# Spirometry reference values Which one to use

Polgar
Knudson
Polgar revised
ECSC
Hankinson
GLI

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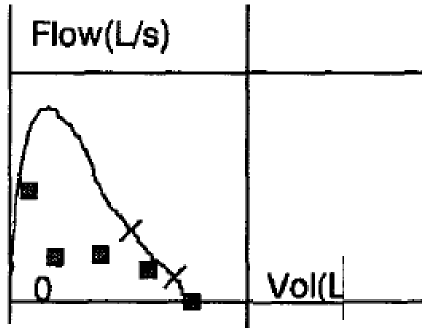
Hipap Mar 2018

# To perform EIA or not

FEV1

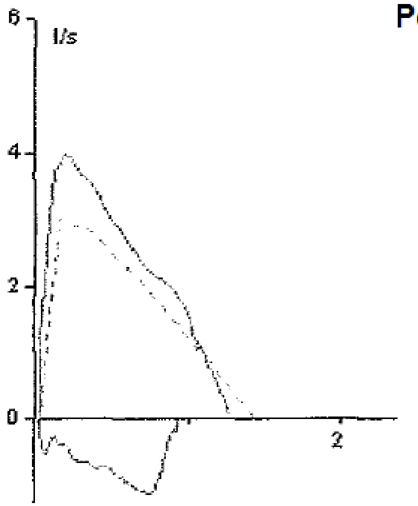
| Age | Meas . | Polgar | %pred | ECSC child | % pred |
|---|---|---|---|---|---|
| 9 | 1.97 | 2.01 | 98 | 2.23 | 88 |
| 10 | 2.01 | 2.28 | 88 | 2.64 | 76 |
| 11 | 1.30 | 1.83 | **71** | 2.06 | **63** |
| 11 | 1.92 | 2.31 | 83 | 2.39 | 80 |
| 12 | 1.12 | 2.07 | 54 | 2.27 | 49 |
| 13 | 2.43 | 3.12 | 78 | 3.38 | 72 |
| 13 | 1.49 | 2.07 | **72** | 2.27 | **66** |
| 14 | 2.92 | 3.11 | 94 | 3.38 | 86 |
| 14 | 2.47 | 2.91 | 85 | 3.16 | 78 |
| 15 | 2.79 | 3.33 | **84** | 3.73 | **75** |
| 15 | 2.08 | 2.63 | **79** | 2.89 | **72** |
| 16 | 4.06 | 4.37 | 93 | 4.66 | 87 |
| 16 | 2.66 | 3.33 | 75 | 3.61 | 74 |

# Problem at the predicted edges

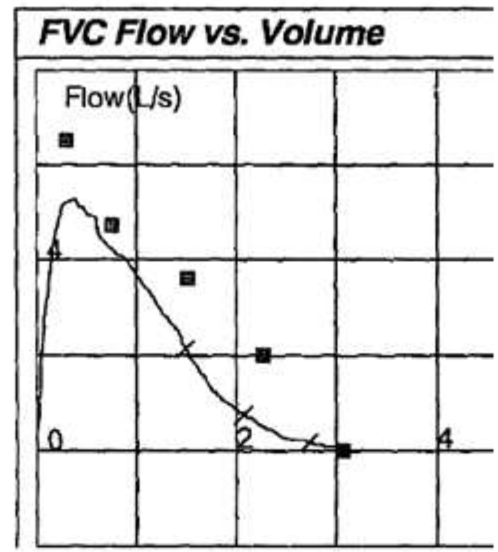



**Polgar revised**

Age 4y




**Age 6 Polgar revised**




**<u>FEV1 passing 18y old</u>.**

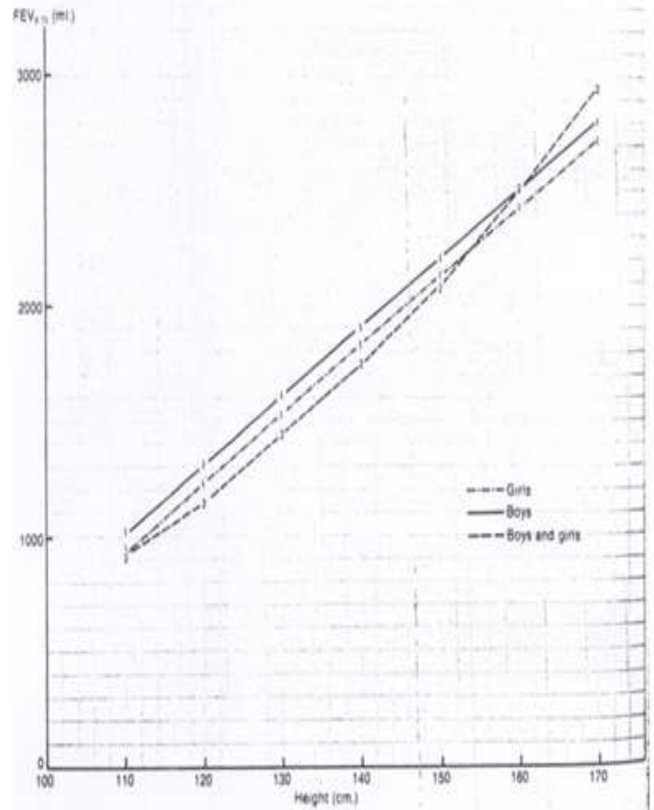
| Age | pred | Actual | %pred | |
|---|---|---|---|---|
| 17.9 | 2.90 | 2.16 | 74 | Polgar revised |
| 18.0 | | 2.24 | 68 | ECSC |
| | | +4% | - 8% | |

