in this category indicated that they were either same-sex attracted exclusively or were same-sex attracted in combination with opposite-sex attraction (such as bisexual, pansexual, etc.). The following responses were written in as "other" for the question about why participants transitioned: "Transitioning to male would mean my attraction to girls would be 'normal'"; "being a 'gay trans man' (female dating other females) felt better than being a lesbian, less shameful"; "I felt being the opposite gender would make my repressed same-sex attraction less scary"; "I didn't want to be a gay man." Some participants described that it took time for them to gain an understanding of themselves as lesbian, gay, or bisexual as seen in the following: "At the time I was trying to figure out my identity and felt very male and thought I was transgender. I later discovered that I was a lesbian…"; and "Well, after deep discovery, I realized I was a gay man and realized that a sexual trauma after puberty might [have] confused my thought. I wanted to live as a gay man again." Several natal female respondents expressed that seeing other butch lesbians would have been helpful to them as shown by the following: "What would have helped me is being able to access women's community, specifically lesbian community. I needed access to diverse female role-models and mentors, especially other butch women."

The *social influence* narrative was identified where participants added information to the question about if they had felt pressured to transition and the response described pressure from a person or people. One-fifth (20.0%) of participants expressed that they felt pressured by a person or people to transition. Example quotes for social influence were described in a previous section.

Of the natal females, 7.2% expressed the *misogyny* narrative. Example quotes include: "…I realized how much of it [dysphoria] may have been caused by internalized misogyny and homophobia"; "Finally realizing there's nothing wrong or disgusting or weak about being female"; and "My transition was a desperate attempt to distance myself from womanhood and femaleness due to internalized lesbophobia and misogyny combined with a history of sexual trauma."

After Detransition

Disposition. At the time of survey completion, most participants had returned to identifying solely as their birth sex (61.0%) with an additional 10.0% identifying as their birth sex plus another identification. Fourteen percent of the participants identified solely as nonbinary with an additional 11.0% identifying as nonbinary plus a second identification. Eight percent of the participants identified solely as transgender with an additional 5.0% identifying as transgender plus another identification. Four percent of the responses did not fit into the above categories and were coded as "other." Figure 1 illustrates the distribution of participants' current gender identification (post-detransition). Only 24.0% of participants had informed

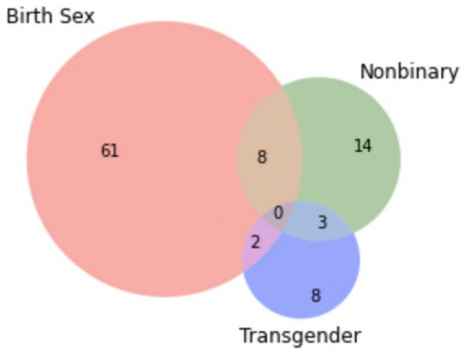

Fig. 1 Distribution of participants' current gender identification (after detransition) (n = 100). *Notes*: The sum of the numbers appearing in the "Birth Sex" circle indicates the number of participants who returned to identifying with their birth sex (71)—either as birth sex alone (61) or birth sex in addition to a second identification (10) represented in the overlap between two circles. For example, eight participants identify as their birth sex and as nonbinary. The sum of the numbers appearing in the "Nonbinary" circle indicates the number of participants who identify as nonbinary (25)—either as nonbinary alone (14) or nonbinary in addition to a second identification (11). The sum of the numbers appearing in the "Transgender" circle indicates the number of participants who identify as transgender (13)—either as transgender alone (8) or transgender in addition to a second identification (5). Four participants had responses that did not fit the categories above and were coded as "other"

the doctor or clinic that facilitated their transitions that they had detransitioned.

Self-appraisal of past transgender identification. Table 7 presents the data for responses endorsed by participants to reflect how they feel currently about having identified as transgender in the past. The statements most frequently selected included: "I thought gender dysphoria was the best explanation for what I was feeling" (57.0%), "My gender dysphoria was similar to the gender dysphoria of those who remain transitioned" (42.0%), "What I thought were feelings of being transgender actually were the result of trauma" (36.0%), "What I thought were feelings of being transgender actually were the result of a mental health condition" (36.0%).

Self-appraisal of transition and detransition. When asked to select which statement best reflects their feelings about their transition, nearly a third (30.0%) indicated that they wish they had never transitioned while 11.0% indicated they were glad they transitioned. Some (34.0%) selected the statement that transition "was a necessary part of [their] journey" but others (21.0%) indicated that the process of transitioning distracted them from what they should have been doing. Responses about whether transition helped or harmed them were also complicated. While 50.5% selected answers consistent with being both helped and harmed, 32.3% indicated that they were only harmed and 17.2% indicated that they were only helped. The majority of respondents were dissatisfied with their decision to transition (69.7%) and satisfied with their decision to detransition (84.7%). At least some amount of transition regret was

Table 7 Self-appraisal of past transgender identification

	Natal female *N* (%) *N* = 69	Natal male *N* (%) *N* = 31
*Self-appraisal about identifying as transgender in the past**		
I thought gender dysphoria was the best explanation for what I was feeling	39 (56.5%)	18 (58.1%)
My gender dysphoria was similar to the gender dysphoria of those who remain transitioned	32 (46.4%)	10 (32.3%)
What I thought were feelings of being transgender actually were the result of trauma	31 (44.9%)	5 (16.1%)
What I thought were feelings of being transgender actually were the result of a mental health condition	28 (40.6%)	8 (25.8%)
Someone else told me that the feelings I was having meant that I was transgender and I believed them	25 (36.2%)	10 (32.3%)
I still identify as transgender	20 (29.0%)	10 (32.3%)
I believed I was transgender then, but I was mistaken	16 (23.2%)	6 (19.4%)
I was transgender then but I am not transgender now	15 (21.7%)	7 (22.6%)
I formerly identified as transgender and now identify as genderqueer/nonbinary	12 (17.4%)	5 (16.1)
My gender dysphoria was different from the gender dysphoria of those who remain transitioned	11 (15.9%)	4 (12.9%)
I was never transgender	8 (11.6%)	3 (9.7%)
I thought I had gender dysphoria but I was mistaken	4 (5.8%)	4 (12.9%)
I never had gender dysphoria	1 (1.4)	2 (6.5%)
N/A as I did not identify as transgender in the past	0 (0%)	1 (3.2%)
Other	18 (26.1%)	5 (16.1%)

*May select more than one answer

common (79.8%) and nearly half (49.5%) reported strong or very strong regret. Most respondents (64.6%) indicated that if they knew then what they know now, they would not have chosen to transition.

Discussion

This study was designed to explore the experiences of individuals who obtained medical and surgical treatment for gender dysphoria and then detransitioned by discontinuing the medications or having surgery to reverse the changes from transition. The findings of this study, however, should not be assumed to be representative of all individuals who detransition. Although this study further documents that detransitioners exist, the prevalence of detransition as an outcome of transition is unknown. Only a small percentage of detransitioners (24.0%) informed the clinicians and clinics that facilitated their transitions that they had detransitioned. Therefore, clinic rates of detransition are likely to be underestimated and gender transition specialists may be unaware of how many of their own patients have detransitioned, particularly for patients who are no longer under their care.

This research demonstrates that the experiences of individuals who detransition are varied and the reasons for detransition are complex. Nearly all participants identified as transgender or nonbinary at the start of their transition and most sought transition because they did not want to be associated with their natal sex, their bodies felt wrong the way they were, and they believed that transition was the only option to relieve their distress. Some were helped by transition and only detransitioned because they were pressured to do so by people in their lives, society, or because they had medical complications. Some were harmed by transition and detransitioned because they concluded that their gender dysphoria was caused by trauma, a mental health condition, internalized homophobia, or misogyny—conditions that are not likely to be resolved with transition. These findings highlight the complexity of gender dysphoria and suggest that, in some cases, failure to explore co-morbidities and the context in which the gender dysphoria emerged can lead to misdiagnosis, missed diagnoses, and inappropriate gender transition. Some individuals detransitioned because their gender dysphoria resolved, because they found better ways to address their symptoms, or because their personal definitions of male and female changed and they became comfortable identifying as their natal sex.

The study sample was predominantly young natal females, many of whom experienced late-onset gender dysphoria which mirrors the recent, striking changes in the demographics of gender dysphoric youth seeking care as well as the youth described by their parents in Littman (2018) (see also Aitken et al., 2015; de Graaf et al., 2018; Zucker, 2019). Concerns have been raised that this new cohort of gender dysphoric individuals is unlike previous cohorts. Professionals have started to call for caution before treating this cohort with interventions with permanent effects because the etiologies, desistance and persistence rates,

expected duration of symptoms, and whether this new population is helped or harmed by gender transition is still unknown (D'Angelo et al., 2021; Kaltiala-Heino et al., 2018). The natal females and natal males in this sample differed on several dimensions, including that natal females were younger than natal males when they sought transition, when they decided to detransition, and at the time of survey completion. Natal females were more likely than natal males to have experienced a trauma less than one year before the onset of their gender dysphoria and were more likely to have felt pressured to transition. Compared to natal males, natal females remained transitioned for a shorter duration of time before deciding to detransition. Additionally, natal females transitioned more recently than natal males, so their experiences may vary due to changing trends in the clinical management of gender dysphoria and the cultural settings in which they became gender dysphoric.

The study findings covered a wide range of detransition experiences that are consistent with the diversity of experiences described in previously published clinical case reports and case series. Overlap of findings include: transition regret; absence of transition regret; re-identification with birth sex; continued identification as transgender; improvement or worsening of well-being with transition; retransitioning; detransitioning due to external social pressures; nonbinary identification; and recognizing and accepting oneself as homosexual or bisexual (D'Angelo, 2018; Djordjevic et al., 2016; Levine, 2018; Pazos Guerra et al., 2020; Turban & Keuroghlian, 2018; Turban et al., 2021; Vandenbussche, 2021). The population in this study is similar to the population in Vandenbussche in that both were predominantly natal females in their mid-20s. Because the current study recruited in 2016–2017 and Vandenbussche recruited in 2019, the similar mean age of participants may reflect the age of individuals who can be reached in online detransitioner communities. Several findings in this study were consistent with Vandenbussche's findings, including similar reasons for detransition (realizing that their gender dysphoria was related to other issues, finding alternatives to address gender dysphoria, gender dysphoria resolved, etc.). Although these two studies were recruited in different years, had different eligibility criteria, and included participants from several countries, it is possible that there may be some overlap of study populations.

The current study findings provide additional insight into the complex relationships between internalized homophobia, gender dysphoria, and desire to transition. Contrary to arguments against the potential role of homophobia in gender transitions (Ashley, 2020), participants reported that their own gender dysphoria and desire to transition stemmed from the discomfort they felt about being same-sex attracted, their desire to not be gay, and the difficulties that they had accepting themselves as lesbian, gay or bisexual. For these individuals, exploring their distress and discomfort around sexual orientation issues may have been more helpful to them than medical and surgical transition or at least an important part of exploration before making the decision to transition. This research adds to the existing evidence that gender dysphoria can be temporary (Ristori & Steensma, 2016; Singh et al., 2021; Zucker, 2018). It has been established that the most likely outcome for prepubertal youth with gender dysphoria is to develop into lesbian, gay, bisexual (LGB) (non-transgender) adults (Ristori & Steensma, 2016; Singh et al., 2021; Wallien & Cohen-Kettenis, 2008; Zucker, 2018). And, temporary gender dysphoria may be a common part of LGB identity development (Korte et al., 2008; Patterson, 2018). Therefore, intervening too soon to medicalize gender dysphoric youth risks iatrogenically derailing the development of youth who would otherwise grow up to be LGB non-transgender adults. Participants who detransitioned because they became comfortable identifying as their natal sex and because their gender dysphoria resolved further support that gender dysphoria is not always permanent.

The data in this study strengthen, with first-hand accounts, the rapid-onset gender dysphoria (ROGD) hypotheses which, briefly stated, are that psychosocial factors (such as trauma, mental health conditions, maladaptive coping mechanisms, internalized homophobia, and social influence) can cause or contribute to the development of gender dysphoria in some individuals (Littman, 2018). Littman also postulated that certain beliefs could be spread by peer contagion, including the belief that a wide range of symptoms should be interpreted as gender dysphoria (and proof of being transgender) and the belief that transition is the only solution to relieve distress. The current study supports the potential role of psychosocial factors in the development of gender dysphoria and further suggests, by participant responses that transitioning prevented or delayed them from addressing their underlying conditions, that maladaptive coping mechanisms may be relevant for some individuals. The potential role of social influence is demonstrated as well. First, when respondents were asked to describe how they currently feel about having identified as transgender in the past, more than a third endorsed the option, "Someone told me that the feelings I was having meant that I was transgender, and I believed them." Second, a subset of participants experienced the unique friendship group dynamics reported in Littman where peer groups mocked people who were not transgender and popularity within the friend group increased when respondents announced their plan to transition. Additionally, respondents identified several social sources that encouraged them to believe that transitioning would help them including: YouTube transition videos, blogs, Tumblr, and online communities. And finally, 20.0% of participants felt pressured to transition by social sources that included friends, partners, and society. More research is needed to further explore these hypotheses.

The current study and the Turban et al. (2021) analysis of the USTS data share some similarities and differences. Similarities include the use of convenience samples, targeted recruitment, and anonymous data collection. The findings of Turban et al. (including external pressures to detransition and transgender

identification after detransition) are a subset of the array of experiences described in the current study. The current study differed from James et al. (2016) and Turban et al. in that it enrolled participants based on the criterion of detransition after medical or surgical transition regardless of how they currently identified, recruited from communities with diverse perspectives about transition and detransition, used a precise definition for detransition that specifies the use of medication or surgery, and included answer options that were relevant to many different types of detransition experiences. In contrast, the USTS only enrolled transgender-identifying individuals regardless of whether they medically or surgically transitioned, recruited from communities likely to have similar perspectives about transition and detransition, and provided multiple choice answer options that were relevant to a narrower range of detransition experiences (James et al., 2016). Further, the definition used by the USTS for "detransitioned" (having "gone back to living as [their] sex assigned as birth, at least for a while") is quite vague. Although Turban et al. provide valuable information about the subset of transgender-identifying people who may have detransitioned, the current study provides a more comprehensive view of individuals who detransition after medical or surgical transition.

Over the past 15 years, there have been substantial changes in the clinical approach to gender dysphoric patients notable for a shift from approaches that employ thorough evaluations and judicious use of medical and surgical transition (the watchful waiting or Dutch approach, the developmentally informed approach, and the medical model of care) to approaches with minimized or eliminated evaluation and liberal use of transition interventions (the affirmative approach and the informed consent model of care) (Cavanaugh et al., 2016; de Vries & Cohen-Kettenis, 2012; Meyer et al., 2002; Rafferty et al., 2018; Schulz, 2018; Zucker et al., 2012b). This trend is prominent in the U.S. where the American Academy of Pediatrics endorsed the affirmative approach in 2018 and Planned Parenthood currently uses the informed consent model to provide medical transition in more than 200 clinics in 35 states (Planned Parenthood, 2021; Rafferty et al., 2018). It is plausible that an unintended consequence of these clinical shifts may be an increase in people who detransition. Many participants in this study believe that they did not receive an adequate evaluation by a clinician before transition. The definition of "adequate evaluation" was not provided in the survey and may be open to respondent interpretation. But given the complexities of the gender dysphoria described in the current study, one might consider a low bar of "adequate" to be the exploration of factors that could be misinterpreted as non-temporary gender dysphoria as well as factors that could be underlying causes for gender dysphoria. The most recently emerging approach to gender dysphoria is called the "exploratory approach" which is a neutral psychotherapeutic approach to help individuals gain a deeper understanding of their gender distress and the factors contributing to their dysphoria (Churcher Clarke & Spiliadis, 2019; Spiliadis, 2019). The study's findings suggest that an exploratory type of approach may have been beneficial to some of the respondents. Future research is needed to determine which patients are best treated by which approaches long term.

Patients considering medical and surgical interventions deserve accurate information about the risks, benefits, and alternatives to that treatment. In this sample, nearly half of the participants reported that the counseling they received about transition was overly positive about the benefits of transition and more than a quarter reported that the counseling was not negative enough about the risks. Several participants felt pressured to transition by their doctors and therapists. If these types of clinical interactions are verified, exploration is needed to determine the extent to which this situation occurs and what measures might be taken to ensure that clinicians provide patients with their options accurately and dispassionately.

There are several obstacles to obtaining accurate rates of detransition and desistance, including stigma and the low numbers of detransitioners who inform their clinicians that they detransitioned. One approach to bypass some of these barriers would be to incorporate non-judgmental questions about detransition and desistance into nationally representative surveys that collect health data. For example, the Behavioral Risk Factor Surveillance System contains an optional module about sexual orientation and gender identity that includes two questions to explore gender issues (Downing & Przedworski, 2018). By changing one existing question, "Do you consider yourself to be transgender?" into two questions, "Have you ever, at any point in your life, considered yourself to be transgender?" and "Do you currently consider yourself to be transgender?" and by adding a follow-up question if answers indicate past but not current transgender identification, "Did you ever take puberty blockers, cross-sex hormones, anti-androgens, or have any surgery as part of your transition?", valuable information about desistance, detransition, and current transgender identification could be obtained. These types of questions may also be of use in clinical practice and electronic medical records. The information gained about rates of detransition and desistance would enhance transgender healthcare by aiding informed consent processes at the start of any medical or surgical transition.

One of the strengths of this study is that it is one of the largest samples of detransitioners to date. Other strengths include the use of a precise definition for detransition, enrollment of detransitioners regardless of their post-detransition gender identification, recruitment from communities with likely divergent views about transition and detransition, and collaboration with two individuals who had detransitioned which helped to create a survey instrument with questions relevant to a variety of detransition experiences and enhanced the recruitment efforts.

There are several limitations to this study that should be considered when interpreting the findings. Like Vandenbussche (2021), James et al. (2016), and Turban et al. (2021), this study

used a cross-sectional design, anonymous surveying, and a convenience sample and therefore shares the same limitations that are inherent to these methodologies. These limitations include that conclusions about causation cannot be determined, identities of participants cannot be verified, and the findings of this study may not be generalizable to the entire population of people who detransition or to people outside of the countries where participants were from. Although this study reached out to communities with differing perspectives about transition and detransition, targeted recruitment and convenience samples always introduce the limitations associated with selection biases which should be addressed in future research. Finally, many of the participants in this study had less than ideal outcomes to their medical and surgical transitions, and it is possible that these experiences may have colored some of the responses.

Additional research is needed to determine the prevalence of detransition as an outcome of transition and to identify and meet the psychological and medical needs of the emerging detransitioned population. Because many individuals who detransition re-identify with their birth sex, are no longer connected to LGBT communities, and don't return to gender clinics, future research about detransition needs to expand recruitment efforts beyond gender clinics and transgender communities. The development and testing of non-medical interventions for gender dysphoria could provide valuable options to be used as alternatives or in conjunction with medical and surgical treatments. Because of the potential for some to experience trauma, mental health conditions, internalized homophobia, and misogyny as gender dysphoria, research needs to be conducted on the evaluation process before transition to find approaches that respectfully and collaboratively explore factors that might contribute to gender-related distress. There continues to be an absence of long-term outcomes evidence for youth treated with medical and surgical transition and a lack of information about the trajectories of youth experiencing late-onset gender dysphoria–research is needed to address these gaps. Continued work is needed to reduce rigid gender roles, increase representation of gender stereotype nonconformity, and to address discrimination and social pressures exerted against people who are transgender, lesbian, gay, bisexual, and gender stereotype non-conforming.

Conclusion

This study described individuals who, after transitioning with medications or surgery, have detransitioned. The prevalence of detransitioning after transition is unknown but is likely underestimated because most of the participants did not inform the doctors who facilitated their transitions that they had detransitioned. There is no single narrative to explain the experiences of all individuals who detransition and we should take care to avoid painting this population with a broad brush. Some detransitioners return to identifying with their birth sex, some assume (or maintain) a nonbinary identification, and some continue to identify as transgender. Some detransitioners regret transitioning and some do not. Some of the detransitioners reported experiences that support the ROGD hypotheses, including that their gender dysphoria began during or after puberty and that mental health issues, trauma, peers, social media, online communities, and difficulty accepting themselves as lesbian, gay, or bisexual were related to their gender dysphoria and desire to transition. Natal female and natal male detransitioners appear to have differences in their baseline characteristics and experiences and these differences should be further delineated. Future research about gender dysphoria and the outcomes of transition should consider the diversity of experiences and trajectories. More research is needed to determine how best to provide support and treatment for the long-term medical and psychological well-being of individuals who detransition. Findings about detransition should be used to improve our understanding of gender dysphoria and to better inform the processes of evaluation, counseling, and informed consent for individuals who are contemplating transition.

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Declarations

Conflict of interest The author has no relevant financial or non-financial conflicts of interest to disclose.

Consent to Participate Electronic consent was obtained from all participants included in the study. On the first page of the online survey, participants were informed of the research purpose and potential risks and benefits of participating, that their participation was voluntary, and were presented with a way to contact the researcher. The research survey questions were displayed only if the participant clicked "agree" which indicated that the participant read the information, voluntarily agreed to participate, and were at least 18 years of age.

Ethical Approval The research was determined to be Exempt Human Research by the Program for the Protection of Human Subjects of the Icahn School of Medicine at Mount Sinai in New York, NY. All procedures were performed in accordance with the ethical standards of the Program for the Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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Exhibit
SL 16

Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline

Wylie C. Hembree,[1] Peggy T. Cohen-Kettenis,[2] Louis Gooren,[3] Sabine E. Hannema,[4] Walter J. Meyer,[5] M. Hassan Murad,[6] Stephen M. Rosenthal,[7] Joshua D. Safer,[8] Vin Tangpricha,[9] and Guy G. T'Sjoen[10]

[1]New York Presbyterian Hospital, Columbia University Medical Center, New York, New York 10032 (Retired); [2]VU University Medical Center, 1007 MB Amsterdam, Netherlands (Retired); [3]VU University Medical Center, 1007 MB Amsterdam, Netherlands (Retired); [4]Leiden University Medical Center, 2300 RC Leiden, Netherlands; [5]University of Texas Medical Branch, Galveston, Texas 77555; [6]Mayo Clinic Evidence-Based Practice Center, Rochester, Minnesota 55905; [7]University of California San Francisco, Benioff Children's Hospital, San Francisco, California 94143; [8]Boston University School of Medicine, Boston, Massachusetts 02118; [9]Emory University School of Medicine and the Atlanta VA Medical Center, Atlanta, Georgia 30322; and [10]Ghent University Hospital, 9000 Ghent, Belgium

*Cosponsoring Associations: American Association of Clinical Endocrinologists, American Society of Andrology, European Society for Pediatric Endocrinology, European Society of Endocrinology, Pediatric Endocrine Society, and World Professional Association for Transgender Health.

Objective: To update the "Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline," published by the Endocrine Society in 2009.

Participants: The participants include an Endocrine Society–appointed task force of nine experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The task force commissioned two systematic reviews and used the best available evidence from other published systematic reviews and individual studies.

Consensus Process: Group meetings, conference calls, and e-mail communications enabled consensus. Endocrine Society committees, members and cosponsoring organizations reviewed and commented on preliminary drafts of the guidelines.

Conclusion: Gender affirmation is multidisciplinary treatment in which endocrinologists play an important role. Gender-dysphoric/gender-incongruent persons seek and/or are referred to endocrinologists to develop the physical characteristics of the affirmed gender. They require a safe and effective hormone regimen that will (1) suppress endogenous sex hormone secretion determined by the person's genetic/gonadal sex and (2) maintain sex hormone levels within the normal range for the person's affirmed gender. Hormone treatment is not recommended for prepubertal gender-dysphoric/gender-incongruent persons. Those clinicians who recommend gender-affirming endocrine treatments—appropriately trained diagnosing clinicians (required), a mental health provider for adolescents (required) and mental health

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Abbreviations: BMD, bone mineral density; DSD, disorder/difference of sex development; DSM, Diagnostic and Statistical Manual of Mental Disorders; GD, gender dysphoria; GnRH, gonadotropin-releasing hormone; ICD, International Statistical Classification of Diseases and Related Health Problems; MHP, mental health professional; VTE, venous thromboembolism.

professional for adults (recommended)—should be knowledgeable about the diagnostic criteria and criteria for gender-affirming treatment, have sufficient training and experience in assessing psychopathology, and be willing to participate in the ongoing care throughout the endocrine transition. We recommend treating gender-dysphoric/gender-incongruent adolescents who have entered puberty at Tanner Stage G2/B2 by suppression with gonadotropin-releasing hormone agonists. Clinicians may add gender-affirming hormones after a multidisciplinary team has confirmed the persistence of gender dysphoria/gender incongruence and sufficient mental capacity to give informed consent to this partially irreversible treatment. Most adolescents have this capacity by age 16 years old. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to age 16 years, although there is minimal published experience treating prior to 13.5 to 14 years of age. For the care of peripubertal youths and older adolescents, we recommend that an expert multidisciplinary team comprised of medical professionals and mental health professionals manage this treatment. The treating physician must confirm the criteria for treatment used by the referring mental health practitioner and collaborate with them in decisions about gender-affirming surgery in older adolescents. For adult gender-dysphoric/gender-incongruent persons, the treating clinicians (collectively) should have expertise in transgender-specific diagnostic criteria, mental health, primary care, hormone treatment, and surgery, as needed by the patient. We suggest maintaining physiologic levels of gender-appropriate hormones and monitoring for known risks and complications. When high doses of sex steroids are required to suppress endogenous sex steroids and/or in advanced age, clinicians may consider surgically removing natal gonads along with reducing sex steroid treatment. Clinicians should monitor both transgender males (female to male) and transgender females (male to female) for reproductive organ cancer risk when surgical removal is incomplete. Additionally, clinicians should persistently monitor adverse effects of sex steroids. For gender-affirming surgeries in adults, the treating physician must collaborate with and confirm the criteria for treatment used by the referring physician. Clinicians should avoid harming individuals (via hormone treatment) who have conditions other than gender dysphoria/gender incongruence and who may not benefit from the physical changes associated with this treatment. ***(J Clin Endocrinol Metab* 102: 3869–3903, 2017)**

Summary of Recommendations

1.0 Evaluation of youth and adults

1.1. We advise that only trained mental health professionals (MHPs) who meet the following criteria should diagnose gender dysphoria (GD)/gender incongruence in adults: (1) competence in using the Diagnostic and Statistical Manual of Mental Disorders (DSM) and/or the International Statistical Classification of Diseases and Related Health Problems (ICD) for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)

1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or the ICD for diagnostic purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)

1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).

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1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 |⊕⊕◯◯)

1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 |⊕⊕⊕◯)

2.0 Treatment of adolescents

2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment, and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 |⊕⊕◯◯)

2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty. (2 |⊕⊕◯◯)

2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 |⊕⊕◯◯)

2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years. (1 |⊕⊕◯◯).

2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 |⊕◯◯◯)

2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment. (2 |⊕⊕◯◯)

3.0 Hormonal therapy for transgender adults

3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and the criteria for the endocrine phase of gender transition before beginning treatment. (1 |⊕⊕⊕◯)

3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment. (1 |⊕⊕⊕◯)

3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 |⊕⊕◯◯)

3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 |⊕◯◯◯)

4.0 Adverse outcome prevention and long-term care

4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every 3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 |⊕⊕◯◯)

4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 |⊕⊕◯◯)

4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 |⊕⊕◯◯)

4.4. We recommend that clinicians obtain bone mineral density (BMD) measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 |⊕⊕◯◯)

4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for non-transgender females. (2 |⊕⊕◯◯)

4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 |⊕◯◯◯)

4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

5.0 Surgery for sex reassignment and gender confirmation

5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically necessary and would benefit the patient's overall health and/or well-being. (1 ⊕⊕◯◯)

5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)

5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)

5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 ⊕◯◯◯)

5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 ⊕⊕◯◯).

5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 ⊕◯◯◯)

Changes Since the Previous Guideline

Both the current guideline and the one published in 2009 contain similar sections. Listed here are the sections contained in the current guideline and the corresponding number of recommendations: Introduction, Evaluation of Youth and Adults (5), Treatment of Adolescents (6), Hormonal Therapy for Transgender Adults (4), Adverse Outcomes Prevention and Long-term Care (7), and Surgery for Sex Reassignment and Gender Confirmation (6). The current introduction updates the diagnostic classification of "gender dysphoria/gender incongruence." It also reviews the development of "gender identity" and summarizes its natural development. The section on clinical evaluation of both youth and adults, defines in detail the professional qualifications required of those who diagnose and treat both adolescents and adults. We advise that decisions regarding the social transition of prepubertal youth are made with the assistance of a mental health professional or similarly experienced professional. We recommend against puberty blocking followed by gender-affirming hormone treatment of prepubertal children. Clinicians should inform pubertal children, adolescents, and adults seeking gender-confirming treatment of their options for fertility preservation. Prior to treatment, clinicians should evaluate the presence of medical conditions that may be worsened by hormone depletion and/or treatment. A multidisciplinary team, preferably composed of medical and mental health professionals, should monitor treatments. Clinicians evaluating transgender adults for endocrine treatment should confirm the diagnosis of persistent gender dysphoria/gender incongruence. Physicians should educate transgender persons regarding the time course of steroid-induced physical changes. Treatment should include periodic monitoring of hormone levels and metabolic parameters, as well as assessments of bone density and the impact upon prostate, gonads, and uterus. We also make recommendations for transgender persons who plan genital gender-affirming surgery.

Method of Development of Evidence-Based Clinical Practice Guidelines

The Clinical Guidelines Subcommittee (CGS) of the Endocrine Society deemed the diagnosis and treatment of individuals with GD/gender incongruence a priority area for revision and appointed a task force to formulate evidence-based recommendations. The task force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation group, an international group with expertise in the development and implementation of evidence-based guidelines (1). A detailed description of the grading scheme has been published elsewhere (2). The task force used the best available research evidence to develop the recommendations. The task force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of the recommendation, strong recommendations use the phrase "we recommend" and the number 1, and weak recommendations use the phrase "we suggest" and the number 2. Cross-filled circles indicate the quality of the evidence, such that ⊕◯◯◯ denotes very low–quality evidence; ⊕⊕◯◯, low quality; ⊕⊕⊕◯, moderate quality; and ⊕⊕⊕⊕, high quality. The task force has confidence that persons who receive care according to the strong recommendations will derive, on average, more benefit than harm. Weak recommendations require more careful consideration of the person's circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the

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values that the task force considered in making the recommendation. In some instances, there are remarks in which the task force offers technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the task force and their preferences; therefore, one should consider these remarks as suggestions.

In this guideline, the task force made several statements to emphasize the importance of shared decision-making, general preventive care measures, and basic principles of the treatment of transgender persons. They labeled these "Ungraded Good Practice Statement." Direct evidence for these statements was either unavailable or not systematically appraised and considered out of the scope of this guideline. The intention of these statements is to draw attention to these principles.

The Endocrine Society maintains a rigorous conflict-of-interest review process for developing clinical practice guidelines. All task force members must declare any potential conflicts of interest by completing a conflict-of-interest form. The CGS reviews all conflicts of interest before the Society's Council approves the members to participate on the task force and periodically during the development of the guideline. All others participating in the guideline's development must also disclose any conflicts of interest in the matter under study, and most of these participants must be without any conflicts of interest. The CGS and the task force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from commercial interests; grants; research support; consulting fees; salary; ownership interests [*e.g.*, stocks and stock options (excluding diversified mutual funds)]; honoraria and other payments for participation in speakers' bureaus, advisory boards, or boards of directors; and all other financial benefits. Completed forms are available through the Endocrine Society office.

The Endocrine Society provided the funding for this guideline; the task force received no funding or remuneration from commercial or other entities.

Commissioned Systematic Review

The task force commissioned two systematic reviews to support this guideline. The first one aimed to summarize the available evidence on the effect of sex steroid use in transgender individuals on lipids and cardiovascular outcomes. The review identified 29 eligible studies at moderate risk of bias. In transgender males (female to male), sex steroid therapy was associated with a statistically significant increase in serum triglycerides and low-density lipoprotein cholesterol levels. High-density lipoprotein cholesterol levels decreased significantly across all follow-up time periods. In transgender females (male to female), serum triglycerides were significantly higher without any changes in other parameters. Few myocardial infarction, stroke, venous thromboembolism (VTE), and death events were reported. These events were more frequent in transgender females. However, the quality of the evidence was low. The second review summarized the available evidence regarding the effect of sex steroids on bone health in transgender individuals and identified 13 studies. In transgender males, there was no statistically significant difference in the lumbar spine, femoral neck, or total hip BMD at 12 and 24 months compared with baseline values before initiating masculinizing hormone therapy. In transgender females, there was a statistically significant increase in lumbar spine BMD at 12 months and 24 months compared with baseline values before initiation of feminizing hormone therapy. There was minimal information on fracture rates. The quality of evidence was also low.

Introduction

Throughout recorded history (in the absence of an endocrine disorder) some men and women have experienced confusion and anguish resulting from rigid, forced conformity to sexual dimorphism. In modern history, there have been numerous ongoing biological, psychological, cultural, political, and sociological debates over various aspects of gender variance. The 20th century marked the emergence of a social awakening for men and women with the belief that they are "trapped" in the wrong body (3). Magnus Hirschfeld and Harry Benjamin, among others, pioneered the medical responses to those who sought relief from and a resolution to their profound discomfort. Although the term transsexual became widely known after Benjamin wrote "The Transsexual Phenomenon" (4), it was Hirschfeld who coined the term "transsexual" in 1923 to describe people who want to live a life that corresponds with their experienced gender vs their designated gender (5). Magnus Hirschfeld (6) and others (4, 7) have described other types of trans phenomena besides transsexualism. These early researchers proposed that the gender identity of these people was located somewhere along a unidimensional continuum. This continuum ranged from all male through "something in between" to all female. Yet such a classification does not take into account that people may have gender identities outside this continuum. For instance, some experience themselves as having both a male and female gender identity, whereas others completely renounce any gender classification (8, 9). There are also reports of individuals experiencing a continuous and rapid involuntary alternation between a male and female identity (10) or men who do not experience themselves as men but do not want to live as women (11, 12). In some countries, (*e.g.*, Nepal, Bangladesh, and Australia), these nonmale or nonfemale genders are officially recognized (13). Specific treatment protocols, however, have not yet been developed for these groups.

Instead of the term transsexualism, the current classification system of the American Psychiatric Association uses the term gender dysphoria in its diagnosis of persons who are not satisfied with their designated gender (14). The current version of the World Health Organization's ICD-10 still uses the term transsexualism when diagnosing adolescents and adults. However, for the ICD-11, the World Health Organization has proposed using the term "gender incongruence" (15).

Treating persons with GD/gender incongruence (15) was previously limited to relatively ineffective elixirs or creams. However, more effective endocrinology-based treatments became possible with the availability of testosterone in 1935 and diethylstilbestrol in 1938. Reports of individuals with GD/gender incongruence who were treated with hormones and gender-affirming surgery appeared in the press during the second half of the 20th century. The Harry Benjamin International Gender Dysphoria Association was founded in September 1979 and is now called the World Professional Association for Transgender Health (WPATH). WPATH published its first Standards of Care in 1979. These standards have since been regularly updated, providing guidance for treating persons with GD/gender incongruence (16).

Prior to 1975, few peer-reviewed articles were published concerning endocrine treatment of transgender persons. Since then, more than two thousand articles about various aspects of transgender care have appeared.

It is the purpose of this guideline to make detailed recommendations and suggestions, based on existing medical literature and clinical experience, that will enable treating physicians to maximize benefit and minimize risk when caring for individuals diagnosed with GD/gender incongruence.

In the future, we need more rigorous evaluations of the effectiveness and safety of endocrine and surgical protocols. Specifically, endocrine treatment protocols for GD/gender incongruence should include the careful assessment of the following: (1) the effects of prolonged delay of puberty in adolescents on bone health, gonadal function, and the brain (including effects on cognitive, emotional, social, and sexual development); (2) the effects of treatment in adults on sex hormone levels; (3) the requirement for and the effects of progestins and other agents used to suppress endogenous sex steroids during treatment; and (4) the risks and benefits of gender-affirming hormone treatment in older transgender people.

To successfully establish and enact these protocols, a commitment of mental health and endocrine investigators is required to collaborate in long-term, large-scale studies across countries that use the same diagnostic and inclusion criteria, medications, assay methods, and response assessment tools (*e.g.*, the European Network for the Investigation of Gender Incongruence) (17, 18).

Terminology and its use vary and continue to evolve. Table 1 contains the definitions of terms as they are used throughout this guideline.

Biological Determinants of Gender Identity Development

One's self-awareness as male or female changes gradually during infant life and childhood. This process of cognitive and affective learning evolves with interactions with parents, peers, and environment. A fairly accurate timetable exists outlining the steps in this process (19). Normative psychological literature, however, does not address if and when gender identity becomes crystallized and what factors contribute to the development of a gender identity that is not congruent with the gender of rearing. Results of studies from a variety of biomedical disciplines—genetic, endocrine, and neuroanatomic—support the concept that gender identity and/or gender expression (20) likely reflect a complex interplay of biological, environmental, and cultural factors (21, 22).

With respect to endocrine considerations, studies have failed to find differences in circulating levels of sex steroids between transgender and nontransgender individuals (23). However, studies in individuals with a disorder/difference of sex development (DSD) have informed our understanding of the role that hormones may play in gender identity outcome, even though most persons with GD/gender incongruence do not have a DSD. For example, although most 46,XX adult individuals with virilizing congenital adrenal hyperplasia caused by mutations in *CYP21A2* reported a female gender identity, the prevalence of GD/gender incongruence was much greater in this group than in the general population without a DSD. This supports the concept that there is a role for prenatal/postnatal androgens in gender development (24–26), although some studies indicate that prenatal androgens are more likely to affect gender behavior and sexual orientation rather than gender identity *per se* (27, 28).

Researchers have made similar observations regarding the potential role of androgens in the development of gender identity in other individuals with DSD. For example, a review of two groups of 46,XY persons, each with androgen synthesis deficiencies and female raised, reported transgender male (female-to-male) gender role changes in 56% to 63% and 39% to 64% of patients, respectively (29). Also, in 46,XY female-raised individuals with cloacal

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Table 1. Definitions of Terms Used in This Guideline

Biological sex, biological male or female: These terms refer to physical aspects of maleness and femaleness. As these may not be in line with each other (*e.g.*, a person with XY chromosomes may have female-appearing genitalia), the terms biological sex and biological male or female are imprecise and should be avoided.

Cisgender: This means not transgender. An alternative way to describe individuals who are not transgender is "non-transgender people."

Gender-affirming (hormone) treatment: See "gender reassignment"

Gender dysphoria: This is the distress and unease experienced if gender identity and designated gender are not completely congruent (see Table 2). In 2013, the American Psychiatric Association released the fifth edition of the DSM-5, which replaced "gender identity disorder" with "gender dysphoria" and changed the criteria for diagnosis.

Gender expression: This refers to external manifestations of gender, expressed through one's name, pronouns, clothing, haircut, behavior, voice, or body characteristics. Typically, transgender people seek to make their gender expression align with their gender identity, rather than their designated gender.

Gender identity/experienced gender: This refers to one's internal, deeply held sense of gender. For transgender people, their gender identity does not match their sex designated at birth. Most people have a gender identity of man or woman (or boy or girl). For some people, their gender identity does not fit neatly into one of those two choices. Unlike gender expression (see below), gender identity is not visible to others.

Gender identity disorder: This is the term used for GD/gender incongruence in previous versions of DSM (see "gender dysphoria"). The ICD-10 still uses the term for diagnosing child diagnoses, but the upcoming ICD-11 has proposed using "gender incongruence of childhood."

Gender incongruence: This is an umbrella term used when the gender identity and/or gender expression differs from what is typically associated with the designated gender. Gender incongruence is also the proposed name of the gender identity–related diagnoses in ICD-11. Not all individuals with gender incongruence have gender dysphoria or seek treatment.

Gender variance: See "gender incongruence"

Gender reassignment: This refers to the treatment procedure for those who want to adapt their bodies to the experienced gender by means of hormones and/or surgery. This is also called gender-confirming or gender-affirming treatment.

Gender-reassignment surgery (gender-confirming/gender-affirming surgery): These terms refer only to the surgical part of gender-confirming/gender-affirming treatment.

Gender role: This refers to behaviors, attitudes, and personality traits that a society (in a given culture and historical period) designates as masculine or feminine and/or that society associates with or considers typical of the social role of men or women.

Sex designated at birth: This refers to sex assigned at birth, usually based on genital anatomy.

Sex: This refers to attributes that characterize biological maleness or femaleness. The best known attributes include the sex-determining genes, the sex chromosomes, the H-Y antigen, the gonads, sex hormones, internal and external genitalia, and secondary sex characteristics.

Sexual orientation: This term describes an individual's enduring physical and emotional attraction to another person. Gender identity and sexual orientation are not the same. Irrespective of their gender identity, transgender people may be attracted to women (gynephilic), attracted to men (androphilic), bisexual, asexual, or queer.

Transgender: This is an umbrella term for people whose gender identity and/or gender expression differs from what is typically associated with their sex designated at birth. Not all transgender individuals seek treatment.

Transgender male (also: trans man, female-to-male, transgender male): This refers to individuals assigned female at birth but who identify and live as men.

Transgender woman (also: trans woman, male-to female, transgender female): This refers to individuals assigned male at birth but who identify and live as women.

Transition: This refers to the process during which transgender persons change their physical, social, and/or legal characteristics consistent with the affirmed gender identity. Prepubertal children may choose to transition socially.

Transsexual: This is an older term that originated in the medical and psychological communities to refer to individuals who have permanently transitioned through medical interventions or desired to do so.

exstrophy and penile agenesis, the occurrence of transgender male changes was significantly more prevalent than in the general population (30, 31). However, the fact that a high percentage of individuals with the same conditions did not change gender suggests that cultural factors may play a role as well.

With respect to genetics and gender identity, several studies have suggested heritability of GD/gender incongruence (32, 33). In particular, a study by Heylens *et al.* (33) demonstrated a 39.1% concordance rate for gender identity disorder (based on the DSM-IV criteria) in 23 monozygotic twin pairs but no concordance in 21 same-sex dizygotic or seven opposite-sex twin pairs. Although numerous investigators have sought to identify specific genes associated with GD/gender incongruence, such studies have been inconsistent and without strong statistical significance (34–38).

Studies focusing on brain structure suggest that the brain phenotypes of people with GD/gender incongruence differ in various ways from control males and females, but that there is not a complete sex reversal in brain structures (39).

In summary, although there is much that is still unknown with respect to gender identity and its expression, compelling studies support the concept that biologic factors, in addition to environmental factors, contribute to this fundamental aspect of human development.

Natural History of Children With GD/Gender Incongruence

With current knowledge, we cannot predict the psychosexual outcome for any specific child. Prospective follow-up studies show that childhood GD/gender incongruence does not invariably persist into adolescence and adulthood (so-called "desisters"). Combining all outcome studies to date, the GD/gender incongruence of a minority of prepubertal children appears to persist in adolescence (20, 40). In adolescence, a significant number of these desisters identify as homosexual or bisexual. It may be that children who only showed some gender nonconforming characteristics have been included in the follow-up studies, because the DSM-IV text revision criteria for a diagnosis were rather broad. However, the persistence of GD/gender incongruence into adolescence is more likely if it had been extreme in childhood (41, 42). With the newer, stricter criteria of the DSM-5 (Table 2), persistence rates may well be different in future studies.

1.0 Evaluation of Youth and Adults

Gender-affirming treatment is a multidisciplinary effort. After evaluation, education, and diagnosis, treatment may include mental health care, hormone therapy, and/or surgical therapy. Together with an MHP, hormone-prescribing clinicians should examine the psychosocial impact of the potential changes on people's lives, including mental health, friends, family, jobs, and their role in society. Transgender individuals should be encouraged to experience living in the new gender role and assess whether this improves their quality of life. Although the focus of this guideline is gender-affirming hormone therapy, collaboration with appropriate professionals responsible for each aspect of treatment maximizes a successful outcome.

Diagnostic assessment and mental health care

GD/gender incongruence may be accompanied with psychological or psychiatric problems (43–51). It is therefore necessary that clinicians who prescribe hormones and are involved in diagnosis and psychosocial assessment meet the following criteria: (1) are competent in using the DSM and/or the ICD for diagnostic purposes, (2) are able to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) are trained in diagnosing psychiatric conditions, (4) undertake or refer for appropriate treatment, (5) are able to do a psychosocial assessment of the patient's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) regularly attend relevant professional meetings.

Because of the psychological vulnerability of many individuals with GD/gender incongruence, it is important that mental health care is available before, during, and sometimes also after transitioning. For children and adolescents, an MHP who has training/experience in child and adolescent gender development (as well as child and adolescent psychopathology) should make the diagnosis, because assessing GD/gender incongruence in children and adolescents is often extremely complex.

During assessment, the clinician obtains information from the individual seeking gender-affirming treatment. In the case

Table 2. DSM-5 Criteria for Gender Dysphoria in Adolescents and Adults

A. A marked incongruence between one's experienced/expressed gender and natal gender of at least 6 mo in duration, as manifested by at least two of the following:
   1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
   2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
   3. A strong desire for the primary and/or secondary sex characteristics of the other gender
   4. A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
   5. A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)
   6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender)

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:
   1. The condition exists with a disorder of sex development.
   2. The condition is posttransitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (*e.g.*, penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

Reference: American Psychiatric Association (14).

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of adolescents, the clinician also obtains information from the parents or guardians regarding various aspects of the child's general and psychosexual development and current functioning. On the basis of this information, the clinician:

- decides whether the individual fulfills criteria for treatment (see Tables 2 and 3) for GD/gender incongruence (DSM-5) or transsexualism (DSM-5 and/or ICD-10);
- informs the individual about the possibilities and limitations of various kinds of treatment (hormonal/surgical and nonhormonal), and if medical treatment is desired, provides correct information to prevent unrealistically high expectations;
- assesses whether medical interventions may result in unfavorable psychological and social outcomes.

In cases in which severe psychopathology, circumstances, or both seriously interfere with the diagnostic work or make satisfactory treatment unlikely, clinicians should assist the adolescent in managing these other issues. Literature on postoperative regret suggests that besides poor quality of surgery, severe psychiatric comorbidity and lack of support may interfere with positive outcomes (52–56).

For adolescents, the diagnostic procedure usually includes a complete psychodiagnostic assessment (57) and an assessment of the decision-making capability of the youth. An evaluation to assess the family's ability to endure stress, give support, and deal with the complexities of the adolescent's situation should be part of the diagnostic phase (58).

Social transitioning

A change in gender expression and role (which may involve living part time or full time in another gender role that is consistent with one's gender identity) may test the person's resolve, the capacity to function in the affirmed gender, and the adequacy of social, economic, and psychological supports. It assists both the individual and the clinician in their judgments about how to proceed (16). During social transitioning, the person's feelings about the social transformation (including coping with the responses of others) is a major focus of the counseling. The optimal timing for social transitioning may differ between individuals. Sometimes people wait until they start gender-affirming hormone treatment to make social transitioning easier, but individuals increasingly start social transitioning long before they receive medically supervised, gender-affirming hormone treatment.

Criteria

Adolescents and adults seeking gender-affirming hormone treatment and surgery should satisfy certain criteria before proceeding (16). Criteria for gender-affirming hormone therapy for adults are in Table 4, and criteria for gender-affirming hormone therapy for adolescents are in Table 5. Follow-up studies in adults meeting these criteria indicate a high satisfaction rate with treatment (59). However, the quality of evidence is usually low. A few follow-up studies on adolescents who fulfilled these criteria also indicated good treatment results (60–63).

Recommendations for Those Involved in the Gender-Affirming Hormone Treatment of Individuals With GD/Gender Incongruence

1.1. We advise that only trained MHPs who meet the following criteria should diagnose GD/gender incongruence in adults: (1) competence in using the DSM and/or the ICD for diagnostic purposes, (2) the ability to diagnose GD/gender incongruence and make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (3) training in diagnosing psychiatric conditions, (4) the ability to undertake or refer for appropriate treatment, (5) the ability to psychosocially assess the person's understanding, mental health, and social conditions that can impact gender-affirming hormone therapy, and (6) a practice of regularly attending relevant professional meetings. (Ungraded Good Practice Statement)

1.2. We advise that only MHPs who meet the following criteria should diagnose GD/gender incongruence in children and adolescents: (1) training in child and adolescent developmental psychology and psychopathology, (2) competence in using the DSM and/or ICD for diagnostic

Table 3. ICD-10 Criteria for Transsexualism

Transsexualism (F64.0) has three criteria:
1. The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatments.
2. The transsexual identity has been present persistently for at least 2 y.
3. The disorder is not a symptom of another mental disorder or a genetic, DSD, or chromosomal abnormality.

Table 4. Criteria for Gender-Affirming Hormone Therapy for Adults

1. Persistent, well-documented gender dysphoria/gender incongruence
2. The capacity to make a fully informed decision and to consent for treatment
3. The age of majority in a given country (if younger, follow the criteria for adolescents)
4. Mental health concerns, if present, must be reasonably well controlled

Reproduced from World Professional Association for Transgender Health (16).

purposes, (3) the ability to make a distinction between GD/gender incongruence and conditions that have similar features (*e.g.*, body dysmorphic disorder), (4) training in diagnosing psychiatric conditions, (5) the ability to undertake or refer for appropriate treatment, (6) the ability to psychosocially assess the person's understanding and social conditions that can impact gender-affirming hormone therapy, (7) a practice of regularly attending relevant professional meetings, and (8) knowledge of the criteria for puberty blocking and gender-affirming hormone treatment in adolescents. (Ungraded Good Practice Statement)

Evidence

Individuals with gender identity issues may have psychological or psychiatric problems (43–48, 50, 51, 64, 65). It is therefore necessary that clinicians making the diagnosis are able to make a distinction between GD/gender incongruence and conditions that have similar features. Examples of conditions with similar features are body dysmorphic disorder, body identity integrity disorder (a condition in which individuals have a sense that their anatomical configuration as an able-bodied person is somehow wrong or inappropriate) (66), or certain forms of eunuchism (in which a person is preoccupied with or engages in castration and/or penectomy for

Table 5. Criteria for Gender-Affirming Hormone Therapy for Adolescents

Adolescents are eligible for GnRH agonist treatment if:

1. A qualified MHP has confirmed that:
- the adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed),
- gender dysphoria worsened with the onset of puberty,
- any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment,
- the adolescent has sufficient mental capacity to give informed consent to this (reversible) treatment,

2. And the adolescent:
- has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility,
- has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,

3. And a pediatric endocrinologist or other clinician experienced in pubertal assessment
- agrees with the indication for GnRH agonist treatment,
- has confirmed that puberty has started in the adolescent (Tanner stage ≥G2/B2),
- has confirmed that there are no medical contraindications to GnRH agonist treatment.

Adolescents are eligible for subsequent sex hormone treatment if:

1. A qualified MHP has confirmed:
- the persistence of gender dysphoria,
- any coexisting psychological, medical, or social problems that could interfere with treatment (*e.g.*, that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start sex hormone treatment,
- the adolescent has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment,

2. And the adolescent:
- has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility),
- has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,

3. And a pediatric endocrinologist or other clinician experienced in pubertal induction:
- agrees with the indication for sex hormone treatment,
- has confirmed that there are no medical contraindications to sex hormone treatment.

Reproduced from World Professional Association for Transgender Health (16).

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reasons that are not gender identity related) (11). Clinicians should also be able to diagnose psychiatric conditions accurately and ensure that these conditions are treated appropriately, particularly when the conditions may complicate treatment, affect the outcome of gender-affirming treatment, or be affected by hormone use.

Values and preferences

The task force placed a very high value on avoiding harm from hormone treatment in individuals who have conditions other than GD/gender incongruence and who may not benefit from the physical changes associated with this treatment and placed a low value on any potential benefit these persons believe they may derive from hormone treatment. This justifies the good practice statement.

1.3. We advise that decisions regarding the social transition of prepubertal youths with GD/gender incongruence are made with the assistance of an MHP or another experienced professional. (Ungraded Good Practice Statement).

1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 ⊕◯◯◯)

Evidence

In most children diagnosed with GD/gender incongruence, it did not persist into adolescence. The percentages differed among studies, probably dependent on which version of the DSM clinicians used, the patient's age, the recruitment criteria, and perhaps cultural factors. However, the large majority (about 85%) of prepubertal children with a childhood diagnosis did not remain GD/gender incongruent in adolescence (20). If children have completely socially transitioned, they may have great difficulty in returning to the original gender role upon entering puberty (40). Social transition is associated with the persistence of GD/gender incongruence as a child progresses into adolescence. It may be that the presence of GD/gender incongruence in prepubertal children is the earliest sign that a child is destined to be transgender as an adolescent/adult (20). However, social transition (in addition to GD/gender incongruence) has been found to contribute to the likelihood of persistence.

This recommendation, however, does not imply that children should be discouraged from showing gender-variant behaviors or should be punished for exhibiting such behaviors. In individual cases, an early complete social transition may result in a more favorable outcome, but there are currently no criteria to identify the GD/gender-incongruent children to whom this applies. At the present time, clinical experience suggests that persistence of GD/gender incongruence can only be reliably assessed after the first signs of puberty.

Values and preferences

The task force placed a high value on avoiding harm with gender-affirming hormone therapy in prepubertal children with GD/gender incongruence. This justifies the strong recommendation in the face of low-quality evidence.

1.5. We recommend that clinicians inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression in adolescents and prior to treating with hormonal therapy of the affirmed gender in both adolescents and adults. (1 ⊕⊕⊕◯)

Remarks

Persons considering hormone use for gender affirmation need adequate information about this treatment in general and about fertility effects of hormone treatment in particular to make an informed and balanced decision (67, 68). Because young adolescents may not feel qualified to make decisions about fertility and may not fully understand the potential effects of hormonal interventions, consent and protocol education should include parents, the referring MHP(s), and other members of the adolescent's support group. To our knowledge, there are no formally evaluated decision aids available to assist in the discussion and decision regarding the future fertility of adolescents or adults beginning gender-affirming treatment.

Treating early pubertal youth with GnRH analogs will temporarily impair spermatogenesis and oocyte maturation. Given that an increasing number of transgender youth want to preserve fertility potential, delaying or temporarily discontinuing GnRH analogs to promote gamete maturation is an option. This option is often not preferred, because mature sperm production is associated with later stages of puberty and with the significant development of secondary sex characteristics.

For those designated male at birth with GD/gender incongruence and who are in early puberty, sperm production and the development of the reproductive tract are insufficient for the cryopreservation of sperm. However, prolonged pubertal suppression using GnRH analogs is reversible and clinicians should inform these individuals that sperm production can be initiated following prolonged gonadotropin suppression. This can be accomplished by spontaneous gonadotropin recovery after

cessation of GnRH analogs or by gonadotropin treatment and will probably be associated with physical manifestations of testosterone production, as stated above. Note that there are no data in this population concerning the time required for sufficient spermatogenesis to collect enough sperm for later fertility. In males treated for precocious puberty, spermarche was reported 0.7 to 3 years after cessation of GnRH analogs (69). In adult men with gonadotropin deficiency, sperm are noted in seminal fluid by 6 to 12 months of gonadotropin treatment. However, sperm numbers when partners of these patients conceive are far below the "normal range" (70, 71).

In girls, no studies have reported long-term, adverse effects of pubertal suppression on ovarian function after treatment cessation (72, 73). Clinicians should inform adolescents that no data are available regarding either time to spontaneous ovulation after cessation of GnRH analogs or the response to ovulation induction following prolonged gonadotropin suppression.

In males with GD/gender incongruence, when medical treatment is started in a later phase of puberty or in adulthood, spermatogenesis is sufficient for cryopreservation and storage of sperm. *In vitro* spermatogenesis is currently under investigation. Restoration of spermatogenesis after prolonged estrogen treatment has not been studied.

In females with GD/gender incongruence, the effect of prolonged treatment with exogenous testosterone on ovarian function is uncertain. There have been reports of an increased incidence of polycystic ovaries in transgender males, both prior to and as a result of androgen treatment (74–77), although these reports were not confirmed by others (78). Pregnancy has been reported in transgender males who have had prolonged androgen treatment and have discontinued testosterone but have not had genital surgery (79, 80). A reproductive endocrine gynecologist can counsel patients before gender-affirming hormone treatment or surgery regarding potential fertility options (81). Techniques for cryopreservation of oocytes, embryos, and ovarian tissue continue to improve, and oocyte maturation of immature tissue is being studied (82).

2.0 Treatment of Adolescents

During the past decade, clinicians have progressively acknowledged the suffering of young adolescents with GD/gender incongruence. In some forms of GD/gender incongruence, psychological interventions may be useful and sufficient. However, for many adolescents with GD/gender incongruence, the pubertal physical changes are unbearable. As early medical intervention may prevent psychological harm, various clinics have decided to start treating young adolescents with GD/gender incongruence with puberty-suppressing medication (a GnRH analog). As compared with starting gender-affirming treatment long after the first phases of puberty, a benefit of pubertal suppression at early puberty may be a better psychological and physical outcome.

In girls, the first physical sign of puberty is the budding of the breasts followed by an increase in breast and fat tissue. Breast development is also associated with the pubertal growth spurt, and menarche occurs ~2 years later. In boys, the first physical change is testicular growth. A testicular volume ≥4 mL is seen as consistent with the initiation of physical puberty. At the beginning of puberty, estradiol and testosterone levels are still low and are best measured in the early morning with an ultrasensitive assay. From a testicular volume of 10 mL, daytime testosterone levels increase, leading to virilization (83). Note that pubic hair and/or axillary hair/odor may not reflect the onset of gonadarche; instead, it may reflect adrenarche alone.

2.1. We suggest that adolescents who meet diagnostic criteria for GD/gender incongruence, fulfill criteria for treatment (Table 5), and are requesting treatment should initially undergo treatment to suppress pubertal development. (2 |⊕⊕◯◯)

2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty (Tanner stages G2/B2). (2 |⊕⊕◯◯)

Evidence

Pubertal suppression can expand the diagnostic phase by a long period, giving the subject more time to explore options and to live in the experienced gender before making a decision to proceed with gender-affirming sex hormone treatments and/or surgery, some of which is irreversible (84, 85). Pubertal suppression is fully reversible, enabling full pubertal development in the natal gender, after cessation of treatment, if appropriate. The experience of full endogenous puberty is an undesirable condition for the GD/gender-incongruent individual and may seriously interfere with healthy psychological functioning and well-being. Treating GD/gender-incongruent adolescents entering puberty with GnRH analogs has been shown to improve psychological functioning in several domains (86).

Another reason to start blocking pubertal hormones early in puberty is that the physical outcome is improved compared with initiating physical transition after puberty has been completed (60, 62). Looking like a man or woman when living as the opposite sex creates difficult

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barriers with enormous life-long disadvantages. We therefore advise starting suppression in early puberty to prevent the irreversible development of undesirable secondary sex characteristics. However, adolescents with GD/gender incongruence should experience the first changes of their endogenous spontaneous puberty, because their emotional reaction to these first physical changes has diagnostic value in establishing the persistence of GD/gender incongruence (85). Thus, Tanner stage 2 is the optimal time to start pubertal suppression. However, pubertal suppression treatment in early puberty will limit the growth of the penis and scrotum, which will have a potential effect on future surgical treatments (87).

Clinicians can also use pubertal suppression in adolescents in later pubertal stages to stop menses in transgender males and prevent facial hair growth in transgender females. However, in contrast to the effects in early pubertal adolescents, physical sex characteristics (such as more advanced breast development in transgender boys and lowering of the voice and outgrowth of the jaw and brow in transgender girls) are not reversible.

Values and preferences

These recommendations place a high value on avoiding an unsatisfactory physical outcome when secondary sex characteristics have become manifest and irreversible, a higher value on psychological well-being, and a lower value on avoiding potential harm from early pubertal suppression.

Remarks

Table 6 lists the Tanner stages of breast and male genital development. Careful documentation of hallmarks of pubertal development will ensure precise timing when initiating pubertal suppression once puberty has started. Clinicians can use pubertal LH and sex steroid levels to confirm that puberty has progressed sufficiently before starting pubertal suppression (88). Reference ranges for sex steroids by Tanner stage may vary depending on the assay used. Ultrasensitive sex steroid and gonadotropin assays will help clinicians document early pubertal changes.

Irreversible and, for GD/gender-incongruent adolescents, undesirable sex characteristics in female puberty are breasts, female body habitus, and, in some cases, relative short stature. In male puberty, they are a prominent Adam's apple; low voice; male bone configuration, such as a large jaw, big feet and hands, and tall stature; and male hair pattern on the face and extremities.

2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 l⊕⊕○○)

Evidence

Clinicians can suppress pubertal development and gonadal function most effectively via gonadotropin suppression using GnRH analogs. GnRH analogs are long-acting agonists that suppress gonadotropins by GnRH receptor desensitization after an initial increase of gonadotropins during ~10 days after the first and (to a lesser degree) the second injection (89). Antagonists immediately suppress pituitary gonadotropin secretion (90, 91). Long-acting GnRH analogs are the currently preferred treatment option. Clinicians may consider long-acting GnRH antagonists when evidence on their safety and efficacy in adolescents becomes available.

During GnRH analog treatment, slight development of secondary sex characteristics may regress, and in a later phase of pubertal development, it will stop. In girls, breast tissue will become atrophic, and menses will stop. In boys, virilization will stop, and testicular volume may decrease (92).

An advantage of using GnRH analogs is the reversibility of the intervention. If, after extensive exploration of his/her transition wish, the individual no longer desires transition, they can discontinue pubertal suppression. In subjects with

Table 6. Tanner Stages of Breast Development and Male External Genitalia

The description of Tanner stages for breast development:
1. Prepubertal
2. Breast and papilla elevated as small mound; areolar diameter increased
3. Breast and areola enlarged, no contour separation
4. Areola and papilla form secondary mound
5. Mature; nipple projects, areola part of general breast contour

For penis and testes:
1. Prepubertal, testicular volume <4 mL
2. Slight enlargement of penis; enlarged scrotum, pink, texture altered, testes 4–6 mL
3. Penis longer, testes larger (8–12 mL)
4. Penis and glans larger, including increase in breadth; testes larger (12–15 mL), scrotum dark
5. Penis adult size; testicular volume > 15 ml

Adapted from Lawrence (56).

precocious puberty, spontaneous pubertal development has been shown to resume after patients discontinue taking GnRH analogs (93).

Recommendations 2.1 to 2.3 are supported by a prospective follow-up study from The Netherlands. This report assessed mental health outcomes in 55 transgender adolescents/young adults (22 transgender females and 33 transgender males) at three time points: (1) before the start of GnRH agonist (average age of 14.8 years at start of treatment), (2) at initiation of gender-affirming hormones (average age of 16.7 years at start of treatment), and (3) 1 year after "gender-reassignment surgery" (average age of 20.7 years) (63). Despite a decrease in depression and an improvement in general mental health functioning, GD/gender incongruence persisted through pubertal suppression, as previously reported (86). However, following sex hormone treatment and gender-reassignment surgery, GD/gender incongruence was resolved and psychological functioning steadily improved (63). Furthermore, well-being was similar to or better than that reported by age-matched young adults from the general population, and none of the study participants regretted treatment. This study represents the first long-term follow-up of individuals managed according to currently existing clinical practice guidelines for transgender youth, and it underscores the benefit of the multidisciplinary approach pioneered in The Netherlands; however, further studies are needed.

Side effects

The primary risks of pubertal suppression in GD/gender-incongruent adolescents may include adverse effects on bone mineralization (which can theoretically be reversed with sex hormone treatment), compromised fertility if the person subsequently is treated with sex hormones, and unknown effects on brain development. Few data are available on the effect of GnRH analogs on BMD in adolescents with GD/gender incongruence. Initial data in GD/gender-incongruent subjects demonstrated no change of absolute areal BMD during 2 years of GnRH analog therapy but a decrease in BMD *z* scores (85). A recent study also suggested suboptimal bone mineral accrual during GnRH analog treatment. The study reported a decrease in areal BMD *z* scores and of bone mineral apparent density *z* scores (which takes the size of the bone into account) in 19 transgender males treated with GnRH analogs from a mean age of 15.0 years (standard deviation = 2.0 years) for a median duration of 1.5 years (0.3 to 5.2 years) and in 15 transgender females treated from 14.9 (±1.9) years for 1.3 years (0.5 to 3.8 years), although not all changes were statistically significant (94). There was incomplete catch-up at age 22 years after sex hormone treatment from age 16.6 (±1.4) years for a median duration of 5.8 years (3.0 to 8.0 years) in transgender females and from age 16.4 (±2.3) years for 5.4 years (2.8 to 7.8 years) in transgender males. Little is known about more prolonged use of GnRH analogs. Researchers reported normal BMD *z* scores at age 35 years in one individual who used GnRH analogs from age 13.7 years until age 18.6 years before initiating sex hormone treatment (65).

Additional data are available from individuals with late puberty or GnRH analog treatment of other indications. Some studies reported that men with constitutionally delayed puberty have decreased BMD in adulthood (95). However, other studies reported that these men have normal BMD (96, 97). Treating adults with GnRH analogs results in a decrease of BMD (98). In children with central precocious puberty, treatment with GnRH analogs has been found to result in a decrease of BMD during treatment by some (99) but not others (100). Studies have reported normal BMD after discontinuing therapy (69, 72, 73, 101, 102). In adolescents treated with growth hormone who are small for gestational age and have normal pubertal timing, 2-year GnRH analog treatments did not adversely affect BMD (103). Calcium supplementation may be beneficial in optimizing bone health in GnRH analog–treated individuals (104). There are no studies of vitamin D supplementation in this context, but clinicians should offer supplements to vitamin D–deficient adolescents. Physical activity, especially during growth, is important for bone mass in healthy individuals (103) and is therefore likely to be beneficial for bone health in GnRH analog–treated subjects.

GnRH analogs did not induce a change in body mass index standard deviation score in GD/gender-incongruent adolescents (94) but caused an increase in fat mass and decrease in lean body mass percentage (92). Studies in girls treated for precocious puberty also reported a stable body mass index standard deviation score during treatment (72) and body mass index and body composition comparable to controls after treatment (73).

Arterial hypertension has been reported as an adverse effect in a few girls treated with GnRH analogs for precocious/early puberty (105, 106). Blood pressure monitoring before and during treatment is recommended.

Individuals may also experience hot flashes, fatigue, and mood alterations as a consequence of pubertal suppression. There is no consensus on treatment of these side effects in this context.

It is recommended that any use of pubertal blockers (and subsequent use of sex hormones, as detailed below) include a discussion about implications for fertility (see recommendation 1.3). Transgender adolescents may

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want to preserve fertility, which may be otherwise compromised if puberty is suppressed at an early stage and the individual completes phenotypic transition with the use of sex hormones.

Limited data are available regarding the effects of GnRH analogs on brain development. A single cross-sectional study demonstrated no compromise of executive function (107), but animal data suggest there may be an effect of GnRH analogs on cognitive function (108).

Values and preferences

Our recommendation of GnRH analogs places a higher value on the superior efficacy, safety, and reversibility of the pubertal hormone suppression achieved (as compared with the alternatives) and a relatively lower value on limiting the cost of therapy. Of the available alternatives, depot and oral progestin preparations are effective. Experience with this treatment dates back prior to the emergence of GnRH analogs for treating precocious puberty in papers from the 1960s and early 1970s (109–112). These compounds are usually safe, but some side effects have been reported (113–115). Only two recent studies involved transgender youth (116, 117). One of these studies described the use of oral lynestrenol monotherapy followed by the addition of testosterone treatment in transgender boys who were at Tanner stage B4 or further at the start of treatment (117). They found lynestrenol safe, but gonadotropins were not fully suppressed. The study reported metrorrhagia in approximately half of the individuals, mainly in the first 6 months. Acne, headache, hot flashes, and fatigue were other frequent side effects. Another progestin that has been studied in the United States is medroxyprogesterone. This agent is not as effective as GnRH analogs in lowering endogenous sex hormones either and may be associated with other side effects (116). Progestin preparations may be an acceptable treatment for persons without access to GnRH analogs or with a needle phobia. If GnRH analog treatment is not available (insurance denial, prohibitive cost, or other reasons), postpubertal, transgender female adolescents may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see adult section).

Remarks

Measurements of gonadotropin and sex steroid levels give precise information about gonadal axis suppression, although there is insufficient evidence for any specific short-term monitoring scheme in children treated with GnRH analogs (88). If the gonadal axis is not completely suppressed—as evidenced by (for example) menses, erections, or progressive hair growth—the interval of GnRH analog treatment can be shortened or the dose increased. During treatment, adolescents should be monitored for negative effects of delaying puberty, including a halted growth spurt and impaired bone mineral accretion. Table 7 illustrates a suggested clinical protocol.

Anthropometric measurements and X-rays of the left hand to monitor bone age are informative for evaluating growth. To assess BMD, clinicians can perform dual-energy X-ray absorptiometry scans.

2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule (see Table 8) after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years (Table 5). (1 |⊕⊕◯◯)

2.5. We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5 to 14 years. As with the care of adolescents ≥16 years of age, we recommend that an expert multidisciplinary team of medical and MHPs manage this treatment. (1 |⊕◯◯◯)

2.6. We suggest monitoring clinical pubertal development every 3 to 6 months and laboratory parameters every 6 to 12 months during sex hormone treatment (Table 9). (2 |⊕⊕◯◯)

Table 7. Baseline and Follow-Up Protocol During Suppression of Puberty

Every 3–6 mo
Anthropometry: height, weight, sitting height, blood pressure, Tanner stages
Every 6–12 mo
Laboratory: LH, FSH, E2/T, 25OH vitamin D
Every 1–2 y
Bone density using DXA
Bone age on X-ray of the left hand (if clinically indicated)

Adapted from Hembree *et al.* (118).

Abbreviations: DXA, dual-energy X-ray absorptiometry; E2, estradiol; FSH, follicle stimulating hormone; LH, luteinizing hormone; T, testosterone;

Table 8. Protocol Induction of Puberty

Induction of female puberty with oral 17β-estradiol, increasing the dose every 6 mo:
- 5 μg/kg/d
- 10 μg/kg/d
- 15 μg/kg/d
- 20 μg/kg/d
- Adult dose = 2–6 mg/d
- *In postpubertal transgender female adolescents, the dose of 17β-estradiol can be increased more rapidly:*
  - 1 mg/d for 6 mo
  - 2 mg/d

Induction of female puberty with transdermal 17β-estradiol, increasing the dose every 6 mo (new patch is placed every 3.5 d):
- 6.25–12.5 μg/24 h (cut 25-μg patch into quarters, then halves)
- 25 μg/24 h
- 37.5 μg/24 h
- Adult dose = 50–200 μg/24 h
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological estradiol levels (see Table 15).*

Induction of male puberty with testosterone esters increasing the dose every 6 mo (IM or SC):
- 25 mg/m^2/2 wk (or alternatively, half this dose weekly, or double the dose every 4 wk)
- 50 mg/m^2/2 wk
- 75 mg/m^2/2 wk
- 100 mg/m^2/2 wk
- Adult dose = 100–200 mg every 2 wk
- *In postpubertal transgender male adolescents the dose of testosterone esters can be increased more rapidly:*
  - 75 mg/2 wk for 6 mo
  - 125 mg/2 wk
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological testosterone levels (see Table 14).*

Adapted from Hembree *et al.* (118).

Abbreviations: IM, intramuscularly; SC, subcutaneously.

Evidence

Adolescents develop competence in decision making at their own pace. Ideally, the supervising medical professionals should individually assess this competence, although no objective tools to make such an assessment are currently available.

Many adolescents have achieved a reasonable level of competence by age 15 to 16 years (119), and in many countries 16-year-olds are legally competent with regard to medical decision making (120). However, others believe that although some capacities are generally achieved before age 16 years, other abilities (such as good risk assessment) do not develop until well after 18 years (121). They suggest that health care procedures should be divided along a matrix of relative risk, so that younger adolescents can be allowed to decide about low-risk procedures, such as most diagnostic tests and common therapies, but not about high-risk procedures, such as most surgical procedures (121).

Currently available data from transgender adolescents support treatment with sex hormones starting at age 16 years (63, 122). However, some patients may incur potential risks by waiting until age 16 years. These include the potential risk to bone health if puberty is suppressed

Table 9. Baseline and Follow-up Protocol During Induction of Puberty

Every 3–6 mo
- •Anthropometry: height, weight, sitting height, blood pressure, Tanner stages

Every 6–12 mo
- •In transgender males: hemoglobin/hematocrit, lipids, testosterone, 25OH vitamin D
- •In transgender females: prolactin, estradiol, 25OH vitamin D

Every 1–2 y
- •BMD using DXA
- •Bone age on X-ray of the left hand (if clinically indicated)

BMD should be monitored into adulthood (until the age of 25–30 y or until peak bone mass has been reached).
For recommendations on monitoring once pubertal induction has been completed, see Tables 14 and 15.

Adapted from Hembree *et al.* (118).

Abbreviation: DXA, dual-energy X-ray absorptiometry.

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for 6 to 7 years before initiating sex hormones (*e.g.*, if someone reached Tanner stage 2 at age 9-10 years old). Additionally, there may be concerns about inappropriate height and potential harm to mental health (emotional and social isolation) if initiation of secondary sex characteristics must wait until the person has reached 16 years of age. However, only minimal data supporting earlier use of gender-affirming hormones in transgender adolescents currently exist (63). Clearly, long-term studies are needed to determine the optimal age of sex hormone treatment in GD/gender-incongruent adolescents.

The MHP who has followed the adolescent during GnRH analog treatment plays an essential role in assessing whether the adolescent is eligible to start sex hormone therapy and capable of consenting to this treatment (Table 5). Support of the family/environment is essential. Prior to the start of sex hormones, clinicians should discuss the implications for fertility (see recommendation 1.5). Throughout pubertal induction, an MHP and a pediatric endocrinologist (or other clinician competent in the evaluation and induction of pubertal development) should monitor the adolescent. In addition to monitoring therapy, it is also important to pay attention to general adolescent health issues, including healthy life style choices, such as not smoking, contraception, and appropriate vaccinations (*e.g.*, human papillomavirus).

