**Onset age as a predictor of mental health problems in adolescents with gender dysphoria**

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**Abstract**

**Background:** Gender dysphoria (GD) in adolescents is often associated with high psychopathological distress. Increasing rates of onset and growing heterogeneity within this group provide evidence for different developmental trajectories and potentially different treatment needs. However, little is known about the onset age, i.e., the early (Early Onset, EO) or late first onset (Late Onset LO) of GD and its significance for mental health problems. The frequency of EO vs. LO courses and the association between OA and psychological distress in adolescents with GD will be examined.

**Methods**: The sample included n = 462 adolescents with a diagnosis of GD who presented to the Hamburg Special Outpatient Clinic for GD between 2013 and 2021. Onset age (EO vs. LO) was assessed using the DSM-5 criteria of GD and psychological distress using the Youth Self-Report.

**Results:** 51% (n =237) of youth with GD had an EO and 49% (n = 225) had an LO. There was a significant association between onset age and psychological distress in that LO was associated with particularly high distress from internalizing problems. LO GD was also associated with more severe peer problems, opposite-sex or asexual orientation, and only moderate crossgender identification.

**Discussion:** The findings highlight that adolescents with LO GD represent a particularly distressed and vulnerable group whose needs should be considered more closely, both diagnostically and treatment-wise. A protocol-based approach to the indication of physical medicine measures can no longer adequately meet the current clinical courses and should be supplemented by a differentiated approach oriented to adolescent developmental dynamics.

**Background**

The current controversial debate among clinicians and researchers about gender dysphoria in adolescence is based on observations that raise more questions than provide answers: worldwide, specialized centers are showing increasing rates of presentation of predominantly biologically female adolescents who place themselves transmasculinely and seek body-modifying interventions (Aitken et al., 2015; Chen M, 2016; de Graaf, N. et al, 2018, 2021; Kaltiala-Heino et al, 2015; Levitan et al, 2019) or who locate themselves as nonbinary, beyond the established gender dualism of male or female (Chew et al, 2020; Hermann et al. 2022, 2023). Similarly, a cluster of adolescents is reported in the United States and Canada who, after gender-conforming development in childhood, first show gender dysphoria until puberty (Hutchinson, 2020; Zucker, 2019) and have a high burden of accompanying psychopathology (Becerra-Culqui et al., 2018; Strang et al., 2018; Thrower et al., 2020).

Overall, significantly increased treatment numbers worldwide (Thompson et al., 2022; Zhang et al., 2020) and the often polarizing reception of these phenomena has led to buzzword-like reductions in the media as a transhype versus liberation through self-determination, with satisfactory explanations lacking so far.

In the meantime, attempts are being made to identify different development paths in the spectrum of increasingly heterogeneous processes. In addition to the Rapid Onset Phenomenon (ROGD) (Littmann, 2018), which describes a sudden onset of gender dysphoria without any previously recognizable clues, other differentiations based on the duration of gender dysphoria and age at first presentation (Arnoldussen, 2022; Sorbara, 2021) are also gaining importance. Similarly, it is useful to differentiate on the basis of the so-called Onset Age (OA), which describes a model for the early or late first onset of GD. Onset age currently gained additional relevance due to the fact that previous treatment and follow-up data, which served as evidence to support recommendations for early use of gender reassignment surgery, now no longer seem comparable to our current clientele, as Abbruzzese et. al. 2023 recently critically discuss.

The attempts to differentiate novel developmental trajectories illustrate the ethical dilemma for practitioners between the well-founded concern of making false indications and feared, numerically still completely unclear detransition rates (Cohn, 2023) and the simultaneous claim, to minimize the suffering of those affected by persistent gender dysphoria through gender reassignment interventions, as recommended, for example, by the current Standards of Care (SOC-8) of the World Professional Association for Transgender Health (WPATH) (Coleman et al., 2022).

A close look at new developmental pathways in the spectrum of heterogeneous self-definitions can provide an important contribution to enable differentiated and individualized treatment planning, on the basis of which a safe indication can only remain guaranteed.

**Definition and diagnosis of GD**

**Gender dysphoria (GD)** describes distress at the perceived discrepancy between perceived identity and physical sex characteristics, as well as the associated social gender role. Operationalized, the experienced gender identity is most often expressed by designating the sex assigned at birth as trans-female (AMAB) or trans-male (AFAB) (APA, 2015).

Most adolescents who turn to specialized centers express the desire for physical medicine measures, in the sense of hormone substitution. A distinction must be made between explicit prerequisites, such as a clinical diagnosis according to DSM-5 or ICD-10 (APA, 2013; WHO, 2019), and implicit prerequisites for an indication, as formulated by SOC-8 (WPATH, 2022) or established treatment protocols (de Vries et al., 2011, 2014). An approach based on the "Dutch Protocol" (Cohen-Kettenis et al., 2003; 2015) has become established in Europe over the past twenty years. Here, strict entry criteria were formulated, such as a retrospective opposite-sex identification going back to childhood, i.e., prepubertal - a so-called **Early Onset (EO)** course (de Vries et al., 2011). In addition, a homogeneous, psychopathologically rather low-stress treatment group was evaluated. Without the presence of EO GD and the absence of concomitant psychopathology, it was almost impossible for adolescents to receive gender reassignment treatment (de Vries et al., 2012). Just recently has the presence of EO GD been formulated more flexibly as a criterion in the SOC-8 (Colemann et al., 2022) in favor of *longer-lasting and consistent GD* and is no longer a basic requirement for the indication of physical medicine treatment.