# Year 1971 - Polgar & Promadaht :

# Predicted values entailed from a set of predicted values.

**Table 1.** Publications on normal values for vital capacity listed chronologically with information on their origin, the subjects tested, and the methods used.

| Origin | | | Subjects | | | | Methods | |
|---|---|---|---|---|---|---|---|---|
| *Authors* | *Year* | *Place* | *Number* | *Population* | *Age-Range* | *Males/Females* | *Technique* | *Body Position* |
| Emerson and Green* | 1921 | U.S.A. | 350 | Orphans, "out-patient normals" | 1-15 | 266/84 | "Wet spirometer" | Not stated |
| Wilson and Edwards | 1921 | U.S.A. | 85 | School children | 6-16 | 44/41 | Krogh spirometer | Sitting |
| Stewart | 1922 | U.S.A. | 2509 | Normals | 4-19 | 1289/1220 | "Wet spirometer" | Not stated |
| Baldwin | 1928 | U.S.A. | >10,000 | School children | 7-17 | Not stated | "Wet spirometer" | Not stated |
| Collins and Clark | 1929 | U.S.A. | 28,674 | School children | 6-15 | 14,318/14,356 | "Wet spirometer" | Not stated |
| Kelly* | 1933 | U.S.A. | 3624 | School children | 11½-18⅔ | 2085/1539 | "Wet spirometer" | Not stated |
| Abernethy | 1936 | U.S.A. | 357 | School children | 8-17 | 179/178 | "Wet spirometer" | Not stated |
| Methenyi | 1941 | U.S.A. | 206 | Normals | 3-6 | 115/91 | "Wet spirometer" | Standing |
| Turner and McLean | 1951 | U.S.A. | 50 | Orphans, "out-patient normals" | 5⅔-14 | 30/20 | Benedict-Roth type | Recumbent |
| Morse et al. | 1952 | U.S.A. | 124 | School children | 10-17 | All males | "Wet spirometer" | Recumbent |
| Ferris et al. | 1952 | U.S.A. | 161 | School children | 5-18 | All males | Benedict-Roth type | Sitting |
| Ferris and Smith | 1953 | U.S.A. | 233 | School children | 5-18 | All females | Benedict-Roth type | Sitting |
| Needham et al. | 1954 | Britain | 150 | School children, orphans | 11-19 | 78/72 | "Wet spirometer" | Sitting |
| Jones | 1955 | Britain | 625 | School children | 6-13⅓ | 324/301 | Benedict-Roth type | Sitting |
| Tatai | 1955 | Japan | 1628 | School children | 8-16 | 835/793 | "Wet spirometer" | Standing |
| Engström et al.* | 1956 | Sweden | 93 | School children | 6-14 | 50/43 | Benedict Roth type | Sitting |
| Kennedy et al. | 1957 | Britain | 175 | School children | 8-14 | All males | "Wet spirometer" | Sitting |
| Helliesen et al. | 1958 | U.S.A. | 82 | "Hospital normals" | 5-17 | 50/32 | Benedict Roth type | Sitting |
| Strang | 1959 | Britain | 418 | School children | 7-18 | 209/209 | "Wet spirometer" forced VC | Sitting |
| Bernstein et al. | 1959 | U.S.A. | 70 | Orphans | 6-15 | Not separated | Benedict Roth type | Sitting |
| Lyons et al. | 1960 | U.S.A. | 1163 | School children | 6-14 | 624/539 | Benedict Roth type | Not stated |
| Cook and Hamann* | 1961 | U.S.A. | 82 | "Hospital normals" | 5-17 | 50/32 | Benedict Roth type | Not stated |
| Cherniack | 1962 | Canada | 521 | "Hospital normals" | 3-17 | 260/261 | Benedict Roth type | Sitting |
| Bjure | 1963 | Sweden | 161 | School children | 7-17 | 79/82 | Benedict Roth type | Sitting |
| Herdegen et al. | 1963 | Czechoslovakia | 164 | Normals | 5-16 | Not separated | "Wet spirometer" | Semirecumbent |
| De Muth and Howatt | 1965a | U.S.A. | 147 | School children | 4-18 | Not separated | Krogh spirometer | Sitting |
| Lunn | 1965 | Britain | 3556 | School children | 6-16 | 1767/1789 | "Wet spirometer" | Not stated |




Method: Wet spirometer
Manual calculations

ew linear regression equations were calculated in relation to height and Sex. (ages 6-18)

**1983- The European Coal and Steel Community (ECSC) published new spirometry reference values for ages 21-70 y**

- Reference values for spirometry are not derived from measured data - Equations are a combination of those from different researchers

- "For each of the regression equations", a new reference values equation was computed as a combination of height and age within the ranges given by the authors

- In most publications, lung function is assumed to decline linearly with age in adults.

- Smoking was not considered.

