

# Harmonising Reference Intervals in Haematology

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# Reference Ranges & What They Mean



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*For basic rules that can help you to make sense of your results, see [Reading your results](#).*

The interpretation of any clinical laboratory test involves comparing the patient's results with the test's "reference range".

The first step in determining a reference range is to define the population to which the range will apply. A large number of individuals from a group who are thought to represent a "normal" population, will be tested for a particular laboratory test. The reference range is then derived mathematically by taking the average value for the group and allowing for natural variation around that value (plus or minus 2 standard deviations from the average). In this way, ranges quoted by labs will represent the values found in 95% of individuals in the chosen 'reference' group. In other words, even in a "normal" population, a test result will lie outside the reference range in 5% of cases (1 in 20). This is why the term "reference range" is preferred over "normal range".

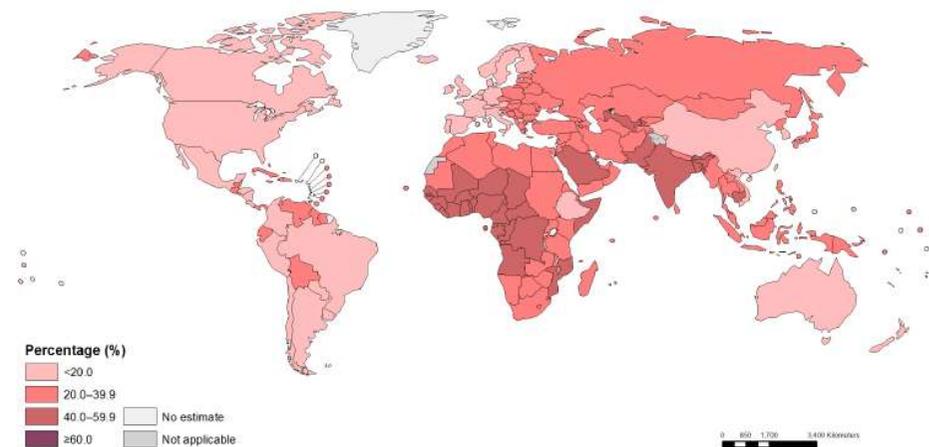
When you examine test results from different populations, you quickly discover that what is "normal" for one group is not necessarily normal for another group. Indeed for tests such as cholesterol the idea of a normal range has been replaced to a large extent by use of target values, achieved either by lifestyle changes or active treatment.

*Whether or not your test result is within the laboratory reference range, the result must be considered within the context of your personal*

# Factors affecting FBC parameters

- Impact of
  - Genetic factors
    - Gender, Ethnicity, Thalassaemia
  - Physiological factors
    - Age, Pregnancy, Diurnal variation
  - Environmental factors
    - Smoking, Altitude
- Consequences for global health economies
  - Thresholds for therapy or investigation

Global estimates of the prevalence of anaemia, all women of reproductive age, 15–49 years, 2011



Source: WHO. The global anaemia prevalence in 2011. Geneva: World Health Organization; 2015.



Reference Ranges & What They | X Anaemia: A disease or symptom | X getpdf.php | X A multicentre study of reference | X A multicentre study of reference | X

tanfonline.com/doi/abs/10.1080/003655104100027977?journalCode=icb20

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Scandinavian Journal of Clinical and Laboratory Investigation  
Volume 64, 2004 - Issue 4

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Article  
**A multicentre study of reference intervals for haemoglobin, basic blood cell counts and erythrocyte indices in the adult population of the Nordic countries**  
G. Nordin, A. Mårtensson, R. Swolin, S. Sandberg, N. J. Christensen, V. Thorsteinsson  
Pages 385-398 | Received 22 Apr 2004, Accepted 03 May 2004, Published online: 08 Jul 2009  
Download citation <https://doi.org/10.1080/00365510410002797>

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### Abstract

Eight haematological quantities were measured in EDTA anticoagulated venous blood specimens collected from 1826 healthy male and female individuals between 18 and 90 years of age in the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden). The samples, collected between November 1999 and November 2001 as part of the Nordic Reference Interval Project (NORIP), were analysed on 12 different types of modern automated haematology instruments currently in use among the 60 laboratories participating in the study. Non-parametric reference intervals (between 2.5 and 97.5 percentiles) have been calculated for B-Haemoglobin (females 117-153 g/l, males 134-170 g/l), R-Erythrocytes (females 3.94-5.16 x 10<sup>12</sup>/l, males

