Establishing Clinical Laboratory Reference Intervals in Africa



A Cross Sectional, Observational Study in Healthy Adults at Multiple African Research Centers

International AIDS Vaccine Initiative

IAVI's mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world.

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iavi International AIDS Vaccine Initiative

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Table of Contents *(click on any title below to jump directly to that section)*

List of Figures

List of Figures *continued*

List of Figures *continued*

List of Tables

List of Tables *continued*

List of Abbreviations and Terms

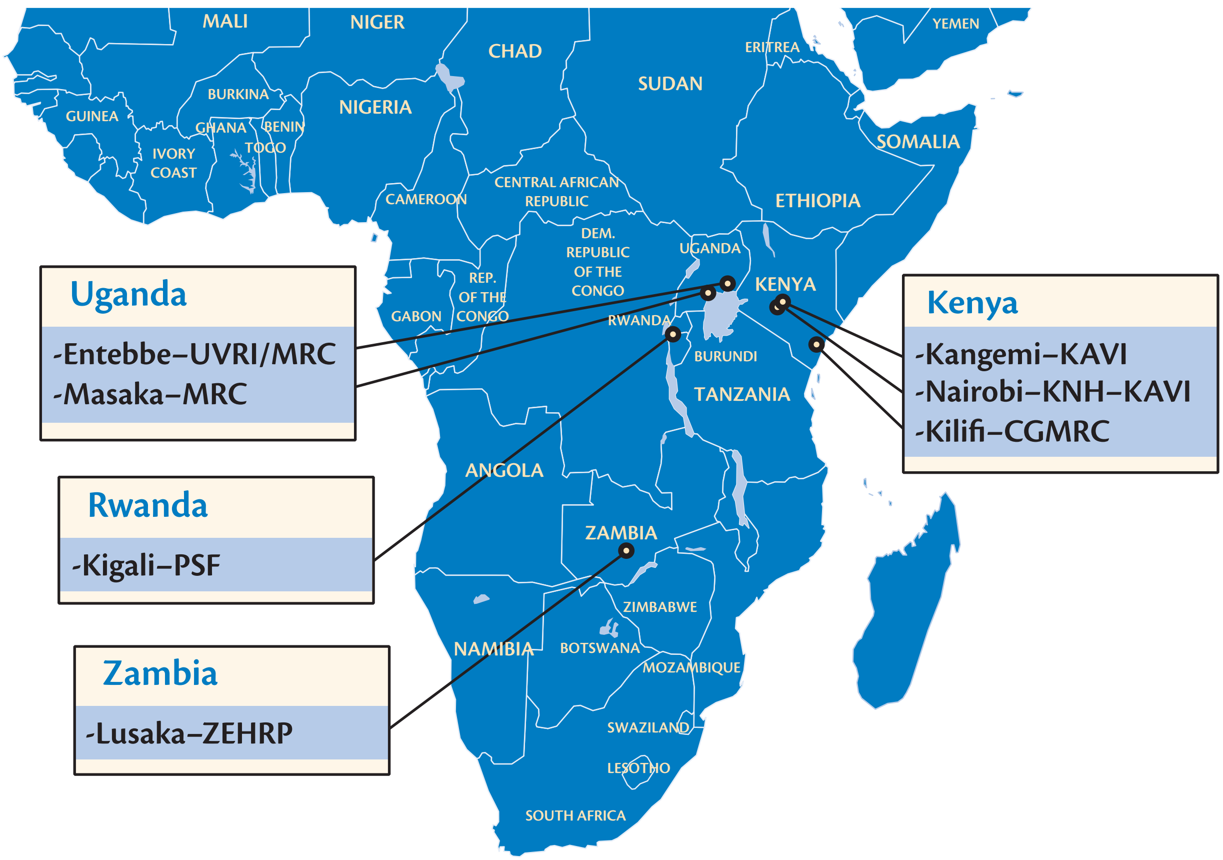
AE: adverse event
ALP: alkaline phosphatase
ALT: alanine aminotransferase (synonymous with SGPT)
AMP: amino methyl propanol
ANOVA: analysis of variance
AST: aspartate aminotransferase (synonymous with SGOT)
CGMRC: Centre for Geographic Medicine-Coast
CLSI: Clinical and Laboratory Standards Institute
CPK: creatine phosphokinase
DAIDS: United States Division of Acquired Immune Deficiency Syndrome
DEA: diethanlamine
dL: deciliter
DGKL: Deutsche Vereinte Gessellschaft für Klinische Chemie und Laboratoriumsmedizin/German Society for Clinical Chemistry and Laboratory Medicine
ELISA: enzyme linked immunosorbent assay
F: female
g: gram
Hb: hemoglobin
HBsAg: hepatitis B surface antigen
HCT: hematocrit
HCV: hepatitis C virus
HIV: human immunodeficiency virus
IAVI: International AIDS Vaccine Initiative
IFCC: International Federation of Clinical Chemistry
IgG: immunoglobulin gamma
ISC: Innovation in Sustainable Chemistry
ISCC: International Symposium on Clinical Chemistry
IU: international units
KAVI: Kenya AIDS Vaccine Initiative
KNH: Kenyatta National Hospital
L: liter
LDH: lactate dehydrogenase
M: male
MCV: mean corpuscular volume
MGH: Massachusetts General Hospital
mg: milligram
MRC: Medical Research Council
µL: microliter
µmol : micromole
NAC: N-Acetyl-L-Cysteine
NCCLS: National Committee for Clinical Laboratory Standards
OOR: out of range
P-L: pyruvate to lactate
PNP: p-Nitrophenol
PSF: Projet San Francisco
RBC: red blood cells
RPR: rapid plasma reagen
SFBC: Société Française de Biologie Clinique (French Society of Clinical Biology)
SD: standard deviation
SGOT: serum glutamic-oxaloacetic transaminase (synonymous with AST)
SGPT: serum glutamate pyruvate transaminase (synonymous with ALT)
US: United States of America
UVRI: Uganda Virus Research Institute
VCT: voluntary counseling and testing (for HIV infection)
WBC: white blood cells
ZEHRP: Zambia Emory HIV Research Project

1. METHODS

1.1. Study Volunteers and Collaborating Institutions

Clinically healthy adult (18-60 years) male and female volunteers were enrolled across seven research centers in four countries in Eastern and Southern Africa (Figure 1). All potential volunteers had received HIV voluntary counseling and testing (VCT) and had negative HIV tests within three months prior to screening for this study. Target enrollments for all institutions were 200 or 400 volunteers, depending on capacity, with equal numbers of men and women by design. Eligibility criteria for this study were similar to those used for HIV vaccine clinical trials and source populations were selected as described below.

Figure 1: Map of study centers



Masaka-Medical Research Council (MRC), Uganda: Eligible volunteers were selected from a rural general population cohort enrolled into prospective HIV incidence studies in preparation for HIV vaccine trials.

Entebbe-Uganda Virus Research Institute (UVRI)/MRC, Uganda: Volunteers for this study were drawn from community members who: 1) had expressed interest to participate in future clinical trials, or 2) were prescreened for a previous HIV vaccine Phase I clinical trial and were not enrolled because the trial had completed enrollment.

Kilifi-Centre for Geographic Medicine Research-Coast (CGMRC), Kenya: Half of this institution's study volunteers were drawn from an HIV prevalence study in Kilifi Town, and half were selected from at-risk individuals who were enrolled in HIV incidence studies in preparation for HIV vaccine trials.

Kangemi-Kenya AIDS Vaccine Initiative (KAVI), Kenya: Volunteers were drawn from an HIV prevalence study conducted in this peri-urban district in western Nairobi in preparation for HIV incidence studies.

Nairobi-Kenyatta National Hospital (KNH) KAVI, Kenya: The majority of volunteers from this teaching hospital in Nairobi included medical students, staff, and professionals from the KNH medical school and hospital facility. Community members not affiliated with the facility were also enrolled.

Lusaka-Zambia Emory HIV Research Program (ZEHRP), Zambia and Kigali-Projet San Francisco (PSF), Rwanda: Half of the volunteers from these two institutions were drawn from large prospective studies of long-term, stable, sexually active couples of HIV discordant status (the volunteer's partner was HIV-infected), and half were drawn from couples identified during couples' VCT as concordant HIV-negative (both partners HIV uninfected).

1.2. Study Procedures

This study was approved by the Institutional Ethics Committees or Institutional Review Boards at each participating institution, namely the National Ethics Committee of Rwanda, the UVRI Science and Ethics Committee, the Uganda National Council for Science and Technology, the Kenya Medical Research Institute, KNH Ethics and Research Committee, the University of Zambia Research Ethics Committee, and the Emory University School of Public Health Ethics Committee.

Each interested potential volunteer was administered a brief screening questionnaire and a symptom-directed examination prior to enrollment. Volunteers were screened out based on significant medical history including current clinical symptoms, immunosuppressive or corticosteroid medication, chemotherapy, hospitalizations, surgery, or blood transfusions in the six months prior to screening. Volunteers with splenomegaly (Grade 2+ by Hackett's classification) were excluded. Menstruating women were asked to return in two weeks, and women who reported being pregnant were not enrolled. Breastfeeding was not an exclusion factor. No information was collected from volunteers who were screened out prior to enrollment except age, gender, and reason for ineligibility.

Following screening, written informed consent was obtained from all eligible volunteers. The consent process included an explanation and discussion of the study procedures, followed by an assessment of the potential volunteer's understanding of the study. Literacy was not a requirement to participate, and illiterate volunteers were consented with an independent third party present to confirm volunteer understanding of the consent process and study procedures. Only those volunteers who could demonstrate a satisfactory understanding following the consenting process were enrolled.

After enrollment, a detailed medical history including reproductive history for women, data on contraception use, investigation of current medications and demographics (socioeconomic status, education, environmental exposures, smoking, and drug and alcohol consumption) were collected from each enrolled volunteer. A physical examination was performed including evaluation of vital signs, weight, and height. Blood was drawn for HIV, syphilis and hepatitis C serology, hepatitis B antigen, hematology (complete blood count and five-part differential), clinical chemistry (aspartate aminotransferase (AST), alanine aminotransferase (ALT), total and direct bilirubin, albumin, total immunoglobulin, creatinine, amylase, creatinine phosphokinase, lactate dehydrogenase (LDH), alkaline phosphatase (ALP), and total protein), and CD4/CD8 T cell count. The assays used for disease screening are shown in Table 1. The majority of analyte methodologies were done as per the manufacturer's instructions; where two or more methods existed, our selections are clarified in Table 2.

The HIV testing algorithm at most research institutions used two concurrent rapid HIV tests followed by a confirmatory enzyme linked immunosorbent assay (ELISA) if either rapid test was positive, except in Uganda (Musaka and Entebbe), where all positive rapid tests were confirmed by two ELISA, with a Western blot done for indeterminate ELISA results. Urinalysis was performed, and urine pregnancy tests performed in women. If needed treatment was not available on-site, volunteers were referred for appropriate care. Enrolled volunteers were excluded from subsequent analysis if the laboratory tests revealed that they were pregnant, positive for HIV-1, HIV-2, hepatitis B surface antigen (HBsAg), antibodies against hepatitis C or rapid plasma reagen (RPR) (suspected syphilis).

Table 1: Summary of laboratory analyte methods

Research Center	Hepatitis B	Hepatitis C	HIV	Pregnancy	Syphilis
Kilifi-CGMRC	Hepanostika HBsAg Uni-Form II MicroELISA system (Biomerieux)	Innotest HCV Ab IV (Innogenetics)	Rapid HIV 1/2 Determine (Abbott), Rapid HIV 1/2 Uni-Gold (Trinity Biotech), discrepant results sent for confirmation at KNH-KAVI	ßhCG reagent strips (Bayer Multistix 10SG)	Macro-Vue RPR Test (Becton Dickinson) with TPHA confirmation
KNH-KAVI	Hepanostika HBsAg Uni-Form II MicroELISA system (Biomerieux)	Innotest HCV Ab IV (Innogenetics)	Rapid HIV 1/2 Determine (Abbott), Rapid HIV 1/2 Uni-Gold (Trinity Biotech), HIV 1/2 ELISA Vironostika Uni-Form II Ag/Ab (Biomerieux), Detect-HIV ELISA (Adaltis, Inc)	ßhCG reagent strips (Bayer Multistix 10SG), Hexagon hCG 1-Step	RPR Test (Forest Diagnostics Ltd)
Kangemi-KAVI	Hepanostika HBsAg Uni-Form II MicroELISA system (Biomerieux)	Innotest HCV Ab IV (Innogenetics)	Rapid HIV 1/2 Determine (Abbott), Rapid HIV 1/2 Uni-Gold (Trinity Biotech), discrepant results sent for confirmation at KNH-KAVI	ßhCG reagent strips (Bayer Multistix 10SG), Hexagon hCG 1-Step	RPR Test (Forest Diagnostics Ltd)
Entebbe-UVRI	Hepanostika HBsAg Uni-Form II MicroELISA system (Biomerieux)	Innotest HCV Ab IV (Innogenetics)	Rapid HIV 1/2 Determine (Abbott), HIV 1/2 ELISA Vironostika Uni-Form II Ag/ Ab (Biomerieux), Murex HIV-1.2.0 ELISA (Abbott), Cambridge Biotech HIV-1 Western Blot Kit (Calypte biomedical),	Hexagon hCG 1-Step	RPR Test (Biotec)
Masaka-MRC	Hepanostika HBsAg Uni-Form II MicroELISA system (Biomerieux)	Innotest HCV Ab IV (Innogenetics)	Rapid HIV 1/2 Determine (Abbott), HIV 1/2 ELISA Vironostika Uni-Form II Ag/ Ab (Biomerieux), Murex HIV-1.2.0 ELISA (Abbott), HIV-1 Western Blot Kit (Calypte biomedical)	ßhCG reagent strips (Bayer Multistix 10SG), Hexagon hCG 1-Step, Cypress Diagnostics hCG slide	RPR Test (Biotec)
Kigali-PSF	HBsAG ELISA (Abbot-Murex version 3)	Anti-HCV (Abbot-Murex version 4)	Rapid HIV 1/2 Determine (Abbott), Rapid HIV 1/2 Capillus (Trinity Biotech), HIV 1/2 ELISA Vironostika Uni-Form II Ag/Ab (Biomerieux)	ßhCG reagent strips (Bayer Multistix 10SG), Cypress-hCG Dipstrip	RPR Carbon (Spinreact)
Lusaka-ZEHRP	HBsAG ELISA (Abbot-Murex version 3)	Anti-HCV (Abbot-Murex version 4)	Rapid HIV 1/2 Determine (Abbott), Rapid HIV 1/2 Capillus (Trinity Biotech), Murex HIV-1.2.0 ELISA (Abbott), HIV 1/2 ELISA Vironostika Uni-Form II Ag/Ab (Biomerieux)	ßhCG reagent strips (Bayer Multistix 10SG), Hexagon hCG 1-Step	RPR Antigen Suspension (Becton Dickinson)

Table 2: Laboratory assays used to evaluate health status of enrolled volunteers

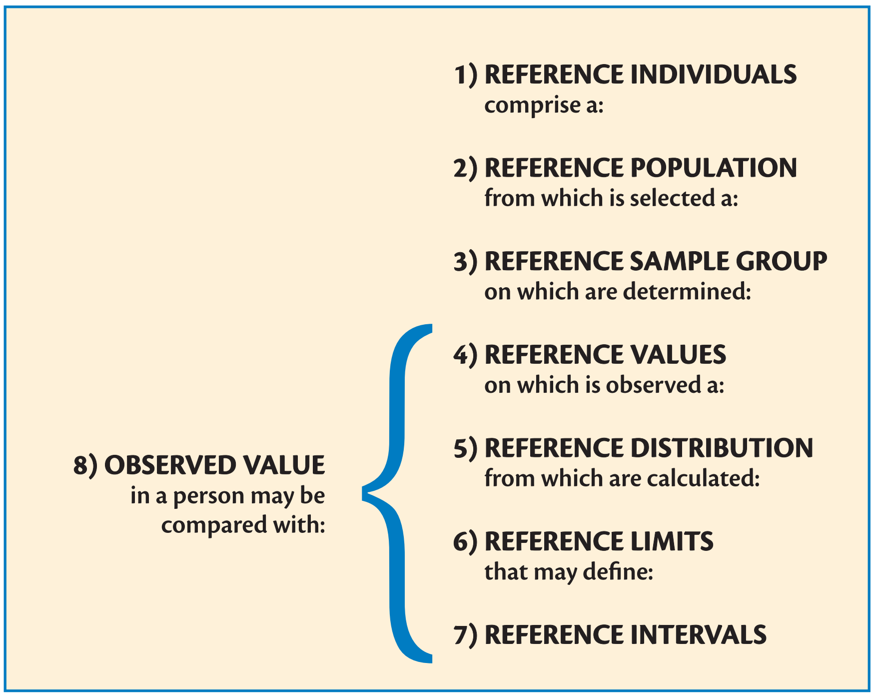
	KAVI (2 sites)	CGMRC	UVRI	MRC	PSF	ZEHRP
Hematology						
Analyzer	Beckman Coulter AcT 5 diff CP Hematology Analyzer (Beckman Coulter, USA)					
Hemoglobin	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Hematocrit	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
RBC	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
MCV	HCT/RBC × 100	HCT/RBC × 100	HCT/RBC × 100	HCT/RBC × 100	HCT/RBC × 100	HCT/RBC × 100
Platelets	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
WBC	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Neutrophils	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Lymphocytes	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Monocytes	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Eosinophils	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Basophils	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Immunology						
Analyzer	FACSCalibur*	FACSCount System (BD Biosciences, USA)				
CD4 T cell	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
CD8 T cell	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Chemistry						
Analyzer	Vitalab Selectra E Clinical Chemistry Analyzer (Vital Scientific, the Netherlands)					
Creatinine	Jaffe (uncompensated)	Jaffe (uncompensated)	Jaffe (uncompensated)	Jaffe (uncompensated)	Jaffe (uncompensated)	Jaffe (uncompensated)
AST (SGOT)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)
ALT (SGPT)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)	IFCC 37°C (-P5P)
Bilirubin Direct	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Bilirubin Total	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Albumin	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output
Total IgG	Immunoturbimetric	Immunoturbimetric	Immunoturbimetric	Immunoturbimetric	Immunoturbimetric	Immunoturbimetric
Amylase	PNP-G7 37°C (IFCC)	PNP-G7 37°C (IFCC)	PNP-G7 37°C (IFCC)	PNP-G7 37°C (IFCC)	PNP-G7 37°C (IFCC)	PNP-G7 37°C (IFCC)
CPK	NAC act. 37°C (IFCC)	NAC act. 37°C (IFCC)	NAC act. 37°C (IFCC)	NAC act. 37°C (IFCC)	NAC act. 37°C (IFCC)	NAC act. 37°C (IFCC)
LDH	DGKL (P-L 37°C)	DGKL (P-L 37°C)	DGKL (P-L 37°C)	DGKL (P-L 37°C)	DGKL (P-L 37°C)	DGKL (P-L 37°C)
ALP	PNP (DEA buffer) 37°C	PNP (AMP buffer) 37°C	PNP (DEA buffer) 37°C	PNP (DEA buffer) 37°C	PNP (AMP buffer) 37°C	PNP (AMP buffer) 37°C
Total Protein	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output	Analyzer output

* (BD Biosciences, USA) Analyzer output is as per manufacturer's instructions for the appropriate analyzer.

1.3. Reference Interval Generation

Data analyses were conducted using STATA (v9.1 College Park, TX, USA) and SAS (v9.1, Cary, NC, USA) software. The terms and guidelines set forth by the Clinical and Laboratory Standards Institute (CLSI, formerly the National Committee for Clinical Laboratory Standards, or NCCLS) for defining reference intervals (NCCLS, 2000) were followed (Figure 2).

Figure 2: CLSI term definitions and schematic



The CLSI procedure summarized below was performed separately for males and females to create consensus intervals. If the overall F-test from an analysis of variance (ANOVA) on mean values was statistically significant ($p<0.05$), a step-wise procedure was performed to evaluate which intervals may be combined into a "consensus reference interval." First, we compared the two most similar center intervals in terms of the p-values obtained from the overall ANOVA, which was adjusted for multiple comparisons using the Tukey method. If the intervals were not different according to the CLSI guidelines, the data were combined and the consensus interval compared with the remaining centers in a new ANOVA. A pairwise comparison was then made between the next most similar interval and the consensus interval, and the data were again combined if not significantly different. This last step was repeated until all remaining centers, if any, were significantly different from the consensus interval. Finally, the consensus intervals for men and women were compared as above, and the data were combined if differences were not statistically significant. For parameters that were not normally distributed, all ANOVA tests were performed after a log transformation and geometric means were compared instead of the arithmetic means. Reference intervals are shown as the interval between the 2.5th and 97.5th percentile, inclusive. As per the CLSI guidelines, we did not exclude outlier values from our healthy study population.

1.4. Comparison with US-Derived Values

US-derived laboratory intervals and the United States Division of Acquired Immune Deficiency Syndrome (DAIDS) adverse events (AE) grading table (DAIDS 2004) were used for comparison. DAIDS AE grading cutoffs for hematology are absolute, and therefore do not vary by population considered. For comparison and calculation of DAIDS chemistry grading criteria, we used values from the Massachusetts General Hospital (MGH) (Katz, et al. 2004), in addition to white blood cell (WBC) differential counts taken from Bakerman's ABCs of Interpretive Laboratory Data (Bakerman, et al 2002) and CD4 and CD8 T cell counts from the Becton Dickinson FACSCount package insert. Collectively, these are referred to as the "comparison intervals."

As the comparison intervals do not provide sample sizes or standard errors, no statistical comparisons with our data are made. Therefore, references to our results being higher or lower than comparison intervals are not confirmed by statistical test. We present the number and percent of volunteers in our study with out-of-range (OOR) values when compared to the comparison intervals. We also present the number and percent of volunteers who would have been considered as a grade one or higher AE when using the US-derived DAIDS AE grading criteria.

2. EXECUTIVE SUMMARY

2.1. Abstract

Clinical laboratory reference intervals have not been established in many African countries and non-local intervals are commonly used in clinical trials to screen and monitor AEs among African participants. Using laboratory reference intervals derived from other populations excludes potential trial volunteers in Africa and makes AE assessment challenging.

The objective of this study was to establish clinical laboratory reference intervals for 25 hematology, immunology, and biochemistry analytes among healthy African adults.

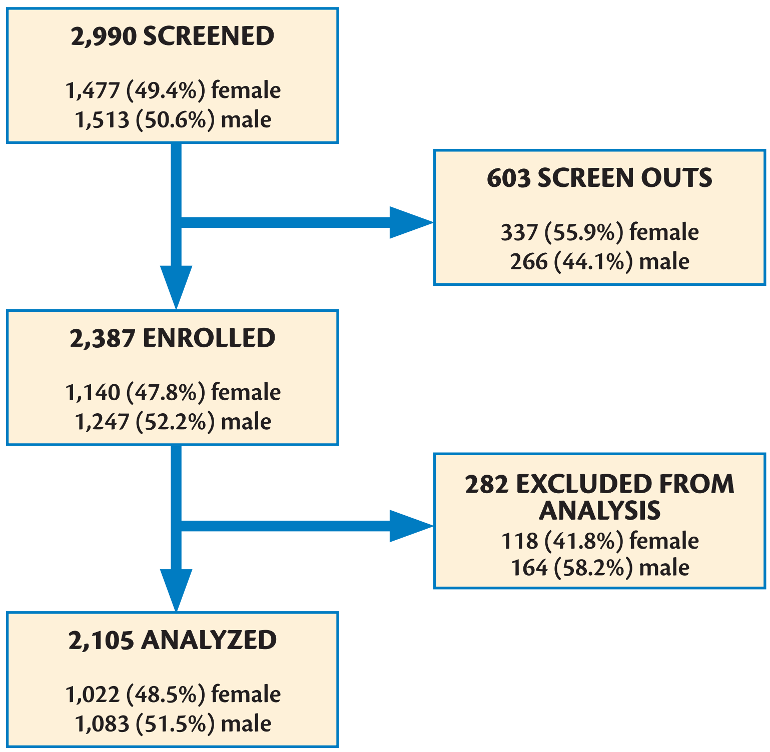
Equal proportions of men and women were invited to participate in a cross-sectional study at seven centers (Kigali, Rwanda; Masaka and Entebbe, Uganda; two centers in Nairobi and one in Kilifi, Kenya; and Lusaka, Zambia). All center laboratories used hematology, immunology, and biochemistry analyzers validated by an independent clinical laboratory. In all, 2,990 potential volunteers were screened, and 2,105 (1,083M, 1,022F) were included in the analysis (Figure 3). While some male and female and regional differences were observed, creating consensus intervals using the complete data was possible for 18 of the 25 analytes. Compared to reference intervals from the US, findings of the study included lower hematocrit (HCT) and hemoglobin (Hb) levels, particularly among women, lower WBC and neutrophil counts, and lower amylase. Both sexes showed elevated eosinophil counts, immunoglobulin G (IgG), total and direct bilirubin, lactate dehydrogenase (LDH) and creatine phosphokinase (CPK), the latter being more pronounced among women. When graded against US-derived DAIDS AE grading criteria, we observed 744 (35.3%) volunteers who would have been considered to have had grade one or higher results had they been in a clinical trial, including 314 (14.9%) with elevated total bilirubin, and 201 (9.6%) with low neutrophil counts. These otherwise healthy volunteers would typically be excluded or require special dispensation to participate in a clinical trial.

The findings of this study represent an important step towards guiding locally-appropriate clinical trial conduct and design and will help inform screening and AE reporting criteria for studies in these regions of Africa.

2.2. Screened, Enrolled, and Analyzed Reference Sample Group

Screening and enrollment began in December 2004 and ended in October 2006. A total of 2,990 individuals were screened across all collaborating institutions, 1,477 women (49.4%) and 1,513 men (50.6%). Approximately 20% of screened volunteers were not enrolled with a further 10% excluded following enrollment for a final reference sample group of 2,105 (Figure 3).

Figure 3: Study screening and enrollment schematic



More women were screened out than men (22.8% versus 17.6%, Fisher's exact 2-tailed test: $p<0.001$), and this was consistent (though not always statistically significant) across all collaborating institutions except Entebbe. Volunteers who were screened out tended to be older than enrolled volunteers (median age: 30 vs. 28 years, Wilcoxon 2-sample test: $p = 0.001$). The most common reasons for screen-outs prior to enrollment were splenomegaly (89/603, 14.8%), inability to demonstrate satisfactory comprehension during the informed consent process (75, 12.4%), hypertension (61, 10.1%), symptoms of upper respiratory infection (51, 8.5%), and menstruating women who did not return for re-screening (44, 7.3%). Some volunteers had more than one reason for exclusion. Most potential volunteers had been pre-screened for HIV; only three potential volunteers were found to be HIV-infected at screening.

Among enrolled volunteers, the prevalence of HBsAg was 4.4% (106/2,387) and of hepatitis C antibody was 4.0% (95/2,387), with significant variations across collaborating institutions. Dual hepatitis B and C infections were uncommon (n=4). Slightly more men than women were excluded from analysis (12.5% versus 9.4%, Fisher's exact 2-tailed test: $p=0.057$), due to a higher prevalence of HBsAg (5.5% vs 3.1%, $p=0.002$) and hepatitis C antibody (6.7% vs. 4.2%, $p=0.005$) in men. Fifty-five volunteers (2.3%) were RPR positive, and this did not vary by gender. After 27 self-reported pregnant women were screened out prior to enrollment, an additional 1.6% (18/1,140) enrolled women were excluded from analysis because they had positive urine pregnancy tests. The final sample of 2,105 volunteers was 48.5% women, 51.5% men. More detailed demographics are shown in Table 3. See Stevens et al. for additional data on the screening, enrollment, and analysis reference sample group (Stevens, 2008).

Table 3: Population characteristics of the reference sample group

	Total		Kigali, Rwanda		Kangemi, Kenya		Kenyatta National Hospital, Kenya		Entebbe, Uganda		Masaka, Uganda		Lusaka, Zambia		Kilifi, Kenya	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Total	2105		373		362		197		194		331		352		296	
Age																
Median	28		28		30		23		25		27		30		27	
Range	18-59		18-53		18-58		18-59		18-55		18-58		18-58		18-55	
Body Mass Index																
Median	21.2		21.1		21.6		21.4		21.8		21.0		20.4		21.5	
95 %ile	17.3-31.3		17.3-29.6		16.6-32.7		17.0-34.8		18.5-30.5		18.0-28.6		17.0-31.5		16.9-31.2	
Gender																
Male	1083	51.4	185	49.6	186	51.4	98	49.7	96	49.5	183	55.3	168	47.7	167	56.4
Female	1022	48.6	188	50.4	176	48.6	99	50.3	98	50.5	148	44.7	184	52.3	129	43.6
Highest Education																
None	161	7.6	71	19.0	18	5.0	1	0.5	2	1.0	29	8.8	12	3.4	28	9.5
Primary	1088	51.7	264	70.8	224	61.9	26	13.2	26	13.4	261	78.9	141	40.1	146	49.3
Secondary	597	28.4	30	8.0	111	30.7	64	32.5	100	51.5	38	11.5	157	44.6	97	32.8
>Secondary	237	11.3	3	0.8	6	1.7	104	52.8	57	29.4	2	0.6	42	11.9	23	7.8
Missing	22	1.0	5	1.3	3	0.8	2	1.0	9	4.6	1	0.3	0		2	0.7
Smoker																
No	1757	83.5	319	85.5	239	66.0	171	86.8	191	98.5	305	92.1	305	86.6	227	76.7
Yes	348	16.5	54	14.5	123	34.0	26	13.2	3	1.5	26	7.9	47	13.4	69	23.3
Alcohol Use																
None	1334	63.4	215	57.6	175	48.3	133	67.5	166	85.6	233	70.4	237	67.3	175	59.1
<Daily	677	32.2	133	35.7	156	43.1	57	28.9	27	13.9	96	29.0	107	30.4	101	34.1
Daily	94	4.5	25	6.7	31	8.6	7	3.6	1	0.5	2	0.6	8	2.3	20	6.8
Recreational drug use																
None	1970	93.6	370	99.2	309	85.4	191	97.0	194	100.0	326	98.5	350	99.4	230	77.7
Marijuana	65	3.1	1	0.3	24	6.6	3	1.5	0		2	0.6	2	0.6	33	11.2
Khat	97	4.6	0		45	12.4	5	2.5	0		0		0		47	15.9
Other*	6	0.3	2	0.5	0		0		0		3	0.9	0		1	0.3

* Other includes cocaine and off-label use of prescription medicines

2.3. Reference Interval Results and Comparison with US-Derived Values

The reference interval results for the 2,105 volunteers are summarized and compared to US-derived intervals in Tables 4 and 5. Table 6 applies DAIDS AE grading criteria to our study results and presents the prevalence of values in our healthy study population that could be considered a laboratory-based AE. For additional information see Laboratory Reference Intervals for Healthy Adults in Eastern and Southern Africa (Karita et al., PloS ONE, on press).