For the induction of puberty, clinicians can use a similar dose scheme for hypogonadal adolescents with GD/gender incongruence as they use in other individuals with hypogonadism, carefully monitoring for desired and undesired effects (Table 8). In transgender female adolescents, transdermal 17β-estradiol may be an alternative for oral 17β-estradiol. It is increasingly used for pubertal induction in hypogonadal females. However, the absence of low-dose estrogen patches may be a problem. As a result, individuals may need to cut patches to size themselves to achieve appropriate dosing (123). In transgender male adolescents, clinicians can give testosterone injections intramuscularly or subcutaneously (124, 125).

When puberty is initiated with a gradually increasing schedule of sex steroid doses, the initial levels will not be high enough to suppress endogenous sex steroid secretion. Gonadotropin secretion and endogenous production of testosterone may resume and interfere with the effectiveness of estrogen treatment, in transgender female adolescents (126, 127). Therefore, continuation of GnRH analog treatment is advised until gonadectomy. Given that GD/gender-incongruent adolescents may opt not to have gonadectomy, long-term studies are necessary to examine the potential risks of prolonged GnRH analog treatment. Alternatively, in transgender male adolescents, GnRH analog treatment can be discontinued once an adult dose of testosterone has been reached and the individual is well virilized. If uterine bleeding occurs, a progestin can be added. However, the combined use of a GnRH analog (for ovarian suppression) and testosterone may enable phenotypic transition with a lower dose of testosterone in comparison with testosterone alone. If there is a wish or need to discontinue GnRH analog treatment in transgender female adolescents, they may be treated with an antiandrogen that directly suppresses androgen synthesis or action (see section 3.0 "Hormonal Therapy for Transgender Adults").

Values and preferences

The recommendation to initiate pubertal induction only when the individual has sufficient mental capacity (roughly age 16 years) to give informed consent for this partly irreversible treatment places a higher value on the ability of the adolescent to fully understand and oversee the partially irreversible consequences of sex hormone treatment and to give informed consent. It places a lower value on the possible negative effects of delayed puberty. We may not currently have the means to weigh adequately the potential benefits of waiting until around age 16 years to initiate sex hormones vs the potential risks/harm to BMD and the sense of social isolation from having the timing of puberty be so out of sync with peers (128).

Remarks

Before starting sex hormone treatment, effects on fertility and options for fertility preservation should be discussed. Adult height may be a concern in transgender adolescents. In a transgender female adolescent, clinicians may consider higher doses of estrogen or a more rapid tempo of dose escalation during pubertal induction. There are no established treatments yet to augment adult height in a transgender male adolescent with open epiphyses during pubertal induction. It is not uncommon for transgender adolescents to present for clinical services after having completed or nearly completed puberty. In such cases, induction of puberty with sex hormones can be done more rapidly (see Table 8). Additionally, an adult dose of testosterone in transgender male adolescents may suffice to suppress the gonadal axis without the need to use a separate agent. At the appropriate time, the multidisciplinary team should adequately prepare the adolescent for transition to adult care.

3.0 Hormonal Therapy for Transgender Adults

The two major goals of hormonal therapy are (1) to reduce endogenous sex hormone levels, and thus reduce

the secondary sex characteristics of the individual's designated gender, and (2) to replace endogenous sex hormone levels consistent with the individual's gender identity by using the principles of hormone replacement treatment of hypogonadal patients. The timing of these two goals and the age at which to begin treatment with the sex hormones of the chosen gender is codetermined in collaboration with both the person pursuing transition and the health care providers. The treatment team should include a medical provider knowledgeable in transgender hormone therapy, an MHP knowledgeable in GD/gender incongruence and the mental health concerns of transition, and a primary care provider able to provide care appropriate for transgender individuals. The physical changes induced by this sex hormone transition are usually accompanied by an improvement in mental well-being (129, 130).

3.1. We recommend that clinicians confirm the diagnostic criteria of GD/gender incongruence and the criteria for the endocrine phase of gender transition before beginning treatment. (1 |⊕⊕⊕◯)

3.2. We recommend that clinicians evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment (Table 10). (1 |⊕⊕⊕◯)

3.3. We suggest that clinicians measure hormone levels during treatment to ensure that endogenous sex steroids are suppressed and administered sex steroids are maintained in the normal physiologic range for the affirmed gender. (2 |⊕⊕◯◯)

Evidence

It is the responsibility of the treating clinician to confirm that the person fulfills criteria for treatment. The treating clinician should become familiar with the terms and criteria presented in Tables 1–5 and take a thorough history from the patient in collaboration with the other members of the treatment team. The treating clinician must ensure that the desire for transition is appropriate; the consequences, risks, and benefits of treatment are well understood; and the desire for transition persists. They also need to discuss fertility preservation options (see recommendation 1.3) (67, 68).

Transgender males

Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males (Appendix A) (113, 114, 131–134). Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism (135). Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range (this is dependent on the specific assay, but is typically 320 to 1000 ng/dL) (Table 11) (136). Sustained supraphysiologic levels of testosterone increase the risk of adverse reactions (see section 4.0 "Adverse Outcome Prevention and Long-Term Care") and should be avoided.

Similar to androgen therapy in hypogonadal men, testosterone treatment in transgender males results in increased muscle mass and decreased fat mass, increased facial hair and acne, male pattern baldness in those genetically predisposed, and increased sexual desire (137).

Table 10. Medical Risks Associated With Sex Hormone Therapy

Transgender female: estrogen
Very high risk of adverse outcomes:
•Thromboembolic disease
Moderate risk of adverse outcomes:
•Macroprolactinoma
•Breast cancer
•Coronary artery disease
•Cerebrovascular disease
•Cholelithiasis
•Hypertriglyceridemia
Transgender male: testosterone
Very high risk of adverse outcomes:
•Erythrocytosis (hematocrit > 50%)
Moderate risk of adverse outcomes:
•Severe liver dysfunction (transaminases > threefold upper limit of normal)
•Coronary artery disease
•Cerebrovascular disease
•Hypertension
•Breast or uterine cancer

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Table 11. Hormone Regimens in Transgender Persons

Transgender females[a]	
Estrogen	
Oral	
Estradiol	2.0–6.0 mg/d
Transdermal	
Estradiol transdermal patch (New patch placed every 3–5 d)	0.025–0.2 mg/d
Parenteral	
Estradiol valerate or cypionate	5–30 mg IM every 2 wk 2–10 mg IM every week
Anti-androgens	
Spironolactone	100–300 mg/d
Cyproterone acetate[b]	25–50 mg/d
GnRH agonist	3.75 mg SQ (SC) monthly 11.25 mg SQ (SC) 3-monthly
Transgender males	
Testosterone	
Parenteral testosterone	
Testosterone enanthate or cypionate	100–200 mg SQ (IM) every 2 wk or SQ (SC) 50% per week
Testosterone undecanoate[c]	1000 mg every 12 wk
Transdermal testosterone	
Testosterone gel 1.6%[d]	50–100 mg/d
Testosterone transdermal patch	2.5–7.5 mg/d

Abbreviations: IM, intramuscularly; SQ, sequentially; SC, subcutaneously.

[a]Estrogens used with or without antiandrogens or GnRH agonist.

[b]Not available in the United States.

[c]One thousand milligrams initially followed by an injection at 6 wk then at 12-wk intervals.

[d]Avoid cutaneous transfer to other individuals.

In transgender males, testosterone will result in clitoromegaly, temporary or permanent decreased fertility, deepening of the voice, cessation of menses (usually), and a significant increase in body hair, particularly on the face, chest, and abdomen. Cessation of menses may occur within a few months with testosterone treatment alone, although high doses of testosterone may be required. If uterine bleeding continues, clinicians may consider the addition of a progestational agent or endometrial ablation (138). Clinicians may also administer GnRH analogs or depot medroxyprogesterone to stop menses prior to testosterone treatment.

Transgender females

The hormone regimen for transgender females is more complex than the transgender male regimen (Appendix B). Treatment with physiologic doses of estrogen alone is insufficient to suppress testosterone levels into the normal range for females (139). Most published clinical studies report the need for adjunctive therapy to achieve testosterone levels in the female range (21, 113, 114, 132–134, 139, 140).

Multiple adjunctive medications are available, such as progestins with antiandrogen activity and GnRH agonists (141). Spironolactone works by directly blocking androgens during their interaction with the androgen receptor (114, 133, 142). It may also have estrogenic activity (143). Cyproterone acetate, a progestational compound with antiandrogenic properties (113, 132, 144), is widely used in Europe. 5α-Reductase inhibitors do not reduce testosterone levels and have adverse effects (145).

Dittrich *et al.* (141) reported that monthly doses of the GnRH agonist goserelin acetate in combination with estrogen were effective in reducing testosterone levels with a low incidence of adverse reactions in 60 transgender females. Leuprolide and transdermal estrogen were as effective as cyproterone and transdermal estrogen in a comparative retrospective study (146).

Patients can take estrogen as oral conjugated estrogens, oral 17β-estradiol, or transdermal 17β-estradiol. Among estrogen options, the increased risk of thromboembolic events associated with estrogens in general seems most concerning with ethinyl estradiol specifically (134, 140, 141), which is why we specifically suggest that it not be used in any transgender treatment plan. Data distinguishing among other estrogen options are less well established although there is some thought that oral routes of administration are more thrombogenic due to the "first pass effect" than are transdermal and parenteral routes, and that the risk of thromboembolic events is dose-dependent. Injectable estrogen and sublingual

estrogen may benefit from avoiding the first pass effect, but they can result in more rapid peaks with greater overall periodicity and thus are more difficult to monitor (147, 148). However, there are no data demonstrating that increased periodicity is harmful otherwise.

Clinicians can use serum estradiol levels to monitor oral, transdermal, and intramuscular estradiol. Blood tests cannot monitor conjugated estrogens or synthetic estrogen use. Clinicians should measure serum estradiol and serum testosterone and maintain them at the level for premenopausal females (100 to 200 pg/mL and <50 ng/dL, respectively). The transdermal preparations and injectable estradiol cypionate or valerate preparations may confer an advantage in older transgender females who may be at higher risk for thromboembolic disease (149).

Values

Our recommendation to maintain levels of gender-affirming hormones in the normal adult range places a high value on the avoidance of the long-term complications of pharmacologic doses. Those patients receiving endocrine treatment who have relative contraindications to hormones should have an in-depth discussion with their physician to balance the risks and benefits of therapy.

Remarks

Clinicians should inform all endocrine-treated individuals of all risks and benefits of gender-affirming hormones prior to initiating therapy. Clinicians should strongly encourage tobacco use cessation in transgender females to avoid increased risk of VTE and cardiovascular complications. We strongly discourage the unsupervised use of hormone therapy (150).

Not all individuals with GD/gender incongruence seek treatment as described (*e.g.*, male-to-eunuchs and individuals seeking partial transition). Tailoring current protocols to the individual may be done within the context of accepted safety guidelines using a multidisciplinary approach including mental health. No evidence-based protocols are available for these groups (151). We need prospective studies to better understand treatment options for these persons.

3.4. We suggest that endocrinologists provide education to transgender individuals undergoing treatment about the onset and time course of physical changes induced by sex hormone treatment. (2 |⊕○○○)

Evidence

Transgender males

Physical changes that are expected to occur during the first 1 to 6 months of testosterone therapy include cessation of menses, increased sexual desire, increased facial and body hair, increased oiliness of skin, increased muscle, and redistribution of fat mass. Changes that occur within the first year of testosterone therapy include deepening of the voice (152, 153), clitoromegaly, and male pattern hair loss (in some cases) (114, 144, 154, 155) (Table 12).

Transgender females

Physical changes that may occur in transgender females in the first 3 to 12 months of estrogen and antiandrogen therapy include decreased sexual desire, decreased spontaneous erections, decreased facial and body hair (usually mild), decreased oiliness of skin, increased breast tissue growth, and redistribution of fat mass (114, 139, 149, 154, 155, 161) (Table 13). Breast development is generally maximal at 2 years after initiating hormones (114, 139, 149, 155). Over a long period of time, the prostate gland and testicles will undergo atrophy.

Although the time course of breast development in transgender females has been studied (150), precise information about other changes induced by sex hormones is lacking (141). There is a great deal of variability among individuals, as evidenced during pubertal development. We all know that a major concern for transgender females is breast development. If we work with estrogens, the result will be often not what the transgender female expects.

Alternatively, there are transgender females who report an anecdotal improved breast development, mood, or sexual desire with the use of progestogens. However, there have been no well-designed studies of the role of progestogens in feminizing hormone regimens, so the question is still open.

Our knowledge concerning the natural history and effects of different cross-sex hormone therapies on breast

Table 12. Masculinizing Effects in Transgender Males

Effect	Onset	Maximum
Skin oiliness/acne	1–6 mo	1–2 y
Facial/body hair growth	6–12 mo	4–5 y
Scalp hair loss	6–12 mo	—[a]
Increased muscle mass/strength	6–12 mo	2–5 y
Fat redistribution	1–6 mo	2–5 y
Cessation of menses	1–6 mo	—[b]
Clitoral enlargement	1–6 mo	1–2 y
Vaginal atrophy	1–6 mo	1–2 y
Deepening of voice	6–12 mo	1–2 y

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157), Wierckx *et al.* (158).

[a] Prevention and treatment as recommended for biological men.

[b] Menorrhagia requires diagnosis and treatment by a gynecologist.

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Table 13. Feminizing Effects in Transgender Females

Effect	Onset	Maximum
Redistribution of body fat	3–6 mo	2–3 y
Decrease in muscle mass and strength	3–6 mo	1–2 y
Softening of skin/decreased oiliness	3–6 mo	Unknown
Decreased sexual desire	1–3 mo	3–6 mo
Decreased spontaneous erections	1–3 mo	3–6 mo
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 mo	2–3 y
Decreased testicular volume	3–6 mo	2–3 y
Decreased sperm production	Unknown	>3 y
Decreased terminal hair growth	6–12 mo	>3 y[a]
Scalp hair	Variable	—[b]
Voice changes	None	—[c]

Estimates represent clinical observations: Toorians *et al.* (149), Asscheman *et al.* (156), Gooren *et al.* (157).

[a]Complete removal of male sexual hair requires electrolysis or laser treatment or both.

[b]Familial scalp hair loss may occur if estrogens are stopped.

[c]Treatment by speech pathologists for voice training is most effective.

development in transgender females is extremely sparse and based on the low quality of evidence. Current evidence does not indicate that progestogens enhance breast development in transgender females, nor does evidence prove the absence of such an effect. This prevents us from drawing any firm conclusion at this moment and demonstrates the need for further research to clarify these important clinical questions (162).

Values and preferences

Transgender persons have very high expectations regarding the physical changes of hormone treatment and are aware that body changes can be enhanced by surgical procedures (*e.g.*, breast, face, and body habitus). Clear expectations for the extent and timing of sex hormone–induced changes may prevent the potential harm and expense of unnecessary procedures.

4.0 Adverse Outcome Prevention and Long-Term Care

Hormone therapy for transgender males and females confers many of the same risks associated with sex hormone replacement therapy in nontransgender persons. The risks arise from and are worsened by inadvertent or intentional use of supraphysiologic doses of sex hormones, as well as use of inadequate doses of sex hormones to maintain normal physiology (131, 139).

4.1. We suggest regular clinical evaluation for physical changes and potential adverse changes in response to sex steroid hormones and laboratory monitoring of sex steroid hormone levels every 3 months during the first year of hormone therapy for transgender males and females and then once or twice yearly. (2 |⊕⊕◯◯)

Evidence

Pretreatment screening and appropriate regular medical monitoring are recommended for both transgender males and females during the endocrine transition and periodically thereafter (26, 155). Clinicians should monitor weight and blood pressure, conduct physical exams, and assess routine health questions, such as tobacco use, symptoms of depression, and risk of adverse events such as deep vein thrombosis/pulmonary embolism and other adverse effects of sex steroids.

Transgender males

Table 14 contains a standard monitoring plan for transgender males on testosterone therapy (154, 159). Key issues include maintaining testosterone levels in the physiologic normal male range and avoiding adverse events resulting from excess testosterone therapy, particularly erythrocytosis, sleep apnea, hypertension, excessive weight gain, salt retention, lipid changes, and excessive or cystic acne (135).

Because oral 17-alkylated testosterone is not recommended, serious hepatic toxicity is not anticipated with parenteral or transdermal testosterone use (163, 164). Past concerns regarding liver toxicity with testosterone have been alleviated with subsequent reports that indicate the risk of serious liver disease is minimal (144, 165, 166).

Transgender females

Table 15 contains a standard monitoring plan for transgender females on estrogens, gonadotropin suppression, or antiandrogens (160). Key issues include avoiding supraphysiologic doses or blood levels of estrogen that may lead to increased risk for thromboembolic disease, liver dysfunction, and hypertension. Clinicians should monitor serum estradiol levels using laboratories participating in external quality control, as measurements of estradiol in blood can be very challenging (167).

VTE may be a serious complication. A study reported a 20-fold increase in venous thromboembolic disease in a large cohort of Dutch transgender subjects (161). This increase may have been associated with the use of the synthetic estrogen, ethinyl estradiol (149). The incidence decreased when clinicians stopped administering ethinyl estradiol (161). Thus, the use of synthetic estrogens and conjugated estrogens is undesirable because of the inability to regulate doses by measuring serum levels and the risk of thromboembolic disease. In a German gender clinic, deep vein thrombosis occurred in 1 of 60 of transgender females treated with a GnRH analog and oral

Table 14. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Male

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
2. Measure serum testosterone every 3 mo until levels are in the normal physiologic male range:[a]
   a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is 400–700 ng/dL to 400 ng/dL. Alternatively, measure peak and trough levels to ensure levels remain in the normal male range.
   b. For parenteral testosterone undecanoate, testosterone should be measured just before the following injection. If the level is <400 ng/dL, adjust dosing interval.
   c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 h after application).
3. Measure hematocrit or hemoglobin at baseline and every 3 mo for the first year and then one to two times a year. Monitor weight, blood pressure, and lipids at regular intervals.
4. Screening for osteoporosis should be conducted in those who stop testosterone treatment, are not compliant with hormone therapy, or who develop risks for bone loss.
5. If cervical tissue is present, monitoring as recommended by the American College of Obstetricians and Gynecologists.
6. Ovariectomy can be considered after completion of hormone transition.
7. Conduct sub- and periareolar annual breast examinations if mastectomy performed. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

[a] Adapted from Lapauw *et al.* (154) and Ott *et al.* (159).

estradiol (141). The patient who developed a deep vein thrombosis was found to have a homozygous C677 T mutation in the methylenetetrahydrofolate reductase gene. In an Austrian gender clinic, administering gender-affirming hormones to 162 transgender females and 89 transgender males was not associated with VTE, despite an 8.0% and 5.6% incidence of thrombophilia (159). A more recent multinational study reported only 10 cases of VTE from a cohort of 1073 subjects (168). Thrombophilia screening of transgender persons initiating hormone treatment should be restricted to those with a personal or family history of VTE (159). Monitoring D-dimer levels during treatment is not recommended (169).

4.2. We suggest periodically monitoring prolactin levels in transgender females treated with estrogens. (2 l⊕⊕◯◯)

Evidence

Estrogen therapy can increase the growth of pituitary lactrotroph cells. There have been several reports of prolactinomas occurring after long-term, high-dose estrogen therapy (170–173). Up to 20% of transgender females treated with estrogens may have elevations in prolactin levels associated with enlargement of the pituitary gland (156). In most cases, the serum prolactin levels will return to the normal range with a reduction or discontinuation of the estrogen therapy or discontinuation of cyproterone acetate (157, 174, 175).

The onset and time course of hyperprolactinemia during estrogen treatment are not known. Clinicians should measure prolactin levels at baseline and then at least annually during the transition period and every 2 years thereafter. Given that only a few case studies reported prolactinomas, and prolactinomas were not reported in large cohorts of estrogen-treated persons, the risk is likely to be very low. Because the major presenting findings of microprolactinomas (hypogonadism and sometimes gynecomastia) are not apparent in transgender females, clinicians may perform radiologic examinations of the pituitary in those patients whose prolactin levels persistently increase despite stable or reduced estrogen levels. Some transgender individuals receive psychotropic medications that can increase prolactin levels (174).

Table 15. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Female

1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of feminization and for development of adverse reactions.
2. Measure serum testosterone and estradiol every 3 mo.
   a. Serum testosterone levels should be <50 ng/dL.
   b. Serum estradiol should not exceed the peak physiologic range: 100–200 pg/mL.
3. For individuals on spironolactone, serum electrolytes, particularly potassium, should be monitored every 3 mo in the first year and annually thereafter.
4. Routine cancer screening is recommended, as in nontransgender individuals (all tissues present).
5. Consider BMD testing at baseline (160). In individuals at low risk, screening for osteoporosis should be conducted at age 60 years or in those who are not compliant with hormone therapy.

This table presents strong recommendations and does not include lower level recommendations.

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4.3. We suggest that clinicians evaluate transgender persons treated with hormones for cardiovascular risk factors using fasting lipid profiles, diabetes screening, and/or other diagnostic tools. (2 ⊕⊕◯◯)

Evidence

Transgender males

Administering testosterone to transgender males results in a more atherogenic lipid profile with lowered high-density lipoprotein cholesterol and higher triglyceride and low-density lipoprotein cholesterol values (176–179). Studies of the effect of testosterone on insulin sensitivity have mixed results (178, 180). A randomized, open-label uncontrolled safety study of transgender males treated with testosterone undecanoate demonstrated no insulin resistance after 1 year (181, 182). Numerous studies have demonstrated the effects of sex hormone treatment on the cardiovascular system (160, 179, 183, 184). Long-term studies from The Netherlands found no increased risk for cardiovascular mortality (161). Likewise, a meta-analysis of 19 randomized trials in nontransgender males on testosterone replacement showed no increased incidence of cardiovascular events (185). A systematic review of the literature found that data were insufficient (due to very low–quality evidence) to allow a meaningful assessment of patient-important outcomes, such as death, stroke, myocardial infarction, or VTE in transgender males (176). Future research is needed to ascertain the potential harm of hormonal therapies (176). Clinicians should manage cardiovascular risk factors as they emerge according to established guidelines (186).

Transgender females

A prospective study of transgender females found favorable changes in lipid parameters with increased high-density lipoprotein and decreased low-density lipoprotein concentrations (178). However, increased weight, blood pressure, and markers of insulin resistance attenuated these favorable lipid changes. In a meta-analysis, only serum triglycerides were higher at ≥24 months without changes in other parameters (187). The largest cohort of transgender females (mean age 41 years, followed for a mean of 10 years) showed no increase in cardiovascular mortality despite a 32% rate of tobacco use (161).

Thus, there is limited evidence to determine whether estrogen is protective or detrimental on lipid and glucose metabolism in transgender females (176). With aging, there is usually an increase of body weight. Therefore, as with nontransgender individuals, clinicians should monitor and manage glucose and lipid metabolism and blood pressure regularly according to established guidelines (186).

4.4. We recommend that clinicians obtain BMD measurements when risk factors for osteoporosis exist, specifically in those who stop sex hormone therapy after gonadectomy. (1 ⊕⊕◯◯)

Evidence

Transgender males

Baseline bone mineral measurements in transgender males are generally in the expected range for their pretreatment gender (188). However, adequate dosing of testosterone is important to maintain bone mass in transgender males (189, 190). In one study (190), serum LH levels were inversely related to BMD, suggesting that low levels of sex hormones were associated with bone loss. Thus, LH levels in the normal range may serve as an indicator of the adequacy of sex steroid administration to preserve bone mass. The protective effect of testosterone may be mediated by peripheral conversion to estradiol, both systemically and locally in the bone.

Transgender females

A baseline study of BMD reported T scores less than −2.5 in 16% of transgender females (191). In aging males, studies suggest that serum estradiol more positively correlates with BMD than does testosterone (192, 193) and is more important for peak bone mass (194). Estrogen preserves BMD in transgender females who continue on estrogen and antiandrogen therapies (188, 190, 191, 195, 196).

Fracture data in transgender males and females are not available. Transgender persons who have undergone gonadectomy may choose not to continue consistent sex steroid treatment after hormonal and surgical sex reassignment, thereby becoming at risk for bone loss. There have been no studies to determine whether clinicians should use the sex assigned at birth or affirmed gender for assessing osteoporosis (*e.g.*, when using the FRAX tool). Although some researchers use the sex assigned at birth (with the assumption that bone mass has usually peaked for transgender people who initiate hormones in early adulthood), this should be assessed on a case-by-case basis until there are more data available. This assumption will be further complicated by the increasing prevalence of transgender people who undergo hormonal transition at a pubertal age or soon after puberty. Sex for comparison within risk assessment tools may be based on the age at which hormones were initiated and the length of exposure to hormones. In some cases, it may be

reasonable to assess risk using both the male and female calculators and using an intermediate value. Because all subjects underwent normal pubertal development, with known effects on bone size, reference values for birth sex were used for all participants (154).

4.5. We suggest that transgender females with no known increased risk of breast cancer follow breast-screening guidelines recommended for those designated female at birth. (2 ⊕⊕◯◯)

4.6. We suggest that transgender females treated with estrogens follow individualized screening according to personal risk for prostatic disease and prostate cancer. (2 ⊕◯◯◯)

Evidence

Studies have reported a few cases of breast cancer in transgender females (197–200). A Dutch study of 1800 transgender females followed for a mean of 15 years (range of 1 30 years) found one case of breast cancer. The Women's Health Initiative study reported that females taking conjugated equine estrogen without progesterone for 7 years did not have an increased risk of breast cancer as compared with females taking placebo (137).

In transgender males, a large retrospective study conducted at the U.S. Veterans Affairs medical health system identified seven breast cancers (194). The authors reported that this was not above the expected rate of breast cancers in cisgender females in this cohort. Furthermore, they did report one breast cancer that developed in a transgender male patient after mastectomy, supporting the fact that breast cancer can occur even after mastectomy. Indeed, there have been case reports of breast cancer developing in subareolar tissue in transgender males, which occurred after mastectomy (201, 202).

Women with primary hypogonadism (Turner syndrome) treated with estrogen replacement exhibited a significantly decreased incidence of breast cancer as compared with national standardized incidence ratios (203, 204). These studies suggest that estrogen therapy does not increase the risk of breast cancer in the short term (<20 to 30 years). We need long-term studies to determine the actual risk, as well as the role of screening mammograms. Regular examinations and gynecologic advice should determine monitoring for breast cancer.

Prostate cancer is very rare before the age of 40, especially with androgen deprivation therapy (205). Childhood or pubertal castration results in regression of the prostate and adult castration reverses benign prostate hypertrophy (206). Although van Kesteren *et al.* (207) reported that estrogen therapy does not induce hypertrophy or premalignant changes in the prostates of transgender females, studies have reported cases of benign prostatic hyperplasia in transgender females treated with estrogens for 20 to 25 years (208, 209). Studies have also reported a few cases of prostate carcinoma in transgender females (210–214).

Transgender females may feel uncomfortable scheduling regular prostate examinations. Gynecologists are not trained to screen for prostate cancer or to monitor prostate growth. Thus, it may be reasonable for transgender females who transitioned after age 20 years to have annual screening digital rectal examinations after age 50 years and prostate-specific antigen tests consistent with U.S. Preventive Services Task Force Guidelines (215).

4.7. We advise that clinicians determine the medical necessity of including a total hysterectomy and oophorectomy as part of gender-affirming surgery. (Ungraded Good Practice Statement)

Evidence

Although aromatization of testosterone to estradiol in transgender males has been suggested as a risk factor for endometrial cancer (216), no cases have been reported. When transgender males undergo hysterectomy, the uterus is small and there is endometrial atrophy (217, 218). Studies have reported cases of ovarian cancer (219, 220). Although there is limited evidence for increased risk of reproductive tract cancers in transgender males, health care providers should determine the medical necessity of a laparoscopic total hysterectomy as part of a gender-affirming surgery to prevent reproductive tract cancer (221).

Values

Given the discomfort that transgender males experience accessing gynecologic care, our recommendation for the medical necessity of total hysterectomy and oophorectomy places a high value on eliminating the risks of female reproductive tract disease and cancer and a lower value on avoiding the risks of these surgical procedures (related to the surgery and to the potential undesirable health consequences of oophorectomy) and their associated costs.

Remarks

The sexual orientation and type of sexual practices will determine the need and types of gynecologic care required following transition. Additionally, in certain countries, the approval required to change the sex in a birth certificate for transgender males may be dependent on having a complete hysterectomy. Clinicians should help patients research nonmedical administrative criteria and

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provide counseling. If individuals decide not to undergo hysterectomy, screening for cervical cancer is the same as all other females.

5.0 Surgery for Sex Reassignment and Gender Confirmation

For many transgender adults, genital gender-affirming surgery may be the necessary step toward achieving their ultimate goal of living successfully in their desired gender role. The type of surgery falls into two main categories: (1) those that directly affect fertility and (2) those that do not. Those that change fertility (previously called sex reassignment surgery) include genital surgery to remove the penis and gonads in the male and removal of the uterus and gonads in the female. The surgeries that effect fertility are often governed by the legal system of the state or country in which they are performed. Other gender-conforming surgeries that do not directly affect fertility are not so tightly governed.

Gender-affirming surgical techniques have improved markedly during the past 10 years. Reconstructive genital surgery that preserves neurologic sensation is now the standard. The satisfaction rate with surgical reassignment of sex is now very high (187). Additionally, the mental health of the individual seems to be improved by participating in a treatment program that defines a pathway of gender-affirming treatment that includes hormones and surgery (130, 144) (Table 16).

Surgery that affects fertility is irreversible. The World Professional Association for Transgender Health Standards of Care (222) emphasizes that the "threshold of 18 should not be seen as an indication in itself for active intervention." If the social transition has not been satisfactory, if the person is not satisfied with or is ambivalent about the effects of sex hormone treatment, or if the person is ambivalent about surgery then the individual should not be referred for surgery (223, 224).

Gender-affirming genital surgeries for transgender females that affect fertility include gonadectomy, penectomy, and creation of a neovagina (225, 226). Surgeons often invert the skin of the penis to form the wall of the vagina, and several literatures reviews have reported on outcomes (227). Sometimes there is inadequate tissue to form a full neovagina, so clinicians have revisited using intestine and found it to be successful (87, 228, 229). Some newer vaginoplasty techniques may involve autologuous oral epithelial cells (230, 231).

The scrotum becomes the labia majora. Surgeons use reconstructive surgery to fashion the clitoris and its hood, preserving the neurovascular bundle at the tip of the penis as the neurosensory supply to the clitoris. Some surgeons are also creating a sensate pedicled-spot adding a G spot to the neovagina to increase sensation (232). Most recently, plastic surgeons have developed techniques to fashion labia minora. To further complete the feminization, uterine transplants have been proposed and even attempted (233).

Neovaginal prolapse, rectovaginal fistula, delayed healing, vaginal stenosis, and other complications do sometimes occur (234, 235). Clinicians should strongly remind the transgender person to use their dilators to maintain the depth and width of the vagina throughout the postoperative period. Genital sexual responsivity and other aspects of sexual function are usually preserved following genital gender-affirming surgery (236, 237).

Ancillary surgeries for more feminine or masculine appearance are not within the scope of this guideline. Voice therapy by a speech language pathologist is available to transform speech patterns to the affirmed gender (148). Spontaneous voice deepening occurs during testosterone treatment of transgender males (152, 238). No studies have compared the effectiveness of speech therapy, laryngeal surgery, or combined treatment.

Breast surgery is a good example of gender-confirming surgery that does not affect fertility. In all females, breast size exhibits a very broad spectrum. For transgender females to make the best informed decision, clinicians should delay breast augmentation surgery until the patient has completed at least 2 years of estrogen therapy, because the breasts continue to grow during that time (141, 155).

Another major procedure is the removal of facial and masculine-appearing body hair using either electrolysis or

Table 16. Criteria for Gender-Affirming Surgery, Which Affects Fertility

1. Persistent, well-documented gender dysphoria
2. Legal age of majority in the given country
3. Having continuously and responsibly used gender-affirming hormones for 12 mo (if there is no medical contraindication to receiving such therapy)
4. Successful continuous full-time living in the new gender role for 12 mo
5. If significant medical or mental health concerns are present, they must be well controlled
6. Demonstrable knowledge of all practical aspects of surgery (*e.g.*, cost, required lengths of hospitalizations, likely complications, postsurgical rehabilitation)

laser treatments. Other feminizing surgeries, such as that to feminize the face, are now becoming more popular (239–241).

In transgender males, clinicians usually delay gender-affirming genital surgeries until after a few years of androgen therapy. Those surgeries that affect fertility in this group include oophorectomy, vaginectomy, and complete hysterectomy. Surgeons can safely perform them vaginally with laparoscopy. These are sometimes done in conjunction with the creation of a neopenis. The cosmetic appearance of a neopenis is now very good, but the surgery is multistage and very expensive (242, 243). Radial forearm flap seems to be the most satisfactory procedure (228, 244). Other flaps also exist (245). Surgeons can make neopenile erections possible by reinervation of the flap and subsequent contraction of the muscle, leading to stiffening of the neopenis (246, 247), but results are inconsistent (248). Surgeons can also stiffen the penis by imbedding some mechanical device (*e.g.*, a rod or some inflatable apparatus) (249, 250). Because of these limitations, the creation of a neopenis has often been less than satisfactory. Recently, penis transplants are being proposed (233).

In fact, most transgender males do not have any external genital surgery because of the lack of access, high cost, and significant potential complications. Some choose a metaoidioplasty that brings forward the clitoris, thereby allowing them to void in a standing position without wetting themselves (251, 252). Surgeons can create the scrotum from the labia majora with good cosmetic effect and can implant testicular prostheses (253).

The most important masculinizing surgery for the transgender male is mastectomy, and it does not affect fertility. Breast size only partially regresses with androgen therapy (155). In adults, discussions about mastectomy usually take place after androgen therapy has started. Because some transgender male adolescents present after significant breast development has occurred, they may also consider mastectomy 2 years after they begin androgen therapy and before age 18 years. Clinicians should individualize treatment based on the physical and mental health status of the individual. There are now newer approaches to mastectomy with better outcomes (254, 255). These often involve chest contouring (256). Mastectomy is often necessary for living comfortably in the new gender (256).

5.1. We recommend that a patient pursue genital gender-affirming surgery only after the MHP and the clinician responsible for endocrine transition therapy both agree that surgery is medically necessary and would benefit the patient's overall health and/or well-being. (1 ⊕⊕◯◯)

5.2. We advise that clinicians approve genital gender-affirming surgery only after completion of at least 1 year of consistent and compliant hormone treatment, unless hormone therapy is not desired or medically contraindicated. (Ungraded Good Practice Statement)

5.3. We advise that the clinician responsible for endocrine treatment and the primary care provider ensure appropriate medical clearance of transgender individuals for genital gender-affirming surgery and collaborate with the surgeon regarding hormone use during and after surgery. (Ungraded Good Practice Statement)

5.4. We recommend that clinicians refer hormone-treated transgender individuals for genital surgery when: (1) the individual has had a satisfactory social role change, (2) the individual is satisfied about the hormonal effects, and (3) the individual desires definitive surgical changes. (1 ⊕◯◯◯)

5.5. We suggest that clinicians delay gender-affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least 18 years old or legal age of majority in his or her country. (2 ⊕⊕◯◯).

5.6. We suggest that clinicians determine the timing of breast surgery for transgender males based upon the physical and mental health status of the individual. There is insufficient evidence to recommend a specific age requirement. (2 ⊕◯◯◯)

Evidence

Owing to the lack of controlled studies, incomplete follow-up, and lack of valid assessment measures, evaluating various surgical approaches and techniques is difficult. However, one systematic review including a large numbers of studies reported satisfactory cosmetic and functional results for vaginoplasty/neovagina construction (257). For transgender males, the outcomes are less certain. However, the problems are now better understood (258). Several postoperative studies report significant long-term psychological and psychiatric pathology (259–261). One study showed satisfaction with breasts, genitals, and femininity increased significantly and showed the importance of surgical treatment as a key therapeutic option for transgender females (262). Another analysis demonstrated that, despite the young average age at death following surgery and the relatively larger number of individuals with somatic morbidity, the study does not allow for determination of

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causal relationships between, for example, specific types of hormonal or surgical treatment received and somatic morbidity and mortality (263). Reversal surgery in regretful male-to-female transsexuals after sexual reassignment surgery represents a complex, multistage procedure with satisfactory outcomes. Further insight into the characteristics of persons who regret their decision postoperatively would facilitate better future selection of applicants eligible for sexual reassignment surgery. We need more studies with appropriate controls that examine long-term quality of life, psychosocial outcomes, and psychiatric outcomes to determine the long-term benefits of surgical treatment.

When a transgender individual decides to have gender-affirming surgery, both the hormone prescribing clinician and the MHP must certify that the patient satisfies criteria for gender-affirming surgery (Table 16).

There is some concern that estrogen therapy may cause an increased risk for venous thrombosis during or following surgery (176). For this reason, the surgeon and the hormone-prescribing clinician should collaborate in making a decision about the use of hormones before and following surgery. One study suggests that preoperative factors (such as compliance) are less important for patient satisfaction than are the physical postoperative results (56). However, other studies and clinical experience dictate that individuals who do not follow medical instructions and do not work with their physicians toward a common goal do not achieve treatment goals (264) and experience higher rates of postoperative infections and other complications (265, 266). It is also important that the person requesting surgery feels comfortable with the anatomical changes that have occurred during hormone therapy. Dissatisfaction with social and physical outcomes during the hormone transition may be a contraindication to surgery (223).

An endocrinologist or experienced medical provider should monitor transgender individuals after surgery. Those who undergo gonadectomy will require hormone replacement therapy, surveillance, or both to prevent adverse effects of chronic hormone deficiency.

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Correspondence and Reprint Requests: The Endocrine Society, 2055 L Street NW, Suite 600, Washington, DC 20036. E-mail: publications@endocrine.org; Phone: 202971-3636.

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Exhibit
SL 17

Pediatric Obesity—Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline

Dennis M. Styne,[1] Silva A. Arslanian,[2] Ellen L. Connor,[3] Ismaa Sadaf Farooqi,[4] M. Hassan Murad,[5] Janet H. Silverstein,[6] and Jack A. Yanovski[7]

[1]University of California Davis, Sacramento, California 95817; [2]University of Pittsburgh, Pittsburgh, Pennsylvania 15224; [3]University of Wisconsin, Madison, Wisconsin 53792; [4]University of Cambridge, Cambridge CB2 0QQ, United Kingdom; [5]Mayo Clinic, Rochester, Minnesota 55905; [6]University of Florida, Gainesville, Florida 32607; and [7]National Institutes of Health, Bethesda, Maryland 20892

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Objective: To formulate clinical practice guidelines for the assessment, treatment, and prevention of pediatric obesity.

Participants: The participants include an Endocrine Society–appointed Task Force of 6 experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The Task Force commissioned 2 systematic reviews and used the best available evidence from other published systematic reviews and individual studies.

Consensus Process: One group meeting, several conference calls, and e-mail communications enabled consensus. Endocrine Society committees and members and co-sponsoring organizations reviewed and commented on preliminary drafts of this guideline.

Conclusion: Pediatric obesity remains an ongoing serious international health concern affecting ~17% of US children and adolescents, threatening their adult health and longevity. Pediatric obesity has its basis in genetic susceptibilities influenced by a permissive environment starting *in utero* and extending through childhood and adolescence. Endocrine etiologies for obesity are rare and usually are accompanied by attenuated growth patterns. Pediatric comorbidities are common and long-term health complications often result; screening for comorbidities of obesity should be applied in a hierarchal, logical manner for early identification before more serious complications result. Genetic screening for rare syndromes is indicated only in the presence of specific historical or physical features. The psychological toll of pediatric obesity on the individual and family necessitates screening for mental health issues and counseling as indicated. The prevention of pediatric obesity by promoting healthful diet, activity, and environment should be a primary goal, as achieving effective, long-lasting results with lifestyle modification once obesity occurs is difficult. Although some behavioral and pharmacotherapy studies report modest success, additional research into accessible and effective methods for preventing and treating pediatric obesity is needed. The use of weight loss medications during childhood and adolescence should be restricted to clinical trials. Increasing evidence

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Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CVD, cardiovascular disease; FDA, Food and Drug Administration; GH, growth hormone; HbA1c, hemoglobin A1c; LAGB, laparoscopic adjustable gastric banding; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; QOL, quality of life; RCT, randomized controlled trial; RYGB, Roux-en-Y gastric bypass; T2DM, type 2 diabetes mellitus; VSG, vertical sleeve gastrectomy; WHO, World Health Organization.

demonstrates the effectiveness of bariatric surgery in the most seriously affected mature teenagers who have failed lifestyle modification, but the use of surgery requires experienced teams with resources for long-term follow-up. Adolescents undergoing lifestyle therapy, medication regimens, or bariatric surgery for obesity will need cohesive planning to help them effectively transition to adult care, with continued necessary monitoring, support, and intervention. Transition programs for obesity are an uncharted area requiring further research for efficacy. Despite a significant increase in research on pediatric obesity since the initial publication of these guidelines 8 years ago, further study is needed of the genetic and biological factors that increase the risk of weight gain and influence the response to therapeutic interventions. Also needed are more studies to better understand the genetic and biological factors that cause an obese individual to manifest one comorbidity vs another or to be free of comorbidities. Furthermore, continued investigation into the most effective methods of preventing and treating obesity and into methods for changing environmental and economic factors that will lead to worldwide cultural changes in diet and activity should be priorities. Particular attention to determining ways to effect systemic changes in food environments and total daily mobility, as well as methods for sustaining healthy body mass index changes, is of importance. (***J Clin Endocrinol Metab* 102: 709–757, 2017**)

Summary of Recommendations

1.0 Diagnosing overweight and obesity

1.1 We recommend using body mass index (BMI) and the Centers for Disease Control and Prevention (CDC) normative BMI percentiles to diagnose overweight or obesity in children and adolescents ≥2 years of age. (1|⊕⊕⊕◯)

1.2 We recommend diagnosing a child or adolescent >2 years of age as overweight if the BMI is ≥85th percentile but <95th percentile for age and sex, as obese if the BMI is ≥95th percentile, and as extremely obese if the BMI is ≥120% of the 95th percentile or ≥35 kg/m^2 (1|⊕⊕◯◯). We suggest that clinicians take into account that variations in BMI correlate differently to comorbidities according to race/ethnicity and that increased muscle mass increases BMI. (2|⊕◯◯◯)

1.3 We suggest calculating, plotting, and reviewing a child's or adolescent's BMI percentile at least annually during well-child and/or sick-child visits. (Ungraded Good Practice Statement)

1.4 We suggest that a child <2 years of age be diagnosed as obese if the sex-specific weight for recumbent length is ≥97.7th percentile on the World Health Organization (WHO) charts, as US and international pediatric groups accept this method as valid. (2|⊕◯◯◯)

1.5 We recommend against routine laboratory evaluations for endocrine etiologies of pediatric obesity unless the patient's stature and/or height velocity are attenuated (assessed in relationship to genetic/familial potential and pubertal stage). (1|⊕⊕⊕◯)

1.6 We recommend that children or adolescents with a BMI of ≥85th percentile be evaluated for potential comorbidities (see Table 2 and Fig. 1). (1|⊕⊕⊕◯)

1.7 We recommend against measuring insulin concentrations when evaluating children or adolescents for obesity. (1|⊕⊕⊕◯)

2.0 Genetic obesity syndromes

2.1 We suggest genetic testing in patients with extreme early onset obesity (before 5 years of age) and that have clinical features of genetic obesity syndromes (in particular extreme hyperphagia) and/or a family history of extreme obesity. (2|⊕⊕◯◯)

3.0 Prevention of obesity

3.1 We suggest that clinicians promote and participate in the ongoing healthy dietary and activity education of children and adolescents, parents, and communities, and encourage schools to provide adequate education about healthy eating (1). (2|⊕◯◯◯)

3.2 We recommend that clinicians prescribe and support healthy eating habits such as:

- avoiding the consumption of calorie-dense, nutrient-poor foods (*e.g.*, sugar-sweetened beverages, sports drinks, fruit drinks, most "fast foods" or those with added table sugar, high-fructose corn syrup, high-fat or high-sodium processed foods, and calorie-dense snacks)
- encouraging the consumption of whole fruits rather than fruit juices. (1|⊕⊕◯◯)

3.3 We recommend that children and adolescents engage in at least 20 minutes, optimally 60 minutes, of vigorous physical activity at least 5 days per week to improve metabolic health and reduce the likelihood of developing obesity. (1|⊕⊕◯◯)

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3.4 We suggest fostering healthy sleep patterns in children and adolescents to decrease the likelihood of developing obesity due to changes in caloric intake and metabolism related to disordered sleep. (2|⊕⊕◯◯)

3.5 We recommend balancing unavoidable technology-related screen time in children and adolescents with increased opportunities for physical activity. (1|⊕⊕◯◯)

3.6 We suggest that a clinician's obesity prevention efforts enlist the entire family rather than only the individual patient. (2|⊕◯◯◯)

3.7 We suggest that clinicians assess family function and make appropriate referrals to address family stressors to decrease the development of obesity. (2|⊕⊕◯◯)

3.8 We suggest using school-based programs and community engagement in pediatric obesity prevention. (2|⊕⊕◯◯)

3.9 We recommend using comprehensive behavior-changing interventions to prevent obesity. Such programs would be integrated with school- or community-based programs to reach the widest audience. (1|⊕⊕◯◯)

3.10 We recommend breast-feeding in infants based on numerous health benefits. However, we can only suggest breast-feeding for the prevention of obesity, as evidence supporting the association between breast-feeding and subsequent obesity is inconsistent. (2|⊕◯◯◯)

4.0 Treating obesity

Lifestyle: general considerations

4.1 We recommend that clinicians prescribe and support intensive, age-appropriate, culturally sensitive, family-centered lifestyle modifications (dietary, physical activity, behavioral) to promote a decrease in BMI. (1|⊕⊕⊕◯)

4.2 We recommend that clinicians prescribe and support healthy eating habits in accordance with the following guidelines of the American Academy of Pediatrics and the US Department of Agriculture:

- decreased consumption of fast foods
- decreased consumption of added table sugar and elimination of sugar-sweetened beverages
- decreased consumption of high-fructose corn syrup and improved labeling of foods containing high-fructose corn syrup
- decreased consumption of high-fat, high-sodium, or processed foods
- consumption of whole fruit rather than fruit juices
- portion control education
- reduced saturated dietary fat intake for children and adolescents >2 years of age
- US Department of Agriculture recommended intake of dietary fiber, fruits, and vegetables
- timely, regular meals, and avoiding constant "grazing" during the day, especially after school and after supper
- recognizing eating cues in the child's or adolescent's environment, such as boredom, stress, loneliness, or screen time
- encouraging single portion packaging and improved food labeling for easier use by consumers. (Ungraded Good Practice Statement)

4.3 We recommend that clinicians prescribe and support the reduction of inactivity and also a minimum of 20 minutes of moderate to vigorous physical activity daily, with a goal of 60 minutes, all in the context of a calorie-controlled diet. (1|⊕⊕◯◯)

4.4 We suggest that clinicians encourage and support patients to limit nonacademic screen time to 1 to 2 hours per day and decrease other sedentary behaviors, such as digital activities. (2|⊕◯◯◯)

4.5 We suggest that the health care team identify maladaptive rearing patterns related to diet and activity and educate families about healthy food and exercise habits. (2|⊕◯◯◯)

4.6 We suggest that the health care team probe for and diagnose unhealthy intrafamily communication patterns and support rearing patterns that seek to enhance the child's or adolescent's self-esteem. (2|⊕◯◯◯)

4.7 We suggest that the health care team evaluate for psychosocial comorbidities and prescribe assessment and counseling when psychosocial problems are suspected. (2|⊕◯◯◯)

4.8 We suggest pharmacotherapy for children or adolescents with obesity only after a formal program of intensive lifestyle modification has failed to limit weight gain or to ameliorate comorbidities (2|⊕◯◯◯). We recommend against using obesity medications in children and adolescents <16 years of age who are overweight but not obese, except in the context of clinical trials. (1|⊕◯◯◯)

4.9 We suggest that Food and Drug Administration (FDA)–approved pharmacotherapy for obesity be administered only with a concomitant lifestyle modification program of the highest intensity available and only by clinicians who are experienced in the use of anti-obesity agents and are

aware of the potential for adverse reactions. (2|⊕○○○)

4.10 We suggest that clinicians should discontinue medication and reevaluate the patient if the patient does not have a >4% BMI/BMI *z* score reduction after taking antiobesity medication for 12 weeks at the medication's full dosage. (2|⊕○○○)

4.11 We suggest bariatric surgery only under the following conditions:

- the patient has attained Tanner 4 or 5 pubertal development and final or near-final adult height, the patient has a BMI of >40 kg/m^2 or has a BMI of >35 kg/m^2 and significant, extreme comorbidities
- extreme obesity and comorbidities persist despite compliance with a formal program of lifestyle modification, with or without pharmacotherapy
- psychological evaluation confirms the stability and competence of the family unit [psychological distress due to impaired quality of live (QOL) from obesity may be present, but the patient does not have an underlying untreated psychiatric illness]
- the patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits
- there is access to an experienced surgeon in a pediatric bariatric surgery center of excellence that provides the necessary infrastructure for patient care, including a team capable of long-term follow-up of the metabolic and psychosocial needs of the patient and family. (2|⊕⊕○○)

4.12 We suggest against bariatric surgery in preadolescent children, pregnant or breast-feeding adolescents (and those planning to become pregnant within 2 years of surgery), and in any patient who has not mastered the principles of healthy dietary and activity habits and/or has an unresolved substance abuse, eating disorder, or untreated psychiatric disorder. (2|⊕○○○)

Method of Development of Evidence-Based Clinical Practice Guidelines

The Clinical Guidelines Subcommittee of the Endocrine Society deemed prevention and treatment of pediatric obesity a priority area in need of practice guidelines and appointed a Task Force to formulate evidence-based recommendations. The Task Force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation group, an international group with expertise in the development and implementation of evidence-based guidelines (2). A detailed description of the grading scheme has been published elsewhere (3). The Task Force used the best available research evidence to develop the recommendations. The Task Force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of a recommendation, strong recommendations use the phrase "we recommend" and the number 1, and weak recommendations ue the phrase "we suggest" and the number 2. Cross-filled circles indicate the quality of the evidence, such that ⊕○○○ denotes very low quality evidence; ⊕⊕○○, low quality; ⊕⊕⊕○, moderate quality; and ⊕⊕⊕⊕, high quality. The Task Force has confidence that persons who receive care according to the strong recommendations will derive, on average, more good than harm. Weak recommendations require more careful consideration of the person's circumstances, values, and preferences to determine the best course of action. Linked to each recommendation is a description of the evidence and the values that the Task Force considered in making the recommendation; in some instances, there are remarks, a section in which the Task Force offers technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the Task Force and their values and preferences; therefore, one should consider these remarks as suggestions.

In this guideline, the Task Force made several statements to emphasize the importance of shared decision making, general preventive care measures, and basic principles of pediatric obesity prevention and treatment. They labeled these as "Ungraded Good Practice Statement." Direct evidence for these statements was either unavailable or not systematically appraised, and thus considered out of the scope of this guideline. The intention of these statements is to draw attention and remind providers of these principles; one should not consider these statements as graded recommendations (4).

The Endocrine Society maintains a rigorous conflict-of-interest review process for developing clinical practice guidelines. All Task Force members must declare any potential conflicts of interest by completing a conflict-of-interest form. The Clinical Guidelines Subcommittee reviews all conflicts of interest before the Society's Council approves the members to participate on the Task Force and periodically during the development of the guideline. All others participating in the guideline's development must also disclose any conflicts of interest in the matter under study, and most of these participants must be without any conflicts of interest. The Clinical Guidelines Subcommittee and the Task Force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from commercial interests; grants; research support; consulting fees; salary; ownership interests [*e.g.*, stocks and stock options (excluding diversified mutual funds)]; honoraria and other payments for participation in speakers' bureaus, advisory boards, or boards of directors; and all other financial benefits. Completed forms are available through the Endocrine Society office.

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The Endocrine Society provided the funding for this guideline; the Task Force received no funding or remuneration from commercial or other entities.

Commissioned Systematic Review

The Task Force commissioned 2 systematic reviews to support this guideline [Treatments of Pediatric Obesity: An Umbrella Systematic Review (5); The Association of Weight Loss and Cardiometabolic Outcomes in Obese Children: Systematic Review and Meta-Regression (6)]. The first was an umbrella review of randomized controlled trials (RCTs) that had a duration >6 months and evaluated medication, surgery, lifestyle, or community-based interventions in overweight or obese children or adolescents. The purpose of this review was to estimate the effectiveness of these interventions and to rate the quality of supporting evidence. This review summarized data from 133 RCTs enrolling 30,445 patients and provided an evidence profile for each intervention. The second was a study-level meta-regression that identified changes in BMI associated with cardiometabolic changes (lipid panel, liver function tests, systolic blood pressure, diastolic blood pressure, hemoglobin A1c (HbA1c), and fasting blood glucose) in pediatric overweight and obese subjects.

The Problem With Obesity

Pediatric obesity is a persistent, epidemic, international problem, and preventing pediatric obesity and its comorbidities is of paramount importance. Treating children or adolescents is difficult and requires changes in diet, activity, and environment. Intensive lifestyle interventions, contacting both patient and family at least monthly (and weekly if possible) for the first 3 months, and providing dietary and nutritional education, a physical activity prescription, and behavioral therapy are poorly reimbursed, which often impedes these services. Additionally, there is inadequate national and international recognition of the value of addressing global obesity prevention and treatment, and we must work with key policymakers to improve this. Elevated BMI among US children and adolescents 6 to 19 years of age is associated with 1.4 billion dollars of additional health care dollars for outpatient visits and other health care expenditures compared with children and adolescents with normal BMIs (7). The Brookings Institution predicted that if all 12.7 million US children and adolescents with obesity became obese adults, the individual average cost would be >$92,000, and the societal costs during their lifetimes might be >$1.1 trillion (8).

1.0 Diagnosing overweight and obesity

1.1 We recommend using BMI and the CDC normative BMI percentiles to diagnose overweight or obesity in children and adolescents ≥2 years of age. (1|⊕⊕⊕◯)

1.2 We recommend diagnosing a child or adolescent >2 years of age as overweight if the BMI is ≥85th percentile but <95th percentile for age and sex, as obese if the BMI is ≥95th percentile, and as extremely obese if the BMI is ≥120% of the 95th percentile or ≥35 kg/m^2 (1|⊕⊕◯◯). We suggest that clinicians take into account that variations in BMI correlate differently to comorbidities according to race/ethnicity and that increased muscle mass increases BMI. (2|⊕◯◯◯)

1.3 We suggest calculating, plotting, and reviewing a child's or adolescent's BMI percentile at least annually during well-child and/or sick-child visits. (Ungraded Good Practice Statement)

1.4 We suggest that a child <2 years of age be diagnosed as obese if the sex-specific weight for recumbent length is ≥97.7th percentile on the WHO charts, as US and international pediatric groups accept this method as valid. (2|⊕◯◯◯)

Definitions

Children and adolescents ≥2 years of age are diagnosed as overweight if the BMI is ≥85th percentile but <95th percentile and obese if the BMI is ≥95th percentile for age and gender on the revised 2000 CDC charts. A child <2 years of age is obese if the weight for recumbent length is ≥97.7th percentile of WHO growth standards (9). Extreme obesity is defined as a BMI ≥120% of the 95th percentile or ≥35 kg/m^2 (10). A recent proposal suggests redefining this state as class 2 obesity, as it relates to the definition of class 2 obesity in adults; class 3 pediatric obesity is proposed (but not yet fully accepted) to be BMI ≥140% of the 95th percentile or ≥40 kg/m^2, as this is considered to represent an even higher risk group. Class 2 and class 3 obesity are increasing significantly in girls of all ages, most clearly between 6 and 11 years of age, and in boys between 12 and 19 years of age with a nonsignificant trend in boys <12 years of age (11).

Evidence

The CDC BMI charts (12) are the accepted standards for US children and adolescents ≥2 years of age and provide a means for determining changes in pediatric obesity prevalence. The US Preventive Services Task Force found that the BMI of children and adolescents correlates reasonably well to percentile rankings of percent body fat measured by more direct methods (13). However, BMI

cannot differentiate muscle from adipose tissue, and thus cannot differentiate between excess adipose tissue and increased lean muscle mass when classifying a child or adolescent as overweight or obese. Pediatric racial/ethnic differences in the percentage of fat at a specific BMI further complicate BMI measures; for example, non-Hispanic black children and adolescents have a lower percentage body fat than do comparable non-Hispanic whites or Mexican Americans at the same BMI, and they are less likely to have high adiposity (14). Additionally, Singapore Chinese adolescents have a higher percentage fat at the same BMI than do white comparison groups (15). Furthermore, in the 1999–2002 National Health and Nutrition Examination Survey obese male Hispanic adolescents had a higher risk of hepatic steatosis than did girls and other ethnic groups, indicating the limits of BMI alone as a risk factor (16). A systematic review found differences in regional mass and body composition in adults between race/ethnic groups when BMI and height are held constant and further differences within the same gender and race/ethnic group by age (17). Therefore, although we do recommend using BMI in clinical practice, it is not an infallible indicator of overweight or obesity. Clinicians should consult endocrinologists when questions arise.

The prevalence of pediatric overweight and obesity in all racial and ethnic groups increased between the 1960s and 1970s until about 2000 when it leveled off in most groups (Table 1). As of 2014, the prevalence of obesity in subjects 2 to 19 years old is 17%. The reason 17% of the population is above the 95th percentile for age is that the CDC only uses weight data prior to 1980 (using NHANES II data) for ages >6 years (before the obesity epidemic developed) and uses height data up to the end of 1994 (the end of NHANES III data collection) for the stature charts. Some recent data suggest a decrease in the prevalence of overweight and obesity in children <5 years of age, but the durability of this potential decline remains unknown. This trend may be explained by the oversampling of Asian preschoolers in that particular dataset; these children had a lower overall BMI.

Different racial and ethnic populations demonstrate differences in the prevalence of obesity and overweight and in the trajectory of change during the last decades (Table 1). Thus, using these BMI definitions may underestimate risk to the health of pediatric Asian patients. Furthermore, a recent meta-analysis including 53,521 patients between a mean age of 4 to 18 years demonstrated that using these BMI cutoffs led to a specificity of 0.93 but a sensitivity of only 0.73 when compared with reference standard methods for measuring body adiposity, such as dual energy X-ray absorptiometry, hydrostatic weighing, air-displacement plethysmography, isotope dilution, bioelectrical impedance analysis, and skin-fold thickness measurements. This suggests that most children and adolescents diagnosed as obese by BMI do indeed have excess fat, but that a normal BMI is compatible with excess body fat in ~25% of subjects (22). Clinical judgment must augment the definitions of obesity based on BMI alone to determine which children or adolescents are actually overfat.

The odds ratio of adult obesity increases for obese adolescents as they approach 18 years of age. The odds ratio of adult obesity rises progressively with the number of parents who are obese, but the greatest predictive effect of parent obesity is found in infancy regardless of the infant's weight (23). Determining overweight or obesity in young children may also help identify which individuals are most likely to become overweight or obese in adulthood. There is an increase in BMI in the first year followed by a fall and then a second rise in BMI at about 6 years of age (termed the adiposity rebound); an early BMI rebound before 5 years of age carries a higher risk for adult obesity. Recent analysis suggests that BMI (or possibly just height) at 7 years of age may provide equally robust predictive ability (24). Longitudinal data from 7738 participants from the National Center for Educational Statistics, Early Childhood Longitudinal Study, Kindergarten Class of 1998–1999 demonstrated the greatest incidence (new onset) of obesity and overweight between the first to third grades; furthermore, there was a fourfold higher risk for obesity at age 14 years in the subjects overweight in kindergarten. These data support a focus on prevention before 9 years of age (25). However, a longitudinal study of 4884 subjects from the National Longitudinal Survey of Youth, the Population Study of Income Dynamics, and the National Health and Nutrition Evaluation Surveys demonstrated that screening for obesity at 5 years of age would miss 50% of those who became obese by 18 years of age, whereas screening at 15 years of age would miss only 9%; the authors recommend using universal prevention methods instituted at a young age and continuing through childhood and adolescence, rather than focusing only on overweight young children (26). These contrasting study conclusions demonstrate a continued need for research into childhood prediction of obesity.

Values and preferences

The Task Force placed a high value on the ease of calculating BMI and familiarity with this measure among providers and patients over other limitations of using BMI. BMI currently is the most reasonable measure for evaluating overweight and obesity, guiding proper

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Table 1. Prevalence of Pediatric Overweight and Obesity in the United States

	Obesity				Combined Overweight and Obesity		
Age	**1963–1970**	**1999–2000**	**2004**	**2011–2014**	**1999–2000**	**2003–2004**	**2011–2012**
0–23 mo	7.20%	11.60%		8.10%			
2–5 y	5	10.50%	13.90%	8.90%	22.0%	26.50%	22.80%
6–11 y	4.20%	15.30%	18.80%	17.50%	29.8%	37.20%	34.20%
12–19 y	4.60%	15.50%	17.40%	20.50%	30.0%	34.30%	34.50%
2–19 y		13.9%	17.1%	17.0%	28.2%	33.60%	31.80%
12–19 y by race			Hispanic	21.90%	43.3	34.3%	38.1
			Boys	22.4	43.6	37.3%	39.6%
			Girls	221.4	42.9	31.1%	36.5%
			African American	19.50%	39.5	36.5%	39.8%
			Boys	18.40%	35.6	31.4%	37.3%
			Girls	20.70%	43.7	42.1%	42.5%
			White	14.70%	26.2	34.7%	31.2%
			Boys	14.30%	27.4	38.70%	31.5%
			Girls	15.10%	24.8	30.4%	31.0%
			Asian	8.60%	—	—	24.6%
			Boys	11.80%	—	—	33.9%
			Girls	5.30%	—	—	15.0%
			All	16.90%	30.0	34.30%	34.5%
			Boys	16.90%	30.0	36.8%	35.1%
			Girls	17.10%	30.0	31.70%	33.8%

Years of study for all ethnicities are noted under the column headings "Obesity" and "Combined Overweight and Obesity." [Derived from Ogden *et al.*, 2015 (18), Hedley *et al.*, 2004 (19), Ogden *et al.*, 2014 (20), and Ogden *et al.*, 2002 (21).]

management, and determining the need for specialist referral (when values rise toward the extreme). The utility of predicting adult obesity and comorbidities from childhood and adolescent BMI calculations may be somewhat limited, supporting a universal prevention approach to obesity that begins in early childhood.

1.5 We recommend against routine laboratory evaluations for endocrine etiologies of pediatric obesity unless the patient's stature and/or height velocity are attenuated (assessed in relationship to genetic/familial potential and pubertal stage). (1|⊕⊕⊕◯)

Evidence

Endocrine and syndromic disorders as a cause of overweight/obesity are rare in children and adolescents and are associated with additional symptoms (26). The distinguishing feature of endocrine causes of obesity, such as growth hormone (GH) deficiency, hypothyroidism, or Cushing syndrome, is that stature and height velocity are decreased, whereas a normal or increased growth rate generally excludes endocrine causes. However, Albright hereditary osteodystrophy/pseudohypoparathyroidism, although associated with short stature in adolescence, may be associated with increased growth velocity in the first 2 to 3 years of life. Pediatric overweight/obesity is also associated with earlier breast development, pubarche, and menarche in girls, and advanced skeletal development in boys that will lead to increased growth rate (27–30). The evidence is stronger in girls than boys because a subgroup of boys with obesity exhibit delayed testicular development (31). Thus, clinicians should not test for endocrine causes of obesity unless the patient is short relative to genetic potential and has decreased growth velocity against the backdrop of continued weight gain (26, 32).

This rule is not inviolable, however, as acquired hypothalamic obesity is a syndrome of intractable weight gain caused by hypothalamic damage from a tumor or its treatment with surgery or radiotherapy (33). Such patients may have adequate growth velocity even when GH deficient but have tumor-related signs and symptoms or have already undergone tumor treatment.

Values and preferences

The Task Force placed a high value on limiting endocrine assessments for the etiology of pediatric overweight or obesity to those rare patients who are obese and short or with decreased height velocity and placed a low value on the unnecessary diagnostic endocrine laboratory screening of children and adolescents who are obese without other signs or symptoms or contributory neurosurgical history.

Remarks

Clinicians can determine a deceleration in height velocity (as needed to account for the stage of puberty) either by using a height velocity (34) curve normalized for age and/or

stage of puberty or by observing that the patient is crossing height percentile curves downward on the standardized height attainment charts (12) for average-maturing, early-maturing, and late-maturing children (35). Clinicians should refer maturing children who are obese with short stature and decreased growth velocity despite continued weight gain to a pediatric endocrinologist, as these patients may have an endocrinopathy.

1.6 We recommend that children or adolescents with a BMI ≥85th percentile be evaluated for potential comorbidities (see Table 2 and Fig. 1). (1|⊕⊕⊕◯)

1.7 We recommend against measuring insulin concentrations when evaluating children or adolescents for obesity. (1|⊕⊕⊕◯)

Evidence

Pediatric overweight and obesity is associated with substantial comorbidities, including prediabetes/type 2 diabetes mellitus (T2DM); dyslipidemia; prehypertension/hypertension; sleep apnea; nonalcoholic fatty liver disease (NAFLD); proteinuria and focal segmental glomerulosclerosis; early subclinical atherosclerosis; hyperandrogenemia/polycystic ovary syndrome (PCOS); slipped capital femoral epiphysis and pseudotumor cerebri (36–42); and cardiovascular disease (CVD) morbidity, and premature mortality in adulthood (43–47). The greater the severity of obesity, the higher the risks of cardiometabolic risk factors, particularly among boys (11). Importantly, the risks of CVD outcomes among children and adolescents who were obese and became nonobese by adulthood appear similar to those who were never obese (46). Thus, clinicians should carefully examine medical and family histories and laboratory assessments of children and adolescents who are overweight or obese to identify comorbidities early and initiate appropriate management.

Values and preferences

The Task Force placed a high value on identifying adiposity-related complications and screening for comorbidities because of their high prevalence and their association with morbidity and mortality. The Task Force also placed a high value on reducing unnecessary testing and evaluation, such as the routine measurements of fasting insulin, because of lack of scientific evidence for its usefulness in clinical practice by general providers.

Remarks

A thorough medical and family history is crucial for assessing obese youths, because obesity and associated comorbidities may be asymptomatic/subclinical but have familial tendencies. The family history should encompass obesity; bariatric surgery (typically not revealed by families unless specifically asked); T2DM; gestational diabetes; dyslipidemia; hypertension; NAFLD; cirrhosis; sleep apnea and use of continuous positive airway pressure; premature CVD events/deaths (such as heart attacks or strokes); and (in women) infertility, PCOS, or hyperandrogenism-associated signs and symptoms. Clinicians should assess the presence of polyuria/polydipsia, blurry vision, fungal vaginitis/discharge in girls, and unexplained weight loss, all of which could be indicative of hyperglycemia. Clinicians should also look for the presence of frequent unexplained headaches, which raise the possibility of hypertension or sleep apnea; habitual snoring, restless sleep, morning headaches, generalized tiredness, and/or excessive daytime sleepiness, as well as hyperactive inattentive behavior in young children as manifestations of sleep apnea (48); gastrointestinal discomfort as a manifestation of NAFLD (39); musculoskeletal symptoms (49); and (in pubertal girls) acne, hirsutism (including the recent use of hair removal techniques that would mask the degree of hirsutism at the time of the examination), and onset and pattern of menses to screen for the possibility of PCOS. Clinicians should obtain a careful history for psychiatric disorders, because children and adolescents who are overweight or obese are more likely to suffer from mental health disorders than their normal weight counterparts (50, 51). Furthermore, clinicians should obtain a history of second-generation antipsychotics use, such as clozapine, risperidone, olanzapine, and quetiapine, because of their association with weight gain (52, 53). Although the various techniques assessing dietary intake are unreliable and subject to error (9, 54), it is still important to estimate the type and quantity of beverage intake, the frequency of dining out and where, and the frequency and type of snacks (among other dietary issues). Clinicians should also obtain a history of sedentary behaviors, such as hours spent on screen activities, and physical activity (*e.g.*, duration, frequency, in school and at home, sports participation, walking to school and stores).

Clinicians should evaluate the following:

- weight, height, and BMI calculation [Even though the International Diabetes Federation includes waist circumference (an indicator of insulin resistance measured at the level of the iliac crest ≥ 90th percentile) as a defining factor for metabolic syndrome in children and adolescents 10 to 16 years of age and as a finding of concern in children 6 to 10 years old (55, 56), given the intermeasurement variability of waist circumference measurements in a clinical setting performed by different support staff, this research tool does not add significantly to what we learn from BMI (57).]

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Table 2. Screening for Comorbidities of Pediatric Overweight or Obesity

Comorbidity	Tests and Interpretation	Source
Prediabetes HbA1c	5.7% to <6.5% (39 to <48 mmol/mol) (note the unpredictability of this test in pediatrics in the text)[a]	American Diabetes Association (59)
IFG (verify fasting status)	Fasting plasma glucose of ≥100 but <126 mg/dL (≥5.6 but <7.0 mmol/L)	
IGT (if OGTT is used)	Two-hour glucose of ≥140 but <200 mg/dL (≥7.8 but <11.1 mmol/L)	
Diabetes mellitus	HbA1c ≥ 6.5% (≥48 mmol/mol)[a,b] Fasting plasma glucose of ≥126 mg/dL (≥7.0 mmol/L) (fasting is defined as no caloric intake for 8 h)[b] Two-hour plasma glucose of ≥200 mg/dL (≥11.1 mmol/L) during an OGTT[b] In a patient with classic symptoms of hyperglycemia, a random plasma glucose of ≥200 mg/dL	American Diabetes Association (59)
Dyslipidemia	Fasting lipids Triglycerides (mg/dL) (multiply by 0.0113 to convert to mmol/L): 0–9 y < 75 (acceptable), 75–99 (borderline high), ≥100 (high); 10–19 y < 90 (acceptable), 90–129 (borderline high), ≥130 (high) LDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <110 (acceptable), 110–129 (borderline high), ≥130 (high) Total cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <170 (acceptable), 170–199 (borderline high), ≥200 (high) HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <40 (low), 40–45 (borderline low), >45 (acceptable) Non–HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L) (can be nonfasting) <120 (acceptable), 120–144 (borderline high), ≥145 (high)	Expert Panel Summary Report (58)
Prehypertension and hypertension	3–11 y: (standardized according to sex, age, and height percentile) BP > 90th percentile to <95th percentile = prehypertension BP ≥ 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP ≥ 99th percentile + 5 mm Hg = stage 2 HTN 12–17 y: (standardized according to sex, age, and height percentile) BP of >90th percentile to <95th percentile or >120/80 = prehypertension BP ≥ 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP ≥ 99th percentile + 5 mm Hg = stage 2 HTN 18 to 21 y: BP ≥ 120/80 to 139/89 mm Hg = prehypertension BP ≥ 140/90 to 159/99 mm Hg = stage 1 HTN BP ≥ 160/100 to 179/109 mm Hg = stage 2 HTN BP > 180/110 mm Hg = stage 3 HTN	Expert Panel Summary Report (58); Mancia *et al.*, 2013 (61)
NAFLD	ALT > 25 U/L (boys) and >22 U/L (girls)	Schwimmer *et al.*, 2010 (62)
PCOS	Free and total testosterone and SHBG, per Endocrine Society PCOS guidelines[c]	Legro *et al.*, 2013 (63)
Obstructive sleep apnea	If positive history, refer to pulmonary for nocturnal polysomnography and if not available overnight oximetry	Wise *et al.*, 2011 (48)
Psychiatric	If positive history, refer to mental health specialist	Zamethkin *et al.*, 2004 (51)

To convert mg/dL to mmol/L, multiply by 0.0555 for glucose, 0.0259 for cholesterol, and 0.0113 for triglycerides.

Abbreviations: BP, blood pressure; HDL, high-density lipoprotein; HTN, hypertension; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LDL, low-density lipoprotein; NAFLD, non-alcoholic fatty liver disease; OGTT, oral glucose tolerance test (1.75 g/kg, maximum 75 g); PCOS, polycystic ovary syndrome.

[a]The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

[b]In the absence of unequivocal hyperglycemia, should be confirmed by repeat testing.

[c]Given variability in testosterone levels and the poor standardization of assays, it is difficult to define an absolute level that is diagnostic of PCOS or other causes of hyperandrogenism (familiarity with local assays recommended) (63). The preferred assay is HPLC tandem mass spectroscopy (64). [Derived from (a) ADA, 2014 (60); (b) Expert Panel 2011 (58); (c) Schwimmer *et al.*, 2010 (62); (d) Legro *et al.*, 2013 (63); (e) Wise *et al.*, 2011 (48); (f) Zametkin *et al.*, 2004 (51)].

- blood pressure [using height/age/sex percentile normalized blood pressure tables to interpret the findings (58)]
- acanthosis nigricans and skin tags
- extreme acne and hirsutism in pubertal girls
- fundoscopic examination for pseudotumor cerebri
- tenderness and range of motion of the knee, leg, or foot
- peripheral edema, thyroid examination for goiter
- physical findings associated with syndromic obesity, particularly if there is a neurodevelopmental abnormality (see section 3).

We list suggested screening tests in Table 2.

In 2009 an International Expert Committee recommended using HbA1c to diagnose diabetes and prediabetes (65). It recommended classifying asymptomatic individuals as having diabetes if they had HbA1c ≥ 6.5% (≥48 mmol/mol) on 2 separate occasions and classifying asymptomatic individuals with prediabetes if they had HbA1c ≥ 6.0% (≥42 mmol/mol) (65), or HbA1c of 5.7% to <6.5% (39 to <48 mmol/mol) (66). Although they based these recommendations on studies in adults with no validation in pediatrics (65), the committee recommended that the same criteria be applied in adolescents. However, several studies have demonstrated poor performance of HbA1c in diagnosing prediabetes or diabetes in pediatrics, underestimating the prevalence of both (67–69). Another pitfall in using the HbA1c is the unresolved issue of racial/ethnic disparities in the correlation between HbA1c and ambient blood glucose (70). Given such drawbacks, HbA1c screening (alone) in overweight or obese children and adolescents is a poor diagnostic tool for prediabetes and T2DM. Additional definitive testing (fasting or random glucose or oral glucose tolerance test) may be necessary in high-risk youths based on medical history, familial risk, race/ethnicity, and/or the presence of additional risk factors for diabetes (71). In a cost effectiveness analysis of various screening strategies for identifying pediatric diabetes and dysglycemia, the preferred strategy for dysglycemia was the 2-hour oral glucose tolerance test with 100% effectiveness (proportion of cases identified) and efficiency (cost per case identified) at $390 per case, and the least effective and efficient was HbA1c (ranges, 7% to 32% and $938 to $3370 per case) (72).

