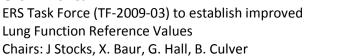


#### **GLOBAL LUNGS INITIATIVE**





July 19, 2015

To: manufacturers - members of the Global Lungs network

## 1 Implementing GLI 2012 regression equations

website

Following the recent endorsement by the ERS, ATS, APSR, ANZRS and TSANZ and ACCP, the Global Lungs Initiative, an ERS Task Force (TF-2009-03) to establish improved Spirometric Lung Function Reference Values, has now published the GLI 2012 regression equations on its <a href="website">website</a> - these complement the Task Force report which has been published in the European Respiratory Journal. These GLI 2012 equations differ from the familiar linear regression equations. Below we explain how software engineers will be able to incorporate them into software and check whether the output is correct.

The predictions depend on three quantities L, M and S, which are functions of sex, age, height and ethnicity. L measures the skewness, S is the coefficient of variation and M is the predicted value of FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC or other indices. The lower limit of normal (LLN) and the z-score are calculated from L, M and S as follows:

Predicted value = M

LLN (5<sup>th</sup> percentile) =  $exp(ln(M) + ln(1 - 1.645 \cdot L \cdot S)/L)$ Z-score =  $((measured/M)^L - 1)/(L \cdot S)$ % predicted =  $(measured/M) \cdot 100$ 

The LMS equations for whites (including Mexican Americans and Latin Americans of Caucasian origin), African Americans, South East Asians, North East Asians and for Other ethnic groups or people of mixed descent, valid from 3-95 years, are of this form, with volumes in litres, age in years, and height in cm:

```
 L = q_0 + q_1 \cdot \ln(Age) + Lspline \\ M = exp(a_0 + a_1 \cdot \ln(Height) + a_2 \cdot \ln(Age) + a_3 \cdot black + a_4 \cdot NEAsia + a_5 \cdot SEAsia + a_6 \cdot Other + Mspline) \\ S = exp(p_0 + p_1 \cdot \ln(Age) + p_2 \cdot black + p_3 \cdot NEAsia + p_4 \cdot SEAsia + p_5 \cdot Other + Sspline)
```

## where

In() = natural log transformation

black = 1 if a subject is African American, otherwise = 0

NEAsia = 1 if a subject is from North East Asia, otherwise = 0 (see map on page 6)

SEAsia = 1 if a subject is from South East Asia, otherwise = 0

Other = 1 if subject is 'other ethnic group' or mixed ethnicity, otherwise = 0

coefficients L<sub>0</sub> ... q depend on the measurement and gender

Mspline, Sspline, Lspline = age-varying coefficients

#### For 3-25 years:

Linearly interpolate Mspline, Sspline and Lspline from lookup tables.

#### For 25-95 years:

Linearly interpolate Mspline, Sspline, Lspline from lookup tables

OR (for systems with limited memory):

 $\begin{aligned} & \text{Mspline} = & b_0 + b_1 \cdot (\text{Age}/100) + b_2 \cdot (\text{Age}/100)^2 + b_3 \cdot (\text{Age}/100)^3 + b_4 \cdot (\text{Age}/100)^4 + b_5 \cdot (\text{Age}/100)^5 \\ & \text{Sspline} = & c_0 + c_1 \cdot (\text{Age}/100) + c_2 \cdot (\text{Age}/100)^2 + c_3 \cdot (\text{Age}/100)^3 + c_4 \cdot (\text{Age}/100)^4 + c_5 \cdot (\text{Age}/100)^5 \\ & \text{Lspline} = & d_0 + d_1 \cdot (\text{Age}/100) + d_2 \cdot (\text{Age}/100)^2 + d_3 \cdot (\text{Age}/100)^3 + d_4 \cdot (\text{Age}/100)^4 + d_5 \cdot (\text{Age}/100)^5 + d_6 \cdot (\text{Age}/100)^6 + d_7 \cdot (\text{Age}/100)^7 \end{aligned}$ 

Given the errors that can arise from truncating age or reporting height simply as integer, every effort should be made to enter height and age to at least 1 decimal place in these equations (Quanjer *et al. Eur Respir J* 2012: 40: 190–197).