**International Journal of Laboratory Hematology**

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ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF LABORATORY HEMATOLOGY

## Recommendation for standardization of haematology reporting units used in the extended blood count

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### RESEARCH ARTICLE

## Complete blood count reference intervals from a healthy adult urban population in Kenya

Geoffrey Omuse<sup>1,2\*</sup>, Daniel Maina<sup>1</sup>, Jane Mwangi<sup>3</sup>, Caroline Wambua<sup>3</sup>, Kiran Radia<sup>3</sup>, Alice Kanyua<sup>4</sup>, Elizabeth Kagotho<sup>1</sup>, Mariza Hoffman<sup>2</sup>, Peter Ojwang<sup>5</sup>, Zui Premji<sup>6</sup>, Kiyoshi Ichihara<sup>7</sup>, Rajiv Erasmus<sup>2</sup>

1 Department of Pathology, Aga Khan University Hospital Nairobi, Nairobi, Kenya, 2 Division of Chemical Pathology, Department of Pathology, Stellenbosch University, Cape Town, South Africa, 3 PathCare Kenya Limited, Nairobi, Kenya, 4 Karen Hospital, Nairobi, Kenya, 5 Department of Pathology, Maseno University, Maseno, Kenya, 6 Formerly of Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania, 7 Faculty of Health Sciences, Yamaguchi University Graduate School of Medicine, Ube, Japan

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### Abstract



# A quick internet search on Hb reference intervals for women

- WHO – defines anaemia as less than 120 g/L
- NCBI – 120 to 160 g/L
- Mayo clinic – 116 to 150 g/L
- Various UK health trusts:
  - 115 to 165 g/L
  - 115 to 155 g/L
  - 120 to 150 g/L



# Haematology WG Terms of Reference

## Project 2: Reference Intervals in Haematology

### **Online Survey to establish:**

- The source of reference ranges in use (laboratory data, healthy volunteer samples, manufacturers' information sheets, published guidelines, text books)
- Are there national guidelines in place in the country / region
- The ranges for the following analytes: WBC, RBC, Hb, Hct, MCV, MCH, Platelet count, neutrophil count and lymphocyte count.
- The units of measurement used. SI Units are preferred and will be used for recommendations.
- Are there different ranges for different patient demographics (Ranges will be requested according to age, gender, ethnic origin and whether the patient is pregnant or not. The definition of ethnicity will be taken from published information, e.g. any WHO definitions).
- Method for determining reference interval



Establish the range and number of haematology  
analysers registered



Establish the range and number of haematology  
analysers registered



Establish how the laboratories establish their  
reference intervals



Comment

## Revisiting WHO haemoglobin thresholds to define anaemia in clinical medicine and public health

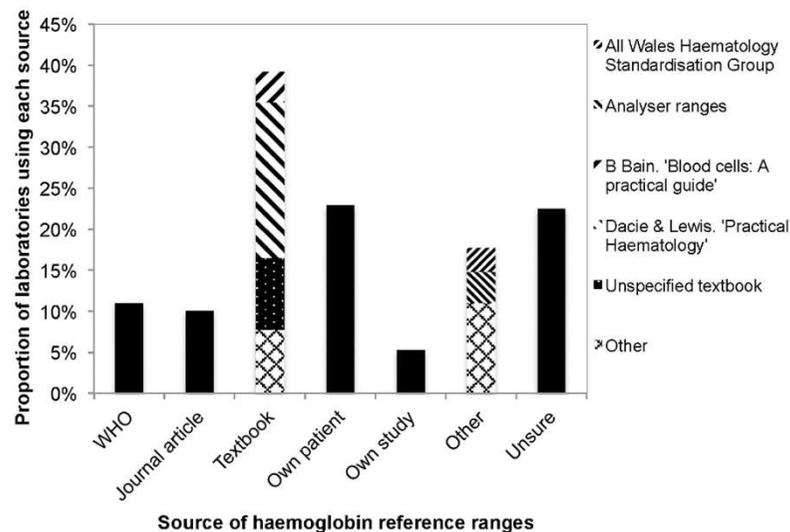


Anaemia exists when circulating red blood cells are insufficient to meet physiological needs. Anaemia is conventionally identified when specific and nutrition-sensitive interventions are predicated on the prevalence of anaemia. Reduction of anaemia might also indicate success of infection control

