New Spirometry and Interpretation Practices

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Allergy & Asthma NETWORK

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1

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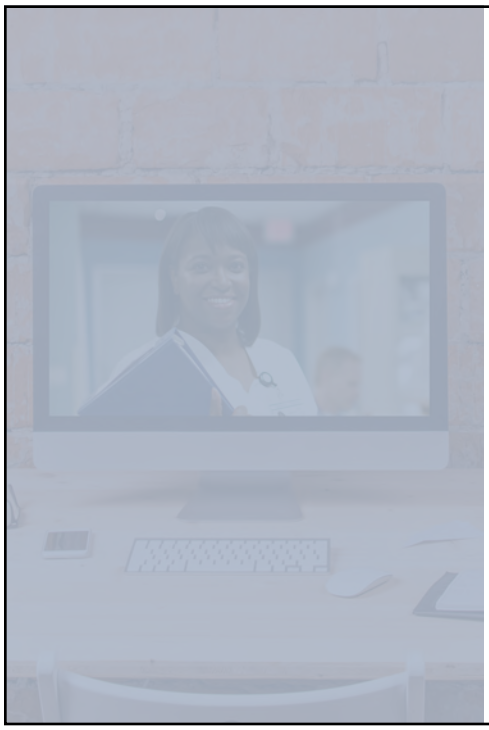
- Rush University
- Chicago, IL

Conflict of Interest

- Member of a working group (Chest, ATS, CTS, and AARC) that is developing a research statement based upon the evidence and gaps for the use of race/ethnicity in interpreting PFTs

2



LEARNING OBJECTIVES

After completion of this presentation, the learner will be able to:

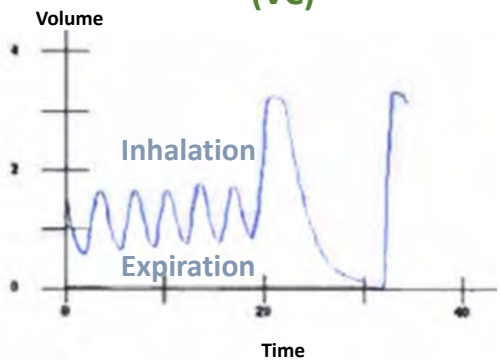
01 Describe the recent changes to the 2019 ATS/ERS technical standards for conducting spirometry tests.

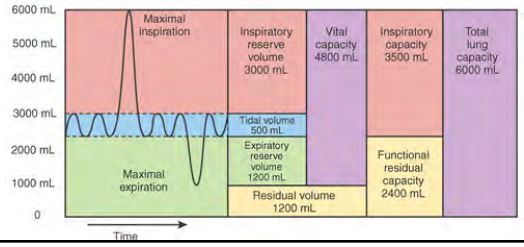
02 Interpret whether spirometry results are normal or if there is bronchodilator responsiveness according to the 2021 ERS/ATS technical standards.

03 Identify issues that result when race and ethnicity are used to predict normal values for lung function tests.

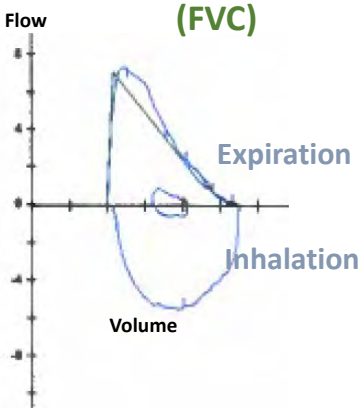
3

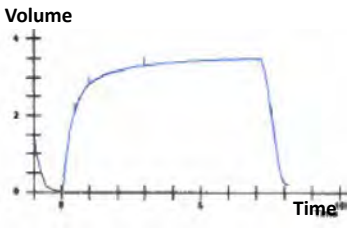
(Slow) Vital Capacity (VC)





Forced Vital Capacity (FVC)



