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Voice dissatisfaction in individuals with a disorder of sex development

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Abstract

Objective: Changes of sex hormone levels in disorders of sex development (DSD) can affect the body, including the vocal folds, during and after foetal development. The voice is a gender characteristic that may also be affected. There is a lack of knowledge on voice alteration in DSD. To explore this in different forms of DSD, we describe the prevalence of voice alterations and investigate patient satisfaction with voice.

Design: The study is part of dsd-LIFE, a multicentre cross-sectional clinical evaluation project assessing the long-term outcomes of surgical, hormonal and psychological interventions in individuals with DSD.

Patients: The study included 1040 individuals with different forms of DSD, that is Turner and Klinefelter syndromes, different degrees of gonadal dysgenesis and 46 XY DSD. Participants were recruited through patient advocacy groups and health care.

Measurements: Satisfaction with voice, Adam's apple, if patient's self-identified gender was mistaken on the phone leading to distress.

Results: A vast majority of the participants with DSD (between 58.3% to 82% in various groups) were not satisfied with their voice, and approximately 15% (n = 147) were mistaken on the phone in accordance with self-identified gender. For 102 participants, this caused distress.

Conclusions: We have identified that voice problems are a cause of distress in all forms of DSD. This result needs to be confirmed and compared with controls. We recommend that evaluation of the voice should be included in future international guidelines for management of DSD.

KEYWORDS
androgens, feminization, gender, hormones, pitch, self-ratings, virilization, voice

Birgit Köhler is a Corporate Member of Freie Universität Berlin.

1 | INTRODUCTION

Disorder of sex development (DSD) is a broad clinical entity defined as an atypical sex development concerning chromosomal, gonadal or phenotypic sex.[1-4] Excess or deficiency of sex hormones is common and, thus, can affect the body during and after foetal development. In some diagnoses, there are no or slight anatomic differences but in the more severe forms one may initially not be able to tell the child's sex after birth. The anatomical differences that characterize males and females include body stature, distribution of muscles and body hair in addition to the anatomy of the genital organs. The differences also include the laryngeal and pharyngeal structures involved in the production of voice and speech. Variations in sex hormones may cause voice virilization in females and lack of voice masculinization in males. The voice is used every day to communicate with other people, but we may not consider how much this influences or confirms our assumptions of the sex of an individual in a social construct. For example, during telephone conversations, it is likely that one can identify the gender and approximate age of the individual. The sound differences are mainly due to the anatomical structures in the vocal folds and pharynx, but also to some extent the vocal behaviour.

The voices of boys and girls sound very similar until entering puberty when the influence of sex hormones causes an alteration in voice function.[5] During puberty, the vocal folds increase in length and the thyroid cartilage, the Adam's apple, becomes more prominent in boys.[6] The voice pitch lowers considerably in boys and less so in girls.[7,8] Adult females speak with a pitch, measured as fundamental frequency (f_o), of approximately 200 Hz, and adult males one octave lower, 100 Hz.[9,10] The pitch is an important feature to perceive a voice as male/masculine or female/feminine.[10,11] The voice pitch has been shown to be correlated with BMI[12] and body height.[13]

1.1 | Voice in patients with DSD

Earlier case reports have described a virilized voice, that is lowering of the voice pitch, in a few females with congenital adrenal hyperplasia (CAH).[14,15] We have recently studied voice characteristics in women diagnosed with CAH divided according to severity in the subgroups: salt-wasting (SW), simple virilizing (SV) and nonclassic (NC). We found that a prolonged period of under-treatment, either due to late diagnosis or suboptimal treatment, increases the risk of severe virilization of the voice, which may concern the individual and cause distress.[12,16] We have also shown that the voice virilization in women probably is due to an androgen effect on the thyroarytenoid muscle in the vocal folds, as observed with MRI examination.[17] Such virilization of the larynx is considered irreversible in contrast to other signs of virilization.[18-20] A virilized voice in women, characterized by unnatural low pitch and loss of high frequencies, may also be hoarse, rough and difficult to project.[21]

If the voice is not congruent with the speaker's sex, that is the pitch is too high for a male voice and too low for a female voice, it may cause distress. This can happen especially when the person is speaking on the phone and is not visible to the listener.