While catamnestic studies of the Dutch cohort showed a clear improvement in the psychological well-being of the treatment group (de Vries et al., 2014), this could not be clearly demonstrated in a much more heterogeneous sample in Germany (Becker- Hebly et al. 2018, 2021), whose selection was not selectively based on a protocol and also included LO courses. In this respect, it must be asked in general whether, in view of the growing diversity of developmental trajectories, a protocol-based treatment approach can still meet the requirements.

**Onset Age**

Early and Late Onset GD (Lawrence, 2010; Person et.al., 1974) are descriptions of the time of initial manifestation **(Onset Age, OA)** of GD. **Early Onset (EO)** manifests in childhood, always before the begin of puberty, and is often accompanied by early gender role change. **Late Onset GD (LO),** on the other hand, manifests later, after the begin or completion of puberty, and is therefore considered more difficult to diagnose, since most affected individuals have already lived in their biological sex for a longer period of time, often without externally recognizable signs of distress. To date, the OA of GD has been considered as a marker of diagnostic certainty in the context of indication for physical medicine interventions in adolescents, with no follow-up data on the persistence of LO GD in the literature to date.

The growing heterogeneity of the clientele and resulting presumed differential developmental trajectories have recently been attempted for the first time to be captured quantitatively (Sorbara, 2021; Arnoldussen, 2022) by distinguishing between the temporal duration of GD and age groups at initial presentation. In initial results from the Netherlands (Arnoldussen, 2022), this showed that older adolescents (younger than 14 years vs. 14 years or older at initial presentation) had an overrepresentation of a female referral gender and greater body-related dissatisfaction, whereas the younger group was more likely to have evidence of gender-nonconforming childhood behavior and more likely to have an indication for gender reassignment procedures. Sorbara (2021) compared the under- and over-15 age groups and found that the older group of adolescents at initial presentation was significantly more psychopathologically distressed, and adolescents presenting younger were significantly more likely to notice their gender incongruence earlier. Without explicitly capturing onset age as a variable in the studies, both findings indicate that older adolescents were more likely to be of female assignment gender at first presentation and were more severely and frequently psychologically distressed than younger adolescents.

While the OA of gender dysphoric experience is a descriptive description along the timeline, the conceptualization of **Rapid Onset GD (ROGD**; Littmann, 2018, 2020, 2021) has been controversial discussed, as etiological assumptions are associated with it. ROGD is understood to be the sudden and surprising onset of GD without any pre-recognizable signs, predominantly in female-born adolescents, usually accompanied by high psychopathological distress in the affected individuals and associated with a strong desire for rapid physical medical treatment. Littmann (2018, 2021) defined ROGD as a subtype of GD and suggested that the gender dysphoric distress resulted less from a persistent and profound opposite-sex identification and was an expression of a different psychological problem. She reported an association between psychological distress and ROGD (76% of respondents had one or more mental disorder diagnoses) and the absence of early signs of GD in childhood. However, statistical analysis by frequencies did not allow conclusions about causality. In addition, all data were collected exclusively by means of third-party assessment by parents who were critical of the trans issue. Turban et al. (2023), who attempted to test Littmann's assumptions, came to different conclusions: they distinguished between early realization of GD (under 10 years of age) and late realization of GD (10 years and older) and found that the two groups did not differ in the extent of psychological distress, with the older group even reporting less distress from suicidal ideation.

**Current clinical impressions and courses**

In addition to the "classic" EO developmental trajectories with social role change already in childhood, little to hardly existing distress until expected puberty, and a predominantly male referral gender in number, we now see a shifted gender ratio in adolescence in the Hamburg special outpatient clinic (84% AFAB vs. 16 AMAB; Hartig et al., 2022; Herrmann et al., 2022; Levitan et al., 2019) with some clinical peculiarities, which are briefly illustrated: there is a high number of adolescents who report a strong and persistent distress about their sex characteristics, with previously psychosexually inconspicuous puberty. In most cases, an etiologically unclear psychopathology with social fear, depressive withdrawal and self-injuries accompanies this course, and often precedes it. Inpatient psychiatric treatments are frequently found in the case histories. Here, too, the psychological distress is usually very serious and must always be taken seriously, but it is highly probable that it has many other origins than GD alone.

In addition, we encounter partial GD in adolescents with female assignment gender: here, often only one specific body feature (mostly the breast) is in the foreground, which should be changed at all costs. The self-definition as trans-male is often intellectually derived from the deep feeling of not being able to be female.

