Worked Example for SI units

Male 30 years old, 178cm, TLCO = 7.7 SI units
Mspline = 0.101788 Sspline = -0.11049

$M = \exp(-8.758548 + 2.151173 \cdot \ln(\text{height}) - 0.027927 \cdot \ln(\text{age}) + \text{Mspline})$
$M = \exp(-8.758548 + 2.151173 \cdot \ln(178) - 0.027927 \cdot \ln(30) + 0.101788)$
$M = 10.970$

$S = \exp(-1.98249 + 0.03430 \cdot \ln(\text{age}) + \text{Sspline})$
$S = \exp(-1.98249 + 0.03430 \cdot \ln(30) - 0.11049)$
$S = 0.139$

$L = 0.38713$

% predicted = (measured/M) ·100
% predicted = (7.7/10.970) ·100
% predicted = 70.191

Lower limit of Normal (LLN) (5th percentile) = $\exp(\ln(M) + \ln(1 - 1.645 \cdot L \cdot S)/L)$
Lower limit of Normal (LLN) (5th percentile) = $\exp(\ln(10.970) + \ln(1 - 1.645 \cdot 0.38713 \cdot 0.139)/0.38713)$
Lower limit of Normal (LLN) (5th percentile) = 8.634

Z-score = $((\text{measured}/M)^{L} - 1)/(L \cdot S)$
Z-score = $((7.7/10.970)^{0.38713} - 1)/(0.38713 \cdot 0.139)$
Z-score = -2.3796

Methodological Differences

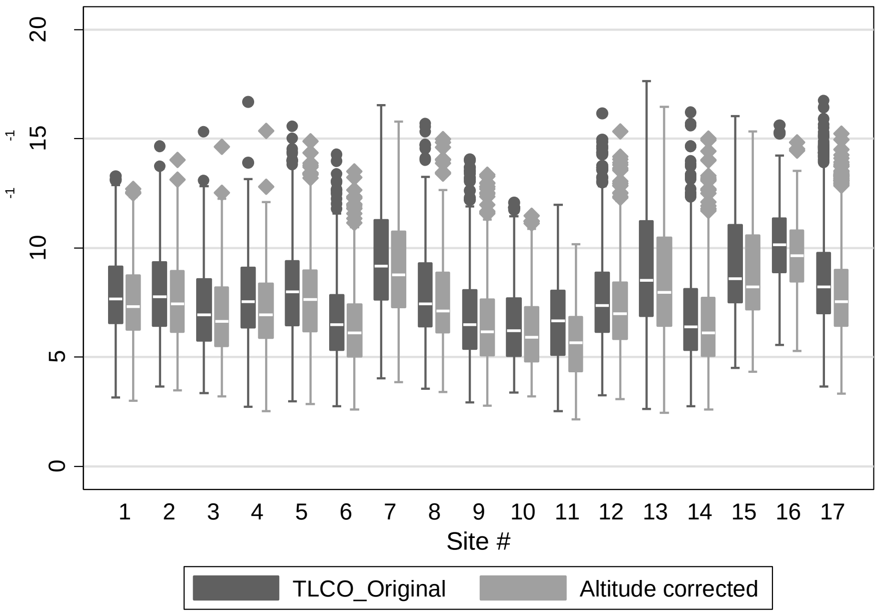

Figure S1. Absolute difference in *T*LCO values prior to, and after correction for partial pressure of oxygen, using centre altitude as a proxy.