In other forms of DSD, like 5-alpha reductase deficiency type 2, 17 beta-hydroxysteroid dehydrogenase type 3 deficiency and 11 beta-hydroxylation defect, one of the initial symptoms can be deepening of the voice in a girl associated with other signs of pubertal virilization.[22-24] In 1968, a study was performed concerning phoniatric data from 23 DSD cases, mainly patients with Turner syndrome.[25] In women with Turner syndrome, a more high-pitched voice is common when untreated, mainly due to shorter stature.[26] Although the voice pitch decreases after treatment with the androgen oxandrolone in combination with growth hormone,[27,28] women with Turner syndrome have reported voice problems, especially those with monosomic or isochrome Turner syndrome as compared to women with the mosaic form.[27] Finally, in one case report a boy with Klinefelter syndrome was described to have a female sounding voice.[29]

Thus, voice alterations can exist for both males and females with different forms of DSD, due to a disrupted hormonal balance. Thus far, these alterations of the voice have been mainly described in individual cases or smaller case series. We aimed to explore whether the voice can be affected to a larger extent in forms of DSD other than CAH and describe the prevalence of voice alterations in a larger sample. We also investigated the patient's self-perception of voice and whether this caused any distress.

2 | MATERIAL AND METHODS

Dsd-LIFE is a multicentre cross-sectional clinical evaluation study assessing the long-term outcomes of surgical, hormonal and psychological interventions in individuals with DSD.[30] The dsd-LIFE consortium consists of 16 partners from six countries (Germany, France, the Netherlands, Poland, Sweden and the United Kingdom). Ethical approval was granted from the local medical ethics committees. Participant recruitment through patients' advocacy groups and clinical records took place from 1 February 2014 to 30 September 2015, with a final participation rate of 37%.

The study included 1040 individuals from 16 years of age and older including the following diagnoses: Turner syndrome, Klinefelter syndrome, 47,XYY, 45,X/46,XY DSD (mixed gonadal dysgenesis (GD)), 46,XX DSD (ovarian dysgenesis, CAH), 46,XX men and 46,XY DSD (complete/partial GD, complete/partial androgen insensitivity syndrome (CAIS/PAIS), hypospadias and others). In the present study, we excluded 40 cases as they belonged to several different small subgroups (n = 28) or classified themselves as open/other/inter gender (n = 12).

We collected patient reported variables including age, height, weight and BMI, as well as whether sex reassignment had occurred after the age of 16 years (n = 5). In the questionnaire, the participants rated the following statements on a 5-point scale: 'I am satisfied with my health', 'I am satisfied with my voice', and 'I am satisfied with my Adam's apple': very dissatisfied (=1), dissatisfied (=2), neutral (=3), satisfied (=4) and very satisfied (=5). The items 'Are you satisfied with your voice' and 'Are you satisfied with your Adam's apple'

TABLE 1 Mean (M) and standard deviation (SD) for age, height, weight, BMI and the number of patients (n) in the (a) different diagnostic groups of DSD and their self-identified gender (F = female, M = male), (b) three subgroups of CAH, all females