NAFLD is usually asymptomatic and thus requires screening for detection. Presently, no screening guidelines exist outside of recognizing those at risk by weight categorization (BMI ≥ 85% for age and sex) (39). Recently new normative standards were proposed for alanine aminotransferase (ALT) concentrations (≤25 U/L for boys and ≤ 22U/L for girls) (62), because pediatric liver biopsy specimens from patients with normal or mildly elevated ALT (≥26 to 50 U/L for boys and ≥23 to 44 U/L for girls) had significant histologic abnormalities, including advanced fibrosis (73). Using highly sensitive research methods of magnetic resonance spectroscopy or magnetic resonance imaging, fatty liver is likely present in most pediatric obesity whether the liver enzymes are high or not. High ALT levels would suggest a more advanced stage of NAFLD, hepatitis, or fibrotic changes. Thus, even though ALT elevation underestimates liver injury in NAFLD, it is still an easily available screen for clinicians to use when assessing children and adolescents who are overweight or obese.

Many clinicians measure insulin values thinking it adds to the diagnosis of comorbidities. In fact it does not, and such measurements are not recommended. Although obesity is associated with insulin resistance/hyperinsulinemia, attempts to diagnose insulin resistance by measuring plasma insulin concentration or any other surrogate (74) in the clinical setting has no merit because it has no diagnostic value. Fasting insulin concentrations show considerable overlap between insulin-resistant and insulin-sensitive youths (74). Therefore, there is no well-defined cut point differentiating normal from abnormal and no universally accepted, clinically useful, numeric expression that defines insulin resistance (75), unlike the case for glucose or lipids. A major requirement for any screening program is the availability of an accurate, reliable, reproducible, standardized, and easily applicable method of measurement. Adult studies have shown that measures of fasting insulin explain no more than 5% to 50% of the variability in insulin sensitivity in nondiabetic subjects (76). Different studies have proposed different cutoffs for so called "insulin resistance values" varying by 2.5-fold (76). In pediatrics, the transient puberty-related insulin resistance that occurs with the completion of puberty further complicates this (77, 78). Moreover, measuring insulin is hampered by the lack of standardized insulin assays, and poor reproducibility of even the same assay (79). Further limitations include race/ethnicity-related differences in insulin concentrations due to differences in the metabolic clearance rate of insulin (80) and the cross-reactivity between insulin and proinsulin. In youths with T2DM, despite severe deficiency in insulin secretion, fasting insulin concentrations are higher than in youths without diabetes (81). Importantly, fasting insulin concentrations are similar in youths who are obese with normal glucose tolerance vs impaired glucose tolerance (82), allowing for the possible danger of missing a diagnosis of impaired glucose tolerance if one uses fasting insulin concentrations as a screening tool. Because of these limitations, measuring plasma insulin concentrations remains a research tool with no clinical value for evaluation of obesity. Measuring fasting

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insulin concentrations to try to diagnose insulin resistance within general practice should be abandoned.

2.0 Genetic obesity syndromes

2.1 We suggest genetic testing in patients with extreme early onset obesity (before 5 years of age) and that have clinical features of genetic obesity syndromes (in particular extreme hyperphagia) and/or a family history of extreme obesity. (2|⊕⊕◯◯)

Evidence

In addition to the obvious environmental drivers, multiple common and rare genetic variants contribute to substantial heritability for BMI and waist circumference (83, 84). Approximately 7% of patients with extreme pediatric obesity may have rare chromosomal abnormalities and/or highly penetrant genetic mutations that drive their obesity (85). This percentage is likely to increase with newer methods for genetic testing.

Values and preferences

When assessing children and adolescents with extreme obesity, clinicians should consider potentially treatable causes and genetic conditions (Fig. 1). The diagnosis of a genetic obesity syndrome can provide information that helps the family and health care providers appropriately manage the child's or adolescent's health and possibly lessen the social stigma. Additionally, clinicians can provide genetic counseling. A genetic diagnosis can inform management, including the possibility of bariatric surgery (many such patients are relatively resistant to weight loss through changes in diet and exercise).

Remarks

It is currently useful to categorize genetic obesity syndromes as those with developmental delay and/or dysmorphism and those without these features, although the clinical spectrum can be quite variable (Table 3). Clinicians should obtain a careful family history to identify potential consanguineous relationships, a family history of severe obesity/bariatric surgery, the ethnic and geographical origin of the child or adolescent, and family members to guide the appropriate use of diagnostic tests (Fig. 1).

Obesity syndromes with developmental delay

Dominant disorders

Prader-Willi syndrome is a methylation disorder caused by the deletion of a critical segment on the paternally inherited chromosome 15q11.2-q12, loss of the entire paternal chromosome 15 with the presence of 2 maternal copies (uniparental maternal disomy), or an imprinting defect that can be sporadic or due to a mutation of the paternally derived imprinting control site of the 15q13 region (88). Plasma ghrelin levels are markedly elevated in children, adolescents, and adults with Prader-Willi syndrome, although the physiological relevance of this finding is unknown (89). GH treatments decrease body fat and increase linear growth, muscle mass, and energy expenditure (90).

Maternal transmission of heterozygous mutations in GNAS1 leads to classical Albright hereditary osteodystrophy and resistance to several hormones that activate heterotrimeric G proteins in their target tissues, whereas paternal transmission leads only to Albright hereditary osteodystrophy (91).

Chromosomal rearrangements and heterozygous mutations involving single-minded 1 brain-derived neurotrophic factor (92, 93), or its receptor, TrkB, lead to hyperphagia and developmental and behavioral abnormalities (94, 95). Clinicians should consider *de novo* mutations if both parents are of normal weight and intelligence quotient.

Recessive disorders

Homozygous mutations that disrupt 1/some of the 16 Bardet-Biedl syndrome genes lead to Bardet-Biedl syndrome (96). Other recessive disorders affecting proteins localized to the basal body of the monocilium, such as Alström syndrome and TUB gene mutations (97), are also associated with obesity.

Obesity syndromes without developmental delay

Rare copy number variants (deletions/duplications) that disrupt multiple genes can cause extreme pediatric obesity without learning difficulties (98). Mutations in specific genes, mostly involving the leptin–melanocortin pathway, cause extreme obesity characterized by hyperphagia (increased drive to eat) and impaired satiety (reduced sensation of fullness after a meal) (Table 3). Clinicians should take a careful history to identify food-seeking behavior, searching for/stealing food, waking at night to find food, and eating food others leave behind, which should prompt genetic investigation (neurologic causes should be excluded in patients with a new history of these behaviors). These behaviors typically occur as a result of the disruption of hypothalamic pathways involved in the regulation of energy balance. Pica syndrome is evident in only a small subset of children and adolescents with hyperphagia.

Dominant disorders

Heterozygous mutations in the melanocortin 4 receptor are found in 2% to 5% of subjects with extreme pediatric obesity, making this the most common genetic form of obesity (99, 100) (Table 3). Homozygous mutations in

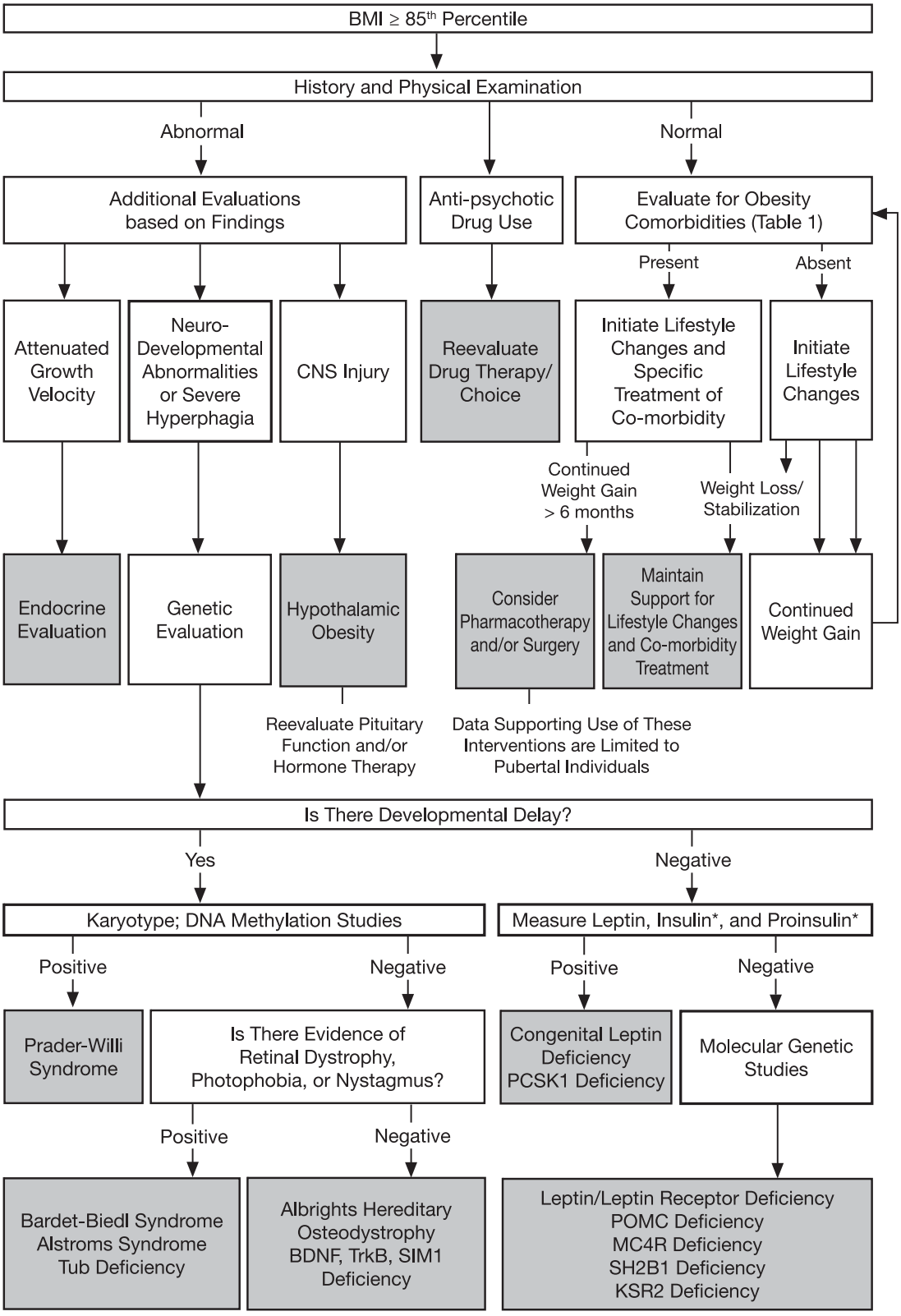

Figure 1. Diagnosis and management flowchart. *Measure insulin and proinsulin in patients with clinical features of PCSK1 deficiency. [Adapted from August GP *et al.* (86) with permission, © Endocrine Society.] [Republished with permission of Springer Science and Bus Media BV from Farooqi S and O'Rahilly S (87); permission conveyed through Copyright Clearance Center, Inc.]

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Table 3. Genetic Obesity Syndromes With and Without Developmental Delay

Genetic Obesity Syndrome	Clinical Features
Obesity with developmental delay	
Dominant	
Prader-Willi syndrome	Hypotonia, failure to thrive in infancy followed by weight gain, short stature (due to GH deficiency), hyperphagia, hypogonadotropic hypogonadism, sleep disturbance, obsessive behaviors
Albright hereditary osteodystrophy	Short stature in some but not all patients, skeletal defects, impaired olfaction, and hormone resistance (*e.g.*, parathyroid hormone) if a mutation is maternally inherited
SIM1 deficiency	Hyperphagia with autonomic dysfunction (characterized by low systolic blood pressure), speech and language delay, neurobehavioral abnormalities, including autistic type behaviors
BDNF/TrkB deficiency	Hyperactivity, impaired concentration, limited attention span, impaired short-term memory and pain sensation
Recessive	
Bardet-Biedl syndrome	Dysmorphic extremities (syndactyly/brachydactyly/polydactyly), retinal dystrophy or pigmentary retinopathy, hypogonadism, renal abnormalities/impairment
TUB deficiency	Retinal dystrophy, deafness
Obesity without developmental delay	
Dominant	
Alström syndrome	Retinal dystrophy; extreme insulin resistance; deafness; dilated cardiomyopathy; progressive pulmonary, hepatic, and renal dysfunction
MC4R deficiency	Hyperphagia, accelerated linear growth, disproportionate hyperinsulinemia, low/normal blood pressure
SH2B1 deficiency	Hyperphagia, disproportionate hyperinsulinemia, early speech and language delay that often resolves, behavioral problems including aggression
KSR2 deficiency	Mild hyperphagia and reduced basal metabolic rate, insulin resistance often with acanthosis nigricans, irregular menses, early development of T2DM
Recessive	
Leptin deficiency	Extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, mild hypothyroidism
Leptin receptor deficiency	Extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, mild hypothyroidism
POMC deficiency	Hyperphagia, cholestatic jaundice or adrenal crisis due to ACTH deficiency, pale skin, and red hair in whites
PCSK1 deficiency	Small bowel enteropathy, hypoglycemia, hypothyroidism, ACTH deficiency, diabetes insipidus

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Abbreviations: ACTH, adrenocorticotropic hormone; BDNF, brain-derived neurotrophic factor; GH, growth hormone; POMC, proopiomelanocortin; T2DM, type 2 diabetes mellitus.

melanocortin 4 receptor have also been identified in offspring from consanguineous families (101). Heterozygous missense mutations affecting proopiomelanocortin-derived peptides and rare variants in melanocortin 2 receptor accessory protein 2 may also contribute to extreme obesity by modulating melanocortin signaling (102, 103). In the near future, selective melanocortin receptor agonists may be feasible therapies for patients with mutations in the melanocortin pathway. Several studies have shown that adolescents and adults with heterozygous melanocortin 4 receptor mutations lose weight following Roux-en-Y gastric bypass (RYGB) surgery (104).

Recessive disorders

Homozygous mutations that reduce the production, secretion, or biological activity of leptin are associated with extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, and mild hypothyroidism; these features can be fully treated with subcutaneous injections of recombinant human leptin (105–107). Recombinant human leptin is currently available on a named patient basis through selected centers.

Serum leptin is a useful test in patients with severe obesity, as undetectable serum leptin is highly suggestive of congenital leptin deficiency. Mutations that result in detectable but bioinactive leptin are rare (107). Serum leptin concentrations are usually appropriate for the degree of obesity in most patients with homozygous mutations in the leptin receptor gene that have comparable clinical features (108) (Table 3).

Children and adolescents who are homozygous or compound heterozygous for mutations in the proopiomelanocortin

gene require long-term corticosteroid replacement, as proopiomelanocortin is a precursor of adrenocorticotropic hormone in the pituitary gland (102). Compound heterozygous or homozygous mutations in the PCSK1 gene, which encodes the processing enzyme (prohormone convertase 1/3), may present in infancy with persistent diarrhea requiring parenteral feeding. An abnormally high level of plasma proinsulin (compared with mature insulin) indicates this possible diagnosis (109).

3.0 Prevention of obesity

The prime objective in addressing the obesity epidemic should be prevention to avoid the comorbidities of obesity. Although beyond the scope of this statement, which addresses postnatal prevention, preconception and prenatal interventions are also of major importance, and the Task Force supports the recommendations of the WHO to address this area of prevention (110).

3.1 We suggest that clinicians promote and participate in the ongoing healthy dietary and activity education of children and adolescents, parents, and communities, and encourage schools to provide adequate education about healthy eating (1). (2|⊕○○○)

Evidence

The authors of the Endocrine Society's previous guideline on pediatric obesity commissioned a meta-analysis (111) which summarized evidence from RCTs that measured the impact of lifestyle interventions to prevent pediatric obesity. The study found modest effects of these interventions; there was decreased sedentary behavior in long-term trials ($P = 0.05$) with a significantly greater effect when directed toward children in contrast to adolescents ($P = 0.02$), reduced unhealthy dietary habits ($P = 0.02$), but only a trend towards increased physical activity ($P = 0.06$–0.07). These beneficial effects did not translate into important changes in BMI (111), but the Task Force recognized that weight maintenance in a growing child or adolescent is as effective as weight loss in an adult. The present committee updated and expanded upon these findings as listed below and in Table 4.

Decreasing caloric intake by consuming more fruits and vegetables and reducing dietary fat and refined carbohydrate intake can decrease the risk of developing obesity and T2DM (152). Many children and adolescents eat fewer than 3 servings of fruits and vegetables a day rather than meeting the US Department of Agriculture dietary recommendation of 5 to 7 fruit and vegetable servings per day. Inadequate consumption of dietary fiber may contribute to excessive weight gain, highlighting the need to continue to address vegetable and whole fruit intake (153). Whole fruit intake increased and fruit juice intake decreased from 2003–2004 to 2009–2010 (154).

Children and adolescents in the public school system in the United States consume up to 40% of their calories at school, so attention to the composition of foods and drinks available to them during the school day is critical (155). New US federal guidelines are encouraging, in that they eliminate trans fat, limit saturated fat, and decrease total sugar content of foods served in schools (156).

Values

The committee places a high value on increasing vegetable and fruit intake to decrease the risk of developing obesity. Calorie-dense, nutrient-poor foods should not be available in the school and school sports environments, where their presence increases their consumption and implies adult assent.

3.2 We recommend that clinicians prescribe and support healthy eating habits such as:

- avoiding the consumption of calorie-dense, nutrient-poor foods (*e.g.*, sugar-sweetened beverages, sports drinks, fruit drinks, most "fast foods" or those with added table sugar, high-fructose corn syrup, high-fat or high-sodium processed foods, and calorie-dense snacks)
- encouraging the consumption of whole fruits rather than fruit juices. (1|⊕⊕○○)

Evidence

Drinking sugar and sugar-sweetened beverages is associated with developing obesity (157, 158). Table sugar consists of 50% glucose and 50% fructose; sugar-sweetened beverages often have a higher percentage of fructose, sometimes up to 65%; and high-fructose corn syrup is found in many foods besides liquid beverages. Metabolic responses differ significantly between fructose and glucose.

Consuming nutrient-poor, calorie-dense, high-fat foods and sugar-sweetened beverages is a risk factor for obesity (156). Reducing sugared-beverage consumption (*e.g.*, soda, fruit drinks, sports drinks, and excessive consumption of fruit juices) is an effective way to reduce ingested calories (159). However, children and adolescents currently consume, on average, 30% to 40% of calories from nutrient-poor, energy-dense foods and drinks (160). Although sugar-sweetened beverage intake is decreasing in younger children, it has actually increased since 2007 in adolescents (161). Fruit juice provides a more concentrated dose of carbohydrates than does whole fruit and may not lead to the feeling of satiety experienced after ingesting whole fruits. Thus, healthy children should limit fruit juice ingestion and children with dental caries or excessive weight should ingest less than the maximal

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recommended volumes. Therefore, fruit juice has no role in the diet of infants under 6 months of age. After 6 months of age, fruit juice must be limited to 4 to 6 ounces per day until children reach 6 years of age, after which 8 to 12 ounces is an acceptable serving, according to the American Academy of Pediatrics policy. In view of the fact that it is easy for children to exceed such limits, the Early Childhood Longitudinal Study—Birth Cohort of >4000 children demonstrated that daily ingestion of fruit juice at 2 years of age resulted in an increase in BMI at 4 years compared with children who had no or infrequent fruit juice. The study also demonstrated that whole fruit provides increased nutritional benefit over juice. This committee encourages the consumption of whole fruits rather than fruit juices (162, 163).

Since 1965, teens have doubled their consumption of sugar-sweetened and fruit-flavored beverages (156, 164). School-based interventions can reduce soda consumption and reduce weight in students at the highest BMI percentiles (152, 165). Although there has reportedly been a 95% decrease in the amount of regular sodas shipped to schools, other sweetened beverages (such as sports drinks) have become more available in schools (166).

However, as of 2014–2015, federal guidelines now restrict the use of such "competitive foods" in the school environment. Obese or normal weight children and adolescents who substituted noncaloric beverages in lieu of sugar-sweetened beverages had less of an increase in BMI at 1 year (115, 116). Because there was no difference in satiety between those who drank sugar-sweetened beverages and those who did not, it appears that a child or adolescent will not compensate for the decreased caloric intake of nonsweetened drinks by increasing his or her caloric intake via other foods or drinks. This lack of compensation may partly explain the reduced weight gain associated with nonsweetened drinks (115, 167).

Although there are reports that reducing glycemic load may have a beneficial effect in the prevention or treatment of obesity, a systematic review of epidemiologic, prospective, and intervention studies did not demonstrate consistent results (168).

Water is frequently recommended as a beneficial replacement for sugar-sweetened beverages. Whereas a systematic review found only a weak association between water consumption and weight control in longitudinal studies, the introduction of water jets to New York City elementary school students led to a 0.022 to 0.025 decrease in BMI and a 0.6% to 0.9% decrease in risk for overweight; this is possibly related to a 12.3% decrease in milk purchases (169). Water remains the most reasonable "drinking" choice for quenching thirst and changing behavior from high-sugar drinking habits (170).

Values

The Task Force placed a high value on decreasing access to sugar-sweetened beverages by children and adolescents as a means of obesity prevention and treatment and a high value on strengthening the message to families that these beverages contribute to pediatric obesity.

Remarks

The costs of comorbidities related to pediatric and adult obesity are spiraling, and we must explore measures to limit nonnutritive excess calories as one means of preventing obesity. No nation can afford the social and financial ramifications of increased obesity incidence left unchecked. The individual practitioner cannot prevent obesity alone; a multidisciplinary health care team including dieticians, mental health practitioners, and nurses provides the optimal setting.

However, the committee agrees with the WHO that such changes must reach beyond the clinical setting and require policy changes at the highest level, as well as the cooperation of commercial entities. The committee supports the suggestion by the WHO for worldwide tax leverage on calorie-dense, nutrient-poor foods (110, 171).

3.3 We recommend that children and adolescents engage in at least 20 minutes, optimally 60 minutes, of vigorous physical activity at least 5 days per week to improve metabolic health and reduce the likelihood of developing obesity. (1|⊕⊕◯◯)

Evidence

A common goal for preventing obesity is to increase physical activity and decrease sedentary time in addition to reducing energy intake. A meta-analysis showed a positive association between sedentary time and the risk for obesity, although the effects were small (172). The 2008 Physical Activity Guidelines for Americans (173) and other sources suggest 1 hour of activity per day for children and adolescents at a minimum; although this is a reasonable aspirational goal, the minimal achievable activity level that produces beneficial effects may be less. Shorter bursts of activity, such as 20 minutes a day 3 to 5 days per week, can improve metabolic measurements in obese children and adolescents in a 3 to 6 month period, and these lower activity levels may also prevent obesity (124). The beneficial effects of exercise are most consistent in the heaviest children and adolescents who previously had not engaged in activity. See Table 4 and section 5 on treatment for more information on how activity and sedentary time affect obesity.

Lack of activity may lead to obesity and overweight, but obesity also decreases the coordination and exercise capacity of affected and adolescents, as well as the

likelihood of being chosen for team sports, resulting in an overall decreased desire for physical activity (174–177).

Values

The Task Force placed a high value on interventions with a low potential for adverse effects and burdens such as increasing physical activity and decreasing sedentary time. The benefits on metabolic fitness are regularly demonstrated, although changes in weight or BMI are less consistent.

3.4 We suggest fostering healthy sleep patterns in children and adolescents to decrease the likelihood of developing obesity due to changes in caloric intake and metabolism related to disordered sleep. (2|⊕⊕◯◯)

Evidence

Disordered sleep length and quality in adults, children, and adolescents affects appetite and decreases insulin sensitivity (150). Table 4 lists 8 studies that show how different sleep durations or changes in sleep duration affect dietary intake in children and adolescents. These results suggest that sleep duration affects obesity development, although 2 other studies challenge these findings, weakening the strength of the evidence (130, 131).

Values

The committee puts a high value on ensuring adequate sleep time for all children and adolescents, although the effect on dietary intake and weight gain is not definitive. The National Sleep Foundation recommends 8 to 11 hours of sleep for school age children and adolescents (178).

3.5 We recommend balancing unavoidable technology-related screen time in children and adolescents with increased opportunities for physical activity. (1|⊕⊕◯◯)

Evidence

A systemic analysis of 24 papers reviewing 15 studies demonstrated strong evidence for decreasing screen time and increasing physical activity to prevent obesity (135); another study reported that decreasing screen time decreases sedentary time (136). A 2-generation study associated increased BMI with >2 hours of screen time per day for both parents and offspring (134). Data from >11,000 preschool children 4 to 6 years of age linked increased caloric intake from snacks and sugar-sweetened beverages to increased screen time (135, 179, 180).

Values

There are frequent requirements for video screen use for schoolwork; as technology becomes more prevalent, such requirements will not decrease. However, the committee put a high value on adhering to the American Academy of Pediatrics guidelines limiting discretionary screen time for children (85, 181).

3.6 We suggest that a clinician's obesity prevention efforts enlist the entire family rather than only the individual patient. (2|⊕◯◯◯)

Evidence

A meta-analysis commissioned by the original Task Force demonstrated a nonsignificant trend associating family involvement with the prevention of obesity, especially if the child is <8 years of age (140, 181).

One recent meta-analysis suggested that family-based therapy is effective for treating obesity (137), and another highlighted the importance of the intensity of parental involvement in the success of family interventions to prevent and treat obesity (138). Furthermore, studies of weight loss in obese children and adolescents demonstrated the importance of including family members in the process; without parental inclusion, the effect on weight loss was not significant (182). However, there is a need for more research into the influence of family participation for the prevention or treatment of pediatric obesity (139, 140, 183). In spite of a general consensus that an authoritative parenting style is optimal and restrictive parenting in terms of food choice is not, there are insufficient data to determine what type of parenting approach is most effective in preventing pediatric obesity (184).

Values

The Task Force placed a high value on involving the entire family in obesity prevention efforts as a practical low-risk approach, while understanding that much of the evidence comes from treatment studies and even those studies are not unanimous on the effects of family intervention.

3.7 We suggest clinicians assess family function and make appropriate referrals to address family stressors to decrease the development of obesity. (2|⊕⊕◯◯)

Evidence

There is evidence for an association between the development of pediatric obesity and family dysfunction as well as exposure to stress (Table 4).

Values

The committee placed a high value on fostering healthy family functioning and minimizing pediatric stress, as

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adverse life events are linked to the development of obesity as well as numerous other complications throughout life.

3.8 We suggest using school-based programs and community engagement in pediatric obesity prevention. (2|⊕⊕◯◯)

Evidence

A school-based program offers the promise of standardization across multiple sites and also can reach large populations of children and adolescents during the early and teenage years.

Numerous school-based interventions focused on reducing obesity rates. The Cardiovascular Health in Children study improved outcomes by decreasing body fat and cholesterol (185). The Cardiovascular Health in Children II study was effective in reducing body fat and blood pressure in middle school children and adolescents (186).

A school-based intervention can reduce body fat and blood pressure in young adolescents (186). One reason the short-term Cardiovascular Health in Children interventions were successful in affecting physiological variables may be the increased time spent in moderate to vigorous physical activity in school (20 minutes per day in elementary schools, 30 minutes in middle schools). Both school design and adult supervision for physical activity affect the amount of physical activity that sixth to eighth graders engage in during free time (187). Additionally, school-based intervention for >4000 middle school children and adolescents at risk for T2DM in the HEALTHY Study Group demonstrated efficacy in decreasing overweight and obesity in both the intervention and control groups, and decreased BMI z score, fasting insulin, prevalence of obesity, and percentage of students with waist circumference > 90th percentile in the intervention group (188). School systems have begun to initiate before- and after-school lifetime fitness programs that appear to be helpful in controlling weight gain (189). As noted, evidence supports prevention efforts in the third grade, which could be carried out in an entire school and preschool environment.

There is moderate evidence that community-based pediatric obesity prevention programs, when combined with a school-based component, can have positive 1-year effects on preventing obesity (145). Community-based participatory research may help enhance school-community involvement, resulting in effective obesity prevention programs (146). A review of multiple settings (early care and education, school, community, health providers, and the home) demonstrated strength for each of these approaches and suggested that a combined approach holds more promise (190).

Values

In making these suggestions, the committee set a high value on the ability of school-based programs to reach a wide population that would benefit from obesity prevention and emphasized the need for additional community-based interventions that used techniques coordinated with a school setting.

3.9 We recommend using comprehensive behavior-changing interventions to prevent obesity. Such programs would be integrated with school- or community-based programs to reach the widest audience. (1|⊕⊕◯◯)

Evidence

A systematic review of RCTs using behavior change techniques to prevent or treat obesity demonstrated that 6 techniques held promise for preventing obesity during a period of at least 6 months. These techniques were:

- providing individualized information on the consequences of behaviors conducive to the development of obesity
- restructuring the environment to make individualized behavior change more successful
- guiding practices expected to decrease the development of obesity
- guiding the identification of role models or advocates to change behavior
- implementing stress management/emotional control training
- providing general communication skills training.

Values

The committee realized the difficulty in providing widespread exposure to behavior change programs but placed a high value on the pursuit of effective techniques of behavior change.

3.10 We recommend breast-feeding in infants based on numerous health benefits. However, we can only suggest breast-feeding for the prevention of obesity, as evidence supporting the association between breast-feeding and subsequent obesity is inconsistent. (1|⊕◯◯◯)

The previous guidelines supported breast-feeding as an effective method of preventing obesity. However, reports on the effect of breast-feeding on preventing obesity are mixed during the last 10 to 15 years. In particular, sibling analyses point to confounding effects

in interpreting the results of cohort studies (151). Furthermore, a 6.5-year-long longitudinal cluster-randomized study of 13,889 subjects demonstrated no effect of breast-feeding on the development of obesity, even among those with more sustained breast-feeding duration (149).

Likewise, 2 meta-analyses showed no strong evidence for the associating between the time of introducing complementary feeding and the development of pediatric overweight or obesity (191, 192).

Values

The committee places high value on promoting breast-feeding to improve infant health but can only suggest breast-feeding as a method for preventing obesity.

Remarks

For most children and adolescents and their families, lifestyle patterns related to eating and exercise are established early, affecting children and adolescents not only when they are young but also throughout life. Health care providers should follow universal prevention methods to avoid the harmful health consequences of less-than-optimal lifestyle choices, conveying to all patients and families in a culturally sensitive and language-appropriate manner the energy needs and essential nutrient requirements of young children, and the importance of physical activity. This is of particular importance when we consider the increased efficacy of prevention trials when directed toward younger children.

The intestinal microflora may influence the development of obesity. Although it is premature to discuss methods of altering the intestinal flora, evidence suggests that *Bacteroides fragilis* is more frequent in the stool of overweight vs normal weight children, adolescents, and adults (193). The intestinal microflora varies between vaginal and cesarean section birth and also due to the composition of early diets, including breast milk. Upcoming results of clinical trials, which modify the microbiome, may suggest new methods of obesity prevention and treatment.

A recent systematic review that looked at the way urban environments affect health behaviors or outcomes for children and adolescents reported some evidence of potential health benefits from urban environment interventions relating to road safety and active travel. However, evidence for the effectiveness of such interventions was weak due to study designs that were opportunistic and nonrandomized, used subjective outcome measures, and did not incorporate follow-up of study participants (194). Nonetheless, health care providers are encouraged to advocate for common sense changes, including providing safe walking/biking areas in parks, school routes, and neighborhoods and providing programs for active play in free time. Environmental change recommendations require additional research with more robust study designs incorporating objective outcome measures to inform meaningful policy change.

4.0 Treating obesity

Lifestyle: general considerations

4.1 We recommend clinicians prescribe and support intensive, age-appropriate, culturally sensitive, family-centered lifestyle modifications (dietary, physical activity, behavioral) to promote a decrease in BMI. (1|⊕⊕⊕◯)

Evidence

The 2015 Endocrine Society Task Force commissioned a systematic review to evaluate the impact of weight change on metabolic outcomes in children and adolescents who are obese (5). The results showed that change in BMI was associated with improvements in triglycerides, high-density lipoprotein, and systolic blood pressure. This analysis is limited by the fact that it used aggregate data. Other studies also showed associations between weight change and other metabolic outcomes (Fig. 2) (195, 196).

Successful weight management, through lifestyle interventions, delays the onset of T2DM in adults (197) and improves cardiovascular fitness (198, 199). Many pediatric weight management programs have found improved body composition and metabolic parameters (13, 200).

A commonly held belief is that lifestyle modification is not sufficiently efficacious. Children and adolescents may not lose weight, or despite initial success, children and adolescents might regain weight after the active phase of the program has ended (201). A factor in weight regain may be lack of continued exercise. The odds for weight regain are twofold greater in those who are sedentary (201). In a 10-year study of adults who participated in the National Weight Control Registry, >87% of participants maintained at least 10% weight loss for 5 to 10 years. A worse outcome was associated with decreased physical activity, decreased dietary restraint, decreased frequency self-weighing, increased energy intake as fat, and increased disinhibition (202).

There is sufficient evidence that intensive lifestyle modification programs can be effective tools for pediatric weight control in the short term (203, 204). Furthermore, implementing a formal maintenance program after the completed treatment phase can be important for

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maintaining achieved weight loss (205). This finding is consistent with the concept of obesity as a chronic disease (206).

A Task Force–commissioned meta-analysis of randomized pediatric trials of combined lifestyle interventions for treating obesity (diet and exercise) showed a modest but significant effect on obesity (equivalent to a decrease in BMI of 1.5 kg/m^2; $P < 0.00001$) when interventions targeted family involvement. When parents were not specifically included, the effect on weight loss was not significant (182). These results suggest involving the family when delivering combined lifestyle interventions.

An additional meta-analysis of RCTs of lifestyle interventions (without an analysis of family involvement) found moderate positive effects from the interventions when compared with no treatment or information-only controls. These effects persisted for an average follow-up period of 15 months (207). Although there was overlap with the Task Force meta-analysis, each study contained reports not covered by the other.

An evidence-based position statement of the American Dietetic Association supports the utility of family-based lifestyle interventions for children and similar multicomponent programs for adolescents (208). These recommendations are consistent with conclusions of a combined CDC and American Medical Association expert committee (209) and an evidence-based review of pharmacological interventions for pediatric obesity that highlighted the importance of concomitant intensive lifestyle interventions, including dietary, exercise, and family counseling (210).

Values and preferences

In making this recommendation, the Task Force placed a high value on promoting healthy, safe pediatric lifestyle modification that included family involvement, with potential wide-reaching benefits.

Remarks

Clinicians should encourage BMI reduction for patients with obesity. A Task Force commissioned meta-analysis demonstrated favorable effects on systolic blood pressure, serum triglycerides, and serum high-density lipoprotein with decreasing BMI or weight (5). When interpreting these data, one must consider that the beneficial effects seen in the 133 RCTs and 16 systematic reviews are for averaged data, not individualized patients; other factors such as age, ethnicity, or genetics may modify individual responses. Very large changes may not be necessary. Although a BMI decrease of 1.5 kg/m^2 (reported in the meta-analysis commissioned by the first Task Force) may seem small, if maintained for the long term, overweight or obese children and adolescents may benefit by maintaining weight as they grow; BMI will decline as linear growth proceeds, and lifestyle modification may reduce fat mass, increase lean body mass, and improve cardiovascular fitness (211). Seven percent weight loss may be a more realistic goal for children and adolescents with extreme obesity. Well-designed RCTs, with large numbers of patients, employing intensive lifestyle intervention and follow-up maintenance programs, will help develop refined techniques. A review of 25 years of behavioral therapy intervention in children and adolescents has demonstrated that long-term weight loss maintenance is possible (212). Other RCTs of diet, physical activity, and/or behavior modification have also demonstrated persistent changes in BMI (212, 213).

Dietary

4.2 We recommend that clinicians prescribe and support healthy eating habits in accordance with the following guidelines of the American Academy of Pediatrics and the US Department of Agriculture:

- decreased consumption of fast foods
- decreased consumption of added table sugar and elimination of sugar-sweetened beverages
- decreased consumption of high-fructose corn syrup and improved labeling of foods containing high-fructose corn syrup
- decreased consumption of high-fat, high-sodium, or processed foods
- consumption of whole fruit rather than fruit juices
- portion control education
- reduced saturated dietary fat intake for children and adolescents >2 years of age
- US Department of Agriculture recommended intake of dietary fiber, fruits, and vegetables
- timely, regular meals, and avoiding constant "grazing" during the day, especially after school and after supper
- recognizing eating cues in the child's or adolescent's environment, such as boredom, stress, loneliness, or screen time
- encouraging single portion packaging and improved food labeling for easier use by consumers. (Ungraded Good Practice Statement)

Evidence

(Refer to section 3.2 for some of the evidence for recommendation 4.2.) Children and adolescents who are overweight are more likely to skip breakfast and consume few large meals per day (214) than do their leaner counterparts who are more likely to consume smaller, more

frequent meals (215). Because snacks tend to be higher in calorie density than meals, frequent snacking (among children and adolescents) is associated with a high intake of fat, sugar, and calories and with overweight (216).

Educating families, children, and adolescents about the need to measure out single snack portions from multiserving packages and place them in single-serving containers can significantly change the amount of food children and adolescents consume (217).

Values and preferences

The committee placed a high value on decreasing snacking and decreasing overall caloric intake to reduce weight gain among children and adolescents.

Remarks

A meta-analysis in children and adolescents suggests that improved weight can be achieved regardless of the macronutrient composition of the diet, and this mirrors similar results found in adults (218). The WHO has recently recommended that adults, children, and adolescents limit sugar to <5% to 10% of total daily energy intake, unless the sugars are contained in fresh fruits and vegetables, which are lower in calories and higher in fiber than processed carbohydrates. The other carbohydrates, which they term "free sugars," include honey; other sweeteners; glucose/fructose; and sugar added by a cook, consumer, or producer. This recommendation was termed "strongly" because of moderate quality evidence that increasing free sugars in one's diet increases body weight, and decreasing free sugars decreases body weight (110).

A dietician familiar with the energy needs of growing children and adolescents should supervise calorie reduction for weight loss or maintenance in patients of this age group. Unbalanced hypocaloric diets (*e.g.*, "fad diets") may be deficient in essential vitamins and minerals.

Physical activity

4.3 We recommend that clinicians prescribe and support the reduction of inactivity and also a minimum of 20 minutes of moderate to vigorous physical activity daily, with a goal of 60 minutes, all in the context of a calorie-controlled diet. (1l⊕⊕○○)

Evidence

In the absence of caloric restriction, moderate exercise does not cause weight loss. However, in combination with decreased caloric intake, exercise can achieve and maintain significant weight loss. Studies performed in the school setting have shown beneficial effects of exercise in children and adolescents (204). The beneficial effects of both aerobic exercise and resistance training can be short-lived, and exercise must be sustained over months. Even 20 minutes of aerobic activity 5 days per week over 13 weeks can decrease body and visceral fat (124). Recent studies in Denmark and elsewhere have demonstrated benefits in mild intensity jogging and in small 10- to 15-minute intervals of exercise, which may be more readily achievable (219, 220).

Physical fitness, even without weight loss, may confer health benefits. Improvements in cardiovascular fitness were associated with improvements in body composition and diabetes risk factors in adolescents (220). In addition to improving metabolic fitness, exercise has been linked to improvements in cognitive function and concentration (124). (Refer to section 4.8 regarding school-based interventions to increase activity.)

Values

The Committee placed a high value on losing weight (in the form of body fat) by decreasing caloric intake and increasing energy expenditure.

Remarks

Although current recommendations state that school children and adolescents (who spend about half their waking hours in school) should receive a minimum of 30 to 60 minutes of moderately vigorous physical activity and at least 60 minutes of aerobic (moderate and vigorous) physical activity each school day, only 5% of school districts in the United States have a requirement for a specific amount of physical education (221–225). Clinicians should place emphasis on increasing a child's or adolescent's activity by helping facilitate:

- the ability to safely walk to and from school
- increased use of stairs (and improved signage to indicate their location)
- increased breaks for movement in the classroom
- increased movement during recess and gym.

Moderate to vigorous exercise is defined as causing some increase in breathing and heart rate; in a healthy person this is usually associated with brisk walking, dancing, swimming, or cycling on flat terrain. In exercise physiology terms, the energy expended should be at least 3 metabolic equivalents (85, 226). Moderate exercise allows talking but not singing, and vigorous exercise makes it impossible to sing and difficult to talk. This generalization should help families understand and identify the difference between moderate and vigorous exercise.

The use of motivational interviews to help an older child or adolescent and/or his or her parent set physical fitness or dietary goals may lead to greater success in

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decreasing BMI (218, 219). In spite of limitations inherent in the method, clinicians should assess a patient's readiness for change when determining how to approach the family.

4.4 We suggest that clinicians encourage and support patients to limit nonacademic screen time to 1 to 2 hours per day and decrease other sedentary behaviors, such as digital activities. (2|⊕○○○)

Evidence

The 2009 Cochrane analysis reported that a combined behavioral approach incorporating both dietary and physical activity changes can produce a significant and clinically meaningful reduction in overweight in children and adolescents (204). A meta-analysis commissioned by the original Task Force of 3 randomized trials of interventions for reducing sedentary activity reported imprecise results (*i.e.*, that these interventions had both a favorable and unfavorable impact on obesity outcomes) (182). Both girls and boys demonstrated small decreases in the amount of screen time in a German study, and these decreases did not correlate with increases in physical activity (227).

Values and preferences

The committee placed a high value on limiting digital access time and other efforts to decrease sedentary time. As our ever-increasing digital environment necessitates increased screen time, a plan for the world's children and adolescents should complement necessary screen time with:

- environments that demand and facilitate movement
- monetary incentives for decreased caloric intake (such as taxes on sugar-sweetened beverages).

The committee agrees with research that finds an association with the presence of a television set in a child's bedroom to increased screen time and increase caloric intake while weakening the positive influence of parents on promotion of healthy habits (228, 229).

Psychological complications of overweight and obesity

Psychosocial

4.5 We suggest that the health care team identify maladaptive rearing patterns related to diet and activity and educate families about healthy food and exercise habits. (2|⊕○○○)

4.6 We suggest that the health care team probe for and diagnose unhealthy intrafamily communication patterns and support rearing patterns that seek to enhance the child's or adolescent's self-esteem. (2|⊕○○○)

4.7 We suggest that the health care team evaluate for psychosocial comorbidities and prescribe assessment and counseling when psychosocial problems are suspected. (2|⊕○○○)

Evidence

In section 4 we discuss the importance of involving the whole family, and not just the child or adolescent, in prevention and treatment interventions.

How interactions between parents and children and adolescents and parenting styles contribute to unhealthy lifestyle habits is a subject of investigation (230, 231). An additional factor to overcome before initiating any intervention may be the parents' inability to recognize that their child or adolescent is overweight, particularly for the preschool child (232–234).

Obesity is associated with QOL, with levels measured in obese children and adolescents equivalent to those seen in pediatric cancer or diabetes (235, 236). In addition to low QOL, children and adolescents with obesity have significant psychosocial comorbidities, including poor self-esteem (237–239), increased risk of depression and anxiety (240–242), and higher-than-average risk of eating disorders and substance abuse. Low self-esteem (243) and perceived or actual higher BMIs are associated with increased likelihood of smoking and alcohol consumption (244).

To remove the bias that might be seen in a clinic sample, the Childhood Growth and Development Study in Australia enrolled healthy weight (n = 158), overweight (n = 77), and obese (n = 27) children from the schools and from families asking to be referred (n = 19). Heights, weights, and psychological testing were done in the schools for the school-based cohort (245). Increasing BMI *z* scores were associated with decreasing self-worth and global self-esteem as well as with decreased athletic competency, social acceptance, and dissatisfaction with their physical appearance. These associations were reported as young as age 8 years, but the association with physical appearance was more pronounced in the older group (246). The presence of psychosocial distress in a population of school children and adolescents not seeking clinic referral, as well as those seeking referral, indicates that psychosocial issues are present in both clinical and nonclinical populations of youths who are obese.

A review of the literature found lower QOL scores for social acceptance, family life, physical appearance, school functioning, and physical functioning in all but 2 of the 34 publications included in the study. Factors influencing lower QOL included degree of obesity, symptoms of

depression, lack of social support from classmates/family, and low socioeconomic status (247).

In general, low self-esteem does not seem to be a significant problem until adolescence, as self-esteem is similar between preteen children who are obese and normal weight. During adolescence, however, self-esteem becomes more closely tied to body image, and rapidly plummets, with those adolescent females who have higher BMIs and body image dissatisfaction having the lowest self-esteem (248).

Individuals with eating disorders tend to define self-worth by their body image (249), possibly explaining the association between eating disorders and youths who are overweight and obese. Surveys from 135 Hispanic and African American girls who are obese or overweight revealed that 52% had been teased about their weight by girls and 60% had been teased about their weight by boys. Of those who were teased, 70% skipped meals, dieted, or starved themselves; 12% reported binge eating; and 33% stated they had "emotional" eating. All of the girls surveyed stated they were unhappy about their weight and wanted to be thinner (250). Eating disorders, including binge eating and anorexia nervosa/bulimia, are more commonly seen in those who have depression, anxiety, and disruptive behavior (251, 252).

Parental reaction to their child's weight affects how the child responds. Bullying by peers and families contributes to poor body image and impaired psychosocial functioning (253).

Some may harass their child, letting them know how unattractive he/she is, resulting in worsening body image and poor self-esteem. A retrospective Internet-based study of college students with great concern about their weight, body shape, and eating behaviors revealed that >80% had a history of parents or siblings making negative comments about their weight, shape, or eating behaviors. Most scored above average in psychometric emotional-abuse tests, with positive associations with negative parental comments and higher weight and negative associations with social support and self-esteem (254). Some parents are overly restrictive, potentially causing their children and adolescents to binge when they have access to unrestricted food (255, 256). Alternatively, adolescents with extreme obesity may develop anorexia bulimia, anorexia nervosa, or purging behaviors in an effort to lose weight. A cross-sectional cohort study of adolescents with extreme obesity and their parents found bulimic symptoms did not correlate with the degree of obesity but were associated with maternal psychopathology, including somatization and anxiety (257).

Youths who are obese are more likely to be teased and bullied and are less likely to have a "best friend" or be considered popular by classmates than their thinner peers (258). Parents, teachers, and peers indicate that youths who are obese are more isolated and have poorer social skills than do their thinner counterparts (259). Those with low self-esteem (243) and perceived or actual higher BMIs are more likely to smoke and drink alcohol than those with higher self-esteem (244). Additionally, they are less athletic and less likely to have romantic relationships, contributing to increased teasing, worsening of self-esteem, loneliness, depression, anxiety, and introverted behavior (260).

In general, those who are most obese report more psychological distress (246, 261). Girls become more depressed with increasing BMI than do boys, and some studies indicate that depression in African American boys is not linked to BMI but rather to peer teasing (246, 262). Race and socioeconomic status (in addition to sex) affect how children and adolescents react to obesity; however, there are conflicting reports on the effect of obesity on psychological status in different groups. One study found that African American children have more body image dissatisfaction and anxiety than do their same-weight white counterparts (262), whereas a study of adolescents found that African Americans and Hispanics are less stigmatized than whites (263). High socioeconomic status adolescents who are obese with psychopathology are less likely to seek help at a weight-loss program than are low socioeconomic status adolescents who are obese (252), possibly due to a more negative perception regarding obesity in high socioeconomic status families.

As adolescents who are obese consistently report high rates of depression, anxiety, and binge eating disorders, all overweight patients should be assessed for psychopathology. Assessment and counseling by a psychologist are often indicated. Clinicians should prescribe antidepressant medications with caution, as atypical antipsychotics cause rapid (often extreme) weight gain (264).

Diuretics, diet pills, and self-induced emesis are not uncommonly used to achieve rapid weight loss by adolescents. One study demonstrated that laxative use, self-induced vomiting, and diet pill ingestion were more common in adolescents who are obese compared with those who are normal weight and overweight (265). Six percent of 6957 middle school children and adolescents in North Carolina used diet pills and 7.1% used laxatives or self-induced vomiting. The case prevalence of diet pills was 3.4 in normal weight, 4.1 in overweight, and 9.5 in adolescents who are obese; the case prevalence of laxatives was 1.3, 0.7, and 3.2, respectively; and the case prevalence of self-induced vomiting was 3.4 in normal weight vs 7.6 in adolescents who are obese. Females more commonly abused substances for weight loss, such as

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tobacco, alcohol, and marijuana; they were also more likely to participate in risky sexual behaviors (265). Clinicians should discuss these maladaptive behaviors at clinic visits, as they are potentially harmful. It is important to emphasize moderation rather than restriction and to counsel against risky weight loss strategies

Remarks

As psychosocial issues are so prevalent, providers should psychologically screen all youths who are obese for the presence of mental health issues, asking questions regarding:

- school absences/refusal
- teasing by peers regarding weight/appearance
- persistent anxiety
- depression/self-harm
- anger outbursts
- sexual activity, alcohol, drug use
- eating disorders—purging, anorexia, binge eating
- family functioning/family attitudes about weight and specifically obesity/parent psychopathology.

Parents and/or children and adolescents should complete a mental health screening measure, such as the Pediatric Symptom Checklist (266). Clinicians can review this during patient visits and refer patients to a mental health professional when indicated. Obesity-related mental health issues are a pervasive problem, and a team-based approach is essential, involving school counselors, nurses, and teachers, as well as health care providers. It might also be helpful to consult with school personnel to initiate school-based counseling. A list of local programs (*e.g.*, YMCA, Boys and Girls Clubs) that offer physical activity programs and healthy snacks is also helpful. Behavioral modification is helpful in determining the child's readiness to change and potential barriers to achieving change (264).

Pharmacotherapy

4.8 We suggest pharmacotherapy for children or adolescents with obesity only after a formal program of intensive lifestyle modification has failed to limit weight gain or to ameliorate comorbidities (2|⊕○○○). We recommend against using obesity medications in children and adolescents <16 years of age who are overweight but not obese, except in the context of clinical trials. (1|⊕○○○)

4.9 We suggest that FDA-approved pharmacotherapy for obesity be administered only with a concomitant lifestyle modification program of the highest intensity available and only by clinicians who are experienced in the use of antiobesity agents and are aware of the potential for adverse reactions. (2|⊕○○○)

4.10 We suggest that clinicians should discontinue medication and re-evaluate the patient if the patient does not have a >4% BMI/BMI *z* score reduction after taking antiobesity medication for 12 weeks at the medication's full dosage. (2|⊕○○○)

Evidence

The FDA recently approved a number of weight-loss medications for adults (216, 267, 268) and considers these medications to be appropriate for those ≥16 years of age who have BMI ≥ 30 kg/m^2 or who have BMI ≥ 27 kg/m^2 and at least 1 weight-related comorbid condition (*e.g.*, hypertension or T2DM). However, although the utility of pharmacotherapy in pediatric obesity has been recently reviewed (269–271), there are no published data directly comparing adult and adolescent outcomes for obesity pharmacotherapy.

Physicians should be discouraged from prescribing weight loss medications off-label to those <16 years old because of: 1) the lack of FDA approval for use; 2) the limited number of well-controlled safety and efficacy studies in obese children and adolescents, 3) the limited efficacy demonstrated in adults for most agents, and 4) the need to weigh the relative risk of drug-induced adverse events in children and adolescents against a medication's long-term theoretical potential for reducing obesity-related morbidity and mortality.

Despite these concerns, the negative health impact of pediatric obesity may justify long-term medication. However, pharmacotherapy should only be prescribed in combination with comprehensive lifestyle modification programs (210, 271–274) that have substantial efficacy (270). The limited available evidence suggests the best pediatric pharmacotherapy outcomes are among patients adherent to lifestyle program recommendations (275).

Among pharmacotherapeutic agents approved for adult obesity (Table 5), only orlistat is FDA approved for obesity treatment of ages 12 to 16 years. Orlistat (299–305) inhibits gastrointestinal lipases, reducing adolescent's fat absorption by ~30% (299). Orlistat reduces BMI significantly in adolescents by ~0.7 to 1.7 kg/m^2 (150, 318), but treatment is associated with significant gastrointestinal side effects (Table 5). Orlistat must be taken with each meal, thus reducing its utility in school-attending adolescents. Orlistat appears to affect the absorption of fat-soluble vitamins E and D (299). Available data suggest that ~50% of pediatric patients that are prescribed orlistat discontinued it within 1 month, 75% stop using it by 3 months, and only 10% remain on orlistat after 6 months (319, 320). Given its limited

Table 4. Factors Associated With Prevention of Pediatric Obesity

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
4.2 Increased sugar sweetened beverages intake			
2- to 5-y-old children from various periods of the National Health and Nutrition Examination Surveys	There was a decrease of 57 calories/d intake of sugar-sweetened beverages between 2003–2004 and 2009–2010 with no appreciable change in sugar intake thereafter up to 2011–2012	Ford *et al.*, 2015 (112)	Probable +
Cross-sectional analysis of 4880 children between 3 and 11 y from the National Health and Nutrition Examination Survey between 1999 and 2004	Sugar-sweetened beverage intake was independently associated with decreased HDL, increased C-reactive protein, and increased waist circumference	Kosova *et al.*, 2013 (113)	+
Longitudinal study of 9600 children in the Early Childhood Longitudinal Survey–Birth Cohort	There was a 1.4 odds ratio for being obese if a 5-y-old child drinks 4 or 5 sugar-sweetened beverages per day but no such risk for 2-y-old; however there was a significant influence on drinking sugar-sweetened beverages at 2 y of age and an increase in BMI *z* score during the next 2 y	DeBoer *et al.*, 2013 (114)	+
Randomized controlled study of 224 teenagers that reduced sugar sweetened beverage intake	There was a decrease in the change in BMI and weight at 1 y but no difference at 2 y	Ebbeling *et al.*, 2012 (115)	+
Eighteen-month study of 642 primarily normal-weight Dutch children aged 4 y 10 mo to 11 y 11 mo who were divided into groups receiving 8 ounces of sugar-free drink or 105 kcal containing sugar-sweetened drinks	There was an increased weight gain and increase in BMI in the sugar-sweetened group	de Ruyter *et al.*, 2102 (116)	+
One hundred forty-six 7- to 11-y-olds drinking sugar-free or sugar-sweetened beverages	There was no difference in the level of satiety experienced; the conclusion is that the child will not compensate for all calories missing from nonsweetened drinks, which may partly explain a lower degree of weight gain with nonsweetened drink ingestion	de Ruyter *et al.*, 2012 (116)	+
4.3 Higher level of activity[a]			
Meta-analysis of 11 RCTs of activity ranging in length from 20 min to >1 h/d and ranging in frequency from twice a week to every day of the school week	There was little effect on BMI, but there were decreases in triglycerides and systolic and diastolic blood pressure when the intervention lasted at least 6 mo; total cholesterol, however, did increase during some studies	Cesa *et al.*, 2014 (117); Vasconcellos *et al.*, 2014 (118)	–
Nine randomized controlled pediatric studies (n = 367) included in a meta-analysis	At least 3 mo of exercise in 3 sessions per week of 60 min each led to decreased fasting glucose and insulin and body fat	Garcia-Hermoso *et al.*, 2014 (119)	–
Meta-analysis of 24 studies of fasting insulin levels and 12 studies on insulin resistance in pediatric normal weight overweight and obese	There was a small but positive effect in improving fasting insulin resistance in children, with the greatest effect occurring in those with the highest BMI standard deviation values	Fedewa *et al.*, 2014 (120)	–
Systematic review of 16 studies of school-based jumping exercises	There was small positive effect of bone-targeted exercise on fat mass (SMD, −0.248; 95% CI, −0.406 to −0.089) and lean mass (SMD, 0.159; 95% CI, −0.076 to 0.394), but there are few studies	Nogueira and Hrovat, 2014 (121)	–
Meta-analysis of 40 studies on the effect of resistance training in pediatric overweight or obese	Resistance training in children and adolescents who are overweight and obese appears to generally have very small to small effects on body composition and moderate to large effects on strength	Schranz *et al.*, 2013 (122)	–
Systematic review of 2 aggregate data meta-analyses representing 14 and 17 studies in 481 and 701 boys and girls, respectively	Exercise decreased the percentage of body fat but does not necessarily have an effect on BMI; therefore, replacing fat tissue with muscle may not necessarily be reflected by characteristic clinic-based anthropomorphic data	Kelley and Kelley, 2013 (123)	–

(*Continued*)

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Table 4. Continued

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
Randomized controlled pediatric study of >200 subjects who experienced 20 or 40 min of fun but nonetheless aerobic activity 5 d/wk during 13 wk	There was a dose response decrease in insulin resistance measured by the area under the curve of an oral glucose tolerance test, decreased total body fat and visceral fat, and a similar improvement in fitness measured by peak VO2; the conclusion is that there is benefit for a child who is obese if the child will actually engage in at least 20 min of aerobic exercise 5 d/wk, (and we expect this may extend to the prevention of obesity)	Davis *et al.*, 2011 (124)	–
4.4 Decreased sleep duration or variation			
A systematic review and unbiased meta-analysis of 11 longitudinal studies of 24,821 children and adolescents	There was a twofold increase in risk for obesity with "short" sleep duration according to sleep standards	Fatima *et al.*, 2015 (125)	+
Sleep duration in a cross-sectional pediatric study (n = 676)	Energy density of the diet, added sugar, and SSBs decreased with increased sleep	Kjeldsen *et al.*, 2014 (126)	+
Variability in sleep duration of 10 min per night	This was positively associated with energy density (P = 0.04), sugar-sweetened beverages intake (P = 0.03), and Children's Sleep Habits Questionnaire score independent of sleep duration	Kjeldsen *et al.*, 2014 (126)	+
One hour decrease in pediatric sleep duration (n = 441) during 200 d	There was a higher intake of added sugar (P = 0.001) and sugar-sweetened beverages (P = 0.002) with no change in energy density of the diet (P = 0.78)	Hjorth *et al.*, 2014 (127); Kjeldsen *et al.*, 2014 (126)	+
Sleeping <10 h at 16 mo of age in 1303 twins	There was a 50 kcal increased intake	Fisher *et al.*, 2014 (128)	+
Increasing pediatric sleep duration an average of 2 h 20 min (n = 37)	There was decreased caloric intake by 134 kcal/d and lowered plasma leptin	Hart *et al.*, 2013 (129)	+
Three hundred eleven term infants; sleep duration at 9 mo, 18 mo, and 3 y of age	There was no relationship between sleep duration and adiposity indicators in 9- to 36-mo-old children: the SKOT cohort	Klingenberg *et al.*, 2013 (130)	None
Eight hundred two 4- to 14-y-old children and adolescents; sleep and intake followed for 7 d	There was no relationship between sleep duration and energy intake, but there was a trend toward a positive association with intake of dietary fiber and vegetables and a negative association with intake of poultry, and a trend toward a negative association with intake of liquid "discretionary calories"	Hoppe *et al.*, 2013 (131)	None
Longitudinal cohort study of 550 children of average age 9.6 y	There was an odds ratio of 2.08 for obesity with <10 h sleep	Chaput *et al.*, 2011 (132)	+
A meta-analysis of 12 studies including 20,003 children	There was a 1.86 odds ratio for obesity with "short" duration of sleep	Cappuccio *et al.*, 2008 (133)	+
4.5 Increased screen time			
Measurements at ~12 y of age of 234 parents from a previously established cohort were compared with 382 of their offspring for screen time and measures of adiposity	Both generations demonstrated a relationship between screen time and obesity at about 12.5 y of age, demonstrating a need to target high-risk families across generations	Steffen *et al.*, 2013 (134)	+
A systematic review of 7 prospective studies on television time and 1 study on computer use	Six studies of varying quality demonstrated a positive relationship between screen time and the development of obesity	te Velde *et al.*, 2012 (135)	+
Seventy children studied every 6 mo during 2 y in a randomized controlled study to decrease television viewing 50% and decrease sedentary activity in the intervention group of 35	The intervention decreased sedentary activity especially in lower socioeconomic group children; there was relationship between decreased television viewing, decreased BMI, and decreased energy, but not increased activity	Epstein *et al.*, 2008 (136)	+

(*Continued*)

Table 4. Continued

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
4.6 Increased family involvement in prevention			
Fifteen RCTs of family-based lifestyle interventions for children and adolescents	Family-based interventions based in behavior theory had more effect than did those theoretically connected to family systems theory	Sung-Chan *et al.*, 2013 (137)	–
A systematic review including 24 studies including parental involvement in long-term weight-control interventions with a nutritional focus	Although there were inadequate data to determine whether parental involvement in prevention programs is important, medium and high levels of parental involvement in obesity treatment programs improved outcomes, suggesting that parental involvement should be studied in prevention	van der Kruk *et al.*, 2013 (138)	Probable +
Fifteen studies (7 were longitudinal) included measures of frequency of family meals although in an inconsistent manner	There was inconsistent and weak evidence of an inverse association between the frequency of family meals and risk of pediatric overweight; there is need for robust longitudinal studies on this topic	Valdes *et al.*, 2013 (139)	None
A systematic review of 9 studies including portion manipulation interventions or portion education/ training interventions	Most studies demonstrated increased intake with increased portion size, and that parents can be educated to estimate portion size more accurately, but there were other studies that contradicted both concepts	Small *et al.*, 2013 (140)	–
4.7 Disordered family function or abuse			
Systematic review of 16 cross-sectional and 1 longitudinal study of family function	Lower levels of family functioning, including poor communication, poor behavior control, poor family cohesion, high levels of family conflict, and low family hierarchy values representing low authority, dominance, and decision power, showed low to moderate relationship to the subject's classification of pediatric obese or overweight; however, out of 4 interventional studies only 2 showed that improved family functioning decreased the risk of obesity, but these studies were suboptimal	Halliday *et al.*, 2014 (141)	+
A meta-analysis of 41 studies including 190,285 participants	Pediatric maltreatment was associated with a 1.36 increased risk ratio for pediatric obesity	Danese and Tam, 2014 (142)	+
Systematic review of 36 studies	Interpersonal violence increased the risk of obesity later in life	Midei *et al.*, 2011 (143)	+
Systematic review of 6 prospective and 2 retrospective studies	Stressful environments during childhood and adolescence, including lack of good care, pediatric anxiety disorders, learning difficulties, low school achievement, and childhood/adolescence abuse, increased adult obesity risk, depression in adolescence, and increased the risk for obesity in girls only	Vamosi *et al.*, 2010 (144)	+
4.8 Increased school involvement			
Nine community-based studies (5 RCTs and 4 non-RCTs) of which 1 was conducted only in the community setting, 3 were conducted in the community and school setting, and 5 were conducted in the community setting in combination with at least 1 other setting, such as the home	There was moderate strength of evidence that a combined diet and physical activity intervention in the community with a school component is effective at preventing obesity or overweight	Bleich *et al.*, 2013 (145)	–
A systematic review of 16 studies involving school prevention programs with community involvement	School programs with more community involvement were more successful than those with less community involvement	Krishnaswami *et al.*, 2012 (146)	–

(*Continued*)

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Table 4. Continued

Study Format	Relationship	Source	Relationship to the Development of Obesity or Metabolic Improvement
Meta-analysis of 37 studies of 27,946 children generally between 6 and 12 y of age	There were beneficial effects of pediatric obesity prevention programs on BMI with school curriculum that includes healthy eating; physical activity and body image; increased sessions for physical activity and the development of fundamental movement skills throughout the school week; improvements in nutritional quality of the food supply in schools; environments and cultural practices that support children eating healthier foods and being active throughout each day; support for teachers and other staff to implement health promotion strategies and activities, as well as parent support and home activities that encourage children to be more active, eat more nutritious foods, and spend less time in screen-based activities; however, weaknesses in studies and potential bias point to the necessity for improved studies in the future	Waters *et al.*, 2011 (147)	–
4.10 Increased breast feeding			
Meta-analysis of 25 studies with a total of 226,508 participants	Breast-feeding was protective of the development of obesity with a dose response effect in 17 studies	Yan *et al.*, 2014 (148); Kramer *et al.*, 2009 (149)	+
A cluster-randomized trial of a breast-feeding promotion intervention of 13,889 subjects (81.5%) followed up at 6.5 y from 31 Belarusian maternity hospitals and affiliated clinics	Although there were substantial increases in the duration and exclusivity of breast-feeding, there was no reduction in obesity at age 6.5 y	Kramer *et al.*, 2009 (149)	None
Meta-analysis of 10 studies of breast-feeding	Five studies showed protective effects and 5 did not; likewise, there were mixed findings on length of breast-feeding and time of introduction of complementary food	Weng *et al.*, 2012 (150)	Mixed
Cohort analyses of 11,998 teenagers from the National Longitudinal Study of Adolescent Health	There was a decreased risk of obesity in girls breast-fed at least 9 mo with similar, but less significant, effects in boys; however, analysis of sibling pairs eliminated any significance from the relationship, demonstrating the effect of confounding effects on cohort analyses	Nelson *et al.*, 2005 (151)	+

Note: Numbers 4.2–4.8 and 4.10 refer to numbered recommendations in the manuscript.

Abbreviations: AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; HDL, high-density lipoprotein; RCT, randomized controlled trial; SKOT, Scottish Childhood Obesity Treatment Trial; SMD, standardized mean difference; TV, television; VO2, oxygen consumption.

[a]Some studies included obese children and adolescents, but results may relate to prevention.

efficacy and low long-term use, orlistat appears of limited benefit in practice.

Additional medications not FDA approved for the treatment of pediatric obesity

Metformin (306–311, 321–334) is not FDA approved for obesity treatment. However, metformin reduces hepatic glucose production, increases peripheral insulin sensitivity, and may reduce appetite (335). Metformin decreases BMI, but with a mean decrease of only 1.16 kg/m^2 over 6 to 12 months (336). Metformin may also possibly be useful in combating the weight gain observed in children and adolescents who are taking atypical psychotropic medications (337, 338) or who have PCOS (324, 331, 339). However, given its limited weight-loss efficacy, metformin is not a considered a weight-loss treatment.

Sibutramine (275, 284, 285, 340–346) was removed from the US market in 2010 because of concerns for

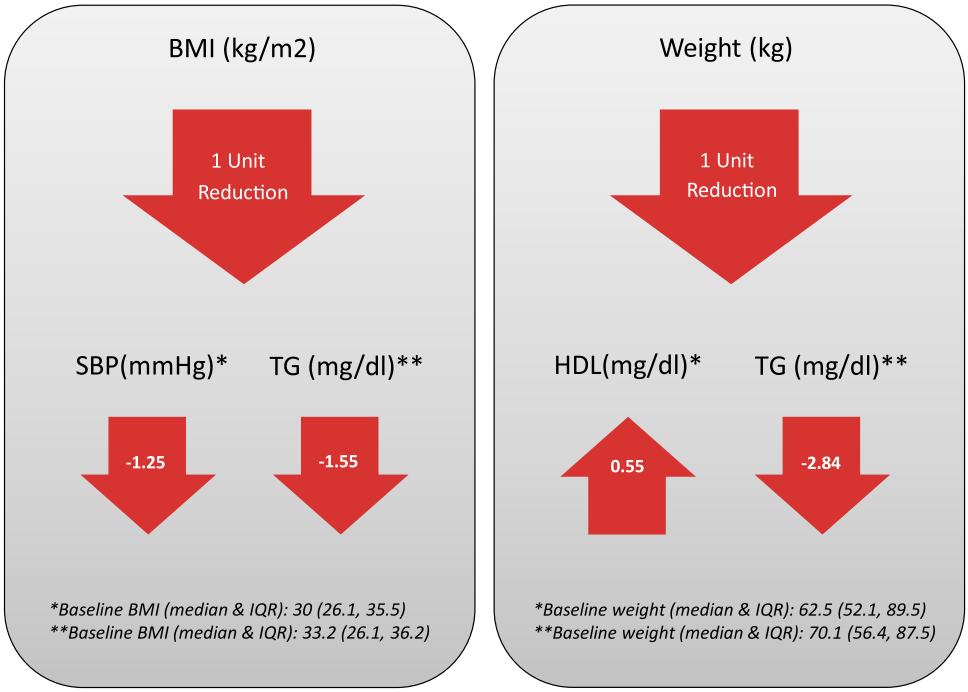

Figure 2. Change in metabolic outcome per unit change in BMI or weight. Abbreviations: HDL, high-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride.

cardiovascular safety but remains available in several other countries.

Other medications approved for obesity treatment of ≥16 years of age or under investigation generally have few relevant pediatric data (297, 298) (Table 5).

Some centrally active, amphetamine-like catecholaminergic and dopaminergic stimulants, such as phentermine and diethylpropion, are FDA approved as short-term monotherapy (a few weeks) for obesity in adults. Recently, lisdexamfetamine dimesylate was FDA approved to treat binge eating in adults (282, 283). Lisdexamfetamine treatment was associated with short-term weight loss, but this medication is not FDA approved for weight management. Because of adverse effect profiles (Table 5), abuse potential (347), and the absence of trials showing long-term weight loss efficacy, none of the amphetamine-like agents is recommended for obesity management in children and adolescents.

Although not FDA approved for the treatment of obesity, GH treatment of children and adolescents with Prader-Willi syndrome, particularly when started early (90), decreases body fat percentage and increases lean body mass (348), with effects that may be sustained for the long term (90). A summary of the benefits and risks of GH treatment (349) and consensus guidelines for GH therapy in Prader-Willi Syndrome are available (350).

Octreotide limits the opening of voltage-gated calcium channels in beta cells (351, 352), decreasing the magnitude of insulin response to glucose (353). In obese adults with insulin hypersecretion, treating with long-acting repeatable octreotide for 6 months resulted in ~2% greater weight loss than in controls (316). Studies have reported weight stabilization, instead of significant weight gain, in children and adolescents with hypothalamic obesity treated with somatostatin analogs (315, 354). Given its side-effect profile, octreotide appears to be potentially beneficial only for those with hypothalamic obesity.

Liraglutide, a glucagon-like peptide 1 analog, is approved for long-term adult obesity treatment; the effective 3 mg dose produced an additional weight loss of 4.5% vs placebo at 1 year, with sustained effects for up to 2 years (355). Small trials suggest that another glucagon-like peptide 1 analog, exenatide, may potentially have efficacy in adolescent obesity; used for >3 months, exenatide reduced BMI by >1 kg/m^2 (compared with control), with continued BMI reduction during a 3-month open-label phase (297, 298).

Leptin therapy in leptin-deficient patients produces significant loss of fat mass (295, 356, 357). Unfortunately, leptin therapy in adults who are not leptin deficient has little effect on body weight (358–360).

Agents that have been recently approved for long-term obesity treatment in adults (Table 5) currently lack pediatric-specific data. The additional weight loss (beyond that achieved with placebo) at 1 year among adults ranges from ~3% (lorcaserin) to ~10% (phentermine plus topiramate) (267), but none is without potential risks. If

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adult patients taking full-dose lorcaserin, bupropion plus naltrexone, liraglutide, or phentermine plus topiramate do not see clinically meaningful weight loss (>3% to 5% of body weight) after 12 weeks, clinicians should discontinue treatment, because significant weight loss after 1 year is unlikely. Similar results were found for adults given orlistat (361). In the largest adolescent orlistat trial (362), 21% of orlistat-treated adolescents decreased their body weight by ≥5% at 12 weeks and went on to decrease body weight by 7.8% after 1 year of treatment; however, those who lost <5% at 12 weeks had a 2.3% weight gain after 1 year (362). Thus, clinicians should discontinue pharmacotherapy agents when sufficient weight loss is not observed after 12 weeks.

Values and preferences

We placed a higher value on avoiding drug side effects and on achieving healthy weight through the incorporation of healthy behaviors. The suggestion to minimize the use of pharmacotherapy in children and adolescents reflects the limited efficacy and small number of long-term pediatric trials for existing agents, along with the imperative to manage pediatric obesity as a serious chronic condition in which long-term success overrides short-term gains.

Remarks

Drug efficacy is based only on reductions of BMI or BMI *z* scores. Antiobesity drugs may have differential effects on obesity-associated comorbidities based on their mechanisms of action. For example, certain medications (*e.g.*, metformin) have more potent effects on glucose tolerance. Clinicians should tailor drug selection to the individual patient and pay strong attention to the patient's concomitant medications, medical conditions, and family history, as well as each medication's efficacy and adverse event profile. The benefits of any drug used to treat pediatric obesity should clearly outweigh its long-term risks. Clinicians should be aware that no obesity medication has been shown to reduce the incidence of cardiovascular morbidity or mortality (267).

The recommendation to discontinue medication when it appears relatively ineffective after 12 weeks of use is consistent with adult obesity pharmacotherapy labeling. The FDA label for liraglutide recommends discontinuation when adults have <4% weight reduction. Most drugs should be discontinued if a 5% decrease in BMI/BMI *z* score does not occur.

Although pediatricians prescribe many medications "off-label", we think pharmacotherapeutic agents not yet approved for the treatment of pediatric obesity should be restricted to large, well-controlled clinical studies.

Bariatric surgery

4.11 We suggest bariatric surgery only under the following conditions:

- the patient has attained Tanner 4 or 5 pubertal development and final or near-final adult height, the patient has a BMI of >40 kg/m^2 or has a BMI of >35 kg/m^2 and significant, extreme comorbidities
- extreme obesity and comorbidities persist despite compliance with a formal program of lifestyle modification, with or without pharmacotherapy
- psychological evaluation confirms the stability and competence of the family unit, psychological distress due to impaired QOL from obesity may be present, but the patient does not have an underlying untreated psychiatric illness
- the patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits
- patient has access to an experienced surgeon in a pediatric bariatric surgery center of excellence providing the necessary infrastructure for patient care, including a team capable of long-term follow-up of the metabolic and psychosocial needs of the patient and family. (2|⊕○○○)

4.12 We suggest against bariatric surgery in preadolescent children; pregnant or breast-feeding adolescents (and those planning to become pregnant within 2 years of surgery); and in any patient who has not mastered the principles of healthy dietary and activity habits and/or has an unresolved substance abuse, eating disorder, or untreated psychiatric disorder. (2|⊕○○○)

Evidence

Clinicians prescribe bariatric procedures for weight loss in adolescents because of the poor success of nonsurgical treatment in achieving and maintaining weight loss in adolescents with extreme obesity.

