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EXPERIMENTAL TREATMENT OF GENDER DYSPHORIA IN PATIENTS WITH NON-BINARY GENDER IDENTITIES: A RETROSPECTIVE REGISTER STUDY AND QUALITY CONTROL

ABSTRACT

The number of people with non-binary gender experience seeking gender-affirming treatment is rising in Finland as in other European countries. The treatments vary, and there is no long-term follow-up data on the benefits of the treatments or the stability of non-binary gender experience. The aim of this study was to evaluate the clinical outcome of empirical gender-affirming treatment among non-binary individuals who were examined in Helsinki University Hospital's Gender Identity Clinic during the period 2010–2018. 50 individuals were included in the study (43 were natal females and 7 natal males) and were sent a questionnaire which 39 individuals completed forming a follow-up group, i.e. respondents. All the patients' psychiatric diagnoses were reviewed. It was found that 8% of patients had no other psychiatric diagnosis in addition to gender disorder diagnosis, and 50% had three or more psychiatric diagnoses, most commonly depression (76%) or anxiety disorder (48%). Neuropsychiatric diagnoses were assigned to 20% and eating disorders to 16%. The use of psychiatric services prior to the examination period was high, in line with the prevalence of psychiatric morbidity. Health-related quality of life (HRQoL) was measured by using the 15D. The results were compared with an age- and gender-standardized sample of the general Finnish population. The mean 15D score among the follow-up group was significantly lower than among the general population. There was no statistically significant difference in the mean 15D score at the beginning of the examination period and at follow-up, suggesting that the treatment of gender dysphoria may not have a large effect on overall HRQoL. The respondents experienced the gender-affirming treatment to be beneficial, and the non-binary gender identity had remained stable among 32 (82%) respondents. The results of this study show that among these non-binary individuals, gender-affirming treatment alleviated gender dysphoria. Moreover, the treatments did not cause any concerning disbenefits, such as regret or unacceptable somatic complications. More research is urgently needed on the effectiveness of gender-affirming treatment among non-binary individuals.

KEYWORDS: GENDER, GENDER IDENTITY, NON-BINARY, TREATMENT

INTRODUCTION

“Biological sex” refers to our reproductive organs, chromosomes and hormones, but birth-assigned sex is usually determined only on the basis of genital appearance, assuming that other components of sex are consistent. “Gender identity” refers to our inner sense of being a man or a woman and “gender presentation” to how we express gender on a feminine to masculine scale. This is defined by local culture, opinion and times in which a person lives. Sex and gender are more likely to fall on continua rather than in dichotomous categories. Variation in how people position themselves on these continua depends on factors such as developmental stage, past and present environment and experience, and nature of relationship with self and others [1,2].

In most cases, gender identity matches the sex assigned at birth and the person is cisgendered. Gender identities which are incongruent with the person’s body, like transsexual, transgender and gender non-conforming identities, have been part of all cultures historically [3]. The emergence of transgender individuals in the western world has only become prominent in recent decades, even though the first research and treatment regarding transgenderism had already been actualized in Germany in the 1920s by Doctor Magnus Hirschfeld, but his work was intercepted and the archives destroyed. Transgenderism as a clinical phenomenon has been described in the literature since the 1940s, and guidelines for diagnosis and treatment since the 1970s [4]. The aetiology of this phenomenon is not fully known, but some evidence suggests that it has a neurobiological basis. Early-life growth conditions and other environmental factors affect the epigenetics of sex differences in the brain and gender expression [5]. Gender identity development seems to involve complex interactions between biological, environmental and cultural factors. Like sexual orientation, gender identity is not a choice [6].

Transgender people experience a discrepancy between the gender they were assigned at birth and their gender identity. People who do not identify within the binary model of gender, but rather hold a gender identity other than male or female, are referred to as non-binary. Non-binary people may identify as both male and female, as different genders at different times, as no gender at all or dispute the very idea of only two genders. Non-binary people may express features of both genders or neither, and often use labels such as “gender neutral” or “gender fluid”. The umbrella terms for such

genders are “genderqueer” or “non-binary” genders [7, 8]. Gender dysphoria is the clinically significant distress, anxiety or discomfort that may occur when a person’s biological sex and gender identity do not align. Suffering caused by gender dysphoria is alleviated with sex reassignment [9]. In the DSM-5 the diagnosis of gender identity disorder has been changed to gender dysphoria [10]. WHO’s new International Classification of Diseases [11] is going to adhere to the DSM-5 system where gender identity disorders belong to the wider “Gender incongruence” diagnosis, where the experienced gender dysphoria is relevant, and gender is considered to be a continuum rather than dichotomous. Implementing ICD-11 means that transgender and non-binary people will get the same diagnosis while now they are still differentiated into two diagnoses, F64.0 Transgenderism and F64.8 Other Gender Identity Disorder. Current examination and treatment in Finland is based on diagnoses according to ICD-10 and Trans Act (Act on Legal Recognition of the Gender of Transsexuals 1053/2002). The new diagnosis system makes the law now, if not earlier, outdated.