	Turner	XX, DSD	CAH	XY, DSD		X/XY		Klinefelter
	F	F	F	F	M	F	M	M
	n = 301	n = 21	n = 207	n = 141	n = 73	n = 31	n = 14	n = 212
(a)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Age (y)	32.2 (13.3)	22.9 (5.2)	29.9 (11.0)	30.7 (12.5)	23.3 (7.7)	30.7 (13.6)	24.6 (7.8)	39.3 (15.3)
Height (cm)	152.7 (7.0)	164.8 (6.7)	160.4 (7.8)	174.2 (7.2)	177.1 (7.8)	156.3 (8.9)	159.9 (6.6)	185.0 (8.4)
Weight (kg)	59.2 (13.2)	58.9 (9.2)	67.7 (16.1)	73.0 (21.7)	76.5 (17.0)	66.1 (18.3)	67.4 (13.9)	89.8 (20.3)
BMI	25.4 (5.3)	21.8 (4.2)	26.4 (6.3)	24.0 (6.5)	24.4 (5.3)	26.8 (6.0)	26.2 (4.4)	26.1 (5.4)

	SW CAH	SV CAH	NC CAH
	n = 109	n = 65	n = 33
(b)	M (SD)	M (SD)	M (SD)
Age (y)	29.1 (9.9)	29.9 (11.2)	32.5 (13.8)
Height (cm)	159.7 (8.1)	159.5 (7.0)	164.0 (7.4)
Weight (kg)	67.7 (15.5)	66.3 (16.7)	70.3 (17.1)
BMI	26.5 (6.2)	26.1 (6.5)	26.3 (6.6)

Note: There were some missing data for height, weight and BMI, but never more than 10% of the total number of persons for each diagnosis.

are part of the Body Image Scale (BIS) used in clinical assessment of patients with gender dysphoria.[31] Finally, two self-constructed questions were added to investigate voice aspects with respect to self-identified gender and rated from the individual's own perspective and perception. The first was 'Some people have an unusually high or low voice so their gender might be mistaken on the phone. Has this happened to you?' This question was answered using the categories 'very often' (=3), 'a few times' (=2) or 'not at all' (=1). The following question was: If so, how much does it concern you? The answer categories: 'a lot '(=3), 'a little' (=2) and 'not at all' (=1) were used.

3 | RESULTS

Altogether, data from 1000 persons with DSD were analysed. Of these, 301 with Turner syndrome, 21 with XX DSD, 207 with CAH, (all females), 214 with different forms of XY DSD (141 females and 73 males), 45 with 45X/46,XY karyotype (31 females and 14 males), and 212 with Klinefelter syndrome, (all males) (Table 1a).

Data on age, height, weight and BMI are presented in Table 1a for each group of diagnosis and separated for males or females, and in Table 1b for the three subgroups of CAH. Sex reassignment after 16 years of age was noted in two CAH and one CAIS, self-identified as females and two XY DSD, self-identified as males. Only one XY DSD was dissatisfied with the voice. In Table 2a and b, we present data on satisfaction with health, voice and Adam's apple. Generally, patients were satisfied with their health. Men with XY DSD and Klinefelter syndrome and women with NC CAH were least satisfied.

3.1 | Satisfaction with the voice

The answers were recorded in 'very satisfied' and 'satisfied' grouped together (4-5), 'neutral' (3) and 'dissatisfied' and 'very dissatisfied' grouped together (1-2) as shown in Table 2a and b, and also in Figure 1. Ratings of the statement 'I am satisfied with my voice' showed that the majority of participants (69.6%) were 'dissatisfied' (4-5) with their voice. For the female participants, the percentage of individuals who were 'dissatisfied' ranged from 64.6% for women with Turner syndrome to 72.4% for the women with XX DSD. Although 65% of women with Turner syndrome had ever received growth hormone treatment, this did not significantly affect the result on voice satisfaction. In the subgroup with CAIS (n = 69), 82% expressed dissatisfaction with their voice. Among women with CAH, 66.8% were not satisfied, results that were similar for the three subgroups of CAH as seen in Table 2a and b.

Among the male participants, the percentage of individuals who were 'dissatisfied' with their voice varied from 58.3% for the 45,X/46,XY group to 77.4% for the Klinefelter group. In total, only 81 participants (9.1%) were satisfied with the voice (Table 2a). Twenty of those participants were 'very satisfied' and 61 were 'satisfied'. In the Klinefelter group, 160/212 (76%) had been treated with testosterone or were on current treatment, and this did not significantly change the result concerning voice satisfaction.

