



**GLOBAL LUNGS INITIATIVE**

ERS Task Force (TF-2009-03) to establish improved Lung Function Reference Values  
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[www.lungfunction.org](http://www.lungfunction.org)



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To: manufacturers - members of the Global Lungs network

**Implementing forthcoming regression equations**

The Global Lungs Initiative, an ERS Task Force (TF-2009-03) to establish improved Lung Function Reference Values, will publish regression equations on its website [www.lungfunction.org](http://www.lungfunction.org) as soon as the manuscript has been accepted for publication. These equations differ from the familiar linear regression equations. Below we explain how software engineers will be able to incorporate them into software.

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

$$\begin{aligned} \text{Predicted value} &= M \\ \text{LLN (5}^{\text{th}} \text{ percentile)} &= \exp(\ln(M) + \ln(1 - 1.645 * L * S) / L) \\ \text{Z-score} &= ((\text{measured} / M)^L - 1) / (L * S) \\ \% \text{ predicted} &= (\text{measured} / M) * 100 \end{aligned}$$

The LMS equations for whites, African Americans and Mexican Americans, valid from 3-95 years, are of this form, with volumes in litres, age in years, and height in cm (**NB this is an example based on data published in Am J Resp Crit Care Med 2008; 177: 253-260**):

$$\begin{aligned} L &= L_0 \\ M &= \exp(a_0 + a_1 * \ln(\text{Height}) + a_2 * \ln(\text{Age}) + a_3 * \text{black} + a_4 * \ln(\text{Age}) * \text{black} + a_5 * \text{hisp} + a_6 * \ln(\text{Age}) * \text{hisp} + \text{Mspline}) \\ S &= \exp(p + q * \ln(\text{Age}) + \text{Sspline}) \end{aligned}$$

where

- ln() = natural log transformation
- black = 1 if a subject is African American, otherwise = 0
- hisp = 1 if a subject is Mexican American, otherwise = 0
- coefficients L<sub>0</sub> ... q depend on the measurement and gender
- Mspline, Sspline = age-varying coefficients

For 3-25 years:

Linearly interpolate Mspline and Sspline from lookup tables

For 25-95 years:

$$\begin{aligned} \text{Mspline} &= b_0 + b_1 * (\text{Age}/100) + b_2 * (\text{Age}/100)^2 + b_3 * (\text{Age}/100)^4 + b_4 * \cos(\text{Age}/b_5) + b_6 * \cos(\text{Age}/b_7) \\ \text{Sspline} &= c_0 + c_1 * (\text{Age}/100) + c_2 * (\text{Age}/100)^2 + c_3 * (\text{Age}/100)^4 + c_4 * \cos(\text{Age}/c_5) + c_6 * \cos(\text{Age}/c_7) \end{aligned}$$

where the cos argument is in units of radians

**Example coefficients for FVC in males**

These are the coefficients for the LMS equations:

L0	0.9345	a2	0.1040	a5	0.0686	q	0.0486
a0	-11.0710	a3	-0.1236	a6	-0.0167		
a1	2.3722	a4	-0.0122	p	-2.2163		

## Implementing lung function regression equations

This table gives values of Mspline and Sspline by whole years of age from 3-25 years, which need to be linearly interpolated to exact age:

Age	Mspline	Sspline	Age	Mspline	Sspline	Age	Mspline	Sspline
3	-0.1174	0.3212	11	-0.0225	-0.0390	19	0.1502	-0.0877
4	-0.0797	0.2307	12	-0.0116	-0.0519	20	0.1571	-0.0886
5	-0.0499	0.1615	13	0.0071	-0.0618	21	0.1603	-0.0889
6	-0.0389	0.1069	14	0.0351	-0.0694	22	0.1607	-0.0885
7	-0.0397	0.0633	15	0.0671	-0.0753	23	0.1593	-0.0875
8	-0.0477	0.0284	16	0.0972	-0.0800	24	0.1565	-0.0860
9	-0.0467	0.0003	17	0.1214	-0.0835	25	0.1511	-0.0826
10	-0.0335	-0.0219	18	0.1387	-0.0860			

These are the Mspline and Sspline coefficients for age 25-95 years:

	Mspline		Sspline
b <sub>0</sub>	0.07502	c <sub>0</sub>	-0.09066
b <sub>1</sub>	0.75883	c <sub>1</sub>	-0.15563
b <sub>2</sub>	-2.03506	c <sub>2</sub>	0.86763
b <sub>3</sub>	0.71649	c <sub>3</sub>	-0.37122
b <sub>4</sub>	-0.00705	c <sub>4</sub>	0.00017
b <sub>5</sub>	5.60114	c <sub>5</sub>	3.78510
b <sub>6</sub>	-0.00925	c <sub>6</sub>	0.00635
b <sub>7</sub>	7.48912	c <sub>7</sub>	8.89271

### THREE WORKED EXAMPLES

#### 1 *White boy*

We wish to calculate the predicted FVC, % predicted, 5<sup>th</sup> percentile LLN and Z-score for a white boy age 4.8 yr, height 107 cm, FVC = 0.800 L.