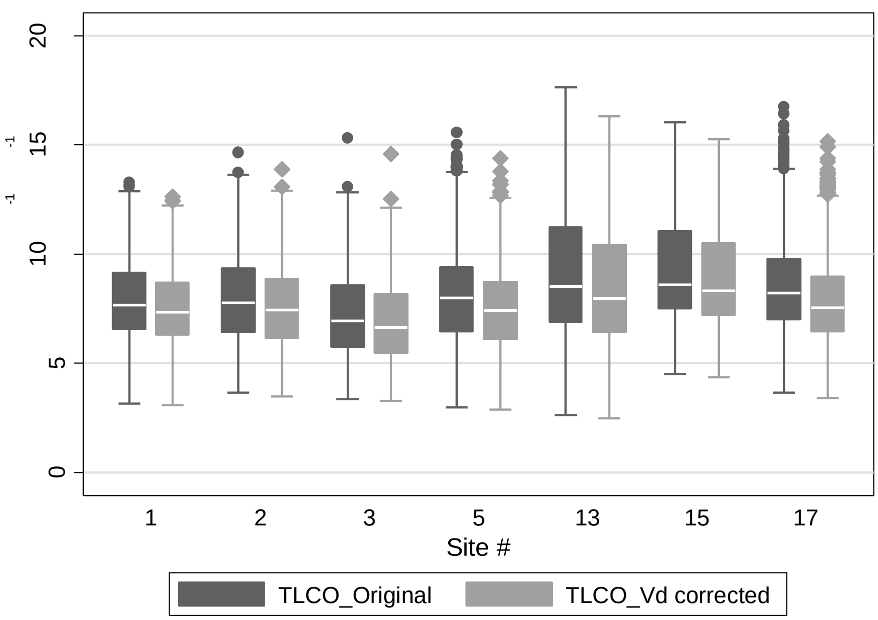

Figure S2. Absolute difference in *T*LCO values prior to, and after correction for anatomic dead space (Vd)

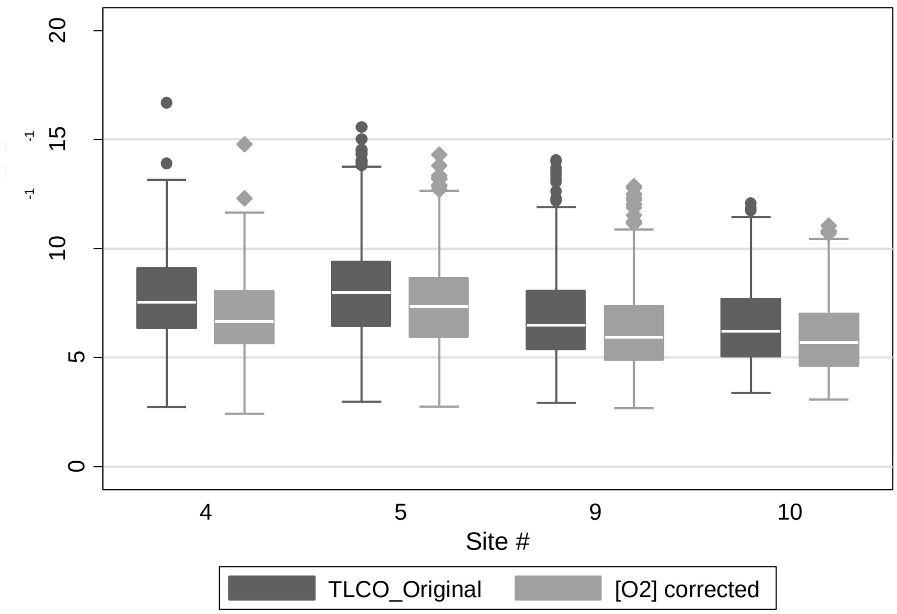

Figure S3. Absolute difference in *T*LCO values prior to, and after corrected for gas concentration.

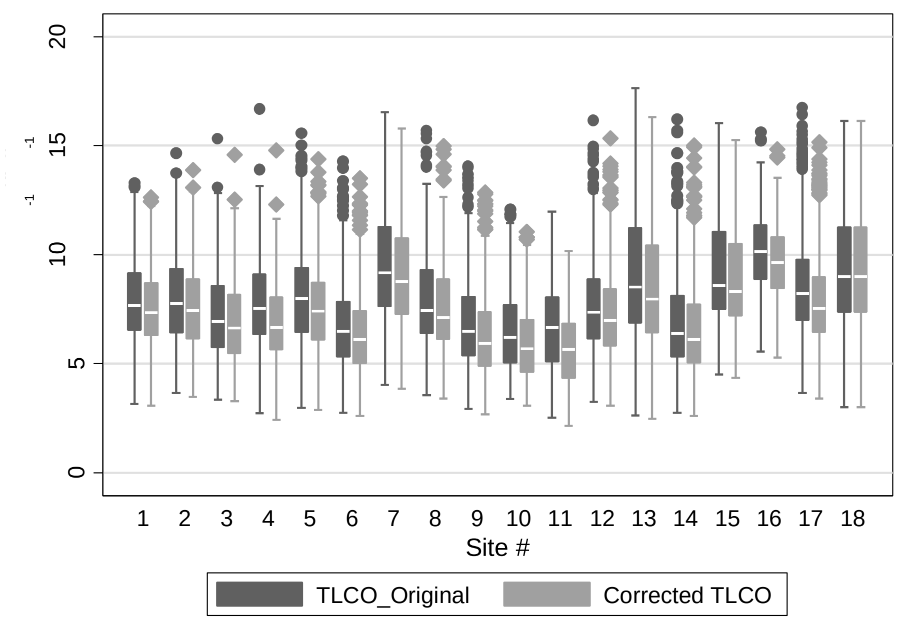

Figure S4. Absolute differences in *T*LCO values prior to, and after correction for anatomic dead space, gas concentration, and partial pressure of oxygen.