3.2 | Satisfaction with Adam's apple

In the group that self-identified as females, the vast majority (416/701 ≈ 59.3%) answered 'nonapplicable' regarding satisfaction with Adam's apple as compared to the male group (19/299;

TABLE 2 Responses in number (%),[a] for the statements 'I am satisfied with my health', 'I am satisfied with my voice' and 'I am satisfied with my Adam's apple' rated using the answer categories 'very dissatisfied' (=1), 'dissatisfied' (=2), 'neutral'=3, 'satisfied' (=4) and 'very satisfied' (=5) (a) for the different diagnostic groups of DSD and patients' self-identified gender, Females (F) and Males (M). Mean values for satisfaction with voice are given for each subcategory, (b) for the three subgroups of CAH, all females

		Turner	XX, DSD	CAH	XY, DSD		X/XY		Klinefelter
		n = 301	n = 21	n = 207	n = 141	n = 73	n = 31	n = 14	n = 212
(a)	Answer categories	F	F	F	F	M	F	M	M
Satisfaction with health	4-5	164 (57.7)	12 (66.7)	119 (60,4)	84 (60.1)	32 (47.8)	16 (53.3)	9 (69.2)	102 (51.0)
	3	83 (29.2)	2 (11.1)	42 (21.3)	31 (22.3)	17 (25.4)	10 (33.3)	2 (15.4)	56 (28.0)
	1-2	37 (13.1)	4 (22.2)	36 (18.3)	50 (36.0)	18 (26.9)	4 (13.3)	2 (15.4)	42 (21.0)
	NA	-	-	-	-	-	-	-	-
	Missing	17	3	10	2	6	1	1	12
Satisfaction with voice	4-5	17 (6.5)	1 (5.9)	19 (10.0)	11 (8.1)	12 (17.9)	1 (4.2)	1 (8.3)	19 (10.2)
	3	75 (28.8)	2 (11.8)	44 (23.2)	26 (19.3)	11 (16.4)	5 (20.8)	4 (33.3)	23 (12.4)
	1-2	168 (64.6)	14 (82.4)	127 (66.8)	98 (72.6)	44 (65.7)	18 (75.0)	7 (58.3)	144 (77.4)
	Mean	2,3	1,9	2,2	2,1	2,3	2,2	2,2	2,1
	NA	16	-	5	3	-	4	-	9
	Missing	25	4	12	3	6	3	2	17
Satisfaction with Adam's apple	4-5	6 (5.4)	0	5 (7.0)	4 (9.1)	3 (4.7)	1 (11.1)	1 (8.3)	11 (6.2)
	3	42 (37.9)	1 (16.7)	19 (26.8)	16 (36.4)	17 (26.6)	3 (33.3)	5 (41.6)	44 (24.6)
	1-2	63 (56.8)	5 (83.3)	47 (66.2)	24 (54.5)	44 (68.8)	5 (55.6)	5 (41.6)	124 (69.3)
	NA	168	11	124	94	2	19	1	16
	Missing	22	4	12	3	7	3	1	17

		SW CAH	SV CAH	NC CAH
(b)	Answer categories	n = 109	n = 65	n = 33
Satisfaction with health	4-5	65 (63.7)	40 (63.5)	14 (43.8)
	3	24 (23.5)	12 (19.1)	6 (18.8)
	1-2	13 (12.7)	11 (17.5)	12 (37.5)
	NA	-	-	-
	Missing	7	2	1
Satisfaction with voice	4-5	10 (10.3)	6 (9.8)	3 (9.4)
	3	22 (22.7)	15 (24.6)	7 (21.9)
	1-2	65 (67.1)	40 (65.6)	22 (68.8)
	NA	3	2	-
	Missing	9	2	1
Satisfaction with Adam's apple	4-5	2 (6.9)	1 (4.4)	2 (10.1)
	3	8 (27.6)	5 (21.7)	6 (31.6)
	1-2	19 (65.5)	17 (73.9)	11 (57.9)
	NA	71	40	13
	Missing	9	2	1

[a]Missing and nonapplicable (NA) data were not included in the per cent measurements.