Table 4: Hematology results, comparison intervals, and OOR values

Analytes	N	Reference Interval	Units	Comparison Interval*	OOR‡	
					N	%
Hemoglobin						
Male	1083	12.2-17.7	g/dL	13.5-17.5	140	12.9
Female	1022	9.5-15.8	g/dL	12.0-16.0	169	16.5
Hematocrit[1]						
Male	799	35.0-50.8	%	41-53	151	18.9
Female	846	29.4-45.4	%	36-46	187	22.1
RBC counts[2]	1929	3.8-6.2	10^6 cells/µL	NA		
Male	1083	4.0-6.4	10^6 cells/µL	4.5-5.9	231	21.3
Female	846	3.8-5.6	10^6 cells/µL	4.0-5.2	141	16.7
MCV	2105	68-98	fl	80-100	403	19.1
Platelet counts	2105	126-438	10^3 cells/µL	150-350	360	17.1
WBC counts	2105	3.1-9.1	10^3 cells/µL	4.5-11.0	602	28.6
Neutrophil counts	2103	1.0-5.3	10^3 cells/µL	1.8-7.7	604	28.7
Percent neutrophils	2103	25-66	%	40-70	721	34.3
Lymphocyte counts	2105	1.2-3.7	10^3 cells/µL	1.0-4.8	18	0.9
Percent lymphocytes	2105	23-59	%	22-44	798	37.9
Monocyte counts	2103	0.20-0.78	10^3 cells/µL	0-0.8	41	2.0
Percent monocytes	2103	4.5-13.1	%	4-11	181	8.6
Eosinophil counts	2104	0.04-1.53	10^3 cells/µL	0-0.45	437	20.8
Percent eosinophils[3]	1921	0.8-21.8	%	0-8	361	18.8
Basophil counts[4]	1750	0.01-0.15	10^3 cells/µL	0-0.2	22	1.3
Percent basophils[5]	1429	0.4-2.5	%	0-3	26	1.8
CD4 T cell counts	2100	457-1628	cells/µL	518-1981	109	5.2
CD8 T cell counts	2100	230-1178	cells/µL	270-1335	146	7.0

* Comparison intervals from (Kratz, 2004), except differential counts (Bakerman, 2002) and CD4/CD8 T cell counts (Beckton Dickinson package insert)
‡ The number and percent of African values outside the comparison interval
1 Excludes males from Kangemi and KNH, and females from Kangemi
2 Excludes females from Kangemi
3 Excludes males from Masaka
4 Excludes all Lusaka volunteers
5 Excludes all Lusaka and Entebbe volunteers, and females from Kilifi

Table 5: Chemistry results, comparison intervals, and OOR values

Analytes	N	Reference Interval	Units	Comparison Interval*	OOR‡	
					N	%
Creatinine	2103	47-109	µmol/L	0-133	3	0.14
SGOT/AST	2103	14-60	IU/L	0-35	244	11.6
SGPT/ALT	2103	8-61	IU/L	0-35	248	11.8
Direct bilirubin[1]	1906	0.4-8.8	µmol/L	1.7-5.1	792	41.6
Total bilirubin	2102	3.9-37.0	µmol/L	5.1-17.0	651	31.0
Albumin	2103	35-52	g/L	35-55	41	2.0
IgG[2]	1919	759-2776	mg/dL	614-1295	1594	83.1
LDH[3]	1674	214-528	IU/L	100 -190	1663	99.3
Amylase	2103	35-159	IU/L	60-180	686	32.6
ALP (DEA buffer)	1082	106-382	IU/L	30-120 **	1029	95.1
ALP (AMP buffer)	1021	48-164	IU/L	30-120 **	142	13.9
CPK	2101	53-552	IU/L	NA		
Male	1080	60-709	IU/L	60-400	119	11.0
Female	1021	49-354	IU/L	40-150	290	28.4
Total protein[4]	1772	58-88	g/L	55-80	290	16.4

* (Kratz, 2004)
‡ The number and percent of African values outside the comparison interval
** (Kratz, 2004) does not specify buffer used
1 Excludes females from Kilifi
2 Excludes males from Masaka
3 Excludes all Masaka volunteers and males from KNH
4 Excludes all Masaka volunteers

Table 6: Frequency of laboratory "adverse events" as defined by US-derived DAIDS AE grading cutoffs*

				Grade 1			Grade 2			Grade 3			Grade 4		
Analytes	N	Consensus Interval	Units	Cutoff	N	%	Cutoff	N	%	Cutoff	N	%	Cutoff	N	%
Hemoglobin															
Male	1083	12.2-17.7	g/dL	≤10.9	2	0.2	≤9.9	1	0.1	≤8.9	3	0.3	≤7.0	0	0
Female	1022	9.5-15.8	g/dL	≤10.9	33	3.2	≤9.9	17	1.7	≤8.9	16	1.6	≤7.0	1	0.1
Platelet counts	2105	126-438	10^3 cells/µL	≤124.9	28	1.3	≤99.9	18	0.9	≤49.9	5	0.2	≤25	0	0
WBC counts	2105	3.1-9.1	10^3 cells/µL	≤2.5	6	0.3	≤1.9	0	0	≤1.49	0	0	≤1	0	0
Neutrophil counts	2103	1.0-5.3	10^3 cells/µL	≤1.3	156	7.4	≤0.99	38	1.8	≤0.749	7	0.3	≤0.5	0	0
Lymphocyte counts	2105	1.2-3.7	10^3 cells/µL	≤0.65	0	0	≤0.59	0	0	≤0.49	0	0	≤0.35	0	0
CD4 T cell counts	2100	457-1628	cells/µL	≤400	11	0.5	≤299	3	0.1	≤199	1	0.1	≤100	0	0
Creatinine	2103	47-109	µmol/L	≥146.3	0	0	≥186.2	0	0	≥252.7	0	0	≥465.5	0	0
AST (SGOT)	2103	14-60	IU/L	≥43.8	103	4.9	≥91.0	20	1.0	≥178.5	3	0.1	≥350.0	0	0
ALT (SGPT)	2103	8-61	IU/L	≥43.8	120	5.7	≥91.0	10	0.5	≥178.5	2	0.1	≥350.0	0	0
Total bilirubin	2102	3.9-37.0	µmol/L	≥18.7	191	9.1	≥27.2	93	4.4	≥44.2	28	1.3	≥85.0	2	0.1
Albumin	2103	35-52	g/L	≤35.0	52	2.5	≤29.0	1	0.1	≤20	0	0	NA		
CPK															
Male	1080	60-709	IU/L	≥1200	7	0.7	≥2400	1	0.1	≥4000	2	0.2	≥8000	0	0
Female	1021	49-354	IU/L	≥450	9	0.9	≥900	2	0.2	≥1500	0	0	≥3000	0	0

* Chemistry cutoffs (DAIDS, 2004) derived from (Kratz, 2004). Hemoglobin, platelet count, WBC, neutrophil, lymphocyte, and CD4 T cell counts provided in (DAIDS, 2004)

3. HEMATOLOGY

3.1. Hemoglobin (Hb)

Results

Table 7 shows the number of subjects with data included in the analysis. Figures 4, 5, and 6 show the Hb distribution overall, by gender and by research center, respectively. Table 8 shows the distribution of Hb by center and gender, together with 95% reference intervals. The same intervals and median value are shown in Figure 7, by center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (g/dL)

	Males	**Females**
Comparison interval:	*13.5 to 17.5*	*12.0 to 16.0*
All centers, consensus interval:	*12.2 to 17.7*	*9.5 to 15.8*

Table 7: Number of observations, hemoglobin

	Male		Female		Total
	N	%	N	%	N
Kilifi	**167**	**56.42**	**129**	**43.58**	**296**
KNH	**98**	**49.75**	**99**	**50.25**	**197**
Kangemi	**186**	**51.38**	**176**	**48.62**	**362**
Entebbe	**96**	**49.48**	**98**	**50.52**	**194**
Masaka	**183**	**55.29**	**148**	**44.71**	**331**
Kigali	**185**	**49.60**	**188**	**50.40**	**373**
Lusaka	**168**	**47.73**	**184**	**52.27**	**352**
Total	**1083**	**51.45**	**1022**	**48.55**	**2105**

Figure 4: Frequency distribution of hemoglobin

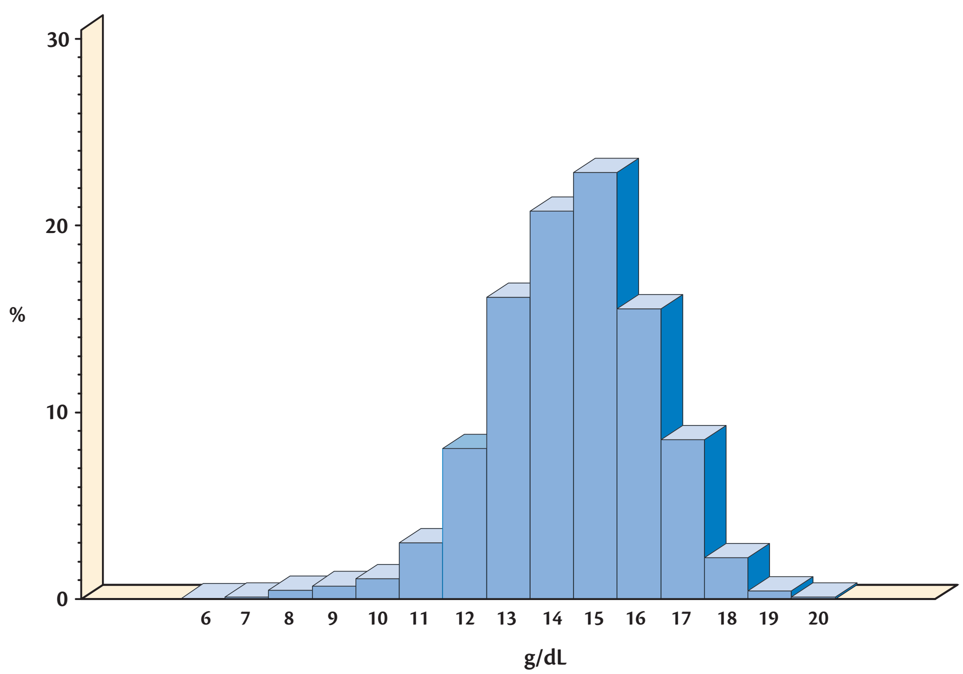


Figure 5: Frequency distribution of hemoglobin by gender

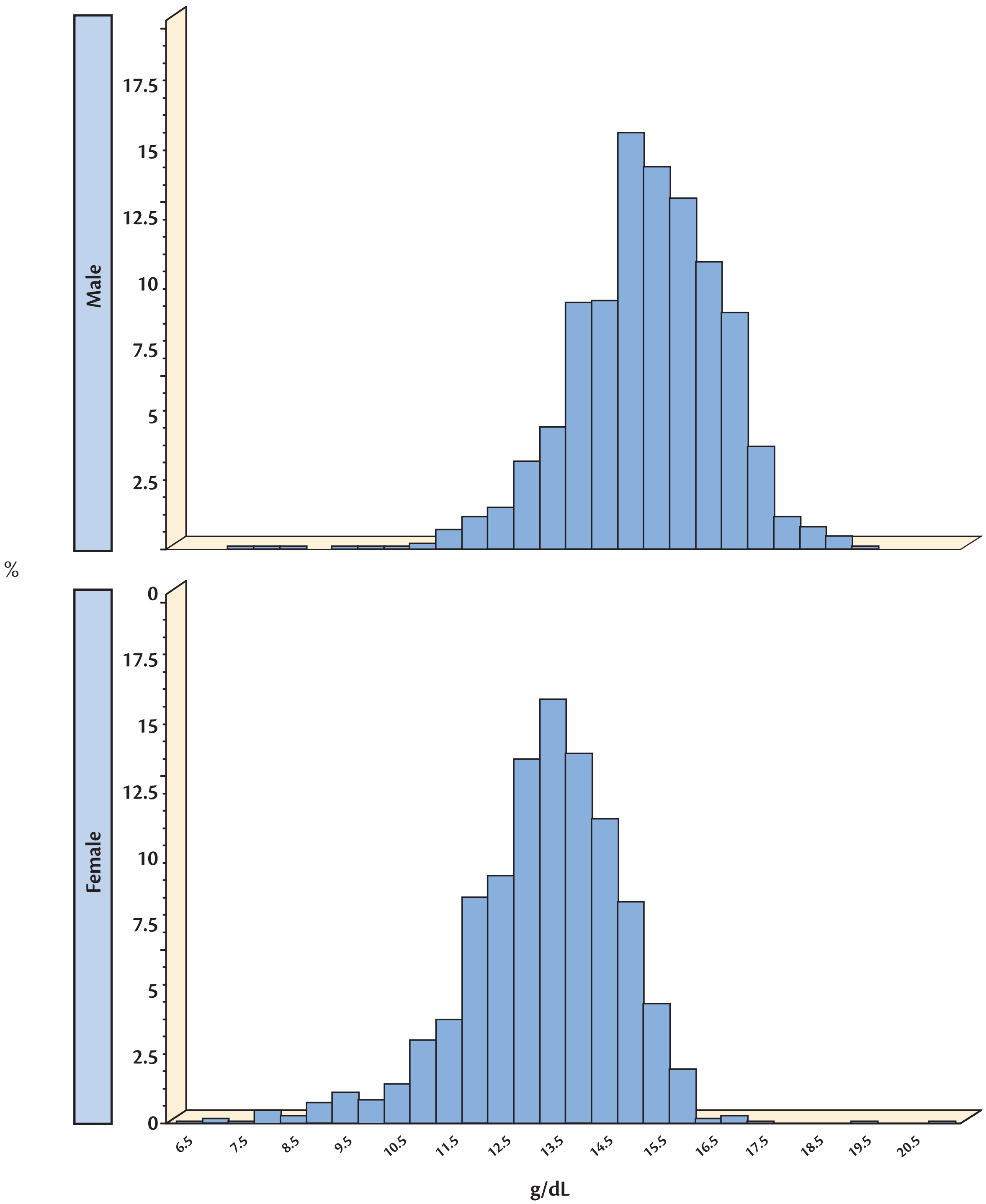


Figure 6: Frequency distribution of hemoglobin by research center

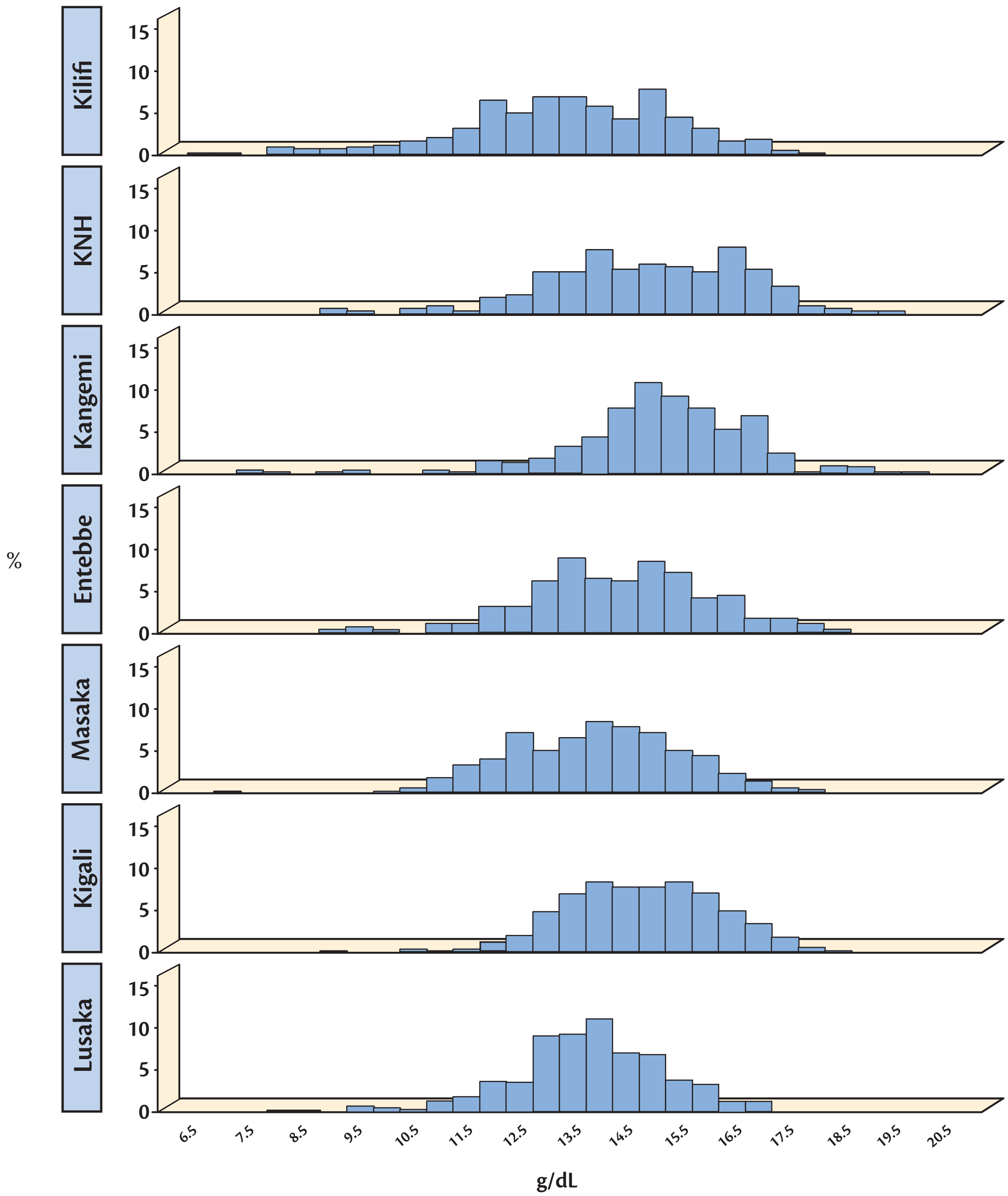


Table 8: Hemoglobin distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	12.0 (1.64)	12.2	8.7 to 15.3	8.0 to 14.9	6.4 to 15.6
	KNH	99	13.5 (1.50)	13.7	10.5 to 16.5	9.4 to 15.8	8.9 to 19.4
	Kangemi	176	14.3 (1.51)	14.6	11.3 to 17.3	9.7 to 16.2	7.6 to 17.3
	Entebbe	98	13.3 (1.32)	13.4	10.6 to 15.9	9.6 to 15.5	8.9 to 15.8
	Masaka	148	12.9 (1.25)	12.9	10.4 to 15.4	10.5 to 15.1	7.1 to 15.6
	Kigali	188	13.8 (1.08)	13.9	11.7 to 16.0	11.4 to 15.8	8.8 to 16.3
	Lusaka	184	12.9 (1.30)	13.1	10.3 to 15.5	9.6 to 15.0	8.1 to 16.1
	Total	1022	13.3 (1.52)	13.4	10.3 to 16.4	9.5 to 15.8	6.4 to 19.4
Male	Kilifi	167	14.5 (1.59)	14.7	11.3 to 17.7	10.6 to 17.0	7.9 to 17.9
	KNH	98	16.3 (1.07)	16.4	14.1 to 18.4	14.0 to 18.4	13.0 to 18.8
	Kangemi	186	16.1 (1.29)	16.2	13.5 to 18.7	13.8 to 18.9	7.7 to 19.5
	Entebbe	96	15.5 (1.26)	15.35	13.0 to 18.0	12.8 to 17.9	12.0 to 18.4
	Masaka	183	14.8 (1.38)	14.9	12.0 to 17.5	11.7 to 17.2	11.3 to 18.2
	Kigali	185	15.8 (1.09)	15.8	13.6 to 17.9	13.2 to 17.7	11.6 to 18.4
	Lusaka	168	14.7 (1.11)	14.6	12.5 to 16.9	12.9 to 16.8	11.2 to 17.2
	Total	1083	15.3 (1.44)	15.4	12.4 to 18.2	12.2 to 17.7	7.7 to 19.5
Total	Kilifi	296	13.4 (2.02)	13.5	9.4 to 17.4	8.5 to 16.9	6.4 to 17.9
	KNH	197	14.9 (1.89)	14.9	11.1 to 18.7	10.7 to 18.1	8.9 to 19.4
	Kangemi	362	15.2 (1.68)	15.3	11.9 to 18.6	11.8 to 18.3	7.6 to 19.5
	Entebbe	194	14.4 (1.71)	14.5	11.0 to 17.8	11.1 to 17.7	8.9 to 18.4
	Masaka	331	14.0 (1.61)	14	10.7 to 17.2	11.1 to 16.9	7.1 to 18.2
	Kigali	373	14.8 (1.45)	14.8	11.9 to 17.7	12.2 to 17.5	8.8 to 18.4
	Lusaka	352	13.8 (1.50)	13.9	10.8 to 16.8	10.1 to 16.4	8.1 to 17.2
	Total	2105	14.3 (1.79)	14.4	10.8 to 17.9	10.5 to 17.5	6.4 to 19.5

Research Center Comparisons

There is no significant difference between centers in hemoglobin, either among males or among females.

Gender Comparisons

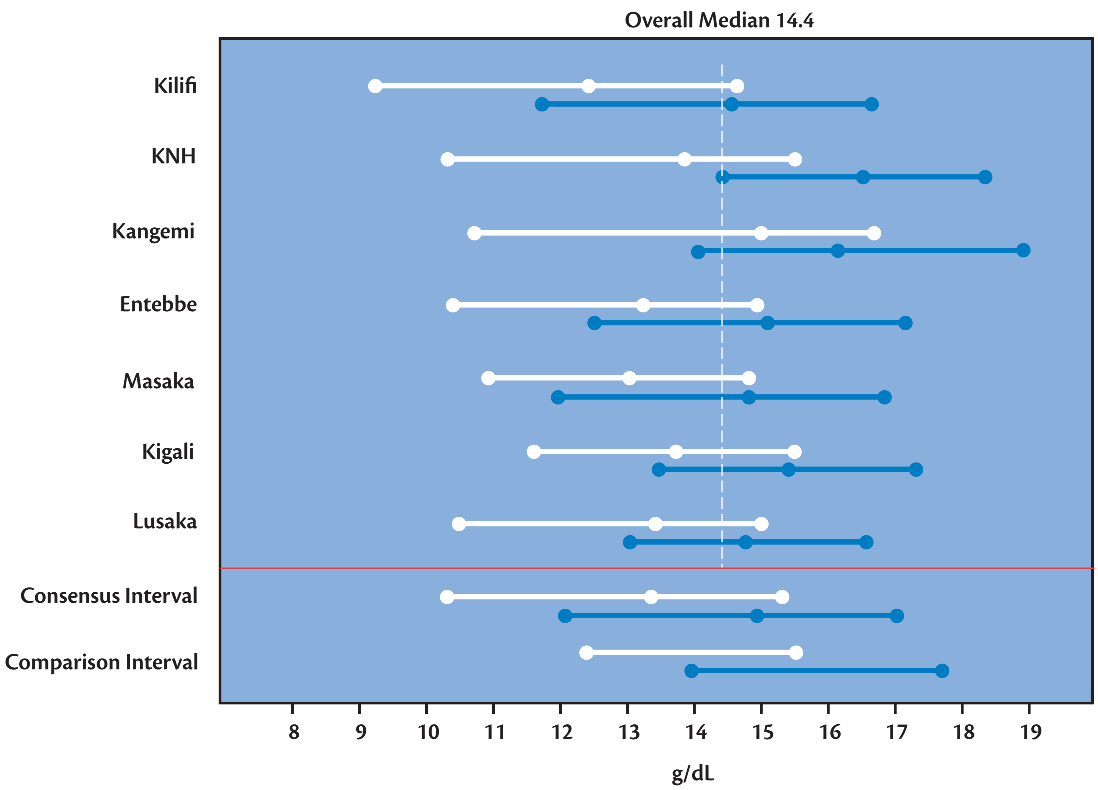
Combining data from all centers, there is a significant difference between males and females in the estimated reference intervals (Table 9, next page) according to the CLSI guidelines. (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment, and either the magnitude of the difference is ≥25% of the overall interval or the ratio of the two interval standard deviations is >1.5.)

Table 9: Evaluation of hemoglobin by gender

All Data Combined	Females		Males		CLSI Guidelines Criteria	
Reference Interval	Reference Interval	Mean (SD)	Reference Interval	Mean (SD)	Difference in Means>25% Ref. Interval	SD ratio > 1.5
10.5-17.5	9.5-15.8	13.31 (1.52)	12.2-17.7	15.32 (1.44)	Yes	No

Figure 7: Hemoglobin 95% intervals and medians by research center and gender

Consensus intervals: 12.2 to 17.7 (M), 9.5 to 15.8 (F)
Comparison intervals: 13.5 to 17.5 (M), 12. to 16.0 (F)
White: Females, Blue: Males



3.2. Hematocrit (HCT)

Results

Table 10 shows the number of subjects with data included in the analysis. Figures 8, 9, and 10 show the HCT distribution overall, by gender and by center, respectively. Table 11 shows the distribution of HCT by center and gender, together with the stratified 95% reference intervals. The same intervals, and median values, are shown in Figure 11, by center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated reference intervals (%)

	Males	Females
Comparison interval:	*41.0 to 53.0*	*36.0 to 46.0*
Consensus interval:*	*35.0 to 50.8*	*29.4 to 45.4*

**Consensus interval excludes males from Kangemi and KNH, and females from Kangemi.*

Table 10: Number of observations, hematocrit

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 8: Frequency distribution of hematocrit

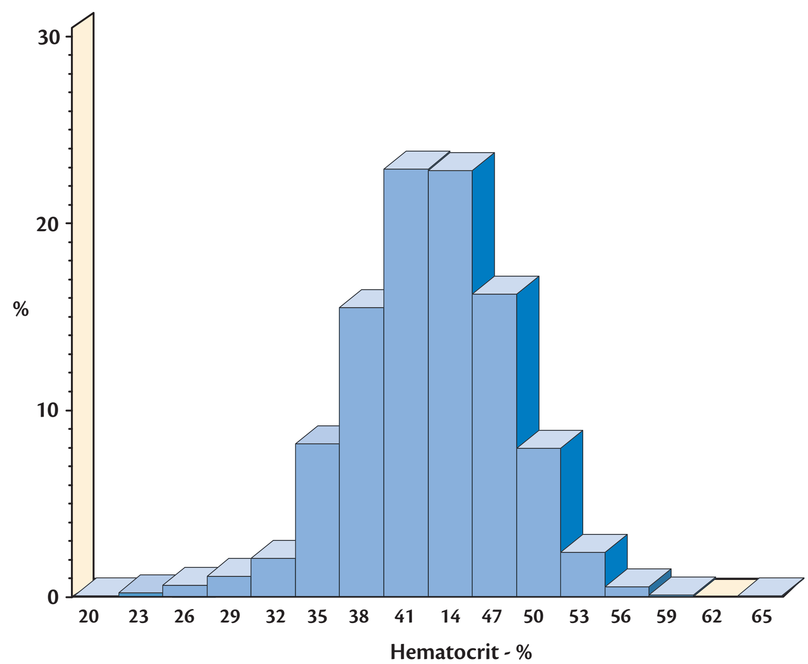


Figure 9: Frequency distribution of hematocrit by gender

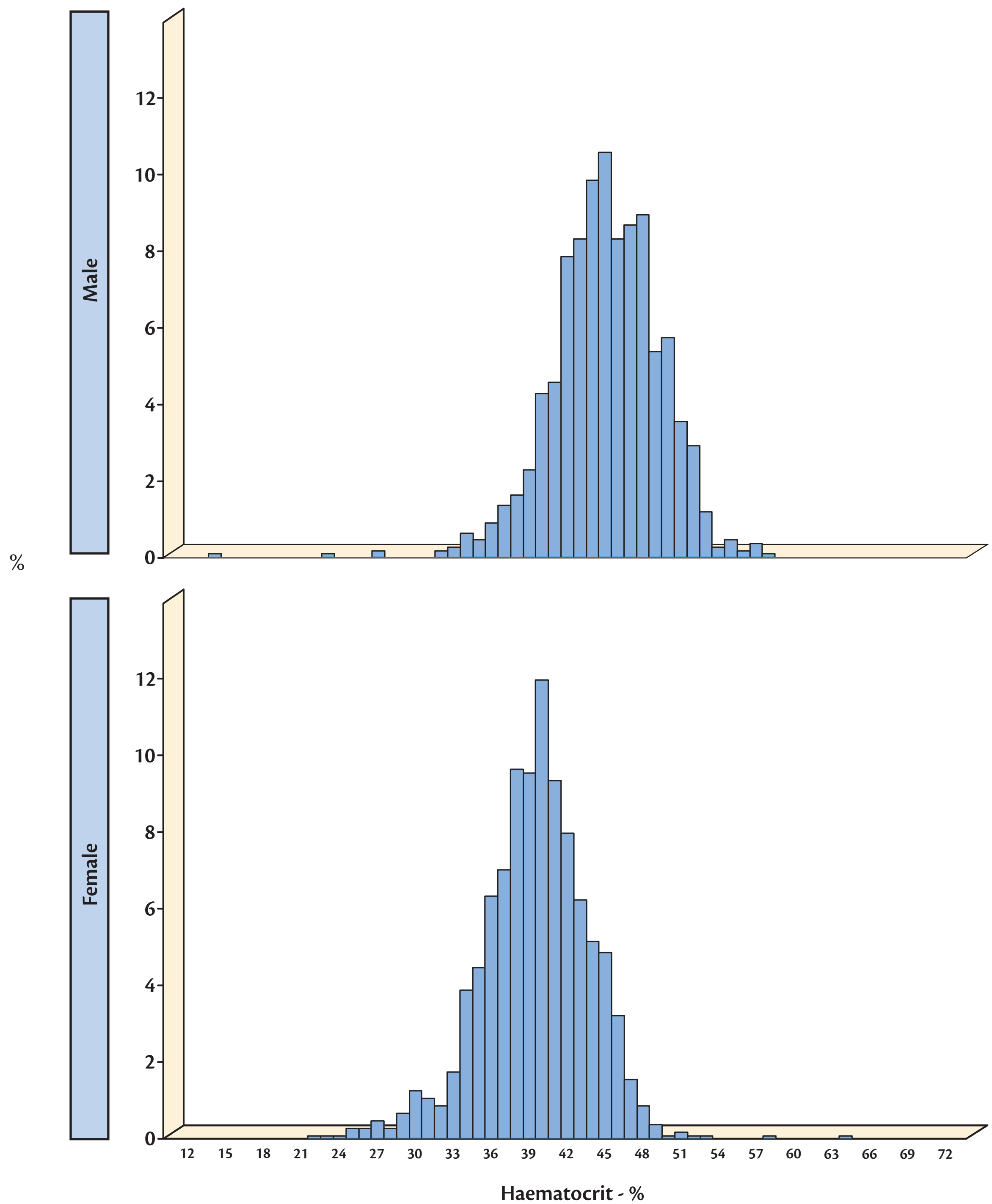


Figure 10: Frequency distribution of hematocrit by research center

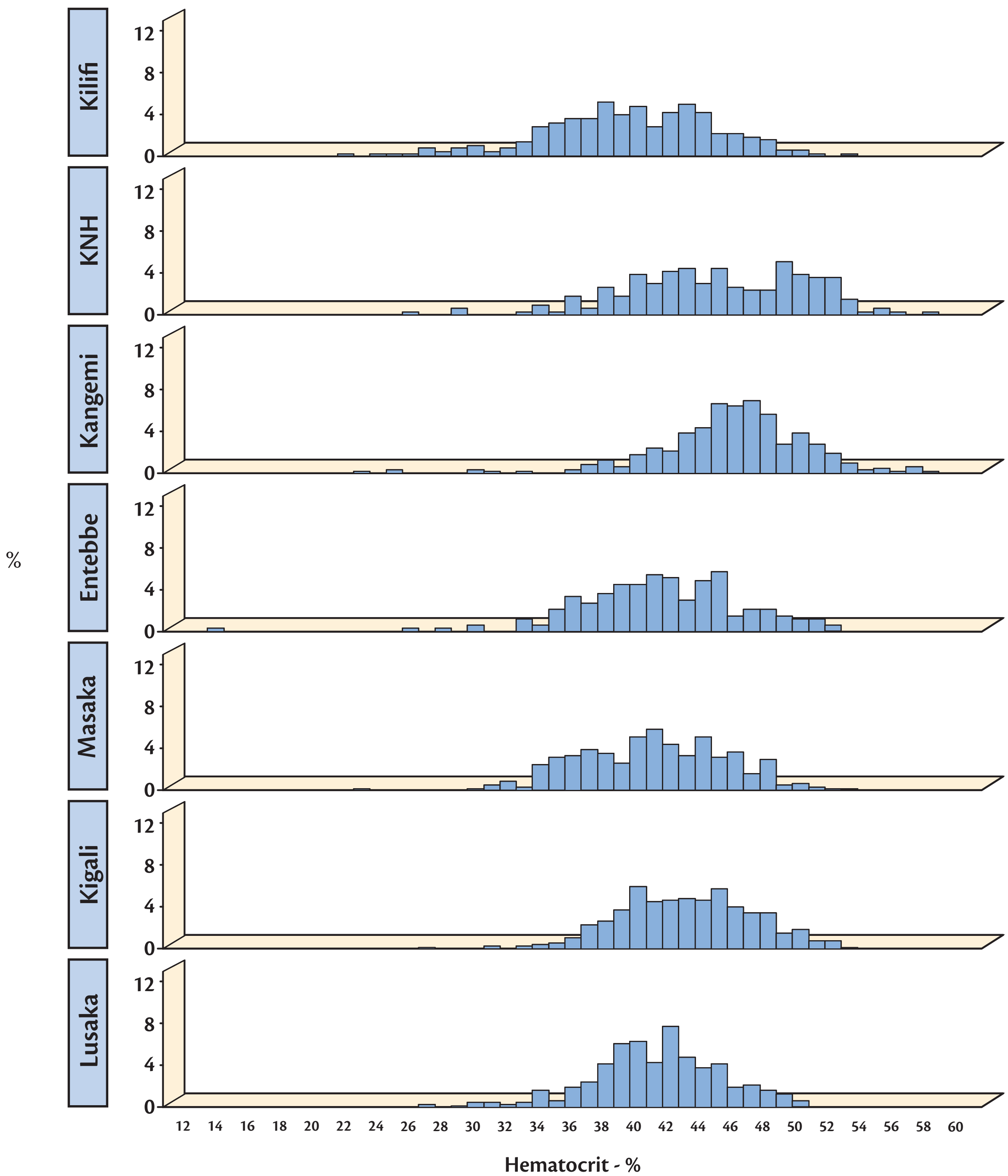


Table 11: Hematocrit distribution by research center and gender

Gender	Site	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	35.6 (4.08)	36.1	27.5 to 43.8	25.9 to 43.1	21.9 to 44.2
	KNH	99	40.7 (4.25)	40.7	32.2 to 49.2	29.4 to 45.9	26.2 to 58.3
	Kangemi	176	43.2 (4.17)	44.3	34.9 to 51.6	30.7 to 49.7	25.0 to 52.5
	Entebbe	98	38.3 (3.43)	38.65	31.5 to 45.2	29.6 to 44.1	26.1 to 45.0
	Masaka	148	37.9 (3.44)	38.05	31.0 to 44.8	31.4 to 43.7	22.7 to 45.6
	Kigali	188	40.2 (3.15)	40.25	33.9 to 46.5	33.5 to 46.0	27.3 to 48.5
	Lusaka	184	38.7 (3.53)	39.25	31.7 to 45.8	29.9 to 44.4	27.1 to 47.6
	Total	1022	39.4 (4.33)	39.65	30.7 to 48.1	29.6 to 46.8	21.9 to 58.3
Male	Kilifi	167	42.4 (4.11)	42.9	34.2 to 50.6	33.9 to 49.6	26.6 to 52.9
	KNH	98	49.0 (3.05)	49.2	42.9 to 55.1	42.5 to 55.0	41.8 to 56.0
	Kangemi	186	48.1 (3.78)	48	40.6 to 55.7	41.3 to 56.8	23.2 to 57.5
	Entebbe	96	44.5 (4.67)	44.6	35.2 to 53.9	36.4 to 51.2	14.3 to 52.3
	Masaka	183	43.3 (3.95)	43.7	35.4 to 51.2	34.6 to 50.2	32.3 to 52.6
	Kigali	185	45.6 (3.21)	45.6	39.2 to 52.0	39.4 to 51.7	33.2 to 52.6
	Lusaka	168	43.6 (3.12)	43.55	37.4 to 49.9	38.1 to 49.4	32.7 to 50.1
	Total	1083	45.1 (4.33)	45.1	36.4 to 53.7	36.2 to 52.6	14.3 to 57.5
Total	Kilifi	296	39.5 (5.29)	39.7	28.9 to 50.0	26.9 to 48.9	21.9 to 52.9
	KNH	197	44.8 (5.58)	44.9	33.7 to 56.0	33.6 to 53.6	26.2 to 58.3
	Kangemi	362	45.7 (4.68)	46.1	36.4 to 55.1	36.5 to 53.6	23.2 to 57.5
	Entebbe	194	41.4 (5.13)	41.35	31.1 to 51.7	30.4 to 51.0	14.3 to 52.3
	Masaka	331	40.9 (4.59)	41.1	31.7 to 50.0	32.4 to 49.3	22.7 to 52.6
	Kigali	373	42.9 (4.17)	43.1	34.5 to 51.2	35.0 to 50.5	27.3 to 52.6
	Lusaka	352	41.1 (4.15)	41.2	32.8 to 49.4	30.8 to 49.1	27.1 to 50.1
	Total	2105	42.3 (5.17)	42.4	32.0 to 52.7	31.6 to 51.7	14.3 to 58.3

Research Center Comparisons

There is a significant difference between centers among males and among females according to the CLSI guidelines. (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment, and either the magnitude of the difference is ≥25% of the overall interval or the ratio of the two interval standard deviations is >1.5.)