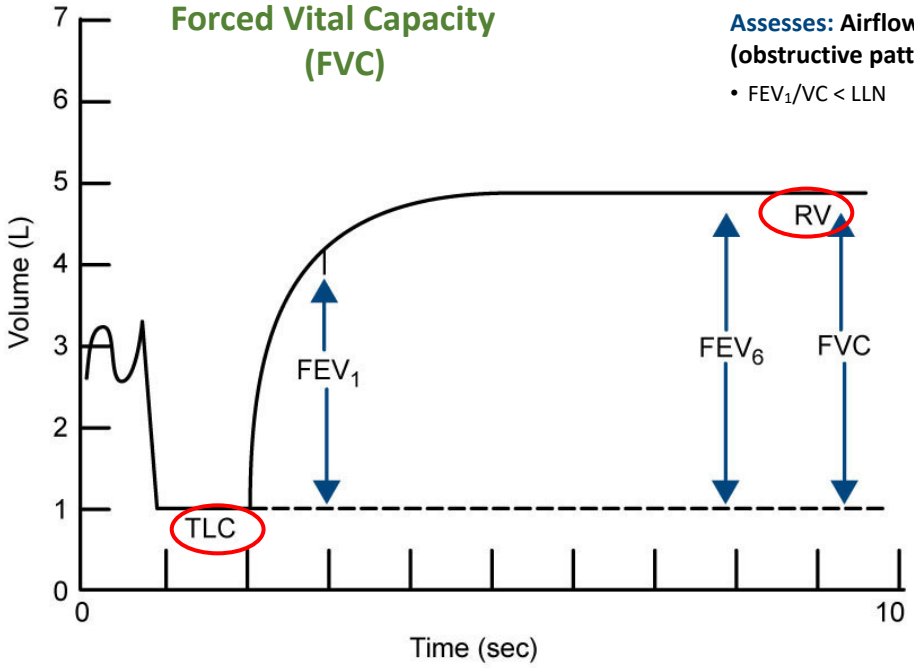


4

Forced Vital Capacity (FVC)

Assesses: Airflow limitation (obstructive pattern)

- $FEV_1/VC < LLN$



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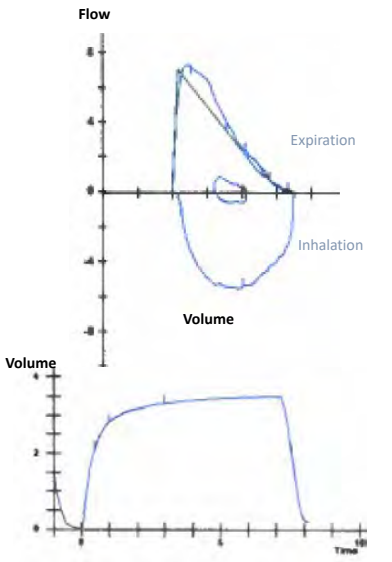
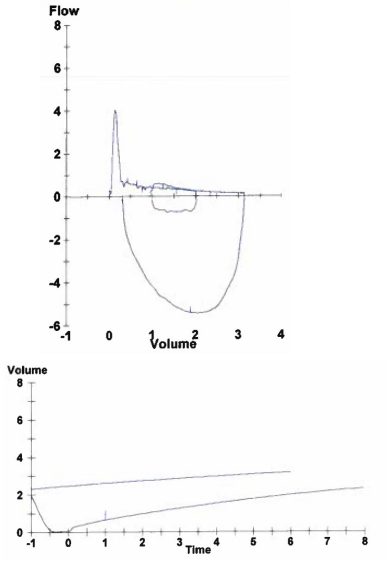
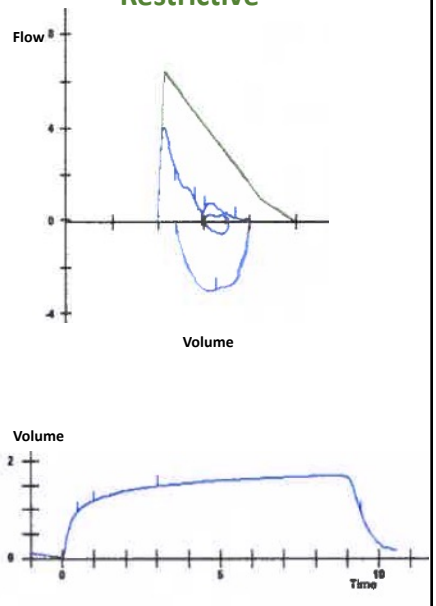
Normal



Obstructive



Restrictive



6

ATS/ERJ Acceptability Criteria

Must have BEV ≤5% of FVC or 0.100 L, whichever is greater
Must have no evidence of a faulty zero-flow setting
Must have no cough in the first second of expiration*
Must have no glottic closure in the first second of expiration*
Must have no glottic closure after 1 s of expiration
Must achieve one of these three EOFE indicators:
1. Expiratory plateau (≤0.025 L in the last 1 s of expiration)
2. Expiratory time ≥15 s
3. FVC is within the repeatability tolerance of or is greater than the largest prior observed FVC†