# 2 Example coefficients for FEV<sub>1</sub> in males

For the purpose of demonstrating how to use the equations in calculating predicted and derived values, let us look at the linear coefficients for calculating  $FEV_1$  in males.

Table E1 – Regression coefficients for  $FEV_1$  (males) for calculating M (predicted value), S (coefficient of variation) and L (skewness). The contributions of splines must be added to the calculated values; they are available in look-up tables.

		Coefficients								
		M			S			L		
Intercept	$a_0$	-10.3420		p <sub>0</sub>	-2.3268		$q_0$	0.8866		
Height	$a_1$	2.2196								
Age	a <sub>2</sub>	0.0574		$p_1$	0.0798		$q_{\scriptscriptstyle 1}$	0.0850		
Afr. Am.	a <sub>3</sub>	-0.1589		$p_2$	0.1096					
N East Asia	a <sub>4</sub>	-0.0351		$p_3$	-0.3973					
S East Asia	<b>a</b> <sub>5</sub>	-0.0881		$p_4$	0.0327					
Other/mixed	<b>a</b> <sub>6</sub>	-0.0708		<b>p</b> <sub>5</sub>	0.0114					
	+	Mspline		+	Sspline		+	Lspline		

Below are the coefficients required to calculate the contribution of splines at specific ages (Age/100 !!), for subjects between 25-95 years. One should never extrapolate beyond these age ranges!

Table E2 – Regression coefficients for splines for  $FEV_1$  in males that may be used to replace look-up tables for ages 25-95 years in systems with limited memory.

	Coefficients							
	ı	Mspline			Sspline		Lsp	line
Intercept	$b_0$	0.3901		C <sub>0</sub>	-1.6902		$d_0$	0
Age	$b_1$	-1.0579		C <sub>1</sub>	17.0986		$d_1$	0
Age <sup>2</sup>	b <sub>2</sub>	1.4743		C <sub>2</sub>	-68.1649		$d_2$	0
Age <sup>3</sup>	b <sub>3</sub>	-2.1077		<b>C</b> <sub>3</sub>	127.1964		d <sub>3</sub>	0
Age <sup>4</sup>	b <sub>4</sub>	-0.1215		C <sub>4</sub>	-109.6777		$d_4$	0
Age <sup>5</sup>	$b_5$	0.8873		<b>C</b> <sub>5</sub>	35.6832		$d_5$	0
Age <sup>6</sup>							$d_6$	0
Age <sup>7</sup>							d <sub>7</sub>	0

#### 3 Five worked examples

Note that in the examples each result is rounded to 4 decimals, unlike in software. Hence there will be slight differences between software output and the results below.

## 3.1 White boy

We wish to calculate the predicted FEV<sub>1</sub>, % predicted,  $5^{th}$  percentile LLN and z-score for a white boy age 4.8 yr, height 107 cm, FEV<sub>1</sub> = 0.800 L.

For linear interpolation for age 4.8 yr we consult the look-up table:

Age Mspline

				0 -	
	0	0.1592	-0.0769	4.75	
	0	0.1535	-0.0752	5	
-4.75)/0.25)·(-0.0752 - (-0.0769)) = -0.0766					

Sspline

Lspline

```
Mspline = -0.0769 + ((4.8-4.75)/0.25) \cdot (-0.0752 - (-0.0769)) = -0.0766

Sspline = 0.1592 + ((4.8-4.75)/0.25) \cdot (0.1535 - 0.1592) = 0.1581

M = FEV1 predicted = \exp(-10.3420 + 2.2196 \cdot \ln(107) + 0.0574 \cdot \ln(4.8) - 0.0766) =

**predicted = (0.800/1.0442) \cdot 100

S = \exp(-2.3268 + 0.0798 \cdot \ln(4.8) + 0.1581) = 0.1296

L = 0.8866 + 0.0850 \cdot \ln(4.8) = 1.0199

LLN = \exp(\ln(1 - 1.644 \cdot L \cdot S)/L + \ln(M))

= \exp(\ln(1 - 1.644 \cdot L \cdot S)/L + \ln(M))

= \exp(\ln(1 - 1.644 \cdot 1.0199 \cdot 0.1296)/1.0199 + \ln(1.0442))

Z-score = ((\text{measured/predicted})^L - 1)/(L \cdot S)

= ((0.800/1.0442)^{1.0199} - 1)/(1.0199 \cdot 0.1296)

= -1.80
```

## 3.2 African American boy

We wish to calculate the predicted FEV<sub>1</sub>, % predicted,  $5^{th}$  percentile LLN and z-score for an African American boy age 12.2 yr, height 152 cm, FEV<sub>1</sub> = 2.405 L.