For males, the combined interval for Kigali, Entebbe, Masaka, Lusaka and Kilifi differs from the combined interval from Kangemi and KNH (35.0 to 50.8 versus 41.8 to 55.2, respectively). For females, the interval for Kangemi (30.7 to 49.7) is significantly different to the interval from all other centers combined (29.4 to 45.4). Hence, males from KNH and Kangemi, and females from Kangemi were not included in the consensus intervals. The Kangemi and KNH centers are the highest elevation of participating study centers.

Table 12: Evaluation of hematocrit by research center

All Centers Combined	Kigali, KNH, Entebbe, Kangemi, Musaka, Kilifi		Lusaka		CLSI Guidelines Criteria	
Reference Interval	Consensus Interval	Mean (SD)	Reference Interval	Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
Males						
36.2-52.6	35.0-50.8	43.86(3.92)	41.80-55.20	48.44(3.57)	Yes	No
Females						
29.6-46.8	29.4-45.4	38.61(3.93)	30.7-49.7	43.21(4.17)	Yes	No

Gender Comparisons

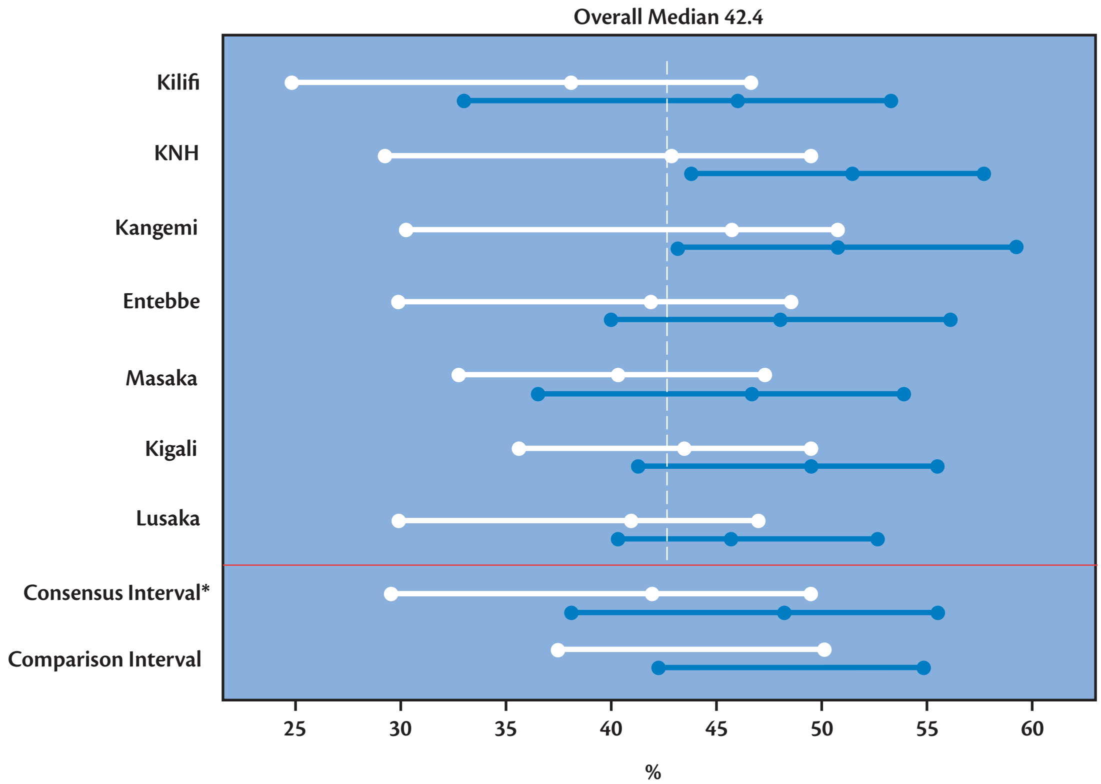
There is a significant difference between males and females (Table 13). Males from KNH and Kangemi, and females from Kangemi were excluded.

Table 13: Evaluation of hematocrit by gender

All Data Combined	Females		Males		CLSI Guidelines Criteria	
Reference Interval	Reference Interval	Mean (SD)	Reference Interval	Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
31.2-49.8	29.4-45.4	38.61(3.93)	35.0-50.8	43.86(3.92)	Yes	No

Figure 11: Hematocrit 95% intervals and medians by research center and gender

*Consensus intervals: 35.0 to 50.8 (M), 29.4 to 45.4 (F)**
Comparison intervals: 41 to 53 (M), 36 to 46 (F)
White: Females, Blue: Males



*Excludes male data from Kangemi and KNH, and female data from Kangemi

3.3. Red Blood Cells (RBC)

Results

Table 14 shows the number of subjects with data included in the analysis. Figures 12, 13, and 14 show the RBC distribution overall, by gender and by center, respectively. Table 15 shows the distribution of RBC by center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 15, by center and gender. Any significant differences that exist across center or gender are presented in Table 16. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (x 10^6 cells/μL)

	Males	**Females**	**Overall**
Comparison interval:	*4.5 to 5.9*	*4.0 to 5.2*	*NA*
Consensus interval:*	*4.0 to 6.4*	*3.8 to 5.6*	*3.8 to 6.2*

** Consensus interval excludes females from Kangemi.*

Table 14: Number of observations, RBC counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.4	129	43.6	296
KNH	98	49.5	99	50.5	197
Kangemi	186	51.2	176	48.8	362
Entebbe	96	49.5	98	50.5	194
Masaka	183	54.9	148	45.1	331
Kigali	185	49.6	188	50.4	373
Lusaka	168	48.0	184	52.0	352
Total	1083	51.4	1022	48.6	2105

Figure 12: Frequency distribution of RBC counts

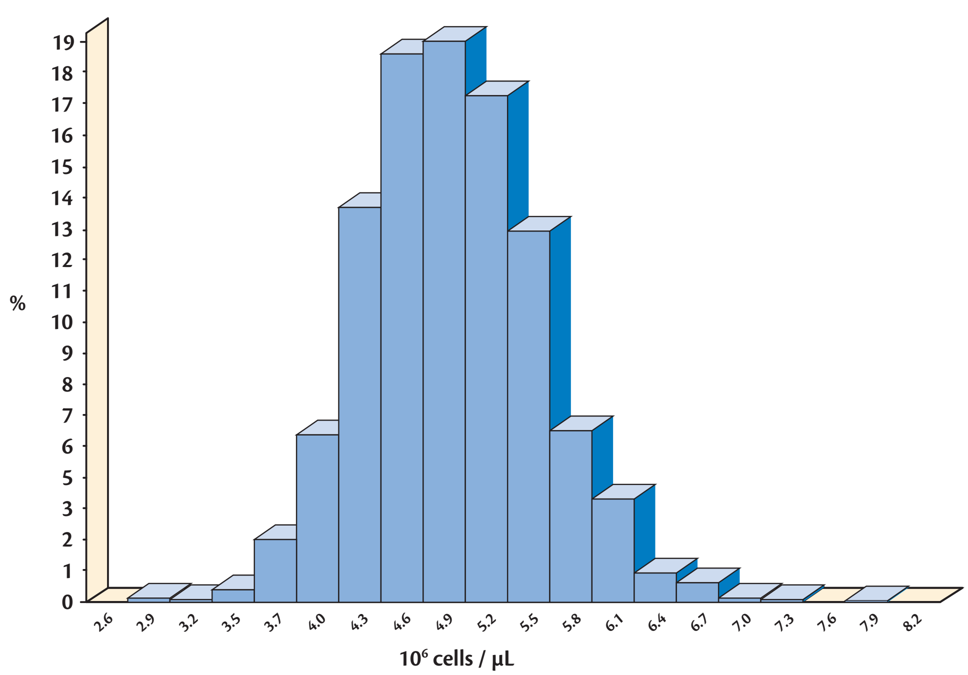


Figure 13: Frequency distribution of RBC counts by gender

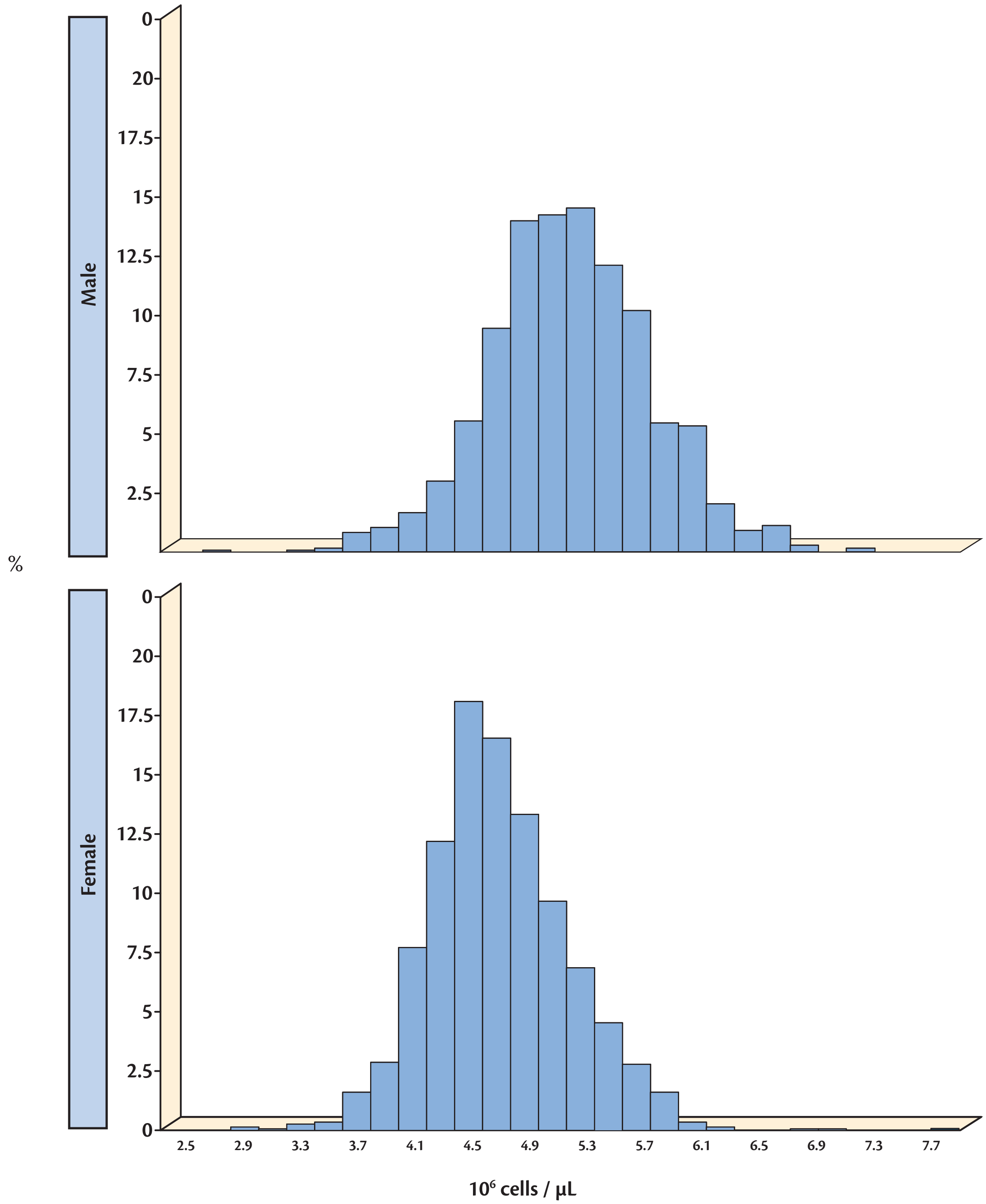


Figure 14: Frequency distribution of RBC counts by research center

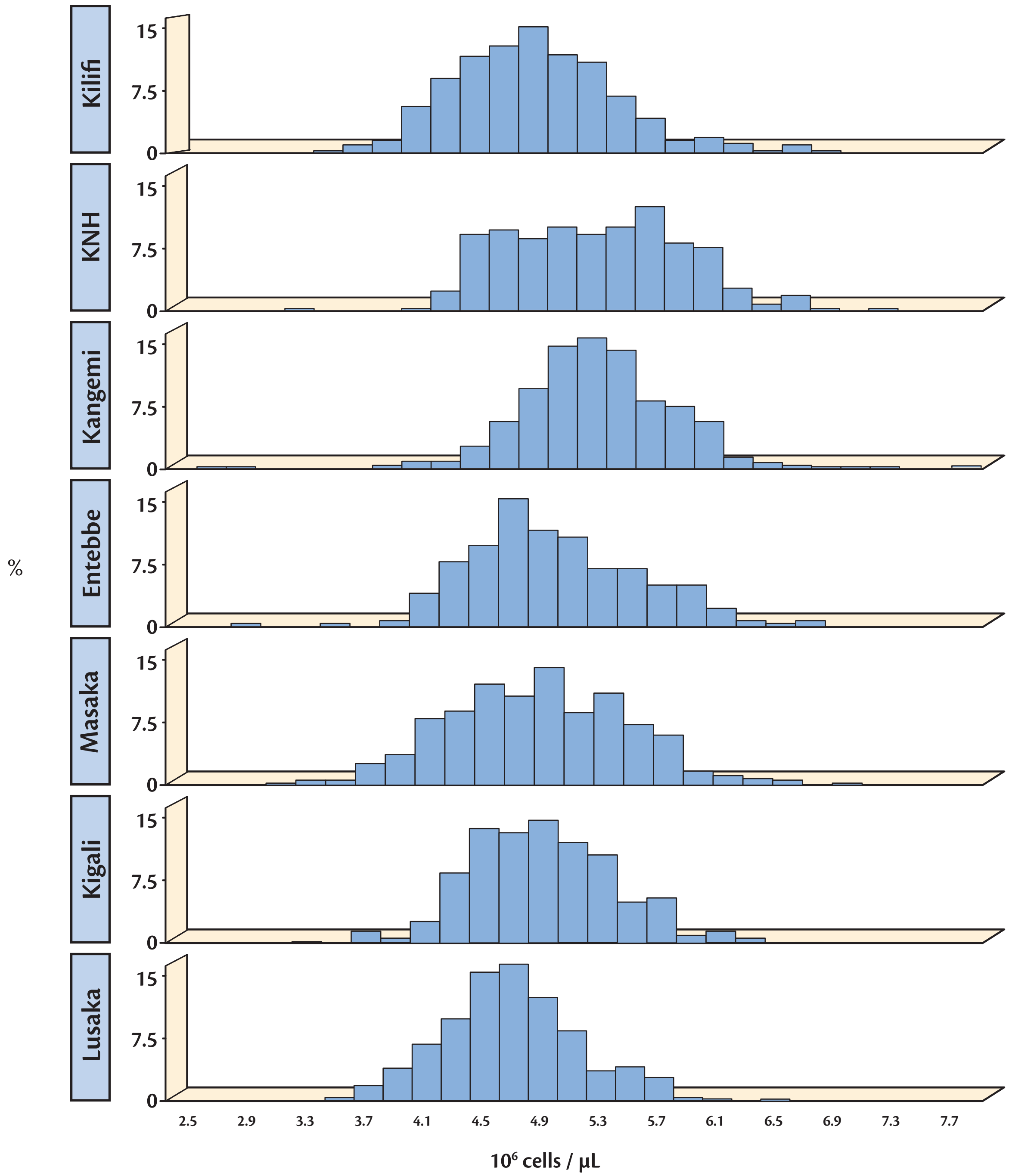


Table 15: RBC counts distribution by research center and gender

Gender	Site	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	4.6 (0.43)	4.54	3.74 to 5.48	3.90 to 5.50	3.72 to 5.94
	KNH	99	4.9 (0.50)	4.89	3.95 to 5.93	4.21 to 5.94	3.20 to 6.92
	Kangemi	176	5.2 (0.52)	5.13	4.14 to 6.20	4.11 to 6.07	2.96 to 7.90
	Entebbe	98	4.6 (0.45)	4.635	3.74 to 5.53	3.92 to 5.61	2.97 to 5.90
	Masaka	148	4.5 (0.49)	4.475	3.52 to 5.46	3.49 to 5.53	3.01 to 5.96
	Kigali	188	4.6 (0.40)	4.6	3.84 to 5.44	3.69 to 5.51	3.37 to 5.89
	Lusaka	184	4.5 (0.44)	4.49	3.66 to 5.41	3.77 to 5.57	3.44 to 5.79
	Total	1022	4.7 (0.52)	4.67	3.68 to 5.75	3.77 to 5.79	2.96 to 7.90
Male	Kilifi	167	5.2 (0.56)	5.13	4.04 to 6.29	4.07 to 6.47	3.43 to 6.93
	KNH	98	5.8 (0.45)	5.72	4.85 to 6.66	5.03 to 6.71	4.65 to 7.26
	Kangemi	186	5.5 (0.54)	5.45	4.41 to 6.57	4.44 to 6.52	2.75 to 7.37
	Entebbe	96	5.3 (0.54)	5.235	4.24 to 6.40	4.28 to 6.55	4.03 to 6.78
	Masaka	183	5.1 (0.58)	5.13	3.93 to 6.24	3.80 to 6.23	3.33 to 6.81
	Kigali	185	5.2 (0.47)	5.16	4.21 to 6.09	4.25 to 6.16	3.69 to 6.71
	Lusaka	168	4.8 (0.49)	4.83	3.85 to 5.83	3.82 to 5.77	3.52 to 6.40
	Total	1083	5.2 (0.58)	5.21	4.06 to 6.39	4.03 to 6.39	2.75 to 7.37
Total	Kilifi	296	4.9 (0.58)	4.89	3.76 to 6.09	3.92 to 6.20	3.43 to 6.93
	KNH	197	5.3 (0.63)	5.35	4.09 to 6.60	4.29 to 6.67	3.20 to 7.26
	Kangemi	362	5.3 (0.55)	5.325	4.23 to 6.44	4.27 to 6.36	2.75 to 7.90
	Entebbe	194	5.0 (0.60)	4.915	3.77 to 6.17	4.03 to 6.24	2.97 to 6.78
	Masaka	331	4.8 (0.61)	4.81	3.60 to 6.05	3.76 to 6.01	3.01 to 6.81
	Kigali	373	4.9 (0.51)	4.86	3.88 to 5.91	3.97 to 6.01	3.37 to 6.71
	Lusaka	352	4.7 (0.49)	4.65	3.70 to 5.66	3.77 to 5.71	3.44 to 6.40
	Total	2105	5.0 (0.61)	4.95	3.76 to 6.19	3.84 to 6.19	2.75 to 7.90

Research Center Comparisons

For females only, there is a significant difference in RBC between Kangemi and the consensus interval of other cemters combined (Table 16) according to the CLSI guidelines. (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment, and either the magnitude of the difference is ≥25% of the overall interval or the ratio of the two interval standard deviations is >1.5.)

Table 16: Evaluation of RBC counts by research center, females

All Centers Combined	Kigali, KNH, Entebbe, Musaka, Lusaka, Kilifi		Kangemi		CLSI Guidelines Criteria	
Reference Interval	Consensus Interval	Mean (SD)	Reference Interval	Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
3.77-5.79	3.76-5.62	4.62(0.46)	4.11-6.07	5.17(0.52)	Yes	No

Gender Comparisons

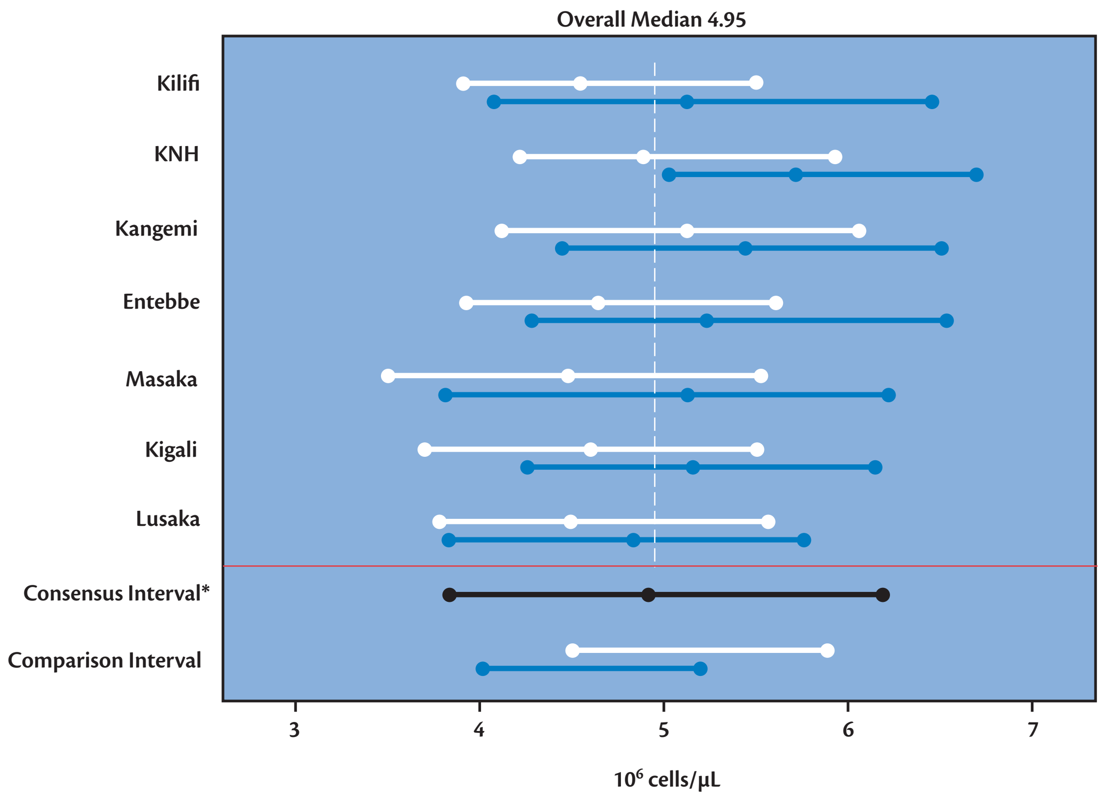
Excluding data from females at Kangemi, the difference between males and females in the remaining sites is significant according to the CLSI guidelines.

Table 17: Evaluation of RBC counts by gender

					CLSI Guidelines Criteria	
Reference Interval	Females Interval	Females Mean (SD)	Males Interval	Males Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
3.83-6.20	3.76-5.62	4.62(0.46)	4.03-6.39	5.22(0.58)	Yes	No

Figure 15: RBC counts 95% intervals and medians by research center and gender

*Consensus intervals: 3.8 to 6.2**
Comparison intervals: 4.5 to 5.9 (M), 4.0 to 5.2 (F)
White: Females, Blue: Males, Black: Overall



*Excludes females from Kangemi

3.4. Mean Corpuscular Volume (MCV)

Results

Table 18 shows the number of subjects with data included in the analysis. Figures 16, 17, and 18 show the MCV distribution overall, by gender and by center, respectively. Table 19 shows the distribution of MCV by center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 19 by center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals MCV (fl)

	Males	**Females**	**Overall**
Comparison interval:	*NA*	*NA*	*80 to 100*
All centers, consensus interval:	*70 to 99*	*65 to 97*	*68 to 98*

Table 18: Number of observations, MCV

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 16: Frequency distribution of MCV

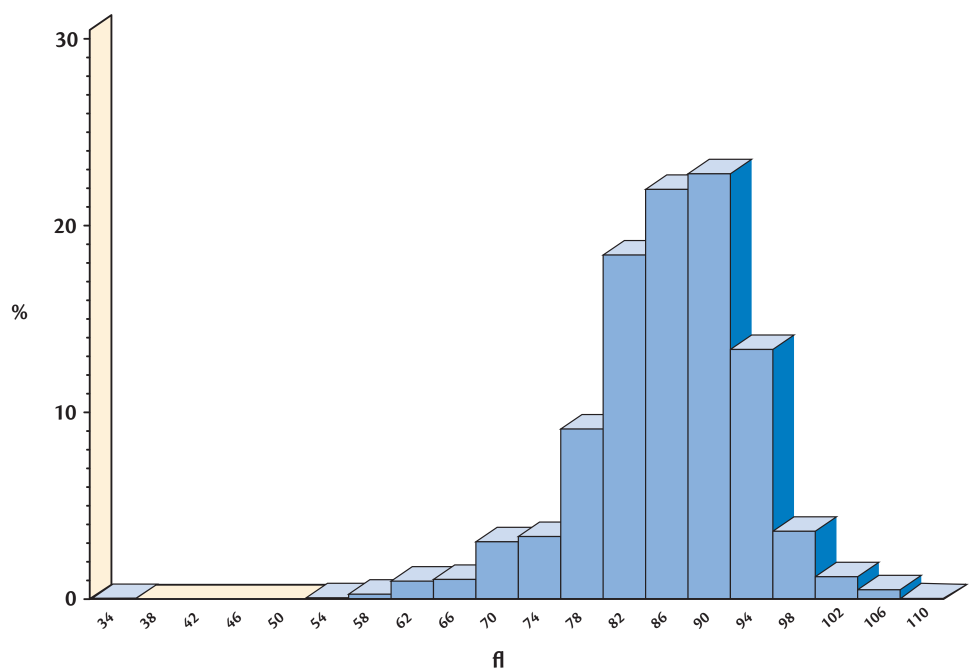


Figure 17: Frequency distribution of MCV by gender

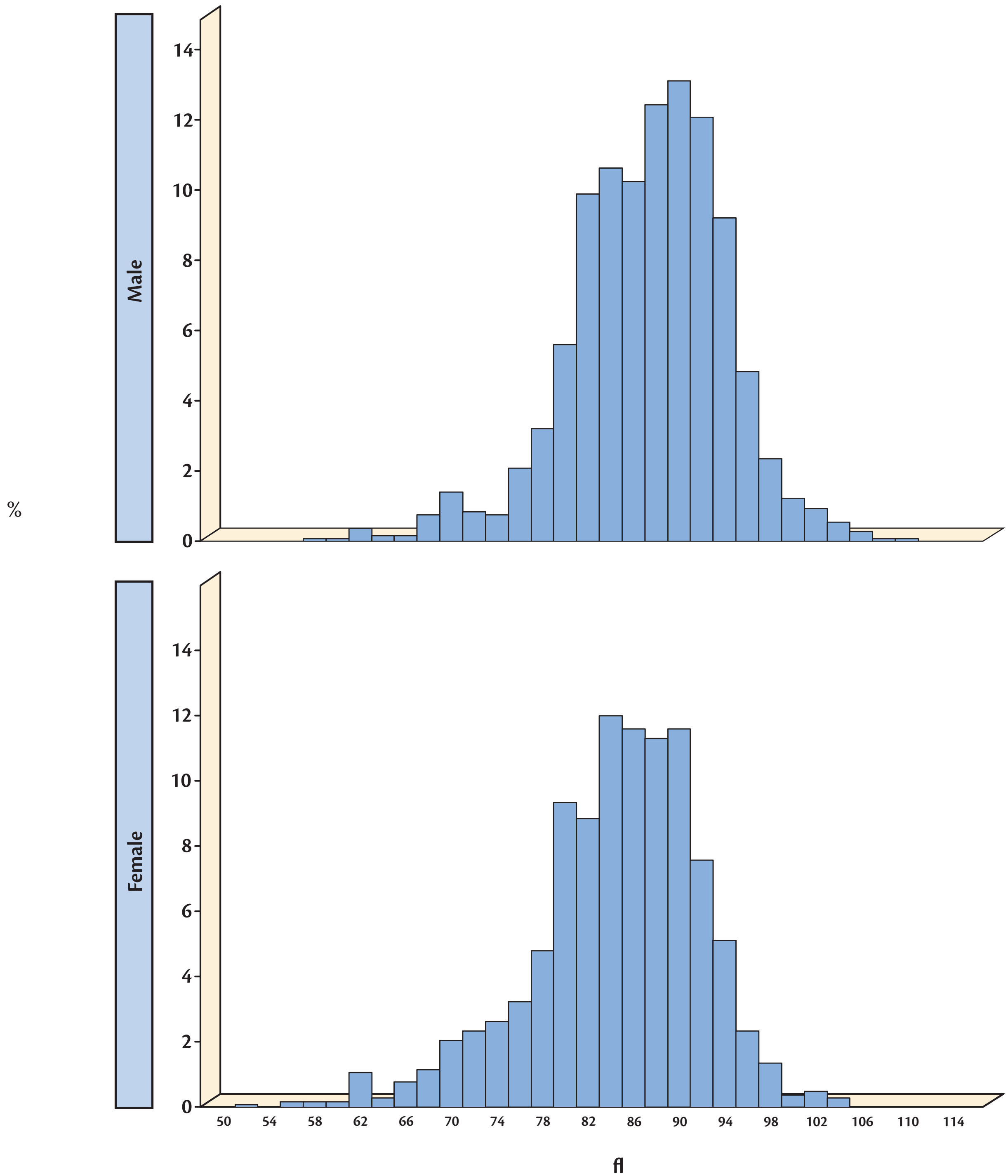


Figure 18: Frequency distribution of MCV by research center

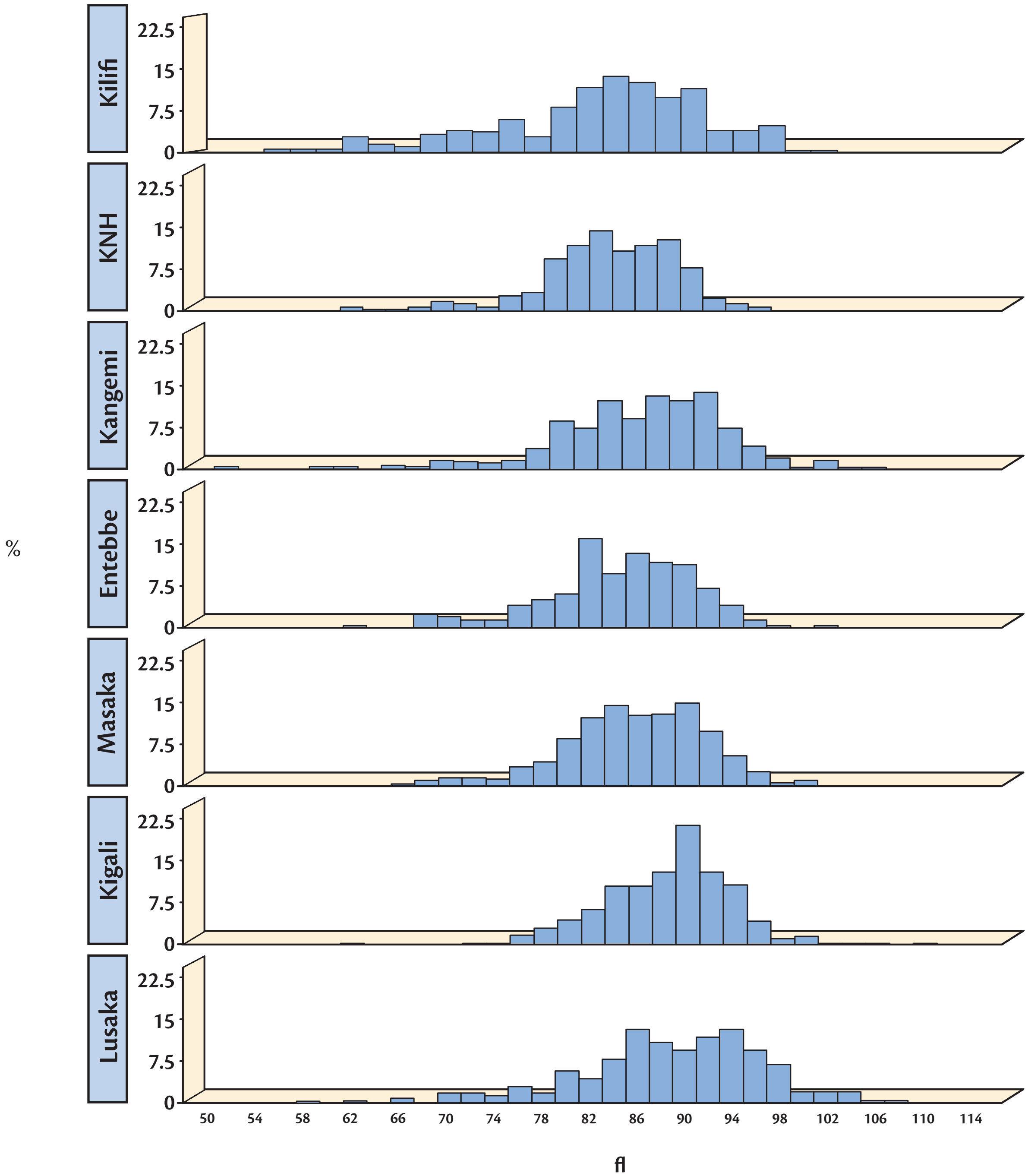


Table 19: MCV distribution

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	77.5 (8.0)	79	61.5 to 93.6	60 to 90	56 to 94
	KNH	99	82.6 (7.2)	83	68.1 to 97.0	63 to 93	62 to 94
	Kangemi	176	84.2 (7.5)	85	69.1 to 99.2	65 to 97	52 to 102
	Entebbe	98	83.0 (6.5)	83.5	70.0 to 96.1	68 to 93	62 to 95
	Masaka	148	84.6 (6.1)	85	72.4 to 96.8	71 to 95	67 to 100
	Kigali	188	86.9 (5.4)	87.5	76.1 to 97.7	76 to 97	62 to 103
	Lusaka	184	85.8 (8.4)	86	68.9 to 102.7	66 to 99	58 to 103
	Total	1022	83.9 (7.6)	85	68.7 to 99.2	65 to 97	52 to 103
Male	Kilifi	167	82.5 (7.8)	83	66.9 to 98.2	62 to 94	58 to 99
	KNH	98	85.4 (5.3)	86	74.8 to 96.1	75 to 96	68 to 98
	Kangemi	186	88.1 (6.2)	89	75.7 to 100.5	76 to 102	69 to 105
	Entebbe	96	84.7 (6.5)	85	71.8 to 97.6	69 to 96	67 to 101
	Masaka	183	85.5 (6.1)	86	73.4 to 97.6	70 to 95	66 to 100
	Kigali	185	88.8 (5.5)	89	77.8 to 99.9	78 to 99	75 to 110
	Lusaka	168	90.6 (7.0)	91.5	76.5 to 104.7	75 to 104	69 to 107
	Total	1083	86.8 (6.9)	87	72.9 to 100.6	70 to 99	58 to 110
Total	Kilifi	296	80.4 (8.3)	82	63.8 to 96.9	61 to 94	56 to 99
	KNH	197	84.0 (6.5)	84	71.0 to 97.0	68 to 95	62 to 98
	Kangemi	362	86.2 (7.1)	87	71.9 to 100.5	70 to 98	52 to 105
	Entebbe	194	83.9 (6.5)	85	70.8 to 96.9	68 to 95	62 to 101
	Masaka	331	85.1 (6.1)	86	72.9 to 97.3	70 to 95	66 to 100
	Kigali	373	87.9 (5.5)	89	76.8 to 99.0	77 to 98	62 to 110
	Lusaka	352	88.1 (8.1)	89	71.8 to 104.4	69 to 103	58 to 107
	Total	2105	85.4 (7.4)	86	70.6 to 100.2	68 to 98	52 to 110

Research Center Comparisons

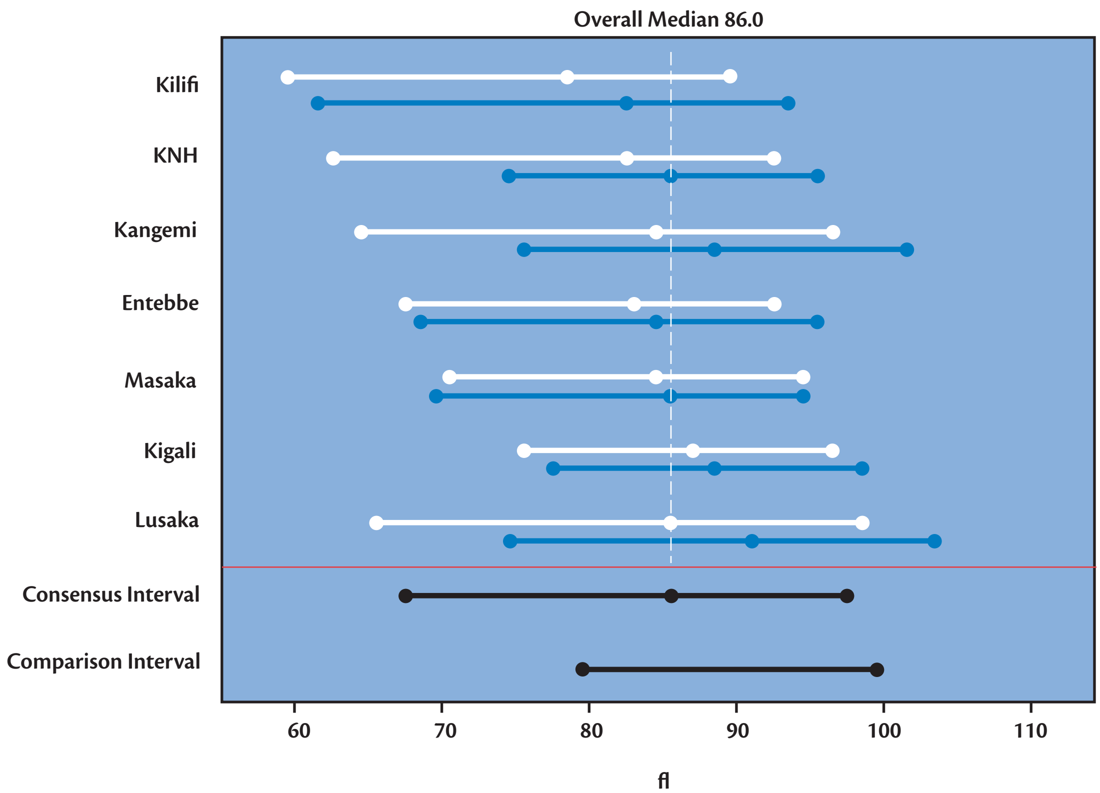
There are no center differences in MCV.