Indications for weight loss surgery include BMI of >35 kg/m^2 with major comorbidities of obesity (T2DM, moderate to extreme sleep apnea, pseudotumor cerebri, debilitating orthopedic problems, and nonalcoholic steatohepatitis with advanced fibrosis). Patients are also candidates for bariatric surgery if they have a BMI of >40 kg/m^2 with mild comorbidities (hypertension, dyslipidemia, moderate orthopedic problems, mild sleep apnea, nonalcoholic steatohepatitis, and extreme psychological distress that is secondary to their obesity) (363).

Because of the beneficial effects on QOL, social relationships, and depression in studies of adolescents (364–367), some as long as 2 to 3 years in duration (368, 369), proponents of bariatric surgery suggest that extreme psychological distress is an indication for

Table 5. Medications Studied for the Long-Term Treatment of Obesity

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Centrally acting anorexigenic agents				
Phentermine, diethylpropion, and mazindol[a]	Approved only for short-term use in adults	Insomnia, elevation in heart rate, dry mouth, taste alterations, dizziness, tremors, headache, diarrhea, constipation, vomiting, gastrointestinal distress, anxiety, restlessness	Monitor HR, BP. These medications are contraindicated in uncontrolled hypertension, hyperthyroidism, glaucoma, agitated states, history of drug abuse, and MAOIs; use caution when prescribing to patients with even mild hypertension	Rauh and Lipp, 1968 (276); Lorber, 1966 (277); von Spranger, 1965 (278); Andelman *et al.*, 1967 (279); Golebiowska *et al.*, 1981 (280); Komorowski, 1982 (281)
Lisdexamfetamine dimesylate[a]	Not FDA approved for obesity. Approved for binge eating disorder in adults and for attention deficit hyperactivity disorder in patients 6 y of age and older	Dry mouth, sleeplessness (insomnia), increased heart rate, jittery feelings, constipation, anxiety	This medication is contraindicated with MAOIs. There is a risk for sudden death in people who have heart problems or heart defects, and stroke and heart attack in adults. Monitor blood pressure and heart rate. May produce psychotic or manic symptoms, such as hallucinations, delusional thinking, or mania. May worsen peripheral vasculopathy, including Raynaud phenomenon	McElroy *et al.*, 2015 (282); McElroy *et al.*, 2015 (283)
Sibutramine	Withdrawn in the US (increased risk of serious cardiovascular events). Still available in some countries such as Brazil	Tachycardia, hypertension, palpitations, insomnia, anxiety, nervousness, depression, diaphoresis	Monitor HR, BP. Do not use with other drugs, MAOIs	Berkowitz *et al.*, 2003 (275); Godoy-Matos *et al.*, 2005 (284); Berkowitz *et al.*, 2006 (285)
Lorcaserin[a]	Approved for long-term use in adults	Headache, dizziness, fatigue, nausea, dry mouth, cough, and constipation; back pain, cough, hypoglycemia in patients with T2DM	There is a risk for serotonin syndrome or neuroleptic malignant syndrome-like reactions. Evaluate patients for signs or symptoms of valvular heart disease. Euphoria, hallucination, and dissociation have been seen with supratherapeutic doses. Interactions with triptans, MAOIs, including linezolid, SSRIs, SNRIs, dextromethorphan, tricyclic antidepressants, bupropion, lithium, tramadol, tryptophan, and St. John's wort	Smith *et al.*, 2010 (286); Fidler *et al.*, 2011 (287)

(*Continued*)

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Table 5. Continued

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Liraglutide[a]	Approved for long-term use in adults	Nausea, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase	Monitor heart rate at regular intervals. This medication is contraindicated in patients with a history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2. Discontinue promptly if pancreatitis is suspected	Zinman *et al.*, 2009 (288); Wadden *et al.*, 2013 (289); Astrup *et al.*, 2009 (290)
Phentermine plus topiramate[a]	Approved for long-term use in adults	Paresthesias, dizziness, taste alterations, insomnia, constipation, dry mouth, elevation in heart rate, memory or cognitive changes	This medication is contraindicated in glaucoma, hyperthyroidism, MAOIs. Concerns about teratogenicity (increased risk of oral clefts) mandate effective contraceptive use and pregnancy test monitoring in females. Metabolic acidosis, hypokalemia, and elevated creatinine have been reported, and periodic monitoring is advised. Abrupt withdrawal of topiramate may cause seizures	Garvey *et al.*, 2012 (291); Allison *et al.*, 2011 (292)
Bupropion plus naltrexone[a]	Approved for long-term use in adults	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea	Monitor HR, BP. Do not administer to patients with a history of seizure disorders or with anorexia or bulimia nervosa or to patients who are using opioids or abruptly discontinuing use of alcohol, benzodiazepines, barbiturates, or antiseizure medications. There is potential increased risk of suicidality	Greenway *et al.*, 2010 (293); Padwal, 2009 (294)
Drugs in development or used off-label that may act centrally as anorexigenic medications				
Recombinant human leptin, metreleptin[a]	This drug is under investigation. In monotherapy it was successful for treating leptin deficiency	Headache, abdominal pain	This drug is useful only in leptin deficiency. Antibodies with neutralizing activity have been identified in patients treated with metreleptin. T cell lymphoma has been reported in patients with acquired generalized lipodystrophy. A risk evaluation and mitigation strategy should be in place to prevent inappropriate prescription	Farooqi *et al.*, 2002 (105); Farooqi *et al.*, 1999 (295)

(*Continued*)

Table 5. Continued

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Exenatide[a]	Not FDA approved for obesity	Nausea, vomiting, diarrhea, feeling jittery, dizziness, headache, dyspepsia	Acute pancreatitis, including fatal and nonfatal hemorrhagic or necrotizing pancreatitis, has been reported. Observe patients carefully for signs and symptoms of pancreatitis. Discontinue promptly if pancreatitis is suspected. Contraindicated in patients with severe renal impairment	Rosenstock *et al.*, 2010 (296); Kelly *et al.*, 2013 (297); Kelly *et al.*, 2012 (298)
Drugs affecting nutrient trafficking				
Orlistat	This drug is FDA approved for treatment of obesity in adolescents ≥12 y old	Oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, increased defecation, fecal incontinence	This drug is contraindicated in chronic malabsorption syndromes and cholestasis. Cholelithiasis and, rarely, severe liver injury, including hepatocellular necrosis and acute hepatic failure leading to death, have been reported. It decreases drug concentrations of cyclosporine and levothyroxine. Doses should be temporally separated from orlistat. Fat-soluble vitamin absorption is decreased by orlistat. Use with caution in those at risk for renal insufficiency. MVI supplementation is strongly recommended. A low- dose preparation is approved for over-the-counter sale	McDuffie *et al.*, 2002 (299); Zhi *et al.*, 2003 (300); Norgren *et al.*, 2003 (301); Ozkan *et al.*, 2004 (302); McDuffie *et al.*, 2004 (303); Chanoine *et al.*, 2005 (304); Maahs *et al.*, 2006 (305)
Drugs affecting internal milieu/metabolic control				
Metformin[a]	This drug is not FDA approved for obesity. It is approved for ≥10 y of age for T2DM	Nausea, flatulence, bloating, diarrhea; usually resolves	Do not use in renal failure or with i.v. contrast. MVI supplementation is strongly recommended. Potential risk for vitamin B12 deficiency when used long-term. Avoid alcohol intake	Freemark and Bursey, 2001 (306); Atabeck and Pirgon, 2008 (307); Love-Osborne *et al.*, 2008 (308); Wilson *et al.*, 2010 (309); Yanovski *et al.*, 2011 (310); Kendall *et al.*, 2013 (311)
Octreotide (for hypothalamic obesity)[a]	This drug is not FDA approved for obesity	Cholelithiasis (can be prevented by concurrent ursodiol), diarrhea, edema, abdominal cramps, nausea, bloating, reduction in T4 concentrations, decreased GH but normal IGF-I	Monitor fasting glucose, FT4, HbA1c. Useful only for hypothalamic obesity. Ursodiol coadministration is strongly recommended	Gambineri *et al.*, 2005 (312); Haqq *et al.*, 2003 (313); Lustig *et al.*, 2001 (314); Lustig *et al.*, 1999 (315); Lustig *et al.*, 2006 (316)

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Table 5. Continued

Drug	Status	Common Side Effects	Monitoring and Contraindications	Source
Recombinant human GH[a]	This drug is not FDA approved for obesity. It is FDA approved in Prader-Willi syndrome to increase height velocity	Edema, carpal tunnel syndrome, death in patients with preexisting obstructive sleep apnea	GH should be used only after screening to rule out obstructive sleep apnea in patients with Prader-Willi syndrome. Clinicians must closely monitor pulmonary function, adrenal function, glucose, HbA1c	Shadid and Jensen, 2003 (317)

Note: All agents are contraindicated in pregnancy. See full prescribing information for all adverse effects, cautions, and contraindications. Pharmacotherapy is not usually considered if the BMI is below the 95th percentile, but there are additional factors to consider. If we initiate pharmacotherapy early in the course of obesity, we may prevent extreme weight gain and metabolic complications, but we may treat an excess of children and adolescents, raise the rate of unwarranted side effects, and increase the costs to individuals and to society. Alternatively, if we begin medication late in the course of obesity, we run the risk of runaway weight gain and long-term morbidity. One approach that reconciles these difficulties is to act aggressively with lifestyle intervention in overweight and mildly obese patients to prevent extreme obesity and to consider pharmacotherapy when the risk of complications is high or soon after complications emerge. The tipping point for pharmacotherapy could be if the family history is strongly positive for a major comorbidity. Lifestyle intervention should precede pharmacotherapy and should be maintained during pharmacotherapy. Derived from August *et al.* (86).

Abbreviations: BP, blood pressure; CNS, central nervous system; FT4, (plasma) free thyroxine; HR, heart rate; IV, intravenous; MAOI, monoamine oxidase inhibitor; MVI, multivitamins; SNRI, selective serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin-reuptake inhibitors; T4, thyroxine.

[a]The use for obesity treatment in children and adolescents <16 y of age of these non–FDA-approved agents should be restricted to large, well-controlled studies.

bariatric surgery (368, 370). Most guidelines now include obesity-related psychological distress an indication for bariatric surgery if the adolescent's BMI is >40 kg/m^2 (363, 370).

A psychologist must assess the bariatric surgery candidate to determine the severity of psychological impairment as well as ability to comply with the requirements for successful outcome. It is essential that all potential candidates have a stable home environment with good family support and the ability to carry out the necessary postoperative behaviors—adherence to dietary guidelines (including macronutrient administration) and physical activity recommendations. Adolescents who are unable to give assent; who have untreated or unstable psychiatric issues other than depression; who are substance abusers; or who are pregnant, planning pregnancy, or breastfeeding are not good candidates for bariatric surgery (370). All candidates for bariatric surgery should agree to psychological evaluation before surgery and in the perioperative period (371).

Surgery can be malabsorptive, restrictive, or combination procedures. Laparoscopic adjustable gastric banding (LAGB) (83) is a purely restrictive procedure that isolates the upper stomach by placing an adjustable silicone ring around the entrance to the stomach [Fig. 3(A)] (223). The LAGB procedure has high reoperation and long-term complication rates, which increase with time and thus it is rarely used anymore (373–375).

Malabsorptive procedures decrease intestinal mucosal function by rearranging the anatomy of the intestine, resulting in malabsorption of nutrients. RYGB is a combination procedure in which the surgeon creates a small stomach pouch and the remainder of the stomach is bypassed. The surgeon inserts a segment of the jejunum in the small gastric pouch, which connects to the proximal portion of the jejunum that drains the bypassed portion of the stomach and the duodenum [Fig. 3(C)]. The RYGB has the restrictive properties of a partial gastrectomy while causing malabsorption and "dumping syndrome" by bypassing much of the stomach.

In vertical sleeve gastrectomy (VSG), a surgeon resects ~85% of the stomach, removing the fundus and greater curvature, leaving a narrow gastric remnant [Fig. 3(F)]. There is no rearrangement of the anatomy, making it less likely that patients having VSG will have malabsorption of micronutrients or postoperative bowel obstruction, as compared with RYGB (370). Because VSG has less surgical complications than the RYGB, patients use it with increasing frequency (373, 376). The Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study (a prospective, multisite observational study at 5 academic centers) performed 52 RYGB and 1 VSG in 2008 vs 24 RYGB and 29 VSG in 2011 (377).

In addition to the anatomic effects of the procedures, both RYGB and VSG decrease the orexigenic hormone ghrelin (87, 378, 379) and increase the anorexogenic incretins glucagon-like peptide 1 and peptide YY (380, 381), thus decreasing appetite and improving insulin sensitivity (382).

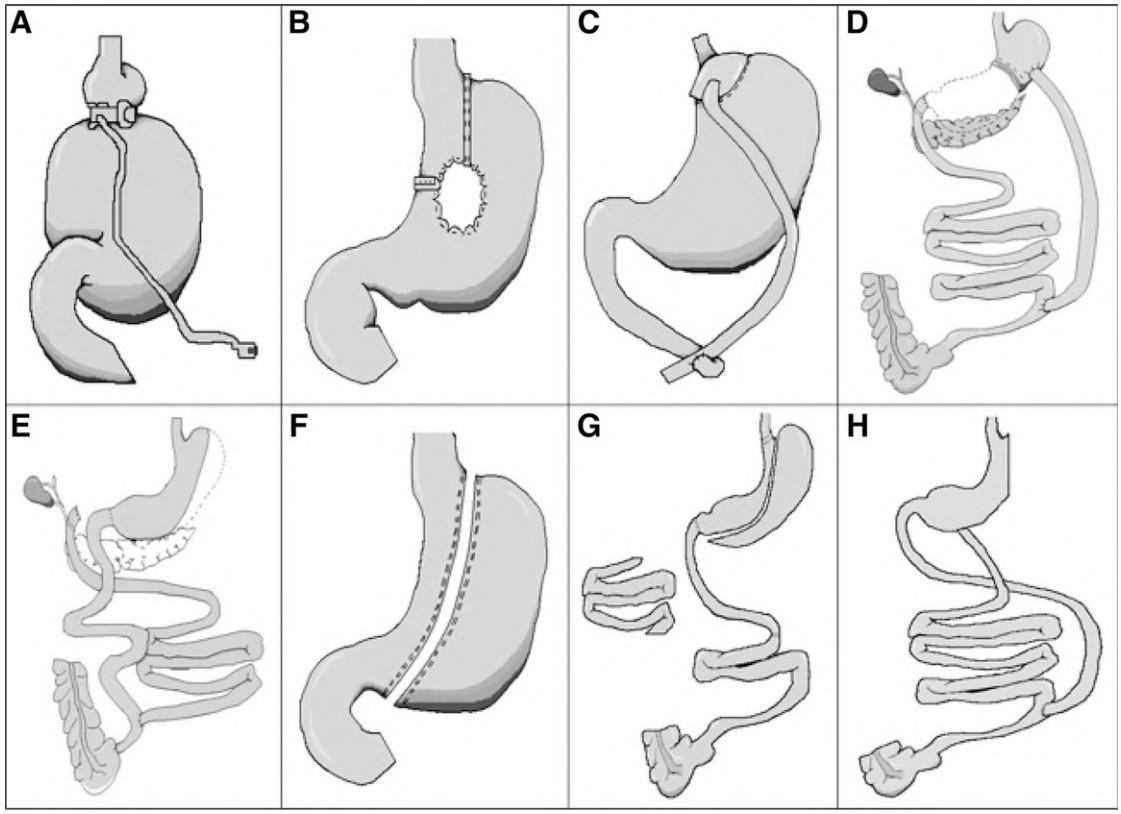

Figure 3. Bariatric surgical procedures. (A) LAGB, (B) vertical banded gastroplasty, (C) RYGB, (D) biliopancreatic diversion, (E) biliopancreatic diversion with duodenal switch, (F) VSG, (G) ileal interposition with sleeve gastrectomy, and (H) Santoro III. (A), (C), and (F) are applicable to section 4 (Bariatric Surgery). [Reproduced from Nandagopal R *et al.* (372), with permission.]

Adolescents having VSG performed between 2008 and 2011 had 61.3% excess weight loss at 1 year (n = 41) and 62.3% excess weight loss at 2 years (n = 8) (383). The largest pediatric study to date found a similar BMI reduction with VSG (37%) (384) as with RYGB (35% to 37%) (385) at 1 year following surgery. This is consistent with the results of the Adolescent Morbid Obesity Study (376), a Swedish study of 81 adolescents with a mean BMI decrease from 45.5 to 29.7 kg/m^2 2 years following RYGB (367). Three-year data from the Teen-LABS study found that the mean BMI decreased overall from 53 to 38 kg/m^2 (a decrease of 27%) with a 28% BMI decrease in those receiving RYGB (n = 161) and a 26% decrease in the teens who had VSG (n = 67) (369).

Regardless of procedure, the percentage of weight loss is independent of initial BMI, so those who are extremely obese will still be obese following surgery (385). Even when obesity persists, most comorbidities associated with obesity improve markedly following the surgery. A study of 22 adolescents who were extremely obese showed positive effects of RYGB on glucose homeostasis parameters with 38% decline in BMI (61 to 39 kg/m^2) 1 year after surgery (386). Positive effects of bariatric surgery have included the reversal of T2DM (387), improvements in glucose homeostasis in nondiabetics (379), improved insulin sensitivity and secretion (388), resolution of sleep apnea (389), improvements in nonalcoholic steatohepatitis (381), improvements in severe arthropathy (371), and improvements in cardiovascular risk factors [dyslipidemia, hypertension, and inflammation (390) and increased adiponeptin and decreased IL-1, IL-8, CRP, and TNF-α (391)], as well as decreased left ventricular mass index, improvements in left ventricular hypertrophy, improvements in diastolic function, and improved rate-pressure product, all of which suggest decreased cardiac workload (392).

The Teen-LABS study indicated that 39% of enrolled patients had more than 4 major comorbid conditions at baseline (376). Three-year follow-up of the patients enrolled in Teen-LABS found a 95% remission of T2DM (19 of 20 teens who had diabetes at the time of surgery), 76% remission of prediabetes (13 of 17 patients), 74% remission of hypertension (56 of 76 with initial high blood pressure), and a 66% normalization of dyslipidemia (84 of 128 patients) (369).

The Teen-LABS study assessed comorbid conditions and surgical complications in the perioperative period in 242 adolescents during the first month following surgery

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(377). There were no procedure-related deaths. Sixty-six percent had laparoscopic RYGB, 28% had VSG, and 6% had LAGB. Major complications occurring within the 30 days following surgery (gastrointestinal leaks, suicidal ideation, anticoagulation for pulmonary embolus) occurred in 7 patients (0.4%), and minor complications occurred in 27 patients (11.2%; 2.5% of patients undergoing RYGB, 3.0% VSG, and 7.1% AGB) (377). The most common complications with both RYGB and VSG were abdominal pain/diarrhea/nausea/dehydration followed by stricture with RYGB and wound infection with VSG (373). Nineteen of 242 patients had major complications within 30 days of surgery (9.3% with RYGB, 4.5% following VSG, and 7.1% with AGB). Late complications occurred in 10% to 15% of patients and included hernias at incision sites, cholelithiasis, small bowel obstruction, stomal stenosis, protein calorie malnutrition, vitamin and mineral deficiencies, and weight regain (376, 377, 393, 394). The Adolescent Morbid Obesity Surgery Study in Sweden had a 33% adverse event rate, with 15% (n = 12) requiring reoperation, 5 for internal hernias, 5 for cholecystectomy, 1 for adhesions, and 1 for pain without surgical findings (364). Seven percent had psychological sequelae, 2 with suicide attempts from medication overdose, 1 with self-destructive behavior and suicidal ideation, and 3 with depression and anxiety. All had psychological problems before surgery. Five patients had excessive use of addictive drugs (none of these patients disclosed the fact that they had preexisting addictions at the time of presurgery assessment) (367). Although most patients have improvement in QOL, self-esteem, anxiety, and depressive symptoms (365), these improvements were not universally maintained at 2 years following surgery (368). Suicidal ideation has been reported, possibly related to unrealistic expectations that their life would be completely different following surgery or to continued poor self-image with weight regain (367). The most recent Teen-LABS study, evaluating 242 adolescents at 3 years after RYGB or VSG, found the mean QOL improved from 63 to 83 based on the total score from the Impact of Weight on Quality of Life–Kids survey (369).

As these procedures all have potential adverse events, it is important to have life-long monitoring for complications. Adherence to prescribed nutritional guidelines is essential for all weight-loss surgery patients postoperatively because low levels of minerals and vitamins can occur due to restricted nutrient intake, decreased gastric acid production, decreased production of intrinsic factor and digestive enzymes, or food intolerance (especially following the dumping syndrome with RYGB) (121, 395). Iron deficiency is the most common mineral deficiency, as RYGB not only causes malabsorption but also has low gastric acid production, further impairing iron absorption (121, 370). Decreased bone mineralization is common, as RYGB decreases cholecalciferol absorption by 25% and calcium and phosphorous concentrations may be low, resulting in significant bone density loss (396). Vitamin deficiencies are common, including deficiencies of vitamins B12, B1, and folate, as RYGB and VSG both reduce the surface of the distal portion of the stomach, resulting in inadequate secretion of intrinsic factor. Annual screening is recommended for patients at risk for developing vitamin deficiencies. As RYGB can result in copper, selenium, and zinc deficiencies, it is recommended that all patients having bariatric surgery receive supplementation with a multivitamin with minerals (370). Patients need to be monitored long term for changes in bone density, hair loss secondary to zinc deficiency, and neurologic complications (363). It is recommended that they avoid alcohol and decrease the intake of sugar and fructose-containing drinks. Despite the importance of nutritional supplementation following bariatric surgery, the Adolescent Morbid Obesity Surgery study found a 67% noncompliance rate with prescribed vitamin and mineral intake at 2 years following surgery. Low ferritin levels were found in 12% of patients before surgery and in 39% of patients 2 years after surgery. Similarly, Vitamin B12 deficiency increased from 1.3% before surgery to 13% after surgery (367). The 3-year follow-up data from the Teen-LABS study found similar results. Low folate levels were found in 3% of youths at baseline and in 8% at 3 years, low vitamin B12 concentrations increased from <1% to 8%, low 25 hydroxyvitamin D levels increased from 37% to 43%, and the percentage of adolescents with low ferritin levels increased from 5% at baseline to 57% at 3 years (369).

These data emphasize the need for a multidisciplinary team that should include a bariatric surgeon, a pediatric obesity specialist to screen and manage the comorbidities, a dietitian to plan the diet and assure adequate nutritional intake, a mental health professional to perform the initial psychological assessment and provide counseling during the postoperative adjustment, a program coordinator to facilitate compliance and follow-up, and a social worker to provide resources to help overcome barriers to care and run support groups (373). Long-term follow-up is essential to maintain compliance with nutritional recommendations.

We agree with the expert panels (226, 227) that suggest bariatric surgery for adolescents with obesity-related comorbid conditions that threaten the adolescent's health—a BMI of >35 kg/m^2 and an extreme comorbidity or a BMI of >40 kg/m^2 and less extreme comorbidity.

Remarks

As adolescents appear to have a greater rate of diabetes resolution and improvement in other obesity-related comorbidities than do adults, it may be beneficial to consider earlier surgery in obese teens, as they likely have less vascular damage than do older individuals.

Values and preferences

The Task Force suggestion of bariatric surgery in adolescents who are extremely obese with serious comorbidities places a high value on amelioration of life-threatening complications and lower value on surgical cost and perioperative complications.

Conclusion

Pediatric obesity remains an ongoing serious international health concern affecting ~17% of US children and adolescents, threatening their adult health and longevity. Pediatric obesity has its basis in genetic susceptibilities influenced by a permissive environment starting *in utero* and extending through childhood and adolescence. Endocrine etiologies for obesity are rare and usually are accompanied by attenuated growth patterns. Pediatric comorbidities are common and long-term health complications often result; screening for comorbidities of obesity should be applied in a hierarchal, logical manner for early identification before more serious complications result. Genetic screening for rare syndromes is indicated only in the presence of specific historical or physical features. The psychological toll of pediatric obesity on the individual and family necessitates screening for mental health issues and counseling as indicated. The prevention of pediatric obesity by promoting healthful diet, activity, and environment should be a primary goal, as achieving effective, long-lasting results with lifestyle modification once obesity occurs is difficult. Although some behavioral and pharmacotherapy studies report modest success, additional research into accessible and effective methods for preventing and treating pediatric obesity is needed. The use of weight loss medications during childhood and adolescence should be restricted to clinical trials. Increasing evidence demonstrates the effectiveness of bariatric surgery in the most seriously affected mature teenagers who have failed lifestyle modification, but it requires experienced teams with resources for long-term follow-up. Adolescents undergoing lifestyle therapy, medication regimens, or bariatric surgery for obesity will need cohesive planning to help them effectively transition to adult care, such as continued necessary monitoring, support, and intervention. Transition programs for obesity are an uncharted area requiring further research for efficacy.

Despite a significant increase in research on pediatric obesity since the initial publication of these guidelines 8 years ago, there remains an unmet need for further study of the genetic and biological factors that increase the risk of weight gain and influence the response to therapeutic interventions. Also needed are more studies to better understand the genetic and biological factors that cause an obese individual to manifest 1 comorbidity vs another or to be free of comorbidities. Continued investigation into the most effective methods of preventing and treating obesity and into methods for changing environmental and economic factors that will lead to worldwide cultural changes in diet and activity should be priorities. Particular attention to determining ways to effect systemic changes in food environs and total daily mobility, as well as methods for sustaining healthy BMI changes, is of importance.

Summary of Changes

Since the publication of the original guidelines 8 years ago there have been an additional 1778 references added to PubMed concerning pediatric obesity. We have incorporated the most relevant data from these to update and enhance the original text.

The epidemiology and definition section contains the latest statistics on trends in childhood obesity, including an apparent recent stabilization of the prevalence. New definitions for extreme obesity are added with a notation that this is the group that continues to rise. The prevalence in ethnic minorities as well a discussion of the limitations of applying the BMI equation to all ethnic groups are addressed.

The evaluation section provides the latest guidelines for utilizing laboratory evaluation for diagnosis and management of comorbidities of obesity. Special emphasis on avoiding endocrine evaluation in most children as well as avoiding measurement of insulin values is provided to prevent unnecessary laboratory testing.

The genetics section has been extensively revised with the latest genomic findings presented in table form and provides guidelines on when to invoke genetic testing in obese children, particularly those with early onset obesity, family history of extreme obesity, and hyperphagia. A combined flowchart demonstrating pathways of diagnosis from history and physical examination to genetic testing is included.

Prevention of obesity is discussed with numerous new studies that support most previous conclusions on lifestyle modification. However, although breast-feeding is beneficial for an infant in numerous ways and was supported as a recommendation to prevent obesity in the

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previous guidelines, recent data weaken support for breast-feeding as a means of preventing obesity and breast-feeding is now a suggestion.

The treatment section focuses on lifestyle changes as the basis of all efforts to treat childhood obesity and supports most previous recommendations and suggestions. A chart demonstrating how much change in systolic blood pressure and lipid values might be expected with a decrease in 1 unit of BMI (kg/m^2) or a decrease of 1 kg of body weight is added.

A discussion of the significant toll childhood obesity takes on the psychological function of a child follows. Guidelines for evaluation of children and access to tools to evaluate child and family function are provided. Referral to appropriate counseling programs is emphasized when psychological problems or aberrant family dynamics are found.

Although noting that all but one of the pharmacological agents targeting obesity are not approved until 16 years of age, agents and their method of action are presented in detail in a table. Lifestyle modification is emphasized as a basis for any additional pharmacological therapy. Should pharmacological therapy be invoked, even off label, guidelines for use and for discontinuation in the case of lack of efficacy are provided. When pharmacotherapy is considered, only clinicians experienced in the use of the agents should use them.

The increasing information on the benefits and risks of bariatric surgery is presented along with a discussion of the types of procedures that might be used. There is emphasis upon contraindications in the use of bariatric surgery in growing children and immature teenagers. Emphasis that procedures should only be carried out in those mature pubertal individuals with severe comorbidities of obesity in the presence of a motivated and compliant patient and family and only in the hands of an experienced surgeon with a dedicated and experienced support team is provided.

The last section sets new goals for future research into the thorny questions of the best method to determine the etiology of childhood obesity and methods to prevent and treat childhood obesity and its comorbidities.

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Address all correspondence and requests for reprints to: The Endocrine Society, 2055 L Street NW, Suite 600, Washington, DC 20036. E-mail: publications@endocrine.org; Phone: 202-971-3636.

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Alfresco Web Script Status 404 - Not Found

The Web Script /alfresco/service/vgr/storage/node/content/workspace/SpacesStore/441006af-62a7-4f19-be73-6d698bf635f5/2018_102 Rapport Könsdysfori.pdf has responded with a status of 404 - Not Found.

404 Description: Requested resource is not available.

Message: Inget dokument med det id:t kunde hittas.
Server: Enterprise v5.2.7 (.2 rde4c74f1-b29) schema 10 095
Time: 2022-apr-26 00:16:05

Diagnostics: Inspect Web Script (se/vgregion/storage/content.get)

Exhibit
SL 18

Summaryx

Exhibit
SL 19

Lääketieteelliset menetelmät sukupuolivariaatioihin liittyvän dysforian hoidossa. Systemaattinen katsaus.

Iris Pasternack, Inka Söderström, Maija Saijonkari, Marjukka Mäkelä

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Arviointiryhmä:

Iris Pasternack, LL, tutkija, toimitusjohtaja, Summaryx Oy
Inka Söderström, VTM, tutkija, Summaryx Oy
Maija Saijonkari, FM, tutkija, Summaryx Oy
Marjukka Mäkelä, LKT, PhD, M.Sc. (ClinEpi), senioritutkija, Summaryx Oy

Summaryx Oy
Tankomäenkatu 8 A 2
00950 HELSINKI

Puhelin: +358 41 4545047
Sähköposti: info@summaryx.eu
Kotisivu: www.summaryx.eu

Summaryx Oy on yhteiskunnallinen yritys, joka tuottaa tietoa terveydenhuollon menetelmistä.

SISÄLLYSLUETTELO

Sisällys

Taustaa

Raportti on Sosiaali- ja terveysministeriön Palveluvalikoimaneuvoston (Palko) toimeksiantona tehty systemaattinen katsaus sukupuolivariaatioihin liittyvän dysforian hoidossa käytettyjen lääketieteellisten menetelmien vaikuttavuudesta ja turvallisuudesta. Koska tulokset tulevat osaksi laajempaa perustelumuistiota, raporttiin ei kirjoiteta tavanomaista johdanto-osaa, jossa kuvataan terveysongelma ja muita taustatietoja sekä määritellään termit. Vaikuttavuustutkimukset ja niiden tulokset esitetään tässä raportissa taulukkomuodossa ja lyhyinä tiivistelminä.

Menetelmät

Aiheen rajaus

Palkon määrittelemä aiheen rajaus PICO-muodossa:

P = terveysongelma / henkilö- tai potilasryhmä (Population, Patient, Problem), jota tutkitaan:

- Transsukupuolisuus: ICD-10: koodi F64.0; Diagnoosikoodiin sisältyy sukupuolenvaihtohalu ja transseksualismi
- Muu sukupuoli-identiteetin häiriö, ICD-10: F64.9, F64.8
- Gender incongruence, ICD-11: HA60 Gender incongruence of adolescence or adulthood
- Gender Dysphoria (DSM5-tautiluokitus; American Psychiatric Association, 2013)
- Gender fluid (sukupuoli-identiteetin vakiintumattomuus/aaltoilu)
- Toimenpiteeseen/hoitoon tyytymättömät henkilöt/potilaat (ei ICD-koodia)

I = Tutkittava interventio/menetelmä, jolla terveysongelmaan pyritään vaikuttamaan:

1. Sukupuoliominaisuuksia muuttavat kirurgiset hoidot
    - Rintakehän tai rintakirurgia, feminisoiva tai maskulinisoiva
    - Kasvojen tai muiden kehonosien kirurginen hoito
    - Kirurgiset hoidot, joissa rakennetaan tai poistetaan joko miehen tai naisen sukuelimet
    - Sukuelinkirurgia, jossa suurennetaan tai muovataan sukuelimiä
    - Äänihuulikirurgia, aataminomenan höyläys
    - Hedelmällisyyden palauttaminen, kun se ensin on identiteettiperustaisen hoidon takia menetetty
    - Kirurgisen toimenpiteen purku tai korjausleikkaus
    - Hiusten siirto
2. Sukupuoliominaisuuksia muuttavat lääkkeelliset hoidot
    - Maskulinisoivat hormonihoidot
        - Testosteroni (geeli tai injektio)
    - Feminisoivat hormonihoidot

    - Estrogeeni (tabletti tai laastari)
    - Antiandrogeeni (tabletti)
- Nuorilla (16-18-v.) lisäksi omaa hormonitoimintaa jarruttava GNRH-analogi-pistoshoito ennen muuntavaa hormonihoitoa ja alkuun myös sen aikana
- Puberteettia jarruttavat GnRH-analogihoidot

3. Muut lääketieteelliset hoidot
    - Hedelmällisyyden säilyttäminen
        - Transnaisille siemennesteenpakastus
        - Transmiehille munasolupakastus
    - Dermatologiset hoidot (transnaiset)
        - Epilaatiohoidot parta-alueelle
        - Karvankasvua estävä voide kasvojen iholle
    - Puheterapia (pääsääntöisesti transnaiset)
    - Apuvälineet, mm. peruukki
4. Psykososiaaliset hoidot
    - mikä tahansa psykoterapia, erityisesti affirmatiivinen, mukaanlukien nettiterapia, mm.
        - kognitiivinen lyhytpsykoterapia
        - transsensitiivinen lyhytterapia
        - psykoedukaatio
        - psykofyysinen fysioterapia
        - kuvataidepsykoterapia
        - neuropsykiatrinen seksuaaliterapia
        - perhe- ja pariterapia, läheistapaaminen,
        - kehoterapia, somatosensorinen terapia

C = Vertailumenetelmä / vaihtoehtoinen menetelmä (Comparison), johon tutkittavaa menetelmää verrataan:

- Ei interventiota tai kahden intervention vertailu

O= Terveyshyöty, terveystulos (Outcome), menetelmän tuottamat terveystulokset, joita halutaan selvittää:

- Hyötyjen lisäksi haitat
- Subjektiivisen hyvinvoinnin paraneminen, elämänlaadun koheneminen, sukupuolidysforian väheneminen

- Ikätasoinen toimintakyky: sosiaaliseen, ammatilliseen tai muuhun tärkeään elämänalueeseen liittyvä toimintakyky
- Parisuhde, perheellistyminen
- Psykiatrisen hoidon tarve, psykiatrinen oireilu, itsetuhoinen käyttäytyminen, rikoskäyttäytyminen, päihdeongelmien väheneminen
- Sairauspoissaolot
- Vaikutukset läheisille ihmisille

Kirjallisuushaku

Sukupuolivariaatioiden hoidon vaikuttavuutta, turvallisuutta, kustannuksia, etiikkaa, laillisuusasioita ja potilasnäkökulmaa käsitteleviä tutkimuksia haettiin seuraavista viitetietokannoista joulukuussa 2018: Medline (PubMed), CLIB, Embase (Scopus), PsychInfo. Joulukuussa 2018 ja helmikuussa 2019 tehtiin lisäksi tarkistushakuja sovituilla avainsanoilla. Hakustrategiat ja viitteiden määrä on kuvattu liitteessä 1.

Haku palveli tutkijajoukkoa, joka valmisteli perustelumuistiota. Tähän raporttiin otettiin mukaan ainoastaan hoitojen turvallisuutta käsittelevistä artikkeleista systemoidut katsaukset, sekä ne sukupuolidysforian lääketieteellistä hoitoa koskevat interventiotutkimukset, joissa lopputuloksena on mitattu seuraavia asioita:

- subjektiivisen hyvinvoinnin paraneminen, elämänlaadun koheneminen, sukupuolidysforian väheneminen
- ikätasoinen toimintakyky: sosiaalisen, ammatillisen tai muuhun tärkeään elämänalueeseen liittyvä toimintakyky
- parisuhde, perheellistyminen
- psykiatrisen hoidon tarve, psykiatrinen oireilu, itsetuhoinen käyttäytyminen, rikoskäyttäytyminen, päihdeongelmien väheneminen
- sairauspoissaolot
- vaikutukset läheisille ihmisille

Aineiston käsittely

Hoitojen vaikuttavuutta käsittelevät tutkimukset ryhmiteltiin intervention ja kohderyhmän perusteella. Vertailuryhmän sisältäviä hoitokokeita oli vain yksi. Suurin osa tutkimuksista oli sellaisia, joissa henkilöjoukon ominaisuuksia ja hoitotuloksia mitattiin ennen ja jälkeen hoitointervention. Ryhmittelimme tutkimukset tutkimustyypin perusteella niihin, joissa 1) relevanttia lopputulosmuuttujaa on mitattu henkilöiltä ennen interventiota ja sen jälkeen, sekä 2) ne tutkimukset, joissa relevanttia lopputulosmuuttujaa on mitattu ainoastaan intervention jälkeen. Ensimmäisen ryhmän, eli ennen-jälkeen-tutkimukset taulukoitiin yksityiskohtaisesti (Liite 2). Jälkimmäisistä otettiin vain ne, joissa oli mitattu tyytyväisyyttä hoitotulokseen ja niiden tiedot taulukoitiin vähemmän yksityiskohtaisesti(Liite 3). Kolme tutkijaa (IS, MS ja IP) taulukoi tutkimukset. Yksi tutkija tarkisti ja yhdenmukaisti taulukoinnit ja kirjoitti tutkimuksia kuvailevan tekstin (IP). Koska tutkimusten menetelmällinen laatu oli jo tutkimustyypin perusteella heikko, ei varsinaista laadunarviointia tai näytön asteen määrittelyä tehty.

Tulokset

Sukupuolidysforian lääketieteellisten hoitojen vaikuttavuuden arviointi perustuu 38 tutkimukseen, joista yksi on kontrolloitu hoitokoe (vaginoplastialeikkauksia koskeva tutkimus, Mate-Kole ym. 1990), yksi

rekisteritutkimus (sukuelinkirurgiatutkimus, Simonsen ym. 2016) ja loput tutkimuksia, joissa mitataan yhden ryhmän tuloksia ennen hoitointerventiota ja sen jälkeen (liite 2). Ennen-jälkeen-tutkimukset olivat joko eteneviä tai sellaisia, joissa alkumittauksia koottiin jälkikäteen potilastiedoista: varsin usein oli epäselvää oliko tutkimus aidosti etenevä. Yhden ryhmän poikkileikkaustutkimuksia, joissa tuloksia mitattiin vain hoidon jälkeen ja joissa mitattiin tyytyväisyyttä hoidon lopputulokseen, oli 25 (liite3).

Sukupuolen muuntoprosessi

Sukupuolen muunto koostuu tyypillisesti tosielämän harjoittelusta, oman sukuhormonituotannon vaimentamisesta hormonilääkityksellä, sekä sukuelimiin, rintoihin ja äänihuuliin kohdistuvista leikkaushoidoista. Toimenpiteitä täydennetään tarvittaessa muun muassa ihokarvojen poistolla ja puheterapialla. Sukupuolen muunto ei ole standardihoito, vaan yksilöllinen valikoima toimenpiteitä, joiden tarkoituksena on parantaa trans- tai muunsukupuolisen henkilön hyvinvointia ja toimintakykyä.

Tutkimusten kuvaus

Transnaisten ja transmiesten sukupuolen muuntoprosessia arvioi seitsemän seurantatutkimusta, joissa oli yhteensä 465 sukupuolen muuntoprosessin läpikäynyttä henkilöä (liite 2, taulukot 1−14). Tutkittujen henkilöiden määrä vaihteli 42:n ja 172:n välillä yksittäisissä tutkimuksissa. Viisi tutkimusta oli tehty Alankomaissa, Belgiassa tai Saksassa, yksi Ruotsissa ja yksi Italiassa. Muuntoprosessit käynnistyivät kahdessa tutkimuksessa 2000-luvun loppupuolella, neljässä tutkimuksessa 2000-luvun alkupuolella ja yhdessä tutkimuksessa 1990-luvulla. Muuntoprosessiin kuului sekä hormonihoitoja että erilaisia leikkaushoitoja. De Vriesin tutkimuksessa (De Vries ym. 2014) prosessin alkuun kuului puberteetin keskeytyshoito. Seurannan kesto oli puolesta vuodesta kahteen ja puoleen vuoteen viimeisimmän leikkauksen jälkeen tai yhdestä viiteen vuoteen muuntoprosessin alusta mitattuna. Ruppinin saksalaistutkimuksessa (Ruppin ym. 2015) seuranta-aika oli muita selvästi pidempi: prosessin alusta alkaen keskimäärin 14 vuotta.

Tutkimukset käsittelivät pääosin transsukupuolisten sukupuolen muuntoprosesseja. Van de Griftin hollantilaistutkimuksen (liite 2, taulukko 1) 5 % henkilöistä edusti muuta diagnoosia kuin DSM-IV:n sukupuoli-identiteetin häiriödiagnoosia. Lisäksi, Johanssonin ruotsalaistutkimuksessa (liite 2, taulukko 4) oli mukana yksi muunsukupuolinen, mutta näiden henkilöiden tuloksia ei kuitenkaan eritelty. Henkilöiden ikä sukupuolen muuntoprosessin alkaessa oli viidessä tutkimuksessa yli 30 vuotta, yhdessä tutkimuksessa ikää ei ollut ilmoitettu (Heylens 2014) ja yhdessä tutkimuksessa (de Vries ym. 2014) henkilöt olivat teinejä, keskimäärin 17-vuotiaita, hoitojen alkaessa. Tutkijat mittasivat useimmiten (taulukko 1) mielialan ja psykologisen kuormituksen muutosta (5 tutkimusta) sekä sukupuoliristiriidan, kehoahdistuksen tai minäkuvan muutoksia (4 tutkimusta).

Taulukko 1. Sukupuolen muuntoprosessin vaikuttavuutta arvioivissa tutkimuksissa käytetyt mittarit.

	Sukupuoliristiriita, kehoahdistus, minäkuva	Mieliala ja psykologinen kuormitus	Yleinen toimintakyky	Persoonallisuus, käyttäytymismallit	Sosiaaliset suhteet, työllisyys	Muuta
Van de Grift ym. 2017	UGDS, BIS					
Ruppin ym. 2015	BSRI	SCL-90		IIP, FPI-R		

de Vries ym. 2014	UGDS, BIS	BDI, STAI, TPI	CGAS			
Heylens ym. 2014		SCL-90			Ihmissuhteet, asuminen, työssäolo	Päihteiden käyttö, seksi
Costantino ym. 2010		oma mielialakysely			Ihmissuhteet	Unen laatu
Johansson ym. 2010						Lääkärin arvio lopputuloksesta
Smith ym. 2005	UGDS, BIS	SCL-90		MMPI		Ammattilaisen arvio fyysisestä olemuksesta (AAI), kokemus hyväksynnästä, tyytyväisyys seksielämään

Vaikuttavuus

Sukupuoliristiriita ja kehoahdistus

Kehoahdistus ja sukupuoliristiriita vähenivät tilastollisesti merkitsevästi kolmessa hollantilaisessa ennen-jälkeen-tutkimuksessa, joissa oli yhteensä 349 henkilöä (van de Grift ym: 2017; de Vries ym. 2014; Smith ym. 2005). Van de Griftin tutkimus ei eritellyt transnaisten ja transmiesten tuloksia. Seuranta-aika tutkimuksissa oli yhdestä kahteen ja puoleen vuoteen viimeisen leikkauksen jälkeen. Kaikissa tutkimuksissa tutkittavat henkilöt olivat saaneet sukupuolen muuntamiseen hormonihoitoa (de Vriesin tutkimuksessa myös puberteetin jarrutushoitoa), transnaisista osa vaginoplastian (van de Griftin tutkimuksessa 61 %) ja transmiehistä osa rintojen poiston (79 %) ja kohdun ja munasarjojen poiston (78 %). Kahdessa tutkimuksessa sukupuolen muuntoprosessiin liittyi transnaisilla myös rintarauhasleikkaukset (van de Griftin tutkimuksessa 30 %) ja transmiehillä falloplastia (van de Grift 27 % ja Smith alle 14 %). Smithin tutkimuksessa oli myös tehty yksi metadoioplastia (klitoriksen suurennus). Van de Griftin tutkimuksessa transnaisille oli lisäksi tehty epilaatioita (86 %), aataminomenan pienennysleikkauksia (8 %) ja feminisoivia kasvoleikkauksia (6 %).

Sukupuoliristiriitaa mittaavat UGDS-pisteet laskivat kaikissa kolmessa tutkimuksessa noin arvosta 50 arvoon 15 (skaala 12−60). Ero oli tilastollisesti merkitsevä. Transmiehillä pisteiden lasku oli suurempaa kuin transnaisilla.

Kehoahdistus väheni BIS-pisteillä mitattuna kaikissa kolmessa tutkimuksessa siten, että pisteet olivat lopussa BIS 2 (tyytyväinen) – 3 (neutraali). Muutos oli tilastollisesti merkitsevä ensisijaisten sukupuoliominaisuuksien (kuten sukuelimet ja rinnat) ja toissijaisten sukupuoliominaisuuksien (esim. lantio ja karvoitus) kohdalla kahdessa tutkimuksessa (Smith ja de Vries, raportoinnin epäselvyys estää van de Griftin tulosten tulkintaa), mutta neutraaleiden ominaisuuksien (kuten pituus ja kasvot) kohdalla de Vriesin tutkimuksen transmiehillä ero alkutilanteeseen nähden ei ollut merkitsevä.

Van de Griftin tutkimuksessa todettiin, että kehoahdistusta hoidon jälkeen ennustivat vaikeampi kehoahdistus alussa ($p<0,001$) sekä heikompi psyykkinen toimintakyky(SCL-90) lopussa ($p<0,001$). Kehoahdistuksen ja sukupuoliristiriidan välillä ei ollut minkään ryhmän kohdalla merkitsevää korrelaatiota alussa eikä lopussa.

Mieliala

Psykologista kuormitusta (SCL-90-mittarilla) mitanneista ennen-jälkeen-tutkimuksista kaikissa kolmessa (Ruppin, Heylens ja Smith, yhteensä 316 henkilöä) mittarin kokonaispisteet alenivat tilastollisesti

merkitsevästi, mikä merkitsee muun muassa vähäisempää masennusta tai ahdistuneisuutta, riittämättömyyden tunnetta, univaikeuksia tai somatisointitaipumuksia. Ruppinin ja Helensin tutkimukset raportoivat sukupuolet yhdessä ja Smithin tutkimuksessa eroteltiin transmiesten ja transnaisten tulokset. Heylensin tutkimuksessa psykologisen kuormituksen väheneminen saavutettiin jo hormonihoidon aikana, eikä leikkaushoidolla saavutettu enää lisähyötyä.

De Vries (55 henkilöä, jotka olivat muuntoprosessin alussa teinejä) käytti masennuksen ja ahdistuneisuuden mittaukseen BDI ja STAI –mittareita, joilla mitattuna masentuneisuus ja ahdistuneisuus laskivat, mutta eivät tilastollisesti merkitsevästi. Mittaustulokset raportoitiin transnaisille ja transmiehille erikseen. Costantinon tutkimuksessa oli ainoastaan transmiehiä. Tutkimuksessa käytettiin itse tehtyä mittaria, jolla mitattuna iloisuus, uupumus, jännittyneisyys, energisyys, onnellisuus, masennus, hikoilu, ärtyneisyys ja aggressiivisuus eivät muuttuneet tilastollisesti merkitsevästi alkutilanteeseen verrattuna.

Tyytyväisyys hoitoihin

Johanssonin ruotsalaistutkimuksessa (n=42) 90% ilmoitti olevansa tyytyväisiä hormonihoitoihin ja 67 % sukuelinkirurgiaan yli viisi vuotta kestäneen seurannan jälkeen. Ruppinin saksalaistutkimuksessa (n=71) oli pitkässä 10−24 vuotta kestäneessä seurannassa sukupuolen muuntoprosessin jälkeen merkittävä nousu tyytyväisyydessä elämään. Smithin englantilaistutkimuksessa vuodelta 2005 (n=158) yksi henkilö katui sukupuolen muuntoprosessiin ryhtymistä. Sukupuoli-identiteettien välillä ei ollut eroja katumisessa.

Liitteeseen 3 koottujen poikkileikkaustutkimusten perusteella transnaisten tyytyväisyysaste vaginoplastiaan oli kahdessa hollantilaistutkimuksessa 70% ja 96%. Rintaimplantteihin tyytyväisiä oli samoissa tutkimuksissa 65 % ja 96 % leikatuista vastaavassa järjestyksessä. Transmiehistä tyytyväisiä rintojenpoistoon oli 23 % ja 94 % ja metadoioplastiaan tai falloplastiaan 44 % ja 100 %.

Pohdintaa

Monien muuttujien, mutta etenkin mielialan mittaustulosten tulkinta on varsin vaikeaa ilman vertailuryhmää, joka ei olisi osallistunut muuntoprosessiin. Etenkin nuorella iällä mielialan muutoksia ja henkistä kasvua tapahtuu monesta muustakin syystä kuin sukupuolen muuntamisesta johtuen. Van de Griftin tutkimus vertasi hoitoja saaneiden tuloksia niiden sukupuolidysforiaa kokeneiden ihmisten tuloksiin, jotka eivät olleet päätyneet muuntoprosessiin, ja totesi, että sekä sukupuoliristiriita että kehoahdistus lievittyivät sekä hoidetuilla että ei-hoidetuilla muutaman vuoden seurannassa: kehoahdistus tosin vain hyvin vähän.

Seuraavassa listataan muutamia havaintoja sukupuolen muuntoprosessin vaikuttavuutta arvioineiden tutkimusten perusteella:

- Transnaisilla oli näissä tutkimuksissa suhteellisesti enemmän myöhäisvaiheen transsukupuolisuusdiagnooseja (Johansson, van de Grift)
- Transnaiset olivat keskimäärin vanhempia hoitoihin hakeutuessaan (Johansson 2010, van de Grift ym. 2017)
- Transnaisten toimintakyky ja tyytyväisyys kehoon oli keskimäärin huonompaa hoitoihin hakeutuessa (van de Grift ym. 2017, Johansson ym. 2010)
- Transmiehille tehtiin vähemmän sukuelinleikkauksia ja heillä tyytymättömyys leikkauksiin oli suurempaa (Ruppin ym. 2015, Smith ym. 2005)
- Toimintakyky parani enemmän transnaisilla (tosin transmiesten toimintakyky oli alun alkaen parempi) (de Vries ym. 2014, Johansson ym. 2010).

Vastausprosentti koko sukupuolen muuntoprosessia koskevissa tutkimuksissa vaihteli 37 %:n (Van de Grift ym. 2017) ja 79 %:n (de Vries ym. 2014) välillä. Ruppinin ym. (2015) tutkimuksessa vastausprosentti oli 50,7 %, Heylensin ym. (2014) tutkimuksessa 63 %, Johanssonin ym. (2010) tutkimuksessa 70 % ja Smithin (2005) tutkimuksessa sitä ei selkeästi ilmaistu. Syinä tutkimukseen osallistumattomuuteen mainittiin, että henkilön uusi osoite ei ollut tiedossa tai hän oli muuttanut ulkomaille (Ruppin, Smith), henkilö oli kuollut (Ruppin, de Vries) tai hän ei halunnut osallistua (Ruppin, Heylens, de Vries, van de Grift). Syitä osallistumisesta kieltäytymiseen mainittiin ajanpuute (Ruppin), somaattinen sairaus (Ruppin, de Vries), integriteettisyyt (Johansson) ja se, että transsukupuolisuus ei ollut enää elämässä ajankohtainen asia (Ruppin).

Van de Grift, Johansson ja De Vries vertasivat tutkimukseen osallistujien ja osallistumattomien ryhmiä keskenään. Van de Griftin ym. (2017) mukaan tutkimukseen osallistuneet henkilöt olivat korkeammin koulutettuja kuin osallistumattomat. Johanssonin ym. (2010) mukaan tutkimuksesta pudonneista valtaosa oli transnaisia (77,8 %) ja heidän toimintakykynsä oli heikompi kuin tutkimukseen osallistuneilla GAF-pisteillä mitattuna (63 vs. 71, p = 0,001). Osallistujat ja osallistumattomat eivät kuitenkaan eronneet toisistaan iältään, diagnoosityypiltään (varhais- vai myöhäisvaiheen diagnoosi) tai seksuaaliselta suuntautumiseltaan. De Vries ym. (2014) ei löytänyt merkitseviä eroja osallistuneiden ja osallistumattomien välillä missään ennen hoitoa mitatussa muuttujassa.

Puberteetin keskeytys

Lapsuudessa esiintyvä voimakaskin identifioituminen vastakkaiseen sukupuoleen katoaa yleensä aikuistumisen myötä (Ristori ja Steensma 2016). Pienellä osalla lapsista identifioituminen vastakkaiseen sukupuoleen kuitenkin lujittuu ja kehoahdistus ilmaantuu tai voimistuu murrosiän alkaessa (Kaltiala-Heino ym. 2018). Niin sanotun Hollannin mallin mukainen hoitolinja suosittaa tällaisessa tilanteessa puberteettikehityksen pysäyttämistä GnRH-agonisteilla eli gonadotropiinien vapauttajahormonin lailla vaikuttavilla lääkkeillä. Osa tutkijoista pitää GnRH-agonisteilla tapahtuvaa hoitoa kuitenkin vielä kokeellisena. Kyseessä on ryhmä kalliita lääkkeitä, joiden antotapa on joko injektio tai implantoitava muoto.

Puberteetin keskeyttämisen tarkoituksena on pysäyttää sekundaaristen ei-toivottujen sukupuoliominaisuuksien kehittyminen, mikä edistää luonnollista lopputulosta ja antaa nuorelle rauhan miettiä, haluaako hän varsinaisia muuntohoitoja. Keskeyttäminen tehdään vasta kun puberteetti on kunnolla käynnistynyt (Tannerin luokitus II-III). Kansainväliset endokrinologi-yhdistykset ovat yhteistyössä tehneet suosituksen, joka puoltaa GnRH-hoidon käyttöä silloin, kun on kyseessä lapsena alkanut ja murrosiän alkaessa jatkuva ristiriita sukupuoli-identiteetin ja kehon välillä (Hembree ym. 2017). Lääkityksen etuna on sen palautuvuus: jos nuori päättää keskeyttää lääkityksen, murrosiän kehitys jatkuu. Toisaalta sukuelinten kehityksen pysäytys voi myöhemmin vaikeuttaa muuntoleikkausten tekoa.

Tutkimusten kuvaus

Puberteetin keskeyttämistä GnRH-analogihoidolla käsitteli kaksi tutkimusta. Niissä oli yhteensä 271 henkilöä, joilla oli lapsena todettu sukupuoli-identiteetin häiriö ja siihen liittyvä ja murrosiässä paheneva sukupuoli- tai kehoahdistus (Liite 2, taulukot 15 ja 16). Tutkimukset on julkaistu vuosina 2015 ja 2011, Britanniassa (Costa ym. 2015) ja Alankomaissa (de Vries ym. 2011). Costan tutkimuksessa osa tutkimukseen osallistuneista siirtyi välittömästi GnRH-hoitoon (n=101), ja ne jotka tarvitsivat lisää kypsyttelyaikaa, aloittivat hormonihoidon vasta myöhemmin (n=100). De Vriesin tutkimus oli yhden ryhmän etenevä ennen-jälkeen-tutkimus.

Costan tutkimuksessa GnRH-analogihoidon rinnalla interventioon kuului WPATH-suosituksen mukainen, psykologinen (supportiivinen) interventio 18 kk ajan ja hormonihoito aloitettiin kuuden kuukauden kohdalla psykoterapian alkamisen jälkeen. De Vriesin tutkimuksessa interventiona oli pelkästään GnRH-analogihoito. Molemmat tutkimukset mittasivat psykososiaalista toiminta kykyä CGAS-mittarilla. De Vriesin

tutkimuksessa mitattiin lisäksi kehoahdistusta (BIS) ja sukupuoliristiriitaa (UGDS), masennusta (BDI) ja ahdistuneisuutta (STAI) sekä käyttäytymistä tai tunteita (CBCL).

Vaikuttavuus

Yleinen toimintakyky koheni CGAS-mittarin pisteiden perusteella molemmissa tutkimuksissa. Costan tutkimuksessa tilastollisesti merkitsevä parannus saavutettiin 12 kk psykoterapian ja 6 kk GnRH-hoidon jälkeen ja vaikutus säilyi vielä ainakin seuraavat kuusi kuukautta. Pelkkää psykoterapiaa saanut vertailuryhmä koheni niin ikään tilastollisesti merkitsevästi 12 ja 18 kuukauden kohdalla.

De Vriesin tutkimuksessa mieliala koheni ja käytöshäiriöiden riski pieneni noin kahden vuoden GnRH-agonistihoidon aikana. Sukupuoliristiriita ei vähentynyt eikä kehon kuvassa ilmaantunut muutoksia.

Turvallisuus

GnRH-hoidon mahdollisia riskejä ovat luun mineralisaation häiriintyminen, hedelmällisyyden aleneminen ja vielä tuntemattomat keskushermostovaikutukset (Hembree ym. 2017). Nuorille, joilla on miehen sukuelimet ja joiden GnRH-analogihoito alkaa jo varhaisessa puberteetissa, tulisi kertoa, että hoidon vuoksi peniksen kudosta ei välttämättä ole riittävästi vaginoplastiamenetelmiä varten, vaan joudutaan käyttämään muita kudossiirteitä.

Hormonihoidot

Transnaisten lääkityksenä on estrogeeni- ja antiandrogeeninen valmiste ja transmiehillä testosteronivalmisteet yksilöllisesti annosteltuna. Lääkkeillä pyritään oman sukuhormonituotannon vaimentamiseen sekä halutun sukupuolen piirteiden aikaansaamiseen ja ylläpitämiseen. Hoidon aloitus ja alkuseuranta tapahtuu HYKS:ssä ja Taysissa osana tosielämän jaksoa, jolloin hoidettava käyttäytyy ja pukeutuu toivotun sukupuolen mukaisesti ja osalle haetaan nimen ja sosiaaliturvatunnuksen muutosta. Hoidon aloittavien ikä vaihtelee paljon, samoin heidän terveydentilansa, taustansa ja toiveensa. Nykyisen käsityksen mukaan hormonilääkityksellä ei ole varsinaista yläikärajaa. Iän myötä annoksia kuitenkin pienennetään ja siirrytään ihon kautta annosteltaviin valmisteisiin. On tärkeää huomioida ja kertoa potilaille, että ylisuuret annokset eivät nopeuta tai lisää elimistössä tapahtuvia muutoksia, vaan saattavat muodostaa terveysriskin. (Tinkanen ym. 2015). Kun sopiva hoito on jatkunut parin vuoden ajan, jatkoseuranta siirtyy muualle, yleensä terveyskeskuksiin. Transsukupuolisten hormonihoidon seurannasta on Pia Dasin kattava artikkeli Suomen Lääkärilehdessä (Das 2019).

Tutkimusten kuvaus

Transnaisten ja transmiesten hormonihoitojen vaikuttavuutta arvioi yksitoista yhden ryhmän ennen ja jälkeen mittauksia tehneitä tutkimuksia, joissa on yhteensä 609 sukupuolen korjaamiseen tähtäävän hormonihoidon läpikäynyttä henkilöä (liite 2, taulukot 17−31). Yksittäisissä tutkimuksissa tutkittavien määrä vaihteli 7:n ja 107:n välillä. Viisi tutkimusta oli tehty Italiassa, kaksi Alankomaissa ja yksi tutkimus Britanniassa, Yhdysvalloissa, Belgiassa ja Turkissa. Tutkimukset on julkaistu vuosina 2000−2018: hormonihoidot toteutettiin 2−7 vuoden aikana päättyen 1−3 vuotta ennen julkaisuvuotta (arvio perustuu viiteen tutkimukseen, joissa hoitojen ajankohta oli ilmoitettu). Tutkitut henkilöt olivat kaikki transsukupuolisia, joiden keskimääräinen ikä oli kahdeksassa tutkimuksessa alle 30 vuotta ja kolmessa tutkimuksessa yli 30 vuotta (Manieri, Miles, Salbbekoorn). Muunsukupuolisia ei hormonitutkimuksissa ollut lainkaan.

Tuloksina mitattiin psykologista kuormitusta, mielialaa ja stressiä (neljä tutkimusta), kehoahdistusta ja sukupuoliristiriitaa (kaksi tutkimusta), aggressiivisuutta, tunteellisuutta tai visuospatiaalisia taitoja (kolme tutkimusta), karvan kasvua (kolme tutkimusta), painoa tai metabolisia muutoksia (kolme tutkimusta), akne

muutoksia tai äänen korkeutta (yksi tutkimus) (taulukko 2). Tulosten mittausajankohta oli yleensä yksi vuosi (7 tutkimusta), pisimmillään kaksi vuotta (Fisher) ja kolmessa tutkimuksessa alle seitsemän kuukautta (Slabbekoorn, Motta ja Turan).

Taulukko 2. Hormonihoitojen vaikuttavuutta arvioivissa tutkimuksissa käytetyt mittarit.

	Sukupuoliristiriita ja kehoahdistus	Elämänlaatu	Psykologinen kuormitus, mieliala ja stressi	Persoonallisuus, kognitio	Karvan kasvu ja akne	Paino, elintavat	Muuta
Motta ym. 2018, Italia				STAXI-2			
Turan ym. 2018, Turkki	BUT		SCL-90			BMI, EAT-40	
Irwig ym. 2017, Yhdysvallat							Äänen korkeus
Fisher ym. 2016, Italia	BUT, GIDYQ-AA		SCL-90-R, BDI		F&G	BMI, vyötärönympärys	
Colizzi ym. 2014, Italia			SCL-90-R, SDS, SAS				
Manieri ym. 2014, Italia		WHOQoL-100				Tupakointi, lipidit ja glukoosi	Kehon muutokset, parisuhde
Wierckx ym. 2014, Belgia					F&G, GAGS		
Colizzi ym. 2013, Italia			PSS, kortisoli				
Miles ym. 2006, Britannia				Verbaalisuus- ja visuospatiaalisuustestejä			
Slabbekoorn ym. 2001, Alankomaat				AIM, ASQ, ACT			
Giltay ja Gooren (G&G) 2000, Alankomaat					F&G, Leeds		

Vaikuttavuus

Transnaiset

Transnaisten hormonihoidon vaikuttavuutta arvioi 7 yhden ryhmän tutkimusta, joissa mittauksia oli tehty ennen ja jälkeen intervention (Fisher ym. 2016; Colizzi ym. 2014; Manieri ym. 2014; Colizzi ym. 2013; Miles ym. 2006; Slabbekoorn ym. 2001; Giltay ja Gooren 2000). Slabbekoornin tutkimuksessa ennen interventioita mittauksia oli tehty viisi kertaa. Seitsemässä tutkimuksessa oli yhteensä 314 henkilöä (21–78 per tutkimus). He olivat kaikki aikuisia, vaikkei sitä Smithin ja Colizzin 2013 tutkimuksessa spesifisti mainittukaan. Ikä oli keskimäärin 30–40 vuotta ja iän kahdessa tutkimuksessa ilmoitettu hajonta 19–66 vuotta.

Hormonihoitona käytettiin 6 tutkimuksessa estradioligeeliä ihon kautta (Fisher, Colizzi 2013 ja 2014, Manieri, Slabbekoorn, G&G), Fisherin tutkimuksessa estradioligeelin vaihtoehtona oli estradiolivaleriaatti suun kautta ja Slabbekoornin ja G&G:n tutkimuksissa etinyyliestradioli suun kautta. Manierin tutkimuksessa estradioligeelin käyttöä edelsi suun kautta annosteltu 17ßestradioli 3 kuukauden ajan, minkä jälkeen hoito jatkui iäkkäillä, tupakoivilla ja tukostaipumuksen omaavilla ihon kautta annostelulla. Milesin tutkimuksessa estrogeenihoito oli suun kautta otettava konjugoitu estrogeeni tai etinyyliestradioli. Antiandrogeenina käytettiin yleisimmin syproteroniasetaattia. Manierin tutkimuksessa käytettiin vaihtoehtoisesti spironolaktonia jos tarvittiin verenpainevaikutusta ja dutasteridia henkilöille, joilla on miestyyppistä hiustenlähtöä. 63 % käytti myös muita antiandrogeeneja. Kahdelle henkilölle, joilla oli lihavuutta ja verenpainetautia, käytettiin syproteroniasetaatin asemesta GnRH-analogia. Milesin tutkimuksessa sypoteroniasetaattia tai medroksiprogesteroniasetaattia käytti vain 8 % henkilöistä. Kolmessa italialaistutkimuksessa henkilöille annettiin hormonihoidon lisäksi psykoterapiaa kerran viikossa (Manieri), psykologista neuvontaa (Colizzi 2013) tai henkistä tukea (Fisher).

Seuranta-aika tutkimuksissa oli yleensä yksi vuosi hormonihoidon aloituksesta. Fisherin tutkimuksessa seuranta-aika oli 2,5 vuotta ja Salbbekoornin tutkimuksessa vain 3,5 kuukautta.

Sukupuoliristiriita ja kehoahdistus

Hormonihoitoa saavien transnaisten sukupuoliristiriitaa ja kehoahdistusta mitattiin yhdessä tutkimuksessa, jossa oli 28 henkilöä (Fisher). Sukupuoliristiriita lievittyi ensin 3 kuukauden kohdalla tilastollisesti merkitsevästi, mutta vaikeutui myöhemmin kohti 2,5 vuoden seurantajakson loppua GIDYQ-AA-mittarin pisteillä. Kehoahdistus lievittyi BUT-AA-pisteillä mitattuna 2,5 vuoden seurannassa tilastollisesti merkitsevästi.

Elämänlaatu

Hormonihoitoa saavien transnaisten elämänlaatua mitattiin yhdessä tutkimuksessa, jossa oli 56 henkilöä (Manieri). Elämänlaatu koheni WHOQOL-100 mittarin pisteillä yhden vuoden hormonihoidon jälkeen tilastollisesti merkitsevästi, keskimäärin pisteistä 62 pisteisiin 72. Mittarin skaala on 0-100. Pisteet yli 50:n viittaavat hyvään elämänlaatuun, joten tutkimukseen osallistuvien henkilöiden elämänlaatu oli jo alkutilanteessa hyvä. Mittarin osa-alueista kehon kuva, sukupuolielämän laatu ja ihmissuhteiden toimivuus näyttivät myös tilastollisesti merkitsevää parannusta.

Psykologinen kuormitus, mieliala ja stressi

Hormonihoitoa saavien transnaisten psykologista kuormitusta mitattiin SCL-90-mittarilla kahdessa tutkimuksessa, joissa oli yhteensä 106 henkilöä (Fisher, Colizzi 2014). Kummassakin tutkimuksessa psykologinen kuormitus väheni yhden vuoden (Colizzi) tai kahden vuoden (Fisher) seurannassa tilastollisesti merkitsevästi. Kokonaispisteet laskivat tasolta 0,75−0,8 tasolle 0,45−0,48. Suomen väestötason kokonaispisteiden arvo 0,65. Colizzin tutkimuksessa todettiin niiden ihmisten osuuden, joilla on merkittäviä psykologisia oireita (SCL>1) laskeneen vuodessa 24 prosentista 11 prosenttiin ($p<0,001$) tai merkittäviä toiminnanrajoituksia SCID-1-mittarin mukaan laskeneen 23 prosentista 10 prosenttiin.

Hormonihoitoa saavien transnaisten masennusta mitattiin kahdessa tutkimuksessa, joissa oli yhteensä 106 henkilöä (Fisher, Colizzi 2014). BDI-II-mittarin pisteet laskivat Fisherin tutkimuksessa kahdessa vuodessa tilastollisesti merkitsevästi, keskimäärin 10,7:stä 4,7:ään. BDI-pisteet 10−18 merkitsevät lievää masennusta ja pisteet alle 10 ei masennusta. Colizzin tutkimuksessa SDS-mittarin masennuspisteet laskivat vuodessa merkitsevästi keskimäärin pisteistä 48 pisteisiin 40. Mittarin skaala on 25−100 ja alle 50:n lukemia pidetään normaaleina. Tutkimukseen osallistujilla oli siis alussa joko vain lievästi tai ei lainkaan masennusoireita. Mittarin lukemien pienenemisellä ei liene näissä tutkimuksissa kliinistä merkitystä.

Hormonihoitoa saavien transnaisten ahdistuneisuutta mitattiin yhdessä tutkimuksessa, jossa oli 78 henkilöä (Colizzi 2014). SDS-mittarin ahdistuneisuuspisteet laskivat vuodessa merkitsevästi keskimäärin 45:stä 38:aan. Mittarin skaala on 25−100 ja alle 50:n lukemia pidetään normaaleina. Tutkimukseen osallistuneilla henkilöillä oli siis alussa joko vain lievästi tai ei lainkaan ahdistuneisuutta. Mittarin lukemien pienenemisellä ei liene näissä tutkimuksissa kliinistä merkitystä.

Hormonihoitoa saavien transnaisten itse koettua stressitasoa mitattiin yhdessä tutkimuksessa, jossa oli 50 henkilöä (Colizzi 2013). PSS-mittarin pisteet laskivat vuoden seurannassa tilastollisesti merkitsevästi, keskimäärin pisteistä 29 pisteisiin 15. Mittarin skaala on 0−40, pienempi arvo viittaa vähäisempään stressiin. Samanikäisessä terveessä väestössä keskiarvo on noin 14.

Karvan kasvu

Hormonihoitoa saavien transnaisten karvan kasvua mitattiin kahdessa tutkimuksessa, joissa oli yhteensä 49 henkilöä (Fisher, G&G). Molemmissa tutkimuksissa karvan kasvu väheni Ferriman-Gallwayn mittarilla yhden tai kahden vuoden seurannassa tilastollisesti merkitsevästi, keskimäärin pisteistä 17 tai 21 pisteisiin 5 tai 10. Pisteet laskivat alle 7 tasolle, joka viittaa siihen, että henkilöillä ei ole seurannan lopussa enää hirsutismin tasoista karvan kasvua.

Paino ja vyötärön ympärys

Hormonihoitoa saavien transnaisten kehon painoa mitattiin kolmessa tutkimuksessa, joissa oli yhteensä 115 henkilöä (Fisher, Manieri, G&G) ja vyötärön ympärysmittaa yhdessä italialaistutkimuksessa, jossa oli 28 henkilöä (Fisher). Kahdessa tutkimuksessa, yhden tai kahden vuoden seurannassa, painoindeksi nousi BMI-mittarilla noin 22:sta noin 23:een. Molemmissa tutkimuksissa muutos oli tilastollisesti merkitsevä. Kolmannessa tutkimuksessa (Manieri) yhden vuoden seurannassa paino nousi kiloissa 66:sta 69:ään, muutos ei ollut tilastollisesti merkitsevä. Vyötärön ympärys suureni Fisherin tutkimuksessa 83:staa 88 senttimetriin ($p<0,01$).

Transmiehet

Transmiesten hormonihoidon vaikuttavuutta arvioi 10 tutkimusta (Motta ym. 2018; Turan ym. 2018; Irwig ym. 2017; Fisher ym. 2016; Colizzi ym. 2014; Manieri ym. 2014; Wierckx ym. 2014; Colizzi ym. 2013; Slabbekoorn ym. 2001; Giltay ja Gooren 2000), joissa oli yhteensä 282 henkilöä (7−52 per tutkimus). Irwigin ja Slabbekoornin tutkimuksissa ennen interventioita tehtyjä mittauksia oli tehty useana ajankohtana. Slabbekoornin tutkimukseen osallistuneet henkilöt olivat 16−44-vuotiaita. Muissa tutkimuksissa henkilöt olivat yli 18-vuotiaita, keskimäärin 25−30 vuotiaita, vaikka Wierckxin ja Colizzin 2013 tutkimuksissa alaikärajaa ei ollut spesifisti mainittu.

Hormonihoitona käytettiin neljässä tutkimuksessa testosteroniestereitä lihaksensisäisesti 2-4 viikon välein (Irwig, Colizzi 2014 ja 2013, G&G), kahdessa tutkimuksessa testosteroniundekanoaattia lihaksensisäisesti noin 3 kk välein (Fisher, Wierckx) ja yhdessä tutkimuksessa testosteroniestereitä lihaksensisäisesti tai testosteroniundekanoaattia lihaksensisäisesti (Irwig) tai suun kautta (Slabbekoorn). Kahdessa tutkimuksessa käytettiin aluksi transdermaalista testosteronia ja sen jälkeen lihaksensisäistä testosteroniundekanoaattia (Motta, Manieri). Neljässä italialaistutkimuksessa henkilöille annettiin hormonihoidon lisäksi psykoterapiaa kerran viikossa (Motta, Manieri), psykologista neuvontaa (Colizzi 2013) tai henkistä tukea (Fisher). Seuranta-aika kuudessa tutkimuksessa yksi vuosi hormonihoidon aloituksesta. Fisherin tutkimuksessa seuranta-aika oli 2,5 vuotta, Mottan ja Turanin tutkimuksissa 6−7 kuukautta ja Salbbekoornin tutkimuksessa 3,5 kuukautta.

Sukupuoliristiriita ja kehoahdistus

Hormonihoitoa saavien transmiesten sukupuoliristiriitaa mitattiin yhdessä tutkimuksessa, jossa oli 26 henkilöä (Fisher). Sukupuoliristiriita lievittyi ensin 3 kuukauden kohdalla tilastollisesti merkitsevästi, mutta vaikeutui myöhemmin kohti 2,5 vuoden seurantajakson loppua GIDYQ-AA-mittarin pisteillä mitattuna. Kehoahdistusta mittasi kaksi tutkimusta (Turan ja Fisher), joissa oli yhteensä 65 henkilöä. Molemmissa tutkimuksissa kehoahdistus lievittyi BUT-AA-pisteillä mitattuna puolen (Turan) tai 2,5 vuoden (Fisher) seurannassa tilastollisesti merkitsevästi.

Elämänlaatu

Hormonihoitoa saavien transmiesten elämänlaatua mitattiin yhdessä tutkimuksessa, jossa oli 27 henkilöä (Manieri). Elämänlaatu koheni WHOQOL-100 mittarin pisteillä yhden vuoden hormonihoidon jälkeen keskimäärin pisteistä 63 pisteisiin 69, mutta muutos ei ollut tilastollisesti merkitsevä. Mittarin skaala on 0−100 ja pisteet yli 50:n viittaavat hyvään elämänlaatuun, joten henkilöiden elämänlaatu oli jo alkutilanteessa hyvä. Mittarin osa-alueista kehon kuva ja ihmissuhteiden toimivuus näyttivät tilastollisesti merkitsevää parannusta.