Gender dysphoria is associated with an increased likelihood of psychiatric disorders [12], like depression and social anxiety, which are considered to be at least partly caused by gender dysphoria and minority stress. Also, more non-suicidal self-injury and other self-harm is clearly reported [13]. People with gender dysphoria have more problems with their body image, like eating disorders [14]. It is also known that people with autism spectrum disorders or qualities from the spectrum suffer more often from gender dysphoria [15].

The psychiatric assessment of both adolescents and adults seeking treatment for gender dysphoria has been centralized in Finland, according to Trans Act, into two university hospitals, Helsinki University Hospital and Tampere University Hospital, and into youth and adult units. In both hospitals, multidisciplinary teams aim at differential diagnosis. Wishes for sex reassignment that are caused by a mental health disorder are excluded. Also, it is important to assure that the patient’s identity is stable and mature enough. Assessment in adolescence is challenging because the identity in youth is still forming. The examination period lasts approximately one year [16]. The publicly funded gender-affirming treatment includes hormone therapy, voice therapy and other phoniatic services, facial hair removal and mastectomy. Legal gender affirmation and genital surgery are available by Finnish law only to transgender people.

There is accumulating evidence that transgender individuals benefit from gender-affirming treatment [17,18]. There is no adequate scientific evidence of the benefits of gender-affirming treatment among non-binary individuals, and their treatment is therefore considered to be experimental.

The aim of this study was to evaluate the clinical outcome of empirical gender-affirming treatment among non-binary individuals, as well as the stability of non-binary gender experience. The follow-up report was originally commissioned by Council for Choices in Health Care in Finland (COHERE Finland), and part of the results will be published in Finnish language as a part of COHERE recommendation.

MATERIALS AND METHODS

STUDY SUBJECTS

This follow-up study was carried out in the (Adult) Gender Identity Clinic of Helsinki University Hospital where approximately half of Finnish individuals, aged 18 and over seeking gender affirming treatment, are examined (Finland's population being 5.5 million). The follow-up group of patients consisted of all individuals who were assigned with a diagnosis of other specified gender identity disorder, F64.8 in ICD-10, from January 2010 to August 2018. These individuals were identified from Helsinki University Hospital electronic patient records. Data retrieval resulted in the identification of 87 individuals with diagnosis F64.8. The patient records of these 87 individuals were reviewed by clinical psychologist (L.T.) and specialist in psychiatry (N.P.). 38 individuals were removed from the dataset: 20 individuals whose diagnoses were reassessed and updated to F64.0 (Transgenderism) by the end of August 2018, 7 individuals who were selected by technical error and 7 individuals whose examination period was interrupted before they had any treatment. Finally, 4 individuals were removed from the dataset because their diagnosis was recently set and they had not yet undergone any treatment. One individual was added to the dataset due to strong identification to non-binary gender despite previous diagnosis of F64.0. In total, 50 individuals were included in the study group, 44 (88%) were female assigned at birth and 6 (12%) male assigned at birth.

BASELINE INFORMATION

Baseline information for the follow-up group was collected retrospectively from the patient records of Helsinki University Hospital by the MD psychiatrist in training (K.K.). The patient records consisted of data entries by nurse, social worker, psychologist and psychiatrist during the multi-vocational examination period. The patient records also included information, obtained with consent, on the individuals' previous psychiatric treatment. During 2010-2018, all individuals underwent psychiatric interview in order to define possible comorbid psychiatric diagnoses before the diagnosis of F64.8. All assigned other psychiatric diagnoses were collected as baseline information. Information on socioeconomic status, such as size of household, marital status and capacity to work/study was recorded. Information on psychiatric history before seeking treatment for gender dysphoria, such as previous psychiatric hospitalizations, treatment in psychiatric outpatient unit and psychotherapy was recorded as part of the baseline data. Details of the examination period in the gender identity unit were recorded (date of initiation, date of diagnosis, age at the time of diagnosis, gender assigned at birth). Scores of available evaluation instruments at the initiation of examination period were recorded (health-related quality of life (HRQoL) data measured by the 15D [19]). Information on the examination period was reviewed in order to learn if the diagnosis of gender identity disorder was postponed due to treatment of other psychiatric conditions.