Gender Comparisons

There are no differences between males and females.

Figure 19: MCV 95% intervals and medians by research center and gender

Consensus interval: 68 to 98
Comparison interval: 80 to 100
White: Females, Blue: Males, Black: Overall



3.5. Platelet Counts

Results

Table 20 shows the number of subjects with data included in the analysis. Figures 20, 21, and 22 show the platelet counts distribution overall, by gender and by center, respectively. Table 21 shows the distribution of platelet counts by center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 23 by center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (10^3 cells/µL)

Comparison interval:	*150 to 350*
All centers, consensus interval:	*126 to 438*

Table 20: Number of observations, platelet counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 20: Frequency distribution of platelet counts

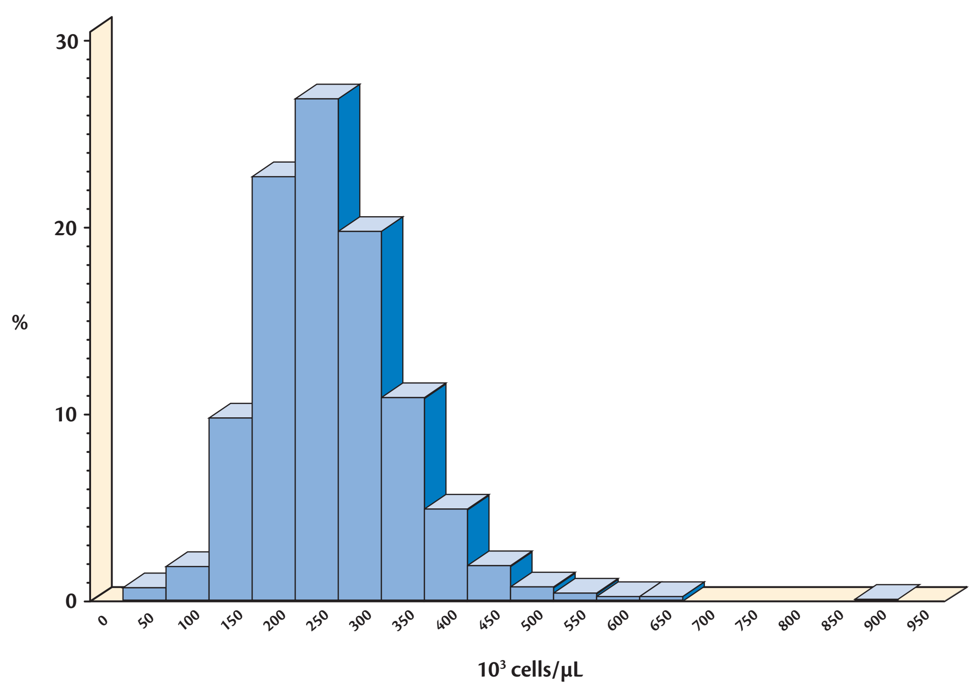


Figure 21: Frequency distribution of platelet counts by gender

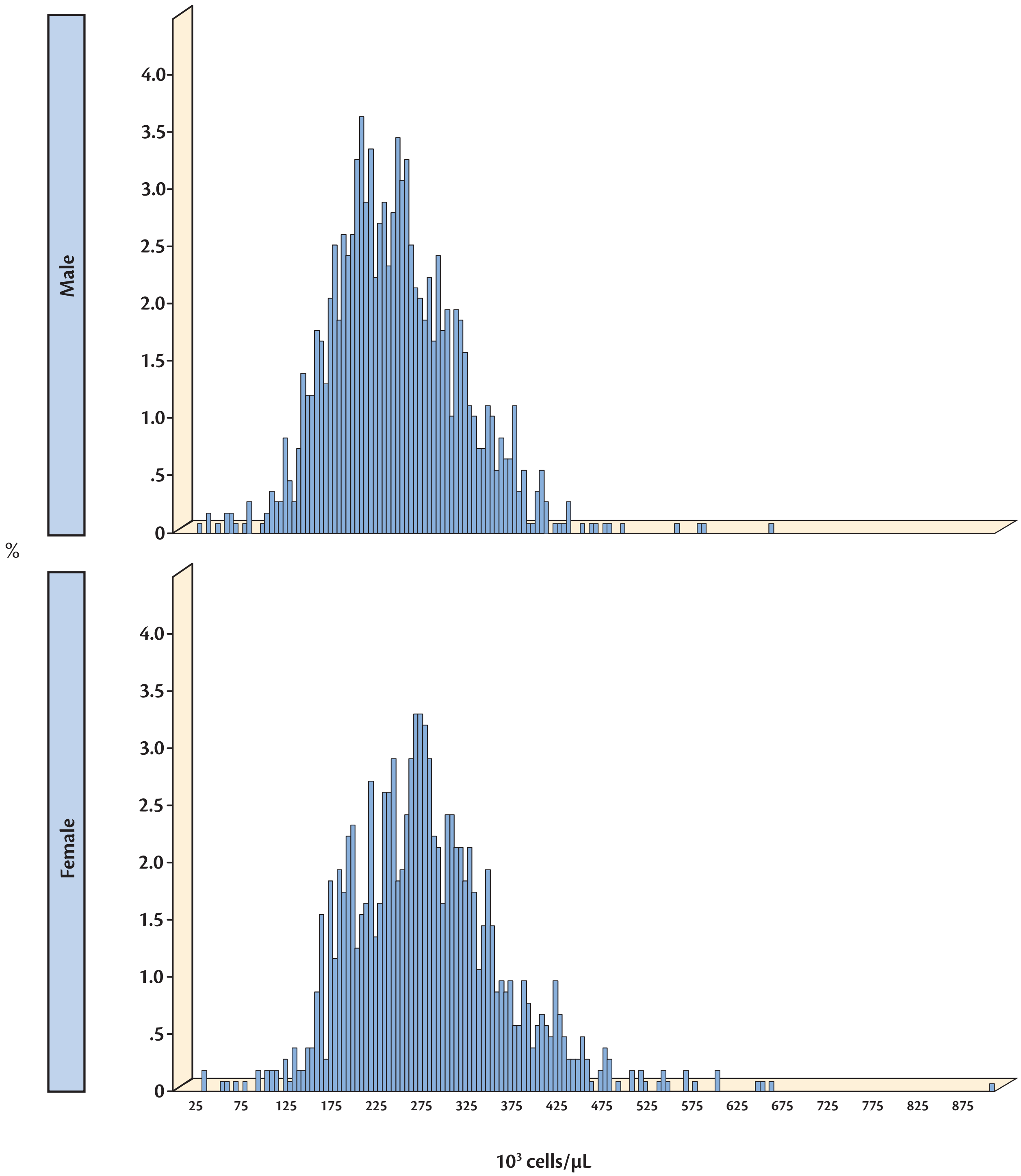


Figure 22: Frequency distribution of platelet counts by research center

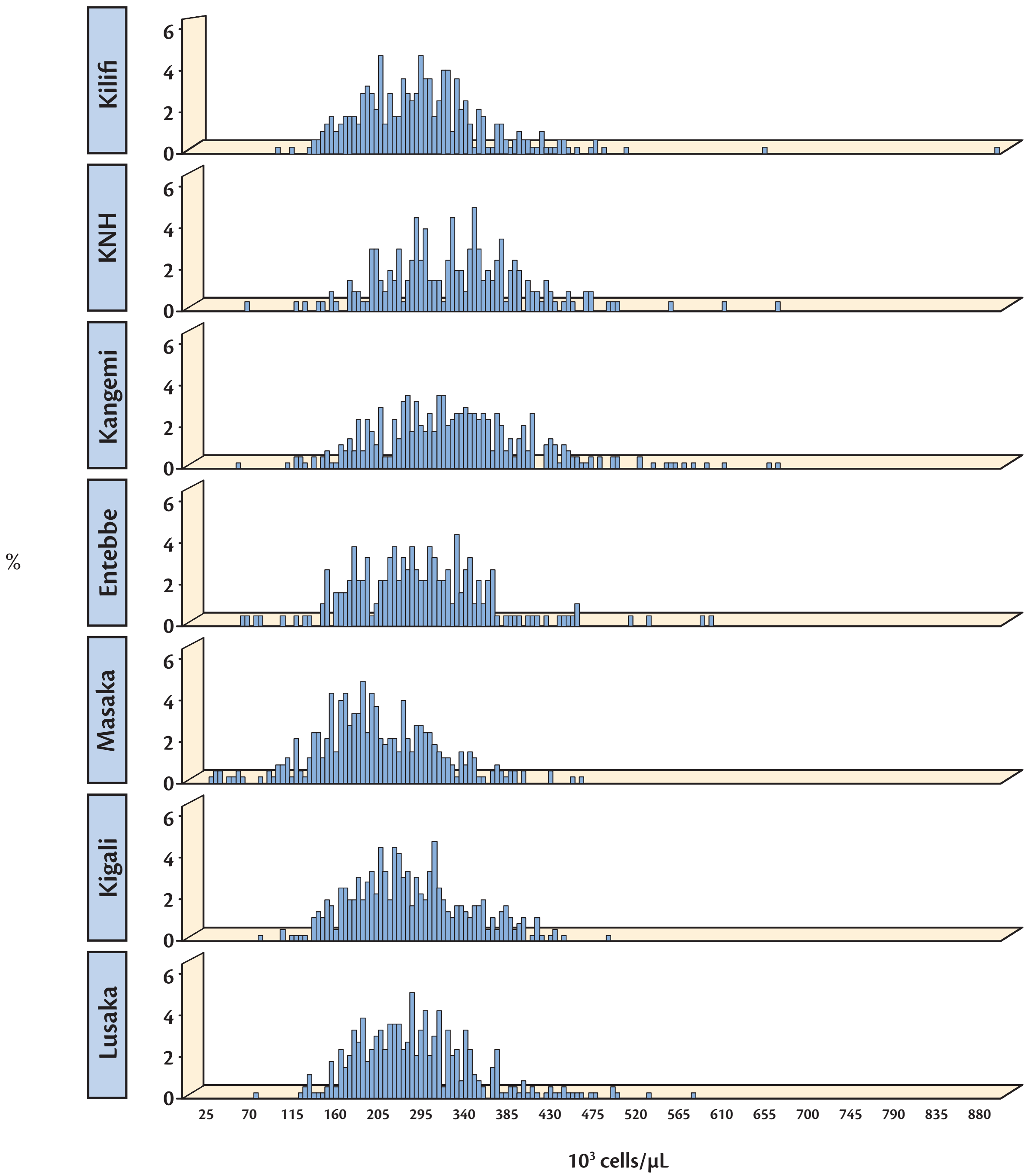


Table 21: Platelet counts distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	292.5 (92.8)	280	107.0 to 478.0	166 to 456	145 to 903
	KNH	99	326.4 (87.8)	320	150.8 to 502.0	181 to 539	67 to 662
	Kangemi	176	311.4 (95.8)	302.5	119.8 to 503.1	151 to 538	110 to 651
	Entebbe	98	263.3 (83.0)	257.5	97.4 to 429.2	153 to 434	76 to 573
	Masaka	148	230.3 (71.7)	230	87.0 to 373.6	90 to 367	30 to 440
	Kigali	188	260.2 (66.7)	255	126.8 to 393.6	153 to 392	106 to 470
	Lusaka	184	280.5 (77.0)	270.5	126.5 to 434.5	162 to 474	126 to 563
	Total	1022	279.1 (86.7)	270	105.7 to 452.6	143 to 474	30 to 903
Male	Kilifi	167	244.4 (66.4)	240	111.6 to 377.2	139 to 398	98 to 467
	KNH	98	271.1 (67.2)	261	136.6 to 405.5	152 to 398	121 to 449
	Kangemi	186	284.5 (83.4)	279.5	117.7 to 451.2	141 to 475	57 to 662
	Entebbe	96	256.8 (81.2)	250.5	94.4 to 419.2	81 to 436	59 to 585
	Masaka	183	197.1 (66.2)	192	64.6 to 329.6	54 to 351	27 to 428
	Kigali	185	235.7 (62.4)	232	110.8 to 360.5	130 to 368	79 to 410
	Lusaka	168	231.9 (53.9)	227.5	124.2 to 339.7	137 to 347	77 to 399
	Total	1083	243.4 (73.9)	238	95.5 to 391.2	118 to 398	27 to 662
Total	Kilifi	296	265.4 (82.4)	259	100.6 to 430.1	150 to 433	98 to 903
	KNH	197	298.9 (82.8)	297	133.2 to 464.5	152 to 475	67 to 662
	Kangemi	362	297.6 (90.5)	289	116.5 to 478.7	151 to 518	57 to 662
	Entebbe	194	260.1 (82.0)	254	96.2 to 424.0	103 to 436	59 to 585
	Masaka	331	211.9 (70.6)	203	70.8 to 353.1	62 to 362	27 to 440
	Kigali	373	248.0 (65.7)	241	116.6 to 379.4	141 to 389	79 to 470
	Lusaka	352	257.3 (71.1)	250.5	115.0 to 399.6	141 to 437	77 to 563
	Total	2105	260.7 (82.3)	254	96.1 to 425.4	126 to 438	27 to 903

Research Center Comparisons

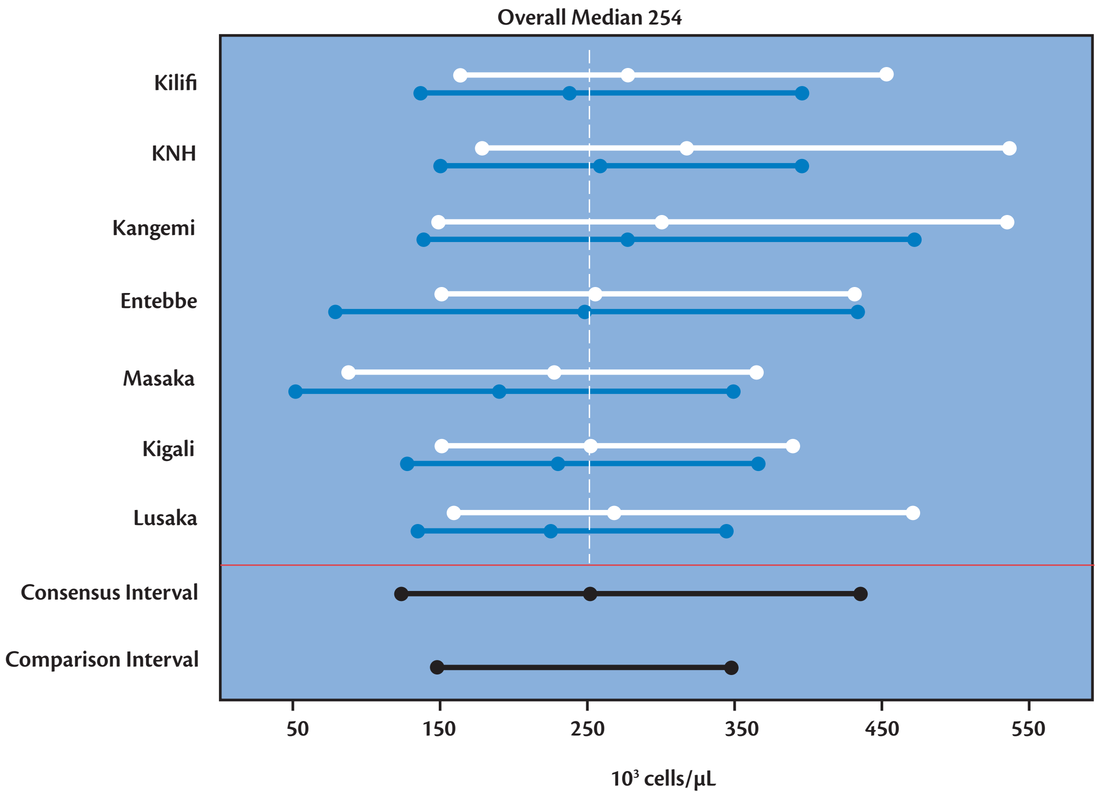
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 23: Platelet counts 95% intervals and medians by research center and gender

Consensus interval: 126 to 438
Comparison interval: 150 to 350
White: Females, Blue: Males, Black: Overall



3.6. White Blood Cell (WBC) Counts

Results

Table 22 shows the number of subjects with data included in the analysis. Figures 24, 25, and 26 show the WBC counts distribution overall, by gender and by research center, respectively. Table 23 shows the distribution of WBC counts by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 27 by research center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (x 10^3 cells/µL)

	Total
Comparison interval:	*4.5 to 11.0*
All centers, consensus interval:	*3.1 to 9.1*

Table 22: Number of observations, WBC counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 24: Frequency distribution of WBC counts

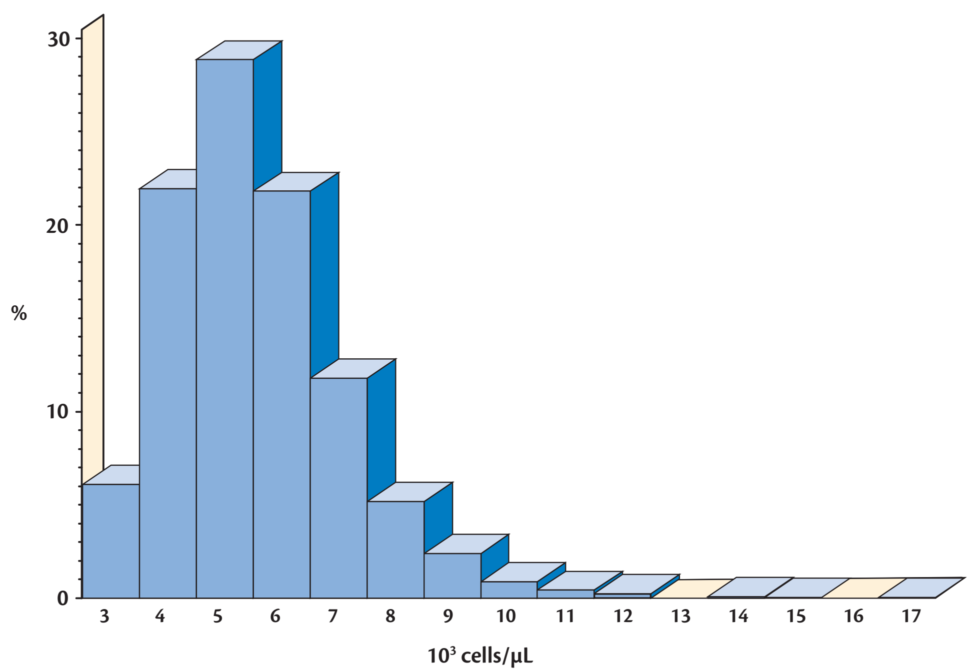


Figure 25: Frequency distribution of WBC counts by gender

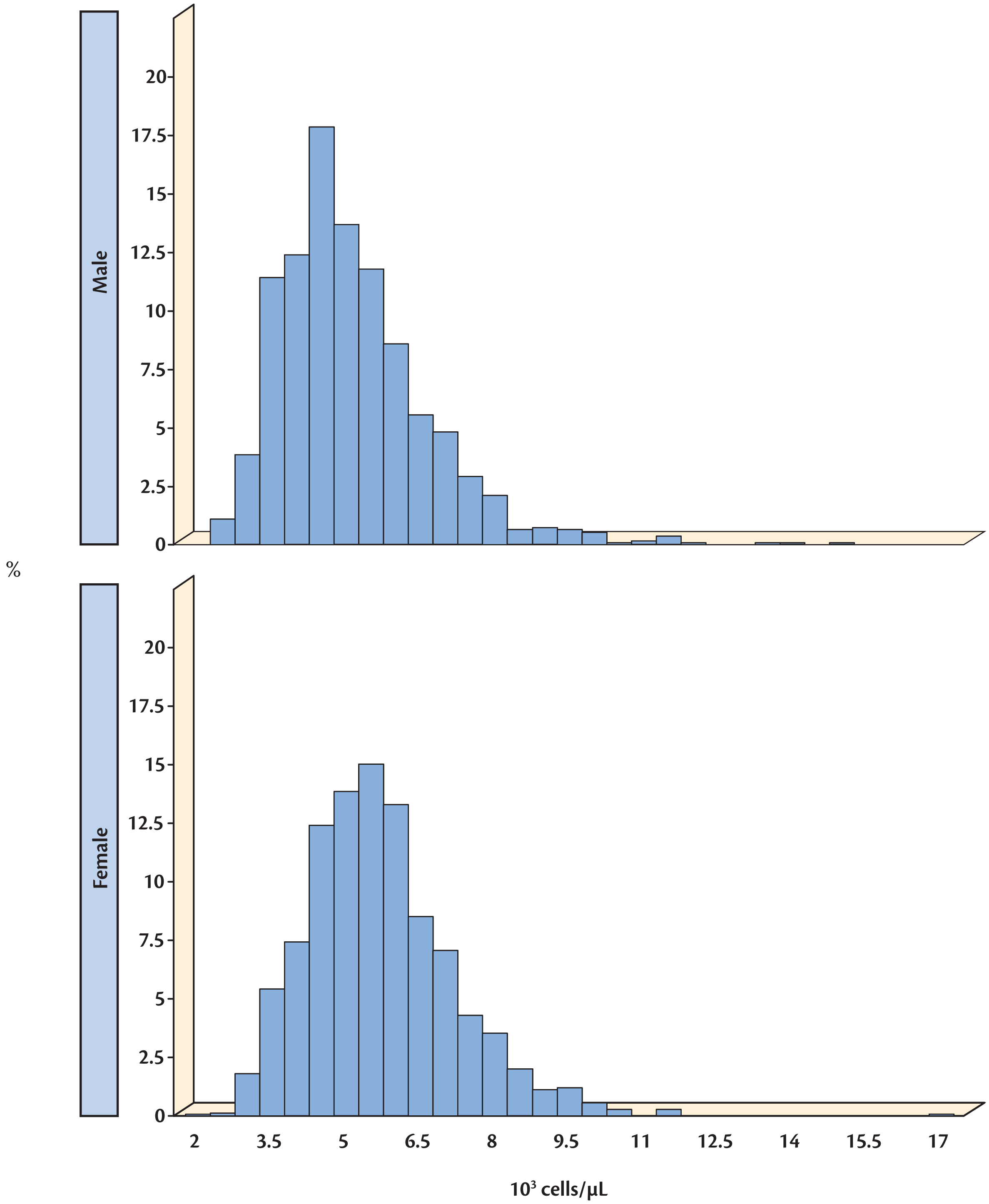


Figure 26: Frequency distribution of WBC counts by research center

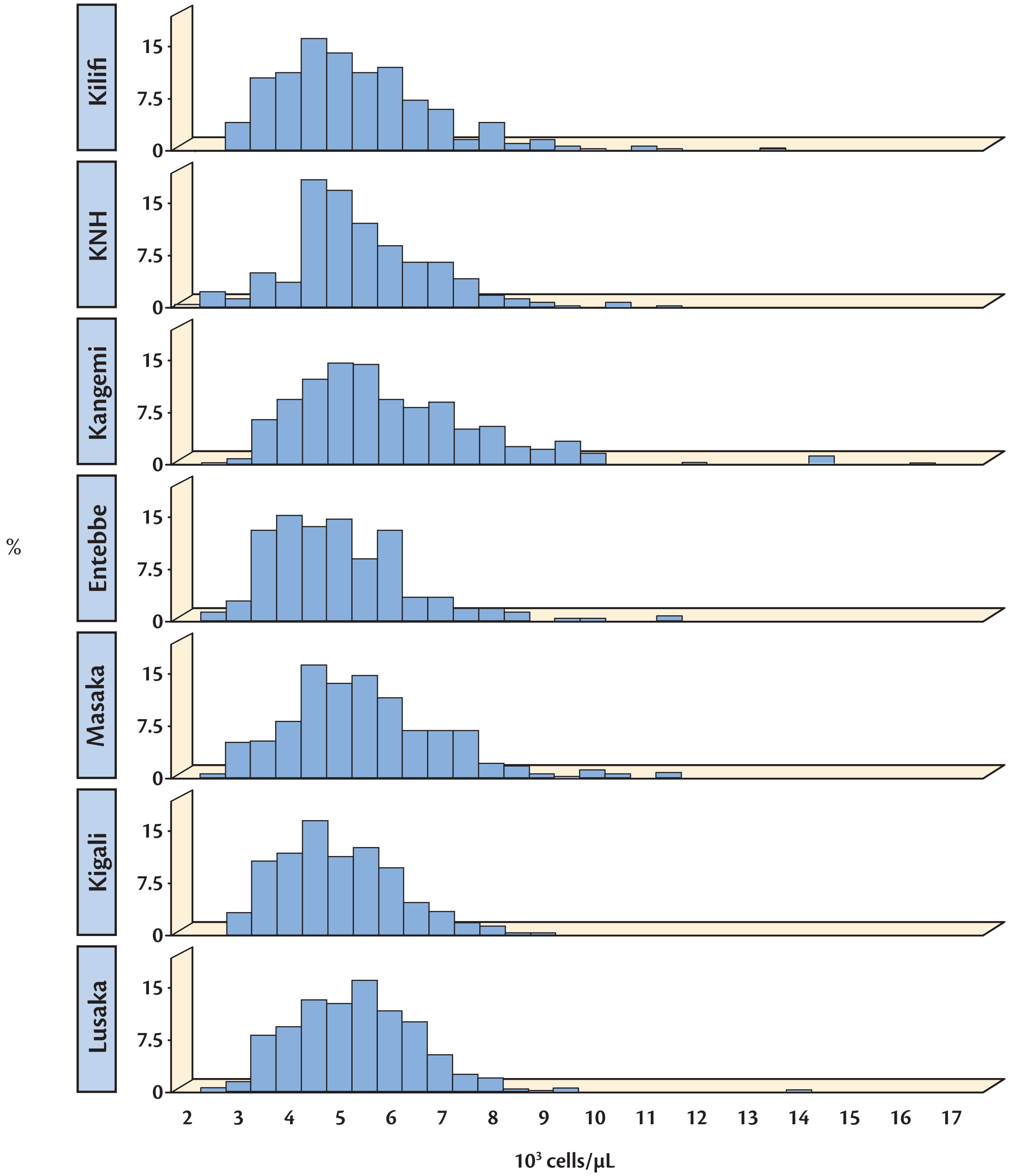


Table 23: WBC counts distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	5.4 (1.4)	5.2	2.59 to 8.21	3.3 to 8.6	2.8 to 9.6
	KNH	99	5.7 (1.4)	5.6	2.94 to 8.55	3.0 to 9.2	2.1 to 10.7
	Kangemi	176	6.3 (1.8)	6.1	2.68 to 9.94	3.6 to 9.6	3.4 to 16.8
	Entebbe	98	5.1 (1.5)	5	2.23 to 8.07	3.1 to 8.4	2.8 to 11.5
	Masaka	148	5.7 (1.7)	5.5	2.40 to 9.06	3.0 to 9.8	2.6 to 11.7
	Kigali	188	5.3 (1.2)	5.35	3.03 to 7.64	3.4 to 7.9	3.2 to 9.2
	Lusaka	184	5.8 (1.2)	5.7	3.37 to 8.25	3.5 to 8.4	3.2 to 9.4
	Total	1022	5.7 (1.5)	5.6	2.68 to 8.67	3.3 to 9.2	2.1 to 16.8
Male	Kilifi	167	5.4 (1.8)	5	1.81 to 8.94	3.0 to 10.1	2.8 to 13.6
	KNH	98	5.1 (1.4)	4.95	2.28 to 7.93	2.7 to 8.3	2.5 to 10.5
	Kangemi	186	5.6 (1.7)	5.2	2.11 to 9.02	3.3 to 9.9	2.7 to 14.8
	Entebbe	96	5.0 (1.5)	4.7	1.93 to 8.04	2.7 to 8.5	2.5 to 11.3
	Masaka	183	5.4 (1.5)	5.3	2.38 to 8.41	3.1 to 9.6	2.7 to 11.7
	Kigali	185	4.7 (1.2)	4.5	2.35 to 7.04	3.0 to 7.5	2.9 to 9.1
	Lusaka	168	4.9 (1.4)	4.7	2.17 to 7.58	3.1 to 7.2	2.3 to 14.2
	Total	1083	5.2 (1.5)	4.9	2.07 to 8.24	3.0 to 9.1	2.3 to 14.8
Total	Kilifi	296	5.4 (1.6)	5.1	2.14 to 8.64	3.1 to 9.2	2.8 to 13.6
	KNH	197	5.4 (1.4)	5.2	2.55 to 8.30	2.7 to 8.8	2.1 to 10.7
	Kangemi	362	5.9 (1.8)	5.5	2.31 to 9.54	3.5 to 9.6	2.7 to 16.8
	Entebbe	194	5.1 (1.5)	4.9	2.08 to 8.05	2.8 to 8.5	2.5 to 11.5
	Masaka	331	5.5 (1.6)	5.3	2.37 to 8.71	3.1 to 9.8	2.6 to 11.7
	Kigali	373	5.0 (1.2)	4.9	2.61 to 7.42	3.2 to 7.8	2.9 to 9.2
	Lusaka	352	5.4 (1.4)	5.3	2.63 to 8.09	3.2 to 8.2	2.3 to 14.2
	Total	2105	5.4 (1.5)	5.2	2.32 to 8.49	3.1 to 9.1	2.1 to 16.8

