HEALTH RELATED QUALITY OF LIFE OF TRANSGENDER ADOLESCENTS UNDERGOING HORMONAL TRANSITION OR ELECTIVE PUBERTAL DELAY

by
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DISSERTATION

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CHAPTER 1
Introduction

The health of adolescents who identify as transgender or gender non-binary has garnered a great deal of attention in the medical community in recent years. While the health of transgender adults is a field still in need of greater research, in comparison, the field of transgender adolescent health is still in its infancy[1]. The aim of this introduction is to lay groundwork for the current state of research in transgender health, transgender health of adolescents, and health related quality of life studies as well as to provide basic definitions to be used throughout this discussion.

Transgender Individuals and The Medical Community

Historically, the United States health system and the United States as a social structure has viewed gender as binary (male and female) and biological sex as an equivalent to gender (again male and female, assigned at birth). However, many societies throughout the ages have accepted a third gender or the notion of gender fluidity, meaning that an individual may identify as not just a third gender but may at different times in their experience identify as either male or female.[2] In these societies, the gender binary was not enforced to the degree it currently is in Western civilization, where the role of gender is tied to biological sex long before the fetus leaves the womb.[3] How the gender binary so fiercely developed in Western civilization is beyond the scope of this discussion, but how the medical community was influenced by the gender binary to dictate medical practices is pertinent. We must look back to set the stage for a discussion on current research and gaps in knowledge regarding care for transgender individuals, and particularly, those minors under the age of eighteen who are

therefore subject to different treatment as a result of age-restricted decision making capacity. [4]

Previously, transgender patients were treated with conversion therapy, aiming to realign the patients gender identity to be concordant with their sex assigned at birth.[2] The notion that these two elements of one's identity- one developed by the individual, the other typically determined by a physician at birth- could be discordant with one another was reacted to with great concern that placed the individual's identity at fault and valued the sex assigned at birth as the ideal biological model, and that their identity could be realigned with their sex assigned at birth through intensive, physically and emotionally painful therapy. This treatment is now considered to be inhumane and not recommended by any medical organization.[4, 5] This history of harmful psychotherapy created a backlash by the transgender community, and now standards of care are dictated by WPATH, the World Professional Association for Transgender Health, which has large participation from transgender individuals and strictly controls membership and publishing of guidelines.[6] The emergence of gender affirming care for adults has given way to groundbreaking work on gender affirming care for adolescents, as transgender adults have long advocated for strategies to prevent younger transgender individuals from experiencing the pubertal changes of their natal sex when their gender identity is not in alignment.[7] Transgender adults (and medical professionals) pushing for the availability of prepubertal interventions for adolescents provide as evidence how well transgender adults themselves have fared with gender affirming therapy, and transgender adults recount that they "knew" at an early age what their true gender identity

was, long before the dramatic changes of puberty. [8] The treatment methodology that has gained the most traction with WPATH and clinicians worldwide when treating transgender adolescents is called the Dutch Protocol, which is discussed in greater detail below.

For the purpose of this discussion, a few definitions are offered by the author. These are by no means an exhaustive list, but merely provide a groundwork for this discussion.

Definitions

Natal sex- sex assigned at birth

Transgender- when one's sex assigned at birth is not congruent with one's gender identity

Transgender Male- natal sex/sex assigned at birth female; gender identity male

Transgender Female- natal sex/sex assigned at birth male; gender identity female

Cisgender- when one's sex assigned at birth is congruent with one's gender identity

Gender affirming therapy- the individualized treatment process for a transgender individual that places the individual's gender identity and their unique needs and wishes for accomplishing an externalized version of that identity at the forefront of their care [6, 9]

Cross Sex Hormone Therapy- administration of manufactured hormones in a transgender patient to achieve the hormonal levels and their desired effects congruent with the patient's gender identity. For transgender females, this is the administration of estrogen. For transgender males, this is the administration of testosterone. [8]

Puberty blockers- first used in precocious puberty, these GnRH agonists are administered to transgender patients to delay the unwanted pubertal changes of their natal sex once they begin to show signs of puberty, which is different for every patient. Puberty blockers may be used

before beginning cross sex hormone therapy, which has been shown to have the greatest benefit to the transgender adolescent as well as the transgender adult.[10] [11]

Androgen blockers- useful in transgender women to decrease the effects of androgens in the body. Examples include Spironolactone.

Health Related Quality of Life Studies

The field of Health Related Quality of Life (HRQoL) emerged in the interest of trying to better quantify the experiences of patients and how their disease processes affected their activities of daily living, outlook on their future, and experience negotiating the world around them.[12] These studies measure the impact of disease on attributes of interest to the researcher and assigns numeric values to statements of opinion in a Likert scale. Many HRQL tools are available and in use in the world today, with the World Health Organization utilizing many different versions of their own tool worldwide in over twenty languages, and the Healthy People 2020 initiative by the United States' CDC includes questions regarding HRQL. While general HRQL tools have existed for over half a century, more and more disease-specific and population-specific (age group, ethnic group, etc) assessments are being validated and published, especially as pharmaceutical companies show interest in being able to prove HRQL benefits for new drugs that otherwise may not receive FDA approval.

GENECIS Clinic at Children's Medical Center, Dallas Texas

This clinic specializes in working with gender-nonconforming adolescents of all ages. The data utilized in this study focuses on patients from the GENECIS clinic enrolled in a

larger study collecting multitudes of data concerning all aspects of their gender experience and medical care. To quantify the HRQoL of the adolescents and their families engaging with the GENECIS clinic, the GENECIS research team determined at the beginning of their study to utilize a well-known and validated tool called the PedsQL, now in the third version. This tool was originally created to capture data regarding the experience of pediatric cancer patients, how their disease impacted their family, and how their family perceived the pediatric patient's daily quality of life had been affected by both disease and treatment. The GENECIS team chose this instrument because of its short length (so as not to burden patients too greatly with longer quality of life scales), validity in many age groups (child, adolescent, teen, young adult, which reflects the wide age range of GENECIS patients), and general applicability in language to this subject group.