As a third line of progression we get to know young adolescents in early puberty who, in addition to a contrary-sex or non-binary identification, have enormous fears of the demands and tasks of the adolescent developmental phase and whose GD first appeared in connection with the feeling of not yet being able to meet these demands. In this group, adolescents are frequently found who hardly participate in social life, show only little interest in contacts with peers and are also clearly inhibited in other areas of identity.

**Psychological distress**

Studies from different countries suggest that more than half of children and adolescents with a GD diagnosis also have at least one other psychiatric diagnosis (Becker et al., 2014; Chen et al., 2016; 2017; Chodzen et al., 2019; Di Ceglie et al., 2002; Hewitt et al., 2012; Holt et al., 2016; Kaltiala-Heino et al., 2015; Katchadourian et al., 2014; Meyenburg, 2020; Nahata et al., 2017; Spack et al., 2012). For example, Kaltiala- Heino et al. (2015) reported at least one preexisting or current mental health disorder in 75% of the youth they studied. Significantly overrepresented compared to the norm sample are also affective and anxiety disorders, self-injurious behavior, suicidal ideation, and suicidal acts in the German studies (Becker et al, 2014; Hartig et al, 2022; Levitan et al, 2019), both in childhood and adolescence (Becker et al, 2018). De Graaf et al. (2022) found consistently elevated rates among female-assigned adolescents in addition to overall elevated incidence of suicidality among transgender adolescents from the Netherlands, Canada, and the United Kingdom.

Questionnaire assessments, mostly conducted with the Child Behavior Checklist (CBCL) or the adolescent version of the CBCL, the Youth Self-Report (YSR) (Achenbach, 1991), consistently showed elevated levels of psychological abnormalities in the clinically relevant range, regardless of assignment gender (Bechard et al., 2017; de Graaf et al., 2019; de Vries et al., 2016; Levitan et al., 2019; Zucker et al. 2012). 45 to 82% of adolescents showed internalizing symptoms such as anxious-depressive moods, social withdrawal behaviors, and somatization tendencies, as well as externalizing abnormalities such as impulse control disorders. Across different countries, there was a clear predominance of internalizing disorders compared to externalizing problems (Cohen-Kettenis et al., 2003; de Graaf et al., 2018; de Vries et al., 2016; Levitan et al., 2019; Röder et al., 2018; Sievert et al., 2020), from which it can be hypothesized that adolescents with GD have higher levels of anxiety, depressive, and somatic complaints, with fewer aggressive-impulsive problems from the externalizing spectrum in comparison.

Further, there is evidence on the importance of **peer relationships** and **family support** as a key protective factor for psychological well-being. Negative experiences with peers emerged as the most important predictor of psychological distress (Aitken et al., 2016; de Graaf et al., 2018; de Vries et al., 2016; Levitan et al., 2020; Sievert et al., 2020; Steensma et al., 2014), assuming that problematic peer relationships may also be an expression of increased psychosocial problems in general and, as a consequence, increased mental health problems. Although cause and effect are not yet sufficiently understood, adolescents with GD have been identified as a particularly vulnerable group to experiences of discrimination and rejection by peers (Toomey et al, 2010) and within the family (Grossman and D'Augelli, 2007).

In addition to OA, various attempts have been made to classify GD subgroups based on **sexual orientation (SO)** (Lawrence, 2010; Nieder 2011; Blanchard, 1987). This was based on the assumption that the original "true transsexualism" (Benjamin, 1966) had to be accompanied by an opposite-sex/heterosexual orientation (after gender reassignment). From a developmental dynamic perspective, the aspect of sexual orientation is interesting less as an attempt at subtyping than as an expression of consolidation of adolescent notions of identity and their testing in interpersonal space, and thus corresponds primarily with the quality of relationships with peers. A differentiated clarity on sexual attraction as well as sexual activity in the sense of "trying oneself out" can influence mental health in adolescence, in line with the findings of Levitan et al. (2019) on the relationship between problematic peer relationships and psychological distress.

**Summary and derivation of research question**

Previous research suggests that differentiating subgroups of adolescents with GD may improve understanding of heterogeneous developmental pathways and, as a result, more individualized treatment steps and services. This seems particularly necessary given the increasingly variable manifestations, and derived different needs, that find little place in current treatment protocols. Therefore, the present study is the first to systematically record a large sample of adolescents with GD with respect to their clinical characteristics of OA and psychological distress for the German-speaking world. Despite numerous clinical hypotheses, which essentially refer to cause-effect relationships, there is so far a lack of differentiating, quantitative studies investigating the relationship between OA and psychological distress in adolescents, controlling for other possible influencing factors, such as gender of assignment, age, intensity of GD, body satisfaction, problematic peer relationships, family functioning level, and SO.

Therefore, the following three research questions will be answered in this paper:

1) What is the distribution of OA among adolescents with GD presenting to a specialized consultation?

2) What is the prevalence of clinically relevant problems in clinically presenting adolescents with GD (compared to the norm sample) and what is the nature of psychological distress?