The 15D instrument includes 15 questions, covering 15 dimensions of HRQoL: mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity. Each dimension is divided into five levels of severity. The 15D can be used as a single index score measure or as a profile. The single index score (15D score), representing the overall HRQoL on a 0-1 scale (1=full health, 0=being dead), and the dimension level values, reflecting the goodness of the levels relative to no problems on the dimension (=1) and to being dead (=0), are calculated from the questionnaire by using a set of population-based preference or utility weights. Mean dimension level values are used to draw 15D profiles for groups [19]. The minimum clinically important change or difference in the 15D score has been estimated to be ± 0.015 [20]. The HRQoL of the patients was also compared with that of an age- and gender-standardized sample of the general Finnish population in the catchment area of the Hospital. For that comparison, patients'

biological gender was used. The population data came from the Health 2011 Health Examination Survey [21].

FOLLOW-UP CONTROL

According to current Finnish law, non-binary patients cannot get legal gender affirmation. Unlike patients with a diagnosis of F64.0, who undergo a one-year real life period before legal gender affirmation, there is no routine follow-up for non-binary patients in Helsinki University Hospital after the diagnosis F64.8 is set. In order to chart the possible healthcare needs of these patients, and to examine the outcome of possible gender-affirming treatment, a follow-up questionnaire was sent to all 50 patients in November 2018 (see Supplementary information). The questionnaire included open questions on received gender-affirming treatment, experienced benefit/harm caused by these treatments and additional treatment wishes. Gender dysphoria, experienced performance and experienced quality of life were mapped with a visual analogue scale (VAS), and the questionnaire also included open questions about these subjects as well as 15D questionnaire. A reminder text message was sent to non-respondents in December 2018. Patients who had not returned the follow-up questionnaire (n=25) were contacted by phone in January 2019 and offered a chance to participate by phone. In total, 39 patients (78%) answered, of these, 37 returned the form and 2 answered by phone. 6 individuals declined to answer and 5 were not reached by phone. Follow-up data of the answers was entered to the corresponding patient record. If concluded that some healthcare intervention was possibly needed, the patients were contacted by treating psychiatrist (K.T.).

STATISTICAL METHODS

The statistical significance of differences in means between independent groups was tested with independent samples t-test, and differences in means of the same group at two different points of time (baseline vs. follow-up) with paired samples t-test. P-values <0.05 were considered statistically significant. The statistical analyses were performed using SPSS.

ETHICAL CONSIDERATION

The study was approved by the ethics committee of Helsinki University Hospital (decision number HUS/2924/2018).

RESULTS

BASELINE DATA

The results cover two patient groups: all the patients who were on an examination period and were diagnosed with F64.8 in 2010–2018 (n=50), and those patients who answered the questionnaire by mail or telephone interview to form the follow-up group, i.e. respondents (n=39). The baseline data of respondents (n=39) and non-respondents (n=11) were compared, and there were no statistically significant differences between the two groups in quality of life, depression, psychiatric history, neuropsychiatric diagnoses, the length of examination period or age at diagnosis.

Among the patients caught by follow-up questionnaire, the diagnosis of F64.8 was set approximately at the age of 27 (standard deviation, SD=6.4; Median, Me=26; Mode, Mo=23). The examination period took approximately 13 months (SD=8.8; Me=9; Mo=9). Two patients had started their examination period at the Tampere University Hospital. 10 (26%) patients had a prolonged examination period due to extra time needed to make sure the gender identity was structured enough, or due to psychiatric treatment.

At the beginning of the examination period, 40 (80%) patients were working or studying full-time. During the examination period this did not change, as 38 of the patients (76%) were working or studying full-time when the examination period ended. The rest were on sick leave or disability pension. When these patients started their examination period, 7 (14%) were married or lived with their partner. By the time the examination process was over, the relationship status was not widely reported. 7 (14%) were married or lived with their partner, 23 (46%) were not, and for 20 (40%) the relationship/marital status was unclear. 46 follow-up patients (92%) were living independently (not with parents or in a care home) when the examination period started and 47 (94%) when it ended.

During the examination period in the Gender Identity Clinic, a psychiatric interview was performed for all individuals seeking gender-affirming treatment. The records of these interviews for all the patients (n=50) were reviewed by MD and psychiatrist in training (K.K.). The results are presented in [Table 1](#).

As there was no statistical difference between respondents and non-respondents, psychiatric diagnoses are reported here for the whole patient group (n=50). Only 4 (8%) patients had no other psychiatric diagnoses in addition to gender disorder diagnosis. 22% (n=11) of the patients had one psychiatric diagnosis and 18% (n=9) had two diagnoses. 16% (n=8) of

the patients had three additional diagnoses and 18% (N=9) had four. 16% of the patients (n=7) had five or six additional diagnoses and one patient (n=1) had 8 additional diagnoses (8%).