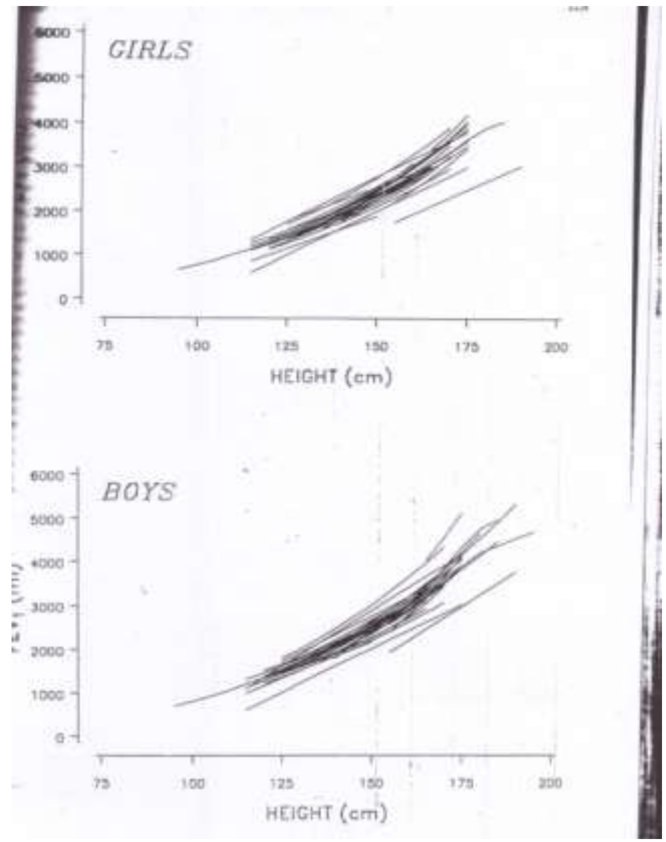
# 1989 - Quanjer et al. Compilation to ECSC of reference values for lung function measurements in children.

REFERENCE VALUES 201s

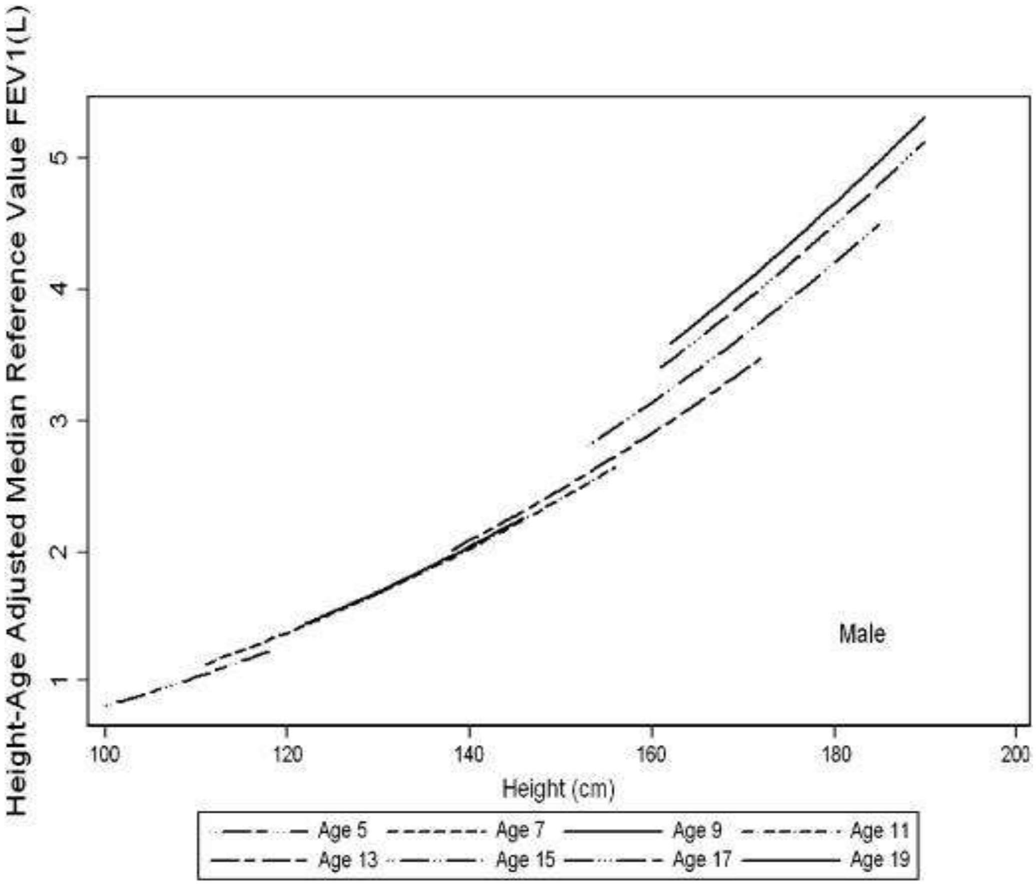
| Reference | Yr | Sex | Regression equation | $S_{SD}$ | RSD | r |
|---|---|---|---|---|---|---|
| Liang | 1975 | M | $-3312 + 40.01H$ | | 218 | 0.90 |
| Lunn | 1965 | M | $-3226 + 40.0H$ | | | 0.90 |
| Palka | 1982 | M | $-10601 + 72H + 216A$ | | 742 | |
| Seely | 1974 | M | $-7641 + 55.95H + 89.41A + 21.41W$ | | 495 | 0.87 |
| Tessier | 1980 | M | $195e^{\text{[illegible]}}$ | | | 0.95 |
| Thiemann | 1976 | M | $3590.10^{-4}H^{\text{[illegible]}}$ | 11.5 | | 0.92 |
| Todisco | 1980 | M | $-4110 + 120A + 35.5H$ | | 580 | 0.89 |
| Warwick | 1977 | M | $788.10^{-4}H^{\text{[illegible]}}$ | 12 | | 0.97 |
| Zapletal | 1969 | M | $7994 - 125.09H + 0.605H^2$ | | 393 | |
| Binder | 1976 | F | $-3380 + 31H + 65A + 10W$ | | 368 | 0.87 |
| Cherniack | 1962 | F | $-2554 + 27.86H + 90.96A$ | | | |
| Dickman[1] | 1971 | F | $-2371 + 30.31H$ | | 171 | 0.83 |
| Dickman[2] | 1971 | F | $-5669 + 46.06H + 102A$ | | 297 | 0.73 |
| Hahurzka | 1976 | F | $-2339 + 32.93H$ | | 388 | 0.74 |
| Higgins[3] | 1973 | F | $-4377 + 106A + 37H$ | | 439 | 0.75 |
| Higgins[4] | 1973 | F | $-4301 + 63A + 40H$ | | 489 | 0.45 |
| Hsu | 1971 | F | $2570.10^{-4}H^{\text{[illegible]}}$ | 14 | | 0.86 |
| Knudson | 1976 | F | $-3469 + 33H + 92A$ | | 500 | 0.87 |
| Knudson[5] | 1983 | F | $-3749 + 43.0H$ | | 373 | 0.75 |
| Knudson[6] | 1983 | F | $-4447 + 41.6H + 69.9A$ | | 497 | 0.73 |
| Lang | 1984 | F | $-5498 + 58H$ | | | 0.66 |
| Liang | 1975 | F | $-2689 + 34.35H$ | | 266 | 0.84 |
| Lunn | 1965 | F | $-2976 + 37.0H$ | | | 0.91 |
| Seely | 1974 | F | $-4069 + 36.36H + 59.72A + 14.25W$ | | 346 | 0.70 |
| Tessier | 1980 | F | $148e^{\text{[illegible]}}$ | | | 0.93 |
| Thiemann | 1976 | F | $2820.10^{-4}H^{\text{[illegible]}}$ | 12.5 | | 0.86 |
| Warwick | 1977 | F | $1015.10^{-4}H^{\text{[illegible]}}$ | 12 | | 0.97 |
| Zapletal | 1969 | F | $169 - 12.17H + 0.189H^2$ | | 263 | |
| Bellon | 1982 | M+F | $123e^{\text{[illegible]}}$ | 9.1 | | 0.95 |
| Dab | 1979 | M+F | $172e^{\text{[illegible]}}$ | | | 0.91 |
| Kunel | 1969 | M+F | $129e^{\text{[illegible]}}$ | 14.6 | | 0.94 |
| Kopetzky | 1974 | M+F | $2444 - 57.6H + 0.41H^2$ | | | |
| Weng | 1969 | M+F | $146e^{\text{[illegible]}}$ | 6.2 | | |