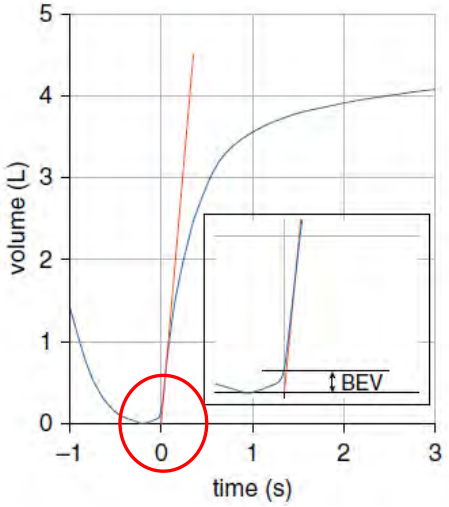
Must have no evidence of obstructed mouthpiece or spirometer
Must have no evidence of a leak
If the maximal inspiration after EOFE is greater than FVC, then FIVC − FVC must be ≤0.100 L or 5% of FVC, whichever is greater‡

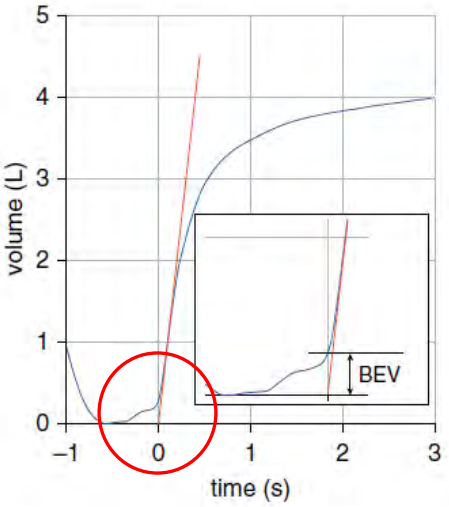
Table 7: Graham 2019, Standardization of Spirometry 2019 Update, *Am J Resp Crit Care Med.*

7

Examples BEV

BEV ≤5% of the FVC or .100 L
- Whichever is greater





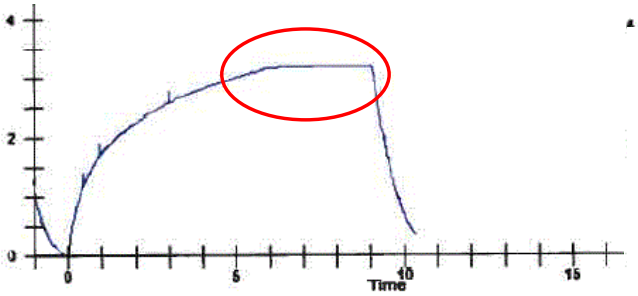
Graham 2019, Standardization of Spirometry 2019 Update, *Am J Resp Crit Care Med*.

8

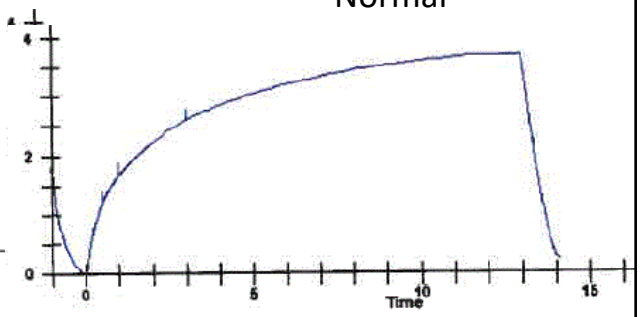
Absence of Glottic Closure

FVC = 3.20 L ----------→ FVC = 3.69 L

Glottic closure



Normal



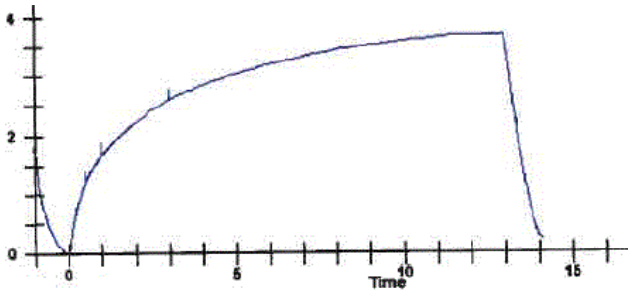
9

End of Forced Exhalation Criteria (EOFE)

Must achieve one of these three EOFE indicators:

1. Expiratory plateau (≤0.025 L in the last 1 s of expiration)
2. Expiratory time ≥15 s
3. FVC is within the repeatability tolerance of or is greater than the largest prior observed FVC†

Table 7: Graham 2019, Standardization of Spirometry 2019 Update, *Am J Resp Crit Care Med.*