GENECIS is one of over forty gender affirming health centers in the United States. Like GENECIS, most other health centers are located within large pediatric facilities and tend to be in large cities. Each facility has their own method of intake, and the intake process for new patients at GENECIS involves a lengthy phone interview, followed by a 3-4 hour in-person screening with a team of health providers including multiple physicians and a psychologist. Patients are then discussed in detail with a multidisciplinary panel of GENECIS employees, in which the goals of care for that individual and a care plan are suggested. Whether a patient receives gender affirming care alone or gender affirming care plus hormonal therapy in the form of pubertal suppression or cross-sex hormones will depend on the goals and age of the patient, the approval of the biological parents (or whomever is legal guardian), and the

discretion of the medical team. Great emphasis is placed on the patient's history of gender experience, mental health status, and support system.

Treatment at GENECIS follows what is known as The Dutch Protocol, as it was developed in the Netherlands.[13] This Protocol was developed to guide clinicians across the globe in providing gender affirming care to gender nonconforming or gender expansive youth of all ages. Briefly, the Dutch Protocol recommends blockade of gender expansive children at Tanner Stage 2, with administration of cross-sex hormones around age 16. The Dutch Protocol recommends surgery following cross-sex hormonal therapy, and not before, and importantly, many, but not all transgender adolescents do want to consider surgery.[10] Surgery is not widely considered a necessary step in transition by the transgender community, but this is not from lack of interest by the community towards surgical options in treatment of gender dysphoria. Current surgical methods are constantly being improved upon, and often the cost of surgery is a limiting factor as few states offer coverage of the surgery as a medically necessary procedure.

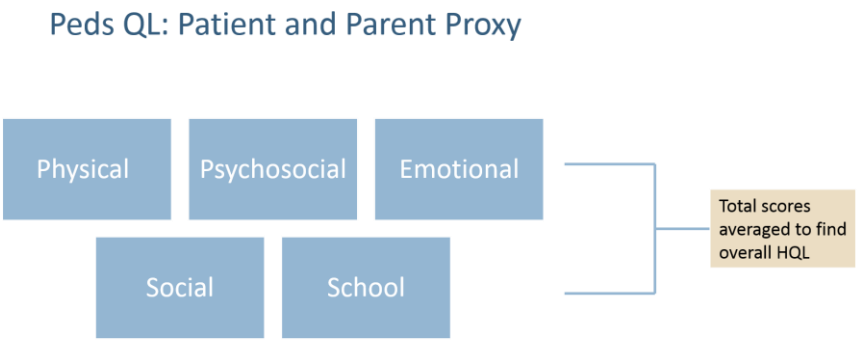
The PedsQL and Family Impact Tools

These HRQOL tools were developed in 1998 by Dr. James Varni, a well-known QOL researcher working with pediatric populations. In developing this tool, Dr. Varni specifically had an interest in pediatric cancer and how the treatments (radiation, chemotherapy), known to have their own vast side effect profile, deeply effected the physical, emotional, social, and school functioning of youth.[14] It has since been utilized to evaluate impact on QOL of a

wide variety of pediatric diseases. The survey was designed to be taken by the patient (adolescent, child, young adult, etc) with another proxy version to be taken by the patient's caregiver/parent. This parent proxy was an excellent comparison tool for how the child was functioning in their daily life from their point of view versus that of an adult. The language for both versions was held to be almost identical, with changes only from first to third person ('you/I' for children vs 'my child/my teen' for the parents). For example, the parent proxy has the phrasing changed to ask "how much of a problem has this been for your child" instead of their child's version which would read "how much of a problem has this been for you".

The wording also includes slight changes based on the age of the patient. For example, in the Social domain the phrase "I have trouble getting along with other kids" becomes "I have trouble getting along with other teens" for the teen group, and the "About School" category asks questions about work for young adults. For the young child survey, emoticons of smiling to frowning faces are used instead of a Likert scale.

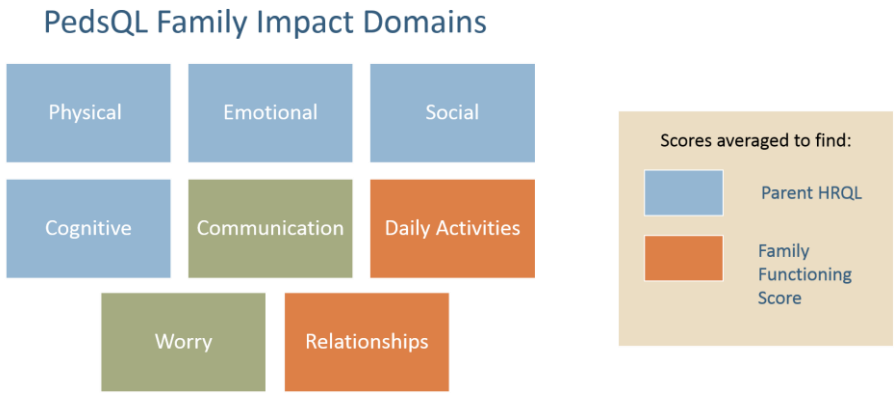
The Peds QL



The PedsQL has five domains: Physical, Psychosocial, Emotional, Social, and School. These five domains are

made up of individual questions that can be averaged to find a score within that domain, and all questions from the survey are averaged to find a patient's overall HQL. The scoring is identical for the parent proxy.

Peds QL: Family Impact



Sensing that further research needed to assist in quantifying how having an ill child at home affected the parent/caregiver's well being (and the family unit as a whole), the same researcher developed the tool known as the PedsQL Family Impact, with scoring that determines the parent's own HRQL as well as the health of the family unit in its response to stress from having an ill loved one. As demonstrated in the graphic above, the Physical, Emotional, Social, and Cognitive domains are averaged to find the Parent HRQL, the counterpart to the PedsQL for the patient. The Daily Activities and the Relationships domains are averaged to find the Family Functioning Score.

CHAPTER 2
Methods

All patients and families at GENECIS complete intake paperwork upon entry into the program, which includes the PedsQL tools among many other psychological assessment tools. This is to monitor the quality of the patient and family experience throughout the treatment course. Those patients and their families who agree to have data collected for research purposes while receiving treatment for their gender dysphoria at GENECIS are consented for the study and have their data pooled anonymously in the encrypted, deidentified survey tool REDCAP. Participation in research has no bearing on the quality or availability of their treatment and the GENECIS team takes every precaution to honor the anonymity of these children and adolescents and their families.