[1] 107–152 cm; [2] 152–198 cm; [3] 10–15 yr; [4] 16–19 yr; [5] >6–<12 yr; [6] >12–<25 yr.

FEV1 ml



# How important is age to FEV1 relationship ??




FEV1 at 8-specific ages for any given height.

Age is as important to consider in determining the reference range, especially during puberty.

## 1995 Quanjer - Polgar revised – Generally used in Europe and Israel up to 2012

Measured spirometric data sets collected in 6 European countries (Netherlands, France, Austria, UK, Spain, and Italy).

Aims:

1. to describe spirometric indices from childhood to adulthood, taking into account the adolescent growth spurt.
2. Population comprised of 2,269 girls (Ht 110-185cm) and 3,592 boys (ht 110-205cm).
3. Age 6-21 years m/f.
4. The model applicable to all data sets was lnFEV1 = a + (b + c x Age (y)) x Ht(cm)

**TABLE 4. Regression of ln FVC and ln $FEV_1$ on Standing Height (H, in Meter) and Age-Height (A · H, A in Years) Interaction and a Variable Indicating the Data Set**

| Index | Regression equation | RSD | $R^2$ |
|---|---|---|---|
| Girls | | | |
| ln FVC | $-1.5371\ (0.0417)^1 + [1.5374\ (0.0364) + 0.0129\ (0.0008) \cdot A] \cdot H + 0.0193\ (0.0056) \cdot k_3$ | 0.1098 | 0.8911 |
| ln $FVC^2$ | $-1.4507\ (0.0503) + [1.4800\ (0.0434) + 0.0127\ (0.0009) \cdot A] \cdot H$ | 0.1063 | 0.8768 |
| ln $FEV_1$ | $-1.6754\ (0.0428) + [1.5564\ (0.0373) + 0.0129\ (0.0008) \cdot A] \cdot H + 0.0551\ (0.0057) \cdot k_3$ | 0.1124 | 0.8884 |
| ln $FEV_1{}^2$ | $-1.5974\ (0.0503) + [1.5016\ (0.0434) + 0.0119\ (0.0009) \cdot A] \cdot H$ | 0.1063 | 0.8754 |
| $FEV_1$% FVC | $88.88\ (0.1344) + 2.48\ (0.2410) \cdot k_3 - 1.44\ (0.6092) \cdot k_4 - 2.53\ (0.3152) \cdot k_5$ | 4.86 | 0.0928 |
| Boys | | | |
| ln FVC | $-1.2217\ (0.0363) + [1.3083\ (0.0327) + 0.0186\ (0.0004) \cdot A] \cdot H + 0.0164\ (0.0041) \cdot k_3$ | 0.1051 | 0.9356 |
| ln $FVC^2$ | $-1.2782\ (0.0462) + [1.3731\ (0.0421) + 0.0164\ (0.0100) \cdot A] \cdot H$ | 0.1033 | 0.9272 |
| ln $FEV_1$ | $-1.2721\ (0.0378) + [1.2326\ (0.0341) + 0.0191\ (0.0008) \cdot A] \cdot H + 0.0571\ (0.0043) \cdot k_3$ | 0.1094 | 0.9305 |
| ln $FEV_1{}^2$ | $-1.2933\ (0.0491) + [1.2669\ (0.0447) + 0.0174\ (0.0011) \cdot A] \cdot H$ | 0.1097 | 0.9138 |
| $FEV_1$% FVC | $86.21\ (0.1470) + 2.22\ (0.2001) \cdot k_3 - 2.48\ (0.7073) \cdot k_5 - 2.39\ (0.3649) \cdot k_5$ | 5.58 | 0.0677 |

[1] Standard errors of regression coefficients in parentheses.