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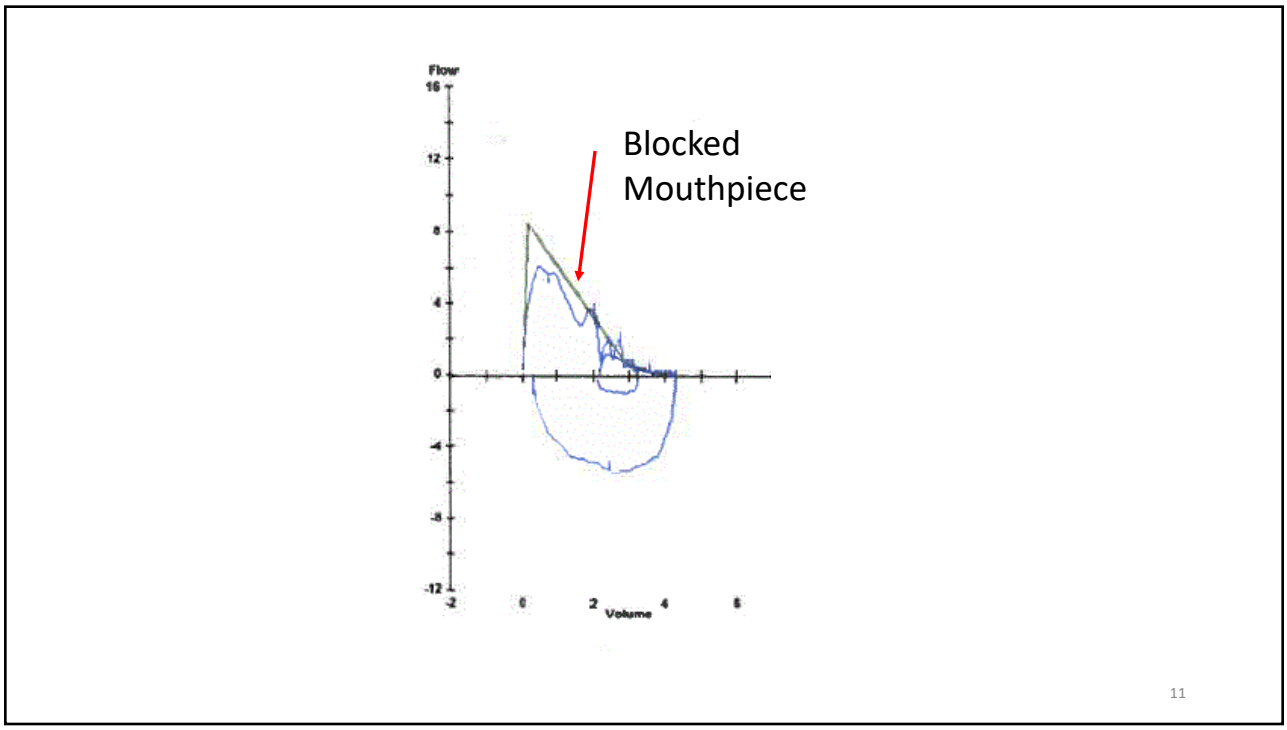
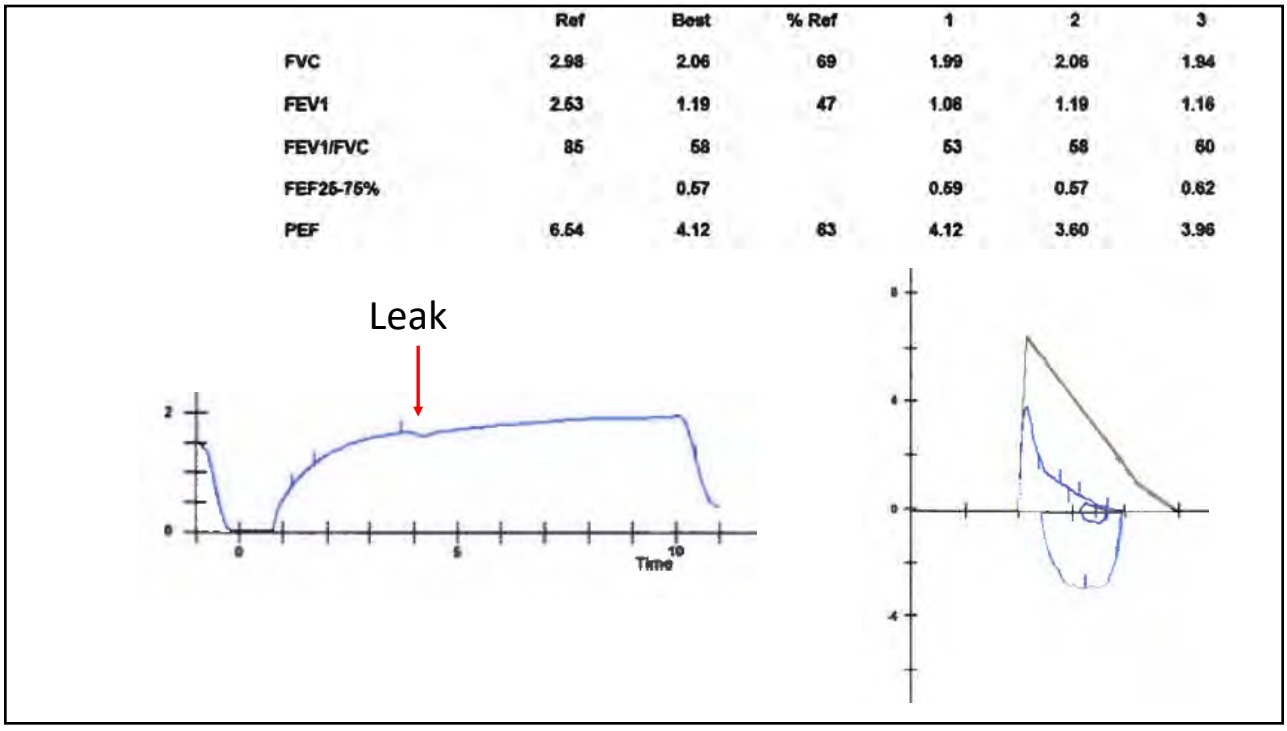