3) What is the relationship between OA and internalizing problems in clinically presenting youth with GD?

Based on previous research, we hypothesize that an LO is related to more internalizing problems.

**Methods**

**Project framework and study design**

At the University Medical Center Hamburg Eppendorf (UKE), the special outpatient clinic for GD in childhood and adolescence (Hamburg Gender Identity Service for children and adolescents, Hamburg GIS) has existed since 2006. According to the current treatment guidelines (cf. AMWF, 2020; Coleman et al., 2022), in addition to diagnostics and psychotherapeutic treatment, indications for gender reassignment measures also take place there. Since 2013, all presenting families have been invited to participate in a study at the Hamburg GIS. Participation is voluntary and data collection takes place at the first appointment, before the start of a diagnostic phase and any use of physical medicine measures. An ethics application for the research project was approved by the Hamburg Chamber of Psychotherapists. The study follows a cross-sectional design with the use of internationally established, psychometrically tested questionnaires (self-report) and expert ratings.

**Sample**

This study examined adolescents who presented to the specialty outpatient clinic between September 2013 and December 2021 and met diagnostic criteria for GD according to DSM-5 (APA, 2013). All diagnoses were rated by clinical experts using standardized diagnostic checklists after a diagnostic period of several months. Since the DSM-5 sets a cut off between the diagnostic classification of childhood vs. adolescence based on age at 11 years, this was adopted and all participants were 11 years or older accordingly. The utilization population comprised a total of 1122 children and adolescents from all northern German states during the survey period. A total of 631 complete data sets are available from the survey. For various reasons, 169 cases had to be excluded (see Fig.1). Thus, for the present study, the complete data of n = 462 adolescents aged 11-18 years with a GD diagnosis and their families were included.

**Figure 1:** *Participants and gender distribution in the HH special outpatient clinic*.

**Sociodemographics and Onset Age**

The following sociodemographic characteristics were included in the analyses: Assignment gender, age at first presentation, nationality, marital status and living situation, and socioeconomic status (SES) of parents (for a detailed description, see Levitan et al., 2019 and Herrmann et al., 2023).

In addition, crossgender identification (experiences of belonging to the "opposite" gender) was recorded for all participants, using a sum score identified in previous studies (e.g., de Vries et al. 2016): In the Youth Self-Report (YSR), items 5 and 110 refer to opposite-sex experiences ("I act like someone of the opposite sex" and "I would like to belong to the opposite sex"). The sum score of the two items can be used as a measure of the intensity of gender incongruence (given a binary understanding of gender identity). The score ranges from 0 to 4, with larger values expressing higher intensity of gender incongruence.

OA was operationalized by dichotomous assignment to EO GD if the DSM diagnosis of GD was already applicable in childhood and LO GD in participants who retrospectively did not meet criteria for GD in childhood but did in adolescence. Thus, two groups of participants emerged: 0) EO (met DSM-5 criteria of GD in both childhood and adolescence) and 1) LO (met DSM-5 criteria of GD only in adolescence). In additional exploratory analyses, within the LO group, we subdivided by duration of GD and labeled all participants whose GD had been present for less than one year as "**Recent Onset GD**".

**Psychological distress**

Internalizing problems were assessed with the 1991 German version of the YSR (Achenbach, 1991; Döpfner et al., 1998) for adolescents aged 11-18 years. The YSR consists of 120 items rated on a 3-point scale ranging from 0 = "not true" to 2 = "true exactly or often." The higher the score, the more pronounced the respective problems are. The total sum of all problem scores is reflected in the total problem score, whereby two main scales can be differentiated (internalizing and externalizing problems). In addition, values in the clinical range (> 90th percentile; T-scores > 63) can be given for these three indices. Norm values of adolescents (aged 11-18 years) from the German general population are available for the different indices and assignment genders (Döpfner et al., 1998). These norm or T values can be used to determine whether the values of our sample are within the normal range. Cronbach's α for the internalizing scale was .91.

For exploratory purposes, the YSR score for externalizing problems and the total problem score were also calculated to examine psychological functioning more broadly. For more information on the calculation of these two indices, see Levitan et al. (2019) or Herrmann et al. (2023). In this study, Cronbach's α for the externalizing and total problem scales was .83 and .93, respectively.

The **Children's Global Assessment Scale (CGAS)** (Shaffer et al., 1983) was used within the exploratory analyses to assess adolescent global functioning using treatment ratings. The CGAS is one of the most widely used assessment scales for measuring everyday functioning in children and adolescents (Schorre et al., 2004). The instrument is divided into 10-point intervals ranging from 10 to 100, with higher scores (above 80) indicating good global functioning.

**Control variables**

**Sexual orientation** was assessed with a self-developed item asking about physical (sexual) attraction in partner choice ("To whom are you more physically (sexually) attracted?") and providing six response categories: "to no one," "to girls," "more to girls, sometimes to boys," "to both girls and boys," "to boys," and "other" (free text response). From these, three categories of SO were formed in relation to assignment gender: 0) Same-sex/homosexual, 1) Opposite-sex/ heterosexual, and 2) Other. The "Other" category was screened and three subgroups were formed: asexual/ uncertain, bisexual, and pansexual.