6.3%). In the subgroup with CAIS, the Adam's apple did not seem to be a large problem, since only 12/69 were dissatisfied. The patients in the male group answered, 'very dissatisfied' or 'dissatisfied' (173/299; 57.9%) as compared to the female group (144/701; 20.5%).

3.3 | Mistaken gender on the phone

Of those 933 persons who responded to these questions, 147 participants (15.8%) stated that they were mistaken in accordance with self-identified gender 'a few times' (11.8%) or 'very often' (4%)

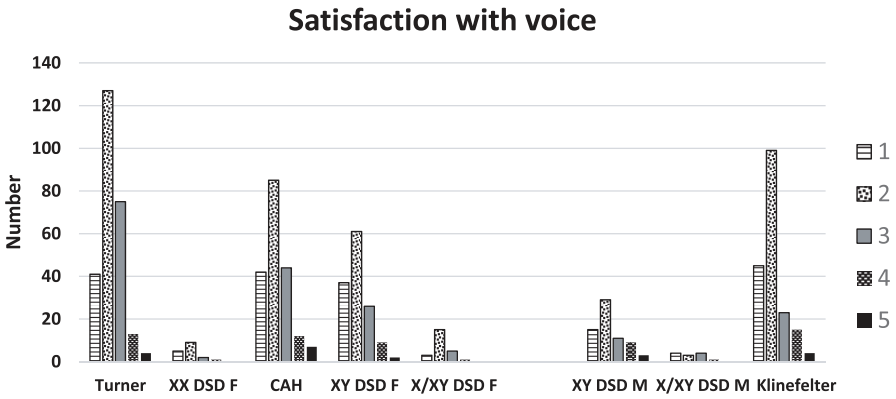

FIGURE 1 Diagram showing responses in number, for the statement 'I am satisfied with my voice' rated using the answer categories 'very dissatisfied' (=1), 'dissatisfied' (=2), 'neutral'=3, 'satisfied' (=4) and 'very satisfied' (=5) for the different diagnostic groups of DSD divided regarding patients' self-identified gender, Females (F) and Males (M). Mean values for each subcategory are given in Table 2a

on the phone (see Table 3 and Figure 2). Forty-five participants (4.8%) were not concerned about this, 64 (6.9%) were concerned 'a little', and 38 (4.1%) were concerned 'a lot'. In the sub group with CAIS, 90% had not been mistaken in accordance with self-identified female gender on the phone. Of the seven individuals (10%) whose gender had been mistaken on the phone, only four were concerned.

When examining responses from women with CAH, 44 (22.4%) were mistaken on the phone 'a few times' or 'very often'. Ten of them were concerned 'a lot': of those, eight had SW CAH. When analysing the data for the three CAH groups, 27/109 (25%) females with SW were mistaken as male on the phone. Of those, six were concerned 'a lot' and 13 'a little' because of this (17%). Similar results were observed for the SV group, with 15/66 (23%) participants mistaken as male on the phone; three were concerned 'a lot' and 8 'a little' (17%). In the NC group, 4/34 participants were mistaken as male on the phone (12%) but only one was concerned 'a little' and one was concerned 'a lot'.

The groups that most commonly answered that their self-identified gender was mistaken on the phone were men and women with XY, DSD (50/204 = 24.5%) as well as men with Klinefelter syndrome (37/196 = 18.9%).

In the group with Turner syndrome, nine of the 301 females (3%) described that they were mistaken as males 'a few times' but only three were concerned 'a little' or 'a lot' (1%).

Among 45 participants with 45,X/46,XY (31 females and 14 males), this was a rare problem as well as the group of XX, DSD with GD.