Focusing on the QOL portion of GENECIS research, upon intake, the family unit (typically mother, father, and patient, or some combination of custodial family) are requested to complete surveys as follows:

Biological mother: Peds QOL Family Impact Survey, Peds QOL Child, Teen, or Young Adult Survey (based on ages; see below)

Biological father: Same as mother

If patient has guardians who are not their biological parents or has a parent that has lost guardianship, the survey tool is provided only to the guardian.

Patient: Peds QOL Child (age 5-8), Adolescent (9-12) Teen (13-18), or Young Adult (18+)

These forms, completed at intake, reflect the family's baseline as they engage with GENECIS for treatment. The type of treatment a child, adolescent, teen, or young adult seeks at GENECIS varies widely based on patient preference but follows GENECIS' own protocol that is most similar to the Dutch protocol. For example, a young child will not be offered puberty blockers until GENECIS clinic staff examinations reveal the child has entered puberty; cross sex hormones will not be begun until an age suitable for the patient, family, and clinical team. GENECIS' program does not offer gender affirming surgery, but often their patients do seek surgical treatment and staff work with those surgeons to ensure any concurrent hormone therapy is administered appropriately throughout the process and recovery period. In this manner, treatment through the GENECIS program is highly individualized and seeks to wrap around patients and their families to provide the top level of psychological, psychosocial, and medical support.

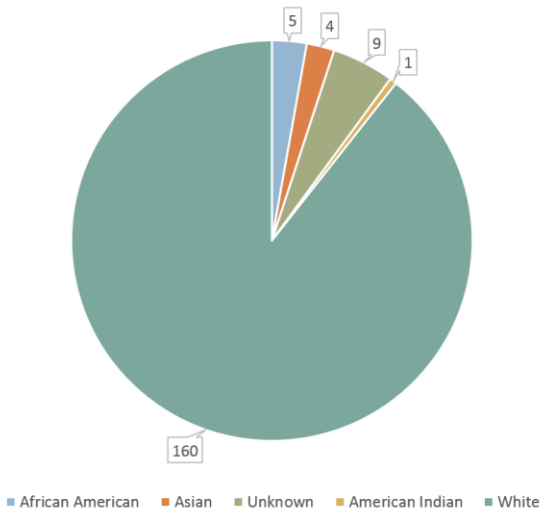
STUDY DESIGN

- Prospective Cohort Study
- Only included patients and families consented to research
- Data de-identified
- Utilized assessments from initial and follow up appointments ~1 year apart

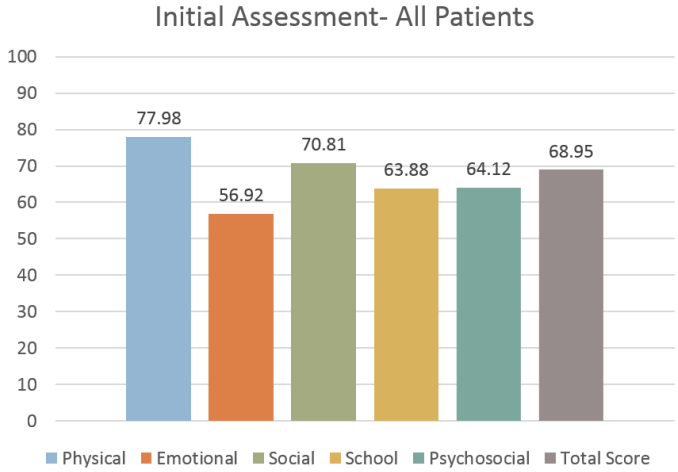
These same forms completed at intake are completed again at yearly follow ups to monitor attitudes the patient and their families have towards the gender affirming care offered at GENECIS and the experience of gender nonconforming adolescents and children over time. All forms are deidentified, with each family unit receiving one study subject family number and each patient receiving their own individual study subject number.

While all patients at GENECIS fill out this paperwork for internal quality measures, only the patients consented to participate in this research study were included in the data pulled for this analysis. Until January of 2018, all forms were physical pen and paper forms and were stored in patient charts under lock and key. Moving forward, all information is now captured via REDCAP surveys that can be either emailed out to patients and caregivers prior to appointments or soon can be offered on tablets in the clinic setting. This will enable better control over completion of surveys; currently, survey questions may be skipped on the pen and paper survey forms but the form will not allow submission with blank entries via REDCAP. This aspect along with the immediate digitization of the data will greatly benefit researchers in the future.

CHAPTER 3
Results
Initial Assessment: A Baseline of QL



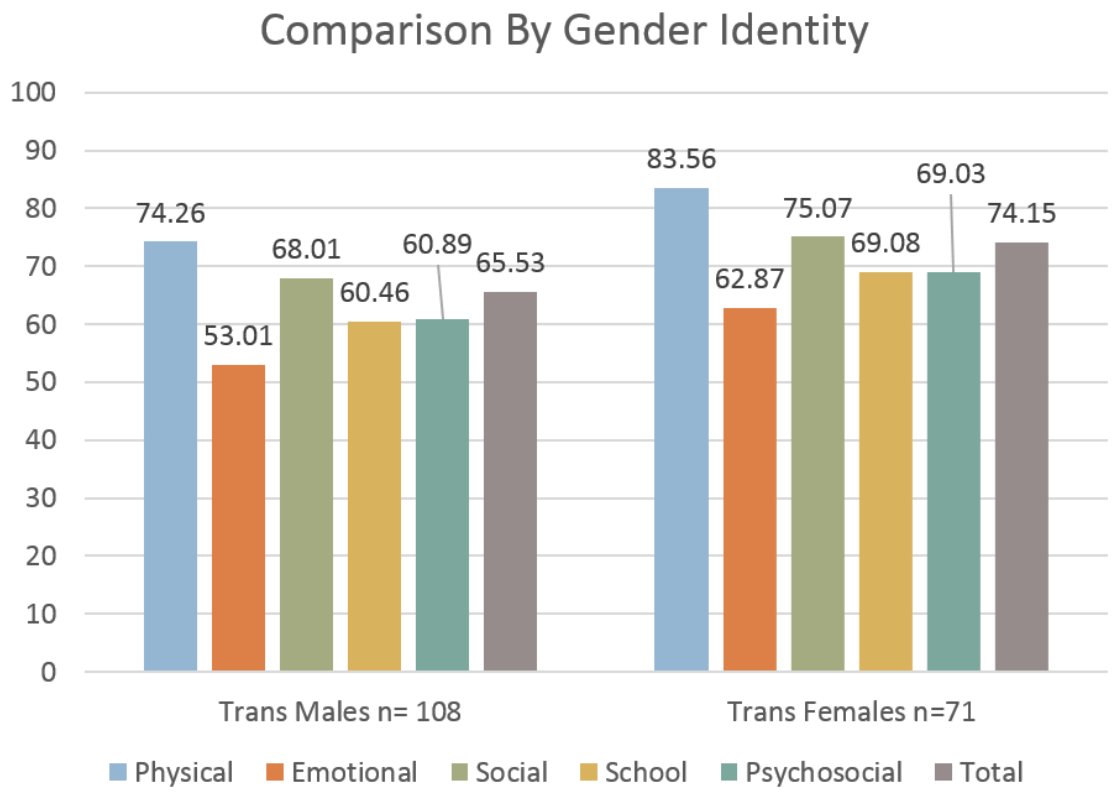
As mentioned, all patients in GENECIS receive a PedsQL upon intake, which becomes what will be referred to as the initial assessment. The initial assessment provided results regarding baseline QL of transgender adolescents. Out of 179 adolescents, 160 identified as White, 5 African American, 1 American Indian/Alaskan Native, 4 Asian, and 9 Unknown. Ethnically, 15 identified as Hispanic or Latino, with 164 identifying as Non-Hispanic or Latino.