Mspline

Sspline

= 2.1860 L

**= 110.0%** 

For linear interpolation to age 12.2 yr we consult the look-up table:

12	-0.0176	-0.0387					
12.25	-0.0101	-0.0339					
Mspline = $-0.0176 + ((12.2-12)/0.25) \cdot (-0.0101 - (-0.0176)) = -0.0116$							
Sspline = $-0.0387 + ((12.2-12)/0.25) \cdot (-0.0339 - (-0.0387)) = -0.0349$							
$M = FEV_1 predicted = exp(-10.3420 + 2.2196 \cdot ln(107) + 0.0574 \cdot ln(12.2) - 0.1589 - 0.0116)$							

Age

 $S = \exp(-2.3268 + 0.0798 \cdot \ln(12.2) + 0.1096 - 0.0349) = 0.1284$ 

 $L = 0.8866 + 0.0850 \cdot ln(12.2) = 1.0992$ 

% predicted =  $(2.405/2.1860) \cdot 100$ 

**LLN** =  $\exp(\ln(1 - 1.644 \cdot L \cdot S) / L + \ln(M))$ 

 $= \exp(\ln(1 - 1.644 \cdot 1.0992 \cdot 0.1284) / 1.0992 + \ln(2.1860))$  = **1.7193** L

**Z-score** =  $((measured/predicted)^{L} - 1)/(L \cdot S)$ 

 $= ((2.405/2.1860)^{1.0992} - 1)/(1.0992 \cdot 0.1284)$  = **0.78** 

# 3.3 South East Asian adult male

We wish to calculate the predicted FEV<sub>1</sub>, % predicted,  $5^{th}$  percentile LLN and z-score for a South East Asian male age 53 yr, height 175 cm, FEV<sub>1</sub> = 2.410 L.

Calculations can be performed using the look-up table for L, M and S, or by replacing the latter with the equations in table E2. First using the look-up tables:

Age	Mspline	Sspline
53	-0.0404	0.0003

```
Mspline = -0.0404
```

Sspline = 0.0003

$$M = FEV_1 \text{ predicted} = \exp(-10.3420 + 2.2196 \cdot \ln(175) + 0.0574 \cdot \ln(53) - 0.0881 - 0.0404) = 3.3911 \text{ L}$$