4 | DISCUSSION

We investigated aspects of voice in over 1000 individuals with various forms of DSD. Across a range of DSD diagnoses, the vast majority (62%) of participants were not satisfied with their voice and approximately 15% were mistaken in accordance with self-identified gender on the phone. Reporting patient perspectives in this large DSD-cohort gives important clinical insights, although the study outcomes were biased by self-report in the absence of objective evidence and control data.

When discussing voice in relation to perceived gender by others and cross–sex hormone treatment, there is an important sex difference since testosterone has an irreversible effect on the voice and larynx. Thus, a male who undergoes reassignment to female after puberty continues to have a virilized voice and will have a higher risk of not being perceived in accordance with self-identified female gender. This may be regarded as a significant problem and cause distress. In contrast, when a female transitions to male, the voice will be virilized due to the testosterone treatment and they will be perceived in accordance with their self-identified male gender.

In contrast, the study participants were generally satisfied with their health. Regarding the Adam's apple, many were 'neutral' or 'satisfied'. Many participants thought that the question about the Adam's apple was not applicable to them, particularly in the female groups. For transwomen, a pronounced Adam's apple can cause distress and therefore thyroid chondroplasty to reduce the prominence is sometimes performed.[32] Our results show that for a high number of women, satisfaction with the Adams apple was not an important issue, demonstrated by the high rate of nonapplicable answers (59%). Among the males, 58% were dissatisfied with the Adam's apple, indicating that this is an important masculine attribute. It is likely that the Adam's apple is underdeveloped due to lack of male hormones during puberty.

Unfortunately, there are no population-based studies that examine how vocally healthy males and females would rate satisfaction with the voice or Adam's apple. A small control group of healthy women (n = 43) gave a mean value of 81 on a 100 mm VAS (with the end-points 0 = not satisfied and 100 = completely satisfied) when asked the question 'Are you satisfied with your voice?'.[16] The BIS[31] can be used for transmen (female sex assigned at birth, male gender identity) and transwomen (male sex assigned at birth, female gender identity). In the BIS, 30 items are rated on a 5-point scale of satisfaction ranging from very satisfied (1) to very dissatisfied (5). Lindgren & Pauly[31] found that 16 transmen and 16 transwomen rated that they were 'dissatisfied' or 'very dissatisfied' with the voice based on group median scores before medical treatment. A recent study by Van de Grift et al[33] showed that 374 transwomen scored a mean value of 3.99, while 286 transmen scored a mean value of 3.86 regarding satisfaction with the voice before medical treatment. Our results show a high prevalence of dissatisfaction

TABLE 3 Results, number (%)[a] shown for each diagnosis for females and males and total for the question 'Some people have an unusual high or low voice so their gender might be mistaken on the phone. Has this happened to you?' The answer categories were 'Not at all', 'A few times' and 'Very Often'. The question 'If so, how much does this concern you?' followed and the answered categories were 'Not at all', 'A little' and 'A lot'

		Self-identified gender mistaken on the phone?	Self-identified gender mistaken on the phone?	How much does it concern you?			Self-identified gender mistaken on the phone?	How much does it concern you?		
Diagnoses	Missing data/NA	Not at all	A few times	Not at all	A little	A lot	Very Often	Not at all	A little	A lot
Females										
Turner n = 301	22	270 (96.8)	9 (3.2)	6	1	2	-	-	-	-
XX DSD F n = 21	4	15 (88.2)	1 (5.9)	-	1	-	1 (5.9)	-	-	1
CAH n = 207	11	152 (77.6)	33 (16.8)	11	16	6	11 (5.6)	2	5	4
XY DSD F n = 141	4	106 (77.4)	25 (18.2)	8	11	6	6 (4.4)	-	2	4
X/XY DSD F n = 31	3	26 (92.9)	2 (7.1)	2	-	-	-	-	-	-
All females n = 701	44	569 (86.6)	70 (10.6)	27 (4.1)	29 (4.4)	14 (2.1)	18 (2.7)	2 (0.3)	7 (0.1)	9 (1.4)
Males										
XY DSD M n = 73	6	48 (71.6)	14 (20.9)	4	7	3	5 (7.5)	-	3	2
X/XY DSD M n = 14	1	10 (76.9)	3 (23.1)	2	1	-	-	-	-	-
Klinefelter n = 212	16	159 (81.1)	23 (11.7)	8	10	5	14 (7.1)	2	7	5
All males n = 299	23	217 (78.6)	40 (14.5)	14 (5.1)	18 (6.5)	8 (2.9)	19 (6.9)	2 (0.7)	10 (3.6)	7 (2.5)
Total n = 1000	67	786 (84.2)	110 (11.8)	41 (4.4)	47 (5.0)	22 (2.4)	37 (4.0)	4 (0.4)	17 (1.8)	16 (1.7)