11

	Ref	Best	% Ref	1	2	3
FVC	2.98	2.06	69	1.99	2.06	1.94
FEV1	2.53	1.19	47	1.08	1.19	1.16
FEV1/FVC	85	58		53	58	60
FEF25-75%		0.57		0.59	0.57	0.62
PEF	6.54	4.12	63	4.12	3.60	3.96



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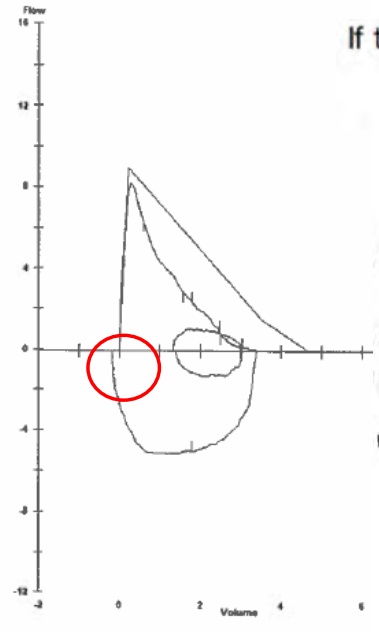


If the maximal inspiration after EOFE is greater than FVC, then FIVC – FVC must be ≤0.100 L or 5% of FVC, whichever is greater‡

Table 7: Graham 2019, Standardization of Spirometry 2019 Update, *Am J Resp Crit Care Med.*

	Ref	Best	% Ref	1	2	3
FVC	4.69	3.62	75	3.32	3.38	3.39
FEV1	3.87	2.62	65	2.42	2.36	2.51
FEV1/FVC	83	72		73	70	74
FIVC	4.67	3.49	75	3.49	3.46	3.56

FIVC = 3.49 L 5% of 3.32 L = 0.17 L

FVC = 3.32 L

0.17 L

13

Interpretation Bronchodilator Responsiveness

$$\text{Bronchodilator Response} = \frac{(\text{Post–bronchodilator value (l)} - \text{Pre–bronchodilator value (l)}) * 100}{\text{Predicted value (l)\#}}$$

A change of >10% is considered a significant BDR response.

#Predicted value should be determined using the appropriate GLI spirometry equation.

Spirometry		Pre	Ref	CI Range	% Ref	Post	% Ref
FVC	Liters	2.90	3.12	(2.5 - 3.8)	93	3.35	107
FEV1	Liters	1.72	2.46	(1.9 - 3.0)	70	2.52	103
FEV1/FVC	%	59	80	(69.8 - 89.3)		75	

FVC Assessment: $\frac{(3.35 - 2.90) \times 100}{3.12} = 14.4\%$

FEV_1 Assessment: $\frac{(2.52 - 1.72) \times 100}{2.46} = 32.5\%$

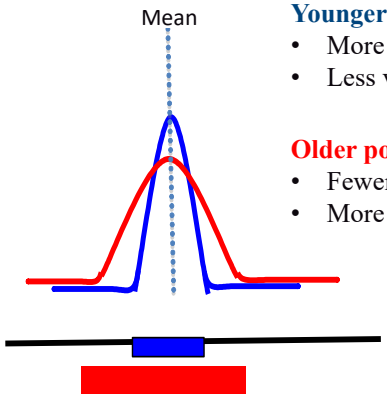
Stanojevic 2021, ERS/ATS Technical Standard on Interpretive Strategies for Routine Lung Function Tests, *Eur Respir J*, Box 1, p. 12.

14

Use LLN for Accurate Measure of Predicted Normal

If you use 80% predicted for older populations:

- Exclude values in the 95% CI (normal) that fall below 80% predicted
  - Incorrectly diagnose patients with obstruction



Younger population
- More measures
- Less variability

Older population
- Fewer measures
- More variability

95% Confidence Intervals

Pellegrino, et al. *ERJ* 2005;26(5):948-968.