[2] Excluding Vitalograph data. RSD, residual standard deviation; $R^2$, explained variance. $k_3$, Austria; $k_4$, UK; $k_5$, Spain; value for $k = 1$ or 0.

Reference: Spirometric reference values for white European children and adolescents: Polgar revisited.
Quanjer PH, Borsboom GJ, Brunekreef B, Zach M, Forche G, Cotes JE, Sanchis J, Paoletti P. Pediatr Pulmonol. **1995** Feb;19(2):135-42.

## Facing the Pitfalls - on the way to GLI

1. Dis-jointed predicted values at the transition from children, adolescence to adulthood.
2. The models poorly fit the measured values, particularly in children.
3. Vary large differences in predicted values by various authors.
4. The “18th birthday effect” is the size of the transition from a pediatric equation to adults ones
5. Children younger than 6y ?
6. Ethnicity ?

# GLI - Global Lungs Initiative -2012

Age and height-based prediction bias in spirometry reference equation.
Quanjer PH1, Hall GL, Stanojevic S, Cole TJ, Stocks J; **Global Lungs Initiative** Eur Respir J. **2012** .
40 Collaborators in alphabetic order: Baur X,……………………, **Vilozni D**, Vlachos H, West S, Wouters EF, Zagami D.

Multi-ethnic reference values for spirometry for the **3-95**-yr age range: the global lung function 2012 equations.
Quanjer PH, **Stanojevic S**, Cole TJ, Baur X, Hall GL, Culver BH, Enright PL, Hankinson JL, Ip MS, Zheng J, Stocks J; ERS **Global Lung Function Initiative**. Collaborators: Eur Respir J**. 2012**

Spirometry centile charts for young Caucasian children: the Asthma UK Collaborative Initiative.
Stanojevic S, Wade A, Cole TJ, Lum S, Custovic A, Silverman M, Hall GL, Welsh L, Kirkby J, Nystad W, Badier M, Davis S, Turner S, Piccioni P, **Vilozni D**, Eigen H, Vlachos-Mayer H, Zheng J, Tomalak W, Jones M, Hankinson JL, Stocks J; Asthma UK Spirometry Collaborative Group. Am J Respir Crit Care Med. **2009**

**Israeli contribution ages 3-6years:**
The role of computer games in measuring spirometry in healthy and "asthmatic" preschool children.
**Vilozni D**, Barak A, Efrati O, Augarten A, Springer C, Yahav Y, Bentur L. Chest. **2005** Sep;128(3):1146-55.
An interactive computer-animated system (SpiroGame) facilitates spirometry in preschool children.
**Vilozni D**, Barker M, Jellouschek H, Heimann G, Blau H. Am J Respir Crit Care Med. **2001**

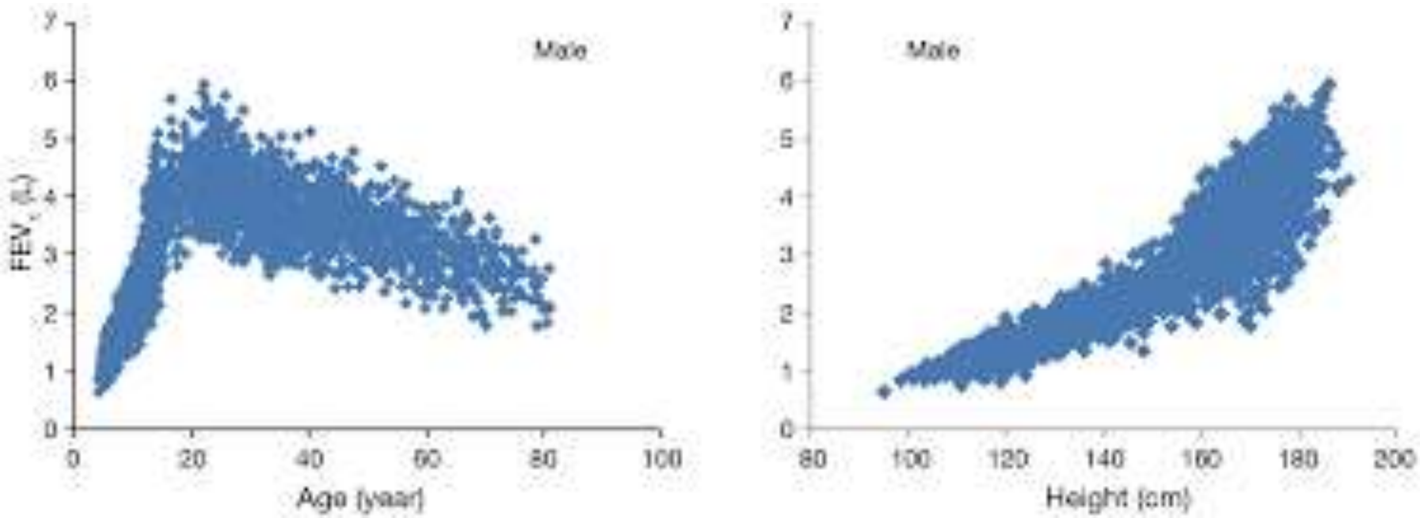
**2012 GLI - Global Lungs Initiative**

- Actual spirometry outcomes from researchers and health care professionals around the world.

- supported by 6-large international respiratory societies.
  World wide network that included clinicians, researchers, technicians, engineers and manufacturers.