Domain means for all adolescents were as follows, with a score of 100 as a perfect score: Physical functioning 77.98, Emotional functioning 56.92, Social functioning 70.81, School functioning 63.88, Psychosocial health summary score 64.12, and Total Score 68.95. Trans males (n=108) had the following domain means: Physical functioning 74.26, Emotional functioning 53.01, Social functioning 68.01, School functioning 60.46, Psychosocial health 60.89, Total score 65.53. Trans females

(n=71) had the following domain means: Physical functioning 83.65, Emotional functioning 62.87, Social functioning 75.07, School functioning 69.08, Psychosocial health 69.03, Total score 74.15.

Interpretation of Results: Overall, trans males and trans females did not achieve close to a perfect score in any domain, suggesting that HRQL of these teenagers is greatly affected by gender dysphoria. When looking at baseline scores by gender identity, that trans males fared worse, on average, than trans females in every category. More research is needed as to why trans males fare worse than trans females, as this was an unexpected result in an area of the United States with no policies in place protecting the health and rights of transgender



individuals. The “tom boy” is an accepted stereotype/gender role in society, but effeminate natal males are not widely accepted and face extreme harassment and bullying. This poses an

interesting research question as to why trans females at baseline score themselves higher than trans males.

Future Research Directions Specific to Peds QL

Of great interest would be the comparison of transgender adolescents at baseline to children with a variety of medical conditions for whom the PedsQL was also administered as well as comparison to "healthy" (no known medical condition/burden) adolescents of similar ages. We need to better understand how transgender adolescents compare to other individuals their age, preferably living within their same school districts and cities. Teenage years, school pressures, navigating new social circles- all these stresses can take a toll on the emotional, social, and physical well-being of a growing individual. Just how much an adolescent's life is affected by gender dysphoria versus the interwoven complexities of home, family, school, and social pressures is difficult to extract from a survey but provides us with an excellent baseline for our patient population. More research questions can be asked and answered by comparing these adolescents to their peers.

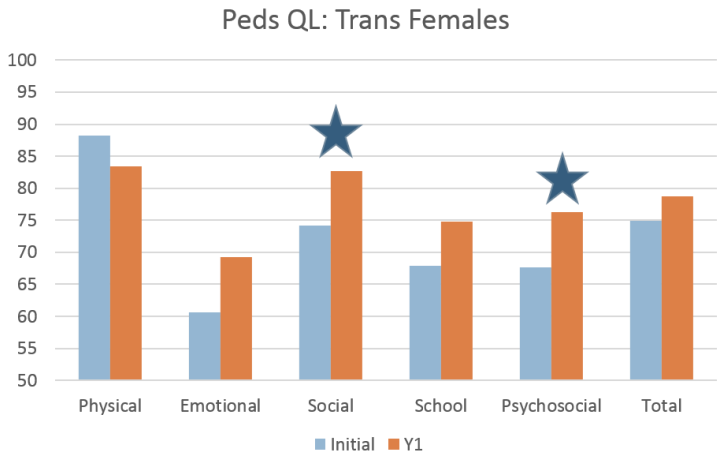
N=71	Initial	Y1	P
Physical	80.76	78.97	.304
Emotional	55.58	64.03	**.004**
Social	72.04	77.82	**.006**
School	65.07	67.68	.396
Psychosocial	64.62	70.49	**.004**
Total Mean Score	70.25	73.41	.065

Paired T Test:

Patient PedsQL

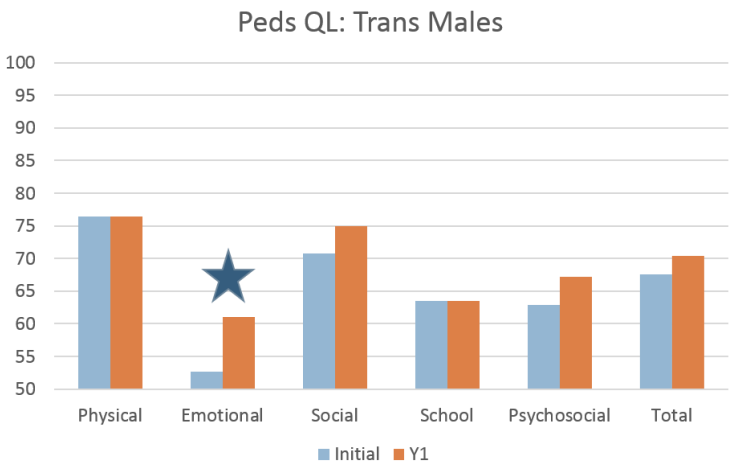
To answer the question of how these patients benefitted

from receiving care in a gender affirming center, patients who completed both an initial PedsQL assessment and one-year reassessment (of the identical PedsQL, appropriate to their age) provided data (n=71) for a Paired T Test (95% CI). These adolescents demonstrated the following results: Physical functioning Initial 80.76, Year 1 78.97, p=.304; Emotional functioning Initial 55.58, Year 1 64.03 p=.004*; Social functioning initial 72.04, Year 1 77.82, p=.006*; School functioning Initial 65.07, Year 1 67.68 p=.396; Psychosocial 64.62, Year 1 70.49, p=.004*; Total score Initial 70.25, Year 1 73.41, p=.065. Of this paired data, Trans Males (n=45) demonstrated the following results:



Physical functioning Initial 76.42, Year 1 76.40, p=.99; Emotional functioning Initial 52.67, Year 1 61.02 p=.01*; Social functioning Initial 70.78, Year 1 75.00, p=.12; School functioning Initial 63.44, Year 1 63.56 p=.97; Psychosocial Initial 62.89, Year 1 67.18, p=.06; Total score Initial 67.58, Year 1 70.36, p=.16. Trans Females (n=26) demonstrated the following results: Physical functioning Initial 88.27, Year 1 83.42, p=.17; Emotional functioning Initial 60.62, Year 1 69.23 p=.14; Social functioning Initial 74.23, Year 1 82.69, p=.01*; School functioning Initial 67.88, Year 1 74.81 p=.17; Psychosocial Initial 67.62, Year 1 76.23, p=.03*; Total score Initial 74.88, Year 1 78.69, p=.24.

Interpretation of Results: When comparing all patients with an initial and one-year follow up PedsQL, there was significance in the Emotional, Social, Psychosocial domains. Surprisingly, trans females had overall higher scores comparing their baseline and year one. There are known societal pressures and dangers for trans females in the US, as documented by the National Center for Transgender Discrimination in their recent landmark survey. With the many ways that transgender adults experience discrimination, trans women tend to face discrimination to the largest degree. Regarding adolescents specifically, a national survey by GLSEN has found that 75% of transgender youth feel unsafe at school, and those who are able to persevere had significantly lower GPAs, were more likely to miss school out of concern for their safety and were less likely to plan on continuing their education. For this reason, it's not surprising that significant gains were not made in the "school" category.

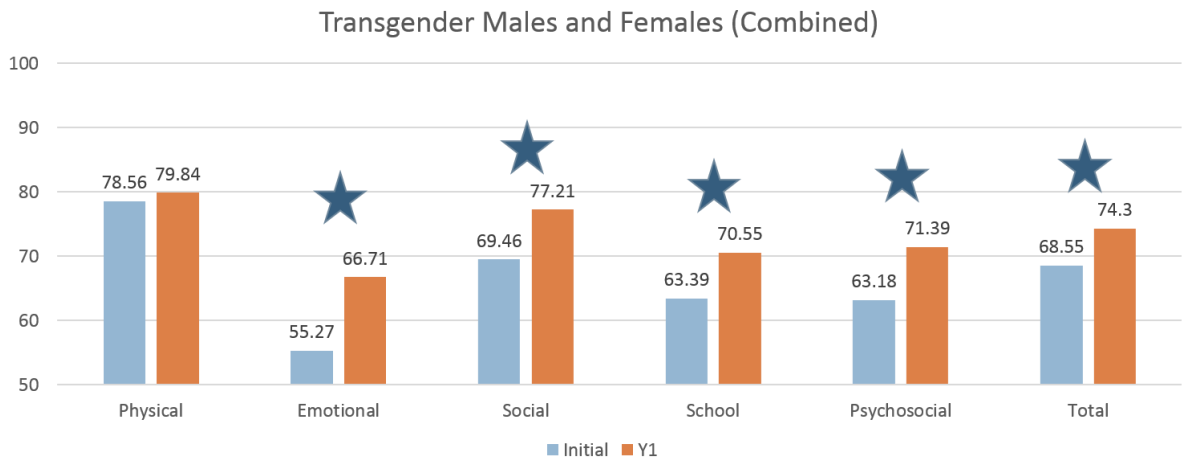


When analyzing this cohort of adolescents with an initial and one year follow up PedsQL, it is important to note this cohort includes patients that may or may not have initiated hormone therapy or been on hormone therapies prior to taking the initial assessment. Therefore, this paired data looked at patients who established care at GENECIS, received whatever care they and their guardians were in favor of, and also completed a one-year

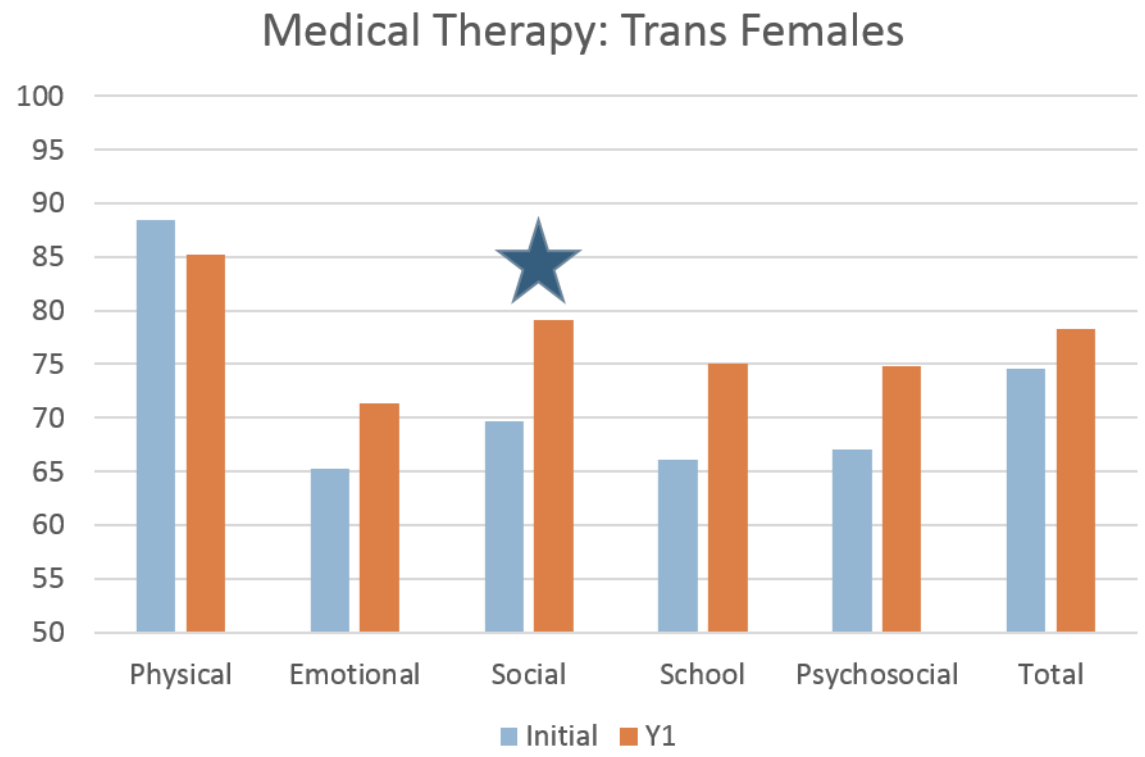
survey. This differs from the following analysis of data which looked strictly at patients receiving medical (hormonal) intervention. Ideally, a case-controlled trial could look at groups of transgender adolescents receiving gender affirming care at a medical center only versus transgender adolescents receiving hormonal therapy only, but as determined by the Dutch Protocol, hormonal therapy should be given in the context of a larger gender affirming approach, so it is impossible and potentially unethical (given the benefits received by the adolescent in having access to mental health counseling, a structured treatment team, and a cohort of other adolescents like themselves receiving care at the center) to distinguish the two groups in an analysis.