15

What is Normal?

- 80-120% of predicted normal value
  - Less accurate
  - Strongly discouraged
- 95% confidence intervals are more accurate
  - Lower limit of normal (LLN)
    - 5th percentile
  - Upper limit of normal (ULN)
    - 95th percentile

Clearly document LLN on PFT report

When results are close to the LLN, consider the person's:

- Medical history
- Physical findings
- Pre-test probability of disease

Stanojevic 2021, ERS/ATS Technical Standard on Interpretive Strategies for Routine Lung Function Tests, *Eur Respir J.*

16

Z – Scores

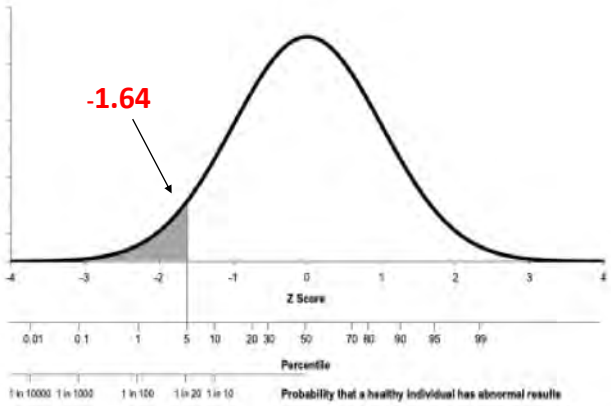


Figure 2. The normal distribution with z-scores and percentiles displayed. Percentile can be interpreted as the probability that a healthy individual has results inside the normal range (i.e., the false positive rate).

$$z = \frac{x - \mu}{\sigma}$$

z = standardized score (z-score)
x = patient's value
μ = mean of the sample
σ = standard deviation of the sample

Stanojevic 2021, ERS/ATS Technical Standard on Interpretive Strategies for Routine Lung Function Tests, *Eur Respir J*

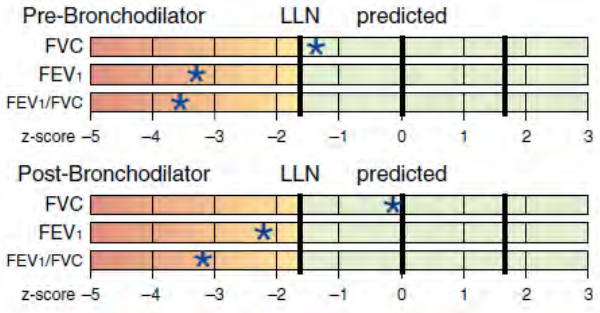
17

17

Practice Interpreting Z-scores

SPIROMETRY

	Pre-Bronchodilator				Post-Bronchodilator				
	Best	LLN	z-score	%Pred	Best	z-score	%Pred	Change	%Chng
FVC (L)	**3.90**	3.70	–1.34	82%	**4.70**	–0.09	99%	600 mL	20%
FEV_1 (L)	**2.02**	2.91	–3.78	54%	**2.61**	–2.21	70%	590 mL	29%
FEV_1/FVC	**0.52**	0.68	–3.54		**0.55**	–3.35			
FET (s)	**10.3**				**11.2**				
Reference values: GLI 2012 Test quality: Pre: FEV_1 - A, FVC - A; Post: FEV_1 - A, FVC - B									



Culver, 2017, *Am J Respir Crit Care Med,* p. 1466.