- GLI Objective: to derive reference equations for spirometry that covered an age range from pre-school children to old age and as many ethnic groups as possible

- The data were collated and analyzed with modern statistical techniques (GLAMS), and led to the GLI-2012 prediction equations.



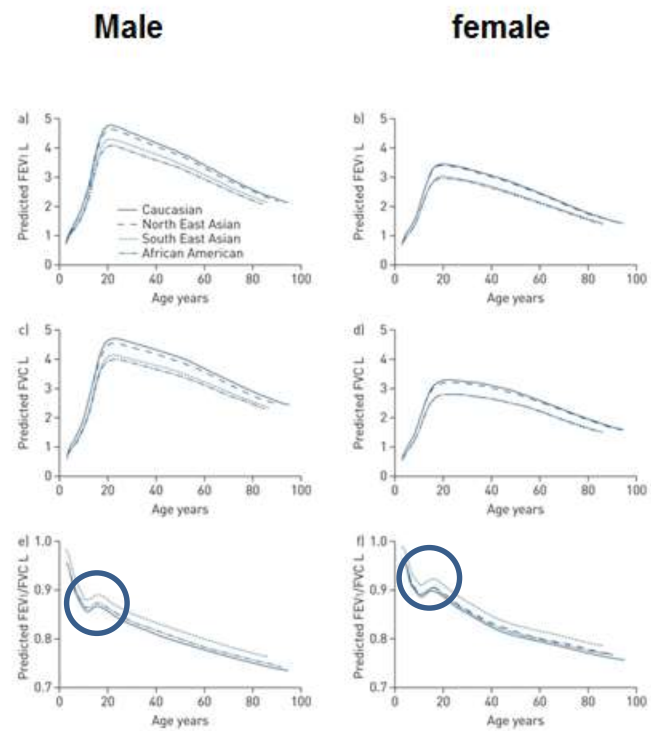

GLI findings:  FEV1 grows during childhood.
FEV1 grows slower in relation to height up so 140-160cm
FEV1 declines with age after puberty

During adolescence the relationship between age, height and spirometry changes
GLI  introduced this relationship and combined them to a single equation

FEV$_1$

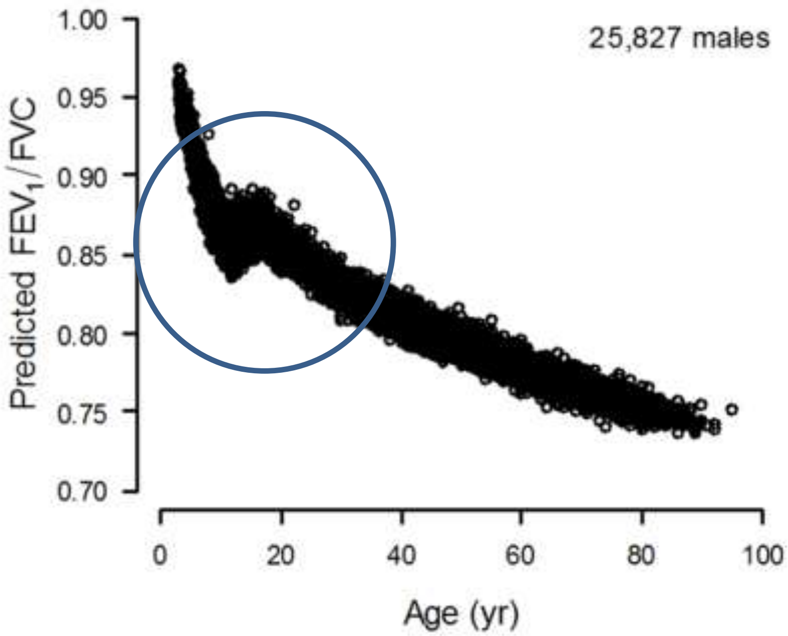
FVC

FEV$_1$/FVC



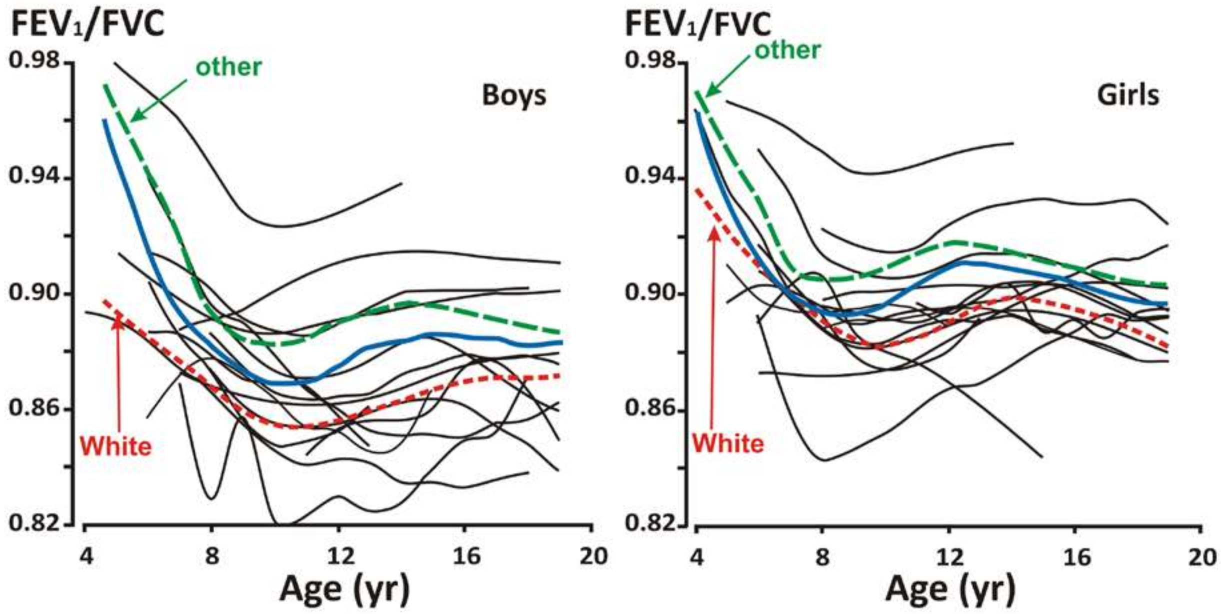

There is a rise and fall in FEV$_1$/FVC around adolescence, due to differential changes in FEV$_1$ and FVC