Three items from the YSR were used to assess **problematic peer relationships (PPR**): Item 25 ("I do not get along with other children or adolescents"), Item 38 ("I am often teased"), and Item 48 ("I am not popular with other children/adolescents"). The PPR has been used in previous studies to measure problematic peer relationships in youth with GD (Levitan et al., 2019; Sievert et al., 2021). The index ranges from 0 to 6, with higher scores reflecting poorer relationships with peers. In the present study, Cronbach's α was .66.

For **general family functioning (GFF)**, the McMasters' Family Assessment Device (FAD, Epstein, Baldwin, & Bishop, 1983) was used. For the present study, only the GFF subscale was evaluated. The GFF scale consists of 12 items, such as family acceptance ("Everyone is accepted as they are"), rated on a 4-point scale (from 1 = "agrees exactly" to 4 = "does not agree at all"). The sum of the 12 items was divided by 12 to create a score ranging from 1 to 4, with higher scores indicating lower levels of family functioning. The cutoff for categorical analyses (problematic or unhealthy family functioning) is 2.17 (Byles et al., 1988). Cronbach's α was .88 in the present sample.

The pictorial measure "**Hamburg Body Drawing Scale" (HBDS**) was used to assess body satisfaction (Appelt & Strauß, 1988; Becker et al., 2016). Participants are asked to rate their satisfaction with various body features and overall appearance on a 5-point scale (from 1 = "very dissatisfied" to 5 = "very satisfied"). The HBDS has been revised and validated for transgender populations (Becker et al., 2016). Internal consistency for the HBDS subscales (Cronbach's α = .63 - .91) is satisfactory (Becker et al., 2016). In the present study, only one item on general body satisfaction was used.

**Statistical analysis**

Confidence intervals (95% CI) were calculated for the prevalence of EO and LO GD. To examine differences between groups (OA and assignment sexes) or associations, t tests and chi-square tests were performed, respectively. Standardized effect sizes (Cohen's d and odds ratios, OR) were calculated to quantify the magnitude of the effect.

Internalizing problems were assessed using raw scores, T scores, and clinical ranges (> 90th percentile; T scores > 63). In addition, confidence intervals for T-scores were calculated to compare the present sample with the age- and sex-equivalent German norm (Döpfner et al., 1998). Whenever the confidence intervals were not within the normal range of the T-distribution (M = 50, SD = 10), a significant difference to the reference group can be assumed. When the confidence intervals overlapped, the results were not significantly different from each other (Cumming & Finch, 2005). For exploratory purposes, the externalizing scale and total problem score were also evaluated as presented.

Multiple linear regression analysis was performed to examine the predictive value of the OA for internalizing problems. For this purpose, the raw scores of the YSR internalizing scale were used, while controlling for assignment sex, age, PPR, GFF, SO, body satisfaction, and crossgender identification. In the exploratory analyses, the same was done to examine the associations between OA and externalizing problems and total problem score. For the total problem score, three items on PPR (items 25, 38, and 48) were also excluded because PPR was a separate predictor in the model. An a priori power analysis (using G\*Power) showed that a small effect (f = 0.02) with a power of 85% could be tested in a multiple regression analysis with n = 462 cases and eight predictors.

In the exploratory analyses, multiple linear regression was also calculated to examine the association between OA (independent variable) and global functionality (dependent variable). The same control variables as described above were used.

Individual missing values were replaced using the expectation maximization algorithm (EM, Little & Rubin, 2019). All statistical analyses were performed using SPSS version 27.

**Results**

**Description of the sample**

Table 1 shows the sociodemographic and clinical characteristics of the participants. The sample (n = 462) consisted of 85% female and 15% male adolescents with a mean age of 15.5 years. EO GD was present in 51% of participants and LO GD in 49%, with the second group being significantly older at initial presentation. There was no association between gender of assignment and OA.

Almost all adolescents were German citizens and came from a family with medium or high SES, with participants with LO GD having significantly higher SES than participants with EO GD.

When asked about problems with peers in the last six months, significantly more LO adolescents reported at least one relevant problem and differed significantly from EO adolescents in this respect. The GFF also showed that LO adolescents experienced problematic family relationships significantly more often than EO adolescents. Furthermore, EO and LO adolescents differed in the intensity of GD experienced, which was significantly more pronounced in EO adolescents than in LO adolescents. No difference was found between the two groups in body satisfaction, which was on average very low regardless of OA.

In the group of LO adolescents, the duration of the experienced GD was additionally asked. Between 23-36% of the adolescents met the criteria for a Recent Onset of GD and reported the first onset of GD less than one year ago (Table 2).

In terms of SO, half of the participants (in relation to assignment gender) located themselves as same-sex oriented and about a quarter as opposite-sex oriented. Significantly more EO youth (63%) were same-sex oriented than LO youth (30%), who were most often opposite-sex oriented or bisexual.