$$\% \text{ predicted} = (2.410/3.3911) \cdot 100$$

$$S = \exp(-2.3268 + 0.0798 \cdot \ln(53) + 0.0327 + 0.0003) = 0.1385$$

$$L = 0.8866 + 0.0850 \cdot \ln(53) = 1.2241$$

$$LLN = \exp(\ln(1 - 1.644 \cdot L \cdot S) / L + \ln(M))$$

$$= \exp(\ln(1 - 1.644 \cdot 1.2241 \cdot 0.1385) / 1.2241 + \ln(3.3911))$$

$$Z - \text{score} = ((\text{measured/predicted})^L - 1) / (L \cdot S)$$

$$= ((2.410/3.3911)^{1.2241} - 1) / (1.2241 \cdot 0.1385)$$

$$= -2.01$$

We can also replace the look-up tables by the equations in Table E2:

```
Mspline = 0.3901 - 1.0579 \cdot (53/100) + 1.4743 \cdot (53/100)^2 - 2.1077 \cdot (53/100)^3 - 0.1215 \cdot (53/100)^4 + 0.8873 \cdot (53/100)^3 - 0.1215 \cdot (53/100)^4 + 0.8873 \cdot (53/100)^4 + 0.8
                                                                                                                                                                  (53/100)^5 = -0.0427
Sspline = -1.6092 + 17.0986 \cdot (53/100) - 68.1649 \cdot (53/100)^2 + 127.1964 \cdot (53/100)^3 - 109.6777 \cdot (53/100)^4 + 127.1964 \cdot (53/100)^3 - 109.6777 \cdot (
                                                                                                                                                                  35.6832 \cdot (53/100)^5 = -0.0007
M = FEV_1 \text{ predicted} = \exp(-10.3420 + 2.2196 \cdot \ln(175) + 0.0574 \cdot \ln(53) - 0.0881 - 0.0427)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     = 3.3833 L
% predicted = (2.410/3.3833) \cdot 100
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     = 71.2%
S = \exp(-2.3268 + 0.0798 \cdot \ln(53) + 0.0327 - 0.0007) = 0.1383
L = 0.8866 + 0.0850 \cdot ln(53) = 1.2241
LLN = \exp(\ln(1 - 1.644 \cdot L \cdot S) / L + \ln(M))
                                                                               = \exp(\ln(1 - 1.644 \cdot 1.2241 \cdot 0.1383) / 1.2241 + \ln(3.3833))
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                = 2.5919 L
Z-score = ((measured/predicted)^{L} - 1)/(L \cdot S)
                                                                               =((2.410/3.3833)^{1.2241}-1)/(1.2241\cdot0.1383)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             = -2.01
```

#### 3.4 South East Asian adult female

Note that South East Asia does *not* refer to India, but to people of Mongoloid extraction. We wish to calculate the predicted  $FEV_1$ , % predicted,  $5^{th}$  percentile LLN and z-score for a South East Asian female age 39.1 yr, height 165 cm,  $FEV_1 = 2.210$  L. Calculations can be performed using the look-up table for L, M and S, or by replacing the latter with the equations in table E3. First using the look-up tables:

Age (yr)	Mspline	Sspline
39	0.1112	-0.0919
39.25	0.1094	-0.0913

Mspline = 
$$0.1112+(0.1/0.25)\cdot(0.1094 - 0.1112) = 0.1105$$
  
Sspline =  $-0.0919 + (0.1/0.25)\cdot(-0.0913 - (-0.0919)) = -0.0917$   
Lspline =  $0$ 

Table E3 – Regression coefficients for  $FEV_1$  (females) for calculating M (predicted value), S (coefficient of variation) and L (skewness). The contributions of splines must be added to the calculated values; they are available in look-up tables.

		Coefficients						
		M		S				L
Intercept	$a_0$	-9.6987		$p_0$	-2.3765		$\mathbf{q}_0$	1.1540
Height	$a_1$	2.1211						
Age	$a_2$	-0.0270		$p_1$	0.0972		$q_{\scriptscriptstyle 1}$	0
Afr. Am.	$a_3$	-0.1484		p <sub>2</sub>	0.1016			
N East Asia	a <sub>4</sub>	-0.0149		<b>p</b> <sub>3</sub>	-0.0109			
S East Asia	$a_5$	-0.1208		p <sub>4</sub>	0.0733			
Other/mixed	$a_6$	-0.0708		<b>p</b> <sub>5</sub>	0.0114			
	+	Mspline		+	Sspline		+	Lspline

We can also replace the look-up tables by equations (table E4):

Table E4 – Regression coefficients for splines for  $FEV_1$  in females that may be used to replace look-up tables for ages 25-95 years in systems with limited memory.

	Coefficients								
	Mspline				Sspline		1	Lspline	
Intercept	$b_0$	0.0552		<b>C</b> 0	-0.0822		$d_0$		0
Age/100	b <sub>1</sub>	1.6029		C <sub>1</sub>	1.4115		$d_1$		0
$(Age/100)^2$	b <sub>2</sub>	-6.4845		C <sub>2</sub>	-11.2797		$d_2$		0
$(Age/100)^3$	b <sub>3</sub>	10.2723		<b>C</b> <sub>3</sub>	29.4613		$d_3$		0
(Age/100) <sup>4</sup>	b <sub>4</sub>	-9.8630		<b>C</b> 4	-29.5597		$d_4$		0
(Age/100) <sup>5</sup>	<b>b</b> <sub>5</sub>	3.8802		<b>C</b> <sub>5</sub>	10.4468		$d_5$		0
(Age/100) <sup>6</sup>							$d_6$		0
(Age/100) <sup>7</sup>							d <sub>7</sub>		0

```
\begin{aligned} \text{Mspline} &= 0.0552 + 1.6029 \cdot (39.1/100) - 6.4845 \cdot (39.1/100)^2 + 10.2723 \cdot (39.1/100)^3 - 9.8630 \cdot (39.1/100)^4 + \\ & 3.8802 \cdot (39.1/100)^5 = 0.1096 \\ \text{Sspline} &= -0.0822 + 1.4115 \cdot (39.1/100) - 11.2797 \cdot (39.1/100)^2 + 29.4613 \cdot (39.1/100)^3 - 29.5597 \cdot (39.1/100)^4 \\ & + 10.4468 \cdot (39.1/100)^5 = -0.0891 \end{aligned}
```

