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Gender Reference Use in Spirometry for Transgender Patients

To the Editor:

Sex is increasingly factoring into pulmonary medicine research (1–3). This advance reflects a broader trend of considering sex, gender, and gender identity in healthcare practice and policy (4). The impact of gender identity on medical practice is pervasive, particularly in binary (e.g., cisgender) references for laboratory and screening tests (5). Historically, this has contributed to healthcare disparities for transgender and gender nonbinary (TGNB) populations (6). Binary, sex-specific references persist for pulmonary function testing (PFT). The 2019 American Thoracic Society (ATS) spirometry guidelines specify that patients, regardless of gender identity, should "be informed" that "birth sex" is a determinant of predicted lung size (7). Anecdotally, reference choice may impact spirometry interpretation and clinical care (8, 9). In this study, we examined PFT reference choice by providers for TGNB patients and the impact on spirometry. Some of the results of these studies have been previously reported in the form of an abstract (10).

Methods

TGNB patients were identified by note keywords, problem list diagnoses, and gender identity demographic fields (11–13) in the electronic health record (EHR) (Epic Corporation) among patients with a primary care provider in a large academic health system between 2015 and 2019. Only patients with PFTs were selected and TGNB identity was confirmed with chart reviews for gender identity (e.g., past medical history, social history). We extracted the following information for each PFT: age, listed gender, testing indication, forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC ratio. Sex recorded at birth, legal sex, race, and any active, concurrent transgender-related hormone therapy prescriptions were captured from the EHR. Obstruction was defined as FEV_1/FVC less than the lower limit of normal (LLN). LLN values using a male versus female reference population were calculated *post hoc* using rspiro: Spirometry equations for R and the Global Lung Function Initiative (GLI)-2012 reference equations (Theodore Lytras (2017), R package version 0.1). In this paper, trans man describes an individual with a male gender identity who was assigned female sex at birth, trans woman describes an individual with a female gender identity who was assigned male sex at birth, and gender nonbinary describes a person whose gender identity does not conform to the binary categories of male or female. For each patient, the first PFT in the EHR with a recorded gender after documented TGNB status was used for the analysis.

Results

Three hundred three patients with PFTs met our initial search criteria. After manual chart review, only 17 patients were confirmed to be transgender. Fifteen patients had full spirometry available including five trans men, eight trans women, and two gender nonbinary individuals (Table 1). Average age at PFT was 44.1 years (range 18.8–67.2 yr) and patients were predominantly white/non-Hispanic (80%). The majority of PFTs (87%) were done in a PFT lab, with primary indications listed as dyspnea (40%), asthma (27%), obstructive sleep apnea (7%), or unlisted (27%).

A female reference population was used by providers for 60% of trans men, 75% of trans women, and 100% of gender nonbinary patients. An active sex hormone prescription was concurrent with 67% of PFTs (100% of trans men, 63% of trans women, 0% of gender nonbinary) including estrogens (50%), testosterones (40%), and spironolactone (10%).

Post hoc calculation of pulmonary function percentiles demonstrated that using the opposite gender as reference did not change the detection of obstruction (FEV_1/FVC $<$LLN) (Table 2). Values above and below LLN changed based on the selected gender reference for FEV_1 in five patients and for FVC in five patients; in three patients, both values were impacted by the reference choice (Table 2).

Discussion

Pulmonary function testing uses a cisgender algorithm for lung function estimation. We found that providers inconsistently use female and male reference ranges for transgender patients, independent of gender identity. The predominant selection of a female reference in our small sample was striking and may signal systemic or unconscious provider biases. The error rate in gender allocation and reference selection in the non-TGNB population (e.g., based on patient names or appearance) is unknown and the impact of the recent ATS guidelines on provider behavior remains to be seen.

Table 1. PFT characteristics for transgender and gender nonbinary patients

Characteristics	Trans Man (*n* = 5)	Trans Woman (*n* = 8)	Gender Nonbinary (*n* = 2)
Age, yr, average	38.0	49.8	36.8
White, %	80	75	100
Concurrent hormone use, %	100	62.5	0
Female gender reference used for PFTs, %	60	75	100
Performed in PFT lab, %	80	100	50
Primary PFT indication, %			
Asthma	20	25	50
Dyspnea	80	25	—
OSA	—	12.5	—
Mean FEV_1, L	2.5	3.3	2.9
Mean FVC, L	2.9	4.0	3.9
Mean FEV_1/FVC	0.85	0.80	0.74

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; OSA = obstructive sleep apnea; PFT = pulmonary function testing.