Psykologinen kuormitus, mieliala ja stressi

Hormonihoitoa saavien transmiesten psykologista kuormitusta mitattiin SCL-90-mittarilla kolmessa tutkimuksessa, joissa oli yhteensä 92 henkilöä (Turan, Fisher, Colizzi 2014). Kaikissa kolmessa tutkimuksessa psykologinen kuormitus väheni joko puolen, yhden tai kahden vuoden seurannassa tilastollisesti merkitsevästi. Colizzin tutkimuksessa todettiin niiden ihmisten osuuden, joilla on merkittäviä psykologisia oireita (SCL>1) laskeneen vuodessa 24 prosentista 11 prosenttiin ($p<0,001$) tai merkittäviä toiminnanrajoituksia SCID-1-mittarin mukaan laskeneen 23 prosentista 10 prosenttiin.

Hormonihoitoa saavien transmiesten masennusta mitattiin kahdessa tutkimuksessa, joissa oli yhteensä 55 henkilöä (Fisher, Colizzi 2014). BDI-II-mittarin pisteet laskivat Fisherin tutkimuksessa kahdessa vuodessa tilastollisesti merkitsevästi, keskimäärin pisteistä 9,2 pisteisiin 4,4. BDI-pisteet alle 10 merkitsevät ”ei masennusta”. Colizzin tutkimuksessa SDS-mittarin masennuspisteet laskivat vuodessa merkitsevästi keskimäärin pisteistä 48 pisteisiin 40. Mittarin skaala on 25−100 ja alle 50:n lukemia pidetään normaaleina. Henkilöillä oli siis alussa joko vain lievästi tai ei lainkaan masennusoireita. Mittarin lukemien pienenemisellä ei liene näissä tutkimuksissa kliinistä merkitystä.

Hormonihoitoa saavien transmiesten ahdistuneisuutta mitattiin yhdessä tutkimuksessa, jossa oli 29 henkilöä (Colizzi 2014). SDS-mittarin ahdistuneisuuspisteet laskivat vuodessa merkitsevästi keskimäärin pisteistä 45 pisteisiin 38. Mittarin skaala on 25−100 ja alle 50:n lukemia pidetään normaaleina. Henkilöillä oli siis alussa joko vain lievästi tai ei lainkaan ahdistuneisuutta. Mittarin lukemien pienenemisellä ei liene näissä tutkimuksissa kliinistä merkitystä.

Hormonihoitoa saavien transmiesten itse koettua stressitasoa mitattiin yhdessä tutkimuksessa, jossa oli 20 henkilöä (Colizzi 2013). PSS-mittarin pisteet laskivat vuoden seurannassa tilastollisesti merkitsevästi, keskimäärin 25:stä 15:een. Mittarin skaala on 0−40 ja pienempi arvo viittaa vähäisempään stressiin. Samanikäisessä terveessä väestössä keskiarvo on noin 14.

Aggressiivisuus

Hormonihoitoa saavien transmiesten aggressiivisuutta mitattiin kahdessa tutkimuksessa, joissa oli yhteensä 99 henkilöä (Motta, Slabbekoorn). Mottan tutkimuksessa aggressiivisuutta mittaavat STAXI-pisteet nousivat seitsemän kuukauden testosteronihoidon jälkeen tilastollisesti merkitsevästi, mikä viittaa lisääntyneeseen

aggressiivisuuteen. Kokonaispisteet pysyivät kuitenkin sekä alussa että seurannan päättyessä normaalialueella. Mitatut testosteronitasot eivät korreloineet aggressiivisuuden tason kanssa, mikä on samansuuntainen tulos kuin tuoreessa suuressa eurooppalaistutkimuksessa (Defreyne ym. 2019b). Slabbekoornin tutkimuksessa ASQ-pisteillä mitattu valmius aggressiiviseen käyttäytymiseen lisääntyi 3,5 kuukauden testosteronihoidon jälkeen vähän, mutta tilastollisesti merkitsevästi. Sen sijaan aggressiivisten tai negatiivisten tunteiden kokemisessa ei tapahtunut merkitsevää muutosta. Slabbekoornin tutkimuksessa (n=47) mitattiin myös tunteisiin reagoinnin voimakkuutta AIM-mittarilla. Tulosten mukaan transmiesten tunteellisuus ja positiivisten tunteiden voimakkuus vähenivät 3,5 kk hormonihoidon jälkeen tilastollisesti merkitsevästi, mutta negatiivisten tunteiden kokemisessa ei tapahtunut merkitsevää muutosta.

Karvan kasvu ja akne

Hormonihoitoa saavien transmiesten karvan kasvua mitattiin kolmessa tutkimuksessa, joissa oli yhteensä 63 henkilöä (Fisher, Wierckx, G&G). Kaikissa kolmessa tutkimuksessa karvan kasvu oli lisääntynyt Ferriman-Gallwayn mittarilla tilastollisesti merkitsevästi, keskimäärin pisteistä 0,5-4 pisteisiin 12-18 yhden vuoden seurannassa tai pisteisiin 25 kahden vuoden seurannassa (Fisher). Wierckxin tutkimuksessa 80 %:lla pisteet nousivat vuoden seurannassa yli 8 tasolle, jota pidetään lievästi kiihtyneenä karvankasvuna. Keskiarvoja tarkastellessa moni saavutti yli 15 pistetason, jota pidetään kohtalaisena tai voimakkaana hirsutismina (naisilla esiintyvä liikakarvoitus). Wiercksin tutkimuksessa (n=20) mitattiin myös aknen kehittymistä vuoden testosteronihoidon jälkeen. Aknemuutoksia, jotka olivat suurimmalla osalla lieviä, oli kasvoissa alussa 35 %:lla ja lopussa 55 %:lla ja selässä vastaavat osuudet olivat 15 % ja 50 %. Miestyyppistä kaljuuntumista ilmaantui Wiercksin tutkimuksessa yhdelle henkilöille. Miestyyppisen kaljuuntumisen riski kasvoi tutkijoiden mukaan heidän toisessa seurantatutkimuksessaan, jossa testosteronihoidon kesto oli yli 10 vuotta.

Paino ja vyötärön ympärys

Hormonihoitoa saavien transmiesten kehon painoa mitattiin neljässä tutkimuksessa, joissa oli yhteensä 117 henkilöä (Turan, Fisher, Manieri, G&G) ja vyötärön ympärysmittaa yhdessä italialaistutkimuksessa, jossa oli 26 henkilöä (Fisher). Kolmessa tutkimuksessa, puolen, yhden tai kahden vuoden seurannassa, paino nousi BMI-mittarilla tilastollisesti merkitsevästi. Fisherin tutkimuksessa henkilöille tuli 2 vuoden testosteronihoidon aikana keskimäärin 10 kiloa lisää kun taas Manierin tutkimuksessa yhden vuoden seurannassa paino nousi kiloissa 65:sta 68:aan, mutta muutos ei ollut tilastollisesti merkitsevä. Vyötärön ympärys pieneni Fisherin tutkimuksessa 100 cm:stä yhdessä vuodessa 90 cm:iin ja palasi kahden vuoden seurannassa 98 senttimetriin.

Äänen korkeus

Hormonihoitoa saavien transmiesten äänen korkeutta mitattiin yhdessä tutkimuksessa, joissa oli 7 henkilöä, jotka eivät olleet saaneet ääniterapiaa tai äänen käytön ohjausta (Irwig). Äänen korkeuden alenemaa pidettiin kliinisesti merkittävänä jo puolen vuoden testosteronihoidon jälkeen kaikkien henkilöiden kohdalla. Ensimmäisen 3 kk aikana tulokset vaihtelivat paljon: toisilla ei tapahtunut äänen muutosta ja toisilla suurin äänen madallus tapahtui juuri tuolloin.

Turvallisuus

Sukupuolen muuntamisen hormonihoitoihin liitettyjä sydän- ja verenkiertoelimistön ja metabolisia riskitekijöitä sekä sairastavuutta ja kuolleisuutta käsitteleviä tutkimuksia on vastikään koottu systemaattiseksi sateenvarjokatsaukseksi (Defreyne ym. 2019). Yhdentoista katsauksen ja 66 alkuperäistutkimuksen perusteella tutkijat totesivat, että transnaisten kohdalla todettiin korkeampi sydäntapahtumien riski. Tuloksen käytettävyyttä heikentää se, että suurimmassa osassa tutkimuksista oli käytetty nyt jo käytöstä poistuvaa etinyyliestradiolia. Nykyaikaisia lääkkeitä käyttävät tutkimukset ovat

suurelta osin takautuvia tutkimuksia, joiden seuranta-ajat ovat riittämättömiä. Laboratoriomarkkerien kohdalla tulokset olivat ristiriitaisia, mikä katsauksen tekijöiden mukaan voi johtua pienestä otoskoosta ja lyhyestä seuranta-ajasta.

Toinen tuore systemoitu katsaus (Velho ym. 2017) rajoittui transmiesten testosteronihoidon sydän- ja verenkiertoelimistön haittoihin. Katsaukseen otetiin mukaan 13 tutkimusta, joissa mittauksia oli tehty ennen hormonihoidon aloitusta ja sen jälkeen. Seuranta-aika vaihteli puolesta vuodesta viiteen vuoteen. Tulosten mukaan painoindeksi nousi hieman. Eri testosteronivalmisteiden verenpainevaikutuksia tarkasteli seitsemän tutkimusta, joista kolmessa havaittiin lievää (kliinisesti merkityksetöntä) nousua verenpainetasoissa. Yhdessä tutkimuksessa kahdelle henkilölle kehittyi verenpainetauti, joka saatiin hallintaan kun testosteronilääkitys purettiin pois. HDL-kolesterolin lasku ja LDL-kolesterolin nousu havaittiin kaikissa lipidejä mitanneissa tutkimuksissa. Kahdeksassa tutkimuksessa havaittiin yhteys testosteronihoidon ja kohonneen hemoglobiinin ja hematokriitin välillä. Arvot eivät kuitenkaan kohonneet niin paljon, että se olisi edellyttänyt testosteronihoidon keskeytystä. Kuusi tutkimusta arvioi maksavaikutuksia, ja ne olivat hyvin lieviä tai niitä ei ollut lainkaan. Yhteenvetona tutkijat toteavat, että testosteronin käyttö assosioituu transmiehillä kohonneeseen painoindeksiin, hemoglobiiniin tai hematokriittiin ja LDL kolesteroliin sekä alentuneeseen HDL-kolesteroliin, mutta näytön aste on alhainen.

Sukupuolen muuntamiseen käytettyjen hormonien ei voida sanoa kasvattavan sukupuolihormoneista riippuvaisten kasvainten riskiä. Tieto perustuu systemaattiseen katsaukseen (McFarlane ym. 2018), jossa on seitsemän aihetta käsittelevää kohorttitutkimusta, kaksi poikkileikkaustutkimusta ja 34 tapausselostusta. Katsauksen tekijät huomauttavat, että tutkitut henkilöt olivat nuoria ja hormonien käyttöajat liian lyhyitä syöpäriskin kunnolliseen arvioimiseen. Tapausselostukset nostavat esiin mahdolliset yhteydet korkea-annoksisen estradiolin ja prolaktinooman sekä antiandrogeenihoidon ja meningeooman välillä.

Pohdintaa

Transnaisten hormonihoidon tulosten tulkinnassa on syytä huomioida tutkimuksissa käytetyt valmisteet. Kahdessa tutkimuksessa (Miles ja GG) käytettiin etinyyliestradiolia, jota ei Suomessa käytetä suurempien vaskulaaristen komplikaatioiden, erityisesti laskimotukosten riskin vuoksi. Suomessa käytetään transnaisten estrogeenivalmisteina estradiolivaleraattia tai estradiolihemihydraattia suun kautta tai ihon kautta annosteltavia estrogeenivalmisteita, jos potilas kuuluu tromboemboliseen riskiryhmään (ylipaino, hypertonia, tupakointi) ja erityisesti potilaan täytettyä 40 vuotta. Yleisimmin käytetyt antiandrogeeniset valmisteet ovat syproteroniasetaatti tai spironolaktoni. Finasteridia voidaan tarvittaessa käyttää kasvojen alueen karvankasvun vähentämiseksi. (Tinkanen 2015)

Rintakirurgia

Tutkimusten kuvaus

Transnaisten ja transmiesten rintakirurgian vaikuttavuutta arvioi kaksi seurantatutkimusta, joissa on yhteensä 35 rintojen silikoni-implanttileikkauksen läpikäynyttä transnaista (Weigert ym. 2013) ja 42 rintojen poistoleikkauksen läpikäynyttä transmiestä (Agarwal ym. 2018) (liite 2, taulukot 32 ja 33). Tutkimukset oli tehty Yhdysvalloissa ja Ranskassa. Sukuelinkirurgiaa koskevissa leikkauksissa oli mukana rinnanpoisto- tai rintaimplanttileikkauksen läpikäyneitä, mutta heidän tuloksiaan ei ole tutkimuksissa eritelty. Silikoni-implantit oli asetettu vuosina 2008−2012 ja rinnan poistot tehty vuosina 2015−2016. Tutkimukset on julkaistu vuosina 2013 ja 2018 ja osallistuneet henkilöt olivat kaikki transsukupuolisia. Keskimääräinen ikä oli transnaisilla 42 vuotta ja transmiehillä 28 vuotta. Molemmat tutkimukset mittasivat elämänlaatua ja rintaleikkauksen jälkeistä tyytyväisyyttä Breast-Q-mittarilla. Transmiehillä mitattiin lisäksi

kehoahdistusta BUT-A-mittarilla. Implanttileikkauksen tuloksia mitattiin vielä vuoden kuluttua ja rintojen poistoleikkauksen tuloksia puoli vuotta leikkauksen jälkeen.

Vaikuttavuus

Elämänlaatua ja tyytyväisyyttä rintaleikkauksen jälkeen mittaavat BREAST-Q-pisteet paranivat tilastollisesti merkitsevästi sekä transnaisilla vuosi rintojen suurennusleikkauksen jälkeen (Weigert) että transmiehillä puoli vuotta rintojen poiston jälkeen (Agarwal). Agarwalin tutkimuksessa transmiesten kehoahdistus väheni BUT-A-mittarin pisteillä mitattuna myös tilastollisesti merkitsevästi.

Liitteen 3 poikkileikkaustutkimuksesta: Transnaisista 95 % oli tyytyväisiä rintojen suurennukseen (1 tutkimus), transmiehistä 79 % rintojen poistoon (1 tutkimus) ja muunsukupuolisista 94-100% rintojen muuntoleikkauksiin (2 tutkimusta).

Pohdintaa

Tyytyväisyyttä rintaleikkauksiin mittaavissa jälkeen-tutkimuksissa vastausprosentti vaihteli 51%:n (De Cuypere ym. 2005) ja 72%:n (Poudrier ym. 2018; Olson-Kennedy ym. 2018) välillä. Syinä osallistumattomuuteen mainittiin tavoittamisen vaikeus esim. muuttuneen asuinpaikan vuoksi (De Cuypere, Olson-Kennedy) ja haluttomuus osallistua haastatteluihin tai tutkimuksiin (Van de Grift, De Cuypere, Olson-Kennedy). De Cuyperen ym. (2005) mukaan pitkä seuranta-aika pienentää usein vastausprosenttia.

Puuttuvien vastausten vuoksi myös osallistuneiden ja osallistumattomien välinen vertailu ja vastausprosentin vaikutusten arviointi lopputuloksen kannalta oli vaikeaa (De Cuypere ym. 2005). Transmiesten tyytyväisyyttä rintaleikkaukseen arvioineen Van de Griftin ym. (2017; vastausprosentti 62%) mukaan tutkimukseen osallistuneet saattavat olla tyytyväisempiä ja toimintakykyisempiä kuin tutkimuksesta pudonneet, koska tutkimukseen osallistuminen vaatii vaivaa ja motivaatiota. Tämä voi vinouttaa tyytyväisyystuloksia hiukan positiivisempaan suuntaan.

Sukuelinkirurgia

Tutkimusten kuvaus

Transnaisten ja transmiesten sukuelinkirurgian vaikuttavuutta arvioi yksi kontrolloitu hoitokoe (Mate-Kole ym. 1990), yksi rekisteritutkimus (Simonsen ym. 2016) ja kahdeksan yhden ryhmän ennen ja jälkeen intervention tehtyjä mittauksia sisältäviä tutkimuksia (Lindqvist ym. 2017; Papadopoulos ym. 2017; van de Grift ym. 2017; da Silva ym. 2016; Lobato ym. 2009; Udeze ym. 2008; Megeri ym. 2007; Smith ym. 2001), joissa on yhteensä 573 leikkauksen läpikäynyttä henkilöä (liite 2, taulukot 34-44). Yksittäisissä tutkimuksissa tutkittavien määrä vaihteli 20:n ja 190:n välillä. Kolme tutkimusta oli tehty Britanniassa, kaksi Alankomaissa, kaksi Brasiliassa ja yksi tutkimus Saksassa, Ruotsissa ja Tanskassa. Tutkimukset on julkaistu vuosina 1990−2017 ja tutkitut henkilöt olivat kaikki transsukupuolisia. Keskimääräinen ikä oli yhdessä tutkimuksessa 20 vuotta (Smith ym. 2001), viidessä tutkimuksessa 30−40 vuotta ja kolmessa tutkimuksessa yli 40 vuotta (Lobaton tutkimuksessa ilmoitettu vain vaihteluväli 21−54). Muunsukupuolisia ei sukuelinkirurgiatutkimuksissa ollut lainkaan.

Tuloksina mitattiin psykologista kuormitusta tai mielialaa (seitsemän tutkimusta), elämänlaatua (neljä tutkimusta), kehoahdistusta ja sukupuolisristiriitaa (kolme tutkimusta), persoonallisuuden piirteitä (kolme tutkimusta) ja virtsaamista (yksi tutkimus) (taulukko 3). Tulosten mittausajankohta oli kuudessa tutkimuksessa yli yksi vuosi viimeisen leikkauksen jälkeen. Kahdessa tutkimuksessa (Papadopolous ym. 2017; Udeze ym 2008) seuranta-aika oli puoli vuotta, ja kahdessa tutkimuksessa (Simonsen ym. 2016; Megeri ym.2007) seuranta-aikaa ei ollut ilmoitettu.

Taulukko 3. Sukuelinkirurgian vaikuttavuutta arvioivissa tutkimuksissa käytetyt mittarit.

	Sukupuoliristiriita ja kehoahdistus	Elämänlaatu	Mieliala, psykologinen kuormitus	Persoonallisuus, kognitio	Muu psykiatrinen diagnoosi	Virtsaaminen	Muuta
Lindqvist ym. 2017, Ruotsi		SF-36					
Papadopoulos ym. 2017, Saksa	RSES	QLS	FPI, PHQ-4				
van de Grift ym. 2017, Alankomaat	BIS, RSES	CL	HADS, SWLS, SHS			IPSS	
da Silva ym. 2016, Brasilia		WHOQOL					
Simonsen ym. 2016, Tanska			ICD-10		ICD-10		Kuolema, päihteet
Lobato ym. 2009, Brasilia				DSQ			t
Udeze ym. 2008, Britannia			SCL-90R		ICD-10		
Megeri ym. 2007, Britannia			HAD, STAI, BDI, GHQ				
Smith ym. 2001, Alankomaat	BIS, UGDS		SCL-90R	NVM			
Mate-Kole ym. 1990, Britannia			CCE	BSRI			

Vaikuttavuus

Transnaiset

Transnaisten sukuelinkirurgian vaikuttavuutta arvioi yhdeksän tutkimusta: yksi kontrolloitu hoitokoe (Mate-Kole ym. 1990), yksi rekisteritutkimus (Simonsen ym. 2016) ja seitsemän yhden ryhmän ennen ja jälkeen intervention tehtyjä mittauksia sisältäviä tutkimuksia (Lindqvist ym. 2017; Papadopoulos ym. 2017; da Silva ym. 2016; Lobato ym. 2009; Udeze ym. 2008; Megeri ym. 2007; Smith ym. 2001). Jälkimmäisistä kaksi oli todennäköisesti etenevää (Udeze, Megeri) ja loput keräsivät alkutietoja takautuvasti. Tutkimuksissa oli yhteensä 491 henkilöä (7−190 per tutkimus). Ikä oli keskimäärin 31−47 vuotta kaikissa tutkimuksissa (hajonta 19−80 vuotta) paitsi Smithin hollantilaistutkimuksessa, jossa leikatut olivat noin 19-vuotiaita.

Kaksi tutkimusta käsitteli ainoastaan vaginoplastiaa (da Silva, Mate-Kole). Yhdessä tutkimuksessa kaikille tehtiin vaginoplastia ja osalle lisäksi muita leikkauksia (Papadopoulos), ja yhdessä vaginoplastia oli yleisin transnaisille tehty leikkaus (Smith). Viidessä tutkimuksessa puhuttiin sukupuolen muuntoleikkauksesta kuvaamatta tarkemmin sisältöjä (Lindqvist, Simonsen, Lobato, Udeze, Megeri). Da Silvan tutkimuksessa kaikki vaginoplastia-leikatut osallistuivat vähintään 2 vuotta supportiiviseen ryhmämuotoiseen psykoterapiaan. Mate-Kolen tutkimuksessa koehenkilöt olivat ennen vaginoplastia-leikkauksia ja niiden jälkeen psykiatrisessa seurannassa. Lobaton tutkimuksessa leikkausta edeltänyt klinikan ryhmäterapia. Seuranta-aika tutkimuksissa vaihteli keskimäärin viidestä vuodesta leikkauksen jälkeen (Lindqvist) pariin vuoteen (4 tutkimusta) ja lyhimmillään puoleen vuoteen leikkauksesta (Papadopoulos, Udeze). Kahdessa tutkimuksessa seuranta-aikaa ei kerrota (Simonsen, Megeri).

Sukupuoliristiriita, kehoahdistus, itsetunto

Smithin tutkimus (7 transnaista ja 13 transmiestä) oli ainoa, jossa vaginoplastian, falloplastian ja rintarauhasleikkausten jälkeen mitattiin sukupuoliristiriitaa UGDS-mittarilla ja kehoahdistusta BIS-mittarilla. Molemmilla mittareilla tilanne parani reilun vuoden seurannassa. Mate-Kolen tutkimuksessa mittarina käytettiin BSRI-pisteitä. Niiden mukaan itse arvioituna, feminiinisisiä tai maskuliinisia persoonallisuuden piirteitä kuvaavissa testituloksissa ei ollut lähtötasossa eroa leikkausryhmän transnaisten ja jonotusryhmän välillä eikä ryhmien välillä havaittu tilastollisesti merkitsevää eroa kahden vuoden jälkeen. Papadopouloksen tutkimuksessa vaginoplastian läpikäyneiden transnaisten itsetunto RSES-pistein mitattuna oli kohentunut hieman (mutta tilastollisesti merkitsevästi) puoli vuotta leikkauksen jälkeen.

Elämänlaatu

Sukuelinleikkauksia läpikäyneiden transnaisten elämänlaatua mitattiin kolmessa tutkimuksessa, joissa oli yhteensä 236 henkilöä (da Silva, Lindqvist, Papadopoulos). Da Silvan brasilialaistutkimuksessa (n=7) elämänlaatua mittaavan HOQOL-mittarin psykologisella ja sosiaalisella ulottuvuudella saatiin merkitsevää parannusta vuosi vaginoplastialeikkauksen jälkeen verrattuna lähtötasoon. Fyysinen terveys ja itsenäisyys sen sijaan heikentyivät merkitsevästi. Lindqvistin ruotsalaistutkimuksessa (n=190) SF-36-mittarilla todettiin useimmissa fyysisen ja psyykkisen toimintakyvyn osa-alueissa ja koetussa terveydessä nousua vuoden kuluttua sukuelinleikkauksesta ja laskua kolmen ja viiden vuoden kuluttua. Muutokset eivät olleet tilastollisesti merkitseviä. Papadopouloksen saksalaistutkimuksessa (n=39) saatiin QLS-mittarilla yleiseen ja terveyteen liittyvään elämänlaatuun tilastollisesti merkitsevää kohenemista puoli vuotta leikkaushoitojen jälkeen. Kaikille oli tehty vaginoplastia ja lähes joka toiselle myös rintojen suurennusleikkaus.

Masennus ja ahdistuneisuus

Sukuelinleikkauksia läpikäyneiden transnaisten masennusta mitattiin Mate-Kolen kontrolloidussa hoitokokeessa (n=40) ja kolmessa ennen-jälkeen -tutkimuksessa, joissa oli yhteensä 133 henkilöä (Papadopolous, Simonsen, Megeri). Mate-Kolen tutkimuksessa masentuneisuus ja ahdistuneisuus oli alkutilanteessa samalla tasolla, mutta kahden vuoden kohdalla leikkausryhmällä oireilu oli vähentynyt ja jonossa olevilla lisääntynyt tilastollisesti merkitsevästi. Papadopouloksen tutkimuksessa PHQ-mittarin masennuspisteet laskivat puolen vuoden kuluttua vaginoplastian ja muiden leikkausten jälkeen tilastollisesti merkitsevästi, väestön keskiarvoon. Simonsenin rekisteritutkimuksessa masennusdiagnoosin omaavien osuus oli suurempi sukupuolen muuntoleikkausten jälkeen kuin ennen sitä. Megerin tutkimuksessa ei havaittu useiden ahdistuneisuutta ja masennusta kuvaavien mittarien tuloksissa merkitsevää eroa ennen ja jälkeen leikkauksen.

Tyytyväisyys hoitoon

Transnaisten tyytyväisyydestä sukuelinkirurgiaan saatiin tietoa Smithin tutkimuksesta ja liitteessä olevista poikkileikkaustutkimuksista. Smithin tutkimuksessa 3/7stä oli tyytyväisiä vaginoplastiaan. Kolmessa poikkileikkaustutkimuksessa vaginoplastiaan tyytyväisten transnaisten osuus oli 70 ja 90 % eikä kukaan katunut leikkaushoitoihin ryhtymistä.

Turvallisuus

Liitteen 3 poikkileikkauksista poimittuna sukuelinleikatuista transnaisista 13 prosentilla esiintyi vakavia komplikaatioita (Revol ym. 2003). Muuntoleikkauksina tehtiin 25 prosentille häpyhuulten leikkauksia ja 13 prosentille neovaginan fisteleiden korjausleikkauksia. Toisessa tutkimuksessa 11 prosentilla leikatuista esiintyi merkittävää verenvuotoa, 7 prosentille kehittyi infektio ja 4 prosentille osittainen nekroosi. Lisäksi neljälle prosentille kehittyi myöhemmin virtsaputken ahtauma ja 7 prosentille tiputtelua (Breton 2017). Kolmannessa tutkimuksessa tehtiin kolme neovaginan purkua, joiden syynä oli nekroosi (10 kuukauden kohdalla) tai ahtauma (yli viiden vuoden kohdalla) (Papadopolous 2017).

Transmiehet

Transmiesten sukuelinkirurgian vaikuttavuutta arvioi yksi tanskalainen rekisteritutkimus (Simonsen ym. 2016) ja kaksi hollantilaista yhden ryhmän ennen ja jälkeen intervention tehtyjä mittauksia sisältäviä tutkimusta, joissa alkutiedot oli kerätty takautuvasti (van de Grift ym. 2017; Smith ym. 2001). Tutkimuksissa oli yhteensä 82 henkilöä (13-48). Ikä leikkausta tehtäessä oli van de Griftin tutkimuksessa keskimäärin 40 vuotta, Simonsenin tutkimuksessa 33 vuotta ja Smithillä noin 19 vuotta. Van de Griftin tutkimuksessa leikkauksena oli falloplastia (n=15) tai metoidioplastia (n=6) ja lisäleikkauksina asetettiin kivesimplantteja sekä tehtiin glansin tai skrotumin plastioita. Smithin tutkimuksessa henkilöille (n=13) tehtiin yksi falloplastia ja kaksi skrotumin plastiaa; suurin osa halusi vain rintojen poiston. Simonsenin rekisteritutkimuksessa leikkauksia ei ollut kuvattu. Seuranta-aika oli Simonsenin rekisteritutkimuksessa yli kymmenen vuotta, van de Griftin tutkimuksessa kaksi ja puoli vuotta ja Smithin tutkimuksessa reilun vuoden.

Sukupuoliristiriita, kehoahdistus, itsetunto

Smithin tutkimus (7 transnaista ja 13 transmiestä) oli ainoa, jossa vaginoplastian, falloplastian ja rintarauhasleikkausten jälkeen mitattiin sukupuoliristiriitaa UGDS-mittarilla ja kehoahdistusta BIS-mittarilla. Molemmilla mittareilla tilanne parani reilun vuoden seurannassa. Van de Griftin tutkimuksessa falloplastian tai metoidioplastian läpikäyneiden transmiesten itsetunnossa ei tapahtunut muutosta RSES-pistein mitattuna pari kolme vuotta leikkauksen jälkeen.

Masennus ja ahdistuneisuus

Sukuelinleikkauksia läpikäyneiden transmiesten masennusta mitattiin kaikissa kolmessa tutkimuksessa. Masennusta kuvaavat HADS-pisteet eivät lisääntyneet van de Griftin tutkimuksessa kahden ja puolen vuoden seurannassa, eikä Simonsenin rekisteritutkimuksessa masennusdiagnoosin omaavien osuudessa ollut eroa ennen ja jälkeen leikkausten. Smithin tutkimuksessa SCL-90-mittarin masennuspisteet laskivat reilussa vuodessa, mutta henkilöiden joukossa oli vain muutama sukuelinkirurgian läpikäynyt transmies.

Sukuelinleikkauksia läpikäyneiden transmiesten ahdistuneisuutta mitattiin kaikissa kolmessa tutkimuksessa. Ahdistuneisuutta kuvaavat HADS- tai SCL-90-pisteet eivät lisääntyneet van de Griftin ja Smithin tutkimuksissa leikkausten jälkeen. Simonsenin rekisteritutkimuksessa ahdistuneisuusdiagnoosin omaavien transmiesten osuus oli leikkausten jälkeen suurempi (11 %) kuin ennen leikkauksia (8 %).

Tyytyväisyys hoitoon

Transmiesten tyytyväisyydestä sukuelinkirurgiaan saatiin tietoa Smithin ja van de Griftin tutkimuksista sekä liitteessä 3 olevista poikkileikkaustutkimuksista (n=10). Smithin tutkimuksessa 8/13:sta oli tyytyväisiä rintojen poistoon. Van de Griftin tutkimuksessa transmiehillä esiintyi falloplastian ja metoidioplastian jälkeen keskivaikeita virtsaamisoireita (IPSS-mittarilla 11 ja 13 pistettä): tyytyväisyys virtsaamiseen oli molempien tekniikoiden jälkeen samaa tasoa (noin 2, skaalalla 0-4). Kummassakaan tutkimuksessa yksikään ei katunut leikkausta. Poikkileikkaustutkimuksista saatiin seuraavaa lisätietoa: Tyytyväisten osuus sukuelinleikkausten jälkeen vaihteli 78 % ja 100 %:n välillä (5 tutkimusta). Falloplastiaan ja metoidioplastiaan tyytyväisten osuus oli noin 90 % (3 tutkimusta).

Turvallisuus

Falloplastiaan ja metadoioplastiaan liittyy merkittävä virtsaputken kuroumien ja fisteleiden riski. Aiheesta ei löytynyt systemaattista katsausta, mutta esimerkiksi Vukadinovicin 2014 tutkimuksessa metadoioplastiaan

liittyi 28: %:lla komplikaatioita ja vakavia komplikaatioita kuten virtsaputken kuroumaa tai fisteliä esiintyi 8 %:lla.

Kurkunpään kirurgia

Tutkimusten kuvaus

Transnaisten kurkunpään kirurgian vaikuttavuutta arvioi viisi seurantatutkimusta, joissa leikkauksena oli joko äänihuulten kiristysleikkaus (Anderson ym. 2007; Orloff ym. 2006) tai kilpiruston höyläysleikkaus (Brown ym. 2000; De Bruyne ym. 1995) ja yhdessä tutkimuksessa tehtiin ilmeisesti molemmat leikkaukset (Kunachak ym. 2010) (liite 2, taulukot 45-49). Tutkimuksissa oli yhteensä 72 henkilöä, 5-31 per tutkimus. Tutkimukset oli tehty Britanniassa, Alankomaissa, Kanadassa, Yhdysvalloissa ja Thaimaassa ja julkaistu vuosina 1995-2010. Kahdessa tutkimuksessa oli ilmoitettu leikkauksen suorittamisen ajankohdaksi noin kuuden vuoden pituinen ajanjakso, joka päättyy 3–4 vuotta ennen julkaisua. Tutkitut henkilöt olivat kaikki transnaisia. Heidän keskimääräinen ikä vaihteli 23:n ja 44:n välillä. Kaikissa tutkimuksissa mitattiin äänenkorkeuden muutosta, seurannan kesto vaihteli puolesta vuodesta kuuteen vuoteen leikkauksen jälkeen. Lisäksi kahdessa tutkimuksessa mitattiin äänen maskuliinisuutta tai feminiinisyyttä ulkopuolisen kuuntelemana, kahdessa tutkimuksessa henkilön tyytyväisyyttä ääneensä ja yhdessä tutkimuksessa ääneen liittyvää toimintakykyisyyttä.

Vaikuttavuus

Äänen korkeus nousi valtaosalla leikatuista naisen normaalikorkeudelle tai lähelle sitä kummallakin leikkaustekniikalla.

Psykoterapia

Tutkimusten kuvaus

Sukupuolidysforian hoitoon tarkoitetun psykoterapian vaikuttavuudesta löytyi yksi pieni yhdysvaltalainen tutkimus (Briggs ym. 2018) (liite 2, taulukko 50). Interventiona oli Somatic Experiencing® -menetelmään perustuva ryhmäterapia, jonka tarkoitus on parantaa masennusta, ahdistusta, somaattisia oireita, elämänlaatua ja syrjinnän kokemuksista selviytymistä. Tutkimukseen osallistui seitsemän aikuista henkilöä, joista 3 oli transsukupuolisia, kaksi sukupuolettomia, yksi muunsukupuolinen ja yksi epäselvä. Ryhmä tapasi kerran viikossa puolitoista tuntia kymmenen viikon ajan. Tuloksena mitattiin elämänlaatua WHOQOL-mittarilla sekä mielialaa ja somaattisia oireita PHQ-SADS-mittarilla.

Vaikuttavuus

Psykologinen elämänlaatu koheni WHOQOL-mittarin pistein mitattuna tilastollisesti merkitsevästi. Masennus- ja somaattiset oireet lievittyivät PHQ-SADS-mittarin pistein hieman, mutta eivät tilastollisesti merkittävästi.

Näytön asteesta

Näyttö sukupuolidysforian lääketieteellisten hoitojen vaikuttavuudesta perustuu yhteen kontrolloituun hoitokokeeseen, yhteen rekisteritutkimukseen ja 36:een yhden ryhmän tuloksia ennen ja jälkeen intervention mitanneisiin tutkimuksiin. Näyttö hoitokeinojen vaikuttavuudesta jää näin ollen heikoksi tai hyvin heikoksi.

Puutteita

Muunsukupuoliset

Suurin osa katsaukseen sisällytetyistä henkilöistä edustaa transsukupuolisia. Alla on lueteltu muunsukupuolisten lukumäärät tutkimuksissa. Muunsukupuolisten tuloksia ei raportoitu erikseen transsukupuolisten henkilöiden tuloksista.

- Van de Grift ym. 2017: 10/201 muu GID-diagnoosi (DSMIV)
- Johansson ym. 2010: 1/42 muunsukupuolinen
- Briggs ym. 2018: 1/7 muunsukupuolinen, 2/7 sukupuoleton, 1/7 ”en tiedä”.

Interventiot

Kaikista aiheen rajauksen sisällyttämistä interventioista ei löytynyt tutkimuksia. Näitä ovat

- Kasvoleikkaukset
- Leikkaustuloksen purku- tai korjausleikkaus
- Hedelmällisyyden säilyttäminen tai palauttaminen
- Hiusten siirto
- Dermatologiset hoidot
- Puheterapia
- Apuvälineet

Psykoterapioista löytyi vain yksi sisäänottokriteerit täyttävä tutkimus, huolimatta täydennyshauista, joita tehtiin käyttämällä spesifejä terapioiden nimiä hakusanoina.

Lopputulosmuuttujat

Aiheen rajauksessa kuvatuista relevanteista lopputuloksista vain osaan löytyi tietoa tutkimuksista. Parhaiten oli raportoitu interventioiden vaikutus mielialaan ja psykologiseen kuormitukseen (18 tutkimusta), sukupuoliristiriitaan ja kehoahdistukseen (10 tutkimusta), elämänlaatuun (10 tutkimusta), persoonallisuuteen, kognitioon tai käyttäytymiseen (9 tutkimusta). Yleistä toimintakykyä tai intervention vaikutusta parisuhteeseen oli mitattu vain neljässä tutkimuksessa. Työssä käyntiä, päihteitä tai psykiatrisia diagnooseja oli tutkittu vain kahdessa tutkimuksessa. Sairauspoissaoloja, terveyspalvelujenkäyttöä, itsetuhoista tai rikollista käytöstä tai vaikutuksia läheisiin ei ollut tutkittu yhdessäkään tutkimuksessa.

Lähdeluettelo

Das P. Transsukupuolisten hormonihoidon seuranta. Suom Lääkäril 2019;74:376-381.

McFarlane T, Zajac JD, Cheung AS. Gender-affirming hormone therapy and the risk of sex hormone-dependent tumours in transgender individuals-A systematic review. Clin Endocrinol (Oxf). 2018 Dec;89(6):700-711

Liite 1 Hakujen kuvaus

Laaja haku, joka palveli useita perustelumuistion tekijöitä

PubMed 14.12.2018	osumia	valittu
#12 Search ((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract]. 1) Filter: systematic review publication type > 26 hits. 2) Systematic review (ti, abs) AND #12 > 25 hits	51	7
(((HTA[Title/Abstract]) OR health technology assessment[Title/Abstract])) AND ((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract]) 1	1	0
Search (((guideline[Title/Abstract]) OR clinical guideline[Title/Abstract])) AND ((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract]	9	5
Search (((((((ethic*[Title/Abstract]) OR moral*[Title/Abstract]) OR integrity[Title/Abstract]) OR justice[Title/Abstract]) OR autonom*[Title/Abstract]) OR human rights[Title/Abstract])) AND ((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])	105	24
Search ((((((legislation[Title/Abstract]) OR legal[Title/Abstract])) AND ((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract]))) NOT (((((((ethic*[Title/Abstract]) OR moral*[Title/Abstract]) OR integrity[Title/Abstract]) OR justice[Title/Abstract]) OR autonom*[Title/Abstract]) OR human rights[Title/Abstract])) AND ((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract]))	55	10

Search (((((cost effectiveness[Title/Abstract]) OR cost*[Title/Abstract]) OR cost utility[Title/Abstract]) OR economic[Title/Abstract])) AND ((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract])))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])	40	0
Search ((((patient perspective[Title/Abstract]) OR values[Title/Abstract]) OR attitudes[Title/Abstract])) AND (((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract])))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])	98	6
#12 Search ((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract])))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract]. 1) Filter: RCT or CCT as publication type.	5	0
Search ((((((((((psychotherap*[Title/Abstract]) OR psychological[Title/Abstract]) OR psychosocial[Title/Abstract])) OR (((speech[Title/Abstract]) OR voice[Title/Abstract]) OR vocal[Title/Abstract])) OR (((hair[Title/Abstract]) OR epilation[Title/Abstract]) OR vaniga[Title/Abstract])) OR ((((((hormone[Title/Abstract]) OR hormonal[Title/Abstract]) OR estrogen[Title/Abstract]) OR antiandrogen[Title/Abstract]) OR testosterone[Title/Abstract]) OR GNRH[Title/Abstract])) OR ((surger*[Title/Abstract]) OR surgical[Title/Abstract])) OR safety[Title/Abstract])) AND (((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract])))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract])	457	22
CLIB 20.12.2018		
'"#1 - ("gender dysphoria"):ti,ab,kw OR (transgender*):ti,ab,kw OR (transsexual*):ti,ab,kw OR (transmen):ti,ab,kw OR (transwomen):ti,ab,kw" (Word variations have been searched)	2 reviews 170 trials	0 34
Scopus 20.12.2018		
Search TITLE-ABS-KEY (ethic* or moral* or justice or human rights) and (transsexual or transgender or transmen or transwomen or non-conforming or non-binary or gender fluid or gender incongruence or genderqueer or dysphoria) and (care or treatment	117	2
Search TITLE-ABS-KEY (gender dysphoria and (cost effectiveness or cost utility or cost* or economic	29	2
Search TITLE-ABS-KEY (gender dysphoria and (legal or legislation or law or juridical)	105	13
Scopus 21.12.2018		
Search (transsexual or transgender or transmen or transwomen or non-conforming or non-binary or gender fluid or gender incongruence or genderqueer or dysphoria) and (patient perspective or values or attitudes)	118	4

Search TITLE-ABS-KEY (psychotherap* OR psychosocial OR psychological OR speech OR voice OR vocal OR hair OR epilation OR vaniga) OR TITLE-ABS-KEY (hormone OR hormonal OR estrogen OR antiandrogen OR testosterone OR gnrh) OR (surger* OR surgical OR vaginoplasty OR phalloplasty OR breast AND masculinization OR breast AND femininization) OR TITLE-ABS-KEY (mastectomy OR metoidioplasty OR metodioplasty OR sex-assignment) AND TITLE-ABS-KEY ((safety OR effectiveness OR efficacy OR outcome OR risk)) AND TITLE-ABS-KEY (gender AND dysphoria) AND TITLE-ABS-KEY (transgender OR transsexual OR non-binary OR non-conforming OR (gender AND incongruence) OR (gender AND fluid) OR genderqueer OR transmen OR transwomen)) AND DOCTYPE (ar OR re)	272	32
PsycInfo 13.12.2018		
Search (gender dysphoria and (ethics or morality or integrity or justice autonomy or human rights)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	27	2
Search (ethics and (care or treatment) and (transsexual or transgender or transman or transmen or transwoman or transwomen)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	45	0
Search (gender dysphoria and (cost effectiveness or cost utility or cost* or economic)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	7	0
Search (transsexual or transgender or transman or transmen or transwoman or transwomen or gender non-conforming or non-binary or gender fluid or gender incongruence or genderqueer) and (legal or legislation or juridic*) and gender dysphoria).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	17	2
Search ((transgender and (legal or legislation or juridic*)) not (lesbian or gay or bisexual)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	159	35
PsycInfo 18.12.2018		
Search ((ethic* or moral* or integrity or justice or autonom*) and (transsexual or transgender or transman or transmen or transwoman or transwomen or gender non-conforming or non-binary or gender fluid or gender incongruence or genderqueer) and gender dysphoria).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	24	1
Search ((patient perspective or values or attitudes) and gender dysphoria).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	57	9
Search ((psychotherap* or psychosocial or psychological or (speech or voice or vocal) or (hair or epilation or vaniga) or (hormone or hormonal or estrogen or antiandrogen or testosterone or gnrh) or (surger* or surgical or vaginoplasty or phalloplasty or breast masculinization or breast femininization or mastectomy or metoidioplasty or metodioplasty) or (safety or effectiveness or efficacy or outcome)) and (transsexual or transgender or transman or transmen or transwoman or transwomen or gender non-conforming or non-binary gender* or gender fluid or gender incongruence or genderqueer) and gender dysphoria) .mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	115	19

Limit to (("0200 clinical case study" or "0300 clinical trial" or "0400 empirical study" or "0430 followup study" or "0450 longitudinal study" or 2100 treatment outcome) and "0110 peer-reviewed journal		
		229
Hakujen ulkopuolelta		93
		322

Täydennyshakuja

CLIB täydennyshaku 20.12.2018 klo 8

- Title abstract transgender* OR transsexual* OR gender incongruence OR gender dysphoria
- 2 katsausta >0,
- 170 trialia > 34 mukaan

Genderqueer-täydennyshaku PubMediin 28.12.2018

Genderqueer (ti, abs) > 40 löydöstä > 11 valittu (ei vaikuttavuutta koskevia)

Psykoterapia-täydennyshaku PubMediin 201.2.2019

PubMed 20.2.2019		
(((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract]) AND cognitive behavioral [Title/Abstract]	1	1
Transsensitive	0	
(psychoeducation[Title/Abstract]) AND (((((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract]))))	1	1
(psychophysical physiotherapy) AND (((((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract]))))	0	0
(art psychotherapy[Title/Abstract]) AND (((((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract]))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract]))))	0	0
(neuropsychiatry[Title/Abstract]) AND (((((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract])	0	0

OR transwomen[Title/Abstract])))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract]))))		
(family therapy[Title/Abstract]) AND (((((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract])))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract]))))	1	1
(couples therapy[Title/Abstract]) AND (((((((((transsexual[Title/Abstract]) OR ((((transman[Title/Abstract]) OR transmen[Title/Abstract]) OR transwoman[Title/Abstract]) OR transwomen[Title/Abstract])))) OR (((((Gender non-conforming[Title/Abstract]) OR non-binary gender*[Title/Abstract]) OR gender fluid[Title/Abstract]) OR gender incongruence[Title/Abstract]) OR Genderqueer[Title/Abstract])) OR gender dysphoria[Title/Abstract])) AND gender dysphoria[Title/Abstract]))))	0	0

Liite 2 Vaikuttavuustaulukot: ennen-jälkeen tutkimukset

n= lukumäärä, ka = keskiarvo, MtF = male-to-female, FtM = female-to-male.

Sukupuolen muuntoprosessi

Transsukupuoliset (MtF ja FtM)

1. van de Grift ym. 2017, Alankomaat, Belgia ja Saksa

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: MtF: ei diagnoosia 11%, varhaisvaiheen GID (DSM-IV) 32%, myöhäisvaiheen GID (DSM-IV) 41%, muu GID-diagnoosi (DSM-IV) 17%. FtM: ei diagnoosia 3%, varhaisvaiheen GID (DSM-IV) 79%, myöhäisvaiheen GID (DSM-IV) 12%, muu GID-diagnoosi (DSM-IV) 5%.		Hormonihoito, sukuelin ja -rintakirurgia, kaulan ja kasvojen leikkaukset, epilaatio.	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin kaikki yli 16-vuotiaat, jotka hakivat sukupuolen muuntohoitoja Amsterdamin, Gentin tai Hampurin klinikoilta vuosina 2007–2009, riippumatta siitä, oliko hoitoja myönnetty. 546 kutsutusta 201 osallistui (37%). Heistä 14% ei ollut saanut sukupuolen muuntohoitoja, 18% oli saanut vain hormonihoitoja ja 68% oli saanut sekä hormoni- että leikkaushoitoja. Ei-osallistujat olivat osallistujiin nähden merkitsevästi vanhempia, koulutetumpia ($p<0,001$) ja tyytyväisempiä kehoonsa ($p=0,01$). Diagnoosien suhteen ei eroja ryhmien välillä.	Yhteensä n=201 • Ei hoitoja n=29 (23 MtF, 6 FtM) • Pelkkä hormonihoito n=36 (heistä 14 aikoi leikkaukseen ja 21 ei aikonut) • Hormonihoito ja leikkauksia n=136 MtF: n=135; tutkimuksen alussa ikä ka 39; koulutustaso korkea 48%, matala 10%. Sukupuolirooli (n): nainen 119, mies 12, ei ilmoittanut 4. Lääkärin arvioima sukupuolenmukainen ulkomuoto (Physical Appearance Scale): pisteet alussa 44 (pienempi pistemäärä kuvastaa toivottuun sukupuoleen liittyvää ulkomuotoa, pisteet >42 viittaavat siihen, että henkilö näyttää enemmän syntymäsukupuolensa mukaiselta). Psykologinen kuormittuneisuus alussa (SCL) 0,5 (alhainen kuormitus). FtM: n=66; ikä ka 31; suurin osa varhaisvaiheen GID-diagnooseja, koulutustaso korkea 41%, matala 12%. Sukupuolirooli (n): nainen 5, mies 60, ei ilmoittanut 1. Ulkomuoto-pisteet 40. Psykologinen kuormittuneisuus alussa (SCL) 0,6 (alhainen kuormitus).	Loppukyselyn aikaan 14% ei ollut saanut mitään interventiota, 18% oli saanut vain hormonihoitoa ja 68% hormonihoitoa ja leikkauksia. MtF: • sukupuolen muuntamiseen tähtäävä hormonihoito 83% • epilaatio 86% • vaginoplastia 61% • rintojen silikoni-implantit 30% • aataminomenan pienentäminen 8% • feminisoiva kasvoleikkaus 6% • aikaa kulunut hormonihoidon alusta ka 4,6 v ja viimeisimmästä leikkauksesta 2,4 v. FtM: • sukupuolen muuntamiseen tähtäävä hormonihoito 91% • rintojen poisto 79%	Kolmen ryhmän (ei hoidetut, vain hormonihoidetut ja hormoni+leikkaushoidetut) ennen-jälkeen mittauksia. Alkumittausten tiedot kerätty takautuvasti. Aineisto kerättiin verkkokyselyllä alussa diagnosointivaiheessa ja lopussa, jolloin aikaa kulunut hormonihoidon alusta ka 4,9 v ja viimeisimmästä leikkauksesta ka 2,6 v. Taustatiedot saatiin potilasrekisteristä. Kunkin ryhmän tuloksia verrattiin alussa ja lopussa ja ryhmiä myös verrattiin keskenään. Joidenkin mittarien kohdalla (SCL-90 ja BIS kehon osa-alueet) alkumittauksien tulokset oli raportoitu vain kaikkien osallistujien (ei kolmen

	Hoitoja saamattomia oli 24. Heistä 71% eli syntymäsukupuolessaan ja 29% vastakkaisessa sukupuolessa.	• munasarjojen / kohdun poisto 78% • neopeniksen rakentaminen 27%	ryhmän) tasolla. Aineiston erittelyä ja vertailuja ei tehty trans- ja muunsukupuolisten henkilöiden kesken.

Sukupuoliristiriita (UGDS)	Kehoahdistus (BIS)	Tulosten tulkintaa
UGDS-pisteet (ka) ennen → jälkeen hoidon, skaala 12–60, pienempi parempi. • Ei hoitoja: 48 → 20* • Vain hormonihoito: 52 → 20 • Hormonihoito ja leikkaus: 54 → 16 Kaikissa ryhmissä sukupuoliristiriita väheni seurannassa. Ei-hoidettujen sukupuoliristiriita oli alussa vähäisempää kuin muiden ryhmien (p<0,001). Hormonihoito ja leikkaus -ryhmän tulos oli parempi kuin ei interventioita -ryhmän (p<0,001). Vain hormonihoitoa ja ilman hoitoa olleiden tuloksissa ei tilastollisesti merkitsevää eroa.	BIS-pisteet (ka) ennen → jälkeen hoidon, skaala 0–5, pienempi parempi. • Ei hoitoja: 3,3 → 3,2* • Vain hormonihoito: 3,3 → 2,7 • Hormonihoito ja leikkaus: 3,3 → 2,5 Kaikissa ryhmissä kehoahdistus väheni. Ei-hoidetut olivat seurantavaiheessa merkitsevästi tyytymättömämpiä kehoonsa kuin hoitoja saaneet. BIS-pisteet eri kehon alueilla: hiukset, pää ja niska, lihaksikkuus ja ryhti, lanteet, rinnat, sukuelimet. Alkumittauksista raportoitu vain kaikkien ryhmien ka. Loppumittaukset hoitoryhmittäin (ei siis saada ennen-jälkeen vertailua). Ei-hoidetuilla pisteet pysyivät seurannassa samalla tasolla kuin alussa. Kaikkein tyytymättömämpiä he olivat rintoihin ja sukuelimiin. Hoitoja saaneilla kehoahdistus väheni ja BIS- pisteet olivat lopussa BIS 2 (tyytyväinen) – 3 (neutraali). Hormoni+leikkaus-ryhmän lopputulokset olivat melkein kaikilla kehon alueilla samankaltaisia kuin vain hormonihoidetuilla: poikkeuksena sukuelimet, joihin leikkaushoidetut olivat tyytyväisempiä kuin hormonihoidetut (p<0,001). Sukuelimiin tyytymättömyys oli seurantavaiheessa suurempaa vain hormonihoitoa saaneella kuin hormoni- ja leikkaushoitoa saaneella ryhmällä (p<0,001). Samanlainen ero havaittiin transnaisten rintoihin tyytymättömyydessä (p=0,009). Muita merkitseviä eroja vain hormonihoitoa ja hormonihoitoa ja leikkaushoitoa saaneiden ryhmien välillä ei havaittu.	Sekä sukupuoliristiriita että kehoahdistus lievittyivät kaikilla ryhmillä (hoidetuilla ja ei-hoidetuilla) muutaman vuoden seurannassa. Miehet olivat tullessa vanhempia ja heidän ulkomuotonsa poikkesi enemmän toivotusta. Hoitotuloksia ei kuitenkaan eritelty sukupuoliryhmittäin (Mtf vs FtM). Tutkijoiden mukaan mittarit eivät sovellu sukupuolten väliseen vertailuun. Kehoahdistusta hoidon jälkeen ennustivat vaikeampi kehoahdistus alussa (p<0,001) sekä heikompi psyykkinen toimintakyky(SCL-90) lopussa (p<0,001). Hoitoja saamattomien kehoahdistus ei pienentynyt seurannassa yhtä paljon kuin sukupuoliristiriita. Heistä (n=29) vain 7 täytti GID-diagnoosin kriteerit ja sukupuoliristiriita oli alun perin lievempi kuin hoitoja saaneiden. Kehoahdistuksen ja sukupuoliristiriidan välillä ei ollut minkään ryhmän kohdalla merkitsevää korrelaatiota alussa eikä lopussa. Tutkijoiden tulkinnan mukaan kehoahdistuksen voimakkuus ei välttämättä korreloi sukupuoliristiriidan voimakkuuteen. Tutkimuksen sovellettavuutta heikentää se, että tutkimukseen osallistuvat ovat nuorempia, vähemmän koulutettuja ja tyytymättömämpiä kehoonsa kuin tutkimuksesta kieltäytyneet.

2. Ruppin ym. 2015, Saksa

Potilaat	Tutkittava interventio	Vertailu ja mittaukset

Diagnoosi: F64.0, ICD-10		Hormonihoito, sukuelin- ja rintakirurgiaa, kaulan alueen leikkauksia	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin yhden klinikan ne potilaat, joilla sukupuolen ja nimen muuttamisesta on kulunut 10 vuotta. Edellytykset nimen muuttamiselle: transsukupuolisuus-diagnoosi, vastakkaiseen sukupuoleen identifioituminen vähintään 3 vuoden ajan sekä vahva todennäköisyys, että identifioituminen on pysyvää. Kutsun vastausprosentti oli 50,7.	n=71 (35 MtF ja 36 FtM), ikä ka = 47,0v. (52,9v. MtF; 41,2v. FtM). Aikaa kulunut aika nimen muutoksesta ka = 13,8v. (10–24v.) (13,7v. MtF; 14,1v. FtM). Seurannan lopussa: Työssä (79%), eläkkeellä (14%), työtön (7,1%). Parisuhteessa 60%. Seksuaalinen suuntautuminen (suhteessa nykyiseen sukup.rooliin): • MF: hetero (35%), bi (18%), homo (29%. 18%:lla ei seksikumppaneita muuntoprosessin jälkeen. • FM: hetero (75%), bi (5,6%), homo (5,6%).	Hormonihoito kaikilla, 2 keskeyttänyt terveyssyistä Psykoterapia 54:llä Leikkaukset (MtF): • vaginoplastia 33:lla • rintojen suurennus 8:lla • kurkunpään leikkaus 6:lla • äänihuulten leikkaus 2:lla leikkaukset (FtM): • rintojen poisto 36:lla • munasarjojen tai kohdunpoisto 33:lla • metoidioplastia 1:llä • falloplastia ”radial forearm flap” -tekniikalla 21:llä	Yhden ryhmän (hoidetut transsukupuoliset) ennen-jälkeen mittauksia (alkutiedot takautuvasti) ennen hoitoja ensimmäisen klinikkakontaktin yhteydessä ja tutkimuskäynnillä keskimäärin 13,8 vuotta (10-24 v.) sen jälkeen. Standardoitu kysely tehty sekä ennen että jälkeen hoitojen. Tutkimuskäynnillä hoitojen jälkeen tehtiin lisäksi puolistrukturoitu haastattelu ja täydentävä seurantakysely elämäntilanteesta ja sukupuoliroolista. Tuloksia ei pääsääntöisesti eritelty eri sukupuoli-identiteettien kesken.

Standardoitu kysely * (ensimmäisen klinikkakontaktin aikaan → seuranta-aikaan)				
Psykologinen kuormitus (SCL-90-R)	Vahingolliset käyttäytymismallit (IIP)	Persoonallisuus (FPI-R)	Sukupuoliroolit (BSRI)	Tulosten tulkintaa
SCL-90-R-pisteet ennen → jälkeen hoitojen. Skaala 0–4, pienempi parempi. Suomen väestötason yhteispisteet (GSI) 0,65. Tulos: Yhteispisteet (GSI): 0,53 → 0,28 (p<0,001) Masennus: 0,70 → 0,32 (p<0,001) Ahdistus: 0,47 → 0,18 (p<0,001) Somatisaatio: 0,39 → 0,31 (NS)	IIP-pisteet ennen → jälkeen hoitojen. Skaala 0–32, pienempi parempi. Dominoiva / kontrolloiva: 5,8 → 3,7 (p=0,003) Kostonhaluinen / itsekeskeinen: 7,8 → 4,9 (p<0,001) Kylmä / etäinen: 8,2 → 4,7 (p<0,001)	FPI-R-pisteet ennen → jälkeen hoitojen. Skaala 0–12, paitsi kahdessa viimeisessä 0– 14. Tyytyväisyys elämään: 4,4 → 8,3 (p<0,001) Sosiaalinen orientaatio: 7,5 → 7,0 (NS) Tarve menestyä: 7,0 → 7,0 (NS) Ujous: 5,1 → 4,7 (NS) Ärtyneisyys: 4,8 → 4,0 (p=0,032)	Sekä MtF- että FtM-transsukupuolisilla minäkuva oli androgyyni. MtF:llä myös ideaalikuva oli androgyyni, mutta FtM:llä lievästi miehinen.	Psykologinen kuormitus ja ihmissuhdeongelmat vähenivät yli 10 vuoden seurannassa ja tyytyväisyys elämään kohentui. Loppumittauksen yhteydessä hyvinvointi oli korkealla tasolla, paitsi tyytyväisyys seksielämään oli muita osa-alueita alhaisempaa. Osallistujat olivat tyytyväisiä hoitoprosessiin. Vain

Pakko-oireisuus: 0,58 → 0,32 (p=0,001) Herkkyys ihmissuhteissa: 0,70 → 0,26 (p<0,001) Vihamielisyys: 0,49 → 0,22 (p<0,001) Fobiat: 0,30 → 0,14 (p=0,004) Paranoidisuus: 0,65 → 0,37 (p<0,001) Psykoottisyys: 0,53 → 0,16 (p<0,001) Psykologinen kuormitus pienempää lopussa. Seurantajakson pituudella ei ollut vaikutusta tuloksiin.	Sosiaalisesti estynyt: 10,4 → 5,5 (p<0,001) Epävarma: 10,7 → 6,3 (p<0,001) Liian sopeutuvainen: 11,6 → 7,0 (p<0,001) Uhrautuva: 10,5 → 7,6 (p<0,001) Tungetteleva / tarvitseva: 8,0 → 4,5 (p<0,001) Ihmissuhdeongelmia vähemmän lopussa. Seurantajakson pituudella ei ollut vaikutusta tuloksiin.	Aggressiivisuus: 3,6 → 3,2 (NS) Stressi: 4,8 → 4,7 (NS) Fyysiset ongelmat: 2,6 → 2,1 (NS) Terveysmurheet: 4,3 → 4,8 (NS) Avoimuus: 6,4 → 5,8 (p=0,033) Ulospäinsuuntautuneisuus: 6,3 → 6,0 (NS) Tunteellisuus: 6,1 → 4,1 (p<0,001) Merkittävä nousu tyytyväisyydessä elämään sekä lasku ärtyneisyydessä, avoimuudessa ja tunteellisuudessa. Seurantajakson pituudella ei merkittävää vaikutusta tuloksiin.	FtM:llä sukupuoliroolin sosiaalinen toivottavuus oli noussut seurantajakson aikana. Muita eroja ei havaittu eri ajankohtina. MtF:llä feminiininen minäkuva oli sitä heikompi mitä pidempi aika lähetteestä oli kulunut.	psykoterapiaan ja leikkausten komplikaatioihin oltiin vähemmän tyytyväisiä. Sukuelinleikkauksien riskit estivät etenkin FtM:llä leikkauksiin hakeutumista. Tutkimuksen vahvuutena pitkä seuranta-aika (yli 10v.): toisaalta pitkä seuranta-aika voi heikentää asioiden muistamista. Tulosten sovellettavuutta saattaa heikentää suhteellisen alhainen osallistumisprosentti (50%). Tutkimuksesta pois jääneiden piirteitä ei tutkittu.

n= lukumäärä, ka = keskiarvo, NS = non-significant, MF = male-to-female, FtM = female-to-male, GSI = Global Severity Index

3. Heylens ym. 2014,Belgia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (ei kuvattu tarkemmin)		Hormonihoito ja leikkaushoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
90 henkilöä, jotka tulleet hormonaaliseen ja kirurgiseen sukupuolenmuuntamiseen Ghentin yliopistosairaalan sukupuoliklinikkaan 2005-2009. 82 antoi suostumuksen tutkimukseen osallistumisesta, näistä 70:llä todettiin GID-diagnoosi, heistä 12 eivät eri syistä käyneet läpi molempia hoitoja, syitä: 1 persoonallisuushäiriö, 1 aivovamma, 10 joko halusi vain	n=57: MtF 46 ja FtM 11	Hormonihoito ja leikkaushoito. Ei kuvattu tarkemmin.	Yhden ryhmän ennen-jälkeen mittauksia: Psykologisen kuormituksen (SCL-90) mittaukset tehtiin ennen hoitojen aloitusta, 3-6 kk hormonihoidon aloituksen jälkeen ja 1-12 kk leikkaushoidon jälkeen. Ensimmäisen ja viimeisen mittauksen väli oli keskimäärin 3 v 3 kk. Vastaajia alussa 56/57, hormonihoidon jälkeen 47 ja leikkauksen jälkeen 42.

hormonihoidon tai päätti jättää kaikki hoidot väliin. 1 teki itsemurhan. 57 tutkimukseen osallistujan joukosta ei kukaan pudonnut seurannasta, mutta 11:lle ei ehditty tehdä leikkausta ennen tutkimuksen päättymistä.			Psykososiaalisia tietoja kerättiin haastattelemalla ja kyselyillä alussa ja viimeisellä vastaanotolla, väli ka 3 vuotta. Vastaajia alussa 54/57 ja lopussa 42. Mittauksia verrattu eri ajankohtina ja suhteessa väestötuloksiin. Tuloksia ei eritelty eri sukupuoliidentiteettien kesken.

Psykologinen kuormitus (SCL-90) ja mieliala	Sosiaaliset suhteet ja työllisyys: % ennen → jälkeen molempien hoitojen	Päihteiden käyttö ennen → jälkeen molempien hoitojen	Tulosten tulkintaa:
SCL-90 yhteispisteet ka • väestössä 118 • alussa→ hormonihoidon jälkeen → leikkaushoidon jälkeen: 156→120 (p<0,001) → 128 (NS) SCL-90 masennus ka • väestössä 22 • alussa→ hormonihoidon jälkeen → leikkaushoidon jälkeen: 35→24 (p<0,001) → 24 (NS) SCL-90 ahdistuneisuus ka • väestössä 13 • alussa→ hormonihoidon jälkeen → leikkaushoidon jälkeen: 17→12 (p<0,001) → 14 (NS) Muissakin mittarin osa-alueissa sama malli: lähtötaso korkeampi kuin väestössä, tilastollisesti merkitsevä lasku hormonihoidon jälkeen, eikä kirurgia tuo enää merkitsevästi lisää. Poikkeuksena avaran tilan kammo ja somatisaatio, joihin ei saatu hoidoilla tilastollisesti merkitsevää parannusta. Potilailta kysyttiin molempien hoitojen jälkeen mielialaa, itseluottamusta ja kehollisia kokemuksia nyt verrattuna aiempaan. Tulokset olivat varsin positiivisia: 80-95% ilmoitti nyt olevan parempi. Ahdistuneisuuden kohdalla tulos ei ollut aivan yhtä hyvä: 81% ilmoitti ahdistuksen vähentyneen, 14% pysyneen samana ja 5% lisääntyneen.	Vakituinen parisuhde: 44% → 43% Asuu yksin: 32% → 43% Asuu kumppanin kanssa: 38% → 38% Asuu vanhempien kanssa: 27% → 12% Hyviä ystäviä: 73% → 88% Ei ihmissuhteita: 12% → 5% Ei seksisuhteita: 38% → 48% Seksiä vain parisuhteessa: 45% → 45% Työssä 66% → 60% Työtön 16% → 14% Muu (opiskelee, eläkkeellä ym) 18% → 26%	Alkoholin väärinkäyttö (abuse) 15% → 2% Kannabiksen käyttö 7% → 0% Muiden päihteiden käyttö 4% → 0%	Keskimäärin noin 3 vuoden muuntohoitojen jälkeen noin 90% koki tilanteen paremmaksi. Päihteiden käyttö näytti vähentyneen, samoin yksinäisyys. Psykologisen kuormituksen väheneminen saavutettiin hormonihoidon aikana: leikkaushoidolla ei saavutettu lisähyötyä. Vastaajien osuus 82% (SCL-90) ja 74% (muut kyselyt).

4. Johansson ym. 2010, Ruotsi

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: F64.0 (ICD-10), varhaisvaiheen transsukupuolisuus (diagnoosi alle 12-vuotiaansa) 62%		Hormonihoidot ja leikkaushoidot	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
60 henkilöä (39 MtF ja 21 FtM) kutsuttiin kahdelta klinikalta, pohjoisesta ja etelästä. Heidät tutkittiin soamaattisesti, psykiatrisesti ja psykologisesti. Osallistumisen edellytyksenä transsukupuolisuus-diagnoosi (F64.0), että on hyväksytty muuntoprosessiin vähintään 5 vuotta sitten ja/tai muuntoprosessi valmis vähintään 2v. sitten. Heistä 42 (70%) päätyi tutkimukseen. Pois jääneistä (14 MtF ja 4 FtM) 1 oli kuollut sukupuolenmuunnosleikkaukseen, 8:aa ei tavoitettu ja 9 ei halunnut osallistua. Pois jääneet olivat enimmäkseen MtF ja heillä oli hieman alempi toimintakyky (GAF-mittarilla). Leikkauskriteerit Ruotsin käytännön mukaisesti: diagnosointi, psykiatrinen arvio, yhden vuoden tosielämäjakso ja hormonihoitoa vähintään 2 vuoden ajan.	n=42: 25 MtF ja 17 FtM; Ikä • alussa ka 33 v. (18–60), MtF 37v ja FtM 28v; FtM nuorempia p<0,05 • muuntoleikkauksen aikaan ka 35v (22–57), MtF 38v, FtM 31v; • lopussa seuranta-ajankohtana ka 43v (25–69), MtF 46v, FtM 39v; Homoseksuaalinen suuntautuminen 69 %:lla (MtF 52%, FtM 94%); Varhaisvaiheen transsukupuolisuus (diagn. alle 12v.) 26:lla (62%) (MtF 44%, FtM 88%), myöhäisiä (diagn. yli 12v.) 16:lla (38 %) (MtF 56%, FtM 12%); MtF:n joukossa oli suhteellisesti enemmän myöhäisiä diagnooseja, p=0,003. Varhaisvaiheen TS / myöhäisvaiheen TS: • sukupuoli MtF: 42 / 88 (p<0,01) • ikä lähetteen aikana (vuosina): 28 / 42 (p<0,01) • ei-homoseksuaalinen suuntautuminen (suhteessa syntymäsukupuoleen): 15 / 56 (p<0,01) Sukupuoli-identiteetti (lopussa): syntymäsukupuoli (0%), vastakkainen kuin syntymäsukupuoli (79%), transsukupuolinen (21%).	Hormonihoito (kaikki saaneet) Leikkaushoidot: 32 potilasta leikattu (76%: MtF 72% ja FtM 82,4%) • 5 odotteli uusia leikkauksia ja • 5 ei halunnut kastraatiota tai muita leikkauksia (4 MtF, 1 FtM, kaikki yli 12-vuotiaana diagnosoituja, 4 käytti edelleen hormoneja, 2 MtF halusi vain rintaimplantit, 1 oli muunsukupuolinen ja 1 epäröi, koska partneri hyväksyi omat genitaalit).	Yhden ryhmän ennen ja jälkeen mittauksia. Alkutiedot takautuvasti. Lääkärit täyttivät standardoituun lomakkeeseen henkilöiden perustiedot rekistereistä ja lähetteestä, postoperatiiviset tiedot ja oman arvion tuloksista sekä GAF-pisteet (arvio toimintakyvystä) hoitoprosessin alusta loppuun asti. Loppumittaus haastatteluin ja samoilla testeillä kuin alussa tehtiin yli 5 vuotta prosessin alusta tai vähintään 2 vuotta leikkausten jälkeen. Seuranta-aika keskimäärin 9 vuotta (4-16 v). Puolet tutkituista oli sellaisia joilla leikkauksesta oli kulunut alle 4 vuotta Vertailuja tehtiin sukupuolten (MtF ja FtM), varhaisen ja myöhäisen diagnoosin, ja seksuaalisen suuntautumisten välillä.

Lääkärin yleisarvio lopputuloksesta (standardoitu kyselylomake)	Sosiaaliset suhteet, työllisyys (standardoitu kyselylomake ja puolistrukturoitu haastattelu)	Tulosten tulkintaa
Yleisarvio: • kokonaistilanne parantunut 62%:lla	Ennen → jälkeen hoitoprosessin, ka 9 vuoden kuluttua. Työssäkäynti: • Töissä tai opiskeli 50% → 62%	Potilaiden tyytyväisyys hoitoprosessiin parempaa kuin lääkäreiden (95% vrt. 60%). MtF-ryhmän tulokset parempia kuin FtM:n. Selityksenä ehkä FtM:n jo alunalkaen parempi toimintakyky.

• tilanne muuttumaton 24 %:lla tilanne huonontunut 14 %:lla Tilanne parantunut: • transnaisilla useammin kuin transmiehillä, p=0.04 (MtF 72% vs FtM 47%) • 60 % heistä, joilla hoidot olivat vielä kesken. • 100 % heistä, jotka eivät halunneet enää lisäleikkauksia. Ei eroa tilanteen paranemisessa • varhaisvaiheen ja myöhäisen diagnoosin välillä, 58% vs 69%, NS. • homoseksuaalisen ja ei-homoseksuaalisen suuntautumisen välillä, 59% vs 69%, NS.	• Työkyvyttömyyseläkkeellä 21% → 28% Oma arvio työtilanteesta: • parantunut 45 % (MF 39, FM 54) • muuttumaton 47 % (MF 48, FM 47) • huonontunut 8 %, n=3 (MF 13, FM 0). Kaksi jäänyt työttömäksi ja yksi miesvaltaisessa työssä, jossa hankaluuksia. Hoitoprosessin jälkeen 38 %:lla oli partneri (MtF 36%, FtM 41%) Oma arvio parisuhteesta:: • parantunut 62 % (MF 70, FM 50) • muuttumaton 30 % (MF 22, FM 43) • huonontunut 8, n=3 (MF 8,7, FM 7,1). Kaksi liittyi seksiin ja yksi rooliongelmiin yleisesti.	FtM-transsukupuoliset olivat MtF-henkilöitä nuorempia ja useammin homoseksuaaleja. Kaikki, joiden muuntoprosessi oli päätöksessä, identifioituivat syntymäsukupuolta vastakkaiseen sukupuoleen. Tutkijat pohtivat, että koska potilaat olivat tuttuja (omia potilaita vuosien ajan), miellyttämisenhalu saattoi vaikuttaa tuloksiin.