 $M = FEV_1 \text{ predicted} = \exp(-9.6987 + 2.1211 \cdot \ln(165) - 0.0270 \cdot \ln(39.1) - 0.1206 + 0.1096) = 2.7775 L$ 

```
% predicted = (2.210/2.77945) \cdot 100 = 79.5% 

S = \exp(-2.3765 + 0.0972 \cdot \ln(39.1) + 0.0733 - 0.0891) = 0.1306 

Lspline = 0 

L = 1.1540 

LLN = \exp(\ln(1 - 1.644 \cdot L \cdot S)/L + \ln(M)) = \exp(\ln(1 - 1.644 \cdot 1.1540 \cdot 0.1306)/1.1540 + \ln(2.7775)) = 2.1702 L 

Z-score = ((\text{measured/predicted})^L - 1)/(L \cdot S) = ((2.210/2.7775)^{1.1540} - 1)/(1.1540 \cdot 0.1306) = -1.54
```

## 3.5 Adult female of mixed descent or 'other group'

We wish to calculate the predicted FEV<sub>1</sub>, % predicted,  $5^{th}$  percentile LLN and z-score for a female age 39.1 yr, height 165 cm, FEV<sub>1</sub> = 2.210 L. She is of mixed ethnic descent.

Calculations can be performed using the look-up table for L, M and S, or by replacing the latter with the equations in table E3.

First using the look-up tables:

**Z-score** =  $((measured/predicted)^{L} - 1)/(L \cdot S)$ 

 $=((2.210/2.9193)^{1.1540}-1)/(1.1540\cdot0.1227)$ 

```
Mspline = 0.1112 + (0.1/0.25) \cdot (0.1094 - 0.1112) = 0.1105
Sspline = -0.0919 + (0.1/0.25) \cdot (-0.0913 - (-0.0919)) = -0.0917
Lspline = 0
M = FEV_1 predicted = exp(-9.6987 + 2.1211 \cdot ln(165) - 0.0270 \cdot ln(39.1) - 0.0708 + 0.1105) =
                                                                                                                                                                                                                                                                                         2.9219 L
% predicted = (2.210/2.9219) \cdot 100
                                                                                                                                                                                                                                                                                              75.6 %
S = \exp(-2.3765 + 0.0972 \cdot \ln(39.1) + 0.0114 - 0.0917) = 0.1224
L = 1.1540
LLN = \exp(\ln(1 - 1.644 \cdot L \cdot S) / L + \ln(M))
                   = \exp(\ln(1 - 1.644 \cdot 1.1540 \cdot 0.1224) / 1.1540 + \ln(2.9219))
                                                                                                                                                                                                                                                                                  = 2.3239 L
Z-score = ((measured/predicted)^{L} - 1)/(L \cdot S)
                   =((2.210/2.9219)^{1.1540}-1)/(1.1540\cdot0.1224)
                                                                                                                                                                                                                                                                                             = -1.95
We can also replace the look-up tables by equations (table E4):
Mspline = 0.0552 + 1.6032 \cdot (39.1/100) - 6.4855 \cdot (39.1/100)^2 + 10.2741 \cdot (39.1/100)^3 - 9.8646 \cdot (39.1/100)^4 + 10.2741 \cdot (3
                            3.8808 \cdot (39.1/100)^5 = 0.1096
Sspline = -0.0825 + 1.4104 \cdot (39.1/100) - 11.2699 \cdot (39.1/100)^2 + 29.4400 \cdot (39.1/100)^3 - 29.5505 \cdot (39.1/100)^4
                            +10.4405\cdot(39.1/100)^5 = -0.0894
M = FEV_1 predicted = exp(-9.6987 + 2.1211·ln(165) - 0.0270·ln(39.1) - 0.0708 + 0.1096)
                                                                                                                                                                                                                                                                                   = 2.9193 L
% predicted = (2.210/2.9193) \cdot 100
                                                                                                                                                                                                                                                                                          = 75.7%
S = \exp(-2.3765 + 0.0972 \cdot \ln(39.1) + 0.0114 - 0.0894) = 0.1227
Lspline = 0
L = 1.1540
LLN = \exp(\ln(1 - 1.644 \cdot L \cdot S) / L + \ln(M))
                            = \exp(\ln(1 - 1.644 \cdot 1.1540 \cdot 0.1227)/1.1540 + \ln(2.9193))
                                                                                                                                                                                                                                                                                  = 2.3204 L
```