By linear interpolation for age 4.8 yr:

$$\begin{aligned}
 \text{Mspline} &= -0.0797 + 0.8 * (-0.0499 - (-0.0797)) = -0.0559 \\
 \text{Sspline} &= 0.2307 + 0.8 * (0.1615 - 0.2307) = 0.1753 \\
 M = \text{FVC predicted} &= \exp(-11.0710 + 2.3722 * \ln(107) + 0.1040 * \ln(4.8) - 0.0559) = \mathbf{1.129 L} \\
 \% \text{ predicted} &= (0.800 / 1.129) * 100 = \mathbf{70.9\%} \\
 S &= \exp(-2.2163 + 0.0486 * \ln(4.8) + 0.1753) = 0.1402 \\
 L &= 0.9345 \\
 \text{LLN} &= \exp(\ln(1 - 1.645 * L * S) / L + \ln(M)) \\
 &= \exp(\ln(1 - 1.645 * 0.9345 * 0.1402) / 0.9345 + \ln(1.129)) = \mathbf{0.870 L} \\
 \text{Z-score} &= ((\text{measured} / \text{predicted})^L - 1) / (L * S) \\
 &= ((0.800 / 1.129)^{0.9345} - 1) / (0.9345 * 0.1402) = \mathbf{-2.10}
 \end{aligned}$$

#### 2 *African American boy*

We wish to calculate the predicted FVC, % predicted, 5<sup>th</sup> percentile LLN and Z-score for an African American boy age 12.2 yr, height 152 cm, FVC = 2.705 L.

By linear interpolation for age 12.2 yr:

$$\begin{aligned}
 \text{Mspline} &= -0.0116 + 0.2 * (0.0071 - (-0.01167)) = -0.0078 \\
 \text{Sspline} &= -0.0519 + 0.2 * (-0.0618 - (-0.0519)) = -0.0539 \\
 M = \text{FVC predicted} &= \exp(-11.0710 + 2.3722 * \ln(152) + 0.1040 * \ln(12.2) - 0.1236 - \\
 &\quad 0.0122 * \ln(12.2) - 0.0078) = \mathbf{2.573 L} \\
 \% \text{ predicted} &= (2.705 / 2.573) * 100 = \mathbf{105.1\%}
 \end{aligned}$$

## Implementing lung function regression equations

$$\begin{aligned}
 S &= \exp(-2.2163 + 0.0486 \cdot \ln(12.2) - 0.0539) = 0.1166 \\
 L &= 0.9345 \\
 \text{LLN} &= \exp(\ln(1 - 1.645 \cdot L \cdot S) / L + \ln(M)) \\
 &= \exp(\ln(1 - 1.645 \cdot 0.9345 \cdot 0.1166) / 0.9345 + \ln(2.573)) = \mathbf{2.083 \text{ L}} \\
 \text{Z-score} &= ((\text{measured}/\text{predicted})^L - 1) / (L \cdot S) \\
 &= ((2.705/2.573)^{0.9345} - 1) / (0.9345 \cdot 0.1166) = \mathbf{0.44}
 \end{aligned}$$

### 3 Mexican American adult male

We wish to calculate the predicted FVC, % predicted, 5<sup>th</sup> percentile LLN and Z-score for an Mexican American male age 53 yr, height 175 cm, FVC = 3.250 L.

Using the equations for age 53 yr:

$$\begin{aligned}
 \text{Mspline} &= 0.07502 + 0.75883 \cdot (53/100) - 2.03506 \cdot (53/100)^2 + 0.71649 \cdot (53/100)^4 - \\
 &\quad 0.00705 \cdot \cos(53/5.60114) - 0.00925 \cdot \cos(53/7.48912) = -0.0374 \\
 \text{Sspline} &= -0.09066 - 0.15563 \cdot (53/100) + 0.86763 \cdot (53/100)^2 - 0.37122 \cdot (53/100)^4 + \\
 &\quad 0.00017 \cdot \cos(53/3.78510) + 0.00635 \cdot \cos(53/8.89271) = 0.0473 \\
 M = \text{FVC predicted} &= \exp(-11.0710 + 2.3722 \cdot \ln(175) + 0.1040 \cdot \ln(53) + 0.0686 - 0.0167 \cdot \ln(53) \\
 &\quad - 0.0374) = \mathbf{4.753 \text{ L}} \\
 \% \text{ predicted} &= (3.250/4.753) \cdot 100 = \mathbf{68.4\%} \\
 S &= \exp(-2.2163 + 0.0486 \cdot \ln(53) + 0.0473) = 0.1386 \\
 L &= 0.9345 \\
 \text{LLN} &= \exp(\ln(1 - 1.645 \cdot L \cdot S) / L + \ln(M)) \\
 &= \exp(\ln(1 - 1.645 \cdot 0.9345 \cdot 0.1386) / 0.9345 + \ln(4.753)) = \mathbf{3.678 \text{ L}} \\
 \text{Z-score} &= ((\text{measured}/\text{predicted})^L - 1) / (L \cdot S) \\
 &= ((3.250/4.753)^{0.9345} - 1) / (0.9345 \cdot 0.1386) = \mathbf{-2.31}
 \end{aligned}$$

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