**Internalizing Problems**

Results on internalizing problems are presented in Table 3. Compared with the German norm population (M = 50, SD = 10), adolescents with GD had significantly higher T-scores (95% CI without M = 50) for internalizing problems. Adolescents with GD scored on average more than 1.5 SD higher on the internalizing problems scale than peers from the YSR reference group.

Regarding OA, it was found that LO GD adolescents were significantly more burdened with internalizing problems than EO GD adolescents. The former had 67% in the clinically salient range, whereas the latter had 49% clinically salient scores (T-scores > 63). Overall, from the sample, 58% of adolescents had clinically relevant levels of distress.

**Onset Age and Internalizing Problems**

The results of the multiple linear regression analysis to test our hypothesis are shown in Table 4. The regression analysis showed a significant relationship between OA and internalizing problems: As hypothesized, the LO GD group was higher by three scale points for internalizing problems in the YSR With respect to the control variables, more internalizing problems were significantly related to gender (female assignment sex), sexual orientation (non-same-sex SO), PPR (poorer peer relationships), GFF (poorer family functioning level), and body satisfaction (less body satisfaction).

Overall, the model resolved 44.5% of the variance in internalizing problems. OA resolved 1.5% of the variance and the control variables a total of 43%.

**Exploratory data analyses: onset age, externalizing problems, and level of functioning**

Exploratory data analyses were conducted to examine the associations between OA and externalizing problems, as well as total problem score and mental functioning level (CGAS) (Appendix Table A1 through A4).

Externalizing problems were less common than internalizing problems in adolescents with GD but still elevated compared with the norm sample (Table A1). 14.5% of cases reported clinically relevant externalizing problems. There were no significant differences between EO and LO youth. Also elevated was the total problem score: youth with GD scored more than 1 SD higher than the reference group, and 46% of participants were in the clinically salient range. LO adolescents were significantly more clinically distressed and tended to be more clinically distressed than EO adolescents. There was also a significant difference in the global level of functioning between the two groups, with LO adolescents having a lower level of functioning.

In the multiple regression analysis for externalizing problems, a significant relationship was found between OA and externalizing problems (Table A2). An inverse relationship was found compared to internalizing problems, i.e., LO adolescents were burdened with fewer externalizing problems. Significant control variables were assigned gender, PPR, and GFF. The model resolved only 16% of the variance in externalizing problems: OA resolved 1% of the variance and the control variables a total of 15%.

Another regression model (Table A3) tested whether OA had an effect on total problem score and global functioning level. OA and total problem score were not related. Significant control variables were assigned sex, PPR, GFF, and body satisfaction. The model resolved 39% of the variance in total problem score.

Table A4 shows the results for the association between OA and global functional level. LO proved to be a significant predictor of worse global functional level. Significant control variables here were PPR and intensity of GD. The model resolved a total of 11.6% of the variance in CGAS: OA resolved 2.2% and the control variables 9.4%.

Last, we explored whether OA was related to internalizing problems when the Recent Onset and LO groups were considered separately (Table A5). Belonging to the LO group was related to significantly higher psychological distress from internalizing problems. Belonging to the Recent Onset group was not related to more internalizing problems, but showed a tendency to do so. Significant control variables were assignment sex, PPR, GFF, body satisfaction, and SO. The model explained a total of 44.5% of the variance in internalizing problems, of which OA accounted for 1.4% and the control variables for 43.1%.

**Discussion**

The aim of the present study was to assess the frequency of EO vs LO courses and to investigate the association between OA of GD and psychological distress in adolescents attending a specialized outpatient clinic for GD.

In the present study, OA emerged as a significant predictor of psychological distress in that LO GD in adolescence was associated with a particularly high burden of internalizing problems.

Numerous relevant differences in sociodemographic and clinical characteristics between EO and LO adolescents (age at first presentation, SES, PPR, GFF, crossgender identification, and SO) also emerged.

The higher burden of the LO group corresponds to recent findings in which a group classification was made on the basis of the age of presentation (Arnoldussen, 2022), pubertal developmental stages and first self-perception of GD (Sorbara, 2021), in which in each case the older study group showed a higher psychological burden. In this context, older age at first presentation and an associated longer suffering from GD is usually understood as an expression of reactive distress or, under certain circumstances, harmful experiences of discrimination. In contrast, our EO and LO groups differed only insignificantly in age (15.2 years to 15.7 years at first presentation). In addition, we found that a longer duration of GD with onset already in childhood (EO) was *not* associated with a higher burden, as previous findings could suggest.

This is also supported by the results we found exploratively for the adolescents with Recent Onset GD: despite the short duration of the gender dysphoric experience of less than one year, they showed a similar or even higher burden of internalizing problems than the rest of the LO group. A more recent study by Turban et al. (2023), which retrospectively asked adults about the Age of Realization of GD (subdivided into under 10 years = childhood and over 10 years = later realization), found a roughly even distribution of OA but, contrary to our findings, an older group significantly less burdened with suicidal thoughts and no differences between groups in overall psychological burden.