The most general psychiatric diagnosis among the non-binary patients was depression (F32-F33), diagnosed in 76% (n=38) of the patients. There were no diagnoses of bipolar disorder. Anxiety disorder (F40-F48) diagnosis was set to 48% (n=24). Personality disorder (F60) was diagnosed among 44% (n=22) of the patients, of which there were 7 diagnoses of borderline personality disorder (F60.3). Patients often had several diagnoses from the same diagnosis main group (for example, panic disorder and post-traumatic stress disorder from the anxiety disorders' group). 6% (n=3) of individuals had suffered from psychosis (F20-F29) and 8% (n=4) had a diagnosis due to psychoactive substance use (F10-F19). 16% (n=8) had eating disorders (F50-F59). Neuropsychiatric diagnosis was set to 10 individuals: 10% (n=5) of individuals had a diagnosis from the diagnosis group F90-98 and 10% (n=5) from the diagnosis group F80-F89.

Before the examination period started, 15% (n=6) of the respondents (n=39) had been treated in psychiatric hospital. 72% (n=28) had had contact with psychiatric healthcare (Finnish Student Health Service YTHS or psychiatric outpatient unit) and 49% (n=19) had had psychotherapy.

FOLLOW-UP QUESTIONNAIRE

In the follow-up questionnaire, individuals were asked to evaluate their performance on a VAS scale from 0 to 100. The results are presented in [Table 2](#).

There was noticeable amount of dispersion in the quality of life and ability to function. Personal ability to function was evaluated to be highest and professional ability to function to be lowest. Most of the respondents reported functioning at a high level and felt that their quality of life was very good.

In the questionnaire patients were asked to select a term that would best describe their gender. 7 patients (18%) chose from the binary gender system describing themselves as "woman" (3, 8%), "man" (1, 3%) or "transman" (3, 8%). 32 (82%) of questionnaire respondents defined their gender from non-binary or gender-queer descriptions: 6 (15%) described themselves as "genderless", 14 (38%) as "gender-queer", 6 (15%) as "non-binary" and 4 (10%) as "other" (2 "transgender", 1 "intersexual", 1 did not specify). Of the 39 respondents, 2 did not answer this question. When the patient

records of the 7 patients describing themselves as binary were examined, it was found that among 3 patients the diagnosis F64.8 had been updated to F64.0 after August 2018, when the data retrieval for this follow-up was made. One patient regretted the received gender-affirming treatment and identified him/herself to his/her gender assigned at birth. The update in diagnosis occurred approximately 2 years after the first gender disorder diagnosis (Me=23.8 months; SD=10.12 months, min 12, 21 months, max=36.87 months). When the updates in gender identity diagnoses were examined among all patients (n=87) found by the original data retrieval, including those who were excluded from the follow-up group, it was found that the diagnoses had been updated approximately a year from the first diagnosis (Me=14.31 months; SD=9.32 months, min=5.68 months, max=36.87 months). There was only one individual whose diagnosis was updated from transgender to non-binary.

The respondents were asked to list all the treatment they had received and whether they found the treatment beneficial or harmful. The answers are listed in [Table 3](#).

More than half of the individuals had gone through mastectomy (59%, n=23) and it was reported to be highly beneficial (4.82 on a scale from 1 to 5). Most of the individuals (62%, n=23) had also received feminizing/masculinizing hormone treatment. The respondents reported lower subjective benefit from hormone treatment (3.91 on a scale from 1 to 5) than from mastectomy (4.82), and 6 individuals had stopped the hormone treatment. Other treatments were reported rarely in the answers. 62% of the individuals had changed their first name but probably did not think to mention it as a treatment, and many were also in psychotherapy even though they did not report in on the questionnaire. Only 2 of the patients had had mastectomy in a private hospital, the rest of the received gender-affirming treatments were given within public healthcare. 6 respondents had not received any kind of gender-affirming treatment nor changed their first name. These individuals reported that they felt that the diagnosis F64.8 was enough or that they wanted to get pregnant first. Mostly the respondents were satisfied with the treatments: they listed 87 positive outcomes or benefits and only 29 disbenefits from the treatments. According to the respondents' answers, the benefits were categorized into physical, mental and other benefits, as can be seen from [Table 4](#).

Table 4 shows that the most significant benefits came from decreased body dysphoria and improved body image. Also, the respondents felt that their mood and self-esteem were better and that they had more social courage. The most mentioned physical changes were the lowering of the voice and decreased pain that was caused by the binding of the breasts. Some felt that the treatments helped them enjoy exercising more and it was easier to get dressed. The respondents mentioned altogether 29 disbenefits from the gender-affirming treatment. The physical disbenefits were mostly problems with the mastectomy: either with pain or bleeding (6 reports) or scars (3 reports). Hormonal treatment-induced acne was a problem for two respondents. Psychological and social disbenefits were depression and anxiety associated with the hormone treatment (2 reports), stress about gender issues and other people's confusion (2 reports). Other disbenefits included expensive medicines that were sometimes out of pharmacy (2 reports) and, for example, dysphoria that got worse (1 report). 34% of the respondents felt that they had gone through all the gender-affirming treatment they needed, while 23% were possibly still thinking to continue with the treatment and 42% were sure they still wanted gender-affirming treatment. Among many of the respondents, gender-affirming treatment was yet to be finished (for example, they were waiting for mastectomy), or they could not get some treatment they wished due to Finnish law or medical reasons.