18

Interpretation Algorithm

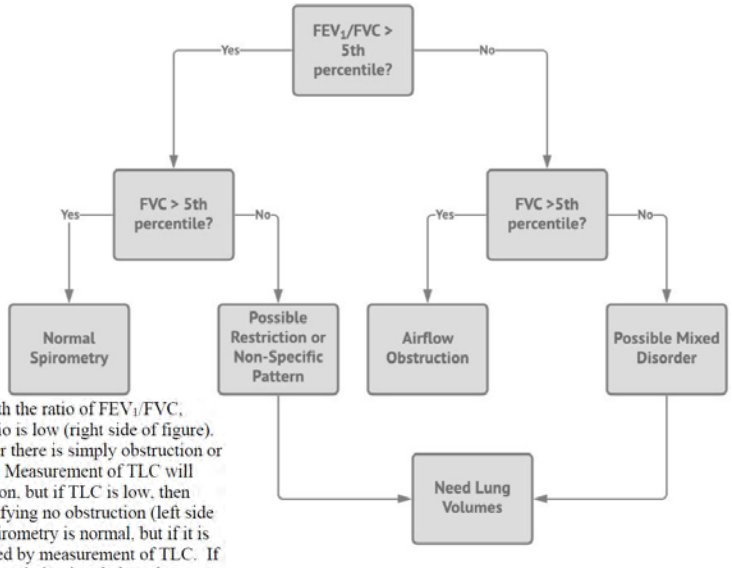


Figure 8. Approach to Interpretation of Spirometry. Beginning with the ratio of FEV_1/FVC, determine whether obstruction is present based on whether the ratio is low (right side of figure). If obstruction is present, then assess the FVC to determine whether there is simply obstruction or whether there may be concomitant restriction ("mixed disorder"). Measurement of TLC will define restriction, so if TLC is normal, then there is only obstruction, but if TLC is low, then there is concomitant restriction. If the FEV_1/FVC is normal, signifying no obstruction (left side of figure), then once again assess the FVC. If it is normal, then spirometry is normal, but if it is low then there may be possible restriction. This must be determined by measurement of TLC. If the TLC is low, then spirometry is consistent with restriction. If restriction is ruled-out by a normal TLC, then the pattern of impairment of low FVC with normal FEV_1/FVC has been dubbed the possible restriction or non-specific pattern, which may include diseases causing obstruction or restriction. Restriction presenting as the "non-specific" pattern is often caused by a chest wall or neuromuscular disorder.

Stanojevic 2021, ERS/ATS Technical Standard on Interpretive Strategies for Routine Lung Function Tests, *Eur Respir J,* p. 42.

19

What Influences Variation?

Spirometry Factors

- Age
- Sex (birth)
- Height/Arm span
- Race or ethnic origin
- Weight

  Not used in prediction equation, but does affect variation

Differ for each pulmonary function test

Normal

- Falls within the confidence interval (CI) range
- In the absence of CI range
  - 80% - 120% reference
  - Less accurate

20

Value #1

Vyas et al, 2020, Hidden in Plain Sight – Reconsidering the Use of Race Correction in Clinical Algorithms, *NEJM*[4]

Are the findings based upon robust evidence and statistical analyses?

21

Spirometry Differences between African Americans and Whites

Citation	Age Group	Sample Size	Differences
Hankinson et al., 2010, *CHEST*[5]	45-84 y	1068	Adjustment for African Americans: • NHANES III = 0.85 • MESA – Lung Study = .81
Burney & Hooper, 2012, *Int J Epidemiol*[6]	45 -64 y	7489	**Sex** / **Race** / **FVC** / **FEV_1** Male / African American / 4.09 (0.64) / 3.10 (0.56) Male / White / 4.82 (0.77) / 3.56 (0.65) Female / African American / 3.00 (0.51) / 2.34 (0.41) Female / White / 3.45 (0.53) / 2.60 (0.44)
Quanjer et al, 2012, *Eur Respir J*[7]	2.5 – 95 y	2545 (AA)	Adjustment for African Americans compared to White: **FVC** • 15.5% decrease for males • 14.4% decrease for females **FEV_1** • 14.7% decrease for males • 13.8% decrease for females

22

Validity and Reliability

Race is a socially constructed term

- May mask modifiable risk factors
  - Nutrition and premature birth[6,8.9]
  - Pollution and environment[6,8-12]
  - Socioeconomic[6-9, 13]
    - *Education*[6,9,12]
    - *Poverty*[6, 9, 11]
    - *Inequalities in access to medical care*[11, 13]

Braun L. Spirometry, measurement, and race in the nineteenth century. *J Hist Med Allied Sci* 2005;60(2):135-169.

Accuracy of measurement

- No established relationship between race and biology[14]
- Race is a broad and less precise term
  - Genetic testing for ancestry is more precise[15]
  - "Island" categorization of race[14]
- Race/ethnicity is not fixed/unchangeable identify[16]
  - Affiliate with multiple categories
  - Personal identities evolve over time
- Self-report vs. measured ancestry
  - An individual may have a complex genetic ancestry
  - Self-report is a poor predictor of genetic ancestry[17]
- Multicultural or multiracial backgrounds
  - 3965 MESA participants who underwent genetic analysis[18]
  - Computed reference equations (sex, age, and height)
    - *Race specific*
    - *Full sample*
      - Lose precision with race-specific equations
      - Had 1/3 higher confidence intervals
- Immigrants and acculturation

23

Race in the Spirometry Literature

Braun et al, 2013, *Eur Respir J*[11]

- Systematic review comparing race (white to others)
- *N* = 226 articles
- Published between 1922-2008

Study characteristics

- **Definition of race/ethnicity**
  - Across entire sample, 39 (17.3%) had definitions
  - Beginning in 2000, 70% of studies with parallel controls had definitions
- **Only 6.1% examined socioeconomic status**
- **Reasons for nonwhites to have lower volumes**
  - 29.4% anthropometric differences
  - 23.1% environmental differences
  - 21.8% inherent differences
  - 24.3% no explanation
- **59.3% of studies had sample sizes 100-999**