Pasricha S-R. [www.thelancet.com/haematology](http://www.thelancet.com/haematology) Vol 5 Feb 2018

WHO Hb thresholds defined 1968  
Epidemiological methods less developed  
Consensus on thresholds limited

### a) Source of ranges used by laboratories



Colman, K.S., *et al*, 2018. Heterogeneous hemoglobin lower thresholds in clinical laboratories. *American journal of hematology*



Establish the range and number of haematology analysers registered



Establish how the laboratories establish their reference intervals



Establish the ranges in use



Reference intervals  
Questionnaire to EQALM  
members' participants

Survey drafted in an  
online platform for  
distribution through the  
EQALM office

- Are there national reference intervals?
  - Give details
- How did you derive your range?:
  - WHO
  - CLSI or other publication
  - Own data
  - Manufacturer's literature
  - Other literature
  - Unknown



Reference intervals  
Questionnaire to EQALM  
members' participants

- How frequently are reference ranges checked / validated?
- When did you last validate your reference ranges?
- Do you include UoM when deriving your reference range?
- Do you use a harmonised reference range (laboratory / network / region etc.)?



Reference intervals  
Questionnaire to EQALM  
members' participants

- Do you have different ranges for according to?:
  - Age
  - M / F / Transgender
  - Physiology, e.g., pregnancy
  - Ethnicity
  - Altitude
  - Etc.
- Reference range data to be gathered for each situation



Reference intervals  
Questionnaire to EQALM  
members' participants

- Do you have critical results action limits in addition to reference ranges?
- What do you do if you receive a sample from a patient that you do not have a suitable reference range for?
- Do you have any instrument-specific parameter reference ranges?
  - How were these validated?
  - Do you report the results clinically?



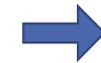
Establish the range and number of haematology  
analysers registered



Establish how the laboratories establish their  
reference intervals



Establish the ranges in use



Publish  
recommendations?



# Pathology Harmony; a pragmatic and scientific approach to unfounded variation in the clinical laboratory

**Jonathan Berg and Vanessa Lane**

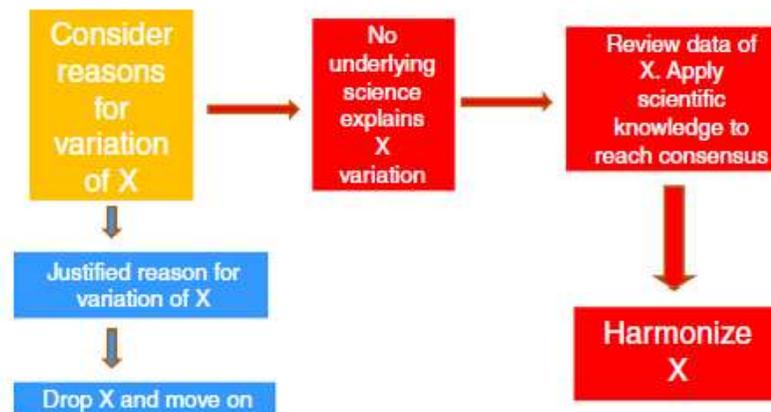
Clinical Biochemistry Department, Sandwell and West Birmingham Hospitals NHS Trust, City Hospital, Birmingham B18 7QH, UK  
Corresponding author: Jonathan Berg. Email: jonathanberg@nhs.net

*Annals of Clinical Biochemistry* 2011; 48: 195–197

Phases I (2007) and II (2009):  
Clinical Chemistry analytes

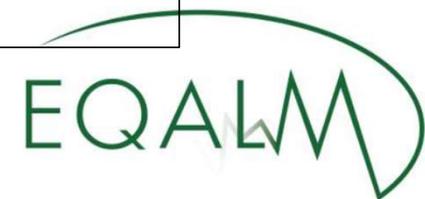
Supported by  
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Phase III (2011): Haematology



Pathology harmony moves on: progress on implementation in haematology  
De la Salle, 2012. BJH, 158 (6): 804-805.

FBC Units only



Establish the range and number of haematology  
analysers registered



Establish how the laboratories establish their reference  
intervals



Establish the ranges in use



Review, compare and map data



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