Research Center Comparisons

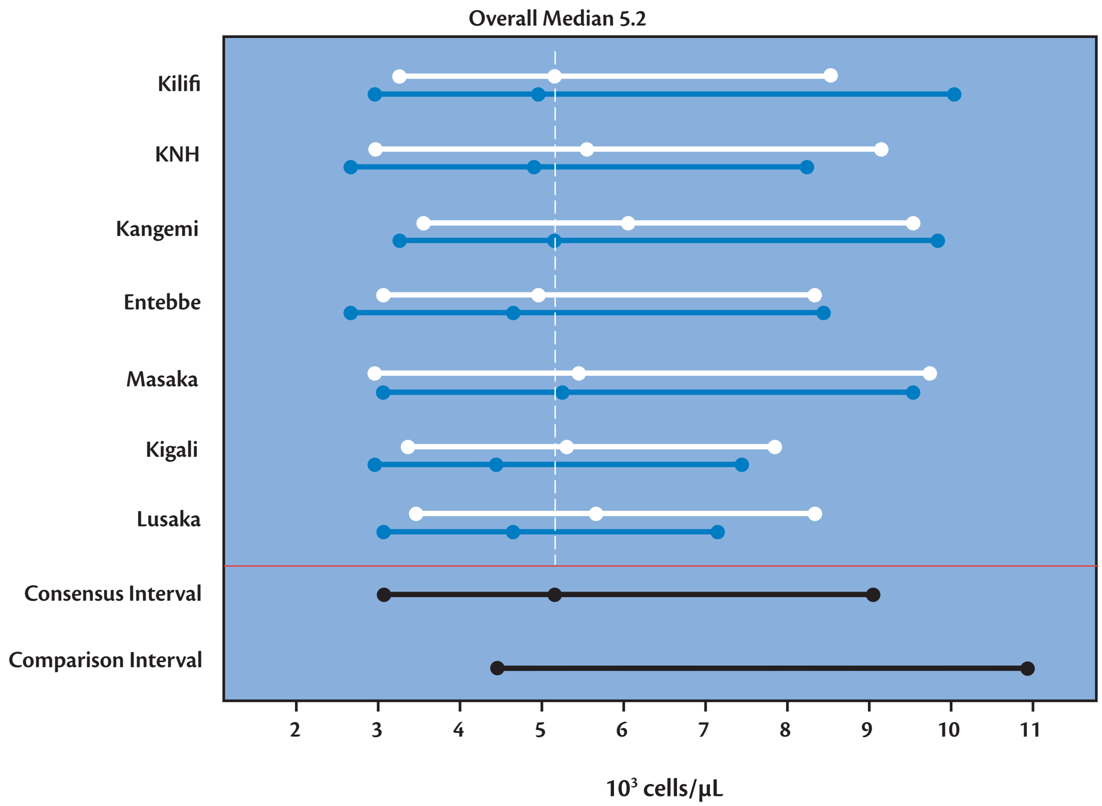
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 27: WBC counts 95% intervals and medians by research center and gender

Consensus interval: 3.1 to 9.1
Comparison interval: 4.5 to 11.0
White: Females, Blue: Males, Black: Overall



3.7. Neutrophils (count and %)

Neutrophil counts (x 10^3 cells/µL)

Results

Table 24 shows the number of subjects with data included in the analysis. Figures 28, 29, and 30 show the neutrophil counts distribution overall, by gender and by research center, respectively. Table 25 shows the distribution of neutrophil counts by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 33 by research center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (x 10^3 cells/µL)

Comparison Interval: 1.8 to 7.7
All centers, consensus interval: 1.0 to 5.3

Table 24: Number of observations, neutrophil counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	185	51.39	175	48.61	360
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1082	51.45	1021	48.55	2103

Figure 28: Frequency distribution of neutrophil counts

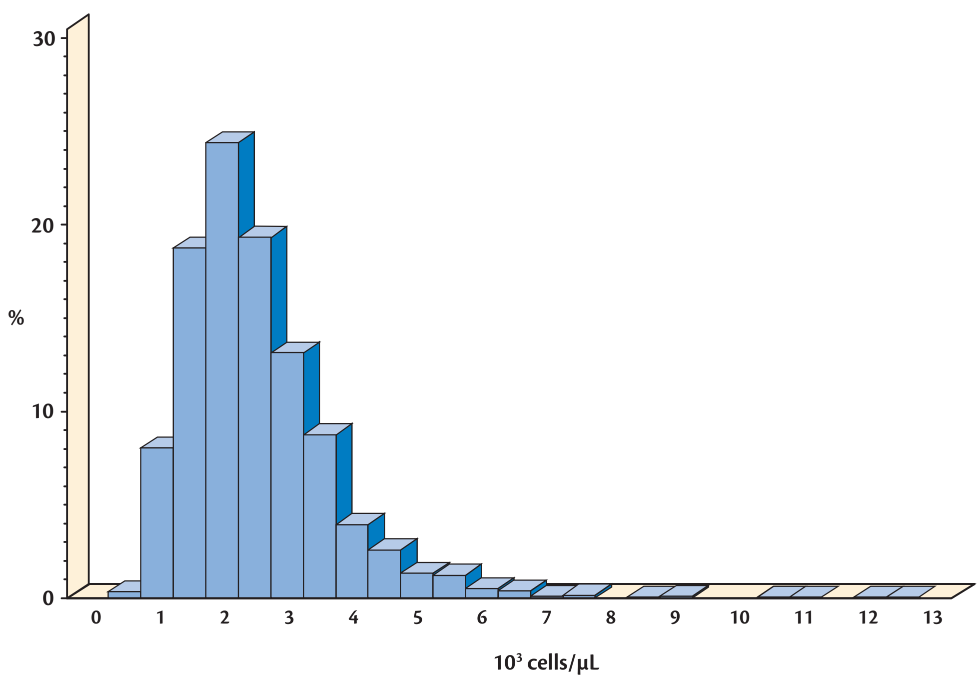


Figure 29: Frequency distribution of neutrophil counts by gender

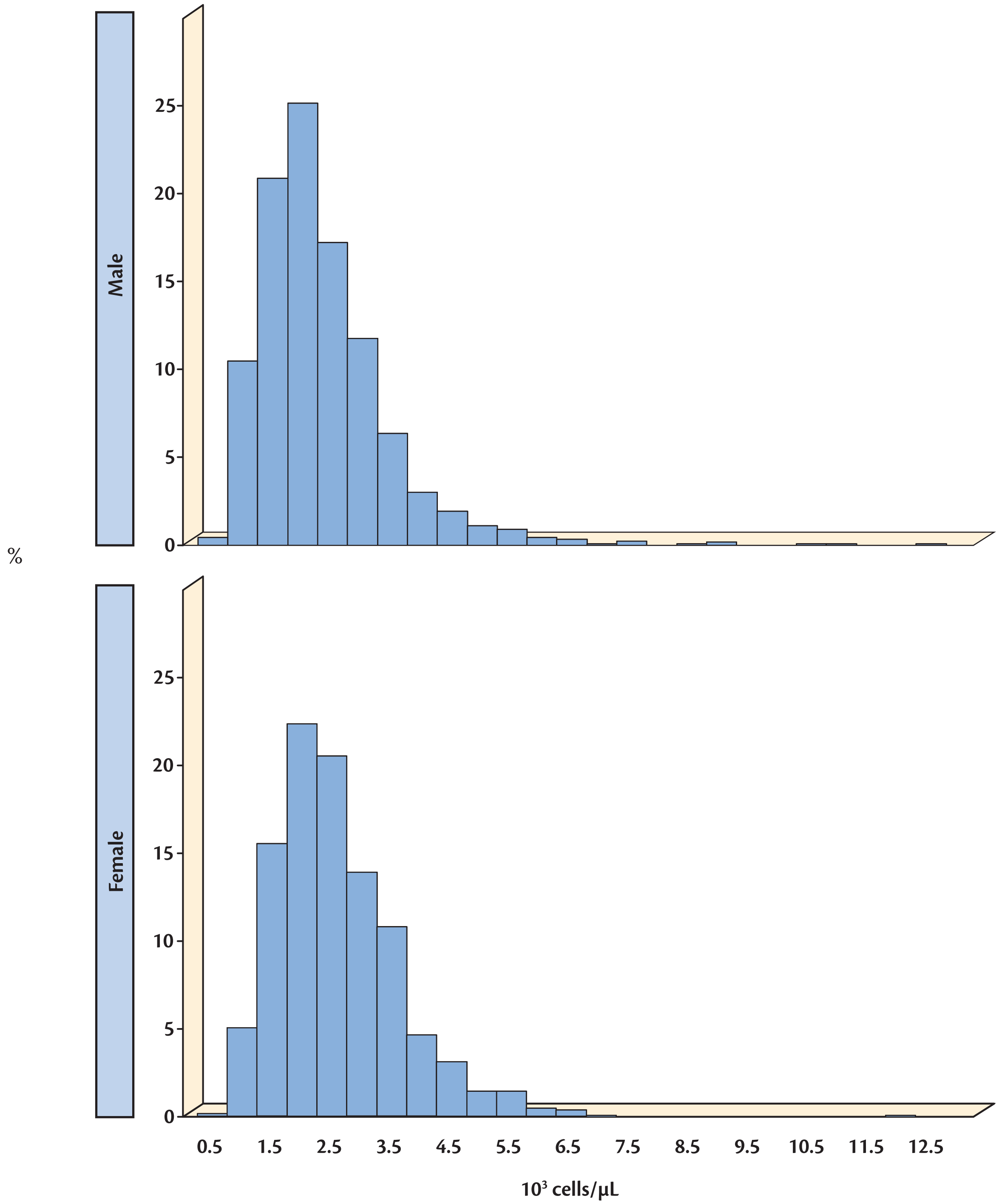


Figure 30: Frequency distribution of neutrophil counts by research center

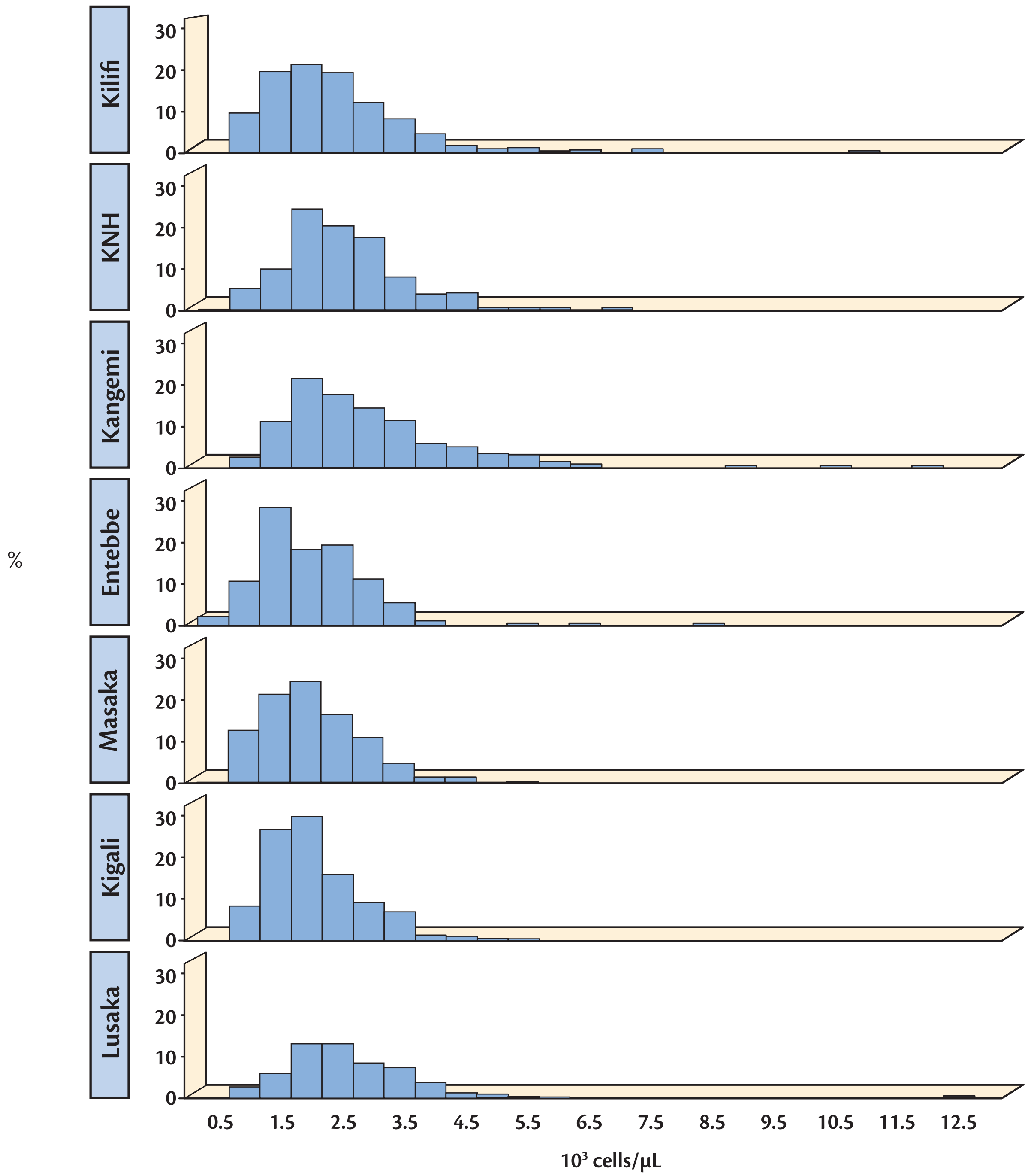


Table 25: Neutrophil counts distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	2.5 (1.0)	2.36	0.43 to 4.55	1.1 to 5.3	0.8 to 6.5
	KNH	99	2.8 (1.1)	2.58	0.68 to 4.89	1.1 to 5.5	0.7 to 7.0
	Kangemi	175	3.1 (1.4)	2.87	0.33 to 5.88	1.3 to 5.9	1.0 to 12.0
	Entebbe	98	2.2 (0.9)	2.02	0.47 to 3.96	1.1 to 3.8	1.0 to 6.4
	Masaka	148	2.2 (0.8)	2.045	0.63 to 3.78	1.0 to 4.3	0.7 to 4.7
	Kigali	188	2.3 (0.8)	2.155	0.68 to 3.92	1.1 to 4.3	1.0 to 5.4
	Lusaka	184	2.9 (0.9)	2.735	1.13 to 4.61	1.5 to 5.0	1.0 to 5.9
	Total	1021	2.6 (1.0)	2.41	0.49 to 4.69	1.1 to 5.2	0.7 to 12.0
Male	Kilifi	167	2.5 (1.4)	2.24	-0.31 to 5.31	0.9 to 6.7	0.8 to 10.8
	KNH	98	2.5 (1.2)	2.245	0.17 to 4.90	1.0 to 6.1	0.8 to 7.2
	Kangemi	185	2.9 (1.4)	2.5	-0.01 to 5.72	1.1 to 6.4	1.0 to 10.5
	Entebbe	96	2.0 (1.1)	1.825	-0.15 to 4.22	0.7 to 4.2	0.5 to 8.6
	Masaka	183	2.1 (0.8)	1.85	0.42 to 3.74	1.0 to 4.0	0.9 to 5.6
	Kigali	185	2.0 (0.8)	1.85	0.37 to 3.69	1.0 to 4.3	0.8 to 5.5
	Lusaka	168	2.4 (1.2)	2.205	0.08 to 4.75	1.1 to 4.4	0.8 to 12.6
	Total	1082	2.4 (1.2)	2.12	-0.02 to 4.74	1.0 to 5.4	0.5 to 12.6
Total	Kilifi	296	2.5 (1.3)	2.265	-0.01 to 5.00	1.0 to 5.7	0.8 to 10.8
	KNH	197	2.7 (1.1)	2.47	0.42 to 4.90	1.0 to 6.1	0.7 to 7.2
	Kangemi	360	3.0 (1.4)	2.63	0.15 to 5.80	1.2 to 6.0	1.0 to 12.0
	Entebbe	194	2.1 (1.0)	1.935	0.15 to 4.11	0.7 to 4.0	0.5 to 8.6
	Masaka	331	2.1 (0.8)	2	0.51 to 3.76	1.0 to 4.0	0.7 to 5.6
	Kigali	373	2.2 (0.8)	2.02	0.51 to 3.83	1.0 to 4.3	0.8 to 5.5
	Lusaka	352	2.7 (1.0)	2.44	0.56 to 4.74	1.1 to 4.8	0.8 to 12.6
	Total	2103	2.5 (1.1)	2.26	0.21 to 4.73	1.0 to 5.3	0.5 to 12.6

Research Center Comparisons

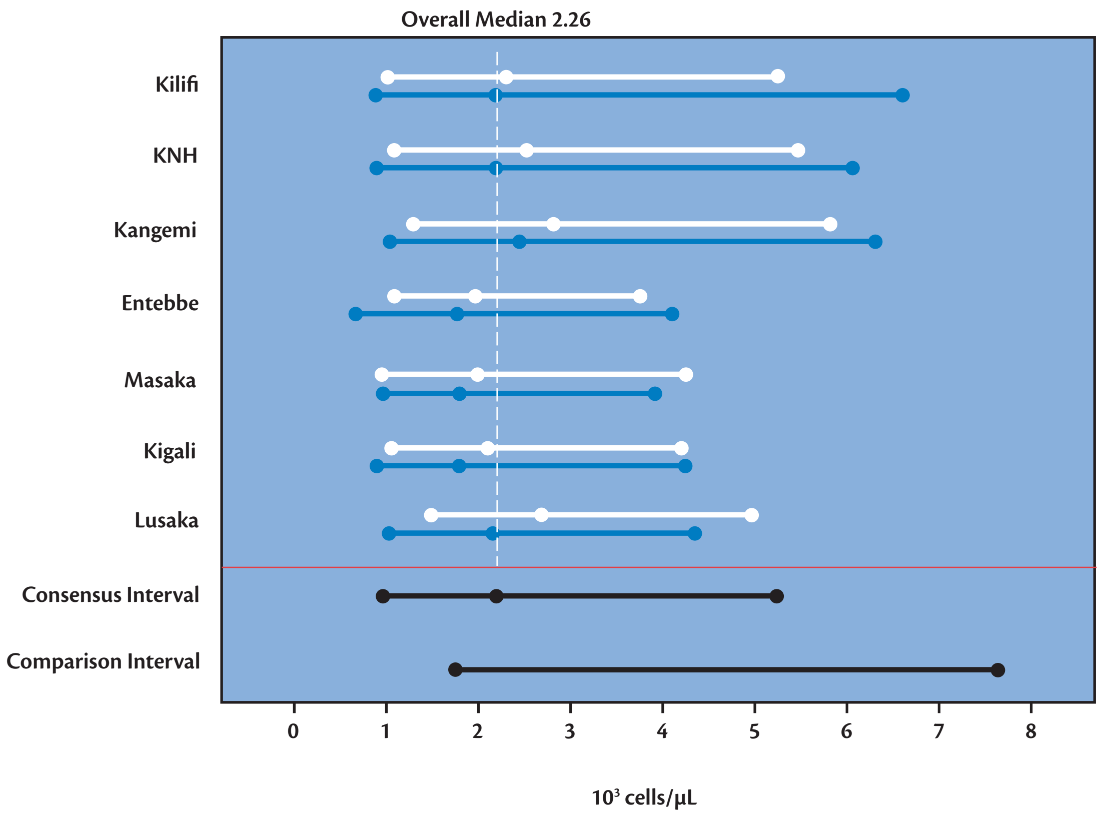
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 31: Neutrophil counts 95% intervals and medians by research center and gender

Consensus interval: 1.0 to 5.3
Comparison interval: 1.8 to 7.7
White: Females, Blue: Males, Black: Overall



Percent Neutrophils

Results

Table 26 shows the number of subjects with data included in the analysis. Figures 32, 33, and 34 show the percent neutrophils distribution overall, by gender and by research center, respectively. Table 27 shows the distribution of percent neutrophils by research center and gender, together with the stratified 95% reference intervals. The same percent intervals and median values are shown in Figure 35, by research center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (%)

Comparison interval: *40 to 70*
All centers, consensus interval: *25 to 66*

Table 26: Number of observations, percent neutrophils

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	185	51.39	175	48.61	360
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1082	51.45	1021	48.55	2103

Figure 32: Frequency distribution of percent neutrophils results

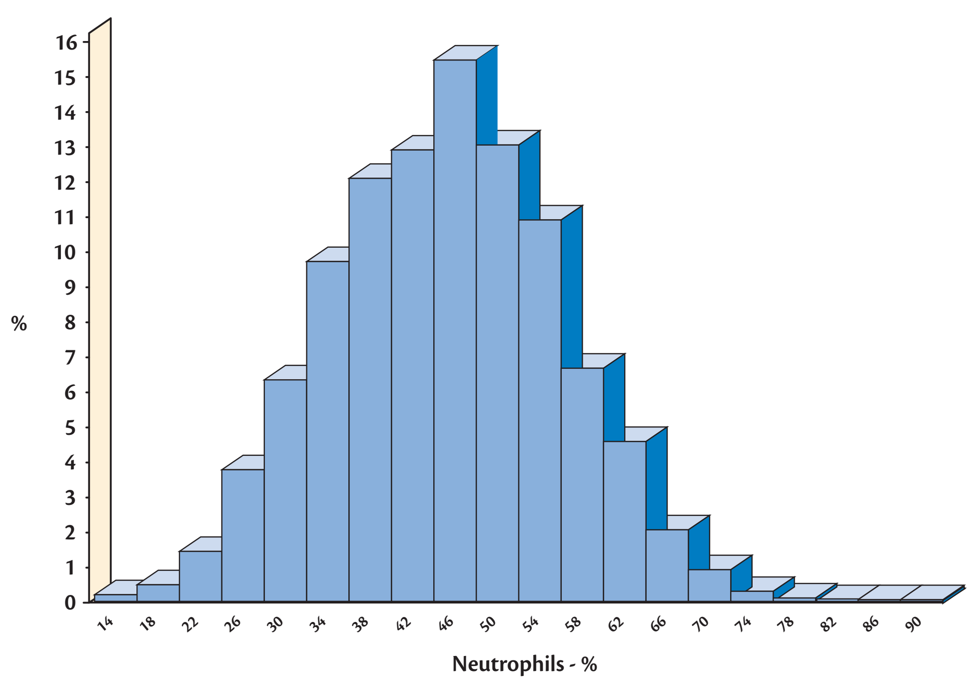


Figure 33: Frequency distribution of percent neutrophils results by gender

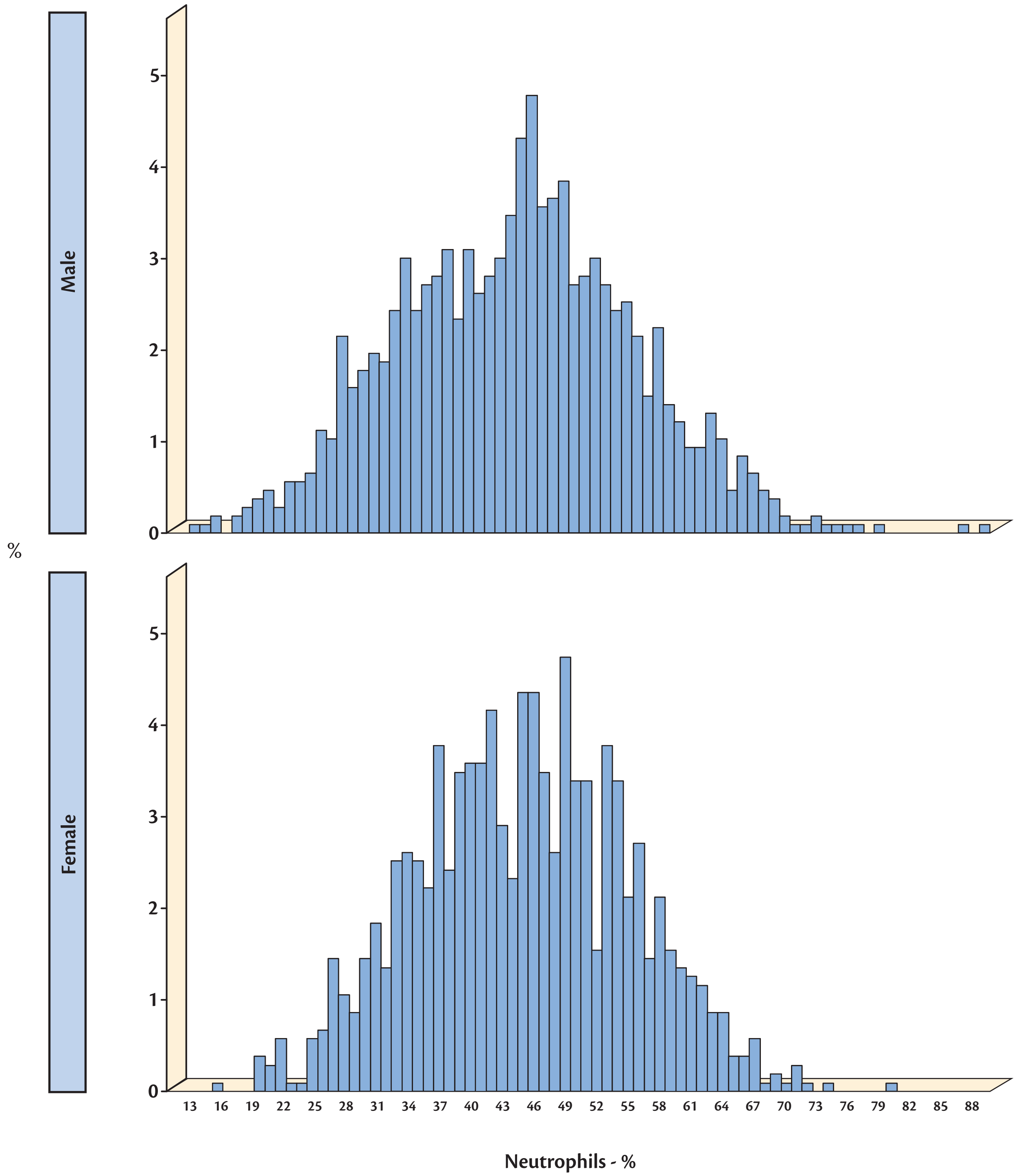


Figure 34: Frequency distribution of percent neutrophils by research center

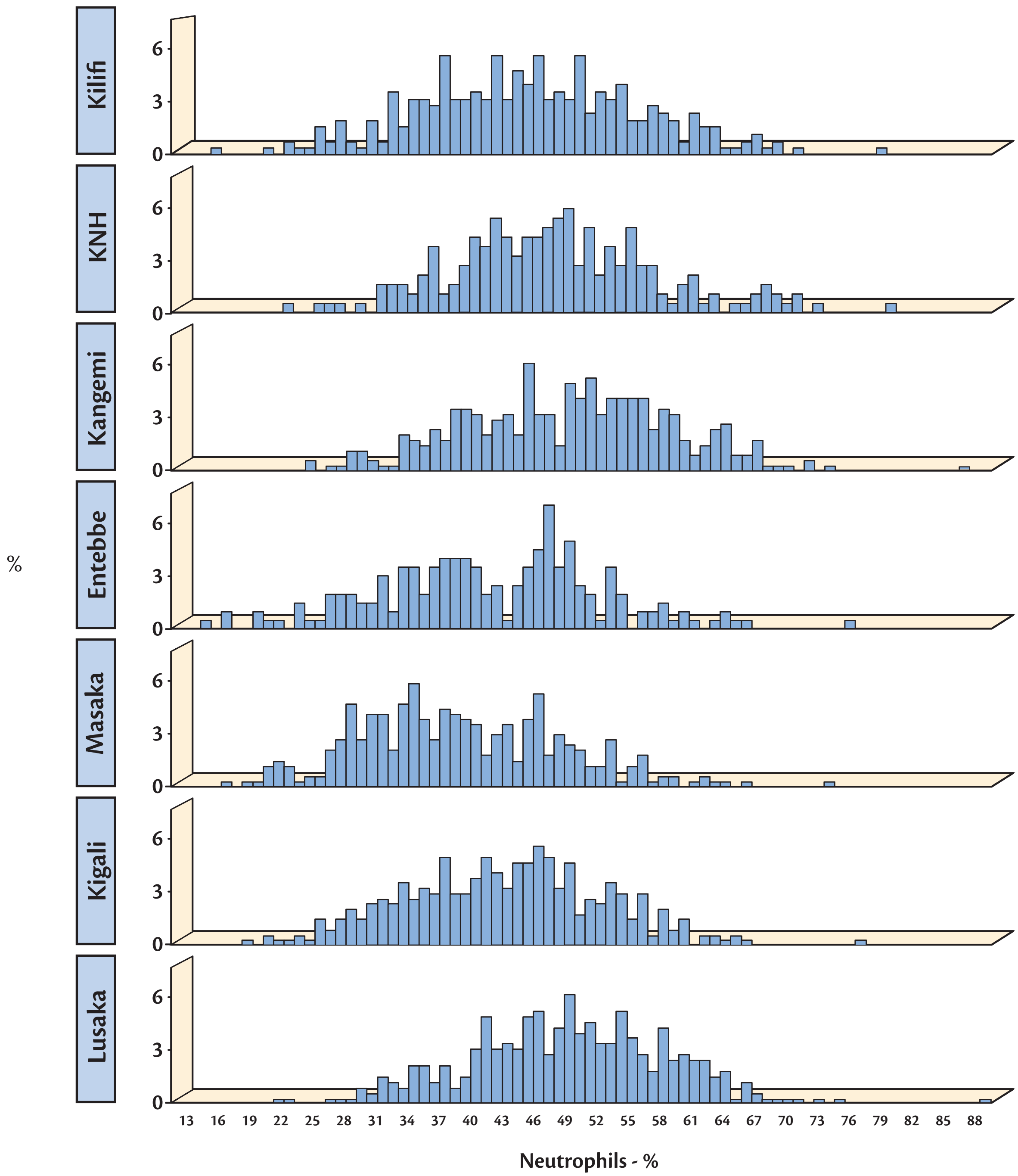


Table 27: Percent neutrophils results by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	45.1 (10.2)	45.2	24.75 to 65.43	26.4 to 63.0	21.5 to 67.4
	KNH	99	47.5 (9.3)	47.8	28.82 to 66.16	30.8 to 67.9	21.8 to 71.2
	Kangemi	175	47.9 (9.6)	48.5	28.70 to 67.01	29.4 to 67.1	27.3 to 73.7
	Entebbe	98	42.7 (9.5)	41.75	23.71 to 61.76	25.6 to 63.8	20.0 to 66.3
	Masaka	148	39.0 (9.7)	38.2	19.63 to 58.44	20.6 to 58.6	15.9 to 62.3
	Kigali	188	42.7 (9.2)	42.35	24.34 to 61.00	24.7 to 58.6	20.4 to 64.5
	Lusaka	184	49.2 (9.1)	49.15	30.92 to 67.43	31.1 to 66.0	21.5 to 71.2
	Total	1021	45.0 (10.1)	45.2	24.85 to 65.11	25.9 to 64.2	15.9 to 73.7
Male	Kilifi	167	45.0 (11.2)	44.6	22.59 to 67.34	24.7 to 68.2	15.4 to 79.1
	KNH	98	47.4 (10.2)	46.65	26.97 to 67.89	28.6 to 69.4	25.4 to 73.3
	Kangemi	185	49.7 (10.5)	49.9	28.60 to 70.74	28.0 to 67.3	24.1 to 86.8
	Entebbe	96	39.9 (11.7)	38.5	16.41 to 63.35	16.4 to 60.4	13.8 to 75.9
	Masaka	183	38.4 (10.0)	37.1	18.42 to 58.46	20.7 to 58.7	17.7 to 73.7
	Kigali	185	42.6 (10.1)	43.5	22.45 to 62.80	23.0 to 62.5	17.6 to 76.9
	Lusaka	168	48.5 (10.5)	48.75	27.58 to 69.41	29.2 to 67.0	21.2 to 89.0
	Total	1082	44.6 (11.3)	44.95	22.03 to 67.15	23.7 to 66.8	13.8 to 89.0
Total	Kilifi	296	45.0 (10.7)	44.85	23.54 to 66.50	25.2 to 67.0	15.4 to 79.1
	KNH	197	47.5 (9.8)	46.9	27.93 to 66.99	28.6 to 69.4	21.8 to 73.3
	Kangemi	360	48.8 (10.1)	49.1	28.57 to 69.00	28.5 to 67.2	24.1 to 86.8
	Entebbe	194	41.3 (10.7)	41.2	19.84 to 62.80	19.2 to 63.8	13.8 to 75.9
	Masaka	331	38.7 (9.9)	37.7	18.98 to 58.43	20.7 to 58.6	15.9 to 73.7
	Kigali	373	42.6 (9.6)	43	23.41 to 61.89	24.7 to 60.4	17.6 to 76.9
	Lusaka	352	48.9 (9.8)	48.9	29.30 to 68.40	30.0 to 66.9	21.2 to 89.0
	Total	2103	44.8 (10.7)	45.1	23.36 to 66.20	24.7 to 65.6	13.8 to 89.0

Research Center Comparisons

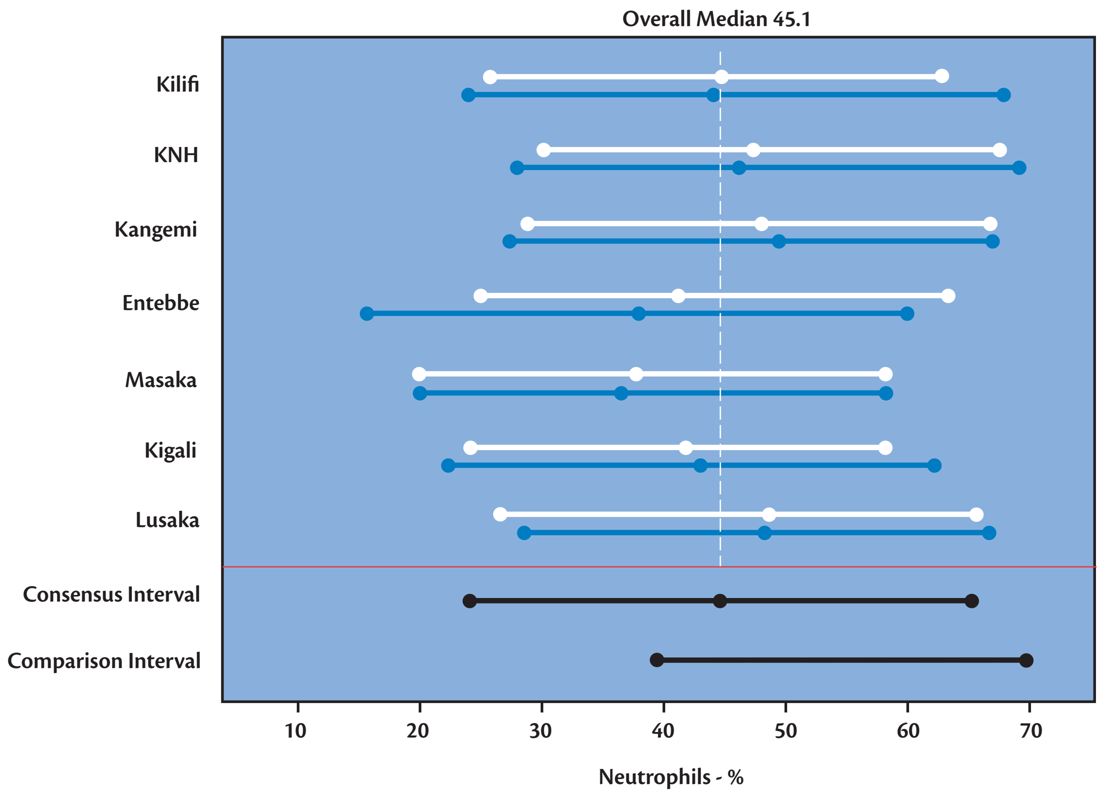
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 35: Percent neutrophils 95% intervals and medians by research center and gender