MtF = male-to-female, FtM = female-to-male, NS = non-significant, ka = keskiarvo, n = lukumäärä

5. Smith ym. 2005, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (DSM-IV)		Hormonihoito ja leikkaushoidot	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin 325 sukupuolen muuntoprosessiin hakeutunutta henkilöä kahdelta yliopistoklinikalta. Sisäänottokriteerejä ei määritelty tarkemmin. Hoitoprosessin kulku Hollannissa: 1) diagnosointivaihe 2) lähete hormonihoitoon ja tosielämäkokeen arvio, 3) lähete sukuelinleikkaukseen. Lääkäri hyväksyy	Lukumäärät: • Muuntoprosessiin hakeneet: n=325 (MtF 220, FtM 105). • Ei-aloittajat (eivät saaneet lähetettä sukupuolen muuntoon): n=103 (MtF 74, FtM 29) • Aloittajat (lähete, aloittivat hormonihoidon): n=222 (MtF 146, FtM 76) • Pudokkaat (lopettivat hormonihoidon): n=34 (MtF 29, FtM 5). • Hoidon päättäneet (kävivät hoidot loppuun): n=188 (MtF 117, FtM 71)	Kaikki hoidon loppuun asti käyneet saaneet hormonihoidon ja sukuelinleikkauksia. Suoritettuja leikkauksia: • vaginoplastia, • rintojen silikoni-implantit, n=52 • falloplastia tai metaidoioplastia, n=10 • rintojen poisto.	Yhden ryhmän mittauksia ennen muuntoprosessia (diagnostiikan yhteydessä) ja sen jälkeen, vähintään 1 vuosi leikkaushoitojen jälkeen. Alkutiedot takautuvasti. Seuranta-aika prosessin alusta loppuun 1–4v. Mittaukset tehtiin haastatteluin ja kyselyin. N= 104 ennen ja 162 jälkeen. Ennen prosessia tehdyt mittaukset: GID in Childhood ja Social Support Scale –mittarit. Ennen ja jälkeen prosessin tehdyt mittaukset: sukupuoliristiriita, kehoahdistus,

leikkaukseen sen mukaan, miten paljon sosiaalinen rooli ja ulkomuoto on muuttunut hormonihoitojen ja tosielämäkokeen myötä, kuinka psykologisesti vakaa henkilö on ja kuinka suuri sukupuoliristiriita on.	• Seurantahaastatteluun osallistuneet: n=158 (MF 94, FM 64) Ikä (hoidon päättäneet): • hakuvaiheessa ka 31v (18–68v.) • hormonihoidon alussa ka 32v (18–68v.) • seurantahaastatteluun osallistuneet ka 35v (21–72v.). MtF 39; FtM 30v. Sosiodemografia (seurantavaiheessa): Työtilanne: työssä (37%), opiskelijoita (5%), eläkkeellä (2%), työttömiä (56%). Asuintilanne: yksin 56%, kumppanin kanssa (ja lasten kanssa tai ilman) 26%, vanhempien luona 2%, yksin lasten kanssa 2%, asuntolassa (8%) Tutkimuksessa käytettiin 162 aikuista. Ennen ja jälkeen muuntoprosessin tehtyihin mittauksiin osallistui 104 ennen ja 162 jälkeen.	Keskimääräinen aika hormonihoidon aloituksen ja leikkauksen välillä oli 20kk (12–73kk). Keskimääräinen aika leikkauksen ja loppuseurannan välillä oli 21 kk (12-47 kk).	fyysinen ulkomuoto ja psykologinen toimintakyky. Kyselyillä kerättiin tietoa 101-126 henkilöltä (riippuen mitatuista asioista). Vain muuntoprosessin jälkeen tehdyt mittaukset: Biografinen kysely ja Symptom Check List, n=101–126. Mittauksia verrattiin yhdessä ryhmässä eri ajankohdissa. Myös eri sukupuoli-identiteettien välisiä ja seksuaalisen suuntautumisen ryhmien tuloksia verrattiin keskenään. Lisäksi tutkijat analysoivat monimuuttujamallituksella sukupuolen muuntoon hyväksytyksi tulemisen ennakoivia tekijöitä

Sukupuoli- ja kehoahdistus (UGDS, AAI ja BIS)	Psykologinen kuormitus ja persoonallisuuden patologiset piirteet (SCL-90 Dutch version ja MMPI Dutch short version)	Kokemus hyväksynnästä (kysely muuntoprosessin jälkeen)	Tyytyväisyys seksielämään (kysely muuntoprosessin jälkeen)*	Tulosten tulkintaa
Sukupuoliristiriita, UGDS-pisteet ennen → jälkeen muuntoprosessin*, skaala 12–60, pienempi parempi: Tulos: 54 → 15, p<0,001 FtM-ryhmässä tulos jopa hieman parempi (→ 14) Fyysinen ulkomuoto kolmen ammattilaisen arvion mukaan (diagnoosin tehnyt lääkäri, hoitaja, tutkija), AAI-pisteet ennen → jälkeen muuntoprosessin, skaala 0–70, pienempi parempi:	MMPI-pisteet ennen → jälkeen muuntoprosessin *, Pienempi parempi pätee myös osa-aluepisteiden tulkintaan paitsi ulospäinsuuntautuneisuutta kuvaavaan kysymykseen, jossa isompi pistemäärä on parempi (tässä listassa viimeisenä). • Negatiivisuus: 23 → 17, p<0,001 • Somatisaatio: 9,1 → 6,6, p=0,003 (alussa korkeampi kuin väestön ka) • Ujous: 15 → 10, p<0,001 • Psykopatologia: 3,2 → 2,4, p=0,006 • Ulospäinsuuntautuneisuus: 13,8 → 15,5, p=0,005. Hoidon jälkeen MtF 13,8 ja FtM 18,0. Arvot keskimääräistä	89% (n=90) koki olevansa useimpien mielestä hyväksytty, 3 % vähän tai ei lainkaan. 83% (n=84) koki saavansa tukea uuteen sukupuolirooliinsa, 6% vähän tai ei lainkaan. 96% (n=99) koki, että on joku kenen puoleen kääntyä, 4% ei kokenut näin. 81% ei ollut kokenut olevansa naurunalainen, kun taas 2% koki niin usein.	Tyytyväisyys seksielämään (heistä joilla kumppani, n=50): tyytyväisiä 89%, tyytymättömiä 6%. Orgasmin saaminen (heistä jotka seksuaalisesti aktiivisia, n=84): aina/usein 63% (MtF 42%; FtM 82%), ei koskaan 18%. Homoseksuaalinen suuntautuminen	Sukupuoliristiriita väheni selvästi. Muuntoprosessin jälkeen ulkomuoto ulkopuolisen arvioimana vastasi henkilön sukupuolikokemusta merkitsevästi enemmän. Psykologinen toimintakyky oli varsin hyvä jo alussa, mutta parani loppumittauksessa kahdella eri mittarilla mitattuna. Sosiaalinen ja seksuaalinen toimintakyky oli kohtuullisen hyvä loppumittauksissa.

Tulos: 45 → 34, p<0,001, n=57. Lopussa MtF 38, FtM 26 Kehoahdistus, BIS-pisteet ennen → jälkeen muuntoprosessin*, pienempi parempi: • Tyytyväisyys ensisijaisiin ominaisuuksiin (esim. rinnat, sukuelimet), skaala 0–35: Tulos: 18 → 7, p<0,001 • Tyytyväisyys toissijaisiin ominaisuuksiin (esim. lantio, karvoitus), skaala 0–65: Tulos: 35 → 25, tulos p<001. • Tyytyväisyys muihin ominaisuuksiin (esim. kasvot, pituus), skaala 0–50: Tulos: 47 → 36, p<0,001	alempia suhteessa hollantilaiseen keskitasoon. MMPI-pisteet loppuvaiheessa vastasivat enimmäkseen hollantilaisia väestökeskiarvoja. SCL-90-Dutch version pisteet ennen → jälkeen muuntoprosessin, kokonaispisteiden skaala 90-450, pienempi parempi. Kokonaispisteet: 140 → 120, p<0,001. MtF 143→123 p=0,001 ja FtM 143 →45, p<0,001 Masennus: 29 → 23 (p<0,001). Hoidon jälkeen MtF 25, FtM 20. Ahdistus: 15 → 13 (p<0,001) Somatisaatio: 18 → 17, p=0,024) Agorafobia: 9,4 → 8,6, p=0,040 Riittämättömyys: 16 → 14, p<0,001 Herkkyys: 28 → 24 (p<0,001) Vihamielisyys: 7,8 → 7,4 (p=0,147) Univaikeudet: 5,4 → 4,6 (p=0,024)	98 % koki että heidät otetaan vakavasti, 2 % koki että vain hyvät ystävät ottavat vakavasti. MtF:t ja FtM:t kokivat tulevansa yhtä hyväksytyksi (eron p=0,4). FtM:t saivat enemmän tukea (p=0,01) ja pystyivät enemmän turvautumaan muihin (p=0,03). MtF:t joutuivat useammin naurunalaisiksi (p<0,001).	(suhteessa syntymäsukupuoleen) 58% (MtF 51%, FtM 71%) yleisempää kuin heteroseksuaalinen (42%) (p=0,04).	Transnaiset olivat vanhempia kuin transmiehet loppumittauksessa: 39v vs 30v). Eroja vaikuttavuudessa: • Transmiehillä tulokset parempia kuin transnaisilla (poikkeuksena suurempi tyytymättömyys leikkauksiin). • Homoseksuaaleilla parempi psykologinen toimintakyky kuin ei-homoseksuaaleilla.

n= lukumäärä, k = keskiarvo, MF = male-to-female, FM = female-to-male, GID = Gender Identity Disorder (sukupuoli-identiteetin häiriö)

* Raportoitu kahden merkitsevän numeron tarkkuudella

Transnaiset (MtF)

6. van de Grift ym. 2017, Alankomaat, Belgia ja Saksa

Potilaat		Tutkittava interventio	Tulos: Psykologinen kuormitus (SCL-90)
Diagnoosi: MtF: ei diagnoosia 11%, varhaisvaiheen GID (DSM-IV) 32%, myöhäisvaiheen GID (DSM-IV) 41%, muu GID-diagnoosi (DSM-IV) 17%.		Hormonihoito, sukuelin ja –rintakirurgia, kaulan ja kasvojen leikkaukset, epilaatio	SCL-90 yhteispisteet (GSI): 0,50 → 0,48 (alhainen kuormitus). Muita tuloksia taulukossa 1.
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		

Tutkimukseen kutsuttiin kaikki yli 16-vuotiaat, jotka hakivat sukupuolen muunnoshoitoja Amsterdamin, Gentin tai Hampurin klinikoilta vuosina 2007–2009, riippumatta siitä, oliko hoitoja myönnetty. 546 kutsutusta 201 osallistui (37%). Heistä 14% ei ollut saanut sukupuolen muuntohoitoja, 18% oli saanut vain hormonihoitoja ja 68% oli saanut sekä hormoni- että leikkaushoitoja. Ei-osallistujat olivat osallistujiin nähden merkitsevästi vanhempia, koulutetumpia ($p<0,001$) ja tyytyväisempiä kehoonsa ($p=0,01$). Diagnoosien suhteen ei eroja ryhmien välillä.	n=119; tutkimuksen alussa ikä ka 39 (koskee koko aineistoa); koulutustaso korkea 48%, matala 10%. Lääkärin arvioima sukupuolenmukainen ulkomuoto: pisteet alussa 44 (pienempi pistemäärä kuvastaa toivottuun sukupuoleen liittyvää ulkomuotoa, pisteet >42 viittaavat siihen, että henkilö näyttää enemmän syntymäsukupuolensa mukaiselta) Psykologinen kuormittuneisuus alussa (SCL) 0,5 (alhainen kuormitus).	• sukupuolen muunnokseen tähtäävä hormonihoito 83% • epilaatio 86% • vaginoplastia 61% • rintojen silikoni-implantit 30% • aataminomenan pienentäminen 8% • feminisoiva kasvoleikkaus 6% • aikaa kulunut hormonihoidon alusta ka 4,6 v ja viimeisimmästä leikkauksesta 2,4 v. • Ei hoitoja 19%	

n= lukumäärä, ka = keskiarvo, MtF = male-to-female, FtM = female-to-male,

van de Grift TC, Elaut E, Cerwenka SC, Cohen-Kettenis PT, De Cuypere G, Richter-Appelt H, Kreukels BPC. Effects of Medical Interventions on Gender Dysphoria and Body Image: A Follow-Up Study. Psychosom Med. 2017 Sep;79(7):815-823.

7. de Vries ym. 2014, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisuus		Sukupuolen muunnokseen tähtäävä hormonihoito ja leikkaushoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yliopistosairaalan sukupuoli-identiteetin klinikkaan vuosina 2000−2008 tulleista 196 peräkkäisestä potilaasta 140 hyväksyttiin sukupuolen muuntoprosessiin ja 111 sai murrosiän keskeytyshoidon	n=55: MtF 22 ja FtM 33. Ikä leikkaushoidon. Ikä (ka): hormonihoidon alussa 17 (14–19)	Murrosiän keskeytys GnRH-analogilla (tulokset	Yhden ryhmän ennen-jälkeen mittaukset. Alkumittausten tulokset takautuvasti.

(Vries ym. 2011). He siirtyivät myöhemmin (2003-2009) sukupuolen muunnokseen tähtäävään hormonihoitoon ja leikkaushoitoihin. . Tähän tutkimukseen valittiin henkilöitä joiden leikkauksista oli kulunut vähintään vuosi. Aineistosta hylättiin 15 henkilöä sukupuolen muuntoleikkauksesta kieltäytymisen (n=2), hoitamattomien oheissairauksien (n=3) tai kontaktiongelmien vuoksi. Yksi henkilö oli kuollut vaginoplastialeikkauksen jälkeen nekrotisoivaan faskiittiin. Kuuden henkilön kohdalla leikkauksesta oli kulunut alle 1 vuosi. Pudonneet 15 henkilöä olivat esitietojen suhteen samankaltaisia kuin tutkimuksessa jatkaneet. 96 henkilöstä 55 henkilöä kutsuttiin tutkimukseen vuosina 2008−2012 (valintatapaa ei kuvattu).	ja leikkauksen ajankohtana 19 (18–21) ja loppumittauksen aikaan 21 (20–23). Älykkyysosamäärä (ka) 99 (70–128) mitattuna WISC-R, WISC-III tai WAIS-III-mittarilla (keskimääräinen älykkyys 90-109).	kuvattu de Vries 2011, taulukko 16). Sukupuolen muunnokseen tähtäävää hormonihoitoa ei kuvattu. Leikkaushoitoina vaginoplastia.	Seurantamittaukset 12 kuukautta leikkaushoitojen jälkeen. Murrosiän keskeyttämisen GnRH-hoidolla tulokset raportoitu tutkimuksessa de Vries ym. 2011 (taulukko 16).

Sukupuoliristiriita (UGDS) ja kehoahdistus (BIS)	Yleinen toimintakyky (CGAS)	Mieliala: masennus (BDI) ja ahdistuneisuus (STAI)	Vihaisuus (TPI)	Tulosten tulkintaa
Sukupuoliristiriita (UGDS) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 12–60, pienempi parempi. N=33. MtF: 47→49→17, p<0.001 Kehoahdistus (BIS), skaala 1-5, pienempi parempi. N=45. Tyytyväisyys ensisijaisiin ominaisuuksiin (esim. rinnat, sukuelimet),: • MtF: 4,0→3,8→2,1, p<0.001 Tyytyväisyys toissijaisiin ominaisuuksiin (esim. lantio, karvoitus) • MtF: 2,6→2,3→1,9, p<0.001 Tyytyväisyys muihin ominaisuuksiin (esim. kasvot, pituus) • MtF: 2,6→2,3→2,1, p=0.014	CGAS ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 0-100, isompi parempi. N=32. • MtF: 74→78→82, p<0.001	Masennus (BDI) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 1-63, pienempi parempi, 1-9 = ei masennusta. N=41 • MtF. 4,7→2,3→3,4, NS Taipumus ahdistuneisuuteen (STAI) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 20-80, pienempi parempi. • MtF:32→32→36, NS	Vihaisuus (TPI) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen. Suurempi pistemäärä kertoo suuremmasta taipumuksesta vastata ärsykkeisiin vihalla. N=32. MtF (n=12):14→14→6, NS	Sukupuoliristiriitaan ja kehonkuvaan liittyvät vaikeudet helpottivat sukupuolen muuntohoitojen (hormoni ja leikkaus) jälkeen. Toimintakyky parani muuntohoitojen jälkeen, mutta vain transnaisilla tilastollisesti merkitsevästi. Mielialassa ei tapahtunut merkitseviä muutoksia. Taipumuksessa vastata ärsykkeisiin vihalla ei havaittu merkitseviä muutoksia, vaikkakin muutostrendi oli laskeva. Tutkimuksen lopussa mitattuna yksikään nuorista ei katunut murrosiän viivästämistä. Kaikki olivat hyvin tai kohtalaisen tyytyväisiä muuntohoitoihin. Elämänlaadussa (WHOQOL) ei ollut merkitsevää eroa verrattuna väestön keskiarvoihin ja ympäristöön liittyvä elämänlaatu oli keskimääräistä parempi (p<0,001).

Lyhenteet: CGAS = Children's global assessment scale; CSH = cross-sex hormones; FtM = Transmies; GnRHa = Gonadotropin-releasing hormone analogs; GRS = gender reassignment surgery; MtF = Transnainen; NS = Ei merkitsevä; e; ÄO = Älykkyysosamäärä

8. Johansson ym. 2010, Ruotsi

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: F64.0 (ICD-10), varhaisvaiheen transsukupuolisuus (diagnoosi alle 12-vuotiaansa) 62%		Hormonihoidot ja leikkaushoidota	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
60 henkilöä (39 MtF ja 21 FtM) kutsuttiin kahdelta klinikalta, pohjoisesta ja etelästä. Heidät tutkittiin somaattisesti, psykiatrisesti ja psykologisesti. Osallistumisen edellytyksenä transsukupuolisuus-diagnoosi (F64.0), että on hyväksytty muunnosprosessiin vähintään 5 vuotta sitten ja/tai muunnosprosessi valmis vähintään 2v. sitten. Heistä 42 (70%) päätyi tutkimukseen. Pois jääneistä (14 MtF ja 4 FtM) 1 oli kuollut sukupuolen muuntoleikkaukseen, 8:aa ei tavoitettu ja 9 ei halunnut osallistua. Pois jääneet olivat enimmäkseen MtF ja heillä oli hieman alempi toimintakyky (GAF-mittarilla). Leikkauskriteerit Ruotsin käytännön mukaisesti: diagnosointi, psykiatrinen arvio, yhden vuoden tosielämäjakso ja hormonihoitoa vähintään 2 vuoden ajan.	n=25 MtF Ikä • alussa ka 37v • muuntoleikkauksen aikaan 38v • lopussa seuranta-ajankohtana ka 46v Homoseksuaalinen suuntautuminen 52%:lla Varhaisvaiheen transsukupuolisuus (diagn. alle 12v.) 44%:lla, myöhäisiä (diagn. yli 12v.) 56%:lla; MtF:n joukossa oli suhteellisesti enemmän myöhäisiä diagnooseja, p=0,003. Varhaisvaiheen TS / myöhäisvaiheen TS: • sukupuoli MtF: 42 / 88 (p<0,01) • ikä lähetteen aikana (vuosina): 28 / 42 (p<0,01) • ei-homoseksuaalinen suuntautuminen (suhteessa syntymäsukupuoleen): 15 / 56 (p<0,01) Sukupuoli-identiteetti (lopussa): syntymäsukupuoli (0%), vastakkainen kuin syntymäsukupuoli (79%), transsukupuolinen (21%).	Hormonihoito (kaikki saaneet) Leikkaushoidot: 72% MtF-potilaista leikattu • 4 ei halunnut kastraatiota tai muita leikkauksia (kaikki yli 12-vuotiaana diagnosoituja), 2 halusi vain rintaimplantit, 1 oli muunsukupuolinen ja 1 epäröi, koska partneri hyväksyi omat genitaali).	Yhden ryhmän ennen ja jälkeen mittauksia. Lääkärit täyttivät standardoituun lomakkeeseen potilaiden perustiedot rekistereistä ja lähetteestä, postoperatiiviset tiedot ja oman arvion tuloksista sekä GAF-pisteet (arvio toimintakyvystä) hoitoprosessin alusta loppuun asti. Loppumittaus haastatteluin ja samoilla testeillä kuin alussa tehtiin yli 5 vuotta prosessin alusta tai vähintään 2 vuotta leikkausten jälkeen. Seuranta-aika keskimäärin 9 vuotta (4-16 v). Puolet tutkituista oli sellaisia joilla leikkauksesta oli kulunut alle 4 vuotta Vertailuja tehtiin sukupuolten (MtF ja FtM), varhaisen ja myöhäisen diagnoosin, ja seksuaalisen suuntautumisten välillä.

Lääkärin yleisarvio lopputuloksesta (standardoitu kyselylomake)	Sosiaalinen toimintakyky (standardoitu kyselylomake ja puolistrukturoitu haastattelu)	Tulosten tulkintaa
Yleisarvio: Tilanne parantunut 72%:lla.	Ennen → jälkeen hoitoprosessin, ka 9 vuoden kuluttua. Oma arvio työtilanteesta: • parantunut 39 % • muuttumaton 48 % • huonontunut 13 %, (Kaksi jäänyt työttömäksi ja yksi miesvaltaisessa työssä, jossa hankaluuksia. Hoitoprosessin jälkeen 36 %:lla oli partneri Oma arvio parisuhteesta:: • parantunut 70 % • muuttumaton 22 % • huonontunut 9%, n=3 Kaksi liittyi seksiin ja yksi rooliongelmiin yleisesti.	Potilaiden tyytyväisyys hoitoprosessiin parempaa kuin lääkäreiden (95% vrt. 60%). MtF-ryhmän tulokset parempia kuin FtM:n. Selityksenä ehkä FtM:n jo alunalkaen parempi toimintakyky. FtM-transsukupuoliset olivat MtF-henkilöitä nuorempia ja useammin homoseksuaaleja. Kaikki, joiden muuntoprosessi oli päätöksessä, identifioituivat syntymäsukupuolta vastakkaiseen sukupuoleen. Tutkijat pohtivat, että koska potilaat olivat tuttuja (omia potilaita vuosien ajan), miellyttämisenhalu saattoi vaikuttaa tuloksiin.

MtF = male-to-female, FtM = female-to-male, NS = non-significant, ka = keskiarvo, n = lukumäärä

9. Smith ym. 2005, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (DSM-IV)		Hormonihoito ja leikkaushoidot	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin 325 sukupuolen muuntoprosessiin hakeutunutta henkilöä kahdelta yliopistoklinikalta. Sisäänottokriteerejä ei määritelty tarkemmin.	Lukumäärät: • Muuntoprosessiin hakeneet: n=325 (MtF 220, FtM 105). • Ei-aloittajat (eivät saaneet lähetettä sukupuolenmuunnokseen): n=103 (MF 74, FM 29)	Kaikki hoidon loppuun asti käyneet saaneet hormonihoidon ja sukuelinleikkauksia.	Yhden ryhmän mittauksia ennen muuntoprosessia (diagnostiikan yhteydessä) ja sen jälkeen, vähintään 1 vuosi leikkaushoitojen jälkeen. Seuranta-aika prosessin alusta loppuun 1–4v. Mittaukset

Hoitoprosessin kulku Hollannissa: 1) diagnosointivaihe 2) lähete hormonihoitoon ja tosielämäkokeen arvio, 3) lähete sukuelinleikkaukseen. Lääkäri hyväksyy leikkaukseen sen mukaan, miten paljon sosiaalinen rooli ja ulkomuoto on muuttunut hormonihoitojen ja tosielämäkokeen myötä, kuinka psykologisesti vakaa henkilö on ja kuinka suuri sukupuoliristiriita on.	• Aloittajat (lähete, aloittivat hormonihoidon): n=222 (MF 146, FM 76) • Pudokkaat (lopettivat hormonihoidon): n=34 (MF 29, FM 5). • Hoidon päättäneet (kävivät hoidot loppuun): n=188 (MtF 117, FtM 71) • Seurantahaastatteluun osallistuneet: n=158 (MtF 94, FtM 64) Ikä (hoidon päättäneet): • hakuvaiheessa ka 31v (18–68v.) • hormonihoidon alussa ka 32v (18–68v.) • seurantahaastatteluun osallistuneet ka 35v (21–72v.). MtF 39; FtM 30v. Sosiodemografia (seurantavaiheessa): Työtilanne: työssä (37%), opiskelijoita (5%), eläkkeellä (2%), työttömiä (56%). Asuintilanne: yksin 56%, kumppanin kanssa (ja lasten kanssa tai ilman) 26%, vanhempien luona 2%, yksin lasten kanssa 2%, asuntolassa (8%) Tutkimuksessa käytettiin 162 aikuista. Ennen ja jälkeen muuntoprosessin tehtyihin mittauksiin osallistui 104 ennen ja 162 jälkeen.	Suoritettuja leikkauksia: vaginoplastia, rintojen silikoni-implantit (n=52). Keskimääräinen aika hormonihoidon aloituksen ja leikkauksen välillä oli 20kk (12–73kk). Keskimääräinen aika leikkauksen ja loppuseurannan välillä oli 21 kk (12-47 kk)	tehtiin haastatteluin ja kyselyin. N= 104 ennen ja 162 jälkeen. Ennen prosessia tehdyt mittaukset: GID in Childhood ja Social Support Scale –mittarit. Ennen ja jälkeen prosessin tehdyt mittaukset: sukupuoliristiriita, kehoahdistus, fyysinen ulkomuoto ja psykologinen toimintakyky. Kyselyillä kerättiin tietoa 101-126 henkilöltä (riippuen mitatuista asioista). Vain muuntoprosessin jälkeen tehdyt mittaukset: Biografinen kysely ja Symptom Check List, n=101–126. Mittauksia verrattiin yhdessä ryhmässä eri ajankohdissa. Myös eri sukupuoli-identiteettien välisiä ja seksuaalisen suuntautumisen ryhmien tuloksia verrattiin keskenään. Lisäksi tutkijat analysoivat monimuuttujamallituksella sukupuolen muunnokseen hyväksytyksi tulemisen ennakoivia tekijöitä

Sukupuoli- ja kehoahdistus (UGDS, AAI)	Psykologinen kuormitus ja persoonallisuuden patologiset piirteet (SCL-90 Dutch version)	Tyytyväisyys seksielämään (kysely muuntoprosessin jälkeen)*	Katuminen ja tyytyväisyys leikkauksiin (kysely muuntoprosessin jälkeen)*	Tulosten tulkintaa

Sukupuoliristiriita, UGDS-pisteet ennen → jälkeen muuntoprosessin*, skaala 12–60, pienempi parempi: Tulos: 54 → 15, p<0,001 kolmen ammattilaisen arvion mukaan (diagnoosin tehnyt lääkäri, hoitaja, tutkija), AAI-pisteet ennen → jälkeen muuntoprosessin, skaala 0–70, pienempi parempi: Tulos: 45 → 38	SCL-90-Dutch version pisteet ennen → muuntoprosessin, kokonaispisteiden skaala 90-450, pienempi parempi. Kokonaispisteet: 143→123 p=0,001 Masennus: 29 → 25 Ahdistus: 15 → 13 (p<0,001) Herkkyys: 28 → 24 (p<0,001) Univaikeudet: 5,4 → 4,6 (	Orgasmin saaminen (heistä jotka seksuaalisesti aktiivisia, n=84): aina/usein 42%; Homoseksuaalinen suuntautuminen (suhteessa syntymäsukupuoleen) 51% .	MtF: • Tyytyväisyys vaginoplastiaan (n=47): 70% oli tyytyväisiä • 22% ei ollut täysin tyytyväisiä koska vagina ei ollut riittävän syvä ja feminiininen • 8% oli tyytymättömiä koska he olivat kyvyttömiä seksuaaliseen nautintoon ja halusivat uusintaleikkausta. Tyytyväisyys rintojen suurentamiseen (n=34): • 65% oli tyytyväisiä • 29% ei ollut täysin tyytyväisiä • 10%:a häiritsi rintojen iso etäisyys toisistaan	Sukupuoliristiriita väheni selvästi, ja vielä enemmän FtM-ryhmällä. MtF-henkilöt olivat vanhempia kuin FtM:t. Psykologinen toimintakyky oli varsin hyvä jo alussa, mutta parani loppumittauksessa kahdella eri mittarilla mitattuna. Sosiaalinen ja seksuaalinen toimintakyky oli kohtuullisen hyvä loppumittauksissa.

Transmiehet (FtM)

10. van de Grift ym. 2017, Alankomaat, Belgia ja Saksa

Potilaat		Tutkittava interventio	Tulos
Diagnoosi: FtM: ei diagnoosia 3%, varhaisvaiheen GID (DSM-IV) 79%, myöhäisvaiheen GID (DSM-IV) 12%, muu GID-diagnoosi (DSM-IV) 5%.		Hormonihoito, sukuelin ja –rintakirurgia	SCL-90 yhteispisteet (GSI): Transmiehillä 0,60 → 0,57 (alhainen kuormitus) Muita tuloksia taulukossa 1.
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin kaikki yli 16-vuotiaat, jotka hakivat sukupuolen muuntohoitoja Amsterdamin, Gentin tai Hampurin klinikoilta vuosina 2007–2009, riippumatta siitä, oliko hoitoja myönnetty. 546 kutsutusta 201 osallistui (37%). Heistä 14% ei ollut saanut sukupuolen muuntohoitoja, 18% oli saanut vain hormonihoitoja ja 68% oli saanut sekä hormoni- että leikkaushoitoja.	n=66; ikä ka 31; suurin osa varhaisvaiheen GID-diagnooseja, koulutustaso korkea 41%, matala 12%. Sukupuolirooli (n): nainen 5, mies 60, ei ilmoittanut 1. Ulkomuoto-pisteet 40. Psykologinen kuormittuneisuus alussa (SCL) 0,6 (alhainen kuormitus).	• sukupuolen muuntamiseen tähtäävä hormonihoito 91% • rintojen poisto 79% • munasarjojen / kohdun poisto 78%	

Ei-osallistujat olivat osallistujiin nähden merkitsevästi vanhempia, koulutetumpia (p<0,001) ja tyytyväisempiä kehoonsa (p=0,01). Diagnoosien suhteen ei eroja ryhmien välillä.	Hoitoja saamattomia oli 24. Heistä 71% eli syntymäsukupuolessaan ja 29% vastakkaisessa sukupuolessa.	• neopeniksen rakentaminen 27%	

van de Grift TC, Elaut E, Cerwenka SC, Cohen-Kettenis PT, De Cuypere G, Richter-Appelt H, Kreukels BPC. Effects of Medical Interventions on Gender Dysphoria and Body Image: A Follow-Up Study. Psychosom Med. 2017 Sep;79(7):815-823.

11. de Vries ym. 2014, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisuus		Sukupuolen muunto: hormonihoito ja leikkaushoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yliopistosairaalan sukupuoli-identiteetin klinikkaan vuosina 2000−2008 tulleista 196 peräkkäisestä potilaasta 140 hyväksyttiin sukupuolen muuntoprosessiin ja 111 sai murrosiän keskeytyshoidon (Vries ym. 2011). He siirtyivät myöhemmin (2003-2009) sukupuolen muunnokseen tähtäävään hormonihoitoon ja leikkaushoitoihin. . Tähän tutkimukseen valittiin henkilöitä joiden leikkauksista oli kulunut vähintään vuosi. Aineistosta hylättiin 15 henkilöä sukupuolen muuntoleikkauksesta kieltäytymisen (n=2), hoitamattomien oheissairauksien (n=3) tai kontaktiongelmien vuoksi. Yksi henkilö oli kuollut vaginoplastialeikkauksen jälkeen nekrotisoivaan faskiittiin. Kuuden henkilön kohdalla leikkauksesta oli kulunut alle 1 vuosi. Pudonneet 15 henkilöä olivat esitietojen suhteen samankaltaisia kuin tutkimuksessa jatkaneet. 96 henkilöstä 55 henkilöä kutsuttiin tutkimukseen vuosina 2008−2012 (valintatapaa ei kuvattu).	n=55: FtM 33. Ikä leikkaushoidon. Ikä (ka): hormonihoidon alussa 17 (14–19) ja leikkauksen ajankohtana 19 (18–21) ja loppumittauksen aikaan 21 (20–23). Älykkyysosamäärä (ka) 99 (70–128) mitattuna WISC-R, WISC-III tai WAIS-III-mittarilla (keskimääräinen älykkyys 90-109).	Murrosiän keskeytys GnRH-analogilla (tulokset kuvattu de Vries 2011, taulukko 16). Sukupuolen muunnokseen tähtäävä hormonihoito (ei kuvattu). Sukupuolen muunnokseen tähtäävät leikkaushoidot: FtM: Rintarauhasten poisto, kohdun ja munasarjojen poisto. Falloplastiaoit ei ollut tutkimuksen päättyessä vielä tehty (osa pitkällä jonotuslistalla).	Murrosiän keskeyttämisen GnRH-hoidolla tulokset raportoitu tutkimuksessa de Vries ym. 2011 (taulukko 16). Tässä tutkimuksessa tulokset 12 kuukautta leikkaushoitojen jälkeen.

Sukupuoliristiriita (UGDS) ja kehoahdistus (BIS)	Yleinen toimintakyky (CGAS)	Mieliala: masennus (BDI) ja ahdistuneisuus (STAI)	Vihaisuus (TPI)	Tulosten tulkintaa

Sukupuoliristiriita (UGDS) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 12–60, pienempi parempi. N=33. FtM: 57→57→15, p<0.001 Kehoahdistus (BIS), skaala 1-5, pienempi parempi. N=45. Tyytyväisyys ensisijaisiin ominaisuuksiin (esim. rinnat, sukuelimet),: • FtM: 4,2→4,1→2,9, p<0.001 Tyytyväisyys toissijaisiin ominaisuuksiin (esim. lantio, karvoitus) • FtM: 2,8→3,2→2,5, p=0.05 Tyytyväisyys muihin ominaisuuksiin (esim. kasvot, pituus) • FtM: 2,2→2,6→2,3, NS	CGAS ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 0-100, isompi parempi. N=32. • FtM: 68→71→76, p=0.02	Masennus (BDI) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 1-63, pienempi parempi, 1-9 = ei masennusta. N=41 • FtM: 10,1→5,1→7,0, NS Taipumus ahdistuneisuuteen (STAI) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen, skaala 20-80, pienempi parempi. • FtM: 44→42→39, NS	Vihaisuus (TPI) ennen hoitoja → jälkeen GnRH-hoidon → 1 vuosi leikkauksen jälkeen. Suurempi pistemäärä kertoo suuremmasta taipumuksesta vastata ärsykkeisiin vihalla. N=32. FtM (n=20): 20→19→17, p=0.05 (	Sukupuoliristiriitaan ja kehonkuvaan liittyvät vaikeudet helpottivat sukupuolen muuntohoitojen (hormoni ja leikkaus) jälkeen. Mielialassa ei tapahtunut merkitseviä muutoksia. Taipumuksessa vastata ärsykkeisiin vihalla ei havaittu merkitseviä muutoksia, vaikkakin muutostrendi oli laskeva. Tutkimuksen lopussa mitattuna yksikään nuorista ei katunut murrosiän viivästämistä. Kaikki olivat hyvin tai kohtalaisen tyytyväisiä muuntohoitoihin. Elämänlaadussa (WHOQOL) ei ollut merkitsevää eroa verrattuna väestön keskiarvoihin ja ympäristöön liittyvä elämänlaatu oli keskimääräistä parempi (p<0,001).

12. Costantino ym. 2013, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (DSM), FtM		Testosteronihoito ja sukuelinkirurgia	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yliopistosairaalan klinikalla 78 GID-potilasta kerättiin 2001-2008. Ei aiempaa hormonihoitoa. Poissulkukriteerit: mielenterveysammattilaisen toteama psykiatrinen sairaus, merkittävä perussairaus, laittomien huumeiden käyttö.	n=50, ikä ka 30 (18-45 v), 46% tupakoi, lukion käyneitä 70%, työssä 70%, opiskelijoita 16%, heteroseksuaaleja 98%, vakituisessa suhteessa 46%, lapsia 4%:lla	Testosteroni yksilöllisellä antotavalla: esim im. testosteronienantaatti 100 mg 10-15 pv välein (n=20), testosteroniundekanoaatti p.o. 40 mg kahdesti päivässä (n=11), testosteroni geeli 50 mg (n=11) ja im testosteroniundekanoaatti 1000 mg alussa ja 6 viikon kohdalla ja sen jälkeen 3-4 kk välein (n=8). Hysterioannexioectomy ja reduktiivinen mammoplastia. Ei falloplastiaa tai muuta rekonstruktiivista sukuelinkirurgiaa.	Yhden ryhmän ennen-jälkeen mittauksia kerättiin ennen hormonihoidon aloitusta, 12 kk hormonihoidon aloituksen jälkeen ja 6 kk leikkaushoidon jälkeen.

Mieliala (tutkijoiden oma kysely)	Unen laatu	Sosiaaliset suhteet	Tulosten tulkintaa
Kysytyt asiat (iloisuus, uupumus, jännittyneisyys, energisyys, onnellisuus, masennus, hikoilu, ärtyneisyys, aggressiivisuus) eivät muuttuneet tilastollisesti merkitsevästi alkutilanteeseen verrattuna.	Unettomuus (p=0,008) ja kuorsaus (p=0,01) lisääntyivät hormonihoidon jälkeen ja jäivät korkeammalle tasolle myös leikkauksen jälkeen.	Vakituisessa suhteessa ennen hoitoja→ 12 kk hormonihoidon aloituksen jälkeen → 6 kk leikkauksen jälkeen: 46%→40%→44%	Raportointi puutteellista eikä validoituja mittareita käytetty.

13. Johansson ym. 2010, Ruotsi

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: F64.0 (ICD-10), varhaisvaiheen transsukupuolisuus (diagnoosi alle 12-vuotiaansa) 62%			
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
60 henkilöä (39 MtF ja 21 FtM) kutsuttiin kahdelta klinikalta, pohjoisesta ja etelästä. Heidät tutkittiin soamaattisesti, psykiatrisesti ja psykologisesti. Osallistumisen edellytyksenä transsukupuolisuus-diagnoosi (F64.0), että on hyväksytty muuntoprosessiin vähintään 5 vuotta sitten ja/tai muuntoprosessi valmis vähintään 2v. sitten. Heistä 42 (70%) päätyi tutkimukseen. Pois jääneistä (14 MtF ja 4 FtM) 1 oli kuollut sukupuolenmuuntoleikkaukseen, 8:aa ei tavoitettu ja 9 ei halunnut osallistua. Pois jääneet olivat enimmäkseen MtF ja heillä oli hieman alempi toimintakyky (GAF-mittarilla). Leikkauskriteerit Ruotsin käytännön mukaisesti: diagnosointi, psykiatrinen arvio, yhden vuoden tosielämäjakso	17 FtM; Ikä • alussa ka 28v; FtM nuorempia kuin MtF p<0,05 • muuntoleikkauksen aikaan ka 31v; • lopussa seuranta-ajankohtana ka 39v; Homoseksuaalinen suuntautuminen 94 %:lla; Varhaisvaiheen transsukupuolisuus (diagn. alle 12v.) 88%:lla, myöhäisiä (diagn. yli 12v.) 12%:lla; FtM:n joukossa oli suhteellisesti vähemmän myöhäisiä diagnooseja, p=0,003.	Hormonihoito (kaikki saaneet) Leikkaushoidot: 82% FtM-potilaista leikattu, 1 ei halunnut kastraatiota tai muita leikkauksia (= yli 12-vuotiaana diagnosoitu).	Yhden ryhmän ennen ja jälkeen mittauksia. Lääkärit täyttivät standardoituun lomakkeeseen potilaiden perustiedot rekistereistä ja lähetteestä, postoperatiiviset tiedot ja oman arvion tuloksista sekä GAF-pisteet (arvio toimintakyvystä) hoitoprosessin alusta loppuun asti. Loppumittaus haastatteluin ja samoilla testeillä kuin alussa tehtiin yli 5 vuotta prosessin alusta tai vähintään 2 vuotta leikkausten jälkeen. Seuranta-aika keskimäärin 9 vuotta (4-16 v). Puolet tutkituista oli sellaisia joilla leikkauksesta oli kulunut alle 4 vuotta Vertailuja tehtiin sukupuolten (MtF ja FtM), varhaisen ja myöhäisen diagnoosin, ja seksuaalisen suuntautumisten välillä.

ja hormonihoitoa vähintään 2 vuoden ajan.			

Lääkärin yleisarvio lopputuloksesta (standardoitu kyselylomake)	Sosiaalinen toimintakyky (standardoitu kyselylomake ja puolistrukturoitu haastattelu)	Tulosten tulkintaa
Tilanne parantunut 47%:lla transmiehistä. Transnaisilla tilanne parani useammin kuin transmiehillä, p=0.04	Ennen → jälkeen hoitoprosessin, ka 9 vuoden kuluttua. Työssäkäynti: • Töissä tai opiskeli 50% → 62% • Työkyvyttömyyseläkkeellä 21% → 28% Oma arvio työtilanteesta: • parantunut 54 % • muuttumaton 47 % • huonontunut 0 %. Hoitoprosessin jälkeen 341%:lla oli partneri Oma arvio parisuhteesta:: • parantunut 50 % • muuttumaton 43 % • huonontunut 7%.	Potilaiden tyytyväisyys hoitoprosessiin parempaa kuin lääkäreiden (95% vrt. 60%). MtF-ryhmän tulokset parempia kuin FtM:n. Selityksenä ehkä FtM:n jo alunalkaen parempi toimintakyky. FtM-transsukupuoliset olivat MtF-henkilöitä nuorempia ja useammin homoseksuaaleja. Kaikki, joiden muuntoprosessi oli päätöksessä, identifioituivat syntymäsukupuolta vastakkaiseen sukupuoleen. Tutkijat pohtivat, että koska potilaat olivat tuttuja (omia potilaita vuosien ajan), miellyttämisenhalu saattoi vaikuttaa tuloksiin.

MtF = male-to-female, FtM = female-to-male, NS = non-significant, ka = keskiarvo, n = lukumäärä

14. Smith ym. 2005, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: **GID (DSM-IV)**		**Hormonihoito ja leikkaushoidot**	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin 325 sukupuolen muuntoprosessiin hakeutunutta henkilöä kahdelta yliopistoklinikalta. Sisäänottokriteerejä ei määritelty tarkemmin.	Lukumäärät: FtM • Muuntoprosessiin hakeneet:105. • Ei-aloittajat (eivät saaneet lähetettä	Kaikki hoidon loppuun asti käyneet saaneet hormonihoidon ja sukuelinleikkauksia. Suoritettuja leikkauksia:	Yhden ryhmän mittauksia ennen muuntoprosessia (diagnostiikan yhteydessä) ja sen jälkeen, vähintään 1 vuosi leikkaushoitojen jälkeen. Seuranta-aika prosessin alusta loppuun 1–4v. Mittaukset tehtiin haastatteluin ja kyselyin. N= 104 ennen ja 162 jälkeen.

Hoitoprosessin kulku Hollannissa: 1) diagnosointivaihe 2) lähete hormonihoitoon ja tosielämäkokeen arvio, 3) lähete sukuelinleikkaukseen. Lääkäri hyväksyy leikkaukseen sen mukaan, miten paljon sosiaalinen rooli ja ulkomuoto on muuttunut hormonihoitojen ja tosielämäkokeen myötä, kuinka psykologisesti vakaa henkilö on ja kuinka suuri sukupuoliristiriita on.	sukupuolenmuunnokseen): 29 • Aloittajat (lähete, aloittivat hormonihoidon): 76 • Pudokkaat (lopettivat hormonihoidon): 5. • Hoidon päättäneet (kävivät hoidot loppuun): 71 • Seurantahaastatteluun osallistuneet: 64 Ikä hoidon päättäneillä ka 30v.	• falloplastia tai metadoioplastia, n=10 • rintojen poisto. Keskimääräinen aika hormonihoidon aloituksen ja leikkauksen välillä oli 20kk (12–73kk). Keskimääräinen aika leikkauksen ja loppuseurannan välillä oli 21 kk 12-47 kk)	Ennen prosessia tehdyt mittaukset: GID in Childhood ja Social Support Scale –mittarit. Ennen ja jälkeen prosessin tehdyt mittaukset: sukupuoliristiriita, kehoahdistus, fyysinen ulkomuoto ja psykologinen toimintakyky. Kyselyillä kerättiin tietoa 101-126 henkilöltä (riippuen mitatuista asioista). Vain muuntoprosessin jälkeen tehdyt mittaukset: Biografinen kysely ja Symptom Check List, n=101–126. Mittauksia verrattiin yhdessä ryhmässä eri ajankohdissa. Myös eri sukupuoli-identiteettien välisiä ja seksuaalisen suuntautumisen ryhmien tuloksia verrattiin keskenään. Lisäksi tutkijat analysoivat monimuuttujamallituksella sukupuolen muuntoon hyväksytyksi tulemisen ennakoivia tekijöitä

Sukupuoliristiriita ja kehoahdistus (UGDS, AAI)	Psykologinen kuormitus (SCL-90) ja persoonallisuuden patologiset piirteet (Dutch version ja MMPI Dutch short version)	Sosiaalinen elämä ja kontaktit (kysely muuntorosessin jälkeen)	Tyytyväisyys seksielämään (kysely muuntoprosessin jälkeen)*	Katuminen ja tyytyväisyys leikkauksiin (kysely muuntoprosessin jälkeen)*	Tulosten tulkintaa
Sukupuoliristiriita, UGDS-pisteet ennen → jälkeen muuntoprosessin*, skaala 12–60, pienempi parempi: Tulos: 54 → 14, p<0,001 Fyysinen ulkomuoto kolmen ammattilaisen arvion mukaan (diagnoosin tehnyt lääkäri, hoitaja, tutkija), AAI-pisteet ennen → jälkeen muuntoprosessin, skaala 0–70, pienempi parempi:	MMPI-pisteet ennen → jälkeen muuntoprosessin *, Pienempi parempi pätee myös osa-aluepisteiden tulkintaan paitsi ulospäinsuuntautuneisuutta kuvaavaan kysymykseen, jossa isompi pistemäärä on parempi. • Ulospäinsuuntautuneisuus: 13,8 → 18,0, p=0,005. alempia suhteessa hollantilaiseen keskitasoon. MMPI-pisteet loppuvaiheessa vastasivat enimmäkseen hollantilaisia väestökeskiarvoja.	MtF:t ja FtM:t kokivat tulevansa yhtä hyväksytyksi (eron p=0,4). FtM:t saivat enemmän tukea (p=0,01) ja pystyivät enemmän turvautumaan muihin (p=0,03).	Orgasmin saaminen (heistä jotka seksuaalisesti aktiivisia): aina/usein 82%., Homoseksuaalinen suuntautuminen (suhteessa syntymäsukupuoleen) 71%.	Sukupuoli-identiteettien välillä ei ollut eroja katumisessa. Katumisessa ei ollut eroa sukupuolten välillä hoitojen aikana (p=0,2) tai sen jälkeen (p=0,3). FtM: Tyytyväisyys rintojen poistoon (n=38): 29% oli tyytyväisiä 58% ei ollut täysin tyytyväisiä 13% oli tyytymättömiä näkyvien arpien vuoksi Tyytyväisyys metadoioplastiaan tai falloplastiaan (n=9):	Sukupuoliristiriita väheni selvästi, ja vielä enemmän FtM-ryhmällä. FtM-potilailla tulokset parempia kuin MtF:llä (poikkeuksena suurempi tyytymättömyys leikkauksiin).

Tulos: 45 → 26, p<0,001, n=57.	SCL-90-Dutch version pisteet ennen → muuntoprosessin, kokonaispisteiden skaala 90-450, pienempi parempi. Kokonaispisteet: 143 →45, p<0,001 Masennus: 29 → 20 (p<0,001).. Ahdistus: 15 → 13 (p<0,001)			• 44% oli tyytyväisiä • 44% ei ollut täysin tyytyväisiä • 11% (n=1) oli tyytymätön virtsaamisongelmien vuoksi	

n= lukumäärä, k = keskiarvo, MF = male-to-female, FM = female-to-male, GID = Gender Identity Disorder (sukupuoli-identiteetin häiriö)

Puberteettikehityksen pysäyttäminen GnRH-agonistilla

15. Costa ym. 2015, Britannia

Potilaat		Tutkittavat interventiot	Vertailu ja mittaukset
Diagnoosi: Varhaislapsuuden GID (DSM-IV-TR) ja GD		**GnRH ja psykologinen interventio**	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
436 perättäistä nuorisoklinikkaan vuosina 2010-2014 lähetettyä potilasta. Ikä ka 16, FtM 1,7-kertaa enemmän. Heistä 201 kävi läpi 6 kk arviointijakson. Hyväksymiskriteerejä: GID varhaislapsuudesta, GD:n paheneminen murrosiässä, ei psykiatrista oheissairautta, hoitojen merkityksen ymmärtäminen. Ryhmä jaettiin kahtia: osa siirtyi välittömästi GnRH-hoitoon (n=101) ja ne jotka tarvitsivat lisää kypsyttelyaikaa (ka 1 v) hoidettiin myöhemmin (n=100). Ei eroja sosiodemografiassa tai toimintakyvyssä (CGAS) tutkimukseen osallistujien ja prosessin keskeyttäneiden välillä.	n=201, ikä ka 15,5 (12-17), 53% elää yhden vanhemman kanssa, 42% kahden vanhemman kanssa, 90% kävi koulua, 23% ei elänyt haluamaansa sukupuoliroolia, 58% oli vaihtanut nimensä. Suurempi osa FtM-henkilöistä toteutti toivomaansa sukupuoliroolia (FtM 87% vs MtF 60% toteutti rooliaan täysin tai osittain) ja kävi koulussa (93% vs 84%). Dysforian taso (UGDS) alussa 55, skaala 12–60, pienempi parempi. FtM-henkilöillä enemmän ahdistusta (56 vs 52, p<0,001). Psykososiaalinen toimintakyky (CGAS) alussa 58, skaala 0-100, isompi parempi. Viittaa vaihtelevaan toimintakykyyn, jossa esiintyy hankaluuksia monilla, mutta ei kaikilla sosiaalisen toimintakyvyn alueilla. Huonompi kuin terveillä verrokeilla (67, p<0,001). FtM-henkilöillä parempi toimintakyky (FtM 59 vs. MtF 55, p=0,03).	Ryhmä 1 (n=101): Klinikan tavanomainen, WPATH suosituksen mukainen, psykologinen (supportiivinen) interventio 18 kk ajan JA alkaen 6 kk kohdalta puberteettikehityksen pysäyttäminen GnRH-analogilla. Ryhmä 2 (n=100): Klinikan tavanomainen, WPATH suosituksen mukainen, psykologinen (supportiivinen) interventio 18 kk ajan	Kahdelle eri interventioryhmälle eri ajankohdissa, ennen ja jälkeen interventioiden, tehtyjä mittauksia. Ryhmien mittaustuloksia ei verrattu keskenään. Mittauksia tehtiin alussa sekä 6, 12 ja 18 kk kohdalla.

Psykososiaalinen toimintakyky (CGAS): skaala 0-100, isompi parempi	Tulosten tulkintaa
Ryhmä 1 GnRH ja psykologinen interventio: mittaustulos alussa → 6 kk kestäneen psykologisen tuen jälkeen → 12 kk kestäneen psykologisen tuen ja 6 kk kestäneen GnRH-hoidon jälkeen →18 kk kestäneen psykologisen tuen ja 12 kk kestäneen GnRH-hoidon jälkeen. Ryhmä 2 pelkkä psykologinen interventio: mittaustulos alussa→ 6 kk → 12 kk →18 kk kestäneen psykologisen tuen jälkeen. Tulokset: Kaikki: 57 →61 (p<0,001)→63 (p<0,001)→65 (p<0,001) (vertailut suhteessa alkutilanteeseen) Ryhmä 1 (n=101): 6 kk pelkkä psykologinen interventio ja 6 kk alkaen myös GnRH 59→61 (NS)→65 (p=0,003)→67 (p<0,001) (vertailut suhteessa alkutilanteeseen) Pelkällä psykologisella interventiolla ei saatu tilastollisesti merkitsevää muutosta, mutta GnRH-hoidon alettua toimintakyky jatkoi kohenemistaan ja välillä 6-18 kk tapahtunut kohentuminen on tilastollisesti merkitsevä (p<0,01). Ryhmä 2 (n=100): pelkkä psykologinen interventio 57→60 (p=0,05)→63 (p=0,005)→63 (p=0,02) (vertailut suhteessa alkutilanteeseen) Tilastollisesti merkitsevä parannus jo ensimmäisen 6 kk kohdalla ja sen jälkeen tilanne säilyi ja jonkun verran koheni edelleen.	Psykososiaalinen toimintakyky koheni 1,5 kestäneiden interventioiden aikana selvästi. Tutkijat eivät verranneet ryhmiä keskenään. Vertailuryhmän (pelkkä psykologinen interventio) CGAS-arvo oli 18 kk kohdalla 63 ja GnRH-ryhmällä 67: eroa on GnRH-ryhmän eduksi mutta eron tilastollinen merkitsevyys ja käytännön merkitys jäävät epäselviksi.

16. de Vries ym. 2011, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Lapsuuden GID ja GD		GnRH	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
196 perättäistä yliopistosairaalaan lähetteellä tullutta potilasta vuosilta 2000-2008. Puberteetin keskeytyksen kriteerit: alle 16-v, GID ja GD lapsesta asti, tukea antava koti, ei psykiatrisia oheissairauksia, puberteetti ainakin Tanner 2-3 tasolla, hormonimittauksin vahvistettuna. 111 kriteerit täyttävää. Arviointivaihe kesti noin puoli vuotta, jonka aikana tosielämän muutoksia ja nimen vaihto useimmille.	Analyysissä 70 ensimmäiset kriteerit täyttävää. Ikä alussa 13,6 (11-17); puberteetin keskeytyksen alkaessa 14,8 (12-18); muuntohoidon (hormoni) alkaessa 16,7 (14-19); leikkauksen aikana 19,2 (18-21). Älykkyys 99 (70-128) (Wechsler Intelligence Scale, isompi parempi, keskimääräinen älykkyys 90-109), kaksi huoltajaa 63%:lla, vanhempien koulutustaso korkea 11%:lla ja matala 23%:lla. 89% ilmoittaa vetoa omaa sukupuolta ja 9% molempia sukupuolia edustaviin.	Puberteetin keskeytys GnRH-analogilla ka 2 vuoden ajan. de Vries ym. 2014 tutkimuksessa raportoidaan saman potilasjoukon myöhempiä muuntohoidon (hormonihoidon ja leikkaushoidon) tuloksia.	Yhden ryhmän ennen-jälkeen mittauksia alussa (n=70) ja juuri ennen muuntohoidon (hormoni) aloitusta (n=54 tai 41 riippuen lopputulosmuuttujasta). Seuranta-aika noin 2 vuotta.

	MtF n=33, ikä alussa ka 13; älykkyys 97, vanhempien koulutustaso korkea 3%:lla ja matala 20%:lla. FtM n=37, ikä ka 14, älykkyys 99, vanhempien koulutustaso korkea 17%:lla ja matala 25%:lla.		

Sukupuoliristiriita (UGDS) ja kehoahdistus (BIS)	Yleinen toimintakyky (CGAS)	Mieliala: masennus (BDI) ja ahdistuneisuus (STAI)	Käyttäytyminen ja tunteet (CBCL)	Tulosten tulkintaa
Sukupuoliristiriita (UGDS) ennen → jälkeen GnRH-hoidon Skaala 12–60, pienempi parempi • Kaikki 53 → 54, NS • MtF: 48 → 50 • FtM: 57→ 57 Kehoahdistus (BIS), skaala 1-5, pienempi parempi. Tyytyväisyys ensisijaisiin ominaisuuksiin (esim. rinnat, sukuelimet),: • Kaikki 4,1 → 4,0, NS • MtF: 4,0 → 3,7 • FtM: 4,2→ 4,2 Tyytyväisyys toissijaisiin ominaisuuksiin (esim. lantio, karvoitus) • Kaikki 2,7 → 2,8, NS • MtF: 2,7 → 2,4 • FtM: 2,8→ 3,2 Tyytyväisyys muihin ominaisuuksiin (esim. kasvot, pituus) • Kaikki 2,4 → 2,5, NS • MtF: 2,6 → 2,3	CGAS ennen → jälkeen GnRH-hoidon, skaala 0-100, isompi parempi • Kaikki 70 → 74, p=0,005 • MtF: 73 → 77 • FtM: 67→ 70	Masennus (BDI) ennen → jälkeen GnRH-hoidon (n=41), skaala 1-63, pienempi parempi, 1-9 = ei masennusta • Kaikki 8,3 → 5,0, p=0,004 • MtF: 5,7 → 3,5 • FtM: 6,4 → 6,4 Taipumus ahdistuneisuuteen (STAI), skaala 20-80, pienempi parempi. • Kaikki 39 → 38, NS • MtF: 4,3 → 4,4 (virhe?) • FtM: 7,0 → 6,2 (virhe?)	Vanhempien arvio käyttäytymisestä ja tunteista: CBCL ennen → jälkeen GnRH-hoidon, skaala 0-100, pienempi parempi, hollantilaisnuorilla pistemäärää yli 63 pidetään kliinisesti merkittävänä. Kokonaispisteet: • Kaikki 61 → 54, p<0,001 • MtF: 59 → 50 • FtM: 62 → 58 Masennus, ahdistus, somatisaatio: • Kaikki 61 → 54, p<0,001 • MtF: 60 → 52 • FtM: 62 → 56 Sääntöjen rikkominen, aggressiivisuus: • Kaikki 58 → 54, p=0,001 • MtF: 55 → 49 • FtM: 61 → 59 Lapsen oma arvio käyttäytymisestä ja tunteista: YSR skaala 0-100, pienempi parempi, hollantilaisnuorilla pistemäärää yli 63 pidetään kliinisesti merkittävänä. Kokonaispisteet: • Kaikki 55 → 50, p<0,001 • MtF: 54 → 48 • FtM: 57 → 52	Noin 2 vuoden GnRH-agonistihoidon aikana: • Sukupuoliristiriita ei vähentynyt • Mieliala koheni ja käytöshäiriöiden riski pieneni. Toisaalta mitatut ominaisuudet olivat alun perinkin normaaliarvoja. Puuttuvia mittauksia suhteellisen paljon: riippuen muuttujasta jopa 40%. Tytöt tulivat hoitoon suhteellisen myöhään, keskimäärin 14-vuotiana, ja suurimmalla osalla oli jo kuukautiset ja rintojen kasvua.

• FtM: 2,2→ 2,6			Masennus, ahdistus, somatisaatio: • Kaikki 56 → 50, p<0,001 • MtF: 56 → 49 • FtM: 56 → 50 Sääntöjen rikkominen, aggressiivisuus: • Kaikki 53 → 50, p=0,009 • MtF: 49 → 47 • FtM: 57 → 53 Taipumus vihaisuuteen (TPI), pienempi parempi • Kaikki 18,3 → 17,9, NS • MtF: 5,2 → 5,0 • FtM: 6,4 → 6,4	

Hormonihoito

Transsukupuoliset (MtF ja FtM)

17. Colizzi ym. 2014, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (DSM-IV-TR)		Hormonihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
118 perättäistä, transsukupuolisuuden vuoksi klinikkaan vv. 2008-2012 tullutta, yli 18 v. henkilöä (MtF ja FtM). Äidinkieli italia. Poissulkukriteerit: Hoitamaton psykiatrinen oheissairaus SCID-I:n mukaisesti; neurologinen tai metabolinen sairaus; intersukupuolisuus. Arvion tekivät 24 viikon aikana transsukupuolisten hoitoon erikoistuneet psykiatrit, psykologit, endokrinologit ja gynekologit, käyttäen haastatteluja, psykometrisia välineitä sekä	n=107: MtF 78, FtM 29. Ikä ka 29, koulutusta ka 11 v., 1/3 ei parisuhteessa, 4/5 elää vanhempien tai partnerin kanssa, 2/3 työssäkäyviä, yli 90% homoseksuaaleja. Ahdistuneisuus alussa lievä (SAS 45). Ei eroja MtF ja FtM välillä. 6:lla stabiili, hoidossa oleva psykiatrinen oheissairaus, johon lääkehoito ka 3 v ajan. (ahdistuneisuus n=2, masennus tai dystymis n=2, bipolaari n=1, päihteiden väärinkäyttö n=1). Heidän soisodemografiset tietonsa samankaltaisia kuin muilla tutkimuspotilailla.	Moniammatillinen arviointijakso ja tosielämän jakso (n=107). Hormonihoito (n=98): MtF: estradioligeeli ihon kautta 1,8 +/- 0,5 mg/pv ja syproteroniasetaatti p.o. 100 mg/pv. FtM: testosteroniesteri im. 250 mg 26 +/- 3 pv:n välein	Yhden ryhmän ennen-jälkeen mittauksia kyselyin ennen hormonihoidon aloitusta sekä noin 12 kk sen jälkeen.

verikokeiden ja kromosomianalyysien tuloksia. Kriteerit täytti 107 henkilöä.	Arviointijakso ja tosielämän jakson jälkeen 9 henkilöä koki tämän riittäväksi interventioksi (7 MtF ja 2 FtM). Loput 98 jatkoivat hormonihoidolla.		

Psykologinen kuormitus (SCL-90R) ja psykologinen toimintakyky (SCID-1)	Masennus (SDS)	Ahdistuneisuus (SAS)	Tulosten tulkintaa
SCL-90 yhteispisteet (GSI) alussa → 12 kk kuluttua hormonihoidon aloituksesta. 0,74 → 0,48, p<0,001. Pienempi parempi. Suomen väestötason GSI arvo 0,65. Tilastollisesti merkitsevää vähenemistä oireissa saavutettiin mittarin osioissa masennus, ahdistuneisuus, pakko-oireisuus ja herkkyys ihmissuhteissa. Kaikissa muissakin osioissa oireet vähenivät, mutta ero ei saavuttanut tilastollista merkitsevyyttä. SCL-90 GSI > 1 (merkittäviä psykologisia oireita) 24% → 11%, p<0,001 Merkittävä toimintarajoitus SCID-1 mukaan 23% → 10%, p<0,001	SDS indeksi (ka) alussa → 12 kk kuluttua hormonihoidon aloituksesta. Skaala 25-100, pienempi parempi, alle 50 pidetään normaalina. Tulos::48 → 40, p<0,001. SDS 25-49 (ei oireita) 58% → 77%, p <0,001 SDS 50-59 (lievä) 29%→17% SDS 60-69 (kohtalainen) 9%→6% SDS 70-100 (vaikea) 4%→0	SAS indeksi (ka) alussa ja 12 kk kuluttua hormonihoidon aloituksesta. Skaala 25-100, pienempi parempi, alle 45 pidetään normaalina. Tulos: 45 → 38, p<0,001. SAS 25-44 (ei oireita) 50% → 80%, p <0,001 SAS 45-59 (lievä) 43%→14% SAS 60-74 (kohtalainen) 5%→3% SAS 75-100 (vaikea) 2%→0	Noin vuoden hormonihoidon jälkeen masennus, ahdistuneisuus ja muu psykologinen kuormitus vähentynyt ja toimintakyky parantunut. Tuloksissa ei eroja MtF ja FtM välillä..

18. Colizzi ym. 2013, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (DSM-IV-TR)		Hormonihoito ja psykologista neuvontaa	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
70 peräkkäistä yliopistosairaalan psykiatrian klinikan sukupuoli-identiteettiyksikön potilasta 2008-2011. Kaksi erikoistunutta psykiatria tutki potilaat ja teki SCID-I haastattelun. Poissulkukriteerit: neurologinen tai psykiatrinen sairaus, metabolinen sairaus tai interseksuaalisuus,	n=70: MtF 50, FtM 20, ikä ka 29, koulutusta ka 12 v, työssä 70%. Aamulla mitattu kortisolitaso ka 29 µg/dl (normaalialue 9-23), minkä tulkittu viittaavan krooniseen stressiin. Ei eroja MtF ja FtM välillä missään mittauksessa.	MtF: estradioli geeli ihon kautta n. ka 1,8 mg/pv ja p.o. syproteroniasetaatti 100 mg/pv. FtM: testosteroni esteri depot 250 mg im injektioina ka 27 pv välein. Lisäksi kaikille psykologista neuvontaa.	Yhden ryhmän ennen-jälkeen mittauksia verikokein ja lomakekyselyin ennen hormonihoidon aloitusta ja n. 12 kk sen jälkeen.

endokrinologin määrittelemänä ja käyttäen verikokeiden ja kromosomianalyysien tuloksia.			

Koettu stressi (PSS)	Kortisolitaso	Tulosten tulkintaa
PSS (ka) ennen hormonihoidon aloitusta→ n. 12 kk sen jälkeen: 28 → 15, p<0,001. Skaala 0-40, pienempi parempi. Samanikäisessä terveessä väestössä ka 14. MtF: 29→15 FtM: 25→15. Ei tilastollisesti merkitseviä eroja MtF ja FtM välillä.	Aamulla mitattu kortisolitaso (ka) ennen hormonihoidon aloitusta → n. 12 kk sen jälkeen: 29 → 16, p=0,001, (normaalialue 9-23): MtF: 32 → 16 FtM: 28 → 15 Ei tilastollisesti merkitseviä eroja MtF ja FtM välillä	Tutkijat mittasivat myös osallistujien varhaisen vuorovaikutuksen tyyliä ja totesivat sen liittyvän kortisolitasoon ja koettuun stressiin, mutta ei siihen kuinka hyvin potilaat hyötyivät hormonihoidosta.

Transnaiset (MtF)

19. Fisher ym. 2016, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GD (DSM-5)		Hormonihoito ja henkistä tukea	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yliopistoklinikasta GD-oireisiini apua hakeva yli 18-vuotias. Diagnoosi tehty usean käynnin jälkeen kahden eri GD-ammattilaisen toimesta. Hoitoaika 2008-2015 (54 hengen alaryhmä 2012-2015). Poissulkukriteerit: intersukupuolisuus, älyllinen kehitysvamma, lukutaidottomuus sukuelinkirurgia tehty. 394 henkilöä valittu poikkileikkaustutkimukseen, jossa verrattiin hormoneja käyttäneitä niihin, jotka eivät olleet käyttäneet hormoneja. Jälkimmäisten joukosta valittiin 60 muuntohoitoja haluavaa henkilöä testosteronihoitokokeeseen. 6 poistui seurannasta. Tiedot puuttuivat 11 potilaalta.	n=54: MtF 28. Ikä ka noin 29.	Kaikki potilaat saivat standardoitua, ammattilaisen antamaa henkistä tukea 3 kk välein. MtF: syproteroniasetaatti suun kautta 50 mg yhdistettynä joko estradiolivaleriaattiin suun kautta (2/3) tai ihon kautta annosteltavaan estradioliin (1/3).	Yhden ryhmän ennen-jälkeen mittauksia ennen hoidon aloitusta sekä 3,6,12 ja 24 kk hormonihoidon aloituksen jälkeen.

Kehoahdistus (BUT) ja sukupuoliristiriita (GIDYQ-AA)	Psyykkinen kuormittuneisuus (SCL-90-R GSI) ja masennus (BDI)	Karvan kasvu (Ferriman-Gallway)	Kehonpaino (BMI, vyötärön ympärys)	Tulosten tulkinta

Kehoahdistus: BUT kokonaispisteet (GSI) ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Pienempi parempi. • MtF 2,4→1,7→1,8→1,5→1,4, p<0,05 Sukupuoliristiriita: GIDYQ-AA ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Isompi parempi. • Kokonaispisteet: noin (pisteet luettu kuviosta) 2,25→2,40→2,10 (p<0,01)→2,05→2,15 • Subjektiivinen osio: merkitsevä nousu 3 kk kohdalla, sen jälkeen laskua. 2 v kohdalla pisteet korkeammat, p<0,01. • Sosiaalinen (p<0,01) ja sosio-laillinen (NS) osio: kummassakin laskeva trendi. Sukupuoliristiriita siis lievittyi ensin, mutta vaikeutui myöhemmin.	Psyykkinen kuormittunen: SCL-90-R kokonaispisteet (GSI) ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Pienempi parempi. Suomen väestötason GSI arvo 0,65. • MtF 0,80→0,48→0,50→0,43→0,45, p<0,05 Masennus: BDI-II ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Pienempi parempi. 1-9-= ei masennusta, 10-18 = lievä masennus. • MtF 10,1→7,5→5,5→4,5→4,7, p<0,05	Ferriman-Gallway ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen, skaala 0-36, pienempi vähemmän. Alle 8= normaali, 8-15 on lievää ja yli 15 on kohtalaista tai voimakasta hirsutismia (karvan kasvu). • MtF 17→13→10→10→5, p<0,001	BMI ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. • MtF 21,9→22,1→22,4→22,9 →23,0, p<0,01 Vyötärön ympärys • MtF 83→84→87→83→88, p<0,01	Kehoahdistus, sukupuoliristiriita ja psyykkinen kuormittuneisuus vähenivät 2 vuoden hormonihoidon aikana. Painoindeksi suureni 1-2 yksikköä, kiloja tuli lisää transnaisilla keskimäärin 2 kg.

Fisher AD, Castellini G, Ristori J, Casale H, Cassioli E, Sensi C, et al. Cross-Sex Hormone Treatment and Psychobiological Changes in Transsexual Persons: Two-Year Follow-Up Data. J Clin Endocrinol Metab 2016 Nov;101(11):4260-4269.

20. Manieri ym. 2014, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (DSM-IV)		Hormonihoito ja psykodynaaminen psykoterapia kerran viikossa	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
GID-diagnoosin teki mielenterveysammattilaisten tiimi ka 8 kk aikana, haastattelujen, psykoseksologisen	n=83 MtF (n=56): ikä ka 33 (+/-9), BMI>30 9%:lla, metabolinen	MtF (n=56): 17βestradioli suun kautta 2 mg/pv ensimmäiset 3 kk ja sen jälkeen 4-6 mg/pv suun kautta tai transdermaalisesti (iäkkäämmät, tupakoivat ja jos tukostaipumusta).	Yhden ryhmän ennen-jälkeen mittauksia ennen hoitojen alkua ja

arvioinnin (omakuva, ruumiinkuva, seksuaalinen suuntautuneisuus, merkittävä psykopatologia) ja persoonallisuustestien perusteella. Kriteereinä: aikuisikä, pysyvä GD, kykenevä tietoiseen päätökseen, lääketieteelliset ja psykologiset/psykiatriset oheissairaudet hoidolla hallinnassa. Tosielämän jakso toimii diagnostisena apuna: kerran viikossa psykoterapia, jossa arvioidaan psykologista ja ihmissuhteissa tapahtuvaa toimintakyvyn kehitystä. Pois suljettu: vakava psykopatologia, mm. psykoottiset häiriöt, päihteiden väärinkäyttö, henkinen kehitysvamma, dementia, MtF-potilaiden synnynnäinen laskimotukosriski.	syndrooma 7%:lla, tupakoivia 39%, heteroseksuaaleja 96%, pysyvässä parisuhteessa 62%. 3:lla HIV.	Antiandrogeeni: Syproteroniasetaatti (CPA) (n=54) alkuun 50 mg/pv, sitten 100 mg/pv ja ylläpito 75mg/pv tai spironolaktoni 100-200 mg/pv (jos tarvittiin verenpainevaikutusta) ja dutasteridi 0,5 mg/pv, henkilöille joilla miestyyppistä hiustenlähtöä. 63% käytti myös muita antiandrogeeneja. 2:lle henkilölle (lihavuus, verenpainetauti) käytettiin CPA:n sijasta GnRH-analogia. Ruokavalio-ohjausta ja glukoosi/kolesterolilääkityksiä tarvittaessa. Kaikille lisäksi: Arviointijakso (RLE), jossa henkilöt elävät uutta kehoaan. Psykodynaaminen psykoterapia kerran viikossa. Hormonimittaukset 3 kk välein, mammografia 8-12 kk kohdalla.	noin 1 vuosi hormonihoidon aloituksen jälkeen.

Elämänlaatu (WHOQOL-100)	Parisuhde tai asuminen	Kehon muutokset	Metaboliset muutokset	Tulosten tulkintaa
WHOQOL-1pisteet alussa → 12 kk hormonihoidon aloituksen jälkeen. Skaala 0-100, isompi parempi, pisteet >50 viittaavat hyvään elämänlaatuun. Elämänlaatu 62 → 72, p<0,05 Kehon kuva 43 → 69, p<0,05 Sukupuolielämän laatu 56→ 62, p<0,05. Ihmissuhteiden toimivuus 50→ 75, p<0,05.	Pysyvä parisuhde tai asuu yhdessä alussa → 12 kk hormonihoidon aloituksen jälkeen: 62% → 64%. 80% koki tunteiden intensiivisyyden, labiiliuden ja herkkyyden ihmissuhteissa lisääntyneen.	Kehon muutokset (ka) alussa → 12 kk hormonihoidon aloituksen jälkeen: • Paino (kg) 66 → 69, NS • Rintarauhasen paksuus kasvoi > 6 cm 61%:lla. • Kivesten tilavuus pieneni 50%. • Iho oheni jo 1. kk jälkeen.	Ei merkitseviä muutoksia lipideissä ja verensokeriarvoissa. Tupakointi väheni.	Transnaisilla elämänlaatu koheni tilastollisesti merkitsevästi eri osa-alueilla. Toivottuja fyysisiä muutoksia yli puolella.

21. Miles ym. 2006, Britannia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset

Diagnoosi: GID (DSM-IV-TR), MtF		Estrogeenihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
103 geneettistä miestä, jotka toivoivat sukupuolen muunnosta naiseksi (MtF). 10 £ palkkio osallistujille.	Ryhmä 1a: ei hormoneja ennen: n=27, ikä ka 37 v. Mittauksia ennen ja jälkeen hormonihoidon aloituksen Ryhmä 1 b: ei hormoneja ennen: n=20, ikä ka 40 v. Mittauksia vain jälkeen hormonihoidon aloituksen. Ryhmä 2: hormoneja käytetty ainakin 28 kk ajan: n=27, ikä ka 40 v. Mitattu hormonien lopettamisen vaikutuksia	Premarin (konjugoitu estrogeeni) 1,25-7,5 mg/pv tai etinyyliestradioli 10 -150 µg/pv. 8%:lla myös syproteroniasetaatti 50-150 mg/pv tai medroksiprogesteroniasetaatti 15 mg/pv.	27 potilasta testattiin ennen hoidon aloitusta ja 3 ja 12 kk sen jälkeen. 27 potilasta, joilla hormonihoito tullessa, testattiin 2 kk estrogeenin lopettamisen jälkeen. 20 potilasta testattiin 3 ja 12 kk hormonihoidon aloittamisen jälkeen.

Verbaalisuus	Visuospatiaaliset taidot	Sanamuisti	Näkömuisti	Tulosten tulkintaa
Tietyllä kirjaimella alkavien sanojen keksiminen ja synonyymejä 6 minuutissa ennen ja 3 ja 12 kk jälkeen hoidon aloituksen: ei eroja.	20 kiertyneen kuvan tunnistaminen 10 minuutissa ja samansuuntaisten viivojen tunnistus ennen ja 3 ja 12 kk jälkeen hoidon aloituksen: ei eroja.	Tarinan toisto ja sanalistan toisto ennen ja 3 ja 12 kk jälkeen hoidon aloituksen: ei eroja.	Värin muistaminen ja muodon muistaminen ennen ja 3 ja 12 kk jälkeen hoidon aloituksen: ei eroja.	Yhden vuoden estrogeenihoidon jälkeen verbaalisissaa ja visuospatiaalisissa testeissä ei gavaittu muutoksia. Tässä on raportoitu vain ennen-jälkeen-ryhmän tulos. Kahden muun ryhmän tulosten merkitys on epäselvä.