- Between 3 - ~10 years of age - The predicted value quickly fall →
- Between ~16 y of age, → ~20y there is a rise in the ratio
  then a gradual non-linear decline in adults



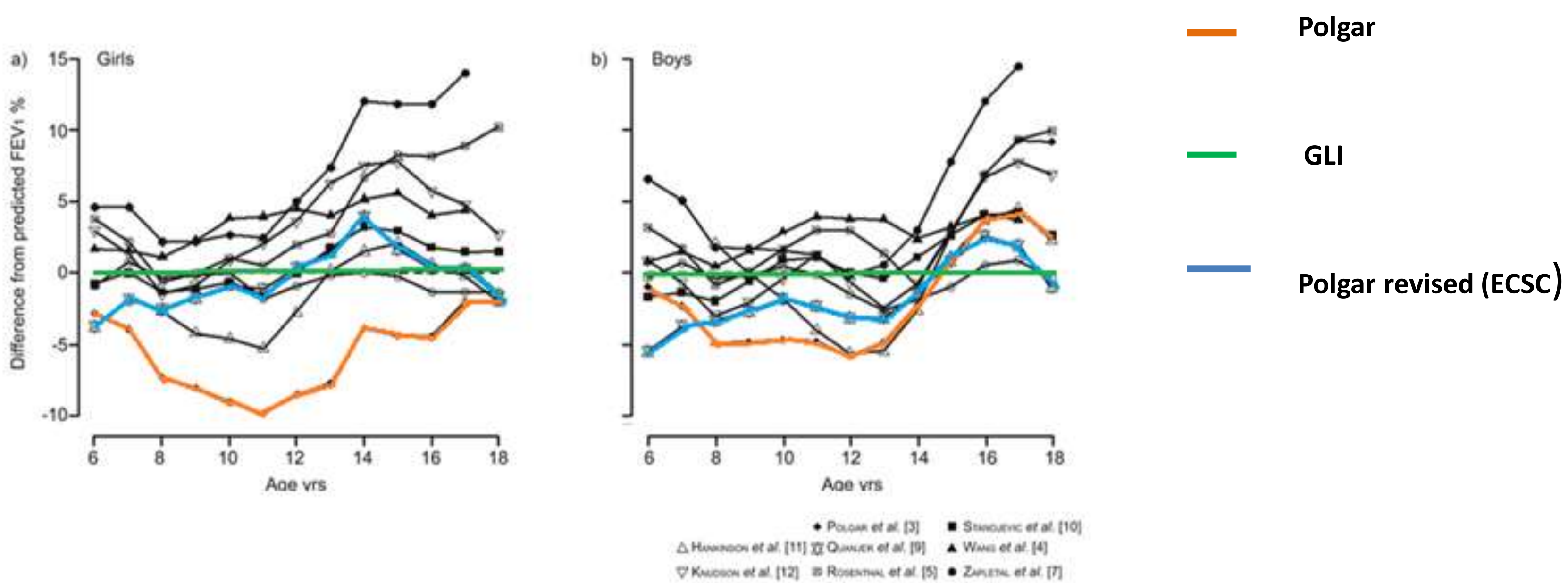

Meaning:
the FEV1 and the VC are not in the same predicted phase:
After birth the VC grows proportionally faster than the FEV1,
This pattern is temporarily reversed during the adolescent growth spurt

Evidence that the findings were not an artifact




GLAMS Analysis of data from boys and girls from 15 difference centers, comprising different ethnic groups.