Note: [a]Missing and nonapplicable (NA) data not included in the per cent measures.

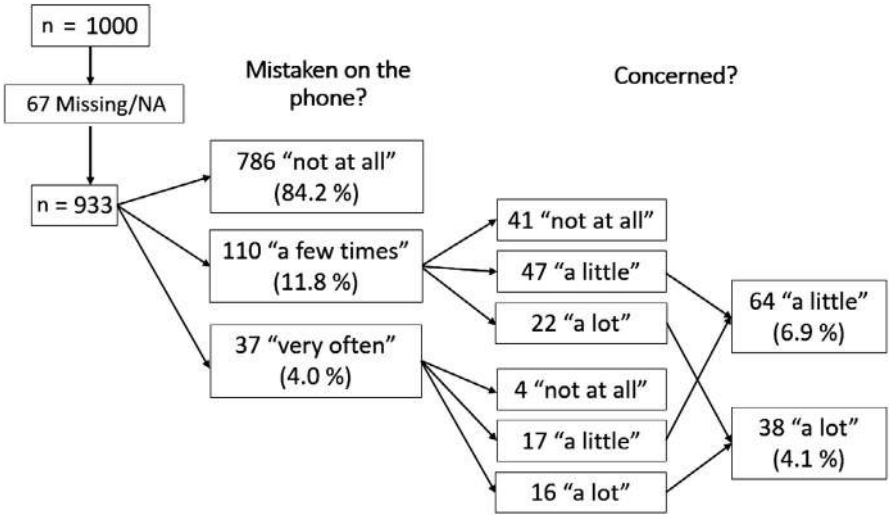

FIGURE 2 Flowchart of answers on the question 'Some people have an unusual high or low voice so their gender might be mistaken on the phone. Has this happened to you?' a few times or very often, and whether that was concerning them 'a lot', 'a little' or 'not at all'

with the voice among patients with DSD between 58.3% and 82.4% in the different groups. Therefore, other factors unrelated to the gender characteristics of the voice, must also contribute to voice dissatisfaction. Initiation of hormonal treatment as well as the normal puberty development may cause voice instability, hoarseness and rough voice quality. Dissatisfaction with the voice may also be caused by low self-esteem or by disliking the characteristics of one's voice or symptoms such as vocal fatigue or strained voice. Some participants declared high satisfaction with the voice despite concerns about not being perceived in accordance with self-identified gender on the phone.

Among the women with no androgen production from the gonads (20 46,XX GD), the general satisfaction with the voice was low and this was also true of women with CAIS (n = 69), without any function of the androgen receptor. Voice and how one perceives one's own voice is a personal and sensitive issue. For example, many people feel awkward hearing their own voice recorded. In the group of women with Turner syndrome, nine had been mistaken in accordance with self-identified gender on the phone, which could be related to an effect of androgen treatment to promote growth during puberty. In this study, however, none of them had had androgen treatment.

