

Online appendix 1: Handling of HbA_{1c} < 4% NGSP

As described in the main text, the HemoCue HbA_{1c} 501 censored HbA_{1c} results < 4% NGSP (20 mmol/mol), and a numerical value had to be assigned to these results before they could be included in analyses.

When assigning a fixed value to measurements < LOQ (limit of quantitation), one of the common approaches¹ is to use $x = \frac{LOQ}{\sqrt{2}}$. Implicitly, this approach assumes that data below the LOQ follow a triangular distribution between zero and LOQ.¹ However, we deemed this an invalid assumption in the case of our data, as an HbA_{1c} of 0% NGSP is most likely incompatible with life.

3% NGSP (9 mmol/mol) is equivalent to an estimated average glucose of 2.2 mmol/l,² so we considered it the lower limit of the physiological range (LLPR) for HbA_{1c}. We assumed that HbA_{1c} values < LOQ followed a triangular distribution between LLPR and LOQ, as shown schematically in Figure A.

Figure A: Schematic presentation of the distribution of HbA_{1c} values, including values < LOQ

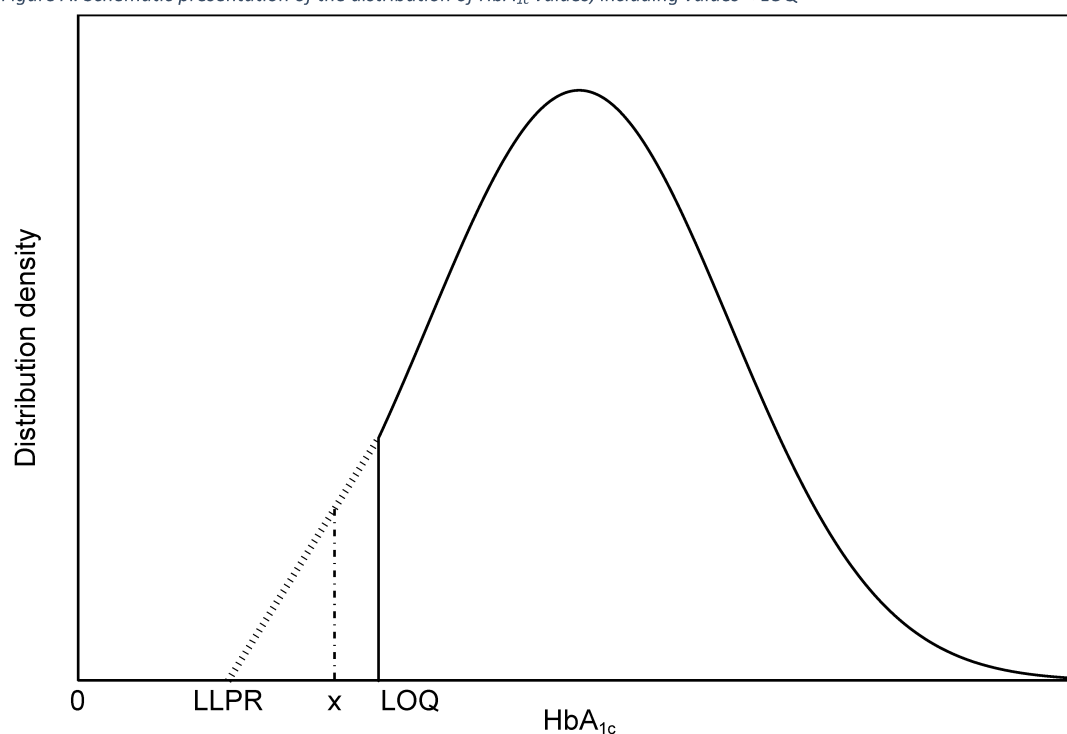


Figure is not to scale.

In the terminology of Figure A, we want to replace all results < LOQ with x , where x is the value of HbA_{1c} that results in the triangle from LLPR to x having half the area of the triangle from LLPR to LOQ.¹ If the slopes of the hypotenuses are called b , this can be written as

Equation A

$$\frac{1}{2} \times \left(\frac{1}{2} \times b \times (LOQ - LLPR)^2 \right) = \left(\frac{1}{2} \times b \times (x - LLPR)^2 \right)$$

By simple algebra, this can be rearranged to

Equation B

$$x = LLPR + \frac{LOQ - LLPR}{\sqrt{2}}$$

The numerical value of x can then be calculated as $x = 3.71\%$ NGSP or $x = 16.8 \text{ mmol/mol}$, which was the value we assigned to all measurements < LOQ.

References for this appendix

- 1 Hornung RW, Reed LD. Estimation of average concentration in the presence of nondetectable values. *Applied occupational and environmental hygiene* 1990;5:46-51.
- 2 NGSP (National Glycohemoglobin Standardization Program). Convert between NGSP, IFCC and eAG. <http://www.ngsp.org/convert1.asp>; accessed 2020-01-14.