= -1.94

As demonstrated above, there are slight differences in the results calculating values using the look-up table or the equations replacing them. The discrepancies are not clinically important; nevertheless use of look-up tables and linear interpolation is the recommended procedure.

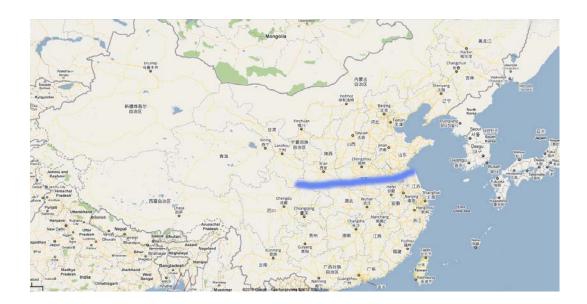
# 4 Valid age range, transformation of variables

Please note that the valid age range varies with the indices, and that age need not always be log transformed:

Index	Age range (yr)	Height	Age
$FEV_1$	3-95	In	In
FVC	3-95	In	In
FEV <sub>1</sub> /FVC	3-95	In	In
FEF <sub>25-75%</sub>	3-90	In	In
FEF <sub>75</sub>	3-90	In	In
$FEV_{0.75}$	3-7	In	linear
FEV <sub>0.75</sub> /FVC	3-7	ln	linear

## 5 North-South divide in East Asia

The group East Asians is comprised of Mongoloid people. The North-South divide in East Asia is formed by the Huaihe River and the Qinling Mountains, as depicted below (blue line):



## 6 GLI2012\_DataConversion.EXE

# 6.1 Transforming existing datasets

This <u>software</u> is available for free. The software is designed for PC ONLY and is provided 'as is', without any warranty. The output has been extensively tested against the output from GAMLSS in R, and found to be accurate.

The software can be used to:

- 1. Add predicted values and z-scores to an existing dataset.
- 2. Check (by IT engineers) whether the implementation in software of the GLI equations and lookup file leads to correct results.

## What the software does:

- 1. Reads a tab-delimited data file (extension .txt)
- 2. Calculates predicted values, their lower limits of normal (5<sup>th</sup> centiles) and z-scores for FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC, FEV<sub>0.75</sub>/FVC, FEF<sub>25-75%</sub>
- 3. Exports the results to a tab-delimited file for manipulation in a spreadsheet or other software.

#### IT IS IMPORTANT TO FOLLOW THE INSTRUCTIONS EXACTLY, TO AVOID ERRORS

- 1) Open your data file in EXCEL
  - a. The maximum number of records is limited to 60,000
- 2) Ensure you have columns for ALL the variables listed below
  - a. If you have not measured a variable, include that column but with all values set to 9999.
  - b. Note that 'South East Asians' refers to people of Mongoloid extraction, and not to the Indian subcontinent.
- 3) Ensure the columns are in the same order as listed
- 4) Ensure the units match and that the data are within the limits specified
  - a. If data are outside the limits the software usually issues a warning and exits, but in some cases the user is allowed to continue if certain that the offending data are correct.
- 5) Code all missing values as 9999
- 6) Ensure that sex, age, height and ethnic group are not missing, and that height and age are entered to at least 1 decimal place to maximise accuracy (Quanjer *et al.*, *Eur Respir J* 2012: 40: 190-197)
- 7) Save the file as a tab delimited text file
- 8) Please note that the file exported by Excel end with a blank line, which causes the conversion software to report an error. Therefore open the file in Endnote and delete the last line.