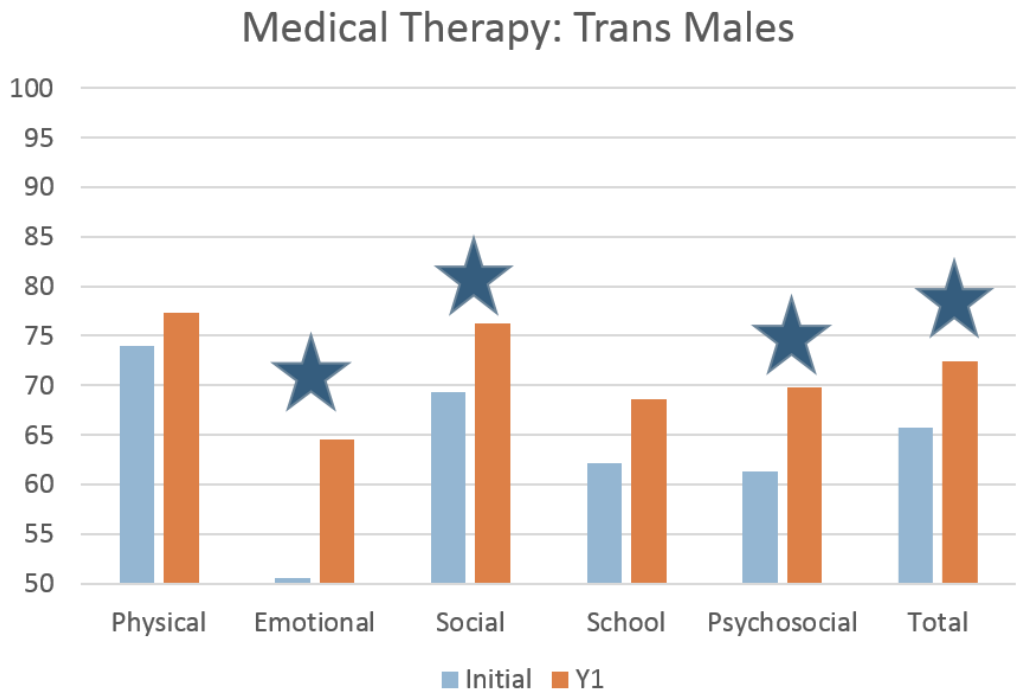
Paired T Test: Patient PedsQL with cross-sex hormonal administration or pubertal delay

Perhaps the study portion of most interest involves PedsQL scores in relation to patients receiving cross sex hormonal therapy or pubertal delay. Patients who completed both an initial PedsQL assessment, began cross-sex hormones or elective pubertal delay following initial assessment, and completed a one year reassessment (n=56) provided data for a Paired T Test (95% CI) with the following results: Physical functioning Initial 78.56, Year 1 79.84, p=.53; Emotional functioning Initial 55.27, Year 1 66.71 p=.0004*; Social functioning Initial 69.46, Year 1 77.21, p=.003*; School functioning Initial 63.39, Year 1 70.55 p=.024*; Psychosocial Initial 63.18, Year 1 71.39, p=.0001*; Total score Initial 68.55, Year 1 74.30, p=.002*.



Of this paired data, Trans Males (n=38) demonstrated the following results: Physical functioning Initial 73.92, Year 1 77.29, p=.17; Emotional functioning Initial 50.53, Year 1 64.50 p=.00003*; Social functioning Initial 69.34, Year 1 76.29, p=.04*; School functioning Initial 62.11, Year 1 68.55 p=.09; Psychosocial Initial 61.34, Year 1 69.76, p=.0009*; Total score Initial 65.71, Year 1 72.39, p=.002*.





Trans Females (n=18) demonstrated the following results: Physical functioning Initial 88.39, Year 1 85.22, p=.38; Emotional functioning Initial 65.28, Year 1 71.39 p=.39; Social functioning initial 69.72, Year 1 79.17, p=.02*; School functioning Initial 66.11, Year 1 75.00 p=.12; Psychosocial Initial 67.06, Year 1 74.83, p=.06; Total score Initial 74.57, Year 1 78.33, p=.26.

Based on the previous results, we can conclude that hormonal therapy significantly improves PedsQL scores. We only see a significance in the improvement of total QL score when including only patients who receive *both* gender affirming care from GENECIS *and* medical therapy in the form of cross-sex hormones or pubertal blockers. **This means only receiving nonmedical therapy from a gender affirming center is not enough to achieve highest potential for total QL scores.**

Analysis: Hormonal Therapy

- Hormonal therapy ***significantly*** improves PedsQL scores.
  - Receiving only nonmedical therapy from gender affirming center NOT ENOUGH to achieve highest potential QL scores and significance

Paired Data Sets	Total Average QL Score	
Patients Initial	70.25	P= .065
Patients Y1	73.41	
Patients Receiving Hormones Initial	68.55	P= .002 ★
Patients Receiving Hormones Y1	74.30	

It is important to note the reasons why some patients do not receive cross-sex hormones or pubertal delay. GENECIS always meets the patient where they are, and respects the decisions of the guardians of the adolescent. Looking at the records of those who do not start hormones or pubertal delay, it is typically due to parental hesitation or insurance reasons. The benefits for cross sex hormones are well established in adults, as it improves psychological outcomes.[8, 10] In adolescents, this is an area that could use greater research.