Contrary to expectations, the gender ratio did not differ between the EO and LO groups, but was balanced with a share of 86% and 84% AFAB, respectively. In this respect, it cannot be assumed that there is an overrepresentation of adolescents with a female assignment sex in the LO group. However, if one considers the physical development of maturity and the fact that girls enter puberty much earlier and usually develop recognizable secondary sexual characteristics well before the age of 12 (Grüters-Kieslich, 2009), this could be a possible explanation for more adolescents with female assignment sex in the EO group. In this context, it is interesting to note the finding that the EO group reported greater intensity of GD and opposite-sex identification with otherwise lower exposure. This could correspond with the assumption of Cohen-Kettenis and Klink (2015) that there is a clinical subtype of female-born adolescents with an early onset course and exceptionally strong GD, which has an early desire for physical medical treatment. At the same time, however, this also shows that a GD with high intensity and suffering pressure does not necessarily have to be connected with strong internalizing problems, but under certain circumstances there are different or independent developmental paths. A clinical approach of understanding seems to be urgently necessary in order to describe these courses more precisely and to be able to make well-founded treatment decisions on this basis.

Limiting causal inferences is the fact that in the Hamburg sample, the proportion of AFAB youth continues to trend upward: from the last data collection in 12/2018 (see, e.g., Levitan, 2019) to our current survey in 12/2021, the proportion of AFAB in the overall sample changed from 74% to 85%. Thus, our sample differs significantly from the Dutch cohort, in which the sex ratio changed only marginally over the long-term (de Graaf et al, 2018; Arnoldussen, 2022).

Considering findings from previous studies on onset age, a developmental dynamic link between female assignment sex and LO GD is suggested, but has not been shown in our study. Nieder et al. (2011) reported 78% EO in an adolescent sample of AFAB subjects presenting to specialized European gender reassignment centers. In contrast, our proportion of 51% EO courses is not only significantly lower, but also contrary to the notion that with increased societal openness and information diversity about transgender might come earlier age-related reflection on the potential discrepancy between body gender and identity experience (e.g., Aitken et al. 2015). Rather, contrary to this expectation, there appears to be a temporal shift to later adolescence, when the incongruence is first perceived.

It is possible, however, that the decrease in stereotypical role expectations and evolved possibilities of expression can also be understood ambiguously: for some, this is associated with a relief from gender templates and more individual freedom; for others, possibly a loss of orientation and the search for new identifications to counteract the insecurity. In both possibilities, the unresolved question arises as to how it is possible to experience puberty without a subjectively noticed pressure of suffering in the case of a LO GD and how it generally comes to the development of dysphoria.

Moreover, given the high burden of internalizing problems and a tendency to withdraw from real interactions with peers in favor of social media and LGBT community contacts (Herrmann et al., 2023), it seems rather questionable whether a creative and individual shaping of gender-nonconforming experiences is possible at all. It can be assumed that an examination of one's own gender identity experience takes place not only in the young person himself, but increasingly also in the virtual interaction with protagonists of social media.

Another interesting finding was revealed in the differences in sexual orientation between the EO and LO groups and the dominance of a same-sex orientation (EO) versus an opposite-sex/other orientation (LO). When SO is viewed less as an etiological indicator (see, e.g., Blanchard, 1987), as it has been in the past, and more in its interpersonal relations, a link to the pronounced problems in peer relationships becomes apparent. The high variance in SO within the LO group is accompanied by stronger problems in peer relationships. Both, the strained relationships and an unclear, only little tested sexuality, as described by Bungener (2017) and Stübler and Becker- Hebly (2017), can significantly complicate a consolidation of adolescent identity ideas as well as lead to a retreat from explorative and progressive adolescent desires and consolidate a persistent insecurity instead of enabling a lively testing.

Strained peer relationships, ambiguity about one's sexual attraction, strong body-related dissatisfaction, and limited family support among LO adolescents point directly to the high symptomatic distress of this group. Identity is a process essentially determined by interaction (Mertens, 1993), both between the individual and relevant others and within the self in the process of reflecting on and testing different conceptions of self. A consolidated and stable experience of identity, also with regard to a grown clarity about one's own gender identity, is accordingly clearly more difficult in the case of high symptomatic stress and conflictual relationships with peers. It can be assumed from this that LO adolescents represent a particularly vulnerable group that can benefit from an individually tailored treatment program in addition to long-term psychotherapeutic support that can help to consolidate their own identity experience and create space for development again.

**Clinical implications**

The results presented raise three major questions: 1) Is there a clinical late onset subtype? 2) On what basis or under what conditions can reliable physical medical indication decisions be made at all? 3) Can a protocol-based approach still meet the needs of those seeking treatment in view of the diversity of courses and the different development paths that can be derived from them?