Consensus interval: 25 to 66
Comparison interval: 40 to 70
White: Females, Blue: Males, Black: Overall



3.8. Lymphocytes (count and %)

Lymphocyte counts (x 10³ cells/µL)

Results

Table 28 shows the number of subjects with data included in the analysis. Figures 36, 37, and 38 show the lymphocyte counts distribution overall, by gender and by research center, respectively. Table 29 shows the distribution of lymphocyte counts by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 39, by research center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (x 10³ cells/µL)

Comparison interval: *1.0 to 4.8*
All centers, consensus interval: *1.2 to 3.7*

Table 28: Number of observations, lymphocyte counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 36: Frequency distribution of lymphocyte counts

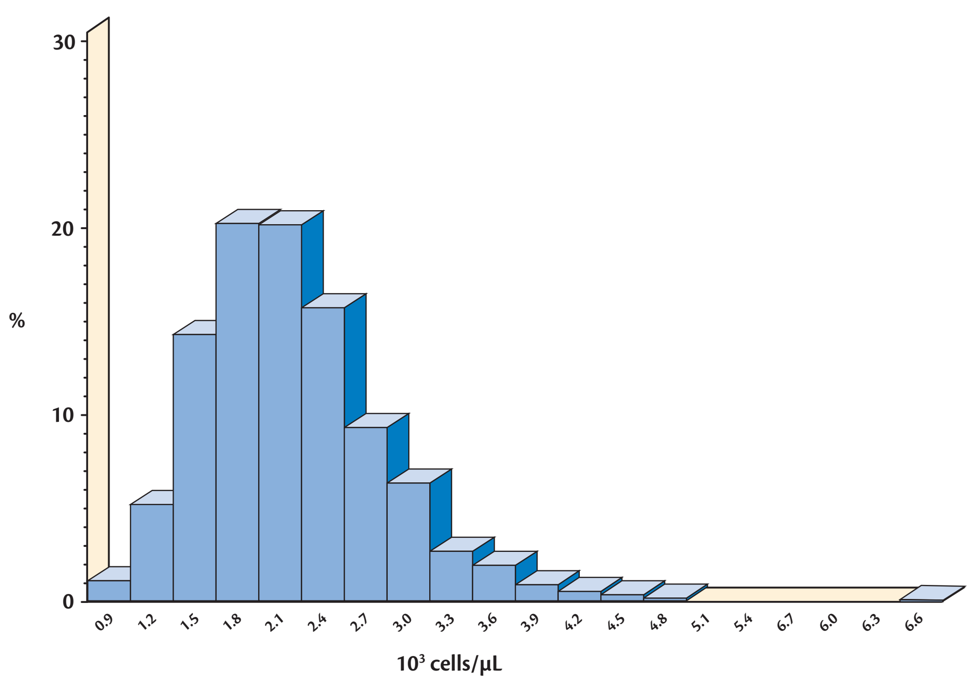


Figure 37: Frequency distribution of lymphocyte counts by gender

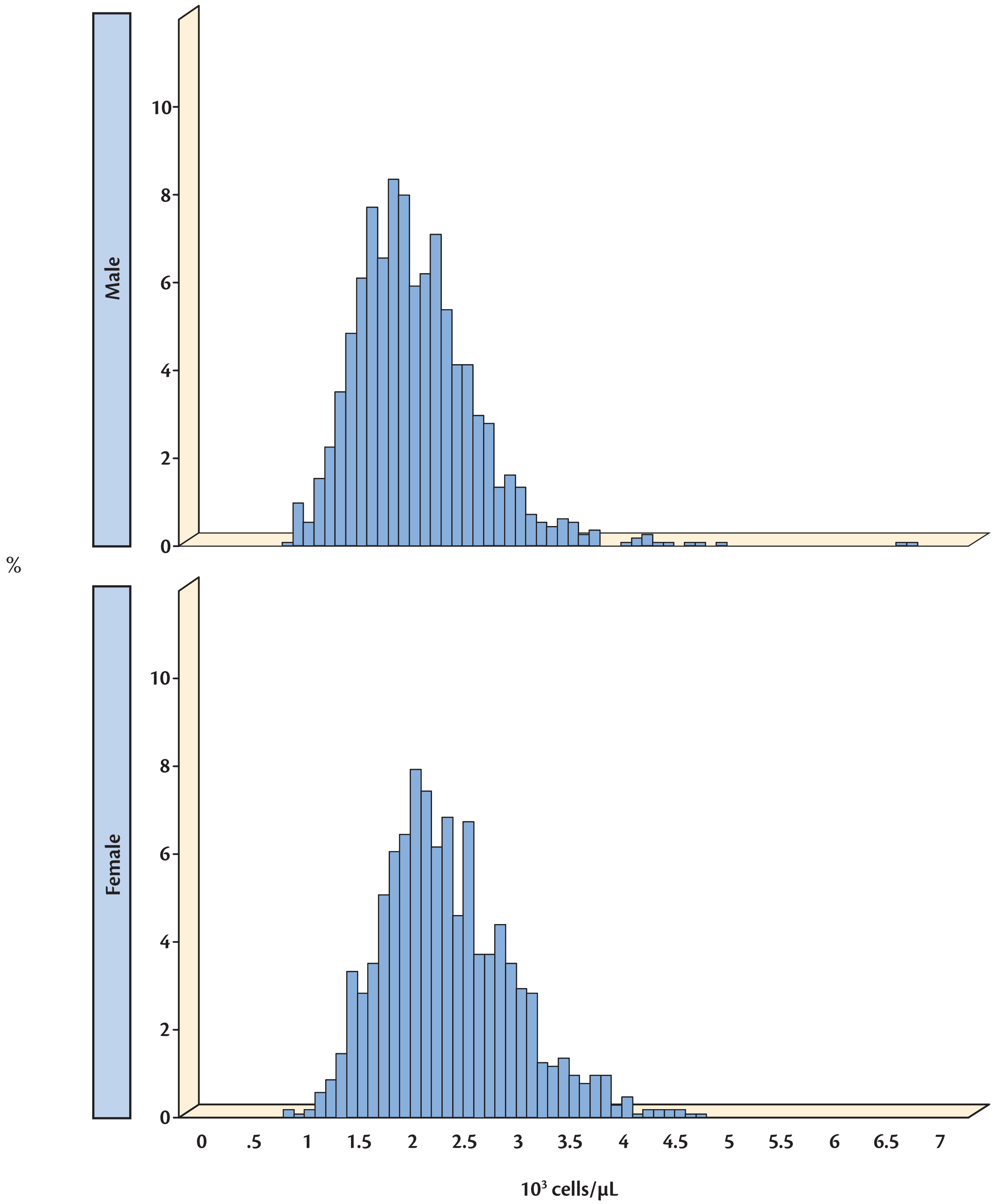


Figure 38: Frequency distribution of lymphocyte counts by research center

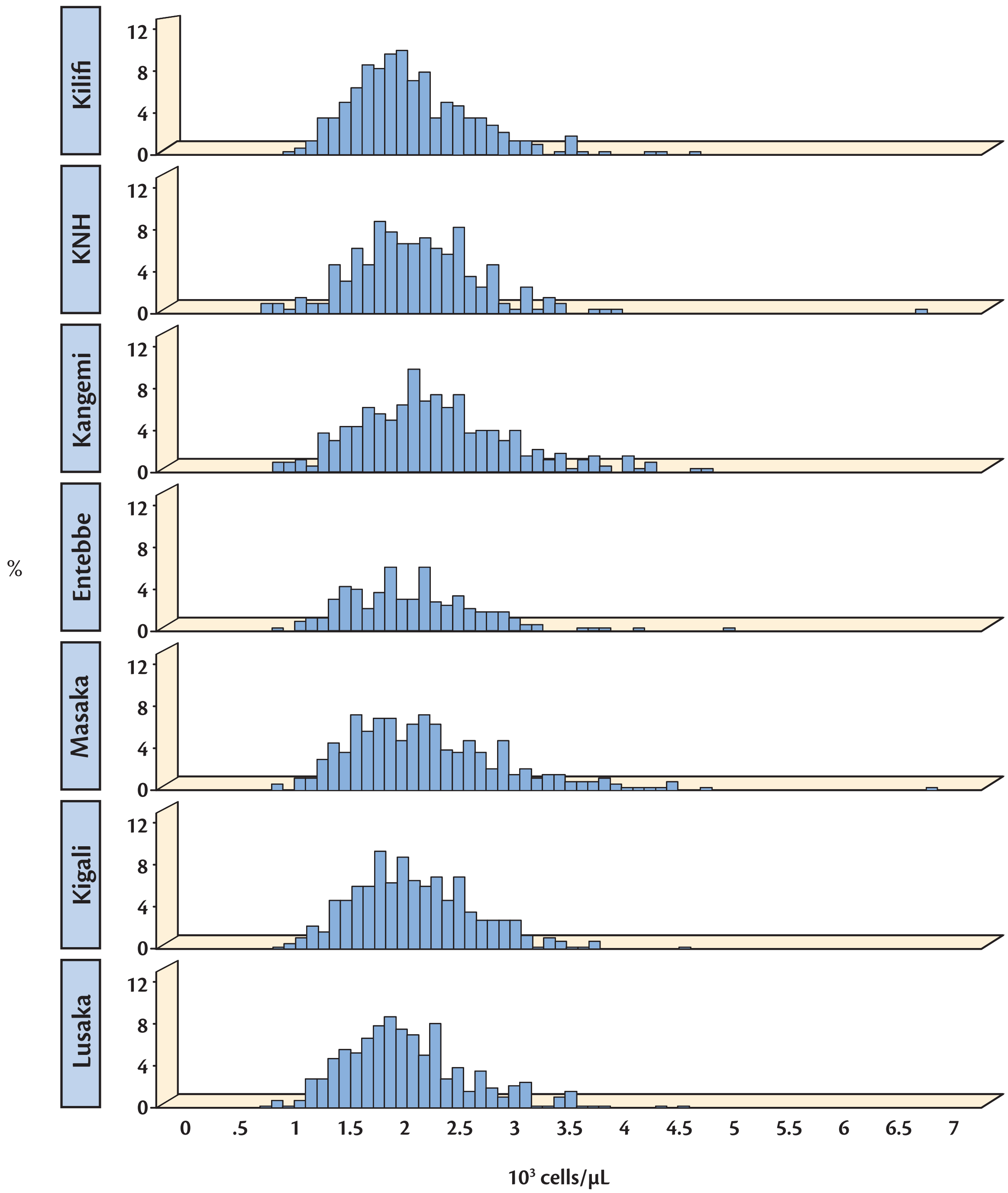


Table 29: Distribution of lymphocyte counts by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	2.2 (0.5)	2.11	1.09 to 3.28	1.3 to 3.5	1.2 to 4.3
	KNH	99	2.3 (0.6)	2.29	1.17 to 3.44	1.0 to 3.4	0.8 to 3.9
	Kangemi	176	2.5 (0.7)	2.42	1.17 to 3.87	1.4 to 4.0	1.0 to 4.6
	Entebbe	98	2.1 (0.6)	2.06	0.95 to 3.33	1.2 to 3.7	1.1 to 4.1
	Masaka	148	2.4 (0.8)	2.205	0.80 to 3.93	1.3 to 4.0	0.9 to 4.7
	Kigali	188	2.3 (0.6)	2.24	1.14 to 3.39	1.2 to 3.5	1.1 to 4.5
	Lusaka	184	2.3 (0.6)	2.135	1.07 to 3.44	1.4 to 3.5	1.1 to 4.5
	Total	1022	2.3 (0.6)	2.21	1.03 to 3.58	1.3 to 3.8	0.8 to 4.7
Male	Kilifi	167	2.0 (0.6)	1.93	0.88 to 3.18	1.2 to 3.5	1.0 to 4.6
	KNH	98	2.0 (0.7)	1.85	0.61 to 3.37	1.1 to 3.4	0.9 to 6.6
	Kangemi	186	2.1 (0.6)	1.995	0.80 to 3.30	1.0 to 3.7	0.9 to 4.7
	Entebbe	96	2.0 (0.6)	1.99	0.86 to 3.22	1.1 to 3.0	0.9 to 4.9
	Masaka	183	2.2 (0.7)	2.09	0.78 to 3.55	1.1 to 3.5	0.9 to 6.7
	Kigali	185	2.0 (0.5)	1.87	0.97 to 2.93	1.1 to 3.0	0.9 to 3.7
	Lusaka	168	1.9 (0.5)	1.83	0.81 to 2.92	1.0 to 3.1	0.8 to 3.6
	Total	1083	2.0 (0.6)	1.93	0.81 to 3.22	1.1 to 3.4	0.8 to 6.7
Total	Kilifi	296	2.1 (0.6)	2	0.96 to 3.23	1.3 to 3.5	1.0 to 4.6
	KNH	197	2.1 (0.6)	2.11	0.85 to 3.45	1.0 to 3.4	0.8 to 6.6
	Kangemi	362	2.3 (0.7)	2.195	0.90 to 3.66	1.1 to 4.0	0.9 to 4.7
	Entebbe	194	2.1 (0.6)	2.03	0.90 to 3.28	1.2 to 3.6	0.9 to 4.9
	Masaka	331	2.3 (0.7)	2.14	0.78 to 3.73	1.2 to 3.9	0.9 to 6.7
	Kigali	373	2.1 (0.6)	2.03	1.01 to 3.21	1.2 to 3.3	0.9 to 4.5
	Lusaka	352	2.1 (0.6)	1.975	0.88 to 3.26	1.2 to 3.5	0.8 to 4.5
	Total	2105	2.2 (0.6)	2.07	0.88 to 3.43	1.2 to 3.7	0.8 to 6.7

Research Center Comparisons

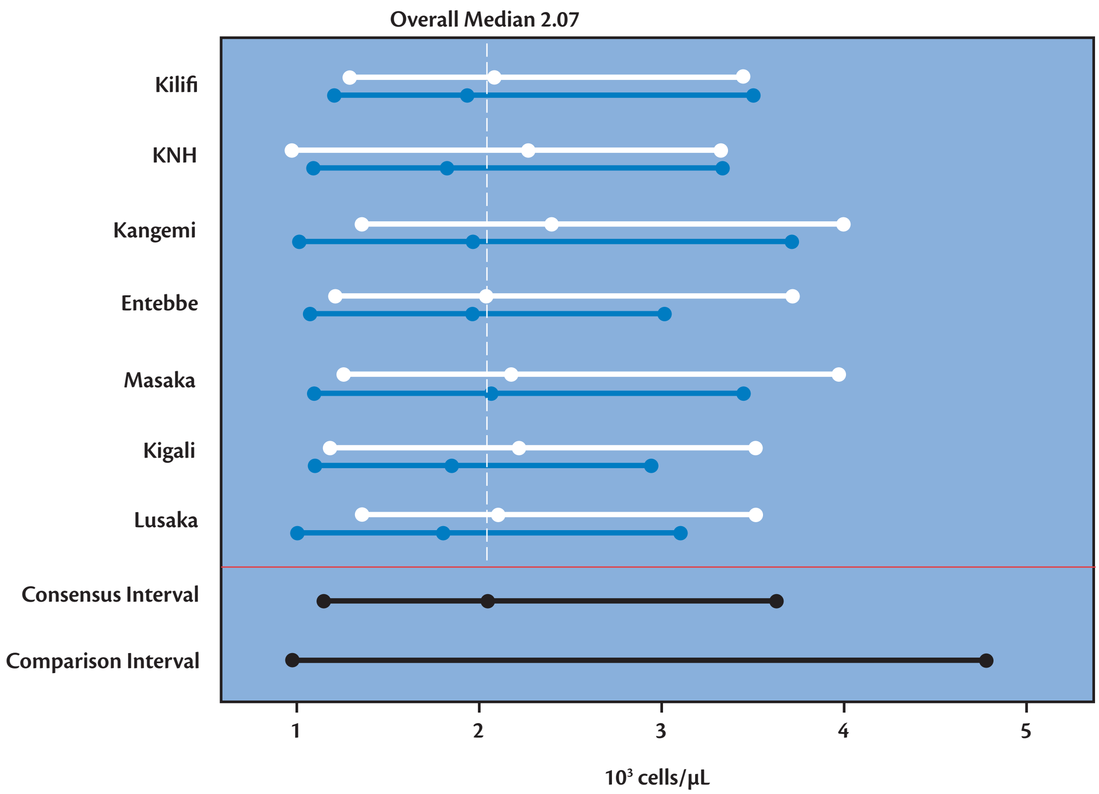
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 39: Lymphocyte counts 95% intervals and medians by research center and gender

Consensus interval: 1.2 to 3.7
Comparison interval: 1.0 to 4.8
White: Females, Blue: Males, Black: Overall



Percent Lymphocytes

Results

Table 30 shows the number of subjects with data included in the analysis. Figures 40, 41, and 42 show the percent lymphocytes distribution overall, by gender and by research center, respectively. Table 31 shows the distribution of percent lymphocytes by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 43, by research center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (%)

Comparison interval: *22 to 44*
All centers, consensus interval: *23 to 59*

Table 30: Number of observations, percent lymphocytes

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 40: Frequency distribution of percent lymphocytes

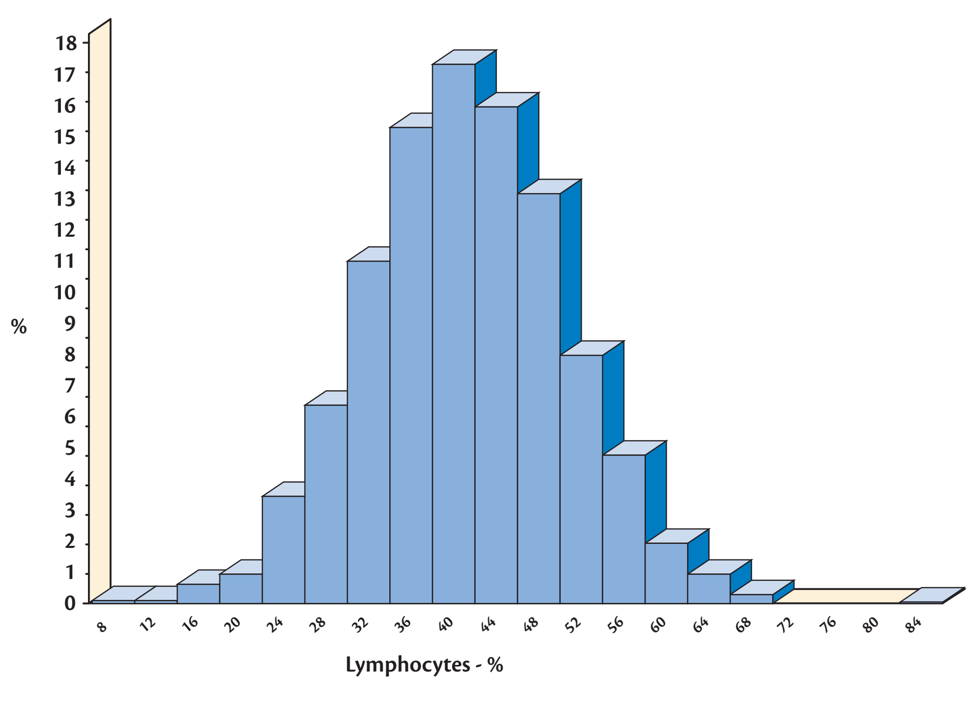


Figure 41: Frequency distribution of percent lymphocytes by gender

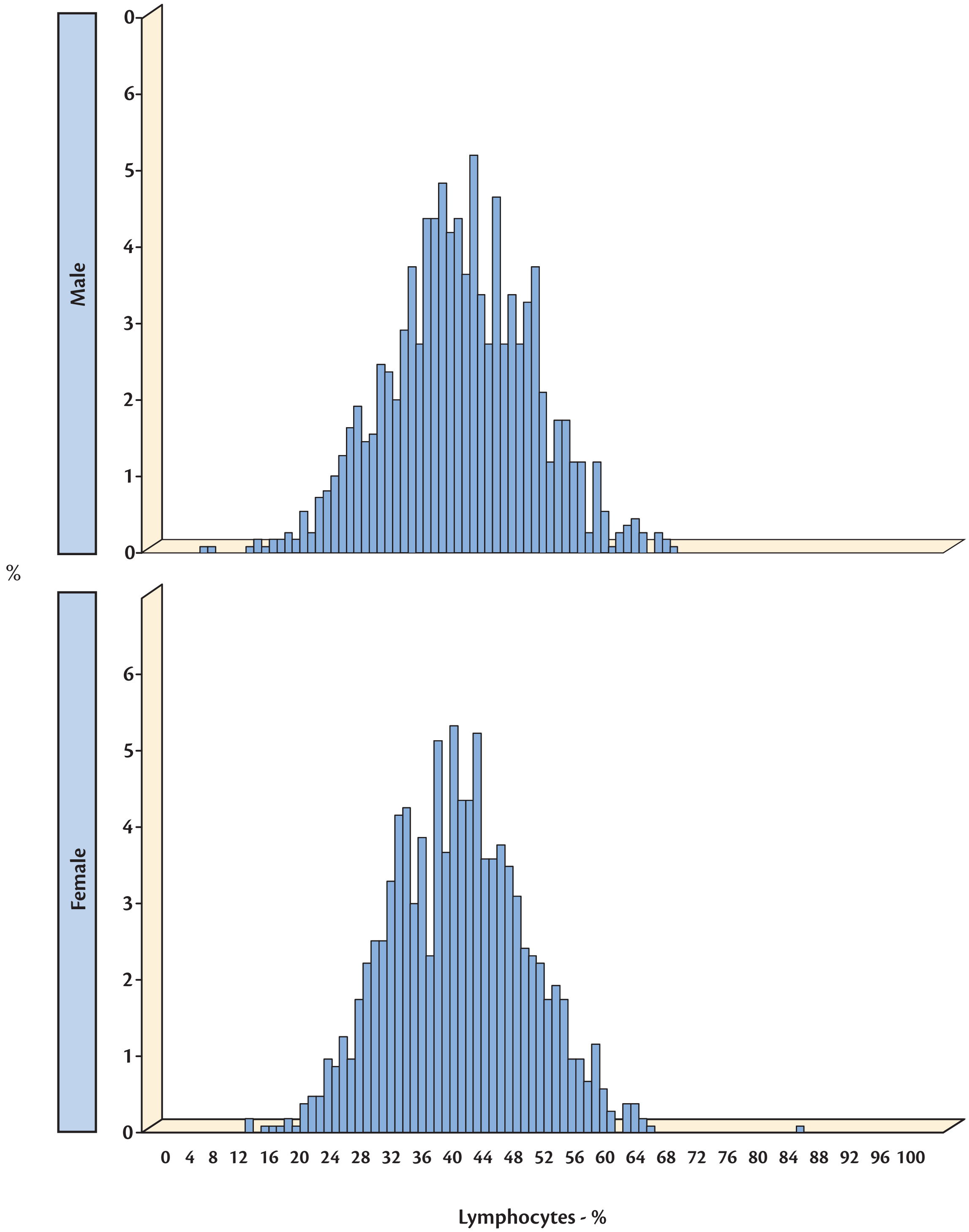


Figure 42: Frequency distribution of percent lymphocytes by research center

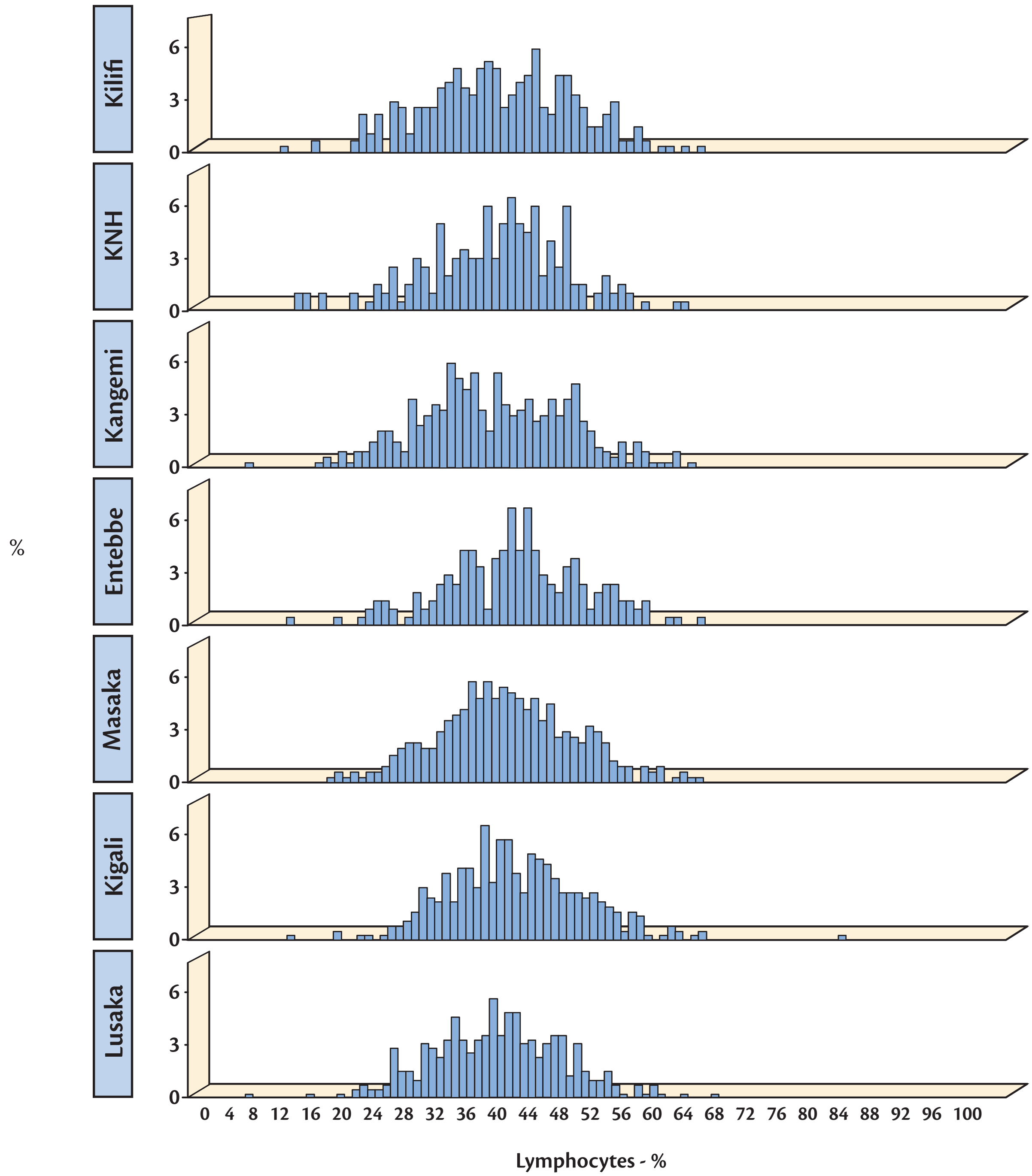


Table 31: Percent lymphocytes distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	41.5 (9.1)	41.1	23.33 to 59.72	25.3 to 57.5	22.5 to 60.6
	KNH	99	40.9 (8.2)	41.4	24.51 to 57.25	23.9 to 56.7	14.5 to 64.1
	Kangemi	176	41.2 (9.2)	41	22.80 to 59.51	23.0 to 59.3	16.5 to 64.9
	Entebbe	98	42.4 (8.2)	42.8	25.99 to 58.88	25.0 to 57.0	20.0 to 59.4
	Masaka	148	42.0 (8.8)	41.8	24.31 to 59.70	24.1 to 60.0	18.9 to 65.1
	Kigali	188	43.5 (9.2)	42.45	25.12 to 61.94	29.4 to 63.4	23.0 to 85.2
	Lusaka	184	39.4 (8.0)	39.75	23.43 to 55.34	24.4 to 54.4	21.3 to 60.0
	Total	1022	41.5 (8.8)	41.4	23.92 to 59.16	25.0 to 59.2	14.5 to 85.2
Male	Kilifi	167	39.6 (9.6)	39.8	20.29 to 58.88	22.0 to 58.0	13.1 to 66.4
	KNH	98	39.5 (9.7)	40.95	20.05 to 58.88	17.7 to 56.0	15.7 to 63.2
	Kangemi	186	38.2 (x 10.1)	37.3	18.04 to 58.26	20.0 to 58.1	8.4 to 63.3
	Entebbe	96	42.4 (9.7)	42.35	22.89 to 61.82	24.2 to 61.6	13.6 to 66.4
	Masaka	183	40.9 (8.8)	40.2	23.28 to 58.46	23.3 to 59.4	19.5 to 65.9
	Kigali	185	42.4 (8.6)	42	25.22 to 59.64	26.4 to 58.6	14.4 to 67.2
	Lusaka	168	39.5 (9.6)	39.1	20.28 to 58.72	22.4 to 59.4	7.0 to 68.1
	Total	1083	40.3 (9.5)	40.2	21.25 to 59.28	22.1 to 58.6	7.0 to 68.1
Total	Kilifi	296	40.4 (9.4)	40.15	21.54 to 59.32	22.7 to 58.0	13.1 to 66.4
	KNH	197	40.2 (9.0)	41.1	22.22 to 58.13	17.7 to 56.7	14.5 to 64.1
	Kangemi	362	39.6 (9.7)	39.45	20.13 to 59.10	21.5 to 59.1	8.4 to 64.9
	Entebbe	194	42.4 (9.0)	42.5	24.44 to 60.35	24.2 to 59.4	13.6 to 66.4
	Masaka	331	41.4 (8.8)	41.1	23.73 to 59.02	24.1 to 59.6	18.9 to 65.9
	Kigali	373	43.0 (8.9)	42.3	25.15 to 60.82	28.0 to 62.3	14.4 to 85.2
	Lusaka	352	39.4 (8.8)	39.4	21.87 to 57.00	23.1 to 57.6	7.0 to 68.1
	Total	2105	40.9 (9.2)	40.9	22.49 to 59.27	23.1 to 59.2	7.0 to 85.2

Research Center Comparisons

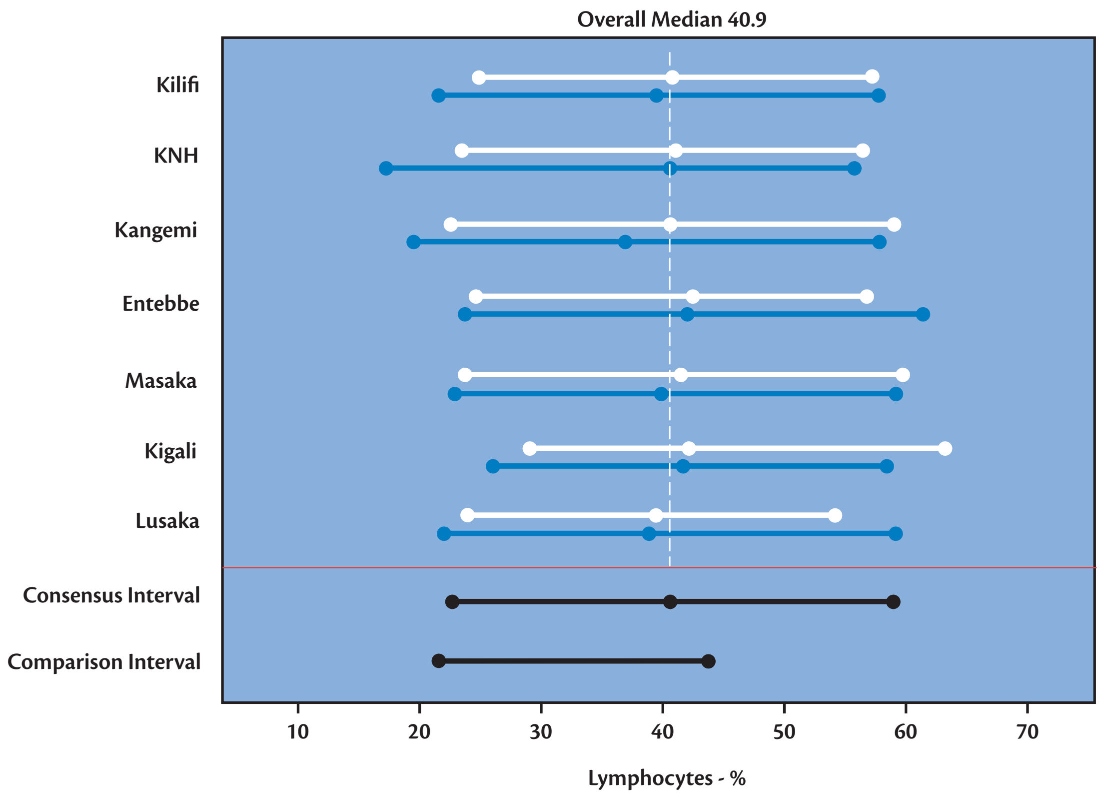
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 43: Percent lymphocytes 95% intervals and medians by research center and gender

Consensus interval: 23 to 59
Comparison interval: 22 to 44
White: Females, Blue: Males, Black: Overall



3.9. Monocytes (count and %)

Monocyte counts (x 10^3 cells/µL)

Results

Table 32 shows the number of subjects with data included in the analysis. Figures 44, 45, and 46 show the monocyte counts distribution overall, by gender and by research center, respectively. Table 33 shows the distribution of monocyte counts by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 47, by research center and gender. The comparison and final estimated consensus reference intervals are shown below.