In the questionnaire, the respondents were asked to evaluate how much they suffer from gender dysphoria on a scale of 0 (none) to 100 (unbearable). Gender dysphoria was divided into two dimensions: social dysphoria and body dysphoria. The respondents reported approximately 51.9 (SD=27.5; Me=60; Mo=70) suffering from social dysphoria. Reported body dysphoria level was 34.5 (SD=25.6; Me=30; Mo=20).

HEALTH-RELATED QUALITY OF LIFE COMPARED TO GENERAL POPULATION BEFORE AND AFTER TREATMENT

As the 15D has been used at the clinic only since 2013, baseline HRQoL data were available for only 22 patients who also participated in the follow-up. The mean 15D score of patients at baseline was 0.876 and that of age- and gender-standardized general population 0.937. The difference is statistically significant ($p=0.002$) and clinically important. The patients were on average statistically significantly worse off than the general population on the dimensions of usual

activities ($p=0.015$), depression ($p<0.001$), distress ($p<0.001$) and vitality ($p=0.032$) (*Figure 1*).

The mean 15D score of patients at follow-up was 0.848 and that of age- and gender-standardized general population 0.937. The difference is statistically significant ($p<0.001$) and clinically important. The patients were on average statistically significantly worse off than the general population on the dimensions of sleeping ($p=0.001$), usual activities ($p<0.001$), mental function ($p=0.0012$), discomfort and symptoms ($p=0.013$), depression ($p<0.001$), distress ($p<0.001$) and vitality ($p<0.001$) (*Figure 2*).

The mean 15D score seems to have deteriorated after the treatments (baseline=0,876, follow-up=0,848). The difference is clinically important, but not statistically significant ($p=0.132$). Of the dimensions, the biggest deteriorations seem to have taken place in usual activities and vitality, but the differences are not statistically significant either ($p=0.084$ and $p=0.062$, respectively) (*Figure 3*).

Table 1.

Lifetime DSM Axis I & II diagnoses of gender identity disorder patients (n=50)		
	n	%
Mood disorders F30-39 (all depressions)	38	76
- of which dysthymia (F34.1)	11	22
Anxiety disorders (F40-48)	24	48
Personality disorder (F60)	22	44
- of which Borderline personality disorder (F60.3)	7	14
Psychotic disorders	3	6
Diagnoses due to psychoactive substance use	4	8
Eating disorders	8	16
Neuropsychiatric disorders:		
F80-89 (Specific developmental disorders)	5	10
F90-98 (Behavioral disorders)	5	10

Table 2.

Self-reported current ability to function on a VASscale from 0 to 100

	Range	SD	Mode	Median
Professional Ability to Function (at work, studies, work search)	0-100	37.94	90	80
Social Ability to Function (relationships, hobbies, personal affairs)	30-100	23.26	80	70
Personal Ability to Function (taking care of self/home)	10-100	25.30	90	80
Quality of life	20-100	22.45	90	70

Table 3.

The treatments the patients had gotten and the benefits and disbenefits reported from them

Treatment	Treated patients, n	Benefits ¹ , mean	Disbenefits ¹ , mean
<u>Gender affirming treatments:</u>			
Hormones	24	3.91 (SD=1.3)	1.68 (SD=1.0)
Mastectomy	23	4.82 (SD=0.85)	1.53 (SD=0.96)
Epilation	2	3.00 (SD=2.83)	1.00 (SD=0)
Hysterectomy	1	5.00 (SD=0)	NR
Breast prosthesis	1	5.00 (SD=0)	1.00 (SD=0)
Drugs to stop periods	2	5.00 (SD=0)	1.00 (SD=0)
<u>Other support measures:</u>			
Name change	4	5.00 (SD=0)	1.00 (SD=0)
Therapy	6	2.86 (SD=1.77)	2.14 (SD=1.68)

¹ On a scale from 1 to 5, 1= not at all, 5 = a lot, NR= not reported

Table 4.