Of important note, trans males made the most significant gains in their PedsQL scores with the administration of cross-sex hormones, which in this case would be testosterone injections. Patients are initiated on testosterone after a very detailed consent process, particularly regarding anticipated side effects as well as effects on future fertility. Testosterone dosing is slowly titrated up to blood levels of natal males over many months, and the desired (effective) dose may vary from individual to individual (some require lower

amounts to feel their best, and therefore do not reach blood levels of natal males). Estrogen dosing for transgender females is also started low and increased gradually. But unlike trans females, Trans males see and feel the desired effects of Testosterone sooner than trans females see/feel the desired effects of estrogen. Also, one of the side effects of testosterone is increased confidence, which could also be an important factor in the improvement in patient scores. Trans Females, on the other hand, may not see estrogen's wanted side effects for 1-2 years. Trans Females also importantly have more difficulty "passing" than trans males, as phenotypically male characteristics like facial hair, broader facial bone structure, Adam's Apple, and taller height are not reversible for trans females who underwent male puberty before presenting to GENECIS.

Also important to note is in this cohort of patients, a greater percentage of trans females were on puberty blockers *only* in comparison to trans males. The gains made in QL scores by trans males over trans females could very much be explained by a larger sample size of trans males receiving cross-sex hormones in comparison to trans females. This points to the need for a larger sample size, and GENECIS is gaining that data every day as we continue to do one year follow ups on our growing patient population.

Now, of importance, is looking at the parent proxy forms to see how parents of transgender adolescents are rating the PedsQL for their own children.

PedsQL- Paired T Test Data from Adolescents vs Parents

ADOLESCENTS n=71	Initial	Year 1	P
Physical	80.76	78.97	.304
Emotional	55.58	64.03	.003
Social	72.04	77.82	.006
School	65.07	67.68	.396
Psychosocial	64.62	70.49	.004
Total Mean Score	70.25	73.41	.065

PARENTS n=90	Initial	Year 1	P
Physical	78.74	81.47	.179
Emotional	59.33	62.81	.08
Social	71.23	76.78	.02
School	69.18	72.36	.28
Psychosocial	66.84	71.02	.03
Total Mean Score	70.96	74.59	.04

Paired T Test: Parent Proxy PedsQL

Parents who also completed an initial PedsQL assessment (parent proxy) and a one year reassessment (n=90) provided data for a Paired T Test (95% CI) with the following results: Physical functioning Initial 78.74, Year 1 81.47 p=.179; Emotional functioning Initial 59.33, Year 1 62.81 p=.08; Social functioning initial 71.23, Year 1 76.78, p=.02*; School functioning Initial 69.18, Year 1 72.36 p=.28; Psychosocial Initial 66.84, Year 1 71.02, p=.03*; Total score Initial 70.96, Year 1 74.59, p=04*.

Interpretation of Results

The results of this Pared T Test demonstrate that the parent proxy is concordant with their adolescent's views, suggesting that parents of transgender adolescents at the GENECIS clinic have a fairly accurate idea of how well (or poorly) their teen is doing. Some domains shared significance between parents and adolescents, particularly the Social and Psychosocial domains.

Importantly, parents also saw their adolescent's overall quality of life improved over the course of one year of treatment at a gender affirming health care center. This is a key point to

take in and emphasize for families coming to GENECIS moving forward: that the gains in health-related quality of life are not only felt by the adolescents receiving care at GENECIS, but they are demonstrated to a level that the parents also can see observable changes in their child.

Family Impact Results

N=94	Initial	Year Y1	P value
Physical	77.95	76.91	.49
Emotional	65.59	71.01	**.02**
Social	75.31	80.18	.07
Cognitive	78.78	80.43	.44
Communication	63.57	68.44	**.047**
Worry	49.34	58.55	**.001**
Daily Activities	74.76	80.73	.09
Family Relationships	69.73	73.56	**.001**
Parent HRQL	74.63	77.82	**.001**
Family functioning	71.68	76.31	.178
Total score	69.70	74.70	.12

Paired T Test: Parent Family Impact Scores

Regarding scores on the PedsQL Family Impact (FI) assessment, a Paired T Test (n=94) had the following results: Physical functioning Initial 77.95, Year 1 79.61 p=.49; Emotional functioning Initial 65.59, Year 1 71.01 p=.02*; Social functioning initial 75.31, Year 1 80.18, p=.07; Cognitive Functioning Initial 78.78, Year 1 80.43 p=.44; Communication Health Summary Initial 63.57, Year 1 68.44, p=.047*; Worry Initial 49.34, Year 1 58.55 p=.001*; Daily Activities Initial 74.76, Year 1 80.73, p=.09; Family Relationships Initial 69.73, Year 1 73.56, p= .001*; Parent HRQL Summary Score Initial 74.63, Year 1 77.82, p= .001*; Family Functioning Summary 71.68, Year 1 76.31, p=.178; Total Score Initial 69.70, Year 1 74.70, p=.12.

These results demonstrate significance in the Emotional, Communication, and Worry domains, and significance in the scores for Family Relationships and Parent HRQL, which themselves are averages of other domains. Of interest, these domains of significance all investigate similar themes of introspection, anxiety and fear, and the ability to convey these concerns to others and receive support. What about this one-year period provided parents with improved resilience? Could it be adjustment to or acceptance of their adolescent's gender identity? Determination to support their adolescent in the face of the discrimination their child faces? Comfort in finding one's tribe- being in contact with other similar parents thanks to GENECIS? We need to look into this further, but importantly, we can tell parents of transgender adolescents establishing care at GENECIS that not only will the child benefit from gender affirming therapy and hormonal treatment but the parent and family unit will also benefit based on the results of this cohort of families.

CHAPTER 4
Limitations, Conclusions and Recommendations

There were limitations to this overall study. This only provides data for one year of treatment. To provide a better picture of the challenges and successes experienced by transgender adolescents in Texas receiving treatment from a gender affirming multidisciplinary center, we need longitudinal data following the same cohort. Additional data for subsequent years to determine how adolescents and their families continue to score, particularly as these adolescents transition into adult care and navigate college, work, or a combination of both, would be invaluable.