Estimated Reference Intervals (x 10^3 cells/µL)

Comparison Interval: *0.0 to 0.8*
All centers, consensus interval: *0.20 to 0.78*

Table 32: Number of observations, monocyte counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	185	51.39	175	48.61	360
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1082	51.45	1021	48.55	2103

Figure 44: Frequency distribution of monocyte counts

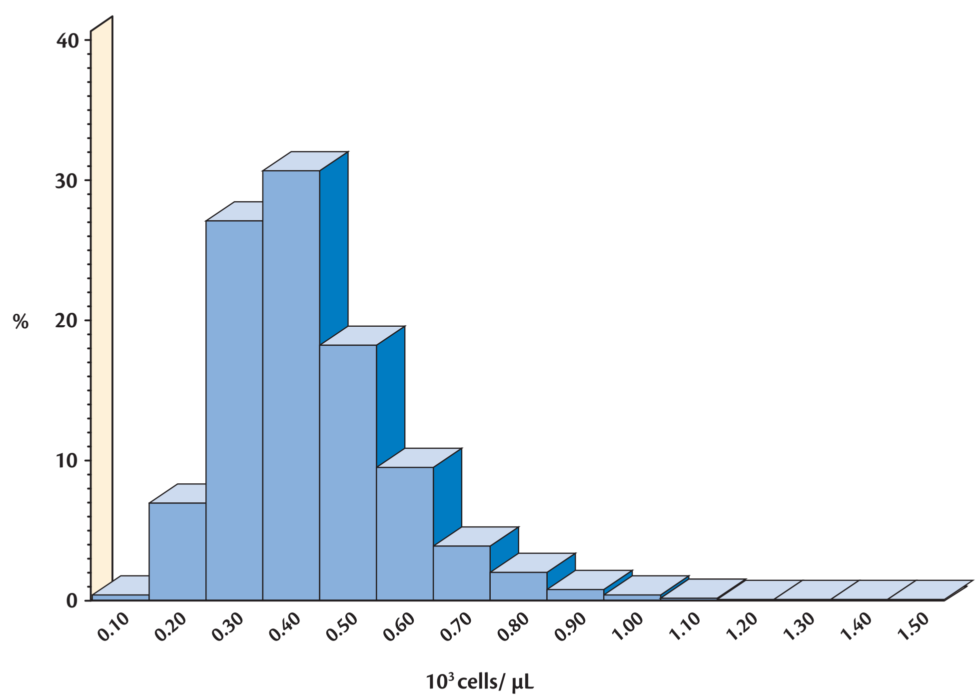


Figure 45: Frequency distribution of monocyte counts by gender

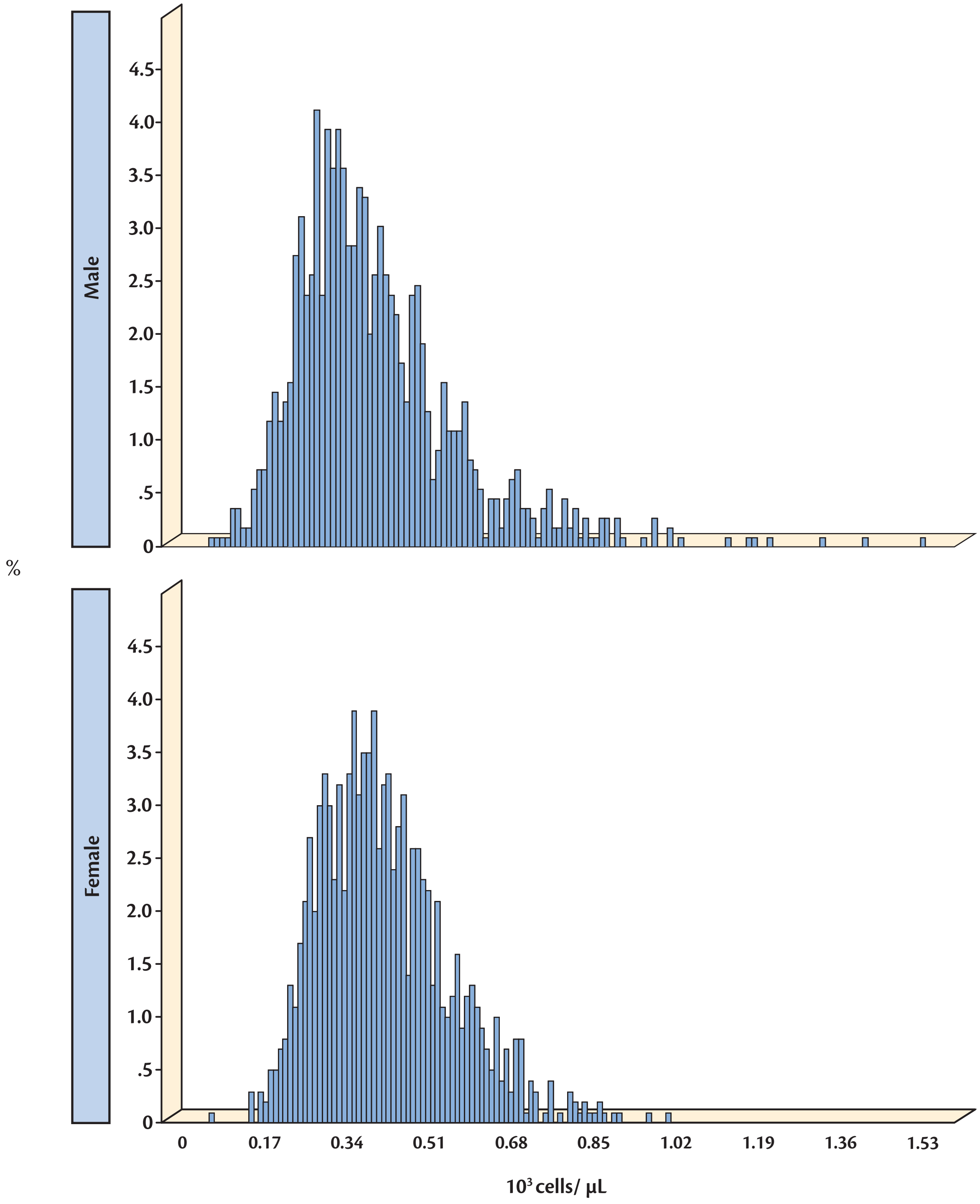


Figure 46: Frequency distribution of monocyte counts by research center

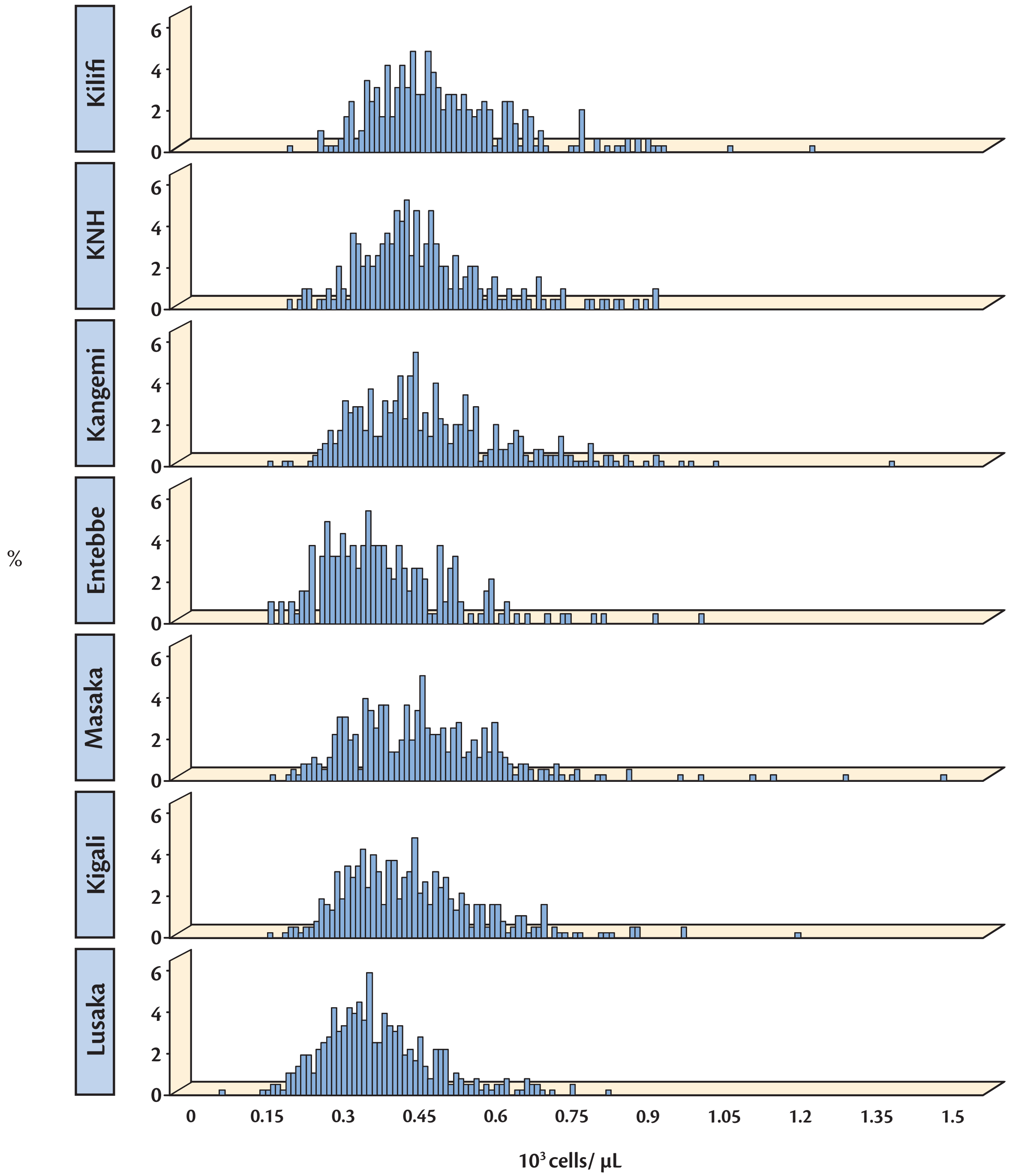


Table 33: Monocyte counts distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	0.4 (0.1)	0.39	0.15 to 0.66	0.21 to 0.72	0.18 to 0.84
	KNH	99	0.4 (0.1)	0.4	0.17 to 0.67	0.20 to 0.68	0.16 to 0.88
	Kangemi	175	0.4 (0.1)	0.41	0.15 to 0.72	0.22 to 0.79	0.14 to 0.89
	Entebbe	98	0.4 (0.1)	0.335	0.11 to 0.61	0.18 to 0.60	0.14 to 0.77
	Masaka	148	0.4 (0.1)	0.42	0.16 to 0.70	0.23 to 0.71	0.19 to 0.99
	Kigali	188	0.4 (0.1)	0.42	0.16 to 0.71	0.22 to 0.79	0.18 to 0.95
	Lusaka	184	0.4 (0.1)	0.36	0.14 to 0.62	0.19 to 0.68	0.06 to 0.75
	Total	1021	0.4 (0.1)	0.39	0.14 to 0.68	0.21 to 0.71	0.06 to 0.99
Male	Kilifi	167	0.4 (0.2)	0.4	0.12 to 0.76	0.23 to 0.82	0.12 to 1.14
	KNH	98	0.4 (0.2)	0.36	0.07 to 0.73	0.16 to 0.84	0.13 to 0.88
	Kangemi	185	0.4 (0.2)	0.4	0.08 to 0.80	0.21 to 0.88	0.11 to 1.35
	Entebbe	96	0.4 (0.1)	0.35	0.09 to 0.67	0.18 to 0.79	0.14 to 0.98
	Masaka	183	0.5 (0.2)	0.45	0.12 to 0.81	0.22 to 0.95	0.20 to 1.46
	Kigali	185	0.4 (0.1)	0.4	0.14 to 0.72	0.23 to 0.80	0.15 to 1.17
	Lusaka	168	0.4 (0.1)	0.345	0.13 to 0.60	0.19 to 0.65	0.15 to 0.82
	Total	1082	0.4 (0.2)	0.39	0.10 to 0.74	0.20 to 0.82	0.11 to 1.46
Total	Kilifi	296	0.4 (0.1)	0.395	0.13 to 0.72	0.22 to 0.80	0.12 to 1.14
	KNH	197	0.4 (0.1)	0.38	0.11 to 0.70	0.17 to 0.81	0.13 to 0.88
	Kangemi	360	0.4 (0.2)	0.4	0.11 to 0.76	0.21 to 0.82	0.11 to 1.35
	Entebbe	194	0.4 (0.1)	0.345	0.10 to 0.64	0.18 to 0.72	0.14 to 0.98
	Masaka	331	0.5 (0.2)	0.44	0.14 to 0.77	0.23 to 0.79	0.19 to 1.46
	Kigali	373	0.4 (0.1)	0.41	0.15 to 0.71	0.23 to 0.79	0.15 to 1.17
	Lusaka	352	0.4 (0.1)	0.35	0.14 to 0.61	0.19 to 0.67	0.06 to 0.82
	Total	2103	0.4 (0.1)	0.39	0.12 to 0.71	0.20 to 0.78	0.06 to 1.46

Research Center Comparisons

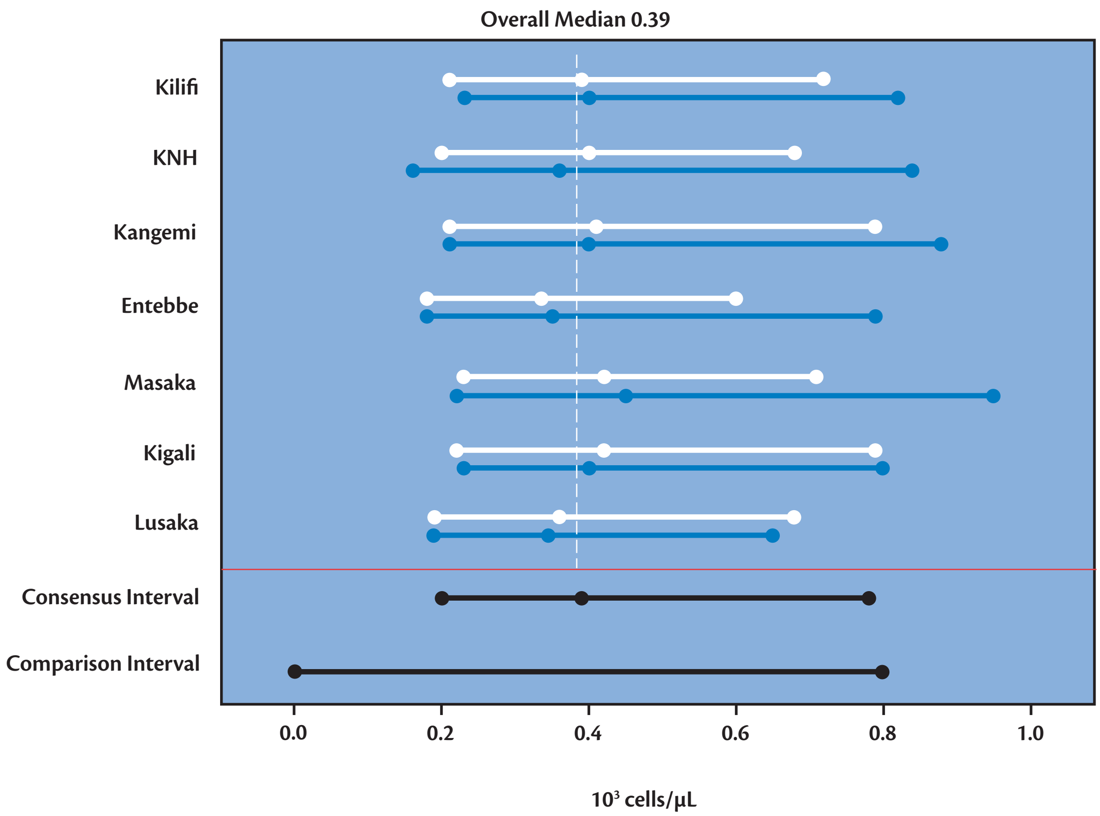
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 47: Monocyte counts 95% intervals and medians by research center and gender

Consensus interval: 0.20 to 0.78
Comparison interval: 0.0 to 0.8
White: Females, Blue: Males, Black: Overall



Percent Monocytes

Results

Table 34 shows the number of subjects with data included in the analysis. Figures 48, 49, and 50 show the percent monocytes distribution overall, by gender and by research center, respectively. Table 35 shows the distribution of percent monocytes by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 51, by research center and gender. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (%)

Comparison interval: *4.0 to 11.0*
All centers, consensus interval: *4.5 to 13.1*

Table 34: Number of observations, percent monocytes

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	185	51.39	175	48.61	360
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1082	51.45	1021	48.55	2103

Figure 48: Frequency distribution of percent monocytes

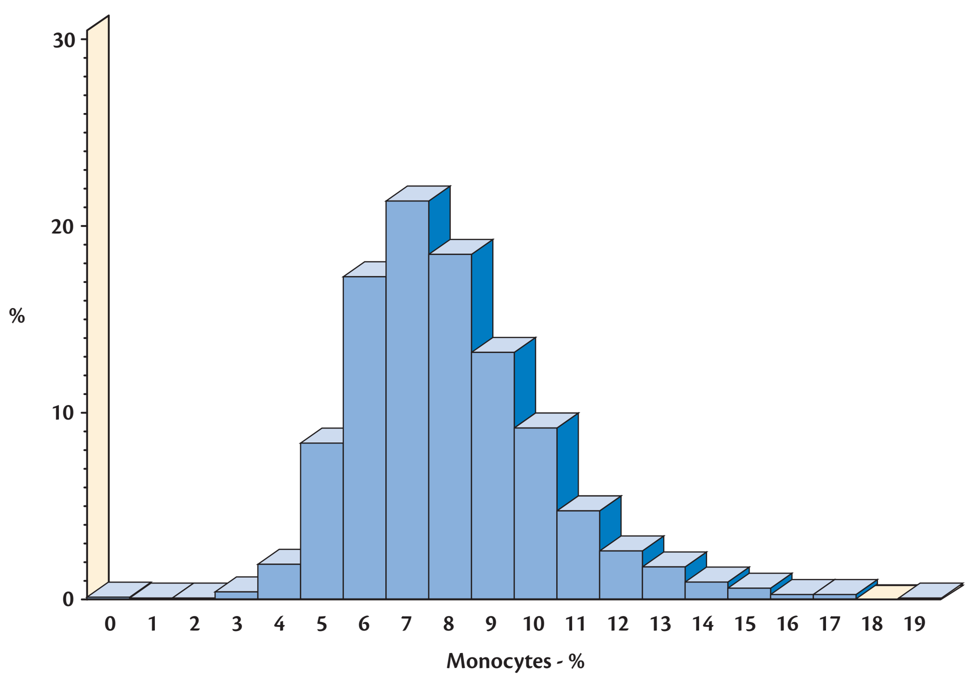


Figure 49: Frequency distribution of percent monocytes by gender

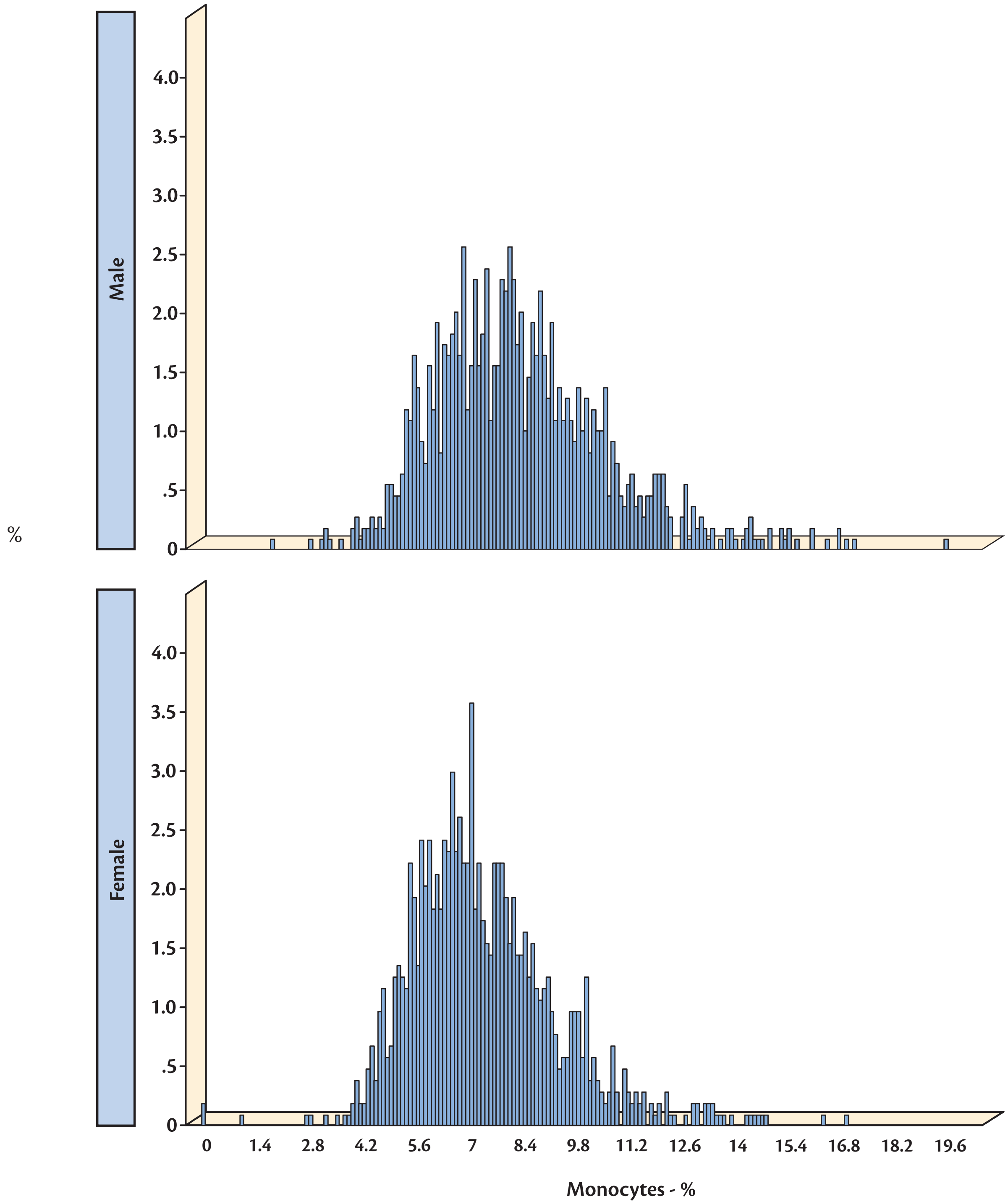


Figure 50: Frequency distribution of percent monocytes by research center

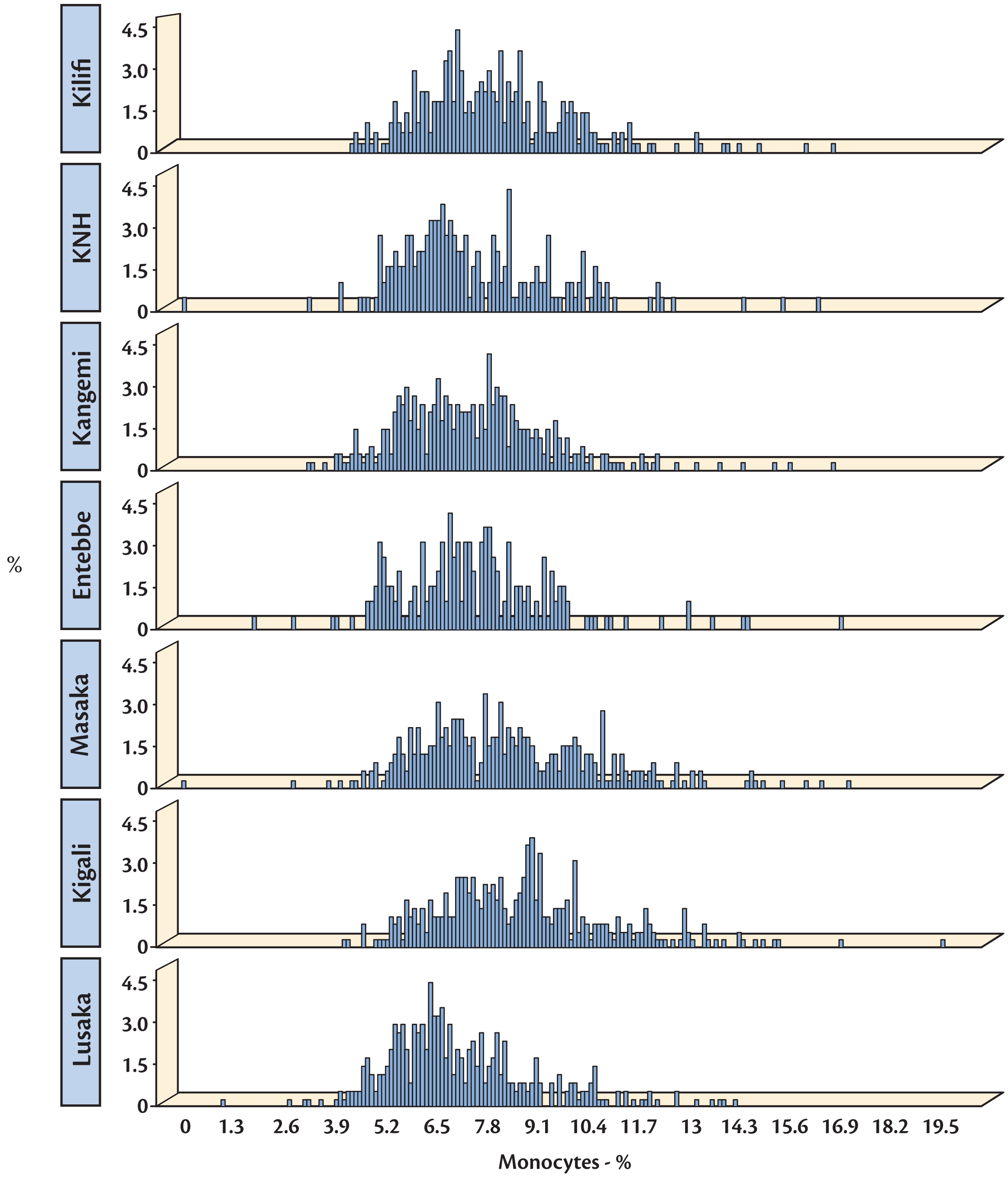


Table 35: Percent monocytes distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	7.6 (1.8)	7.4	4.02 to 11.13	4.6 to 11.4	4.3 to 14.7
	KNH	99	7.4 (2.1)	6.9	3.22 to 11.60	4.7 to 12.2	4.0 to 16.2
	Kangemi	175	6.9 (1.6)	6.8	3.70 to 10.14	4.3 to 11.0	3.2 to 12.1
	Entebbe	98	7.1 (2.1)	6.9	2.95 to 11.25	4.7 to 12.9	3.8 to 16.8
	Masaka	148	7.7 (2.1)	7.35	3.54 to 11.90	4.0 to 12.6	0.0 to 14.5
	Kigali	188	8.1 (2.0)	7.9	4.19 to 12.06	5.0 to 13.3	4.1 to 14.6
	Lusaka	184	6.6 (1.7)	6.4	3.10 to 10.05	4.0 to 11.1	1.0 to 13.8
	Total	1021	7.3 (2.0)	7	3.43 to 11.26	4.4 to 12.1	0.0 to 16.8
Male	Kilifi	167	8.3 (2.1)	8.1	4.09 to 12.52	5.3 to 13.8	4.4 to 16.6
	KNH	98	7.6 (2.0)	7.1	3.59 to 11.59	4.5 to 11.9	3.2 to 15.3
	Kangemi	185	7.9 (2.2)	7.8	3.57 to 12.26	4.1 to 13.7	3.3 to 16.6
	Entebbe	96	7.8 (1.9)	7.7	3.90 to 11.65	3.9 to 12.2	1.8 to 14.3
	Masaka	183	8.9 (2.5)	8.5	3.93 to 13.78	4.9 to 14.8	4.6 to 17.0
	Kigali	185	9.2 (2.4)	8.9	4.44 to 13.95	5.4 to 14.8	4.6 to 19.4
	Lusaka	168	7.7 (2.1)	7.4	3.43 to 11.87	4.2 to 12.1	3.1 to 14.1
	Total	1082	8.3 (2.3)	8	3.71 to 12.83	4.8 to 13.8	1.8 to 19.4
Total	Kilifi	296	8.0 (2.0)	7.75	3.99 to 11.98	4.7 to 13.1	4.3 to 16.6
	KNH	197	7.5 (2.0)	7	3.41 to 11.59	4.6 to 12.2	3.2 to 16.2
	Kangemi	360	7.4 (2.0)	7.3	3.47 to 11.39	4.2 to 12.0	3.2 to 16.6
	Entebbe	194	7.4 (2.0)	7.3	3.37 to 11.50	4.3 to 12.9	1.8 to 16.8
	Masaka	331	8.3 (2.4)	8.1	3.61 to 13.08	4.8 to 14.4	0.0 to 17.0
	Kigali	373	8.7 (2.2)	8.5	4.17 to 13.14	5.3 to 13.8	4.1 to 19.4
	Lusaka	352	7.1 (2.0)	6.6	3.10 to 11.08	4.1 to 11.9	1.0 to 14.1
	Total	2103	7.8 (2.2)	7.6	3.46 to 12.18	4.5 to 13.1	0.0 to 19.4

Research Center Comparisons

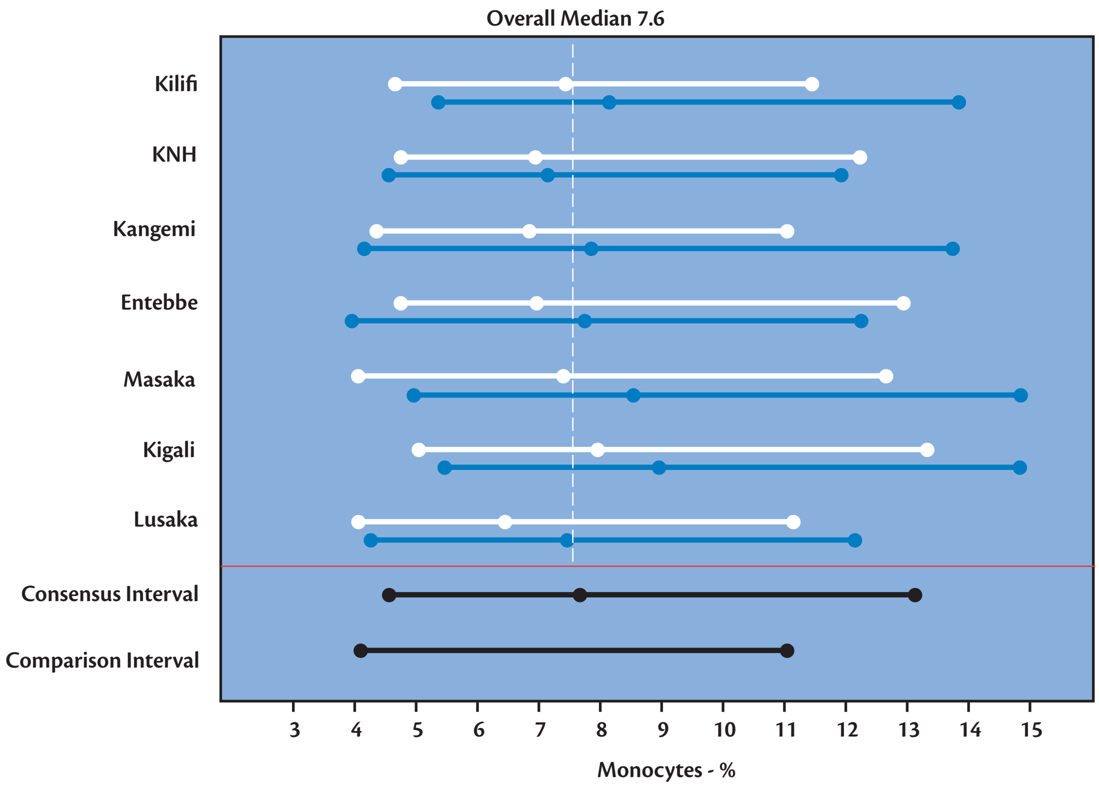
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 51: Monocyte counts 95% intervals and medians by research center and gender

Consensus interval: 4.5 to 13.1
Comparison Interval: 4.0 to 11.0
White: Females, Blue: Males, Black: Overall



3.10. Eosinophils (count and %)

Eosinophil counts (x 10³ cells/μL)

Results

Table 36 shows the number of subjects with data included in the analysis. Figures 52, 53, and 54 show the eosinophil counts distribution overall, by gender and by research center, respectively. Table 37 shows the distribution of eosinophil counts by research center and gender, together with the stratified 95% reference intervals. Since the distribution of eosinophil counts is highly skewed to the left, the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 55. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (x 10³ cells/μL)

Comparison interval: *0 to 0.45*
Consensus interval: *0.04 to 1.53*

Table 36: Number of observations, eosinophil counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	167	47.58	184	52.42	351
Total	1082	51.43	1022	48.57	2104