Benefits from the treatments

Physical	How many times mentioned
Lowering of the voice	7
No more periods	2
Facial hair, change in hair	4
More muscle, body more masculine	3
No need to use binder any more (less pain, better posture)	6
<u>Psychological</u>	
Looking better	2
Less body dysphoria, more whole body image	21
Mood and quality of life better, less anxiety	7
Better self-esteem/self-image	5
Identity stronger, own situation dearer	5
More self-assurance, social situations easier	9
<u>Other</u>	
Easier to dress up	6
Easier to exercise, exercising more	4
Getting more sexual, easier to enjoy sexuality	2
Less pain	2
Change in way of thinking	1
Taking better care of oneself	1

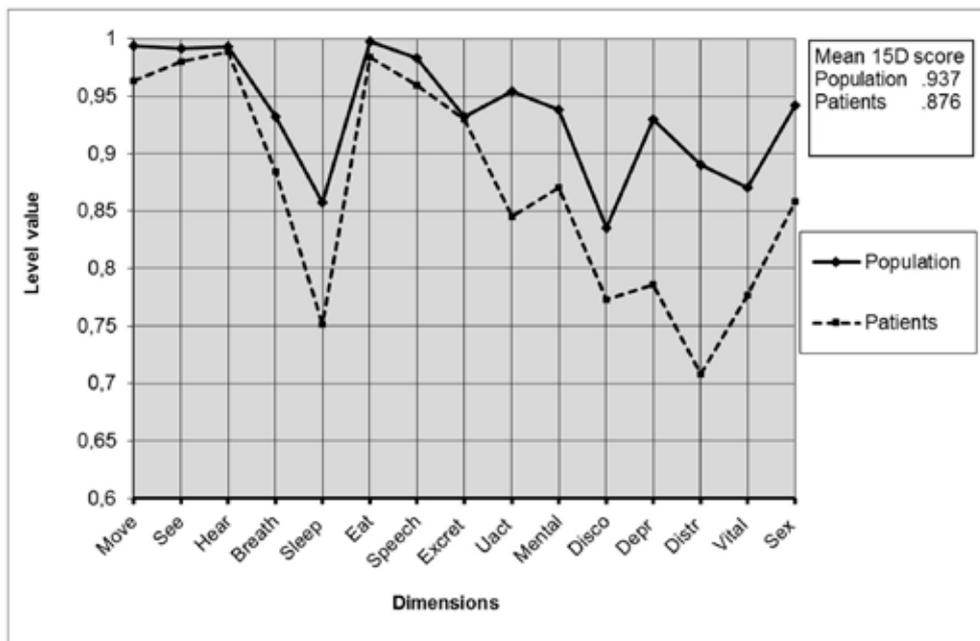


Figure 1. The mean 15 D profile of non-binary individuals (n=22) at baseline and that of age-and gender-standardized general population

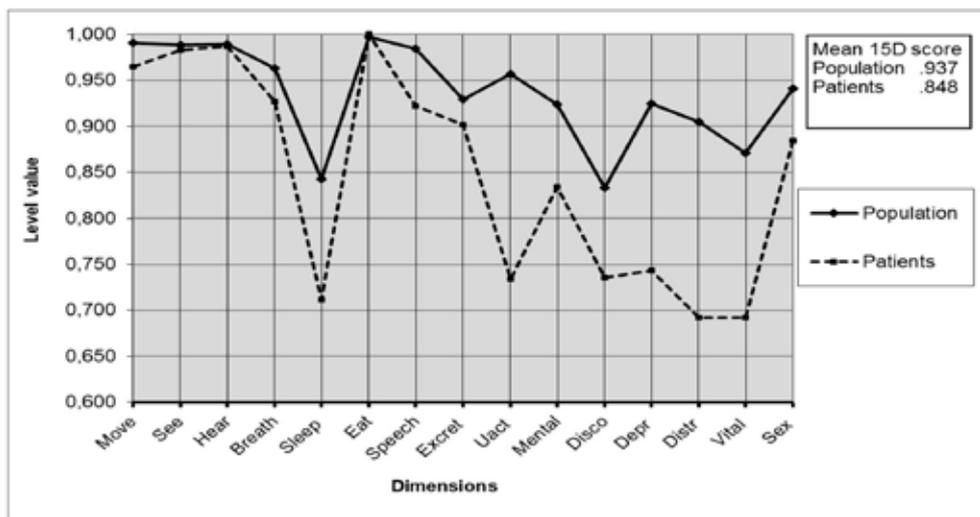


Figure 2. The mean 15 D profile of non-binary individuals at follow-up and that of age- and gender-standardized general population