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Table 2. PFT by gender reference ranges

Gender Identity	Measured FEV_1	Calculated		Measured FVC	Calculated		Measured FEV_1/FVC	Calculated	
		FEV_1 LLN (Male)	FEV_1 LLN (Female)		FVC LLN (Male)	FVC LLN (Female)		FEV_1/FVC LLN (Male)	FEV_1/FVC LLN (Female)
Trans woman	2.37	2.36	1.99*	2.75	3.12	2.57*	0.78	0.64	0.66*
Trans woman	3.45	2.56	2.16*	4.08	3.35	2.78*	0.85	0.65	0.66*
Trans woman	2.37	2.43	2.04*	3.80	3.26	2.66*	0.62	0.63	0.65*
Trans woman	3.13	2.64	2.23*	3.82	3.40	2.85*	0.82	0.67	0.67*
Trans woman	2.39	2.72*	2.30	3.11	3.52*	2.94	0.77	0.66*	0.67
Trans woman	4.42	3.31	2.84*	5.37	4.19	3.58*	0.82	0.69	0.70*
Trans woman	3.02	3.22	2.77*	3.64	3.87	3.25*	0.83	0.75	0.76*
Trans woman	5.09	3.24*	2.83	5.64	3.81*	3.23	0.90	0.76*	0.79
Trans man	3.16	2.88	2.53*	3.85	3.53	3.07*	0.82	0.72	0.72*
Trans man	1.38	2.26	1.94*	1.55	2.83	2.43*	0.89	0.69	0.69*
Trans man	2.23	2.17	1.78*	2.74	2.63	2.18*	0.81	0.73	0.73*
Trans man	3.27	2.76*	2.39	3.59	3.22*	2.73	0.91	0.74*	0.76
Trans man	2.38	2.88*	2.49	2.87	3.35*	2.84	0.83	0.74*	0.76
Gender nonbinary	3.04	3.09	2.67*	3.57	3.85	3.32*	0.85	0.70	0.70*
Gender nonbinary	2.67	2.91	2.56*	4.26	3.52	3.03*	0.63	0.73	0.73*

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; LLN = lower limit of normal; PFT = pulmonary function testing.
Measured data were extracted from spirometry in the electronic health record. Calculated data were obtained *post hoc* by examining both male and female gender reference ranges for each patient.
Dark shading indicates patients who would no longer have a measured value <LLN if the opposite reference range was used.
Light shading indicates patients who would no longer have a measured value >LLN if the opposite reference range was used.
*Denotes the calculated gender reference range, which is the opposite of the sex reported on the PFT from the electronic health record.

Use of the opposite gender reference affected interpretation of FEV_1 and FVC in our sample. These findings suggest that use of male predicted FEV_1 and FVC values, for a female-sized body, could result in a pseudo-restriction and the reverse scenario may mask a true restriction. However, the presence of obstruction based on predicted FEV_1/FVC was not affected by gender reference assignment. This provides an important discussion point for pulmonary providers and PFT technologists with TGNB patients. Additionally, as spirometry is increasingly incorporated into bioinformatic algorithms phenotyping pulmonary disease (14), our findings support the importance of extracting and reporting full PFTs particularly for transgender patients.

We used multiple methods to identify potential TGNB patients based on published algorithms and EHR demographic fields. The sensitivity and specificity of these methods ranged widely (11, 13). The resulting small sample size aligns with recently published findings that U.S. health centers have a high percentage of missing sexual orientation and gender identity data (15). Our study supports the need for increased use of sexual orientation and gender identity data collection for clinical application in pulmonary disease.

Accurately measuring lung function is a fundamental step to addressing healthcare disparities in pulmonary disease globally (16). Notably, cigarette (17) and e-cigarette use (18) is more prevalent among transgender individuals than the general population. ATS guidelines reinforce a cisgender approach and favor sex recorded at birth as reference. This contrasts with guidelines in other clinical specialties where providers and patients may consider using both binary reference ranges as an option in shared decision making (19). Finally, the majority of patients in our study were on concurrent hormone therapy at the time of PFTs, yet the impact of hormone therapy—particularly pubertal blockade—and surgical interventions on longitudinal lung function remains unknown. This is a compelling area of future study given the emerging research on the roles of estrogen, progesterone, and testosterone in lung pathophysiology (3). Until then, risks for disparities—despite guidelines—will persist.

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Effect of Face Masks on Gas Exchange in Healthy Persons and Patients with Chronic Obstructive Pulmonary Disease

To the Editor:

Current evidence, from observational studies to systematic reviews and epidemiologic modeling, supports the use of masks by the public, especially surgical masks, for mitigating coronavirus disease (COVID-19) transmission and deaths (1–5). However, public mask use has been heavily politicized with inconsistent recommendations by authorities leading to divided public opinion. Despite evidence to the contrary, an online UK/U.S. survey found that only 29.7–37.8% of participants thought that wearing a surgical mask was "highly effective" in protecting them from acquiring COVID-19 (6). Another reason commonly argued against mask use involves safety concerns, as mask discomfort has been attributed to rebreathing CO_2 and hypoxemia, with some even considering that masks are lethal (7).

Objective

To evaluate whether gas exchange abnormalities occur with the use of surgical masks in subjects with and without lung function impairment.

Methods and Findings

To demonstrate the changes in end-tidal CO_2 and oxygen saturation as measured by pulse oximetry before and after