22. Slabbekoorn ym. 2001, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolinen		Hormonihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yliopistosairaalan sukupuoliyksikön potilaita, kaikki soveltuvia sukupuolen uudelleen määrittelyyn. Diagnoosin vahvisti psykologi ja psykiatri,	n=101 MtF: n=54, ikä ka 33 (19-66) v. FtM: n=47, ikä ka. 26 (16-44) v. FtM olivat nuorempia, p<0,001	MtF: Syproteroni asetaatti suun kautta (Androcur) 50 mg x2/pv JA etinyyliestradioli suun kautta 0.05 mg x2/pv (Lynoral), n=32 TAI or 17ß estradiolilaastareita (Estraderm TTS) 0.1 mg/pv, n=22.	Yhden ryhmän ennen-jälkeen mittauksia. 5 kyselyä tehtiin ennen hoidon aloitusta ja 14 viikon kohdalla hoidon aloituksen jälkeen tai testosteroniesterin käyttäjillä 6 pv viimeisen injektion jälkeen. Kuusi im testosteroniestereitä käyttävää henkilöä osallistui lisäksi tiheämpiin mittauksiin kahden viikon sykleissä

			nopeasti muuttuvan testosteronitason mukaisesti. Heitä pyydettiin täyttämään päiväkirjaa 11 viikon ajan alkaen, 5 kertaa, 2 viikon välein, alkaen 1 vko ennen hoitoa.

Tunteisiin reagoinnin voimakkuus tai tunteellisuus (AIM)	Vihaisuus (ASQ)	Ei-verbaalinen ilmaisu (ACT)	Tulosten tulkintaa
AIM kokonaispisteet (skaala 40-240) ennen hormonihoitoa →14 viikon kohdalla hoidon alusta • 141→145, p<0,001 Transnaisten tunteellisuus kasvoi AIM positiiviset tunteet (skaala 28-168) • 100→102, NS AIM negatiiviset tunteet (skaala 12-72) • 43→43, NS	Vihaisuuden voimakkuus ennen hormonihoitoa →14 viikon kohdalla hoidon alusta. Suuremmat pisteet viittaavaat voimakkaampaan vihaisuuteen: 3,5 → 3,3, NS Negatiivisten tunteiden voimakkuus: 2,8 → 2,7, NS Transnaisilla negatiiviset tunteet voimakkaampia kuin transmiehillä, p<0,001. Aggressiivinen käyttäytyminen (ASQ anger readiness) 57 → 62, p<0,05	ACT ennen hormonihoitoa →14 viikon kohdalla hoidon alusta. Skaala 13-117, suuremmat pisteet merkitsevät enemmän ei-verbaalista tunteiden ilmaisua. MtF: 63 → 67, p<0,001 Transnaisilla ei-verbaalinen tunteiden ilmaisu lisääntyi	Ennakoituja muutoksia tunteellisuudessa ja tunteiden ilmaisussa (transnaisilla nousua). Negatiivisten tunteiden kokemisessa ei muutoksia, mutta aggressiivisen käyttäytymisen pisteissä nousua. Aggressiivinen käyttäytyminen lisääntyi. Sukupuoli-identiteettien välillä ei tilastollisesti merkitsevää eroa aggressiivisen käyttäytymisen tasossa. Seuranta-aika lyhyt, 3,5 kk.

23. Giltay ja Gooren 2000, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID		Hormonihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Ei kuvattu	MtF n=21, kaikki valkoihoisia, ikä md 30 (20-44) v.; BMI 22, yhdellä oli insuliinihoitoinen diabetes	Etinyyliestradioli 100 µg/pv suun kautta (Lynoral) n=10 tai 17ß-estradioli ihon kautta (Estraderm) n=11. Lisäksi syproteroniasetaatti 100 mg/pv.	Yhden ryhmän ennen-jälkeen mittauksia ennen hoitoa ja 4, 8 ja 12 kk kuluttua hoidon aloituksesta.

Karvan kasvu	Paino	Akne (Leeds)	Tulosten tulkintaa

Ferriman-Gallway 0-36 0→4 →8 →12 kk kohdalla, hormoniriippuvaisten alueiden yhteispisteet 9x4=36. 0 on ei karvaa, >7 tulkitaan hirsutismiksi. 21→15→13→10, p<0,01	BMI 0→4 →8 →12 kk kohdalla 22,0 →22,5→23,1→23,3, p<0,001	Leeds-pisteet 0-10, 0→4 →8 →12 kk kohdalla, 1:ä suuremmat merkitsevät kliinistä akneta. Kasvot 0→0→0→0 Selkä 0→0→0→0	Painoindeksi nousi noin yhden yksikön, karvan kasvu muuttui toivottuun suuntaan.

Transmiehet (FtM)

24. Motta ym. 2018, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GD (DSM-5), FtM		Testosteronihoito ja psykoterapia kerran viikossa	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
GD-keskuksen yli 18-vuotiaita FtM-potilaita vuosilta 2013-2015. Soveltuvuus sukupuolen muunnokseen tehty WPATH-kriteerein.	n=52, ikä ka 28 +/-8, BMI 25, koulutusta 11 v, työssä 46%, pysyvässä suhteessa 54%. Psykiatrisia häiriöitä 36%:lla: yleisimpänä mielialahäiriöt ja riippuvuudet (näistä noin puolet lääkehoidossa), persoonallisuushäiriöitä 15%:lla. Kuormittava elämäntilanne (itsemurhayritys, hyväksikäytön uhri, fyysinen vamma tms) ollut 33%:lla.	Ensimmäiset 3 kk transdermaalinen testosteroni, sitten antotapa valittiin yksilöllisesti, useimmille lihaksensisäinen testosteroniundekaneoaatti. Suurin osa kävi kerran viikossa psykoterapiassa, jossa seurataan hormonihoidon psykososiaalisia vaikutuksia ja ennakoidaan aggressiivisuuden lisääntymistä.	Yhden ryhmän ennen-jälkeen mittauksia ennen hoitoa ja 7 kk testosteronihoidon aloituksen jälkeen.

Aggressiivisuus (STAXI-2)	Haitat	Tulosten tulkintaa
Staxi-pisteet alussa → 7 kk hormonihoidon aloituksen jälkeen. Isompi merkitsee enemmän aggressiivisuutta. Pisteitä >75 tutkijat pitivät normaaliarvon ylittävinä. Yleisarvio 49 →74, p<0,001 Voimakkuus 45 →72, p<0,001 Yleisyys 45 →56, p<0,001 Ilmaisu 46 →76, p<0,001 Peittäminen 47 →79, p<0,001 Hallinta ilmaisun estolla 50 →73, p<0,001 Hallinta rauhoittelulla 56 →78, p<0,001	Ei hoidon keskeytyksiä, ei uusia psykiatrisia diagnooseja tai hoitoja	Testosteronitasot eivät korreloineet aggressiivisuuden kanssa. Ne, joilla kuukautiset jatkuivat testosteronihoidosta huolimatta, olivat aggressiivisempia kuin muut.

25. Turan ym. 2018, Turkki

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GD (DSM-5), FtM		Testosteronihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
41 yliopistosairaalan FtM-muuntohoitopotilasta, ikä yli 18, kaksi GD-ammattilaista teki diagnoosin. Poissuljettu: neurologiset, endokrinologiset, metaboliset patologiat ja interseksuaalisuus; aikaisempi sukupuolta korjaava hormonihoito; henkinen kehitysvamma; lukutaidottomuus. Laki vaatii naimattomuutta ja pysyvää hedelmättömyyttä.	n=37, ikä ka 25 +/- 5, koulutus 12 v, työssä 38%, opiskelijoita 51%, ihmissuhteessa 54%, seksuaalinen suuntautuneisuus kohti omaa biologista sukupuolta 100%	Lihaksensisäisesti testosteroniesteri 250 mg depot (30 mg testosteronipropionaatti, 60 mg testosteronifenyylipropionaatti, 60 mg testosteroni-isokaproaatti ja 100 mg testosteronidekanoaatti) 3–4 viikon välein, tai 1000 mg testosteroniundekanoaatti 12–14 viikon välein.	Yhden ryhmän ennen-jälkeen mittauksia ennen hoitoa ja 6 kk hormonihoidon aloituksen jälkeen. Ryhmän tuloksia verrattiin myös 40 vapaaehtoisen, koulutustason mukaan vakioidun naisen mittaustuloksiin.

Kehoahdistus (BUT)	Psykologinen kuormitus (SCL-.90)	Paino ja asenteet syömiseen (BMI ja EAT-40)	Tulosten tulkintaa
BUT-A ennen → 6 kk hormonihoidon aloituksen jälkeen • GSI 2,5 →2,0, p=0,002 (pienempi parempi), terveillä verrokeilla 0,6 • painofobia 2,8→2,3, NS • huoli kehonkuvasta 3,3→2,5, p=0,001 • välttely 2,1→1,6, NS • pakonomainen itsetarkkailu 1,6→1,3, NS • depersonalisaatio 2,3→1,7, p=0,002 Huoli eri ruumiinosiin liittyen (BUT-B) ei muuttunut tilastollisesti merkitsevästi 6 kk seurannassa.	SCL-pisteet ennen hoitoa→ 6 kk hormonihoidon aloituksen jälkeen, pienempi parempi, terveillä verrokeilla 38. • Yhteispisteet (GSI) 48→44, NS, • Herkkyys ihmissuhteissa 51→46, p=0,002 • Psykoottiset piirteet 50→45, p<0,001 Kaikki muut mittarin osa-aluepisteet (somatisaatio, pakko-oireisuus, masennus, ahdistuneisuus, vihamielisyys, foobisuus, paranoidisuus) pienenivät, mutta ero ei ollut tilastollisesti merkitsevä.	BMI suureni hormonihoidon aikana, p<0,001 Asenteet syömiseen (EAT-40) ennen hoitoa→ 6 kk hormonihoidon aloituksen jälkeen, skaala 0-120, pienempi parempi, pisteet >30 merkitsevät suurentunutta syömishäiriön riskiä: • 20 → 18, NS, • terveillä verrokeilla 19	Tutkijat eivät havainneet korrelaatioita iän, koulutustason, painon ja psykologisten oireiden välillä. Lähtötilanteessa kehoahdistus transsukupuolisilla vaikeampia kuin terveillä verrokeilla (kaikilla BUT-osa-alueilla paitsi painofobia), p<0,001.

26. Irwig ym. 2017, Yhdysvallat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transukupuolisia, FtM		Testosteronihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin vuosina 2013-2014 transsukupuolisia miehiä, jotka eivät aikaisemmin olleet käyttäneet testosteronihoitoa. Äänitestauksista henkilöt saivat rahallisen korvauksen.	n=7, ikä 18-39; 2 valkoista, 2 mustaa, 3 mix (oma ilmoitus); 1 tupakoi. Lähtötilanteessa perustaajuus oli 4/7:lla henkilöllä cis-naisen skaalan matalimmassa päässä ja 3/7 henkilöllä neutraali tai korkean cis-miesäänen mukainen.	Kaikki saivat tavanomaista, saman endokrinologin antamaa hoitoa 3 kk välein 12 kk ajan. Testosteroniesterit olivat ensisijainen hoitovaihtoehto: testosteronienantaatti tai –syprionaatti aloitusannoksella 50 mg joka toinen viikko ja annosta nostettiin tarvittaessa seurantamittausten perusteella tähdäten miesten keskimääräiseen testosteronitasoon. Potilaita ja/tai läheisiä ohjattiin lihaksensisäisen testosteronin käyttöön. Heitä kannustettiin käymään verinäytteessä n viikon kuluttua pistoksesta. Testosteronihoidon toteutumista seurattiin joka käynnillä seerumin testosteroni- ja estradioloimittauksin.12 kk kohdalla testosteroniannokset: aloitusannos (n=1), 50 mg kerran viikossa (n=1), 100 mg 2 viikon välein (n=4) tai 150 mg 2 viikon välein (n=1). Ei ääniterapiaa tai äänen käytön ohjausta. (Ilmeisesti jotkut olivat osallistuneet ääniterapiaan ennen tutkimusta.)	Yhden ryhmän äänen mittauksia kahdesti ennen hormonihoidon aloitusta sekä 3, 6, 9 ja 12 kk hormonihoidon aloituksen jälkeen. Äänimittaus sisälsi kolmesti toistetun, pitkän a-vokaalin ja standarditekstin nauhoituksen

Äänen korkeus (Hz ja ST)	Tulosten tulkintaa
ST on taajuuden arvo puolisävelinä. Yhdessä oktaavissa on 12 ST-yksikköä. Hertsit mitataan logaritmisesti ja äänen korkeus puolisävelien intervalleina. Esimerkiksi 50 Hz muutos matalassa miesäänessä vastaa noin 7 ST-yksikköä ja 50 Hz muutos korkeassa naisäänessä vastaa noin 4 ST-yksikön muutosta. ST-alenema, ka (vaihteluväli), verrattuna alkutilanteeseen ensimmäisen 3 → 6 → 9 → 12 kk jälkeen: 2,2 (0-6) →4,7 (2-10) →5,8 (2-10) →6,4 (2-10). Hz-alenema ka (vaihteluväli), verrattuna alkutilanteeseen ensimmäisen 3 → 6 → 9 → 12 kk jälkeen: 19 (2-52) →37 (17-78) →44 (15-74) →49 (17-79). 12 kk kohdalla äänen korkeus lukutestissä oli 87-128 Hz (F2-C3). Cis-miesten puhekorkeus on keskimäärin 100–130 Hz. Äänen korkeuden alenemaa pidetään kliinisesti merkittävänä 6 kk kohdalla kaikkien 7 henkilön kohdalla.	Ensimmäisen 3 kk aikana tulokset vaihtelivat paljon: toisilla ei tapahtunut äänen muutosta ja toisilla suurin äänen madallus tapahtui juuri tuolloin. Testosteronitaso alussa feminiininen ja seurannassa kohonnut, mikä viittaa hyvään kompliansiin.

27. Fisher ym. 2016, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GD (DSM-5)		Hormonihoito ja henkinen tuki	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yliopistoklinikasta GD-oireisiini apua hakeva yli 18-vuotias. Diagnoosi tehty usean käynnin jälkeen kahden eri GD-ammattilaisen toimesta. Hoitoaika 2008-2015 (54 hengen alaryhmä 2012-2015). Poissulkukriteerit: intersukupuolisuus, älyllinen kehitysvamma, lukutaidottomuus sukuelinkirurgia tehty. 394 henkilöä valittu poikkileikkaustutkimukseen, jossa verrattiin hormoneja käyttäneitä niihin, jotka eivät olleet käyttäneet hormoneja. Jälkimmäisten joukosta valittiin 60 muuntohoitoja haluavaa henkilöä testosteronihoitokokeeseen. 6 poistui seurannasta. Tiedot puuttuivat 11 potilaalta.	n= 26. Ikä ka noin 29.	Testosteroniundekanoaatti 1000 mg lihaksen sisäisenä injektiona, aluksi 0, 6 ja 12 viikon kohdalla ja sen jälkeen pistosväli määriteltiin yksilöllisesti hormonimittausten perusteella (10-14 viikkoa). Kaikki potilaat saivat standardoitua, ammattilaisen antamaa henkistä tukea 3 kk välein.	Yhden ryhmän ennen-jälkeen mittauksia ennen hoidon aloitusta sekä 3,6,12 ja 24 kk hormonihoidon aloituksen jälkeen.

Kehoahdistus (BUT) ja sukupuoliristiriita (GIDYQ-AA)	Psyykkinen kuormitus (SCL-90-R) ja masennus (BDI)	Karvan kasvu (Ferriman-Gallway)	Kehonpaino (BMI, vyötärön ympärys)	Tulosten tulkinta
Kehoahdistus: BUT kokonaispisteet (GSI) ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Pienempi parempi. • FtM 2,3→1,9→1,8→1,7→1,6, p<0,05 Sukupuoliristiriita: GIDYQ-AA kokonaispisteet ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Isompi parempi. • Kokonaispisteet: noin (pisteet luettu kuviosta) 2,2→2,3 (p<0,05)→2,1→2,1→2,1 (p<0,05) • Subjektiivinen osio: merkitsevä nousu jo 3 kk ja vielä 6 kk kohdalla, sen jälkeen laskua.	Psyykkinen kuormittunen: SCL-90-R kokonaispisteet (GSI) ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Pienempi parempi. Suomen väestötason GSI arvo 0,65. • FtM 0,57→0,59→0,46→0,40→0,35, p<0,05 Masennus: BDI-II ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. Pienempi parempi. 1-9-= ei masennusta, 10-18 = lievä masennus. • FtM 9,2→7,5→5,6→4,5→4,4, p<0,05	Ferriman-Gallway ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen, skaala 0-36, pienempi vähemmän. Alle 8= normaali, 8-15 on lievää ja yli 15 on kohtalaista tai voimakasta hirsutismia (karvan kasvu). • FtM 4→7→14→18→25, p<0,001	BMI ennen hoitoa →3→6→12→24 kk hoidon aloituksen jälkeen. • FtM 24,9→25,6→25,8→25,6 →27,7 p<0,01 Vyötärön ympärys • FtM 100→91→90→90→98 p<0,01	Kehoahdistus, sukupuoliristiriita ja psyykkinen kuormittuneisuus vähenivät 2 vuoden hormonihoidon aikana. Painoindeksi suureni 1-2 yksikköä, kiloja tuli lisää transmiehillä keskimäärin 10 kg.

mutta 2 v kohdalla pisteet vielä korkeammat, p<0,01. • Sosiaalinen ja sosio-laillinen osio: kummassakin laskeva trendi (p<0,01). • Sukupuoliristiriita siis lievittyi ensin, mutta vaikeutui myöhemmin.				

Fisher AD, Castellini G, Ristori J, Casale H, Cassioli E, Sensi C, et al. Cross-Sex Hormone Treatment and Psychobiological Changes in Transsexual Persons: Two-Year Follow-Up Data. J Clin Endocrinol Metab 2016 Nov;101(11):4260-4269.

28. Manieri ym. 2014, Italia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID (DSM-IV)		Hormonihoito ja psykodynaaminen psykoterapia kerran viikossa.	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
GID-diagnoosin teki mielenterveysammattilaisten tiimi ka 8 kk aikana, haastattelujen, psykoseksologisen arvioinnin (omakuva, ruumiinkuva, seksuaalinen suuntautuneisuus, merkittävä psykopatologia) ja persoonallisuustestien perusteella. Kriteereinä: aikuisikä, pysyvä GD, kykenevä tietoiseen päätökseen, lääketieteelliset ja psykologiset/psykiatriset oheissairaudet hoidolla hallinnassa. Tosielämän jakso toimii diagnostisena apuna: kerran viikossa psykoterapia, jossa arvioidaan psykologista ja ihmissuhteissa tapahtuvaa toimintakyvyn kehitystä. Pois suljettu: vakava psykopatologia, mm. psykoottiset häiriöt, päihteiden väärinkäyttö, henkinen kehitysvamma, dementia, MtF-henkilöillä synnynnäinen laskimotukosriski.	FtM (n= 27): ikä ka 30 (+/- 8), BMI >30 22%:lla, metabolinen syndrooma 4 %:lla, tupakoivia 41%, heteroseksuaaleja 100%. 2:lla polykystiset ovariot. Ei lisääntynyttä lisämunuaisen androgeenieritystä.	Aluksi transdermaalinen testosteroni 25 mg/pv tai lihaksensisäisesti 100 mg 10-15 pv välein. Sitten lihaksensisäisesti testosteroniundekanoaatti 1000 mg 3-4 kk välein. Ruokavalio-ohjausta ja glukoosi/kolesterolilääkityksiä tarvittaessa. Kaikille lisäksi: Arviointijakso (RLE), jossa henkilöt elävät uutta kehoaan. Psykodynaaminen psykoterapia kerran viikossa. Hormonimittaukset 3 kk välein, mammografia 8-12 kk kohdalla.	Yhden ryhmän ennen-jälkeen mittauksia ennen hoitojen alkua ja noin 1 vuosi hormonihoidon aloituksen jälkeen.

Elämänlaatu (WHOQOL-100)	Psykososiaalinen toimintakyky	Kehon muutokset	Metaboliset muutokset	Tulosten tulkintaa
WHOQOL-pisteet alussa → 12 kk hormonihoidon aloituksen jälkeen. Skaala 0-100, isompi parempi, pisteet >50 viittaavat hyvään elämänlaatuun. • Elämänlaatu 63 → 69, NS • Kehon kuva 22 → 63, p<0,05 • Sukupuolielämän laatu 50→ 56, NS. • Ihmissuhteiden toimivuus 50→ 81, p<0,05.	85% koki impulsiivisuuden ja aggressiivisuuden lisääntyneen 12 kk hormonihoidon aloituksen jälkeen.	Paino (kg) alussa → 12 kk hormonihoidon aloituksen jälkeen 65→ 68, NS Lihasmassa ja akne lisääntyivät jo ensimmäisinä kuukausina, parran kasvu vasta 6 kk kohdalla. Kuukautiset loppuivat ensimmäisen 3 kk aikana 88%:lla.	Ei merkitseviä muutoksia lipideissä ja verensokeriarvoissa. Tupakointi väheni.	Transmiehillä elämänlaatupisteet kohenivat, mutta vähemmän kuin transnaisilla.

29. Wierckx ym. 2014, Belgia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolinen (DSM-IIIR ja DSM-IV, 302.85), FtM		Testosteronihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin 20 yliopistoklinikan tutkimukseen tullutta valkoista transmiestä, joita ei ollut vielä hoidettu hormonein tai leikkauksin.	n=20, FtM, ikä ka 27, BMI 23,7, tupakoivia 25%	Kaikille im. testosteroniundekanoaatti 1000 mg 3 kk välein. Seurantakäynnit 3 kk välein 12 kk ajan.	Yhden ryhmän mittauksia ennen hormonihoidon aloitusta sekä 6 ja 12 kk sen jälkeen. Tutkijat raportoivat tuloksia myös toisesta poikkileikkauskohortista ja niihin viitataan tulosten tulkintaosiossa.

Karvan kasvu (Ferriman ja Gallwey)	Akne (GAGS)	Tulosten tulkintaa
F&G-pisteet alussa → 12 kk hormonihoidon jälkeen 0,5 → 12 (vaihteluväli 2-25). F&G-pisteet olivat yli 8 (joka tarkoittaa naisilla hirsutismia) 6 kk kohdalla 54%:lla ja	Akne kasvoissa (osuus henkilöistä) alussa → 6kk →12kk testosteronihoidon aloituksen jälkeen 35%→82%→55% Akne selässä ja/tai rinnassa (osuus henkilöistä) alussa → 6kk →12kk testosteronihoidon aloituksen jälkeen 15%→88%→50%.	Seerumin testosteronitasot eivät korreloineet iho-ja karvamuutosten kanssa. Testosteronihoito lisäsi kasvojen ja vartalon karvan kasvua kaikilla henkilöillä 12 kk aikana. Tutkijoiden mukaan karvan kasvu voi vielä lisääntyä sen jälkeenkin. Enin osa akne-muutoksista ilmaantui ensimmäisen 6-9 kk aikana ja vähenivät 12 kk jälkeen, mikä voi johtua hoidoista.

12 kk kohdalla 80%:lla. Yhdelle henkilölle kehittyi lievä ohimoiden ja otsan (androgeenityyppinen) kaljuuntuminen.	Suurimmalla osalla aknemuutokset olivat lieviä, 20%:lla kohtalaisia, vaikeita ei ollut ollenkaan. Ensimmäisen vuoden aikana 50% käytti iholle annosteltavia aknelääkkeitä ja 3/20 turvautui antibioottiin aknen hoitamiseksi.	Pidemmässä seurannassa aknemuutokset eivät lisääntyneet eikä aknearpia kehittynyt kovinkaan monille. Myös miestyyppisen kaljuuntumisen riski kasvoi tutkijoiden toisessa seurantatutkimuksessa, joissa testosteronihoidon kesto oli yli 10 vuotta.

Wierckx K, Van de Peer F, Verhaeghe E, Dedecker D, Van Caenegem E, Toye K, et al. Short- and Long-Term Clinical Skin Effects of Testosterone Treatment in Trans Men. Journal of Sexual Medicine 2014;11(1):222-229.

30. Slabbekoorn ym. 2001, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolinen		Hormonihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yliopistosairaalan sukupuoliyksikön potilaita, kaikki soveltuvia sukupuolen uudelleen määrittelyyn. Diagnoosin vahvisti psykologi ja psykiatri,	FtM: n=47, ikä ka. 26 (16-44) v.	Testosteroniesteri lihaksensisäisesti 250 mg 2 viikon välein (Sustanon), n=42 TAI Testosteroniundekanoaatti suun kautta 200 mg/pv (Andriol).	Yhden ryhmän ennen-jälkeen mittauksia. 5 kyselyä tehtiin ennen hoidon aloitusta ja 14 viikon kohdalla hoidon aloituksen jälkeen tai testosteroniesterin käyttäjillä 6 pv viimeisen injektion jälkeen. Kuusi im testosteroniestereitä käyttävää henkilöä osallistui lisäksi tiheämpiin mittauksiin kahden viikon sykleissä nopeasti muuttuvan testosteronitason mukaisesti. Heitä pyydettiin täyttämään päiväkirjaa 11 viikon ajan alkaen, 5 kertaa, 2 viikon välein, alkaen 1 vko ennen hoitoa.

Tunteisiin reagoinnin voimakkuus (tunteellisuus) (AIM) ennen hormonihoitoa →14 viikon kohdalla hoidon alusta	Vihaisuus (ASQ) ennen hormonihoitoa →14 viikon kohdalla hoidon alusta	Ei-verbaalinen ilmaisu (ACT)	Mieliala ja hyvinvointi (päiväkirja transmiehillä).	Tulosten tulkintaa

AIM kokonaispisteet (skaala 40-240) 144 → 141, p<0,001 Transmiesten tunteellisuus väheni. AIM positiiviset tunteet (skaala 28-168) 103 → 101, p<0,05 Transmiesten postiivisten tunteiden kokemisen voimakkuus väheni AIM negatiiviset tunteet (skaala 12-72) 41 → 39, NS Ei muutosta	Vihaisuuden voimakkuus (Suuremmat pisteet viittaavaat voimakkaampaan vihaisuuteen): FtM: 3,4 → 3,5, NS Negatiivisten tunteiden voimakkuus: FtM: 2,1 → 2,2, NS Aggressiivinen käyttäytyminen (ASQ anger readiness) 59 → 62, p<0,05 Molemmilla identiteettiryhmillä aggressiivinen käyttäytyminen lisääntyi. Ryhmien välillä ei tilastollisesti merkitsevää eroa.	ACT ennen hormonihoitoa →14 viikon kohdalla hoidon alusta. Skaala 13-117, suuremmat pisteet merkitsevät enemmän ei-verbaalista tunteiden ilmaisua. 61 → 61, NS	Mielialan vaihtelut: ei muutoksia eri mittausajankohdissa. Ärtyneisyys ja impulsiivisuus: ei muutoksia eri mittausajankohdissa. Hyvinvointi: ei muutoksia eri mittausajankohdissa. Vetäytyminen ja väsyneisyys: ei muutoksia eri mittausajankohdissa.	Ennakoituja muutoksia tunteellisuudessa ja tunteiden ilmaisussa. Negatiivisten tunteiden kokemisessa ei muutoksia, mutta aggressiivisen käyttäytymisen pisteissä nousua. Seuranta-aika lyhyt, 3,5 kk.

31. Giltay ja Gooren 2000, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GID		Hormonihoito	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Ei kuvattu	n=17, 14/17 valkoihoisia, ikä md 25 (18-37) v., BMI 24; 16/17 säännöllinen kuukautiskierto	Testosteroniesteri 250 mg 2 viikon välein lihaksensiäisesti (Sustanon)	Yhden ryhmän ennen-jälkeen mittauksia ennen hoitoa ja 4, 8 ja 12 kk kuluttua hoidon aloituksesta.

Karvan kasvu	Paino	Akne	Tulosten tulkintaa: mm.
Ferriman-Gallway 0-36 0→4 →8 →12 kk kohdalla, hormoniriippuvaisten alueiden yhteispisteet	BMI 0→4 →8 →12 kk kohdalla 23,9 →25,2→24,7→24,7, p=0,009	Leeds, 0-10, 0→4 →8 →12 kk kohdalla, 1:ä suuremmat merkitsevät kliinistä akneta. Kasvot 0,0→0,1→0,1→0,1, p=0,005 Selkä 0,0→0,1→0,5→0,25, p=0,003	Painoindeksi nousi noin yhden yksikön, karvan kasvu muuttui toivottuun suuntaan, transmiehillä ilmaantui lievää aknea.

9x4=36. 0 on ei karvaa, >7 tulkitaan hirsutismiksi. 2 →11→13→16, p<0,001			3 henkilöä oli käyttänyt hormoneja ennen tutkimusta (2 FtM ehkäisytabletteja ja 1 MtF etinyyliestradiolia useita tabletteja). Muut eivät olleet käyttäneet hormoneja 3 vuoteen, mikä vahvistui myös laboratoriokokeilla.

Rintakirurgia

Transnaiset (MtF)

32. Weigert ym. 2013, Ranska

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: MtF transsukupuoliset		Rintojen suurennusleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Potilaiksi kutsuttiin kaikki peräkkäiset yli 18-vuotiaat saman kirurgin MtF transsukupuoliset, joilta saatiin tietoinen ja informoitu suostumus rintaleikkaukseen ja hoidettiin 2008-2012. Kaikille tehty sukuelinleikkaus (ka 16kk ennen rintaleikkausta) ja kaikki saaneet vähintään 12 kk ajan estrogeenihormonihoitoa (etinyyliestradiolia), ei aiempaa rintaleikkausta. Kaikki leikkaukset suoritettiin saman kirurgin tekemänä ajalla 7/2008-7/2012. Kaikki leikkaukset oli hyväksytty korvattaviksi julkisella sairasvakuutuksella.	n=35, kaikki MtF-transsukupuolisia. Ikä ka 42v. (19–63v.), pituus ka 174 cm, paino 69 kg, BMI 22,7 kg/m2. Rintojen leveys 13,1 cm, etäisyys kaulaloven ja nännin välissä 21,6 cm. Sosioammatillinen asema: yrittäjä 34%, työntekijä 29%, eläkeläinen 11%, työtön/opiskelija/muu 26%. Aktiivinen tupakoija 34%.	Rintojen anatomiset silikoni implantit, leikkausta ei kuvattu tarkemmin. Hormonihoidon kesto ka 4,9 v. Sukuelinleikkauksesta kulunut aika ka 16 kk.	Yhden ryhmän ennen-jälkeen mittauksia kyselyin 3kk ennen rintaleikkausta (n=35), 4kk sen jälkeen (n=35) ja yli 12kk sen jälkeen (n=21). Potilas- ja hoitotiedot järjestelmästä ennen ja jälkeen leikkauksen. Kyselyn tuloksia verrattiin eri ajankohdissa.

Elämänlaatu ja tyytyväisyys rintaleikkauksen jälkeen (BREAST-Q)*	Komplikaatiot	Tulosten tulkintaa
BREAST-Q pisteet (md) ennen leikkausta → 4kk leikkauksen jälkeen → yli 12kk leikkauksen jälkeen, skaala 0–100, isompi parempi. Tyytyväisyys rintoihin (md): 19 → 77 → 68	Kenelläkään ei merkittäviä komplikaatioita (infektio	Rintojen suurennusleikkaus paransi potilaiden hyvinvointia tilastollisesti merkittävästi jo 4kk leikkauksen jälkeen, ja se pysyi korkealla myös yli 12kk sen jälkeen.

Tyytyväisyyden muutos (pistettä): 0⟶ +59 ⟶ +47 (p<0.0001) Psykososiaalinen hyvinvointi (md): 36 ⟶ 85 ⟶ 76 Hyvinvoinnin muutos (pistettä): 0⟶ +48 ⟶ +37 (p<0.0001) Seksuaalinen hyvinvointi (md): 29 ⟶ 72 ⟶ 72 Hyvinvoinnin muutos (pistettä): 0 ⟶ +34 ⟶ +33 (p<0.0001) Fyysinen hyvinvointi (md): 100 ⟶ 79 ⟶ 79 Hyvinvoinnin muutos (pistettä): 0 ⟶ -10 ⟶ -6 (NS) Tyytyväisyys rintoihin, psykososiaalinen ja seksuaalinen hyvinvointi paranivat tilastollisesti merkitsevästi 4kk leikkauksen jälkeen. Yli 12kk leikkauksen jälkeen ne eivät enää kasvaneet, mutta pysyivät korkealla tasolla. HUOM. 12kk seurannassa osallistujajoukko pieneni (35 ⟶ 21). Keskimääräistä pienempien ja suurempien implanttien saajilla ei tilastollisesti merkittävää eroa tuloksissa, lukuun ottamatta seksuaalista hyvinvointia 4kk leikkauksen jälkeen (pienempirintaiset olivat tyytyväisempiä kuin suurempirintaiset, p<0.0001).	0%, hematooma 0%, kapseloituminen 0%)	Rajoituksia: • Iso osa potilaista tippui pois viimeisessä seurannassa (14 35:stä eli 40%). Pois pudonneiden tyytyväisyys oli kuitenkin parantunut 1. seurannassa, mikä tukee tulosten tulkintaa. • Seksuaaliseen hyvinvointiin saattanut vaikuttaa myös edeltävä sukuelinleikkaus. • Kaikille asetettiin anatomiset implantit, joten ei mahdollisuutta vertailla eri implantteja tai tekniikoita.

NS = non-significant, ei tilastollisesti merkitsevä, n = lukumäärä, MF = male-to-female, md = mediaani

* Raportoitu kahden merkitsevän numeron tarkkuudella

Transmiehet (FtM)

33. Agarwal ym. 2018, Yhdysvallat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: GD (DSM-5), FtM transsukupuoliset		Rinnanpoistoleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Kaikki yli 18v. halukkaat leikkaukseen tulijat, ei poissulkukriteerejä. Leikkauskriteerit WPATH:n hoitostandardien mukaan	n=42, ikä ka 28v (18–50); BMI ka=28 (vaihteluväli 17-41) Ihonväri: valkoinen 88%, afroamerikkalainen 2%, aasialainen 2%; etnisyys: latino 12%, muu 88% Seksuaalinen suuntautuminen: hetero 40%, biseksuaali 10%, homo 12%, lesbo 2%, muu 37%. Parisuhdestatus: naimaton (83%), naimisissa (10%), eronnut (5%), leski (2%).	Rinnanpoistoleikkaus. Tekniikat: *double incision technique with free nipple grafts* (90%) ja *periareolar technique* (10%). Leikkaukset suoritti sama kirurgi. Kaikki käyneet läpi mielenterveysneuvonnan, ja 93%	Yhden ryhmän ennen-jälkeen mittauksia: itse täytetty kysely 1-2vk ennen leikkausta ja 6kk leikkauksen jälkeen.

(versio 7). Leikkaukset tehty 4/2015-6/2016.	Koulutusaste: lukio kesken 5%, lukiotutkinto 12%, yliopisto kesken 51%, yliopistotutkinto 17%, jatko-opiskelija 14%. Työmarkkinatilanne: työssäkäyvä (55%), opiskelija (12%) Tulotaso: 0-19k USD (33%), 20-39k USD (33%), >80k USD (9%). Mielenterveys: ei diagnoosia (50%), ahdistus (14%), ahdistus ja masennus (26%), masennus (5%), muu (5%).	saanut hormonihoitoa. Ei aiempia leikkauksia.	

Elämänlaatu ja tyytyväisyys rintaleikkauksen jälkeen (Breast-Q)	Kehoahdistus (BUT-A) * (ennen leikkausta → leikkauksen jälkeen)	Komplikaatiot	Tulosten tulkintaa
BREAST-Q ennen ja → jälkeen leikkauksen, skaala 0–100, isompi parempi). Rintoihin tyytyväisyys: 17 → 85 Psykososiaalinen hyvinvointi: 31 → 79 Seksuaalinen tyytyväisyys: 31 → 71 Fyysinen hyvinvointi: 65 → 80 (kaikissa p < 0,0001) Kaikki osa-alueet paranivat tilastollisesti merkitsevästi leikkauksen jälkeen. Ei tilastollisesti merkittävää korrelaatiota kyselytulosten ja taustamuuttujien (ikä, sukupuoli-identiteetti, seksuaalinen suuntautuminen ym.) välillä.	Kehoahdistus BUT-A ennen leikkausta → leikkauksen jälkeen, skaala 0–5, pienempi parempi. - Yhteispisteet (GSI): 2.7 → 1.2, p<0.0001 Huoli kehonkuvasta: 3.5 → 1.3 Välttelevä käytös: 2.5 → 0.7 Pakonomainen itsetarkkailu: 1.6 → 1.3 Depersonalisaatio: 2.4 → 0.8 (kaikissa p<0.0001). Kaikki osa-alueet ja yhteispisteet vähenivät leikkauksen jälkeen tilastollisesti merkitsevästi. Korrelaatio mielenterveysongelmien ja yhteispisteiden (GSI) välillä: mitä heikompi mielenterveys potilaalla oli, sitä suurempi kehoahdistus oli ennen leikkausta ja sitä enemmän se parani leikkauksen jälkeen.	- Uusintaleikkaus 5% - Serooma 7% - Hematooma 5% Ei tilastollisesti merkitsevää yhteyttä komplikaatioasteen ja leikkaustekniikan tai muiden taustamuuttujien välillä.	Rintojen poisto paransi tilastollisesti merkittävästi tutkittavien elämänlaatua ja toimintakykyä ja vähensi kehoahdistusta. Tulokset samansuuntaisia aiempien tutkimusten kanssa. Mastektomia paransi etenkin mielenterveysongelmista kärsivien potilaiden elämänlaatua ja kehotyytyväisyyttä. Ei tietoa korrelaation suunnasta: aiheuttiko kehoahdistus ennen leikkausta mielenterveysongelmia vai toisin päin. Rajoitteita: pieni kohortti, pieni etninen diversiteetti, mahdollinen vinouma (vastasivatko tyytyväiset kyselyyn enemmän). Mittarit oli kehitetty muille potilasryhmille, ja eri tutkimukset käyttäneet eri mittareita. Jatkossa kehitettävä erityisiä mittareita transsukupuolisten tutkimiseen.

WPATH = the World Professional Association for Transgender Health, GD = gender dysphoria, k = ”kilo”, tuhat (20k = 20 000), ka=keskiarvo, NS = non-significant, n= lukumäärä, FM = female-to-male

Sukuelinkirurgia

Transsukupuoliset (MtF ja FtM)

34. Smith ym. 2001, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transseksuaalisuus			
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
20 peräkkäistä yliopistoklinikalla sukuelinkirurgisen muunnosleikkauksen läpikäynyttä henkilöä sekä 21 henkilöä (joista 7:llä tiedot riittämättömiä), joilta sukupuolen muuntoprosessiin pääsy evättiin tai jotka vetivät hakemuksensa pois. Leikkauksesta tuli olla kulunut ainakin vuosi. Seurantakyselyt tehty 1995-1999 ja leikkaukset oli tehty 1-4 vuotta aikaisemmin.	Leikatut: n=20, MtF 7, FtM 13; Lähtötilanteessa ikä (ka) 17 v, (15–19), älykkyysosamäärä ka 107 (85-140). 10 oli aloittanut hormonihoidon 16-18-vuotiaana. Seurantahaastattelun ajankohtana (ka 1,3 v leikkauksen jälkeen) ikä oli ka 21 v. (19-23), opiskelijoita 9, töissä 5, työtön 5. Asui yksin 10, partnerin kanssa 1 ja vanhempien kanssa 8. Ei-leikatut: n=14, miehiä 9, naisia 5. Lähtötilanteessa ikä (ka) 17 v (14–20), älykkyysosamäärä ka 104 (89-130). Seurantahaastattelun ajankohtana ikä oli ka 22 (16-26). Asui yksin 6, partnerin kanssa 1 ja vanhempien kanssa 7, yksi psykiatrisessa laitoksessa.	Sukupuolen muuntoleikkaus. • MtF: vaginoplastia yleisin • FtM: Rintojen poisto yleisin leikkaus. 1 falloplastia ja 2 neoskrotum-leikkausta	Kahden ryhmän (leikattujen ja ei-leikattujen) ennen-jälkeen mittauksia, Leikatuilla ensimmäinen kysely tehty sukupuolen muuntoprosessiin hakuvaiheessa ja toinen keskimäärin 1,3 (1–4) v viimeisen leikkauksen jälkeen. Ei-leikatuilla kyselyt tehty sukupuolen muuntoprosessiin hakuvaiheessa ja kielteisen päätöksen jälkeisen seurantavaiheen lopussa, ka 4,2 v (1–7) kuluttua alkumittauksesta. Tutkijoiden mukaan ryhmiä verrattu keskenään, mutta ainoastaan sukupuoliristiriitaa kuvaavien UGDS-pisteiden osalta on raportoitu ryhmien välinen ero muutoksessa. Mittaustuloksia on verrattu myös hollantilaisen väestön tuloksiin. Tiedot on kerätty osittain takautuvasti.

Sukupuoliristiriita (UGDS) ja kehoahdistus (BIS)	Psykologinen kuormitus (SCL-90R)	Persoonallisuuspiirteet (NVM)	Tyytyväisyys hoitotulokseen	Tulosten tulkintaa
Mittausten ajankohdat: Leikatuilla ennen leikkausta → ka 1,3 v sen jälkeen. Ei-leikatuilla leikkaukseen haettaessa → ka 4,2 v sen jälkeen				
Sukupuoliristiriita:UGDS-pisteet, skaala 12-60, pienempi parempi. • Leikatut 56→14, p<0,001, • Ei-leikatut 47→31, p=0,002	SCL-pisteet alaryhmittäin, pienempi parempi. Alaviitteissä tieto siitä miten paljon tulos poikkeaa hollantilaisesta väestöstä. Psykoneuroottisuus: • Leikatut: 145[4]→129[3], NS	NVM-pisteet alaryhmittäin. Korkeammat pisteet merkitsevät vahvempaa persoonallisuuspiirrettä. Alaviitteissä tieto siitä miten paljon tulos poikkeaa hollantilaisesta väestöstä:	Leikatut: Kukaan ei katunut kirurgiaa. 16/20 oli tyytyväisiä tai hyvin tyytyväisiä leikkaukseen, yksi oli hyvin tyytymätön ja kaksi suhtautui neutraalisti asiaan. Tyytyväisiä - rintojen poistoon 8/13	Tyytyväisyys omaan kehoon lisääntyi leikatuilla selvästi. Myös ei-leikatuilla keskimääräinen kehoahdistus lieveni jonkun verran neljän vuoden seurannassa ja tyytyväisyys sukuelimiin ja rintoihin lisääntyi merkitsevästi. Toisaalta ei-leikattujen joukossa melkein

Sukupuoliristiriita pieneni leikatuilla enemmän kuin ei-leikatuilla, p=0,002 Kehoahdistus BIS, pienempi parempi. Tyytyväisyys ensisijaisiin ominaisuuksiin (esim. rinnat, sukuelimet),: • Leikatut 18→10, p<0,001 • Ei-leikatut 16→13, p=0,04 Tyytyväisyys toissijaisiin ominaisuuksiin (esim. lantio, karvoitus) • Leikatut 32→25, p=0,001 • Ei-leikatut 30→28, NS	• Ei-leikatut: 159[4]→163[4*], NS Ahdistuneisuus: • Leikatut: 16[4]→13[3], NS • Ei-leikatut: 20[4]→18[4], NS Agorafobia: • Leikatut: 9[4]→8[4], NS • Ei-leikatut: 9[4]→9[4], NS Masennus: • Leikatut: 28[4]→22[3], p<0,05 • Ei-leikatut: 32[4]→35[5], NS Somatisaatio: • Leikatut: 16[3]→15[2], NS • Ei-leikatut: 20[4]→18[3], NS	Taipumus kokea negatiivisia tunteita, kuten ahdistusta ja huolta. • Leikatut: 22[2]→21[2], NS • Ei-leikatut:23[2]→26[4], NS Taipumus kokea lääketieteellisesti selittämättömiä somaattisia oireita (somatisaatio): • Leikatut: 8[2]→8[2], NS • Ei-leikatut: 8[2]→10[4], NS Taipumus kokea hermostuneisuutta ihmissuhteissa ja hämmentyy helposti (ujous): • Leikatut: 13[2]→12[2], NS • Ei-leikatut: 12[2]→12[2], NS Psykopatologisuus: • Leikatut: 3[2]→3[2], NS • Ei-leikatut: 6[4]→6[4], NS Taipumus kokea positiivisia tunteita sosiaalisissa tilanteissa (ekstroversio): • Leikatut: 17[2]→17[2], NS • Ei-leikatut: 16[1]→15[1], NS	- vaginoplastiaan 3/7 - seksielämään 7/10 (vakituinen partneri) Orgasmikyky tallella 11/16 Sosiaaliset suhteet: - kaikki lähipiirissä hyväksyneet ja tukeneet uudessa sukupuolessa 16/20 - ei yksinäisyyttä 15/20 Ei-leikatut: 11/14 ei enää harmitellut sitä, että leikkausta ei tehty. 3 harmitteli jonkun verran: 1 nainen 2 miestä. Sosiaaliset suhteet: -12/14 (hyvin) tyytyväisiä sosiaalisiin suhteisiin vastakkaisen ja 9/14 saman sukupuolisten kanssa - ei yksinäisyyttä 6/14	puolet oli seurannan lopussa edelleen hyvin tyytymätön kehonkuvaansa. Psykologinen kuormitus näyttää olevan sekä leikatuilla, että ei-leikatuilla korkeammalla tasolla kuin hollantilaisväestössä keskimäärin. Negatiivisia persoonallisuuspiirteitä kuvaavat NVM-pisteet olivat leikatuilla saman tasoisia kuin hollantilaisessa väestössä keskimäärin. Ei-leikatuilla pisteet olivat suurempia tai ylärajoilla väestön pisteiden kanssa.

[1]=alle keskiarvon, [2]=keskiarvoinen, [3]=yli keskiarvon, [4]=korkea, [5]= hyvin korkea verrattuna väestöarvoihin; *p<0,05

Transnaiset (MtF)

Vaginoplastia

35. da Silva ym. 2016, Brasilia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisuus (ICD-10) tai GID (DSM-IV), MtF		Vaginoplastia	

Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
5/2000–8/2006 klinikassa tutkitut yli 16-vuotiaat transnaiset (n=190). Diagnoosin teki klinikan moniammatillinen tiimi. 160 kävi läpi hormonihoidot ja leikkauksen. Näistä 47 täytti kyselyt ennen ja jälkeen hoitojen. Klinikan sukupuolen muuntoleikkaukseen pääsyn kriteerit: ≥2 vuoden moniammatillinen seuranta, ikä ≥21 v. (liittovaltiotason vaatimus). Poissulkukriteeri: mielenterveyden häiriö psykiatrin tai psykologin toteamana, kehitysvamma tai päihteiden väärinkäyttö.	n=47, ikä ka 31 (16–54) v. Parisuhteessa 11 %, yliopistotutkinto 15%:lla, yli 8 vuoden koulutus 49%:lla. HIV-positiivisia 15%, sukupuolitauti 11%:lla.	Klassinen inversiovaginoplastia, jotka teki yksi kokenut kirurgi. Lisäksi osalle potilaista lisäleikkauksia: uretroplastia virtsaputken sulkijan ahtauman korjaamiseksi (n=9) ja neovaginan uusintaleikkaus genitaalialueen ulkopuolisin ihosiirtein (n=6). Kaikki osallistuivat vähintään 2 vuotta supportiiviseen ryhmämuotoiseen psykoterapiaan, 1 tunti 1-2 viikon välein.	Yhden ryhmän ennen-jälkeen mittauksia klinikkaan tulon yhteydessä ja vähintään 12 kk leikkauksen jälkeen.

Elämänlaatu (WHOQOL, the Brazilian version)	Tulosten tulkintaa
Verrattuna lähtötasoon, elämänlaadun kahdella ulottuvuudella, psykologisella ja sosiaalisella, tapahtui merkitsevää parannusta leikkauksen jälkeen. Fyysinen terveys ja itsenäisyys sen sijaan heikentyivät merkitsevästi. Ympäristöön, hengellisyyteen, uskontoon ja uskomuksiin liittyvässä elämänlaadussa ei tapahtunut merkitseviä muutoksia. Ulottuvuuksien alakysymyksistä seksuaalinen aktiivisuus, vapaus, fyysinen turvallisuus sekä sosiaali- ja terveydenhuollon saatavuus ja laatu kohenivat leikkausten jälkeen. Sen sijaan energisyys, uni ja lepo, liikkuvuus, jokapäiväisistä toiminnoista selviytyminen ja fyysinen ympäristö heikkenivät ja negatiiviset tuntemukset lisääntyivät vastaavana aikana.	Tulosten raportointi niukkaa. Elämänlaatumittarin lähtöarvoja ei ilmoitettu, vaan pelkästään ajankohtien ero. Iän raportoinnissa epäselvyyksiä: Klinikan leikkauskriteereissä vaadittiin 21-vuoden ikää, mutta tutkimukseen otettiin myös 16-vuotiaita.

36. Mate-Kole ym. 1990, Britannia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisuus 302.5 (ICD-9), MtF			
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Psykiatri kävi läpi klinikkaan tulevat lähetteet käyttäen standardoitua formaattia, joka kattoi potilaan ja hänen perheensä lääketieteelliset ja psykiatriset taustatiedot sekä potilaan kehitysasteen, koulutuksen, työstatuksen, sosiaaliset ja seksuaaliset suhteet ja transsukupuolisuuden alun ja etenemisen. Leikkauskelpoisuuden arvioinnissa käytettiin IGDA-kriteerejä: diagnoosi varmistettu psykiatrisella arvioinnilla ja ≥6 kk:n hoidolla, ei psykoosia, yli 2v kestänyt vakaa tahto vaihtaa sukupuolta ja potilas osoittanut kykenevänsä elämään > 1v naisen roolissa. Leikkauskelpoisista potilaista 40 suostui	n=40, kaikki transnaisia (MtF), ikä ka=33 (21-53); melkein kaikki kävivät töissä. Alkutilanteessa leikkausryhmä/jonotusryhmä (%) • 1. asteen sukulaisilla psykiatrisia sairauksia: n=20% / 30% • Lapsuudessa neuroottisia piirteitä: 35% / 45%;	Vaginoplastia: siittimen ja kivesten poisto ja neovaginan rakentaminen yhdellä leikkauksella. Ennen leikkauksia ja niiden jälkeen psykiatrinen seuranta.	Kontrolloitu hoitokoe. Ryhmiin jako perustuu joka toisen henkilön valintaan listalta. Kummankin ryhmän tuloksia verrattiin seurannan alussa ja kaksi vuotta leikkauksen jälkeen. Lisäksi jonkun verran

sukupuolenvaihdosleikkaukseen, johon normaalikäytännön mukaan kuului 1-2 vuoden odottelu. 40 hengen listalta joka toiselle tarjottiin mahdollisuutta päästä leikkaukseen heti. Interventioryhmä (n=20) sai leikkaushoidon heti (3 kk sisällä jonoon pääsystä), jonotusryhmän jäsenet (n=20) jäivät leikkausjonoon (tavanomainen hoitokäytäntö).	• Saaneet psykiatrista hoitoa muuhun kuin sukupuoleen liittyviin ongelmiin: 30% / 25% • Itsemurhayrityksiä: 5% / 10%		ryhmien tulosten keskinäistä vertailua.

Psykoneuroottinen oireilu (CCEI)	Feminiiniset ja maskuliiniset persoonallisuuspiirteet (BSRI)	Sosiaalinen, seksuaalinen ja työelämään liittyvä aktiivisuus	Tulosten tulkintaa
Vapaa ahdistus, foobisuus, pakkoneuroottisuus, ahdistuksen somatisointitaipumus, masentuneisuus, hysteerisyys: lähtötasoissa ei ollut merkitsevää eroa ryhmien välillä millään osa-alueella. 2 v kohdalla leikatuilla oireilu oli vähentynyt kaikilla osa-alueilla ja jonossa olevilla lisääntynyt kaikilla osa-alueilla. Ero ryhmien välillä oli merkitsevä kaikilla osa-alueilla, tosin ahdistuksen kohdalla p oli raja-arvoinen 0,05.	Itse arvioituna, feminiinisisiä tai maskuliinisia persoonallisuuden piirteitä kuvaavissa testituloksissa ei ollut lähtötasossa eroa ryhmien välillä. Lähtötason ja 2v. kohdalla mitattujen tulosten välillä ei ollut merkitsevää eroa kummassakaan ryhmässä vaikkakin interventioryhmässä maskuliinisuuspisteissä muutoksen suunta oli nouseva.	Verrattuna lähtötasoon interventioryhmän jäsenet kokivat olevansa kahden vuoden kohdalla merkitsevästi aktiivisempia sosiaalisesti ja seksuaalisesti, verrokkiryhmä ei. Ryhmien välillä oli myös merkitsevä ero interventioryhmän hyväksi ryhmässä tai yksin harrastetussa liikunnassa, perheen tai ystävien luona vierailussa, tanssimisessa, ulkona syömisessä ja seksuaalisessa aktiivisuudessa, mutta eroa ei ollut sosiaalisessa juomisessa ja työstatuksessa.	Lähtötason BSRI-pisteet raportoitu, mutta 2v. seurantatulokset kuvataan sanallisesti. Muutoksen suunnan (BSRI) raportoinnin yhteydessä viitataan toisaalla julkaistuihin tuloksiin (Mate-Kole ym. 1988), jossa kuitenkin eri tutkimusryhmä, N =150. On ilmeistä, että sosiaalinen, seksuaalinen ja työelämään liittyvä aktiivisuus on mitattu ainoastaan 2 v kohdalla, ja vastaajat arvioivat muistinvaraisesti lähtötason/ muutoksen lähtötasoon.

Yhdistelmäleikkaukset (tai ei kuvattu)

37. Lindqvist ym. 2017, Ruotsi

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: F64.0 (ICD-10), MtF		Transnaisen sukuelinleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Kaikki Karoliinisessa sairaalassa vuosina 2003–2015 leikkaukseen hyväksytyt transnaiset (MtF).	n=190, ikä ka 36 v (19–76).	sukupuolen muuntoleikkaus (ei tarkempaa kuvausta)	Yhden ryhmän ennen-jälkeen mittauksia itse täytettävällä kyselyllä ennen leikkausta sekä 1, 3 ja 5 vuotta leikkauksen jälkeen. Tuloksia verrattu eri ajankohdissa ja suhteessa väestötuloksiin.

			Suurin osa vastasi kyselyyn vähintään kaksi kertaa ja 17 vastasi kaikilla neljällä kerralla.

Elämänlaatu (SF-36)	Tulosten tulkintaa
• Fyysinen toimintakyky, fyysinen roolitoiminta, kivuttomuus, sosiaalinen toimintakyky, psyykkinen roolitoiminta, psyykkinen hyvinvointi ja tarmokkuus: useimmissa lievää nousua 1 vuoden kohdalla ja laskua 3 ja 5 vuoden kohdalla; NS. • Koettu terveys: 1 vuoden kohdalla parantunut (2,4 → 2,1, p<0,05). 3 ja 5 vuoden kohdalla huonontunut (2,4 →2,8, NS). (Asteikko 1-5, pienempi parempi, 1 = paljon parempi nyt ja 5 = paljon huonompi nyt)	Elämänlaatu parani 1 vuoden kohdalla leikkauksesta. 3 ja 5 vuoden kohdalla elämänlaatu jopa lähtötilannetta matalampi. Tulosta verrattu väestömittauksiin (kaikki iät) ja kyseisenä ajanjaksona elämänlaadussa havaittu laskua myös väestössä. Mittaukseen osallistui: ennen leikkausta 146, 1 vuosi jälkeen 108, 3 vuotta jälkeen 64 ja 5 vuotta leikkauksen jälkeen 43. Voi olla, että 3 ja 5 vuoden kohdalla vastasivat vain ne, joilla oli komplikaatioita mikä voi selittää negatiivista tulosta. Toisaalta ennen leikkausta elämänlaatu voi mittauksessa näyttäytyä tavallista parempana suurten odotusten vuoksi.

Lyhenteet: ka = keskiarvo; MtF=Male to Female; n = otoskoko; NS=Tilastollisesti ei merkitsevä; v = vuotta

38. Papadopoulos ym. 2017, Saksa

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transnaiset (MtF)			
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Mukaan otettiin kaikki aikuiset transnaiset (MtF), jotka olivat menossa yliopistoklinikan sukupuolen muuntamisenensimmäiseen leikkaukseen 9/2012-1/2014. Poissulkukriteerit: aiemmin tehty sukuelinten leikkauksia, huono saksankielen taito. Sisäänottokriteerit täytti 49 henkilöä, näistä 2 ei halunnut osallistua tutkimukseen ja 8 ei palauttanut kyselyä/kyselyjä.	n=39, ikä ka 39 ±13 v, transidentiteetin kesto ka 3 v, naimattomia 62%, lapsettomia 64%, keski- tai korkea-asteen tutkinto 59%. Kaikki osallistuneet psykoterapiaan ennen 1. leikkausta (Saksassa edellytys julkisin varoin tehtävälle leikkaukselle), 24% 2. leikkauksen jälkeen.	Kiveksen ja siittimen poisto ja vaginoplastia. 46%:lle lisäksi rintojen silikoni-implantit. Muuntoleikkaus tai leikkauksia tehtiin noin 6 kk ensimmäisestä leikkauksesta. 87%:lle tehtiin kaksi tai useampia leikkauksia tutkimusaikana. Kaikki leikkaukset toteutti yksi kokenut kirurgi.	Etenevä tutkimus. Yhden ryhmän ennen-jälkeen mittauksia ennen ensimmäistä leikkausta (sairaalassa) ja ka 11±3 k kohdalla, 6 kk toisen leikkauksen jälkeen (kysely postitse kotiin).

Elämänlaatu (QLS)	Emotionaalinen tila (FPI)	Itsetunto (RSES)	Masennus (PHQ-4)	Tulosten tulkintaa
QLS-pisteet (isompi parempi) ennen 1. leikkausta → 6 kk toisen leikkauksen jälkeen. Yleinen: 40→60, p<0,05 (väestön keskiarvo 60) Terveys: 62→80, p<0,05 (väestön keskiarvo: 74) Kehonkuva: 86→155, p<0,01	FPI-pisteet (pienempi parempi) ennen 1. leikkausta → 6 kk toisen leikkauksen jälkeen. 6,5→4,7, p<0,03 (väestön keskiarvo 6,2)	RSES-pisteet (isompi parempi) ennen 1. leikkausta → 6 kk toisen leikkauksen jälkeen. 32→35, p<0,01 (väestön keskiarvo 31,7)	PHQ-4-pisteet (pienempi parempi) ennen 1. leikkausta → 6 kk toisen leikkauksen jälkeen. 4,0→1,8, p<0,01 (väestön keskiarvo 1,8)	QLS-mittarilla elämänlaatu parani kaikilla kolmella osa-alueella ja erityisesti kysymyksissä ”kumppanuus”, ”rentoutumiskyky”, ”energisyys”, ”vapaus ahdistuneisuudesta”, ”hiukset”, ”rinnat” ja ”penis/vagina”. Leikkauksen jälkeen potilaat tunsivat itsensä myös tasapainoisemmiksi, heidän itsetuntonsa parani ja masennuksensa väheni verrattuna lähtötasoon. Seuranta-aika oli 8–14 kk, pidemmällä seuranta-ajalla tulokset yleensä heikommat.

Lyhenteet: ka = keskiarvo; kk=kuukausi; MtF=Male to Female; n = otoskoko; v = vuotta;
Papadopulos NA, Zavlin D, Lellé JD, Herschbach P, Henrich G, Kovacs L, Ehrenberger B, Machens HG, Schaff J. Male-to-Female Sex Reassignment Surgery Using the Combined Technique Leads to Increased Quality of Life in a Prospective Study. Plast Reconstr Surg. 2017 Aug;140(2):286-294.

39. Simonsen ym. 2016, Tanska

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: F64.0 (ICD-8/ICD10)		Sukupuolen muuntoleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Rekistereistä (Danish Psychiatric Central Research Register ja potilastietojärjestelmät) poimittu 98% Tanskassa vuosina 1978–2010 sukupuolen muuntoleikkauksen läpikäyneistä henkilöistä. 2%:n puuttumiselle ei annettu selitystä. Klinikkaan saapuessa arviointijakso: verikokeet kromosomi- ja hormonitoiminnan häiriöiden selvittämiseksi, fyysinen ja psykiatrinen tutkimus, psykologinen testaus ja kuukausittaiset tapaamiset psykologin tai psykiatrin kanssa. Tanskassa juridiset kriteerit kastraatiolle ja sukuelinten muuntoleikkaukselle olivat tutkimusaikana seuraavat: F64.0, vakaa halu kastraatioon ja ymmärrys sen seurauksista, vähintään 21 v. ikä, edeltävästi 1,5 vuoden arviointijakso.	n=56 MtF, Ikä (ka), kun: • lähete: 30±10, • hormonihoidon aloitus: 32±10 • leikkauspäätös: 37±10,	Sukupuolen muuntoleikkaus: ei tarkempaa kuvausta. Klinikkakäyntejä (kpl): • 1–30 kpl 30 (53,6%), • 31–60 kpl: 20 (35,7%), • >60 kpl: 4 (7%), • Ei tietoa: 2 (4%), Leikkauksen jälkeinen seuranta-aika, v (ka): 16±7	Rekisteritiedoista kerätty tieto psykiatrisesta sairastavuudesta ennen leikkausta ja sen jälkeen, ajalta 1970–2013., Kuolleisuustieto kerättiin kuolinsyyrekistereistä vuosilta 1978–2014.

Osuus henkilöistä (%), joilla kyseinen diagnoosi ennen leikkausta → leikkauksen jälkeen. Seuranta-aikaa ei ilmoitettu.							
Kuollut leikkauksen jälkeen	Masennus (ICD10)	Ahdistuneisuus (ICD10)	Päihteiden väärinkäyttö (ICD10/8)	Personallisuus-häiriö (ICD10/8)	Psykoosi (ICD10/8)	Mikä tahansa psykiatrinen diagnoosi	Tulosten tulkintaa
MtF 6 (11%), keski-ikä 54±8;	MtF: 5→16	MtF: 0→ 11	ICD10: MtF: 0→0, ICD8: MtF: 0→0,	ICD10: MtF: 0→9	MtF: 2→4	MtF: 49→22,	104 henkilöstä (sis sekä MtF että FtM) kaikkiaan 29:llä (28 %) oli vähintään yksi psykiatrinen diagnoosi ennen leikkausta ja 23:lla (22 %) sen jälkeen. 22:lla oli psykiatrinen diagnoosi tai diagnooseja ainoastaan ennen leikkausta, 16:lla ainoastaan leikkauksen jälkeen ja 7:llä sekä ennen että jälkeen. Kuolinsyyt: itsemurha 2, tupakoinnin ja alkoholin aiheuttamat sairaudet 4, sydänsairaudet 2, syöpä 1, haavat 1.

40. Lobato ym. 2009, Brasilia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisuus (ICD-10) tai sukupuoli-identiteetin häiriö (DSM-IV-T), MtF		Sukupuolen muuntoleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Klinikassa tehty 48 sukupuolen muuntoleikkausta. Leikkauksen edellytyksenä oli 21 v ikä (mukana kuitenkin 16-vuotiaita, ilmeisesti siksi, että potilaat olleet mukana tutkimuksessa hormonihoidon alusta asti) ja poissulkukriteereinä psykoosi, kehitysvamma tai päihteiden väärinkäyttö. Leikkaukseen haluavien ohjelmaan kuului kaikille pakollinen, kaksi vuotta kestävä supportiivinen ryhmäterapia (ryhmässä 14 henkeä), yksi tunti 1-2 viikon välein, psykiatrin ja sosiaalityöntekijän vetämänä. Tarvittaessa potilaita ohjattiin yksilöpsykoterapiaan. Kaksi potilasta ei halunnut osallistua ja 14:ltä puuttui seurantatietoja.	n=32, kaikki transnaisia (MtF), ikä 16−54 v. (ilmeisesti lähtötilanteessa). Hormonihoito ollut 11-42-vuotiaana.	Sukupuolen muuntoleikkaus (ei kuvattu tarkemmin). Leikkausta edeltänyt klinikan ryhmäterapia ja (useimmilla?) hormonihoito.	Yhden ryhmän ennen-jälkeen mittauksia alussa ja 12 kk leikkaushoidon jälkeen.

Puolustusmekanismit (DSQ)	Tulosten tulkintaa
Puolustusmekanismi, DSQ alussa → leikkauksen jälkeen, pienempi parempi Ennakointi: 6,8→5,8, p<0,05 Idealisointi: 4,5→3,7, p=0,05	Verrattuna lähtötasoon eri puolustusmekanismeista vain ennakoinnissa ja idealisoinnissa nähtiin merkitsevä positiivinen muutos leikkausten jälkeen. Kypsissä, neuroottisissa ja epäkypsissä puolustustyyleissä ei vastaavina ajankohtina havaittu merkitseviä muutoksia.

41. Udeze ym. 2008, Britannia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisuus (DSM-IV), GD, MtF		Sukupuolen muuntoleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Leicesterin klinikan psykiatri kävi läpi lähetteet käyttäen standardoitua formaattia, joka kattoi perheen taustatiedot sekä henkilön demografiset tiedot, taustatiedot erityisesti GD-tuntemusten ja kokemusten osalta, lääketieteelliset ja psykiatriset taustatiedot sekä tiedon lääkityksistä, työstatuksesta ja sosiaalisista ja seksuaalisista suhteista. Henkilöä pyydettiin esittämään sukupuoleen liittyvän ”elämäntarinansa”. Moniammatillinen Gender Panel arvioi leikkauskelpoisuuden käyttäen HBIGDA (myöhemmin lyhenne WPATH) -kriteereitä. Leikkausjonoon hyväksytyille seuranta ja arviointi säännöllisesti. Tutkimukseen otettiin mukaan 40 satunnaisesti valittua, leikkausjonoon hyväksyttyä transnaista, jotka palauttivat SCL-90R-kyselyn. Odotusaika leikkaukseen ka 14 kk (2 kk–6 v)	MtF, n=40; ikä ka=47 (25–80)	Sukupuolen muuntoleikkaus (ei kuvattu tarkemmin).	Yhden ryhmän ennen-jälkeen mittauksia alussa ja max 6 kk leikkaushoidon jälkeen.

Psykologinen kuormitus (SCL-90R)	Psykiatriset ICD-10 diagnoosit (muut kuin GID)	Tulosten tulkintaa
SCL-90R ennen →jälkeen leikkauksen, pienempi parempi. Kokonaispisteet 48 →49 NS Merkitsevää eroa ei myöskään ollut yhdelläkään mittarin osa-alueista (masennus, ahdistuneisuus, somatisaatio, paranoidiset ajatukset, psykoottiset piirteet, herkkyys ihmissuhteissa, vihamielisyys, pakko-oireisuus ja fobiat).	Ei diagnooseja ennen eikä jälkeen leikkauksen	SCL-90R-mittarin kokonaispisteissä ei ollut merkitsevää eroa ennen ja jälkeen leikkauksen.

42. Megeri ym. 2007, Britannia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisuus F64 (ICD-10), MtF		Sukupuolen muuntoleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
40 ensimmäistä Leicesterin sukupuoli-identiteetin klinikalla leikattua transnaista, jotka palauttivat kyselykaavakkeen ennen ja jälkeen leikkauksen. Ajankohtaa ei ilmoitettu selkeästi; oletettavasti vuodesta 1994 alkaen. Klinikkaan tullessaan henkilöä pyydettiin esittämään elämäntarinansa. Moniammatillinen Gender Panel päätti sen ja ammattilaisten tekemän arvion perusteella sukupuolen muunnosprosessiin pääsystä. Odotusaika leikkaukseen 2 kk–6 v.	n=40; kaikki transnaisia (MtF), ikä ka=42 (23-75). Kenelläkään ei ahdistuneisuuteen viittaavia piirteitä tai aiempia psykiatrisia sairauksia.	Sukupuolen muuntoleikkaus (ei kuvattu tarkemmin).	Yhden ryhmän ennen-jälkeen mittauksia kotiin lähetetyllä kyselyllä, alussa ja leikkaushoidon jälkeen.

Ahdistuneisuus ja masennus (HAD, STAI, BDI ja GHQ)	Tulosten tulkintaa
Ahdistuneisuutta ja masennusta kuvaavien mittarien tuloksissa ei havaittu merkitsevää eroa ennen ja jälkeen leikkauksen, p>0.05 kaikilla mittareilla ja niiden osa-alueilla.	Ennen leikkausta potilaat eivät ehkä myöntäneet oireilua, koska halusivat esittää itsensä myönteisessä valossa päästäkseen leikkaukseen.

Transmiehet (FtM)

43. van de Grift ym. 2017, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transmies			
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen kutsuttiin kaikki 34 transmiestä, jotka olivat olleet sukupuolen muuntoleikkauksessa vv. 2011–2015. 12 ei vastannut	Lopullinen n=21, ikä 40±10 v, BMI 25,6. Ei parisuhteessa 26%, naispartneri 63%:lla ja miespartneri 11 %:lla. Hormonihoidon kesto ka.12 v.	Falloplastia (n=15) käyttäen • varrellista reisikielekettä (ALTF), n=8 • vapaata kyynärvarsisiirrettä (FRFF), n=2	Yhden ryhmän ennen-jälkeen mittauksia ennen ja ka 31 kk leikkauksen jälkeen. Leikkauksen jälkeen mitattuja tuloksia verrattiin myös väestön keskiarvoihin ja eri leikkaustekniikoiden kesken (metoidioplastia-falloplastia)

kyselyihin ja 1 ei osallistunut ajanpuutteen vuoksi. Leikkauskelpoisuuden kriteerit olivat olleet: ei tupakointia, BMI 18–30 kg/m^2. Lisäksi oli edellytetty preoperatiivista ohjausta, jossa psykologin/seksologin, plastiikkakirurgin ja urologin konsultaatiot.	Aikaisemmat leikkaukset (osuus) • Rintarauhasten poisto 100 % • Kohdun ja munasarjojen poisto 100 % • Emättimen poisto 76 %.	• FRFF + ALTF, n=5 Metoidioplastia (n=6): • virtsaputken pidennyksellä, n=2 • ilman virtsaputken pidennystä, n=4 Lisäleikkauksia: • Kivesimplantit, n=10 • Glansin plastia, n=3 • Skrotumin plastia, n=3 Kirurginen hoito oli toteutettu WPATH-standardien mukaan.	Taustatiedot koottiin potilasrekistereistä ja itseraportoiduista kyselyistä. Leikkaustekniikoihin ja komplikaatioihin liittyvä tieto koottiin rekistereistä. Toiminnallisiin tuloksiin (virtsaaminen ja peniksen toiminta) liittyvä data kerättiin leikkauksen jälkeen IPSS-kyselyllä, 24 h virtsaamispäiväkirjalla ja tutkijoiden laatimalla kyselyllä. Motivaatio ennen leikkausta ja tyytyväisyys/kokemukset leikkauksen jälkeen selvitettiin kyselyillä. Psykoseksuaaliset tulokset ja elämänlaatu selvitettiin kyselyllä ennen ja jälkeen leikkauksen.

Kehoahdistus (BIS) ja itsetunto (RSES)	Mieliala (HADS), tyytyväisyys elämään (SWLS), onnellisuus (SHS) ja elämänlaatu (CL)	Virtsaaminen (IPSS)	Tyytyväisyys hoitoon	Tulosten tulkintaa
Kehoahdistus BIS leikkauksen jälkeen (ka), vertailuna väestön keskiarvo, pienempi parempi. Hiukset 2,2 • väestön ka 2,3, NS Pää ja niska 2,1 • väestön ka 2,0, NS Lihakset 2,5 • väestön ka 2,2, NS Lantio 2,8 • väestön ka 2,2, p<0.05 Rintakehä 2,8 • väestön ka 2,3, NS Sukuelimet 2,5 • väestön ka 2,0, NS	HADS-pisteet (ka) ennen→ älkeen leikkauksen, pienempi parempi: Ahdistuneisuus 5,2→6,5 NS Masennus 3,5→4,4 NS Tyytyväisyys elämään SWLS-pisteet ennen ja jälkeen leikkauksen (ka), isompi parempi. 22,0→21,7, NS • väestön ka 26, p<0.05. Onnellisuus SHS-pisteet pisteet ennen ja jälkeen leikkauksen (ka), isompi parempi. 4,8→4,6 NS	IPSS-pisteet leikkauksen jälkeen (ka) eri leikkaustekniikoilla, pienempi parempi, <7 tulos viittaa lieviin, 8–18 keskivaikeisiin ja >18 vaikeisiin oireisiin: • Falloplastia 11 • Metoidioplastia 13 Tyytyväisyys virtsaamiseen leikkauksen jälkeen eri leikkaustekniikoilla*, skaala 0-4, isompi parempi: • Falloplastia 1,9; • Metoidioplastia 2,0	Yksikään ei katunut sukupuolen muuntoleikkausta. Yksi olisi valinnut metoidioplastian sijaan falloplastian ja yksi päinvastoin. Leikkauksen jälkeen potilaat harrastivat enemmän masturbaatiota ja seksiä partnerin kanssa kuin ennen leikkausta. Oma arvio seksielämästä ka 5,5 (skaala 1-10). Kuinka moni (osuus) sai leikkauksen jälkeen merkittävää helpotusta itseä vaivaaviin asioihin: • Maskuliininen identiteetti 70 % • Aktiivinen yhdyntä 17 % • Virtsaaminen seisten 44 %	Leikkauksen vaikutuksesta kehoahdistukseen ei raportoitu seurantatuloksia, vaan pelkästään väestöön suhteutettuja leikkauksen jälkeisiä tuloksia. Tyytyväisyydessä elämään, itsetunnossa ja mielialassa ei tapahtunut selviä muutoksia leikkauksen jälkeen. Leikkauksen jälkeisiä komplikaatioita oli vähemmän metoidioplastiaryhmässä (esim virtsaputken ahtauma 80% falloplastia vs 33% metoidioplastiaryhmässä). Virtsaaminen onnistui ja vakavia urologisia ongelmia esiintyi

Itsetunto RSES ennen→jälkeen leikkauksen Feminiinisyys 31→31, NS väestön ka 32 Maskuliinisuus 1,6→1,6, NS	• väestön ka 4,9. Elämän laatu CL-pisteet, skaala 0-10. 7,0→6,6 NS • väestön ka 6,8.	Seksuaalinen tyytyväisyys: • Falloplastia 1,3 • Metoidioplastia 3,0, p<0.05	• Miestenhuoneen käyttö 44 % • Vaivaantuneisuus uusissa suhteissa 32 % • Vaivaantuneisuus saunoissa tms. 16 %	kummankin leikkausmenetelmän jälkeen saman verran. Metoidioplastia-menetelmällä leikatut olivat tyytyväisempiä seksiin.