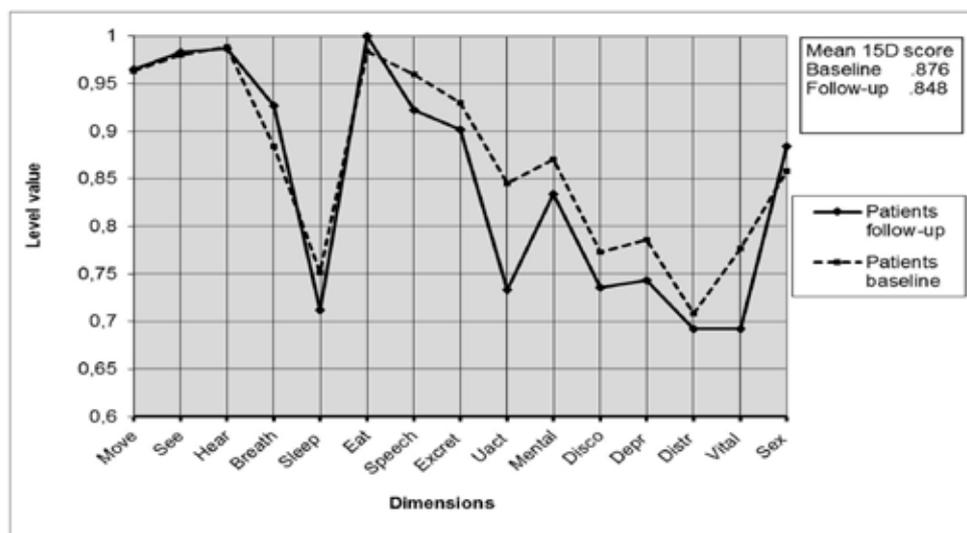


Figure 3. The mean 15 D profile of non-binary individuals at baseline and follow-up

DISCUSSION

There is paucity of long-term follow-up data on the stability of non-binary gender experience as well as outcomes of empirical gender-affirming medical treatment among non-binary population [8]. This is one of the first studies on the subject. This database follow-up study was designed when a need for follow-up data for clinical purposes emerged as the number of patients with non-binary gender experience seeking gender-affirming treatment started to increase rapidly in Finland, in line with other European countries [22,23]. Simultaneously, the Ministry of Social Affairs and Health Council for Choice in Health Care in Finland (COHERE) commenced a preparation for a recommendation concerning gender-affirming medical treatment. This study was partly funded by COHERE Finland and a part of the results will be published in the Finnish language as COHERE Finland recommendation's background material.

There are only two publicly funded gender identity clinics with roughly a similar number of patients in Finland, and therefore this clinical follow-up reached approximately half of all non-binary individuals seeking medical treatment in Finland during the period 2010-2018. As most of the psychiatric specialized healthcare in Finland is publicly funded, the patient records from psychiatric units were available with the permission of the patient. The percentage of patients that were reached either by questionnaire or telephone was high (78%), which shows that the study was also found to be of importance among the patients.

When the patient records of individuals diagnosed with F64.8 other gender identity disorder were reviewed, it became evident that even the vocabulary concerning this phenomenon was only forming during the study period 2010-2018. During the first years of this sample, individuals with non-binary gender experience were referred to as "transgender" in English language as there was no word for this in Finnish. Towards the end of the study, 2016-2017, diagnosis was "other gender" ("muunsukupuolinen" in the Finnish language). As the whole concept of non-binary gender experience was only forming in a medical context, the study population examined was fairly diverse. As the study population consisted of individuals diagnosed with F64.8 in Helsinki, individuals with non-binary gender experience who did not seek medical treatment for gender dysphoria were not included in this study. In addition, individuals who had somatic or psychiatric conditions warranting acute treatment during the study period 2010-2018 were not included, as the treatment of more acute conditions was prioritized over the examination period. Due to the long examination period, the

phase of the treatment varied among the study population when the follow-up questionnaire was conducted, and not all of the individuals had yet undergone all the desired gender-affirming treatment.

In this retrospective study setting it was not possible to do before and after treatment comparisons for most of the examined variables, excluding the 15D [19], which was filled in by part of the study population prior to treatment. A prospective study is ongoing, where the aim is to correct this problem. Finally, according to Finnish law, the gender identity clinic serves as a gatekeeper to publicly funded gender-affirming treatment, and this may have had some effect on the follow-up questionnaire answers.

The patient population consisted of working age individuals, and the majority of them were studying or working full-time at the time of their examination period. Almost all were living independently. However, being married or cohabiting with a partner was less common among these non-binary individuals than would be expected according to their age.

The majority of non-binary individuals in this study had more than one psychiatric diagnosis. Especially depression and anxiety disorders were clearly more prevalent than in the Finnish general population, where the lifetime prevalence of depression is estimated to be 6.5% and anxiety disorders 4.5% [24]. This is consistent with previous findings among non-binary populations, and minority stress is suggested to be one of the explaining factors [25]. The use of psychiatric services prior to the examination period was high, in line with the prevalence of psychiatric morbidity, which can be seen as a positive thing showing that the patients had sought help and it was available. Substance use disorders were rare among this study population. Neuropsychiatric diagnoses were assigned to 20% and eating disorders to 16%, which is consistent with previous studies stating that these disorders are more common in individuals with gender dysphoria compared to the general population [14,15].