Variables	Units	Example	Limits	Valid age range (years)
ID	integer	4, 7, 411		
Sex	integer	1(male), 2(female)	1-2	
Age	year	45.57	3.0 - 95.0	
Height	cm	143.7	50 –250	
Ethnicity	integer	1(white), 2(black),	1-5	
		3(NE Asia*), 4(SE Asia*),		
		5(Other/mixed <sup>§</sup> )		
$FEV_1$	litre	3.456	0.2 - 9.0	3 – 95
FVC	litre	4.035	0.3 - 11.0	3 – 95
FEV <sub>1</sub> /FVC	1/s	0.85	0.15 - 1.0	3 – 95
$FEV_{0.75}$	L/s	2.862	0.2 - 6.0	3 – 7
FEV <sub>0.75</sub> /FVC	1/s	0.76	0.2 - 1.0	3 – 7
FEF <sub>25-75%</sub>	L/s	3.786	0.1 - 11.0	3 – 90
FEF <sub>75</sub>	L/s	2.305	0.02 - 8.0	3 – 90

<sup>\*</sup> Applies to Mongoloid group (see section 5). The dividing line between Korea and China (North East) and South East Asia is the Huaihe River and Qinling Mountains (see paragraph 5). § Other group or mixed ethnic descent.

Upon opening GLI2012\_DataConversion.EXE, 'Database conversion' is checked by default in 'Select Output' (Figure 1). Click 'File' and select the file that you want to convert. The content of the file and a button 'Calculate' are displayed (Figure 2). Click on the button and save (see under 'File') the resulting file (with extension .txt) when prompted.

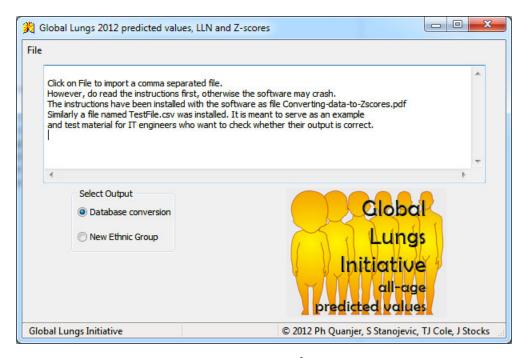


Figure 1 – Opening screen of GLIZscores.EXE

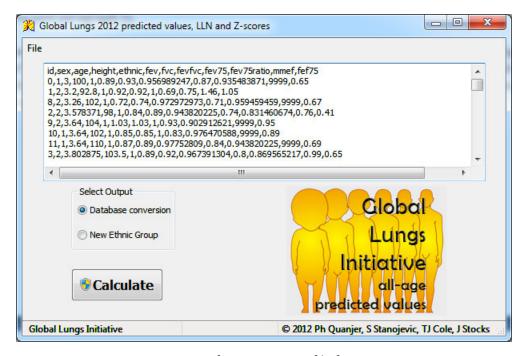


Figure 2 – Screen after importing a file for conversion.

If the software crashes and you are confident that your dataset contains no errors, please note carefully what steps led to the crash and report these (for the attention of P. Quanjer).

#### 6.2 Countries which contributed data

Caucasians Europe, Israel, Australia, USA, Canada, Mexican Americans, Brazil, Chile, Mexico,

Uruguay, Venezuela, Algeria, Tunisia

Blacks African Americans

South East Asians Thailand, Taiwan and China (including Hong Kong) south of the Huaihe River and

**Qinling Mountains** 

North East Asians Korea and China north of the Huaihe River and Qinling Mountains