Differences between predicted equations and the meaning of using them



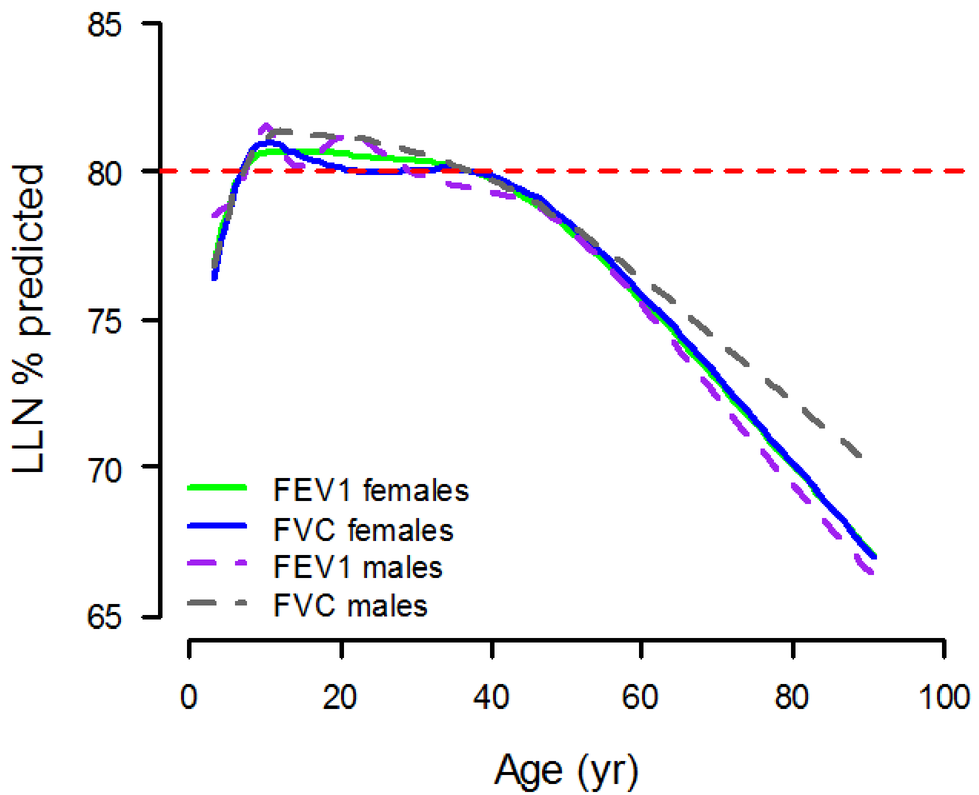

A difference of 0% indicates that the predicted values perfectly match the GLI 2012 data.

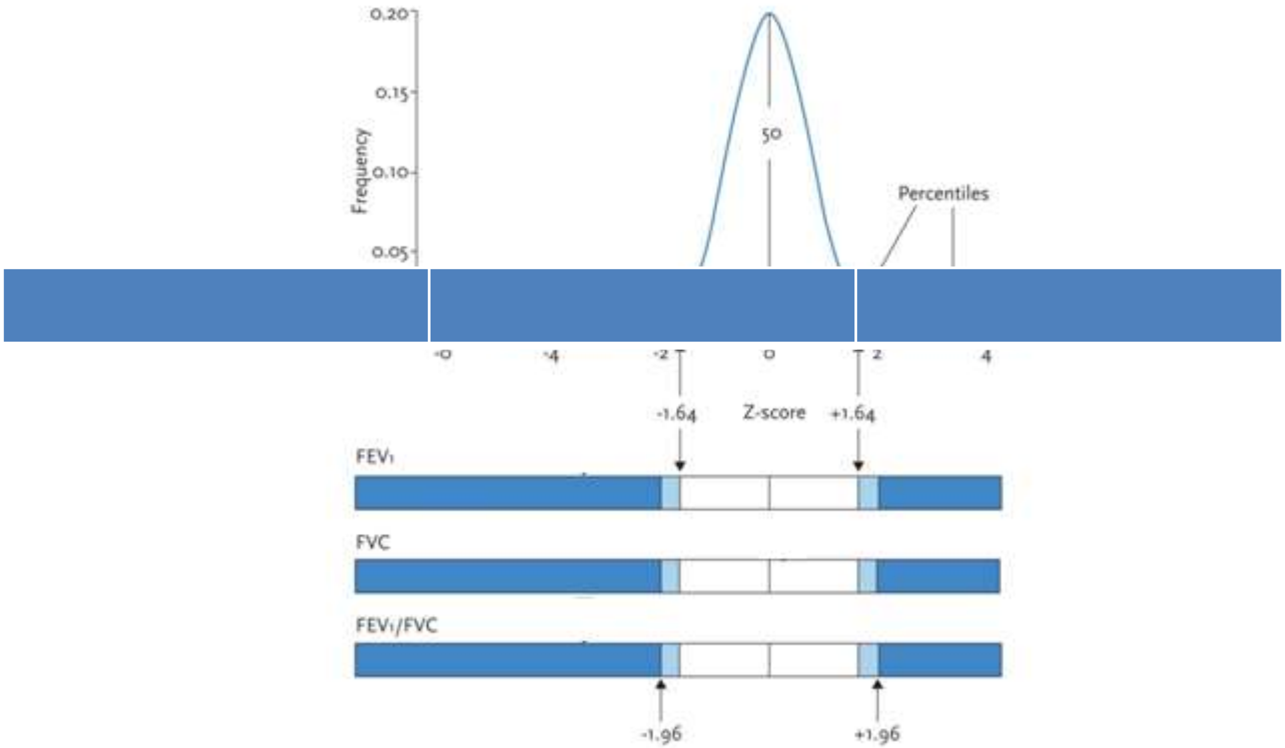
# The differences between predicted values for $FEV_1$ at 17.99 and 18.0 yrs for 282 boys of identical height (mL) according–various reference equations.

| FEV1 | Age 17.99 yrs | vs. | Age 18.0 yrs |
|---|---|---|---|
| | GLI 2012 | | |
| | Absolute error mL | | (Error %from GLI) |
| Hankinson | -33–268 | | (-1-5%) |
| ECCS children/adults | 263–450 | | (-7-12%) |
| Polgar | 192–538 | | (4-22%) |

# The lower limit of normal (LLN) defines between normal and abnormal

The lower limit of normal (LLN) for FEV1 and FVC expressed as a %%
of the GLI-2012 predicted values in the 3-95 year age range.






# Grading system for categorization of airways obstruction

| | %predicted | zScore |
|---|---|---|
| MILD | 0 - 70 | > -2 |
| Moderate | 60-69 | -2.5 - -2 |
| Moderately severe | 50-59 | -3.0 - -2.5 |
| Severe | 35-49 | -4.0 - -3.0 |
| Very Sever | <35 | < -4 |

# Point for discussion

1. By continuing using  Polgar,  values can be “too good”
2. Which equation should we use ?  Given that the GLI includes FVC, FEV1, FEV0.75, FEF25-75. (Lung volumes were already presented)
3. Can  we use any single equation for follow-up?
4. How to announce this change?
5. To use the GLI equations one must upgrade the spirometer