In total, 147 participants (88 females and 59 males)/1000 (~15%) have experienced being mistaken in accordance with self-identified gender over the telephone, with the highest prevalence among participants with XY DSD of both sexes (especially males), and females with CAH. Among those, 45 participants declared that this was not a problem. For 786 participants the situation to be mistaken on the phone was not reported at all.

As stated already by Böhme several decades ago,[25] evaluation of the voice should be part of the treatment of patients with DSDs, especially in XY DSD and CAH. It is important to be aware of voice change and to inform the patients that the voice may change with hormonal treatment.[34] Voice documentation has also been recommended for women with Turners syndrome since the voice can be altered during androgen treatment.[35] Despite these recommendations, voice evaluations are not routine part of the clinical programs today. Our results support the need for a voice evaluation-based on self-reported dissatisfaction with voice. There is also a need for increased knowledge about the specific voice issues faced by various patients with DSD. Furthermore, personal perception of voice at both ends (speaker and listener) should be evaluated with voice recordings and listening tests.

The strength with this descriptive study is that it covers a spectrum of DSD diagnoses and investigates novel elements of voice satisfaction and not being recognized as one's self-identified gender on the phone. A major limitation was the lack of available reference data from vocally healthy people and the limited number of participants in some of the groups. Further studies should aim to elucidate the reasons for voice dissatisfaction, apart from being mistaken in accordance with self-identified gender.

In conclusion, we have shown that a vast majority of DSD participants are not satisfied with their voice, and approximately 15% have been mistaken on the phone in accordance with self-identified gender leading to a lot of concern. Further work is needed to confirm and explore these findings in patients with DSD. We recommend that satisfaction with voice should form part of the medical history in patients with DSD and that evaluation of voice should be included in future international guidelines for the management of DSD.

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Availability of data and materials: The data sets analysed during the current study will not publicly available until analyses of other primary outcomes of dsd-LIFE are complete. The data will be made available to researchers by the principle investigator upon request after publication of the primary outcomes described in the grant by the consortium.

Patient involvement: Patients with DSD or their representatives participated in the study design through: work in focus groups for the development of condition-specific self-constructed items, work on the scientific advisory board and recruitment through patient advocacy groups. Representatives of the scientific advisory board were involved throughout study development and data collection.

CONFLICT OF INTEREST

All authors declare no support from any organization for the submitted work; no relationship with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. Therefore, the authors declare that they have no competing interests. The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

TRIAL REGISTRATION

German Clinical Trials Register: Registration identification number: DRKS00006072, date of registration April 17th, 2014. DRKS00006072 (German Clinical Trials Register).

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

We obtained ethical approval as appropriate for each country.

Germany: Ethics Commission of the Charité – University Medicine of Berlin (Germany); Reference number EA2/069/13. Approval May 24th, 2013. Ethics Commission of the Universitat zu Lübeck , reference number 13–144. Approval July 22nd, 2013. Ethics Commission of the Medical Faculty of the Westfalische Wilhelms-Universitat Münster , reference number 2013–500-b-S, approval September 13th, 2013. Ethics Commission of the Ludwig-Maximilians Universitat Munich, reference number 450–13. Approval October 2nd, 2013.

France: Comite de Protection des Personnes – Ile de France 1, reference number 13352. Approval November 5th, 2013 (Joint application for France Assistance Publique – Hopitaux de Paris, Le Centre Hospitalier Universitaire de Toulouse, Centre Hospitalier Universitaire de Montpellier, Université Claude Bernard, Lyon 1/Hospices Civils de Lyon).

Poland: Medical University of Lodz, Komisja Bioetyki Uniwersytetu Medycznego w Lodzi, reference number RNN/242/13/KE. Approval September 30th, 2013. Komisja Bioethycnej przy intytucie 'Pomnik-centrum Zdrowia Dziecka, Warsaw, reference number 103/KBE/2013. Approval September 30th, 2013.

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We obtained written informed consent from all participants in all study sites, and if the participant was below age 18, both the participants and their parents provided written informed consent at all sites.

DATA SHARING STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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