*Toiminnallisia tuloksia arvioitiin väittämillä: ”Olen tyytyväinen virtsaamiseen ja seksuaalisiin toimintoihini” ja ”Kadun, että lähdin sukuelinkirurgiseen leikkaukseen” ja ”Nykyisellä kokemuksella olisin valinnut toisen tyyppisen sukuelinleikkauksen”, skaala kaikissa 0=Täysin eri mieltä ja 4=Täysin samaa mieltä.

van de Grift TC, Pigot GLS, Boudhan S, Elfering L, Kreukels BPC, Gijs LACL, Buncamper ME, Özer M, van der Sluis W, Meuleman EJH, Bouman MB, Mullender MG. A Longitudinal Study of Motivations Before and Psychosexual Outcomes After Genital Gender-Confirming Surgery in Transmen. J Sex Med. 2017 Dec;14(12):1621-1628.

44. Simonsen ym. 2016, Tanska

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: F64.0 (ICD-8/ICD10)		Sukupuolen muuntoleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Rekistereistä (Danish Psychiatric Central Research Register ja potilastietojärjestelmät) poimittu 98% Tanskassa vuosina 1978–2010 sukupuolen muuntoleikkauksen läpikäyneistä henkilöistä. 2%:n puuttumiselle ei annettu selitystä. Klinikkaan saapuessa arviointijakso: verikokeet kromosomi- ja hormonitoiminnan häiriöiden selvittämiseksi, fyysinen ja psykiatrinen tutkimus, psykologinen testaus ja kuukausittaiset tapaamiset psykologin tai psykiatrin kanssa. Tanskassa juridiset kriteerit kastraatiolle ja sukuelinten muuntoleikkaukselle olivat tutkimusaikana seuraavat: F64.0, vakaa halu kastraatioon ja ymmärrys sen seurauksista, vähintään 21 v. ikä, edeltävästi 1,5 vuoden arviointijakso.	N=48 FtM, Ikä (ka), kun: • lähete 27±9 • hormonihoidon aloitus 30±8 • leikkauspäätös 33±8	Sukupuolen muuntoleikkaus: ei tarkempaa kuvausta. Klinikkakäyntejä (kpl): • 1–30: 23 (48%) • 31–60: 22 (46 %) • >60: 2 (4%) • Ei tietoa: 1 (2%) Leikkauksen jälkeinen seuranta-aika, v (ka) 10±6 v.	Rekisteritiedoista kerätty tieto psykiatrisesta sairastavuudesta ennen leikkausta ja sen jälkeen, ajalta 1970–2013., Kuolleisuustieto kerättiin kuolinsyyrekistereistä vuosilta 1978–2014.

Osuus henkilöistä (%), joilla kyseinen diagnoosi ennen leikkausta → leikkauksen jälkeen. Seuranta-aikaa ei ilmoitettu.

Kuollut leikkauksen jälkeen	Masennus (ICD10)	Ahdistuneisuus (ICD10)	Päihteiden väärinkäyttö (ICD10/8)	Personallisuus-häiriö (ICD10/8)	Psykoosi (ICD10/8)	Mikä tahansa psykiatrinen diagnoosi	Tulosten tulkintaa
FtM 4 (8%), keski-ikä 54±7	FtM 6→6	FtM 8→11	ICD10: FtM 4→8 ICD8: FtM 2→0	ICD10: FtM 8→6 ICD8*: FtM 17→0	FtM 4→4	FtM 41→17, p<0,01	104 henkilöstä (sis sekä MtF että FtM) kaikkiaan 29:llä (28 %) oli vähintään yksi psykiatrinen diagnoosi ennen leikkausta ja 23:lla (22 %) sen jälkeen. 22:lla oli psykiatrinen diagnoosi tai diagnooseja ainoastaan ennen leikkausta, 16:lla ainoastaan leikkauksen jälkeen ja 7:llä sekä ennen että jälkeen. Kuolinsyyt: itsemurha 2, tupakoinnin ja alkoholin aiheuttamat sairaudet 4, sydänsairaudet 2, syöpä 1, haavat 1.

Nielukirurgia

Transnaiset

45. Kunachak, S. ym. 2010, Thaimaa

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: MtF transsukupuoliset		Nieluleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Kaikki nieluleikkaukseen vuosina 1990-1996 valitut kutsuttiin tutkimukseen. Kilpirusto ja sisäiset kurkunpään rakenteet olivat kaikilla maskuliinisia. Kaikkien ääni oli maskuliininen, teennäisestä äänen korottamisesta huolimatta. Leikkauskriteerit: fyysinen ja psykologinen arvio ennen leikkausta -> arvioitu psyykkisesti vakaiksi. Estrogeeni- ja keltarauhashormonihoito kaikilla vuosien ajan. 5/6 käynyt läpi sukuelinleikkauksen.	n=6, ikä ka 23v (20–27v.)	Kilpiruston ja äänihuulten pienennys. Leikkaukset tehty vuosina 1990-1996.	Yhden ryhmän ääninäytteiden vertailu ennen ja jälkeen leikkauksen. Seuranta 2 viikon välein1. kk ajan, sen jälkeen 1krt/1-2kk enintään 6 vuoteen asti.

Äänenkorkeus (Hz)	Komplikaatiot	Tulosten tulkintaa

Mittaustuloksia ka ennen leikkausta → leikkauksen jälkeen:max 6 vuoteen asti Perustaajuus (*fundamental frequency*): 147 Hz → 315 Hz. (Tutkimusten mukaan tyypillisiä frekvenssejä ~120 Hz faikuislla miehilla ja 220 Hz aikuisilla naisilla.) Värinä, äänen frekvenssin (korkeuden) instabiilius *(jitter):* 2,35% → 0,98%. (Terveiden aikuisten mittaustuloksia: miehet 0,6%, naiset 0,33%, Teixeira 2014). *Äänen amplitudin (voimakkuuden) instabiilius (shimmer):* 0,82dB → 0,69dB. (Terveiden aikuisten mittaustuloksia: miehet 0,20dB, naiset 0,23dB, Teixeira 2014). Tutkimuksissa standardideviaatiot ovat tyypillisesti suuria. Maksimaalinen ääntöaika (*maximum phonation time)*: 15 sekuntia → 14 sekuntia. Normaalisti miehet pystyvät pitämään yllä vokaalin ääntöä 25-35 sek ja naiset 15-25 sekuntia.	2 potilaalle kehittyi kurkunpään anterior commissure alueelle (äänihuulten yhtymäkohtaan) granulaatiokudosta 1-2 viikkoa leikkauksen jälkeen:	• Kilpiruston leikkaustekniikka näyttää korottavan äänenkorkeuden naiselle tyypilliselle tasolle tehokkaasti ja pitkäkestoisesti. • Äänenkorkeus nousi käytetyllä uudella leikkaustekniikalla enemmän kuin aiemmilla tekniikoilla (*cricothyroid approximation, vocal fold webbing, vocal ligament tightening* ja *partial thyroarytenoid myectomy*). • Tekniikan haittapuolet: ○ Potilas on nukutettuna, joten ääntä ei voi monitoroida ja testata leikkauksen aikana. ○ Se on invasiivinen -> tekniikkaa pitää vielä kehittää ja tutkia lisää. • Puheterapiasta voi olla hyötyä äänenkorkeuden nousemiselle sekä ennen että jälkeen nieluleikkauksen.

MF = male-to-female, ka = keskiarvo, n= lukumäärä

João Paulo Teixeiraa, Paula Odete Fernandesa. Jitter, Shimmer and HNR classification within gender, tones and vowels in healthy voices. Procedia Technology 2014;16;1228 – 1237.

46. Anderson ym. 2007, Kanada

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolinen MtF ja F		Kurkunpääleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Osallistujat oli lähetetty klinikalle transsukupuolisia hoitavilta lääkäreiltä. Sisäänottokriteerit: 25–60-vuotias, 3 vuotta hormonihoitoa takana (jos MF-transsukupuolinen), lähete hoitavalta lääkäriltä, ei aikaisempia kurkunpään sairauksia tai aktiivista keuhkosairautta, ei	n=6: MtF 5 ja F 1. Naispotilaalle oli kehittynyt androfonia (matala äänenkorkeus) androgeenisten stereodien käytöstä ja hän halusi siihen muutosta leikkauksella. MtF:ien ikä ka 36 (26-50), naispotilaan ikä 27 ikä Kaikilla transsukupuolisilla osallistujilla takana usean vuoden hormonihoito, ja useimmilla takana sukupuolen muuntoleikkaus sekä mm. rintojen suurennus ja aataminomenan höyläys.	Äänihuulten leikkaus: endoscopic laryngeal web formation with a Gelfoam augmentation.	Yhden ryhmän haastattelu ja mittaukset ennen leikkausta sekä 1 ja 6 kk leikkauksen jälkeen.

aikaisempia puheen, kielen tai kuulon häiriöitä. Poissulkukriteerit: lääketieteellinen soveltumattomuus yleiselle anestesialle, epärealistiset odotukset äänenkorkeuden noston vaikutuksista.	Aiemmat nieluleikkaukset: tyypin IV thyroplastia (2 potilasta), laser micro (2 potilasta), vocal fold stripping (1 potilas) ja epäonnistunut laser web formation (1 potilas).		

Äänen korkeus (perustaajuus Hz)	Äänenvoimakkuus (dB)	Tulosten tulkintaa
Alussa taajuus keskimäärin 134 Hz (vaihtelu 96-155 Hz). Seurannassa äänen korkeus nousi kolmella henkilöllä yli 100 Hz ja kolmella henkilöllä 50-90 Hz. Puheäänen taajuuden vaihtelu pieneni leikkauksen jälkeen, mutta pysyi normaalin rajoissa.	Äänen voimakkuus alussa keskimäärin 59 dB (vaihtelu 56-64). Se pysyi melko samana leikkauksen jälkeen.	Kaikkien osallistujien perustaajuus oli leikkauksen jälkeen naisen normaalin perustaajuuden vaihteluvälin sisällä ja yhdellä sen yläpuolella. Osallistujien mukaan heidän äänenvoimakkuutensa väheni ainakin 6 kuukaudeksi leikkauksen jälkeen.

47. Orloff ym. 2006, Yhdysvallat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transnaiset (MtF)		Nieluleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Kaikki leikkaukseen v. 1997-2003 otetut valittiin tutkimukseen, ei poissulkukriteerejä. Etnisiä ryhmiä ei poissuljettu. Leikkauskriteerit: yli 18 vuoden ikä, riittävän hyvä terveydentila leikkaukseen osallistumiseksi (ASA luokka I tai II). 5 potilasta käynyt toisen fonokirurgisen toimenpiteen. Moni oli käynyt puheterapiassa ja aataminomenaa pienentävässä toimenpiteessä.	n=31, kaikki MtF, ikä ka 44v (26-60v.)	Äänenkorkeutta nostava fonokirurginen laserleikkaus (*laser-assisted voice adjustment, LAVA),* vuosina 1997-2003	Yhden ryhmän ennen-jälkeen mittauksia: • Potilastyytyväisyys kysely (itse laadittu) ennen leikkausta ja 12kk sen jälkeen. • Ääninäytteiden mittauksia ennen leikkausta ja 10-52 viikkoa leikkauksen jälkeen. Leikkauksen jälkeen tehtyjä mittauksia: • Toimintakykyä mittaava VHI-kysely 3kk leikkauksen jälkeen • Äänen ja oletetun sukupuolen välinen yhteys. Ääninäytteet otettiin myös cis-vertailuryhmältä (20 naista ja 20 miestä). 5 kuuntelijaa arvioi.

Äänen korkeus (Hz)	Ääneen liittyvä toimintakykyisyys (VHI)	Äänen ja oletetun sukupuolen välinen yhteys	Potilastyytyväisyys (itse rakennettu kysely)	Komplikaatiot	Tulosten tulkintaa
Ääninäytteiden mittauksia ennen leikkausta ja 10-52 viikkoa leikkauksen jälkeen. • Perustaajuus nousi ka 26 Hz (p<0.0025). 78%:lla perustaajuus nousi keskimäärin 37 Hz, kun taas 22%:lla se ei muuttunut lainkaan tai laski.	VHI-pisteet 3 kk leikkauksen jälkeen, yhteispisteiden skaala 0–100, osa-alueiden skaala 0–40, pienempi parempi. • VHI yhteispisteet ka 51 (vastaa keskivertoa äänivammaa). Eri osa-alueiden pisteet (ka): fyysinen 16, funktionaalinen 18, emotionaalinen 17.	Ääninäytteet 10 potilaalta (58%) ja cis-verrokeilta sekä 5 kuuntelijaa. • 60% (6/10) oletettiin äänen perusteella naiseksi kaikkien kuuntelijoiden mielestä. • 30% (3/10) oletettiin osan kuuntelijoista mielestä naiseksi, osan mieheksi • 10% (1/10) oletettiin kaikkien kuuntelijoiden mielestä mieheksi.	Kyselyn pisteet (ka) ennen leikkausta → 12kk sen jälkeen, skaala 6–30, isompi parempi. • Kokonaistyytyväisyys: 18.67 → 18.67, ei muutosta, NS • Tyytyväisyys ääneen lisääntyi: NS • Äänen yhteensopivuus omakuvan kanssa lisääntyi. NS • Äänen selkeys, voimakkuus ja ääniala pienenivät. NS Kyselyyn vastasi vain 6 potilasta (19%).	1 lle leikatuista muodostui granulaatiokudosta äänihuulten pinnalle (*superior vocal fold surface)*. Potilaalla oli taustalla ruokatorven refluksitauti.	Toimintakykykysely ja äänen kuunteluttaminen ulkopuolisilla suoritettiin vain leikkauksen jälkeen, mikä tekee tulosten vertailun mahdottomaksi. Leikkauksen jälkeinen ääninäyte saatiin vain 58%:lta potilaista ja tyytyväisyyskysely vain 19% potilaista, mikä vaikeuttaa tulkintaa. Artikkelin kirjoittajien mukaan puheterapia leikkauksen jälkeen parantaa LAVA:n tuloksia, mutta tästä ei ole esitetty tuloksia.

48. Brown, M. ym. 2000, Britannia ja Australia

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: MtF transsukupuoliset		Kilpirustoleikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Tutkimukseen valituilla fysiologisesti normaali kurkunpää, sukuelinleikkaus suoritettu samassa sairaalassa. Itse hakeutuneet nieluleikkaukseen äänen parantamiseksi. Ei tarkempaa tietoa leikkaus- tai valintakriteereistä.Estrogeeni-hormonihoito käynnissä.	n=14, - ikä ka = 37;5v. (27;0–52;8), 12:lla äidinkielenä englanti, yksi tupakoija, kaikki elivät täysipäiväisesti naisena.	Äänenkorkeutta nostava nieluleikkaus (*crico-thyroid approximation, kilpiruston höyläys*) saman lääkärin suorittamana. Kaikki saaneet puheterapiaa ennen leikkausta.	Yhden ryhmän mittauksia ennen ja jälkeen leikkauksen: • Ääninäytteitä ennen leikkausta, 2vk leikkauksen jälkeen (n=14) ja 6kk leikkauksen jälkeen (n=4). • Äänen kuunteluttaminen 10 fysioterapeutilla (n=8)

Tyytyväisyys hoidon lopputulokseen	Äänenkorkeus (puheäänen taajuus Hz)	Äänen ja oletetun sukupuolen välinen yhteys	Tulosten tulkintaa
2/14 oli tyytymättömiä tulokseen, loput tyytyväisiä tai eivät osanneet sanoa	Äänentaajuus (Hz) ennen leikkausta → 2 vko leikkauksen jälkeen → 6kk leikkauksen jälkeen) Keskimääräinen frekvenssi (Hz): 152.21 (n=14) → 154.79 → 156.50 (n=4) (NS) Modal frequency (Hz, ka). Resonoiva äänenkäyttö (ns rintaääni), jota käytetään vokaalien lausumisessa, edellyttää sopivaa ilmavirtaa ja kurkunpään jännitystä. Yhdessä tutkimuksessa keskimääräiset arvot miehillä 116 Hz ja naisilla 217 Hz (Fitch 1970). Tulos: 142.07 → 174.64 → 185.50 (p < 0.01)	Vain 8 potilasta tutkittu. Korrelaatio modaalisen äänenkorkeuden (*modal frequency*) ja naiseksi olettamisen välillä tilastollisesti merkitsevä (p<0.01). Ei korrelaatiota keskiarvoisen äänenkorkeuden (*mean frequency*) ja naiseksi olettamisen välillä. Puolet kuulijoista oletti puhujan naiseksi, kun *modal frequency* > 173 Hz. Kaikki kuulijat olettivat puhujan naiseksi, kun *modal frequency* > 238 Hz. Äänen teennäinen korotus ennen leikkausta ei edistänyt puhujan olettamista naiseksi.	• Modaalinen äänenkorkeus näyttää olevan hyvä oletetun sukupuolen ja nieluleikkauksella saadun muutoksen mittari. Toisaalta modaalisessa äänekorkeudessa, kuten myös muissa äänimittausten parametreissa, on iso vaihteluväli. • Leikkaus korotti modaalista äänenkorkeutta, ja vähensi äänen teennäisen korottamisen tarvetta. • Äänen teennäinen korotus ennen leikkausta on tutkijoiden mukaan paitsi haitallista äänelle myös tehotonta naiseksi olettamisen kannalta. • Potilaskato oli suuri: 6kk seurannassa mukana vain 4/14, ääninäytteiden esittämisessä 8

James L. Fitch, Anthony Holbrook. Modal Vocal Fundamental Frequency of Young Adults. Archives of otolaryngology 1970; 92(4):379-82

49. De Bruyne 1995, Alankomaat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisia, MtF		Kilpiruston leikkaus	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Ei kuvattu	n=5. Kaikki olivat ennen leikkausta tietoisestikorottaneet ääntään, ja heidän äänenkorkeutensa oli jo ennen leikkausta keskimääräistä miehen äänenkorkeutta korkeampi	Cricothroid approximation (kilpiruston höyläys). Sama lääkäri suoritti leikkauksen kaikille potilaille.	Yhden ryhmän ääninäytteet ennen leikkausta ja 1-3 kertaa leikkauksen jälkeen 17 kk aikana. Ääninäytteenä potilaat lukivat saman 5min tekstinäytteen.

Äänen korkeus	Tulkintaa
Keskimääräinen perustaajuus (Hz): Alussa taajuus keskimäärin 156 Hz (vaihtelu 126-160 Hz). Seurannassa äänen korkeus nousi yhdellä henkilöllä 83Hz, kahdella henkilöllä noin 55 Hz, yhdellä 16 Hz ja yhdellä vain 1 hertsin.	Neljä viidestä leikatusta saavutti naisen normaalin äänenkorkeuden.

Korkein perustaajuus nousi selvästi kaikilla osallistujilla. Matalimmassa perustaajuudessa muutos ei ollut niin suuri kuin korkeimmassa ja keskiarvoisessa, mutta sekin nousi kaikilla tai pysyi samana.	

Psykologiset interventiot

50. Briggs, P. ym, 2018, Yhdysvallat

Potilaat		Tutkittava interventio	Vertailu ja mittaukset
Diagnoosi: Transsukupuolisia GD (DSM-5) n=3/7, sukupuoleton 2/7, muunsukupuolinen 1/7, ei-tiedä n=1/7		Ryhmäpsykoterapia	
Potilasvalinta	Lukumäärä, ikä, sosiodemografia		
Yli 18-vuotiaita osallistujia tavoitettiin Portlandin transyhteisön kautta. Heidän piti identifioitua transsukupuoliseksi tai muunsukupuoliseksi (transgender, gender non-conforming or gender variant). Kaikki 8 aluksi suostuneet ilmaisivat olevansa sukupuolen muuntoprosessissa. 3 sai paraikaa hormonihoitoa, 1 oli käynyt läpi rintaleikkauksen ja munasarjojen poiston.	n=7 (yksi tippui pois), ikä yli 18v., - etnisyys: valkoinen (8), alkuperäiskansaa (1), latino (1). Parisuhdestatus: yksin elävä (5), parisuhteessa (3), sosioekonominen asema: työssä (4), opiskelija (3), asumismuoto: yksin (2), ystävien kanssa (4), lasten kanssa (1), puolison kanssa (1). Mielenterveys: masennusoireita (7), ahdistusoireita (5), ärtymysoireita (7), nukkumisvaikeuksia (3), kipua (7). Päihteidenkäyttö: tupakka (2), alkoholi (päivittäin) (2), kannabis (3), muut laittomat huumeet (0). Syntymätodistuksen sukupuoli: nainen (5), mies (3). Sukupuoli-identiteetti (n=7): • Trans-MtF n=2 • Trans-FtM n=1 • Sukupuoleton transnainen n=1 • Sukupuoleton nainen/mies n=1 • Muunsukupuolinen n=1 • ”en tiedä” n=1.	Somatic Experiencing® -menetelmään perustuva ryhmäterapia, jonka tarkoitus parantaa masennusta, ahdistusta, somaattisia oireita, elämänlaatua ja syrjinnän kokemuksista selviytymistä. Ryhmä tapasi kerran viikossa, 90min/krt, 10 vk ajan. Osallistujille ilmainen.	Yhden ryhmän ennen ja jälkeen mittauksia kyselyin ennen ryhmäterapiaa ja 10 viikkoa kestäneen ryhmäterapian jälkeen.

Elämänlaatu (WHOQoL)	Mieliala ja somaattiset oireet (PHQ-SADS)	Tulosten tulkintaa

WHOQoL-pisteet ennen terapiaa → terapian jälkeen, skaala 0–100, isompi parempi. Psykologinen elämänlaatu: 42 → 58 (p = 0,003) Terveys: 55 → 61 (NS) Sosiaalinen elämänlaatu: 68 → 66 (NS) Ympäristö: 56 → 52 (NS)	PHQ-SADS pisteet ennen terapiaa → terapian jälkeen), skaalat • PHQ-9 0–27 • PHQ-15 0–30 • GAD-7 0–21 - Masennusoireet (PHQ-9): 8.6 → 7 (NS), Pisteet 5-10 viittaavat lieväoireiseen masennukseen. - Somaattiset oireet (PHQ-15): 10.7 → 9.2 (NS). Pisteet 5-10 viittaavat lieväoireiseen ja 10-15 kohtalaiseen somaattiseen oireiluun. - Ahdistusoireet (GAD-7): 7.4 → 8.9 (NS). Pisteet 5-10 viittaavat lieväoireiseen ahdistukseen. Yksi vastaaja poikkesi huomattavasti keskiarvosta, ja hänet poissulkiessa analyysistä positiivinen muutos muuttui kliinisesti ja tilastollisesti merkitsevämmäksi.	Osallistujien psykologinen elämänlaatu nousi terapian myötä tilastollisesti merkitsevästi. Se voi tutkijoiden mukaan viitata parantuneeseen resilienssiin stressaavia elämäntapahtumia ja syrjinnän kokemuksia kohtaan. Osallistujien mielialaoireet olivat alussa lieväoireisella tasolla ja somaattiset oireet kohtalaisella tasolla. Oireilu lievittyi hieman joka kategoriassa (ei tilastollisesti merkitsevää eroa). Rajoitteita: • pieni aineisto • pieni etninen diversiteetti (kaikki valkoisia) • seurantakyselyt suoritettiin pian Orlandon homobaarin ampumatapauksen jälkeen, millä voi olla vaikutus tuloksiin

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Liite 3 Tyytyväisyys hoitoon

Taulukko tutkimuksista, joissa mittauksia tehty ainoastaan hoitointervention jälkeen

Sukupuolen muuntoprosessi

Transnaiset ja transmiehet

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % tai tasopisteet hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
Ruppin ym. 2015, Saksa	71 (MtF 35, FtM 36)	4,7/5	Sukupuoli-identiteetti	10 v	0 katui tai toivoi perumista
		4,5/5	Kosmeettinen tulos		
		3,6/5	Sukupuolielämä		
Johansson ym. 2010, Ruotsi	42 (MtF 25, FtM 17)	90%	Hormonihoito	<5 v	
		67%	Sukuelinkirurgia		

		95%	Yleinen tai toiminnallinen tyytyväisyys		5% tyytymättömiä prosessiin (ongelmat liittyivät pääosin sukuelinkeikkauksiin). 12% tyytymättömiä sukuelinleikkauksiin. 1 tyytymätön hormonihoitoon, syynä allerginen reaktio
		70% (MtF 67%, FtM 75%)	Sukupuolielämä		
Smith ym. 2005, Alankomaat	158 (MtF 94, FtM 64)	89% .(heistä joilla oli kumppani, n=50)	Sukupuolielämä	1-4 v	1 katui ja 1 katui vähän, mutta tekisi silti prosessin uudelleen. Homoseksuaalit (suhteessa syntymäsukupuoleen) katuivat vähemmän kuin ei-homoseksuaalit. 6% tyytymättömiä seksielämään

Transnaiset (MtF)

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
van de Grift ym., 2018, Alankomaat	81	96%	Vaginoplastia	>2,6 v.	Kukaan ei katunut paljon. 3% koki kosmeettisia haittoja äänihuulileikkauksesta, mastektomiasta ja vaginoplastiasta. Yhdelle kroonista kipua vaginoplastiasta, yhdelle rintaimplanttien kapseloitumista.
		96%	Rintaimplantit		
		100%	Kilpiruston leikkaus		
		100%	Feminisoiva kasvoleikkaus		
		0%	Äänihuulten leikkaus		
Smith ym. 2005, Alankomaat	94	70%	Vaginoplastia	1-4 v	2% ei ollut täysin tyytyväisiä koska vagina ei ollut riittävän syvä ja feminiininen. 8% oli kyvyttömiä seksuaaliseen nautintoon ja halusivat uusintaleikkausta. 29% ei ollut täysin tyytyväisiä rintoihin, 10%:tä häiritsi rintojen iso etäisyys toisistaan
		65%	Rintaimplantit		

Transmiehet (FtM)

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
van de Grift ym., 2018, Alankomaat	51	94%	Rintojen poisto	>2,6	Kukaan ei katunut paljon. Yhdelle tunnottomuutta rintojen poistosta.
		97%	Kohdunpoisto		
		100%	Falloplastia		
		100%	Metadoioplastia		
		94%	Rintojen poisto		

Smith ym. 2005, Alankomaat	64	29% 44%	Rintojen poisto Metadoioplastia tai falloplastia	1-4 v	58% ei ollut täysin tyytyväisiä rintojen poistoon. 13%:lla syynä oli näkyvät arvet. Yksi henkilö oli tyytymätön virtsaamisongelmien vuoksi

Rintaimplantit

Transnaiset (MtF)

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
de Cuypere ym. 2005, Belgia	32	95%	Yleinen ja toiminnallinen tyytyväisyys	3,8 v	Kukaan ei ollut hyvin tyytymätön
Kanhai ym. 1999, Hollanti	201			1-20 v	11%:lla komplikaatioita: kapseloituminen 5%:lle. 4 (2%) sairastui rintasyöpään.

Rintojen poisto

Transmiehet (FtM)

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % tai tasopisteet hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
van de Grift ym. 2017, Hollanti	54 (	7/10	Yleinen ja toiminnallinen tyytyväisyys	6-12 kk	Tyytyväisyys samaa luokkaa molemmissa leikkaustekniikoissa: *concentric circular ja inframammary skin resection with free nipple graft. Muuntoleikkauksia* 38%:lle ja *14%:lle vastaavassa järjestyksessä.*
de Cuypere ym. 2005, Belgia	23	79%	Yleinen ja toiminnallinen tyytyväisyys	6,2 v	Hyvin tyytymättömiä 0.

Muunsukupuoliset

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
Olson-Kennedy ym. 2018, Yhdysvallat	68 (mies tai muunsukupuolinen, nuoria, ikä ka 19 v)	100%	Yleinen ja toiminnallinen tyytyväisyys	0-5 v	0 katui, 41%:lle rintojen tunnottomuus, 32%:lle nännien tunnottomuus.
Poudrier ym. 2018, Yhdysvallat	58 (mies 43%, transmies 66%, muunsukupuolinen 22%, muu 5%)	94%	Yleinen ja toiminnallinen tyytyväisyys	0-6 v (90%) >6 v (10%)	0 katuu koko ajan, 4% katuu joskus. 1/58 tyytymätön. 24% tyytymättömiä nännien tunneherkkyyteen. 15%:lla keloidiarpia.

Sukuelinkirurgia

Transnaiset (MtF)

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % tai tasopisteet hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
Özata ym. 2018, Turkki	11	82%	Yleinen tai toiminnallinen tyytyväisyys	>1 v	Korkeat komplikaatioluvut. 2 toivoi uusintaleikkausta
le Breton ym. 2017, Kanada	28	0,6–1,3 skaalalla (⁻2–2)	Sukupuolielämä	3-49 kk	Haittoja: 11% verenvuoto, 4% virtsaputken ahtauma, 7% tiputtelu, 7% infektio, 4% osittainen nekroosi
Papadopoulos ym. 2017, Saksa	47			>1 v	Kukaan ei katunut. Muuntoleikkauksia: 25%:lle häpyhuulten leikkaus ja 13%:lle neovaginan fistelin korjaus. 3 neovaginan purkua: syynä 1 nekroosi (10 kk) ja 2 ahtaumaa (5 ja 6,5 v kohdalla). Jälkimmäisille tehtiin uusi neovagina.
Bouman ym. 2016, Alankomaat	31 (nuoria, ikä ka 19)	65% ja 8/10	Vaginoplastia: yleinen ja toiminnallinen tyytyväisyys	1 v	1 tyytymätön. Viidellä henkilöllä tyytyväisyys-pisteet neovaginan toiminnallisuuteen oli <6/10. Syinä neovaginan ahtauma (n=2), limaneritys (n=1), muut (n=2). 8%lla virtsaamisvaikeuksia. 41%l:le korjausleikkauksia.
		82%	Vaginoplastia: tulos odotusten mukainen		
		83% ja 8/10	Vaginoplastia: riittävän feminiinisen näköinen lopputulos		
Van der Sluis ym. 2016, Alankomaat	9	7,4/10	Vaginoplastia: yleinen ja toiminnallinen tyytyväisyys	4-44 v.	
Hess ym. 2014, Saksa	119	72%	Yleinen ja toiminnallinen tyytyväisyys	1-7 v	

		85%	Sukupuoli-identiteetti		
Wagner ym. 2010, Saksa	50	98%	Yleinen ja toiminnallinen tyytyväisyys	3 v	1 katui, masentui, yritti kahdesti itsemurhaa 2 v aikana 10%:lla neovaginan kurouma, jota korjattu leikkauksella.
		90%	Kosmeettinen tulos		
Lawrence ym. 2003 ja 2006, Yhdysvallat	232 (22% ei täyttänyt HBIGDA-kriteerejä).	86%	Yleinen ja toiminnallinen tyytyväisyys	>1 v	6% katuu joskus, 0 pysyvästi. Haittoja: 9% sukuelinten kipu, 4% virtsaputken ahtauma, 12% muita komplikaatioita (infektiot, inkontinenssi, tunnottomuus, verenvuoto). (
Lobato ym. 2006, Brasilia	8			1-2,5 v	Kukaan ei katunut
Zimmermann ym. 2006, Saksa	24	88%	Yleinen ja toiminnallinen tyytyväisyys	0,5–19 v	
		92%	Sukupuoli-identiteetti		
		54%	Sukupuolielämä		
de Cuypere ym. 2006, Belgia	35	85%	Yleinen ja toiminnallinen tyytyväisyys	4 v	1 katui toisinaan (psykoosi komorbiditeettina)
de Cuypere ym. 2005, Belgia	32	48%	Sukupuolielämä	4 v	3% hyvin tyytymättömiä vaginoplastiaan
		86%	Vaginoplastia		
Goddard ym. 2007, Britannia	70	80%	Yleinen ja toiminnallinen tyytyväisyys	3 v	
		76%	Kosmeettinen tulos		
de Roche ym. 2004, Sveitsi	9	89%	Yleinen ja toiminnallinen tyytyväisyys	0,7-8 v	
Revol ym. 2003, Ranska	22	7,6/10	Yleinen ja toiminnallinen tyytyväisyys	3,5	
		8,0/10	Kosmeettinen tulos		
		7,0/10	Sukupuolielämä		
	63			1-10 v	13%:lla vakavia komplikaatioita (nekrooseja, fisteleitä)
Rauchfleisch ym. 1998, Saksa	13			5-20 v	3/13 katui, 8 ei kokenut seksuaalista nautintoa. Kahdelle tehty palautusleikkaus. 3:lla virtsaamisvaivoja, joihin korjausleikkaus. 4:llä häiritsevää karvoitusta emättimessä.

Transmiehet (FtM)

Tekijä, vuosi, maa	Osallistujien lkm	Tyytyväisiä % tai tasopisteet hoidon jälkeen	Tyytyväisyyden aihe tai kohde	Seuranta-aika	Katuminen, haitat ja tyytymättömyys hoidon jälkeen
Özata ym. 2018, Turkki	9	78%	Yleinen ja toiminnallinen tyytyväisyys	>1 v	2/9 toivoi uusintaleikkausta sukuelinten ulkonäön parantamiseksi.
Garcia ym. 2014, Britannia	25	9/10	Falloplastia	2-6 v	Kukaan ei katunut
Vukadinovic ym. 2014, Serbia	97	100%	Yleinen ja toiminnallinen tyytyväisyys (virtsaaminen)	2,5 v	4% tyytymättömiä ulkonäköönsä metoidioplastian jälkeen, 5% tyytymätön sukupuolielämään. 11%:lle kosmeettisia toimenpiteitä. 8%:lla vakavia komplikaatioita (virtsaputken fisteli, kurouma), 28%:lla lievempiä komplikaatioita (useimmiten uretroplastiaan liittyviä).
		84%	Kosmeettinen tulos		
		88%	Metadoioplastia		
Leriche ym. 2008, Ranska	56	90%	Falloplastian kosmeettinen tulos	9 v	55% virtsaputken fisteli tai virtsaumpi, 25% kielekkeen komplikaatiot
		83%	Neofalloksen tuntoherkkyys		
		9%	Erogeeninen herkkyys		
		93%	Maskuliininen ulkoasu		
Hage ym. 2006, Alankomaat	70			8 v	89%:lla komplikaatioita (metoidioplastiasta), 33%:lla välittömiä komplikaatioita, 37%:lla virtsaputken fisteli, 37%:lla virtsaputken kurouma, 49%:lla kivesproteesin sijoiltaanmeno, 31%:lla virtsaputken menetys, 24%:lle falloplastia lisätoimenpiteeksi
Lobato ym. 2006, Brasilia	1				Kukaan ei katunut
Zimmermann ym. 2006, Saksa	16	88%	Yleinen ja toiminnallinen tyytyväisyys	0,5-19 v	
		100%	Sukupuoli-identiteetti		
		60%	Sukupuolielämä		
de Cuypere ym. 2006, Belgia	27	89%	Yleinen ja toiminnallinen tyytyväisyys	8 v	1 katui
de Cuypere ym. 2005, Belgia	23	76%	Sukupuolielämä	6 v	19% oli tyytymättömiä sukupuolielämään. Kukaan ei ollut hyvin tyytymätön falloplastiaan.
		89%	Falloplastia		
de Roche ym. 2004, Sveitsi	4	100%	Yleinen ja toiminnallinen tyytyväisyys	0,7-8 v.	

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Liite 4 Mittarit

AAI = Appraisal of Appearance Inventory on mittari, jolla ammattilainen arvioi kohdehenkilön feminiinisiä tai maskuliinisia piirteitä 14 ominaisuuden perusteella: hiukset, kasvojen karvoitus, nielu, ääni, figuuri, pituus, iho, kädet/jalat, lihaksikkuus, posket, nenä, leuka, puhe ja eleet/liikkeet. Kuhunkin osioon vastataan 0–5. Mitä pienempi lukuarvo, sitä paremmin ulkonäkö vastaa uutta sukupuolta.

ABCL = Child/Adult Behavior Checklist. Katso CBCL/ABCL = Child/Adult Behavior Checklist.

ACT = The Affective Communication Test. Mittaa ei-verbaalisia ilmaisutapaa. Kyselyssä kuvataan 13 tilannetta tapahtumasta ja siitä miten henkilö itse reagoin siihen. Kunkin kohdalla vastaaja arvioi 9-portaisesti missä määrin hän on samaa mieltä tai eri mieltä. Yhteispisteet 13-117. Suuremmat pisteet merkitsevät enemmän ei-verbaalista tunteiden ilmaisua. Naisilla pisteet ovat yleensä suuremmat. Lähde: Friedman, H.S., Prince, L.M., Riggio, R.E., and DiMatteo, M.R. (1980) Understanding and assessing nonverbal expressiveness: the Affective Communication Test. Journal of Personality and Social Psychology, 39: 333-351.

AIM= The Affect Intensity Measure. Itse täytettävä kysely, 40 kysymystä tunteiden kokemisen voimakkuudesta. Kutakin esimerkkiväitettä arvioidaan 6 pisteen asteikolla: 1 (ei koskaan)- 6 (aina). Yhteispisteet 40-240. Erikseen on pisteytykset negatiivisten tunteiden (kuten syyllisyys ja häpeä) kokemisen voimakkuudelle, 12 kohtaa, yhteispisteet 12-72 ja positiivisten tunteiden (kuten onnellisuus ja innostus) kokemisen voimakkuudelle, 28 kohtaa, yhteispisteet 28-168. Suuremmat pisteet merkitsevät enemmän tunteellisuutta. Naisten on todettu kokevan sekä positiiviset että negatiiviset tunteet voimakkaammin kuin miehet. Lähde: Larsen, R.J. and Diener, E. (1987) Affect intensity as an individual difference characteristic: a review. Journal of Research in Personality, 21: 1-39.

ASQ=The Short Anger Situation Questionnaire. Mittari vihaisuudelle, negatiivisille tunteille ja vihastustaipumuksille. Lomakkeessa kuvataan 17 tilannetta, joissa henkilön tulee kuvitella olevansa. Jokaisessa on kolme kysymystä, joihin voi vastata 5 portaisesti. Kysymykset: Mitä tunnet tilanteessa? (1= ei mitään- 5 = vihainen), 2) kuinka voimakas tunteesi on? (1= tuskin mitään- 5= hyvin voimakas) ja 3) mitä olet taipuvainen tekemään tällaisessa tilanteessa? (5 toimintavaihtoehtoa). Negatiivisten tunteiden voimakkuus (ASQ Emot. Intens) on 2-pisteiden keskiarvo silloin kun henkilö on vastannut 1-kysymykseen vastauksilla 2-4 (surullisuus, avuttomuus, pettymys). Vihaisuuden voimakkuus (ASC Anger Intens.) on 2-pisteiden keskiarvo silloin kun henkilö on vastannut 1-kysymykseen vastauksella 5 eli vihainen. Valmius vihaisuuteen (ASQ Anger Readiness) lasketaan itsevarmuutta ja agressiivisuutta kuvaavien vastusten prosenttiosuustena. Suuremmat pistemäärät viittaavaat voimakkaampaan vihaisuuteen tai aggressiivisen käyttäytymiseen. Koska kysely oli aluksi suunniteltu naisten vihaisuuden tutkimiseen, monet esimerkkitilanteet liittyvät enemmän naisia vihastuttaviin tilanteisiin. On todettu naisten saavan miehiä suuremmat pisteet tästä kyselystä. Lähde: Van Goozen, S.H.M., Frijda, N.H., Kindt, M., and Van de Poll, N.E. (1994) Anger proneness in women: development and validation of the Anger Situation Questionnaire (ASQ). Aggressive Behavior, 20: 79-100.; Van Goozen S.H.M., Cohen-Kettenis, P.T., Gooren, L.J.G., Frijda, N.H., and Van de Poll, N.E. (1995) Gender differences **in behavior: activating** effects of cross-gender hormones. Psychoneuroendocrinology, 20: 343-363**.**

BDI = Beck depression index, Beckin depressiokysely. Itse täytettävä kyselylomake, joka on kehitetty alunperin masennusoireiden vaikeusasteen arviointiin kliinisessä tilanteessa. Beckin depressiokyselystä on olemassa useita kansainvälisiä versioita, joista vakiintuneessa kliinisessä käytössä Suomessa on 21-osioinen, Terveysportista löytyvä versio (Beck ym. 1979). Sen antama pistemäärä voidaan luokitella seuraavasti: 1–9 = ”ei masennusta” , 10–18 = ”lievä masennus”, 19–29 = ”keskivaikea masennus”, 30–63 = ”vaikea masennus”. http://www.thl.fi/toimia/tietokanta/mittariversio/83/. BDI:n käytön ongelmana ovat erilaiset käännösversiot, vaihtelevat seularajat ja tarkastelujaksot. Lähde: Beck AT, Rush AJ, Shaw BF, Emery G. Cognitive therapy of depression. Guilford Press, New York 1979.

BIS = Body Image Scale, jossa 30 kysymystä, joihin vastataan asteikolla 1–5. Suurempi tulos kuvaa suurempaa tyytymättömyyttä kehonkuvaan. Erotellaan ensisijaiset ominaisuudet (esim. rinnat, sukuelimet), toissijaiset (esim. lantio, karvoitus) ja neutraalit (esim. kasvot, pituus). (Lähde: Lindgren TW, Pauly IB. A body image scale for evaluating transsexuals. Arch Sex Behav 1975;4:639-656.

BREAST-Q. Elämänlaatua ja tyytyväisyyttä rintaleikkauksen jälkeen mittaava mittari. Elämänlaatu ja tyytyväisyys koostuvat molemmat kolmesta osa-alueesta: psykososiaalinen hyvinvointi, fyysinen hyvinvointi ja seksuaalinen hyvinvointi, sekä tyytyväisyys rintoihin, tyytyväisyys tulokseen ja tyytyväisyys annettuun hoitoon. Tiedot syötetään BREAST-Q-ohjelmaan, joka muuttaa ne skaalaksi 0–100; isompi lukema merkitsee parempaa tulosta. Lähde: Dean, N.R. & Crittenden, T. (2016) A five year experience of measuring clinical effectiveness in a breast reconstruction service using the BREAST-Q patient reported outcome measure: A cohort study. Journal of Plastic, Reconstructive & Aesthetic Surgery, 69, 1469-1477.

BSRI = Bem Sex Role Inventory. Tutkittava arvioi 60 persoonallisuudenpiirrettään 7-portaisella Lickertin asteikolla ja määrittää näin maskuliiniset ja feminiiniset piirteensä erillisinä osa-alueina. Lähteet: 1) Bem S. The measurement of psychological androgyny. Journal of Consulting and Clinical Psychology 1974, 42, 155-162. 2) Bem S. On the utility of alternative procedures for assessing psychology androgyny. Journal of Consulting and Clinical Psychology, 1977. 45, 196-205.

BUT-A = The Body Uneasiness Test. Kehoahdistuksen mittari. Itse täytettävä kysely, jossa 71 kysymystä, joihin vastaukset annetaan 6-portaisella Likert-skaalalla. Koostuu kahdesta osasta: BUT-A (mittaa painofobiaa, huolta kehonkuvasta, välttelevä käytöstä, pakonomaista itsetarkkailua ja depersonalisaatiota (irrallisuutta omasta kehosta)) ja BUT-B (mittaa huolta tietyistä kehon osista tai toiminnoista). Yhteistuloksena on BUT GSI, Global Severity Index, missä suurempi numero merkitsee suurempaa kehoahdistusta. Lähde: Cuzzolaro M, Vetrone G, Marano G, Battacchi MW. BUT, Body Uneasiness Test: a new attitudinal body image scale. Psichiatr Infanz Adolesc . 1999;66:417–428.

CBCL/ABCL = Child/Adult Behavior Checklist. Kysely lapsille / aikuisille lapsen ongelmakäyttäytymisen tunnistamiseen. Lapsen kyselyn (6–18v.) täyttää lapsen läheinen aikuinen. Yhteensä 118 kysymystä, kuhunkin kysymykseen vastataan asteikolla 0–2. Kysymykset liittyvät käyttäytymiseen, koulusuoriutumiseen ja vuorovaikutukseen. Tuloksia ryhmitellään ”sisäisiin” (ahdistus, masennus, vetäytyminen, somaattiset vaivat) ja ”ulkoisiin” (sääntöjen rikkominen, aggressiivisuus). Pisteet on skaalattu siten että 50 merkitsee iän- ja sukupuolenmukaista keskiarvoa. Kokonaispistemäärä >63 osoittaa kliinisesti merkittävää ongelmakäyttäytymistä. Lähde: Achenbach TM, Edelbrock CS. Manual for the Child Behavior Checklist and Revised Child Behavior Profile. Burlington, VT: University of Vermont, Department of Psychiatry; 1983.

CCEI = Crown Crisp Experiential Index. Koostuu 48 kysymyksestä, joilla mitataan erityyppistä psykoneuroottista oireilua. Kyselystä lasketaan kuusi asteikkopistemäärää (vapaa ahdistus, foobisuus, pakkoneuroottisuus, ahdistuksen somatisointitaipumus, masentuneisuus, hysteerisyys), jotka kukin koostuvat kahdeksasta osiosta. Lähde: Crown S. & Crisp A. (1979) Manual of the Crown Crisp Experiential Index. London: Hodder & Stoughton.

CL = the Cantril Ladder, jossa vastaaja arvioi elämäänsä asteikolla 0 (äärimmäisen huono) –10 (erinomainen). Lähde: Cantril H. The pattern of human concern. New Brunswick, NJ: Rutgers University; 1965.

CGAS = Children’s global assessment scale mittaa lapsen/nuoren toimintakykyä skaalalla 0–100. Suurempi luku viittaa parempaan toimintakykyyn. Lähde: Shaffer D, Gould MS, Brasic J, et al. A children’s global assessment scale (CGAS). Arch Gen Psychiatry. 1983;40(11):
1228–1231

DSQ = Defensive Style Questionnaire, Brazilian Portuguese version on itsearviointikysely, jonka 40 kysymystä mittaavat taipumusta eri puolustusmekanismeihin. Kysymykset voidaan ryhmitellä siten, että voidaan arvioida vastaajan taipumusta kypsään, neuroottiseen ja epäkypsään puolustustyyliin. Kysymyksiin vastataan 10-portaisella Lickert-asteikolla (1−9). Lähde: Blaya C, Kipper L, Heldt E, Isolan L, Ceitlin LH, Bond M, Manfro GG. Brazilian-Portuguese version of the Defense Style Questionnaire (DSQ-40) for defense mechanisms measure: a preliminary study. Rev Bras Psiquiatr. 2004;26(4):255-8.

EAT-40. Mittari syömishäiriön riskin arviointiin. Itse täytettävä 40-kohtainen kysely, joka pyrkii tunnistamaan poikkeavia syömiseen liittyviä asenteita ja käytösmalleja. Vastaukset annetaan asteikolla 1= ei koskaan, 6= aina. Kokonaispisteet 0-120, suuremmat pisteet merkitsevät enemmän häiriöitä syömiseen liittyvissä asenteissa ja

käyttäytymisessä. Pisteet yli 30 merkitsevät kohonnutta syömishäiriön riskiä. Lähde: Garner, D. M., & Garfinkel, P. E. (1979). The Eating Attitudes Test: An index of the symptoms of anorexia nervosa. Psychological Medicine, 9, 273–279.

Ferriman-Gallway. Karvan kasvun mittari. Karvan kasvua arvioidaan 9 alueella: ylähuuli, posket, yläselkä, alaselkäkyynärvarsi, olkavarsi ja kyynärvarren takaosa, reidet ja sääret. Kussakin pisteytys 0-4: 0 merkitsee ei karvan kasvua, 1 vähäistä, 2 kohtalaista, 3 tiheää ja 4 hyvin tiheää karvan kasvua. Kokonaispistemäärä on 0-36: alle 8 on normaali, 8-15 on lievää hirsutismia, yli 15 on kohtalaista tai voimakasta hirsutismia. Lähde: Ferriman D, Gallwey JD: Clinical assessment of body hair growth in women. Journal of Clinical Endocrinology 1961; 21:1440–1447.

FPI / FPI-R = Freiburg Personality Inventory. 12 osioon jaettu elämänlaadun mittari, joka koostuu kaiken kaikkiaan 138 väittämästä, joihin vastataan ”oikein” tai ”väärin”. Kutakin osiota voi käyttää myös itsenäisesti. Osio Emotionality arvioi potilaan emotionaalista tilaa, stressinhallintakykyä, ahdistuneisuutta ja luonnetta. Pisteet 0–4 viittaavat hyvään emotionaalisesti tasapainoon, 5–7 tasapainoon ilman käytösoireita ja 8–14 ongelmalliseen epätasapainoon. Lähde: Fahrenberg J, Hampel R, Selg H. Das Freiburger Persönlichkeitsinventar FPI. Revidierte Fassung FPI-R und teilweise geänderte Fassung FPI-A1. Göttingen: Hogrefe-Verlag; 1994.

GAD-7 = Generalized Anxiety Disorder. 7 kysymyksen ahdistuneisuuskysely. Kysymykset asteikolla 0–3, yhteisskaala 0–21. Pisteistä 5–9 viittaa lievään, 10–15 kohtalaiseen ja 16–21 vaikeaan ahdistuneisuuteen. Lähde: http://www.thl.fi/toimia/tietokanta/mittariversio/109/; Kurt Kroenke, Robert L.Spitzer, Janet B.W.Williams, Bernd Löwe. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. General Hospital Psychiatry. Volume 32, Issue 4, July–August 2010, Pages 345-359.

GHQ = GHQ-12, 12-item General Health Questionnaire. Mittarin osiot kartoittavat psyykkisen kuormittuneisuuden aiheuttamia ongelmia normaaleista toiminnoista suoriutumisessa. Osiot käsittelevät ahdistuneisuutta ja masentuneisuutta, sosiaalista kanssakäymistä ja itseluottamusta. Vastausasteikko osioissa on Likert-asteikko, joka vaihtelee välillä 0–3. Lähde: Goldberg, D. P. and Williams, P. A user's guide to the General Health Questionnaire. NFER-Nelson, 1978.

GIDYQ-AA = Gender Identity/Gender Dysphoria Questionnaire for Adolescents and Adults. Itse täytettävä kysely, 27 kysymystä kokemuksista viimeisen 12 kuukauden ajalta, joihin vastataan 5-portaisella skaalalla. Aiheet liittyvät henkilökohtaiseen sukupuolityytyväisyyteen, sosiaalisiin tilanteisiin, kehollisiin oireisiin ja laillisen aseman hankkimiseen. Alemmat pisteet merkitsevät enemmän sukupuoliahdistusta. Tulos alle 3 pistettä viittaa vahvasti sukupuoli identiteetin poikkeamaan (sensitiivisyys 90,4%, spesifisyys 99,7%). Lähde: Deogracias JJ, Johnson LL, Meyer-Bahlburg HF, Kessler SJ, Schober JM, Zucker KJ. The gender identity/gender dysphoria questionnaire for adolescents and adults. J Sex Res . 2007;44:370–379.

HADS = The Hospital Anxiety And Depression Scale. Pisteytys 0-21, erikseen masennukselle ja ahdistuneisuudelle, isompi numero merkitsee enemmän oireita. Lähde: Snaith RP. The Hospital Anxiety And Depression Scale. Health Qual Life Outcomes. 2003; 1: 29.

IIP = Inventory of Interpersonal Problems. Mittaa vahingollisia käyttäytymismalleja ihmistenvälisissä suhteissa. Koostuu 127:stä kysymyksestä, jotka on jaettu kahteen osa-alueeseen: ihmistenväliset puutteet ja estot (78 kysymystä) ja kohtuuttomuudet ja pakko-oireet (49 kysymystä). Analysoi kahdeksaa eri piirrettä: dominoimista / kontrolloimista, kostonhaluisuutta / itsekeskeisyyttä, kylmyyttä / etäisyyttä, sosiaalista estyneisyyttä, epävarmuutta, liikaa sopeutuvaisuutta, uhrautuvuutta ja tungettelevuutta / tarvitsevuutta. Osallistujat vastaavat kysymyksiin asteikolla 0–4. Lähteet: Horowitz, L. M., Rosenberg, S. E., Baer, B. A., Ureno, G., & Villasenor, V S. (1988). Inventory of interpersonal problems: Psychometric properties and clinical applications. Journal of Consulting and Clinical Psychology, 56, 885-892.; Horowitz, L. M., Rosenberg, S. E., & Bartholomew, K. (1993). Interpersonal problems, attachment styles, and outcomes in brief dynamic psychotherapy. Journal of Consulting and Clinical Psychology, 61, 549-560.

IPSS = International Prostate Symptom Score on 7-osainen virtsaamisoirekysely, jossa <7 tulos viittaa lieviin, 8–18 keskivaikeisiin ja >18 vaikeisiin oireisiin. Lähde: Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992;148:1549-1557.

MINI = Mini International Neuropsychiatric Interview on mielenterveyshäiriöitä kartoittava haastattelu, joka sisältää masennuksen, dystymian, bipolaarihäiriön, itsetuhoisuuden, paniikkihäiriön, julkisten paikkojen, sosiaalisen ja määräkohteisen pelon, pakko-oireisen häiriön, yleistyneen ahdistuneisuushäiriön, päihteiden väärinkäytön ja riippuvuuden (huumeet ja alkoholi erikseen), syömishäiriöiden, posttraumaattisen stressihäiriön, psykoottisen oireilun sekä antisosiaalisen persoonallisuushäiriön kartoittamisen. MINI-diagnoosit on jaettu eri osa-alueisiin (yllä mainitut) ja tarkentaviin kysymyksiin siirrytään vasta, mikäli seulontakysymykset viittaavat häiriöön. Mittarista voidaan käyttää myös tiettyyn osa-alueeseen kohdistuvaa sovellusta. Lähteet: Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59:22–33. Amorim P. Mini International Neuropsychiatric Interview (MINI): validation of a short structured diagnostic psychiatric interview. Rev Bras Psiquiatr. 2000;22:106–115.

MMPI = Minnesota Multiphasic Personality Inventory. Katso NVM. Standardoitu testi aikuisten persoonallisuuden ja psykopatologian testaukseen. Erilaisia versioita testistä käytetään muun muassa differentiaalidiagnostiikkaan, oikeuspsykologian kysymysten ratkaisuun, henkilökunnan valintaprosesseissa ja osana hoidollista arviointia. Versioita MMPI (1943), MMPI-2 (1989), MMPI-2-RF (2008), nuorille (14-18-vuotiaille) kehitelty versio MMPI-A (1992).

NVM = Dutch Short MMPI (Minnesota Multiphasic Personality Inventory). Mittari persoonallisuuden patologisten piirteiden arvioimiseen. Testissä on 83 väittämää (pitää paikkansa-ei pidä paikkaansa –tyyppistä), joista lasketaan pistemäärä viidelle kliinisesti määritellylle ominaisuudelle: negativismi (taipumus kokea negatiivisia tunteita, kuten ahdistusta ja huolta), somatisaatio (taipumus kokea lääketieteellisesti selittämättömiä somaattisia oireita), ujous (taipumus kokea hermostuneisuutta ihmissuhteissa ja hämmentyy helposti), vaikea psykopatologia ja ulospäinsuuntautuneisuus (taipumus kokea positiivisia tunteita sosiaalisissa tilanteissa). Kokonaispisteiden skaala 90-450, pienempi parempi. Pienempi parempi pätee myös osa-aluepisteiden tulkintaan paitsi ulospäinsuuntautuneisuutta kuvaaviin kysymyksiin, joissa isompi pistemäärä on parempi. Lähde: Luteyn F, Kok AR, van der Ploeg FAE (1980), NVM Nederlandse Verkorte MMPI, Handleiding. Lisse, the Netherlands: Swets en Zeitlinger.

PHQ = The Patient Health Questionnaire. Lyhyt mittari, joka mittaa stressiä, somaattisia oireita, ahdistusta ja masennusta. PHQ-9 (skaala 0-27), PHQ-15 –versiossa (skaala 0-30) sekä GAD-7:ssä (skaala 0-27) pisteet 5-10 viittaavat lieväoireiseen masennukseen/ahdistukseen/somaattiseen oireiluun, 10-15 kohtalaiseen, 15-20 kohtalaisen vaikeaan ja >20 pistettä vaikeaoireiseen oireiluun. .Lähde: Spitzer RL, Williams JW, Kroenke K. Patient Health Questionnaire—SADS.

PHQ-4 = Patient Health Questionnaire. Lyhyt masennuksen seulontaan ja masennusoireiden vakavuuden mittaukseen käytetty menetelmä. Pisteet >3 viittaavat masennushäiriöön, 3–5 lieväasteinen masennushäiriö, 6–8 keskivaikea masennushäiriö, ≥9 vaikeaoireinen masennushäiriö. Lähde: Lowe B, Wahl I, Rose M, et al. A 4-item measure of depression and anxiety: Validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. J Affect Disord. 2010;122:86–95.

PHQ-9 = Patient Health Questionnaire. 9 kysymyksen kysely masennuksen vakavuuden seulontaan. Pisteet 0–4 ei lainkaan vakava / minimaalinen, 5–9 lievä, 10–14 keskivakava, 15–19 keskivakava / vakava, 20–27 vakava. Lähde: Kurt Kroenke, Robert L.Spitzer, Janet B.W.Williams, Bernd Löwe. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. General Hospital Psychiatry. Volume 32, Issue 4, July–August 2010, Pages 345-359.

PHQ-15 = Patient Health Questionnaire. 15 kysymyksen kysely somaattisten oireiden ja niiden vakavuuden seulontaan. Skaala 0–30. Lähde: Kurt Kroenke, Robert L.Spitzer, Janet B.W.Williams, Bernd Löwe. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. General Hospital Psychiatry. Volume 32, Issue 4, July–August 2010, Pages 345-359.

PHQ-SADS = Patient Health Questionnaire - Somatic, anxiety, and depression symptoms. Laajennettu PHQ-kysely mittaamaan somaattisia, ahdistus- ja masennusoireita. Sisältää kyselyt PHQ-9, GAD-7 ja PHQ-15 sekä kysymyksiä paniikkikohtauksista. Eri osa-alueiden kysymyksiin vastataan asteikolla 0–3. Oireiden vakavuus

yhteispisteiden mukaan: 0–4 minimaalinen, 5–9 lievä, 10–14 keskivaikea, ≥15 vaikea. Lähde: Kurt Kroenke, Robert L.Spitzer, Janet B.W.Williams, Bernd Löwe. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. General Hospital Psychiatry. Volume 32, Issue 4, July–August 2010, Pages 345-359.

Physical Appearance Scale. Mittaa arvioijan havaintoja henkilön maskuliinisesta/feminiinisestä ulkomuodosta. 14 kysymystä, joihin vastataan asteikolla 1–5 (1 = hyvin feminiininen, 5 = hyvin maskuliininen). Pisteet luokitellaan syntymäsukupuolen ja koetun sukupuolen mukaan. Korkeammat pisteet merkitsevät ulkomuodon heikompaa yhdenmukaisuutta koetun sukupuolen kanssa (”passing”). Tulokset, joiden yhteispisteiden arvo on yli 42, merkitsevät, että ulkomuoto on yhdenmukaisempi syntymäsukupuolen kuin koetun sukupuolen kanssa. Lähde: van de Grift TC, Elaut E, Cerwenka SC, Cohen-Kettenis PT, De Cuypere G, Richter-Appelt H, Kreukels BPC. Effects of Medical Interventions on Gender Dysphoria and Body Image: A Follow-Up Study. Psychosom Med. 2017 Sep;79(7):815-823.

PSS = Perceived Stress Scale. Itse täytettävä kysely, 10 kysymystä. Yhteispisteet 0 (alhainen koettu stressi) – 40 (korkea koettu stressi). Lähde: Cohen S, Williamson G. Perceived stress in a probability sample of the United States. In: Spacapan S, Oskamp S, eds. Social psychology of health. Newbury Park, CA: Sage;1988:31–68.

QLS = The Questions on Life Satisfaction, Modules (German version) on standardoitu elämänlaadun mittari, joka koostuu kolmesta osa-alueesta: yleinen tyytyväisyys, terveyteen liittyvä tyytyväisyys ja kehonkuvaan liittyvä tyytyväisyys. Jokainen osio koostuu alakysymyksistä ja vastaaja arvioi kunkin alakysymyksen tärkeyden itselleen ja kokemansa tyytyväisyyden skaalalla -12–20; -12 = vähiten tyytyväinen ja 20 = erittäin tyytyväinen. Mittarin saksalaiset väestöarvot ovat saatavilla yleisen ja terveyteen liittyvän tyytyväisyyden osalta. Lähde: Papadopulos N, Zavlin D, Lellé JD, Herschbach P, Henrich G ym. Male-to-Female Sex Reassignment Surgery Using the Combined Technique Leads to Increased Quality of Life in a Prospective Study. Plast. Reconstr. Surg. 140: 286, 2017.

RSES = **Rosenberg self-esteem scale** on itsetuntoa kartoittava mittari, jonka skaala on 10–40. Tarkkoja lukuarvoja tulkinnalle ei anneta, mutta <15 voi viitata ongelmallisen heikkoon itsetuntoon. Lähde: Schmitt DP, Allik J. Simultaneous administration of the Rosenberg Self-Esteem Scale in 53 nations: Exploring the universal and culture-specific features of global self-esteem. J Pers Soc Psychol. 2005;89:623–642.

RSQ = Response Styles Questionnaire tai RRS The ruminative response scale on potilaan omaan arvioon perustuva mittari, joka kuvaa henkilön vastetta masentuneeseen olotilaan. Ruminaatio merkitsee märehtimistä. Mittari koostuu 22 kysymyksestä ja kolmesta osatekijästä (masennus, murehtiminen ja reflektio). Jokaiseen kysymykseen vastataan 4-portaisella Lickert-asteikolla, jossa 1 = ei koskaan ja 4 = aina. Kokonaistulos voi olla välillä 22–88; mitä suurempi lukuarvo sitä korkeampi on ruminaatio-oireiden aste. Mittarista käytetään myös sovelluksia, joissa on mukana vain yhtä tai kahta osatekijää koskevat kysymykset. Lähteet: Treynor W, Gonzalez R, Nolen-Hoeksema S. Rumination reconsidered: a psychometric analysis. Cognit Ther Res. 2003;27:247–259. Lei X, Zhong M, Liu Y, Xi C, Ling Y ym. Psychometric properties of the 10-item ruminative response scale in Chinese university students. BMC Psychiatry. 2017; 17: 152. Published online 2017 Apr 28. doi: 10.1186/s12888-017-1318-

SAS= Zung Self-Rating Anxiety Scale. Itse täytettävä kysely, 20 kysymystä koskien yleiseen ahdistuneisuuteen viittaavia oireita edeltävän viikon ajalta. Vastaukset annetaan neljäportaisella asteikolla: 1 = ei oireita ja 4= vaikeita oireita. Yhteispistemäärä 20-80 jaetaan 80:llä ja kerrotaan 10:lla jotta saadaan indeksi 25 (vähäinen ahdistuneisuus) – 100 (vaikea ahdistuneisuus). Indeksiä 45 ehdotettu kliinisesti merkityksellisen ahdistuneisuuden rajaksi. Lievä-kohtalainen ahdistuneisuus = 45-59, merkittävä tai vaikea ahdistuneisuus 60-74, hyvin vaikea ahdistuneisuus = 75 tai suurempi. Lähde: Zung, W.W.K., 1971. A rating instrument for anxiety disorders. Psychosomatics 12, 371—379.

SDS= Zung Self-Rating Depression Scale. Itse täytettävä kysely, 20 kysymystä, mittaa depression oireiden vaikeutta nyt tai edeltävän viikon aikana henkilöillä, joilla on todettu depressio. Käytetty myös tutkimuksissa hoidon tehon seurannassa. Vastaukset annetaan neljäportaisella asteikolla: 1 = ei oireita ja 4= vaikeita oireita. Yhteispistemäärä 20-80 jaetaan 80:llä ja kerrotaan 10:lla jotta saadaan indeksi 25 (vähäinen masennusoireilu) – 100 (vaikea oireilu). Indeksiä alle 50 pidetään normaalina. Lieväoireinen masennus 50-59, kohtalainen 60-69, vaikea yli 70. Lähde: Zung, W.W.K., 1967. Factors influencing the Self-Rating Depression Scale. Arch. Gen. Psychiatry 16, 543—547.

SCID-I = Structured Clinical Interview for DSM-IV-TR Axis-I Disorders. Lähde: Michael B., Williams Janet B.W., Spitzer Robert L., and Gibbon, Miriam: Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Clinical Trials Version (SCID-CT). New York: Biometrics Research, New York State Psychiatric Institute, 2007

SCL-90-R. Symptom Checklist-90-Revised. Psykologisten oireiden ja psykologisen stressin tai psykoneuroottisuuden mittari. Voidaan käyttää terveiden seulontaan tai erilaisissa sairaustiloissa. Itse täytettävä kysely, 90 kysymystä 9 alueelta: masennus, ahdistuneisuus, somatisaatio, paranoidiset ajatukset, psykoottiset piirteet, herkkyys ihmissuhteissa, vihamielisyys, pakko-oireisuus ja fobiat. Kysymyksiin vastataan 5-portaisella asteikolla. Yhteispistemäärä ilmaistaan käsitteillä GSI global severity index, PSDI Positive Symptom Distress Index tai PST Positive Symptom Total. Korkeammat pisteet merkitsevät enemmän psykopatologiaa. Mittaria on käytetty mm. Mini-Suomi- ja Terveys 2000-tutkimuksissa. Suomen väestötason GSI arvo 0,65 ja mielenterveyden avopotilailla 1,56. Lähteet: Derogatis LR. SCL-90-R: Administration, Scoring and Procedure Manual—II. Towson, MD: Clinical Psychometric Research; 1992. Matti Holi. Assessment of psychiatric symptoms using the SCL-90. Academic dissertation, University of Helsinki 2003. https://helda.helsinki.fi/bitstream/handle/10138/22453/assessme.pdf?sequence=2

SF-36 = The Short Form (36) Health Survey. Terveyteen liittyvän elämänlaadun mittari, joka koostuu kahdeksasta osiosta, jotka sisältävät kysymyksiä liittyen fyysiseen toimintakykyyn, fyysiseen roolitoimintaan, kivuttomuuteen, koettuun terveyteen, sosiaaliseen toimintakykyyn, psyykkiseen roolitoimintaan, psyykkiseen hyvinvointiin ja tarmokkuuteen. Kussakin osiossa pisteet 0-100: suurempi pistemäärä kertoo paremmasta tuloksesta. Lähde: Ware J Jr, Kosinski M, Keller SD. 1996. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 34(3), 220–33. http://www.thl.fi/toimia/tietokanta/mittariversio/143/

SHS = the Subjective Happiness Scale on 4 kysymystä käsittävä mittari, johon vastataan 1−7 Lickertin asteikolla. Suurempi tulos viittaa suurempaan onnellisuuteen. Lähde: Lyubomirsky S, Lepper HS. A measure of subjective happiness: preliminary reliability and construct validation. Soc Indicat Res 1999;46:137-155.

STAI = State-Trait Anxiety Inventory. Ahdistuneisuuden itsearviointimittari. Sisältää kaksi osaa: nykyiset oireet ja yleinen taipumus ahdistuneisuuteen. Kummassakin osassa 20 kysymystä, yhteensä 40 kysymystä. Kummankin osan pisteskaala on 20-80, suurempi pistemäärä kertoo vaikeammasta ahdistuneisuudesta. Nykyoireita kuvaavassa osassa pistemäärä 39-40 katsotaan edustavan kliinisesti merkittävää ahdistuneisuutta, iäkkäämmillä pisteraja lienee lähempänä 54-55-tasoa. Lähde: Spielberger C. Manual for the State-Trait Anxiety Inventory. rev. ed. Consulting Psychologists Press; Palo Alto (CA): 1983.

STAXI-2 = Spielberger's State-Trait Anger Expression Inventory. Itse täytettävä 56-osainen kysely, joka mittaa aggressiivisuuden voimakkuutta, esiintymistä ja hallintakeinoja. Vastaukset annetaan 4-portaisesti (ei lainkaan – melkein aina). Tuloksena yleisarvio (Anger Expression Index) ja kuusi alaryhmää: aggression voimakkuus, yleisyys, ilmaisu, peittäminen, hallinta ilmaisua lieventämällä ja hallinta rauhoittelulla. Lähde: Charles Donald Spielberger. STAXI-2 : State-Trait Anger Expression Inventory-2 : professional manual. Odessa 1999.

SWLS = the Satisfaction With Life Scale on 5-portainen mittari, jossa suurempi tulos viittaa suurempaa tyytyväisyyteen. Lähde: Diener ED, Emmons RA, Larsen RJ, et al. The satisfaction with life scale. J Pers Assess 1985;49:71-75.

ToL= Tower of London test. Neuropsykologinen testi, joka mittaa erityisesti käyttäytymisen hallinnassa tärkeitä ominaisuuksia: huomion kiinnittämistä, työmuistia, ongelmanratkaisutaitoja ja kognitiivista joustavuutta. Lähde: Shallice, T. (1982). "Specific impairments of planning". Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences. 298 (1089): 199–209.

TPI = Spielberger's Trait Anger. Vihan/kiukun itsearviointimittari, joka koostuu 10 kysymyksestä, joihin vastataan asteikolla 1–4. Suurempi pistemäärä kertoo suuremmasta taipumuksesta vastata ärsykkeisiin vihalla. Lähde: Spielberger CD. Manual for the State-Trait Anger Expression Inventory (STAXI). Odessa, FL: Psychological Assessment Resources; 1988.

UGDS = Utrecht Gender Dysphoria Scale koostuu 12 väittämästä, joihin vastataan 5-portaisella asteikolla 1–5, kokonaispistemäärän skaala 12–60. Mitä suurempi lukuarvo, sitä vahvempi sukupuolidysforia vastaajalla on. Cohen-Kettenis PT, van Goozen SHM (1997), Sex reassignment of adolescent transsexuals: a follow-up study. J Am Acad Child Adolesc Psychiatry 36:263–271.

VHI = Voice Handicap Index. Mittaa äänenkäyttäjän käsitystä ääniongelmistaan ja ääneen liittyvää toimintakykyisyydestään. Kaikkien osa-alueiden kumulatiivisen VHI-arvon maksimi on 120. Eri osa-alueiden maksimi on 40. Lähde: Jacobson, B. H., Johnson, A., Grywalski, C., Silbergleit, A., Jacobson, G., Benninger, M. S. & Newman C. W. (1997). The Voice Handicap Index (VHI): development and validation. American Journal of Speech-Language Pathology, 6, 66–70.

Wagnild and Young Resilience Scale, suom. resilienssiasteikko, mittaa resilienssin viittä ulottuvuutta: mielentyyneyttä, sinnikkyyttä, itseluottamusta, mielekkyyden tunnetta, ja olemassaolon ainutlaatuisuuden kokemusta. Mittarin 25 kysymykseen vastataan asteikolla 1–7, jossa 1 = Olen täysin eri mieltä ja 7 = Olen täysin samaa mieltä. Kokonaistulos voi olla välillä 25–175; mitä suurempi lukuarvo, sitä suurempi resilienssikapasiteetti hankilöllä on. Lähde: Wagnild GM, Young HM. Development and psychometric evaluation of the Resilience Scale. J Nurs Measurement 1993;1:165–78.

Wechsler Intelligence Scale on psykologinen testi, joka koostuu tehtävistä, joista suoriutumisen perusteella henkilön älykkyyttä arvioidaan. Älykkyystestin tulos pyrkii kuvaamaan testatun henkilön kognitiivisia kykyjä tilastollisesti keskiarvoon 100 suhteutettuna: tulos, joka on alle keskiarvon tarkoittaa keskimääräistä alhaisempaa älykkyyttä ja tulos, joka on yli keskiarvon kuvaa keskimääräistä korkeampaa älykkyyttä. Lähde: Wikipedia: https://fi.wikipedia.org/wiki/%C3%84lykkyysosam%C3%A4%C3%A4r%C3%A4

WHOQoL = The World Health Organization Quality of Life. Sensitiivinen ja laadukas mittari elämänlaadun mittaamiseen neljällä osa-alueella: psykologinen, terveyteen liittyvä, sosiaalinen ja ympäristöön liittyvä. Vastausvaihtoehdot Likert-asteikolla 1–5, josta ne lasketaan skaalapisteiksi joko 4-20 tai 0-100. Parempi tulos merkitsee parempaa elämänlaatua. Lähde: authorship i No. World Health Organization Quality of Life–BREF [Database record] (n.d). Retrieved from PsycTESTS.10.1037/t01408-000

WHOQoL = The World Health Organization Quality of Life, The Brazilian version. Sensitiivinen ja laadukas mittari elämänlaadun mittaamiseen kuudella ulottuvuudella: I) fyysinen terveys (kipu, energisyys, uni ja lepo), II) psykologinen (positiiviset tunteet, ajattelu, itsetunto, kehonkuva, ulkonäkö), III) itsenäisyys (liikkuminen, aktiviteetit, riippuvaisuudet, työkyky), IV) sosiaalinen (henkilökohtaiset suhteet, sosiaalinen tuki, seksuaalinen aktiivisuus), V) ympäristö (vapaus, fyysinen turvallisuus, kotiympäristö, taloudelliset resurssit, terveyden- ja sosiaalihuollon saatavuus ja laatu, vapaa-aika, fyysinen ympäristö, liikennöinti) sekä VI) hengellisyys, uskonto ja uskomukset. Vastausvaihtoehdot Likert-asteikolla 1–5, jossa korkeampi lukuarvo merkitsee parempaa elämänlaatua. Lähde: Fleck MP, Louzada S, Xavier M, et al. Application of the Portuguese version of the instrument for the assessment of quality of life of the World Health Organization (WHOQOL-100). Rev Saude Publica 1999;3:198-205.

YSR/ASR = Youth/Adult Self-Report. Katso CBCL/ABCL. Nuoren (11–18v.) itsensä täyttämä kysely, jonka tarkoitus on seuloa tunne-elämän ja käyttäytymisen ongelmia. 112 kysymystä, joihin vastaukset annetaan kolmiportaisella asteikolla (0-2). Tuloksia ryhmitellään ”sisäisiin” (ahdistus, masennus, vetäytyminen, somaattiset vaivat) ja ”ulkoisiin” (sääntöjen rikkominen, aggressiivisuus). Pisteet on skaalattu siten että 50 merkitsee iän- ja sukupuolenmukaista keskiarvoa ja kokonaispisteet >63 osoittaa kliinisesti merkittävää käytösongelmaa. Osa ASEBA-kyselylomakesarjaa. Lähde: Achenbach, Thomas M.; Rescorla, Leslie A. (2001). Manual for the ASEBA School-Age Forms & Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families. pp. 16–17.