Study Population

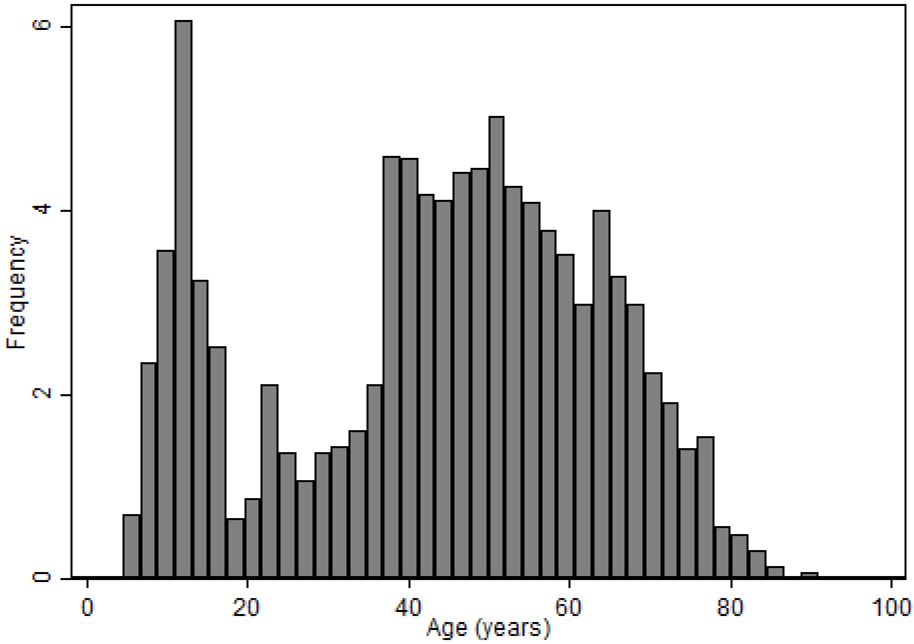

Figure S5: Age distribution of study population (median 45 years; inter-quarter range 26 to 57)

Details regarding the correction for anatomical dead space

The dead space, V_D, is composed of the equipment dead space ($V_{D,equip}$) plus the anatomic dead space ($V_{D,an}$):

$V_D = V_{D,equip} + V_{D,an}$

The equipment dead space, which includes the filter, is fixed and is reported by the equipment manufacturer.

The alveolar volume, V_A, is calculated from the inspired volume of test gas, V_I, minus the dead space times the inspired tracer gas fractional concentration (F_{ITr}) divided by the tracer gas fractional concentration in the exhaled gas (F_{ETr}) :

$V_A = (V_I – V_D) * F_{ITr} / F_{ETr}$ (1)

To calculate T_{LCO}, V_A is converted to STPD and multiplied by the logarithmic decay in CO divided by time and divided by barometric pressure. However, T_{LCO} is directly proportional to V_A so that any percent change in V_A translates to an equal percent change in $T_{L,CO}$.

Some systems use a fixed anatomic dead space ($V_{D,an,fixed}$) of 150 mL since this is an option specified in the 2005 ATS/ERS standards.(1)

The anatomic dead space in mL can be estimated ($V_{D,an,est}$) in subjects with BMI ≤ 30 kg/m^2 as 2.2 mL/kg(2) and in subjects with BMI > 30 kg/m^2 as height^2/189.4.(1)

In order to adjust T_{LCO}, it must be recalculated using an estimated anatomic dead space in place of a fixed anatomic dead space.

If V_I and $V_{D,equip}$ are known, then T_{LCO} can be recalculated relatively simply by dividing by (V_I-$V_{D,equip}$- $V_{D,an,fixed}$) and multiplying by (V_I-$V_{D,equip}$ - $V_{D,annest}$):

$T_{LCO}' = T_{LCO} * (V_I - V_{D,equip} - V_{D,an,est})/(V_I - V_{D,equip} - V_{D,an,fixed})$ (2)

Where V_I was not available, we assumed V_I = FVC. Although V_I usually tends to be larger than FVC because of dynamic gas trapping, the amount of error in the adjusted T_{LCO} introduced by using FVC instead of V_I will usually be less than 0.1%.

The change in T_{LCO} calculated using a fixed anatomic dead space and adjusted to an estimated anatomic dead space is typically 6% for a 20 kg child and -2% for a 100 kg adult.

References

1. Macintyre N, Crapo RO, Viegi G, Johnson DC, van der Grinten CP, Brusasco V, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. Eur Respir J. 2005;26(4):720-35.
2. Cotes JE. Lung Function. 5th ed. London: Blackwell Scientific Publication; 1993.