When the stability of experienced gender was examined, it appeared that among 32 (82%) of the respondents, non-binary gender identity had remained stable. This suggests that non-binary gender experience per se is not a sign of undeveloped or unstable gender identity. 7 (18%) of the respondents reported that their experienced gender had changed from non-binary towards binary transgenderism. In addition, another 20 individuals were excluded from the study because their diagnosis had been corrected to F64.0 earlier. This suggests that among some individuals, non-binary gender experience may be an intermediate phase. Furthermore, the

transition from non-binary towards transgender may reflect them representing the same continuum, with the difference in identification to social gender roles. The cultural trends of challenging traditional gender roles also become visible among patients with gender dysphoria. It is also possible that received gender-affirming treatment affects gender experience. On average, the change of diagnosis from F64.8 to F64.0 was actualized very fast, within a year from first gender dysphoria diagnosis. Clinically it seems that if the diagnosis changes quickly from F64.8 to F64.0 it is because the gender identity is already leaning towards binary transgenderism, and then the physiological treatment strengthens that identity. When the patient records of these individuals were reviewed, it appeared that none of the individuals whose diagnosis was changed from F64.8 to F64.0 regretted the received gender-affirming treatment. On the contrary, additional measures such as genital surgery and legal gender affirmation became available for these individuals after their diagnosis was corrected to F64.0 (as stated in Finnish law). One individual (3%) reported a gender identity corresponding to their gender assigned at birth and reported to regret the received gender-affirming treatment. The statistical power of this study did not permit any conclusions on the prevalence or characteristics of non-binary individuals who regretted treatment.

In general, the respondents experienced the gender-affirming treatment received as beneficial. According to the open questions in the questionnaire, respondents stated that their body image felt more intact and their gender dysphoria decreased after treatment, which is considered the primary goal of gender-affirming treatment. This finding is consistent with previous Finnish studies among binary transgender patients [26,27]. Elevated self-confidence and mood were also reported, which can be interpreted as a consequence of decreased gender dysphoria. Mastectomy was reported to be highly beneficial, although many small complications occurred during the procedure. The respondents were not as content with the received hormonal treatment, and some individuals had ceased the hormonal treatment altogether. The respondents listed considerably more often benefits than disbenefits, and the reported disbenefits did not expose any common problem with the treatments. 42% of the respondents reported that they had not received all the treatments that they wanted. The reasons for this were medical (for example, too high body mass index) or juridical (Finnish law does not permit genital surgery for non-binary individuals). A part of the respondents felt that the diagnosis F64.8 per se was enough to validate their gender experience and did not wish any gender-affirming treatment. At the time of the study, when

most of the individuals had received some gender-affirming treatment, social gender dysphoria was reported to be higher than dysphoria related to the body. This can be attributed to difficulties in being perceived and treated as non-binary in a society where the mainstream view of gender is still mostly binary.

When the baseline data for the respondents was reviewed, completed HRQoL (15D) questionnaires at the beginning of the examination period were found for 22/39 individuals, as the 15D evaluation had only been used at the Gender Identity Clinic since 2013. There was no statistically significant difference in the mean 15D score at the beginning of the examination period and at follow-up. This suggests that the treatment of gender dysphoria may not have a large effect on overall HRQoL. However, this finding has to be confirmed in a larger study population. According to clinical experience, it often seems that individuals who seek treatment for gender dysphoria tend to under-report their health concerns and over-report their HRQoL at the beginning, due to worries that their gender dysphoria treatment may be postponed if a lot of other problems are detected. At the follow-up it is easier to report true problems more accurately. Their mean 15D profiles, however, were quite similar before and after the follow-up, suggesting a minor bias in degree of quantitative reporting instead of profound discrepancy. In comparison to Finnish age- and gender-standardized general population, the mean HRQoL was statistically significantly and clinically importantly poorer among non-binary individuals. When the different dimensions of the 15D were examined, it was found that poorer HRQoL occurred primarily on dimensions concerning psychiatric health. This is consistent with previous studies [28] that psychiatric morbidity is higher among gender dysphoria patients compared to the general population. This may be at least partially attributed to minority stress [26].

In conclusion, the results of this study show that among these non-binary individuals, gender-affirming treatment alleviated gender dysphoria. Moreover, the treatments did not cause concerning disbenefits. Psychiatric morbidity was high and HRQoL was lower compared to the general population. According to these preliminary results, there is no reason to change the treatment regime for non-binary patients at the Gender Identity Clinic of Helsinki, provided that a routine, structured follow-up is organized, similar to that of transgender patients, and that special attention be directed to treating comorbid psychiatric problems. In order to formulate evidence-based treatment protocols for non-binary patients, studies on the effectiveness of gender-affirming treatments among non-binary individuals are urgently needed.

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