First, the present findings indicate that increasing heterogeneity is not only apparent in clinical course observations of treatment-seekers, but is also reflected within the sample between EO and LO courses. In the results, the LO group was found to be significantly more psychologically distressed, with more pronounced peer problems, opposite-sex or asexual orientation, and only moderate crossgender identification. Neither the duration of the gender dysphoric experience nor the intensity of crossgender identification can be convincingly assumed to be causal for the overall very high psychological distress, so that other influences involved are likely.

Drawing on the clinical manifestations briefly outlined at the beginning, we can assume that for a substantial proportion of adolescents with long psychiatric histories, late-onset GD will have a different developmental trajectory than a deeply felt incongruence between identity gender and body. Contrary to Littmann's (2018) assumption, we consider a developmentally derivable transgender belief to be etiologically different in understanding, but not milder in course or less in need of treatment. Rather, the question here is what interventions would benefit this particularly vulnerable group of youth with LO, beyond the desire for physical medicine interventions.

Second, an indication for physical health interventions based purely on descriptive and external criteria appears neither purposeful nor feasible given the reciprocal overlap of gender dysphoric experiences and other developmental conflicts (Edwards- Leeper, 2017; Zucker et.al., 1995).

Our proposal is therefore: A comprehensive process-oriented diagnosis including psychosexual development, own narratives about identity development, as well as a detailed anamnesis for other relevant adolescent issues and conflicts forms the basis for an assessment of the course, in the context of which considerations about body-modifying measures can become an issue at all. A focus is placed on the interaction between GD and relevant developmental conflicts, thus enabling a deeper understanding of the individual path and the development of a narrative of one's own. An accompanying psychopathology does not represent a clear contraindication for physical medical measures, as long as it can be understood in terms of developmental dynamics. Nonetheless, the psychodynamic review makes clear that a substantial proportion of adolescents at the time of the diagnostic phase benefit less from physical medicine interventions than from adjunctive and developmental psychotherapy. Given concerns about increasing numbers of detransitions (Cohn, 2023), persistent distress despite body-modifying interventions (Roberts et. al., 2022; Diaz et. al., 2023), and ambiguity regarding the stability of GD experience over time, cautious and intensely reflective indications for this group of adolescents appear essential.

Third, our study group is characterized by a particularly high degree of burden with internalizing problems, also in comparison with other European samples (see de Graaf et al., 2018). This, as well as the shifted gender ratio toward a dominance of AFAB trajectories, make our study group not directly comparable to the Dutch cohort from the follow-up studies. Abbruzzese et al. (2023) point out the inapplicability of the Dutch results to heterogeneous, nonpreselected treatment groups, which include nonbinary, psychiatrically troubled youth. A normative, criteria-based approach no longer seems appropriate. The growing diversity of developmental trajectories in adolescents, with varying intensity of gender dysphoric distress and concomitant, interacting psychopathology, demonstrates the need for an individualized treatment setting. The guiding question "what works for whom, at what time, and in what setting" enables a differential indication (Dorr et. al., 2020) for outpatient or inpatient psychotherapy, physical medicine measures, or low-frequency accompaniment oriented to individual needs.

**Limitations**

Our findings should be considered in light of several limitations. Data collection in the form of a cross-sectional design cannot provide information on long-term trajectories or influencing factors. This is especially true for the control variables studied, such as intensity of GD, sexual orientation, and body satisfaction, which should be considered snapshots and may change over time.

Another difficulty is the operationalization of LO and EO trajectories. Even though retrospective assessment by expert ratings after a diagnostic process is based on adolescents' self-descriptions, it is selective boundary setting because of the DSM-5 classification based on age 12 years. Given the average age difference between male and female puberty and the now advanced timing of female pubertal development, the results are likely to be of limited value to some participants. For future studies, a clearer determination based on physical maturational development would be useful. For example, it is known that puberty and the associated onset of body-related complaints is a key time for many children and adolescents with GD to become aware of their own incongruence (Steensma et.al., 2013).

Similarly, while the collection of psychological distress using YSR data is widespread, a categorical diagnostic using standardized questionnaires for ICD-10/-11 would be important. Another aspect that should be considered in future studies is the systematic collection of data on the course of treatment for the sample, as this will make it clearer to what extent there are also differences in the indication given the subgroups found. Last but not least, it has to be stated restrictively that with the chosen methods the great variety - also of possible further - development paths in the group of GD adolescents can only be represented in an excerpt and thus certainly cannot do justice to the diversity of the population, so that clinical experience values can also only be represented statistically with difficulty.

**Conclusions**

The present study showed that about half of the adolescents who turn to a specialized center because of GD report an LO course. A LO course proved to be associated with a very high burden of internalizing problems, which are also still significantly higher than those known in comparable populations in European countries.

The findings point to a specific subgroup of LO adolescents in the growing spectrum of heterogeneous trajectories and are understood against the background of different etiological developmental pathways. The diversity of trajectories and the presence of particularly vulnerable subgroups highlight the need to move away from a protocol-based approach toward a more individualized approach based on developmental dynamics in the sense of differential indication.

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