Reporting Race

- Provide rationale for using race
- Self-identify/chart review
- No consensus on categories
- Open-ended question/fixed categories[16]
- Aggregating data

Historical Explanations

- Implied inferiority

Currently

- Unexplained[6]
- Consider all relevant factors[16]

24

Value #2

Vyas et al, 2020, Hidden in Plain Sight – Reconsidering the Use of Race Correction in Clinical Algorithms, *NEJM*[4]

Consider if race-adjustment would relieve or exacerbate health inequities

25

Clinical Decisions

Diagnosis

Consider the clinical picture in addition to diagnostic testing results

- The ratio (FEV_1/FVC) is not affected[6, 19]
- An important concern in restrictive conditions[6]
  - *Make the diagnosis on other variables*[20]
- Issues more prominent when values are near threshold[9]

Prognosis (mortality)

Do not race-adjust FVC[20]

- Consider the functional role of VC
  - The absolute value of VC is critical for survival

Borrell et al, 2021, *NEJM*[15]

Underestimate impairment

- *Reduce probability of treatment/compensation*

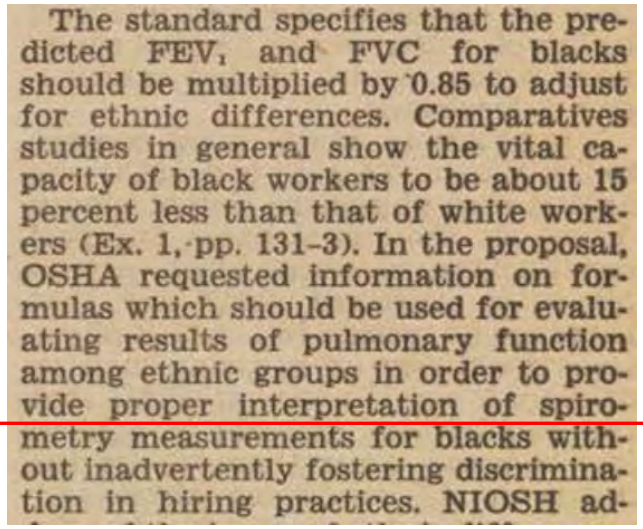
Overestimate impairment

- *Unnecessary testing*
- *Higher life-insurance premiums*
- *Ineligible for certain professions*
- *Withhold certain treatments*
- *Anxiety*

Inclusion in clinical trials

26

Occupational Health: 1978 Cotton Dust Standards



The standard specifies that the predicted FEV_1 and FVC for blacks should be multiplied by 0.85 to adjust for ethnic differences. Comparatives studies in general show the vital capacity of black workers to be about 15 percent less than that of white workers (Ex. 1, pp. 131-3). In the proposal, OSHA requested information on formulas which should be used for evaluating results of pulmonary function among ethnic groups in order to provide proper interpretation of spirometry measurements for blacks without inadvertently fostering discrimination in hiring practices. NIOSH ad-

Federal Register: https://www.govinfo.gov/app/details/FR-1978-06-23, p. 27391

27

Value #3

Vyas et al, 2020, Hidden in Plain Sight – Reconsidering the Use of Race Correction in Clinical Algorithms, *NEJM*[7]

Evaluate plausible causal mechanisms

28

Epidemiology Research on Disparities

Differential Approach to Race

- Epidemiologic analysis vs. clinical guidelines

Target Needs

Explore how social and physical environments influence lung function[9, 10]

Collect Race Data

Ignoring race counterproductive[15]

- *Promotes inequity*
- *Limits opportunities for societal interventions*

Interpretation

Do not use race-adjusted values[20]

- Masks potential social and environmental disadvantage[20, 21]
- Interpret racial disparities as injustices to solve vs. simple facts

29

Next Steps

Reference Values

- Consider when and if race/ethnicity adjustment is warranted
  - Clinical outcome
  - Occupational health
  - Epidemiology
- Consider using composite race/ethnicity equations

Evaluate Use of Race on Outcomes[9]

- Do race/ethnicity adjustments in PFTs impact clinical outcomes?
- How do PFT results fit into clinical decisions/guidelines?
- What effectively reduces health disparities?

Mindfully consider how we measure, use, and report "race"

Kaplan & Bennett. Use of Race and Ethnicity in Biomedical Publication. *JAMA* 2003;289:2709-2716.[16]

30

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31

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32

Questions?

We'll get to as many questions as we can!

33

Thank you for listening!

We appreciate you being here.

NEXT Webinar:

Long COVID-19: A Fresh Perspective on the Condition & Concerns

April 28, 2022

4:00 PM ET

34

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35