Also, the patient population in this study is majority white, with larger numbers of trans males than trans females. We need to look into barriers to care for minorities- why are fewer adolescents of color presenting for care to GENECIS? We also need to look into why the clinic sees, on average, more trans males than trans females. Looking at the intake forms from these patients, similar stories emerge– that the adolescent can look back to early childhood for feelings of gender identity discordance. So we cannot simply say "trans males 'know sooner' than trans females'" and that is why we see fewer in this adolescent clinic. We also cannot say "there are just more trans males than trans females in the general population" as an explanation. A controversial hypothesis this researcher would like to posit is that families of trans females may be more reluctant to permit their adolescents to pursue hormonal therapy or even gender affirming care due to familial desire, whether conscious or not, to maintain a perceived "male"

family member for status or financial reasons. We cannot deny the fact that males make more than females, and males enjoy certain privileges in society that females do not. Do families feel they concede too much by consenting to a trans female child's gender identity?

Also, this study was limited in reflecting gender fluidity in this population; for ease of discourse a gender binary model was utilized which is not reflective of the views of the trans population as a whole. Greater efforts are being made in future data collection to better categorize transgender adolescents who identify as gender fluid.

Also of importance is that the PedsQL and FI tool has excellent validity but was not designed for this population. Some parents noted that they found the term "disease" problematic in the Family Impact tool (and understandably so- while the DSM V categorizes what these adolescents are experiencing as a disorder, it is *not* a disease). Social scientists are only now beginning to examine the far-reaching effects that societal views have on gender expression and the lived experiences of transgender individuals as a product of social constructs, versus biology (or as previously thought, pathology). As another example of the tool's difficulty in capturing the experiences of this special population, in the treatment category of the FI tool, parents are asked about whether they worry about their child's treatments and side effects. Many patients at GENECIS are not on any form of medical treatment for gender dysphoria when they first present for initial assessment, so that creates confusion. Of note, the physical functioning domain was designed for cancer patients in mind, in whom chemo can cause significant impacts on physical health. For this reason, it is not

surprising that adolescents receiving care at GENECIS did not experience any gains of QL in this domain.

By focusing on functionality as demonstrated by the PedsQL, this research has demonstrated that transgender adolescents achieve a significant improvement across multiple QOL domains via medical care rooted in a gender-affirming approach, but adolescents achieved the greatest gains in QOL scores when medical therapy in the form of cross-sex hormones or pubertal suppression was introduced. Trans males had greater improvements in QOL scoring, possibly explained the larger sample size of trans males in the GENECIS clinic, the faster onset of desired side effects of testosterone administration versus estrogen, and the larger percentage of trans males on cross-sex hormones in versus pubertal blockers alone.

The similarities in how adolescents reported their quality of life compared to the reported observations of their guardian suggest parents of adolescents at GENECIS can accurately estimate the impact gender dysphoria has on their child's life, and adolescent self-reporting is as accurate to parental proxy. This potentially has great importance for future informed decision making, particularly age at which cross-sex hormones are administered. The PedsQL Family Impact instrument provided strong data suggesting that not only do adolescents benefit from receiving care from a gender affirming center (as demonstrated by the PedsQL tool) but that the family unit and the parent also achieve an improved quality of life.

Based on these findings, we conclude that this early research on QOL in transgender adolescents continues to support administration of cross-sex hormones and pubertal blockade and consider lowering the age of transition below sixteen years of age as improvement in QOL of the adolescent and family unit is demonstrable and desirable.

Future Directions

GENECIS is making extraordinary strides to best capture valuable data on this vulnerable and high need population. Future study questions can not only better inform how GENECIS patients and their caregivers are presented with challenges during care, but also how those participating in GENECIS research may compare to other treatment cohorts at comparable gender affirming care centers across the country and even world. Potential study questions include the following:

-*How does HRQL of GENECIS patients correlate with screening methodologies for suicidality and depression?* Does the similarity of parental HRQL scores for parents and children hold when looking at patients who score poorly (are high risk) for suicidality screenings? This study could better inform if parents and caregivers are adequately picking up on suicide risk and suicidal behaviors in their adolescents.

-*What specifically accounts for the parents' improvement Peds QL Family Impact scores at GENECIS once the adolescent begins gender affirming treatment?* As previously discussed, this researcher can only hypothesize that it could not only be the parents viewing improvement in their child's functioning but also that parents could

benefit greatly from having their experiences supported and normalized by an interdisciplinary team of experts. Perhaps a qualitative study with focus groups of parents could best inform this study question, which could potentially spearhead formalized support groups and networks for parents and families.

- *What difficulties do these teens face at school, and do transgender adolescents who home school fare better (have improved PedsQL scores) than transgender adolescents in the school system?* Being a transgender adolescent in Texas' current sociopolitical climate is tough. Many respondents to the PedsQL survey reported homeschooling. The impact of the school environment on PedsQL scores could provide important information for parents looking to make tough decisions for their teen, and provide potential legal grounds for widespread establishment of laws designed to protect LGBTQ youth.

-*What accounts for the greater baseline PedsQL score in Transgender Females vs. Transgender Males?* A series of focus groups (or individual interviews for more privacy) on why these groups scored their QL the way they did would be very informative, particularly if the focus groups occurred immediately following their taking of the survey.

-*What accounts for the greater improvement in PedsQL scores at baseline and one year follow up for Transgender Males receiving hormonal therapy in comparison to*

Transgender Females receiving hormonal therapy? As mentioned in the discussion, this could be due to the earlier onset of desirable hormonal side effects from testosterone that Transgender Men experience versus Transgender Women, but warrants further discussion.

-*Why does GENECIS see far fewer Transgender Women than Men?* The demographics of this study pointed out a very skewed sample; this warrants investigation into if families of Transgender Females are more reluctant than families of Transgender Males to consent to treatment.

-*What prevents more patients of color from accessing care at GENECIS?* The topic of racial and class discrimination in healthcare systems is a large topic, and transgender youth, particularly transgender youth of color, are a very at-risk population. Cultural barriers need to be investigated, especially as these youths are relying on parental consent to treatment, but decreased access to health care generally for patients of color cannot be ignored, and this is a topic that deserves intense investigation to better serve our community of adolescents.

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VITAE

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