# 6.3 Test file for manufacturers – IT engineers

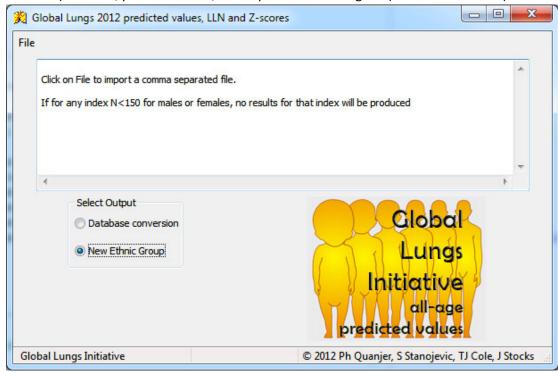
Manufacturers can test whether their implementation of equations in software leads to correct results. To that end they can compare their output to that in Validate.txt, using the same age, height *etc*. as in that file. The GLI2012\_DataConversion.EXE software is also accompanied by TestFile.txt; when imported and processed by the software, the output file contains the same data as Validate.txt: the original data, predicted values, lower limit of normal (5<sup>th</sup> centile) and z-scores to 4 decimal accuracy. The txt file and the GLI2012\_DataConversion software are included in the installation file, available from <a href="here">here</a>.

## 6.4 Deriving coefficients for additional ethnic groups

The GLI2012\_DataConversion.EXE software can be used to derive coefficients for additional ethnic groups from the GLI-2012 equations. A prerequisite is that a sufficiently large group of healthy nonsmokers, studied according to current international standards and appropriate quality control, is available. A minimum group size is 150 males and 150 females. Please note that samples of this size may differ by up to  $\pm$  0.4 z-scores from the true population mean, and by up to  $\pm$ 0.3 z-scores even if sample size exceeds 1,000 subjects (*Eur Respir J* 2011; 37: 658–664). It is obviously best to increase sample size by combining datasets, but the separate datasets need to give similar constants when analysed separately

In order to add coefficients for a new group (e.g. Inuit, highlanders in Bolivia, Australian aboriginals) to the set of equations, proceed as follows.

- 1. Format the group as indicated as in section 6.1. The only difference is that the ethnicity must be recorded as 1 (Caucasian), in order to calculate how much the new group differs from the Caucasian group.
- 2. Start the GLI2012\_DataConversion software, select "New Ethnic Group', open your (tab-delimited) data file, press Calculate, and export the resulting file (with .txt extension).



The following output is produced for FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC, FEF<sub>25-75%</sub>, and FEF<sub>75</sub>:

• Average z-scores for males and females. Thus avgFEVM and avgFEVF are the mean z-scores for FEV<sub>1</sub> in males and females, respectively.

- The standard deviation (SD) of z-scores for the various indices. Thus sdFVCM and sdFVCF represent the SD for the z-scores for FVC in males and females, respectively.
- The coefficients for M and S for your new group. Thus Mratiogroup and Sratiogroup represent the coefficients for FEV<sub>1</sub>/FVC to be applied to your new group. These coefficients should be applied to both males and females.

Note that no output will be produced for  $FEV_{0.75}$  and  $FEV_{0.75}$ /FVC, as GLI 2012 predicted values for these indices are only available for Caucasians. Even so, your data file should be formatted as delineated in section 6.1, where these indices may be coded as missing (code value as 9999).

As shown in the GLI-2012 report, there are essentially no inter-group differences in the FEV $_1$ /FVC ratio. If you find a large difference in this ratio between your new group and predicted values for Caucasians, you should be concerned about your measurements.

## 6.5 Implementing additional coefficients into commercial lung function devices

It will be possible for software manufacturers to implement the facility to enter additional coefficients for calculating predicted values for new ethnic groups, provided written agreement has been obtained from the GLI analytical team. This will be subject to the following conditions:

Individuals or groups requiring inclusion of such updates need to provide the GLI team with the following:

- 1. Written confirmation that data were collected with full ethical approval and with agreement for publication.
- 2. Confirmation that data were collected using international standards for technical acceptability, valid at time of measurement.
- 3. Agreement to share the data from which coefficients have been derived with the GLI, so that it can be incorporated into any future dataset or combined with other similar ethnic groups.
- 4. Submission of individual spirometry test results, and relevant background details (age, sex, height, ethnic group, *etc.*) in standardised anonymised format.
- 5. Agreement that details of the additional coefficients should be open access/shared with all manufacturers.

Analytical Team of Global Lung Function Initiative

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