Figure 52: Frequency distribution of eosinophil counts

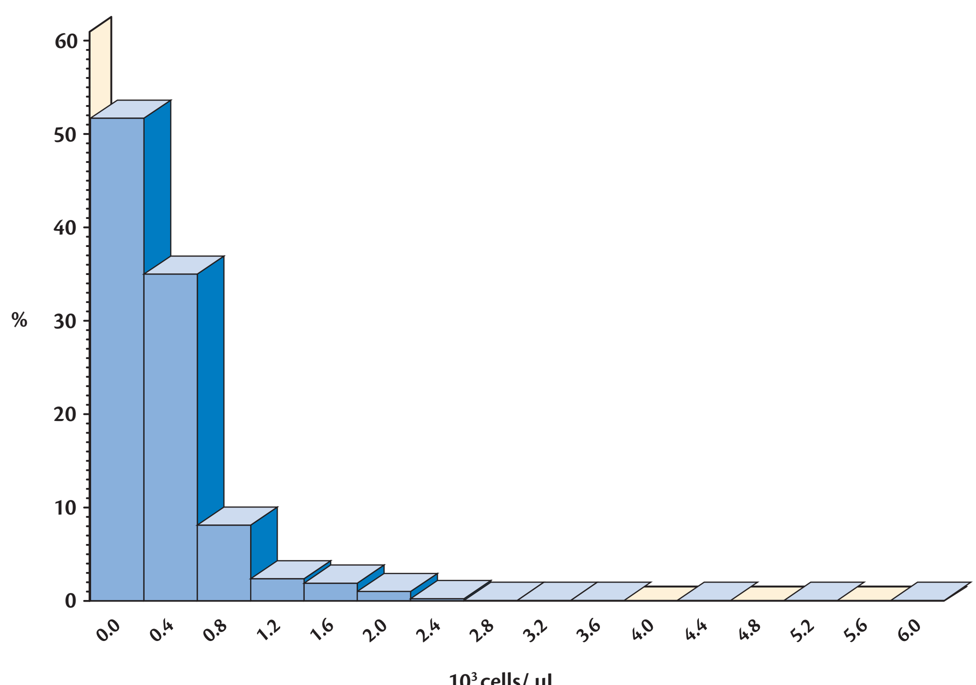


Figure 53: Frequency distribution of eosinophil counts by gender

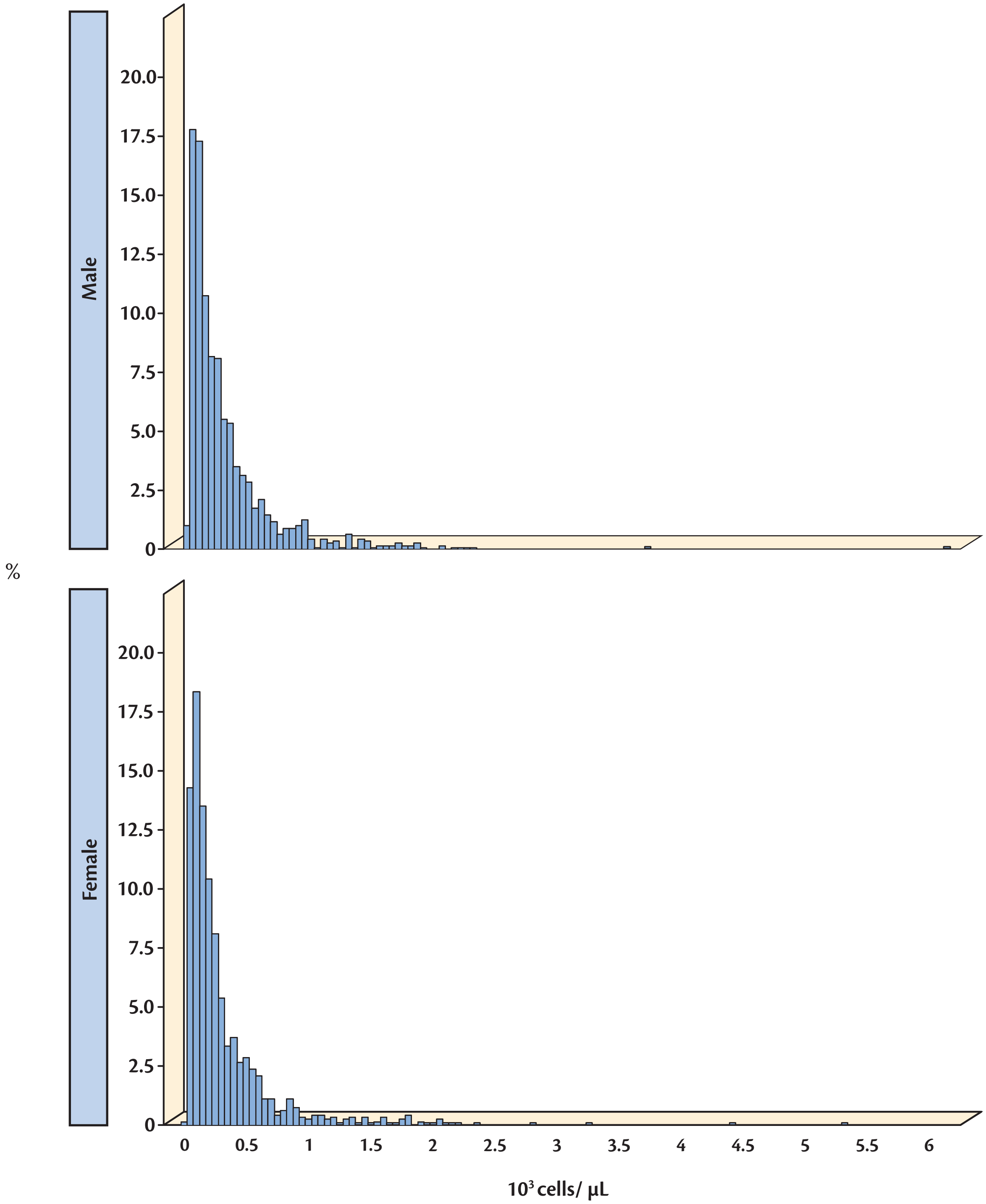


Figure 54: Frequency distribution of eosinophil counts by research center

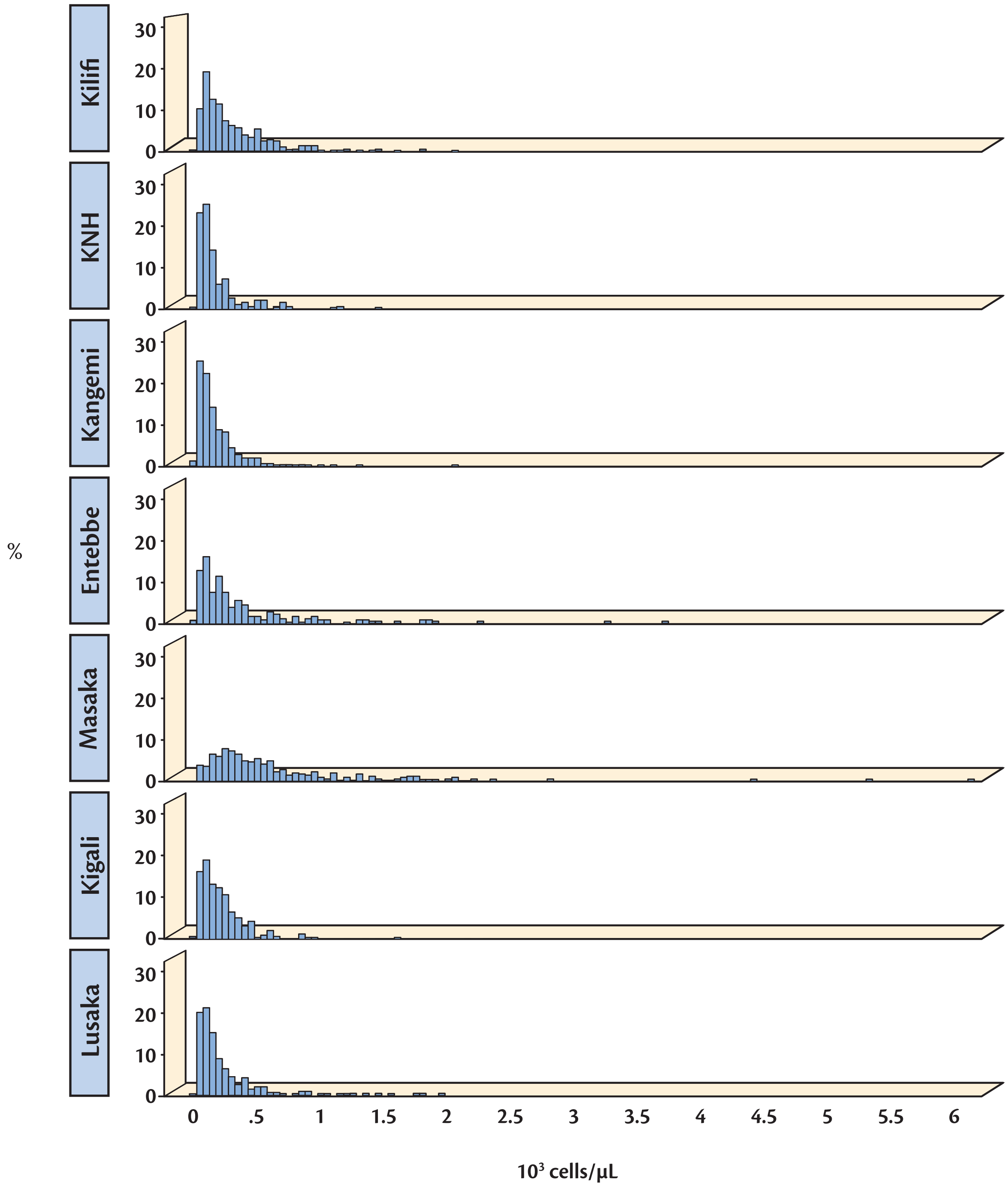


Table 37: Eosinophil counts distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	0.211 (0.177)	0.20	0.04 to 1.13	0.05 to 1.20	0.02 to 2.07
	KNH	99	0.131 (0.106)	0.12	0.03 to 0.67	0.03 to 1.09	0.03 to 1.44
	Kangemi	176	0.151 (0.120)	0.15	0.03 to 0.74	0.04 to 0.72	0.02 to 2.04
	Entebbe	98	0.204 (0.214)	0.20	0.02 to 1.66	0.04 to 1.80	0.04 to 3.24
	Masaka	148	0.425 (0.396)	0.42	0.07 to 2.74	0.05 to 2.34	0.04 to 5.31
	Kigali	188	0.205 (0.163)	0.20	0.04 to 1.01	0.05 to 1.22	0.04 to 1.60
	Lusaka	184	0.187 (0.167)	0.16	0.03 to 1.12	0.05 to 1.43	0.03 to 1.94
	Total	1022	0.204 (0.190)	0.19	0.03 to 1.31	0.04 to 1.59	0.02 to 5.31
Male	Kilifi	167	0.239 (0.221)	0.24	0.04 to 1.51	0.03 to 1.29	0.02 to 1.80
	KNH	98	0.138 (0.121)	0.12	0.02 to 0.79	0.04 to 0.73	0.02 to 1.14
	Kangemi	186	0.118 (0.100)	0.10	0.02 to 0.64	0.03 to 0.75	0.02 to 1.28
	Entebbe	96	0.301 (0.305)	0.30	0.04 to 2.28	0.05 to 1.85	0.02 to 3.71
	Masaka	183	0.436 (0.382)	0.45	0.08 to 2.51	0.06 to 1.88	0.04 to 6.09
	Kigali	185	0.155 (0.135)	0.16	0.03 to 0.89	0.03 to 0.95	0.02 to 2.30
	Lusaka	167	0.142 (0.126)	0.14	0.02 to 0.84	0.03 to 0.89	0.02 to 1.54
	Total	1082	0.195 (0.195)	0.19	0.03 to 1.45	0.03 to 1.46	0.02 to 6.09
Total	Kilifi	296	0.227 (0.201)	0.22	0.04 to 1.34	0.04 to 1.29	0.02 to 2.07
	KNH	197	0.134 (0.113)	0.12	0.02 to 0.72	0.04 to 0.77	0.02 to 1.44
	Kangemi	362	0.133 (0.110)	0.13	0.03 to 0.70	0.03 to 0.72	0.02 to 2.04
	Entebbe	194	0.247 (0.259)	0.23	0.03 to 2.01	0.04 to 1.85	0.02 to 3.71
	Masaka	331	0.431 (0.388)	0.44	0.07 to 2.61	0.05 to 2.07	0.04 to 6.09
	Kigali	373	0.178 (0.151)	0.18	0.03 to 0.97	0.04 to 0.97	0.02 to 2.30
	Lusaka	351	0.164 (0.148)	0.15	0.03 to 0.99	0.03 to 1.19	0.02 to 1.94
	Total	2104	0.199 (0.193)	0.19	0.03 to 1.38	0.04 to 1.53	0.02 to 6.09

Research Center Comparisons

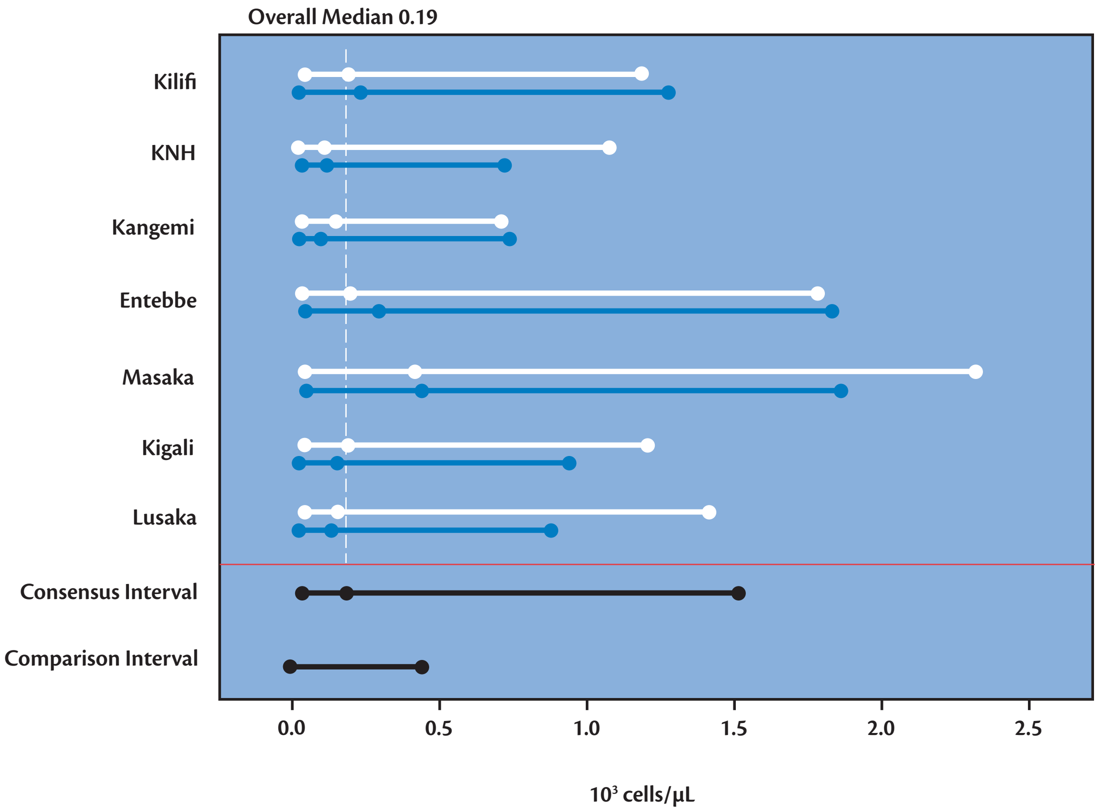
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 55: Eosinophil counts 95% intervals and medians by research center and gender

Consensus interval: 0.04 to 1.53
Comparison interval: 0 to 0.45
White: Females, Blue: Males, Black: Overall



Percent Eosinophils

Results

Table 38 shows the number of subjects with data included in the analysis. Figures 56, 57, and 58 show the percent eosinophils distribution overall, by gender and by research center, respectively. Table 39 shows the distribution of percent eosinophils by research center and gender, together with the stratified 95% reference intervals. Since the distribution of percent eosinophils is highly skewed to the left, the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 58. Significant differences across center or gender will be presented in Table 40. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (%)

	Males	**Females**	**Overall**
Comparison interval:	*NA*	*NA*	*0 to 8.0*
Consensus interval:*	*0.7 to 16.6*	*0.9 to 21.4*	*0.8 to 21.8*

** Excludes data from males at Masaka.*

Table 38: Number of observations, percent eosinophils

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	167	47.58	184	52.42	351
Total	1082	51.43	1022	48.57	2104

Figure 56: Frequency distribution of percent eosinophils

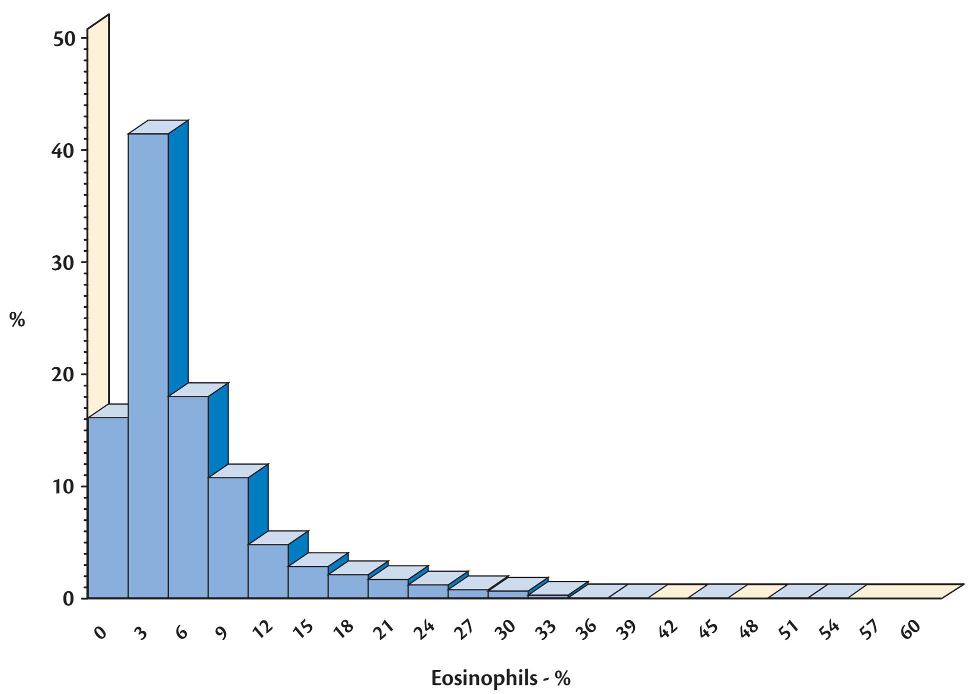


Figure 57: Frequency distribution of percent eosinophils by gender

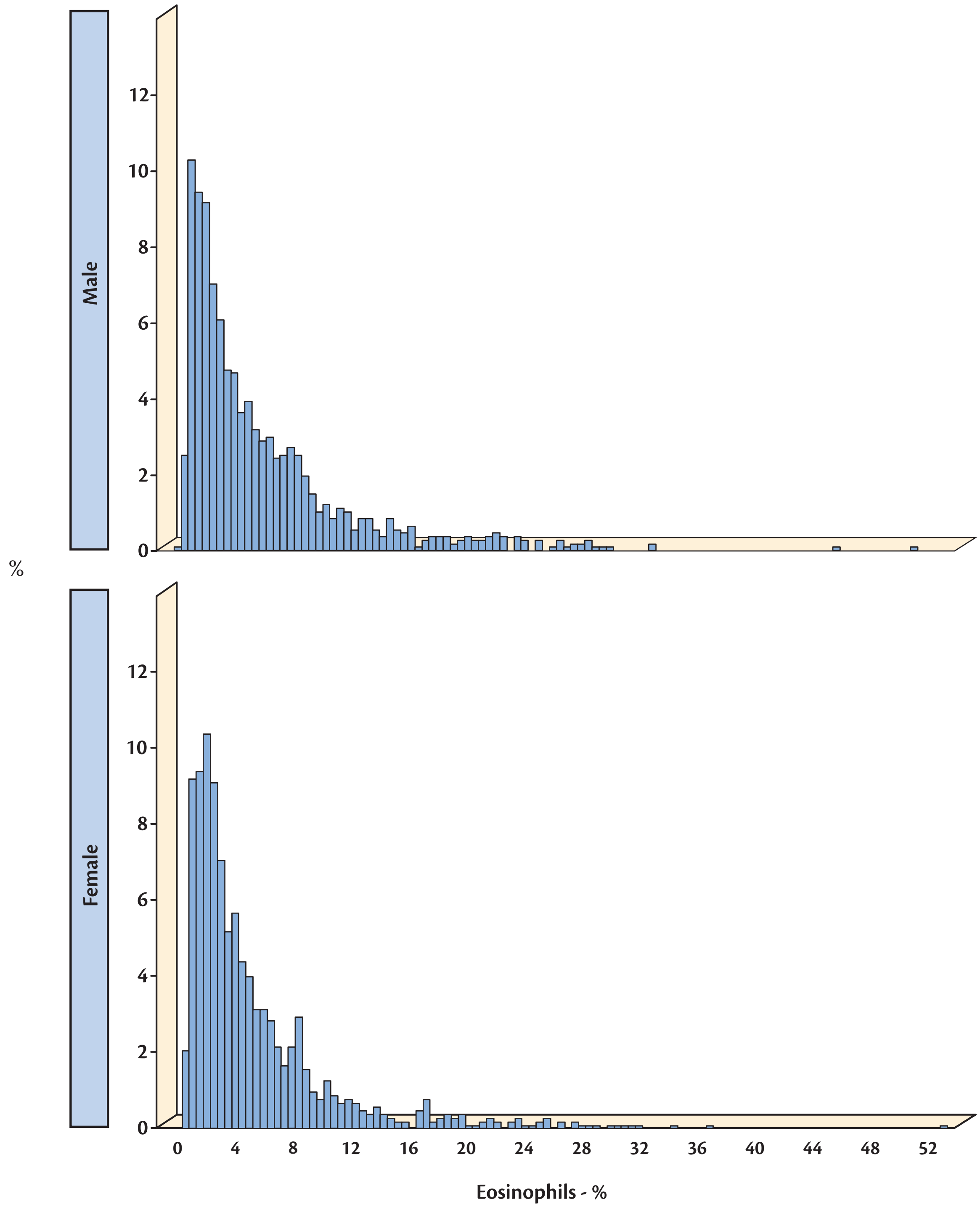


Figure 58: Frequency distribution of percent eosinophils by research center

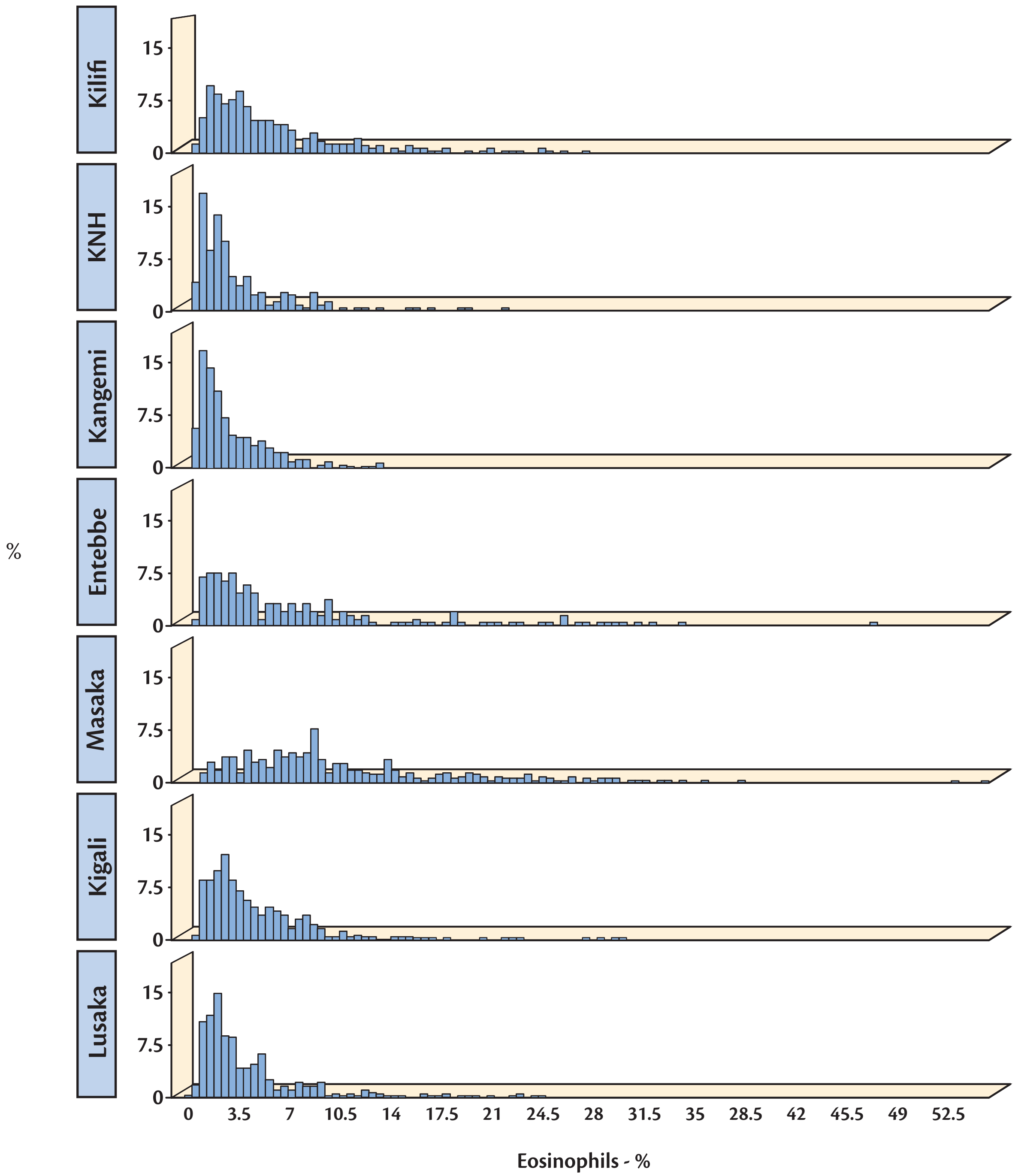


Table 39: Percent eosinophils distribution by research center and gender

Log transformation used, values are back-transformed (i.e., the geometric mean is shown)

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	3.94 (2.92)	3.8	0.9 to 17.4	1.1 to 17.6	0.5 to 25.5
	KNH	99	2.35 (1.83)	2.0	0.5 to 11.1	0.7 to 18.4	0.6 to 21.4
	Kangemi	176	2.43 (1.81)	2.4	0.5 to 10.8	0.7 to 10.4	0.5 to 20.1
	Entebbe	98	4.10 (3.87)	4.0	0.6 to 27.0	0.9 to 29.0	0.7 to 31.7
	Masaka	148	7.85 (6.27)	8.3	1.6 to 38.7	1.1 to 32.2	0.8 to 54.0
	Kigali	188	3.93 (2.92)	3.8	0.9 to 17.3	0.9 to 17.7	0.8 to 22.6
	Lusaka	184	3.19 (2.62)	2.8	0.6 to 16.4	0.8 to 19.6	0.3 to 24.0
	Total	1022	3.68 (3.21)	3.5	0.6 to 21.0	0.8 to 22.6	0.3 to 54.0
Male	Kilifi	167	4.67 (3.99)	4.6	0.8 to 25.8	1.0 to 22.1	0.7 to 27.0
	KNH	98	2.78 (2.35)	2.6	0.5 to 15.1	0.6 to 14.9	0.5 to 16.4
	Kangemi	186	2.18 (1.73)	1.9	0.4 to 10.7	0.6 to 12.1	0.3 to 21.8
	Entebbe	96	6.31 (5.84)	7.2	1.0 to 40.2	1.2 to 30.5	0.5 to 46.3
	Masaka	183	8.39 (6.49)	8.7	1.8 to 39.4	1.5 to 28.9	0.9 to 52.1
	Kigali	185	3.42 (2.70)	3.2	0.7 to 16.5	0.9 to 16.6	0.7 to 29.3
	Lusaka	167	3.05 (2.46)	2.9	0.6 to 15.4	0.8 to 16.7	0.6 to 22.3
	Total	1082	3.93 (3.67)	3.9	0.6 to 25.5	0.8 to 23.9	0.3 to 52.1
Total	Kilifi	296	4.33 (3.51)	4.2	0.9 to 21.9	1.0 to 21.6	0.5 to 27.0
	KNH	197	2.55 (2.08)	2.3	0.5 to 13.0	0.6 to 15.3	0.5 to 21.4
	Kangemi	362	2.30 (1.77)	2.1	0.5 to 10.8	0.6 to 10.4	0.3 to 21.8
	Entebbe	194	5.07 (4.85)	4.7	0.7 to 34.4	0.9 to 29.6	0.5 to 46.3
	Masaka	331	8.14 (6.38)	8.4	1.7 to 39.1	1.4 to 30.0	0.8 to 54.0
	Kigali	373	3.67 (2.81)	3.5	0.8 to 17.0	0.9 to 16.6	0.7 to 29.3
	Lusaka	351	3.12 (2.54)	2.9	0.6 to 15.9	0.8 to 18.7	0.3 to 24.0
	Total	2104	3.81 (3.44)	3.7	0.6 to 23.2	0.8 to 23.7	0.3 to 54.0

Research Center Comparisons

For males, there is a significant difference in percent eosinophils between Masaka and the other sites combined (Table 39) according to the CLSI guidelines, (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment and either the magnitude of the difference is ≥25% of the overall interval or the ratio of the two interval standard deviations is >1.5.) No site differences were seen among females.

Table 40: Evaluation of percent eosinophils by research center

All Centers Combined	Kigali, KNH, Entebbe, Kangemi, Lusaka, Kilifi		Masaka		CLSI Guidelines Criteria	
Reference Interval	Consensus Interval	Mean (SD)	Reference Interval	Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.70 to 23.90	0.70 to 20.50	1.22(0.89)	1.50 to 28.90	2.13(0.77)	Yes	No
		3.37(2.99)*		8.39(6.49)*		

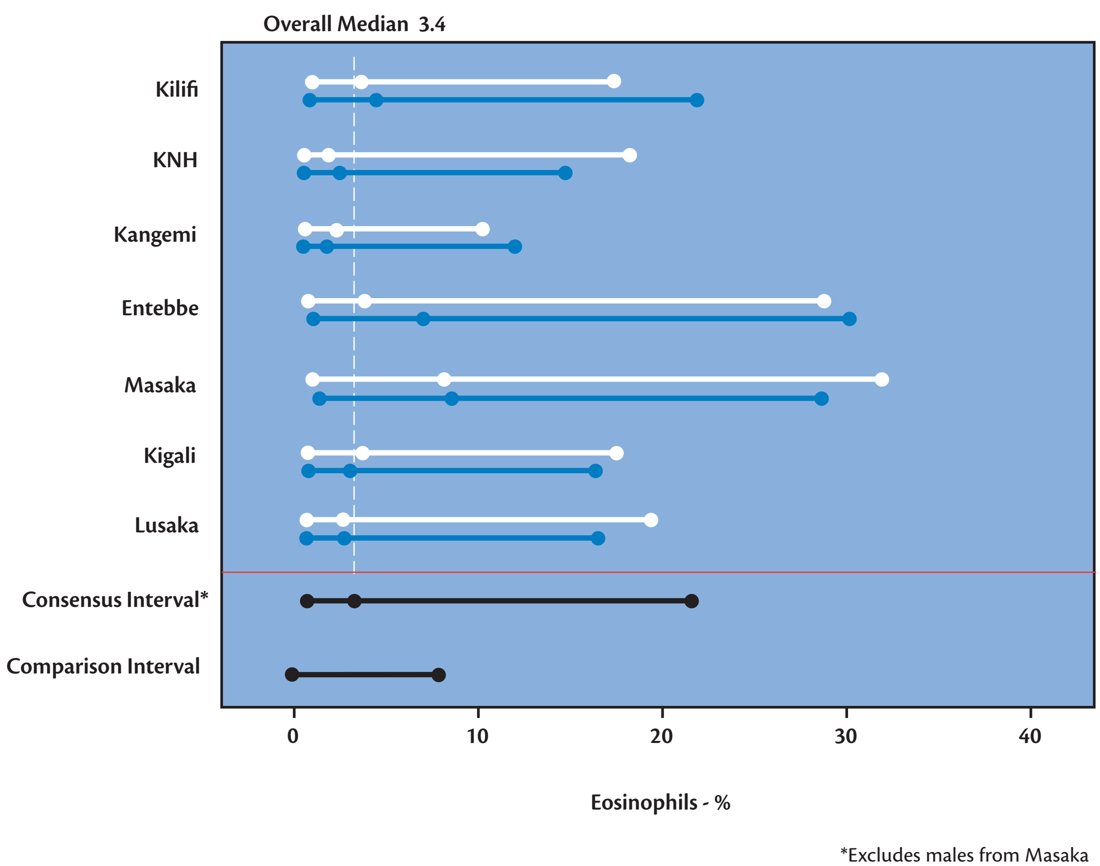
* Back-transformed log values

Gender Comparisons

Excluding data from males at Masaka, the difference between males and females in the remaining centers is not significant according to the CLSI guidelines.

Figure 59: Percent eosinophils 95% intervals and medians by research center and gender

*Consensus interval: 0.8 to 21.8**
Comparison interval: 0 to 8.0
White: Females, Blue: Males, Black: Overall



3.11. Basophils (count and %)

Basophil counts (x 10³ cells/µL)

Results

Table 41 shows the number of subjects with data included in the analysis. Figures 60, 61, and 62 show the basophil counts distribution overall, by gender and by research center, respectively. Table 42 shows the distribution of basophil counts by research center and gender, together with the stratified 95% reference intervals. Since the distribution of basophil counts is highly skewed to the left, log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 63. Any significant differences that exist across center or gender will be presented in Tables 43 and 44, respectively. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (x 10³ cells/µL)

Comparison interval: *0 to 0.2*
Consensus interval:* *0.01 to 0.15*
** Excludes data from Lusaka.*

Table 41: Number of observations, basophil counts

	Male		Female		Total
	N	%	N	%	Data
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 60: Frequency distribution of basophil counts

Excludes two subjects with values 1.53 (female from Entebbe) and 1.89 (male from KNH)

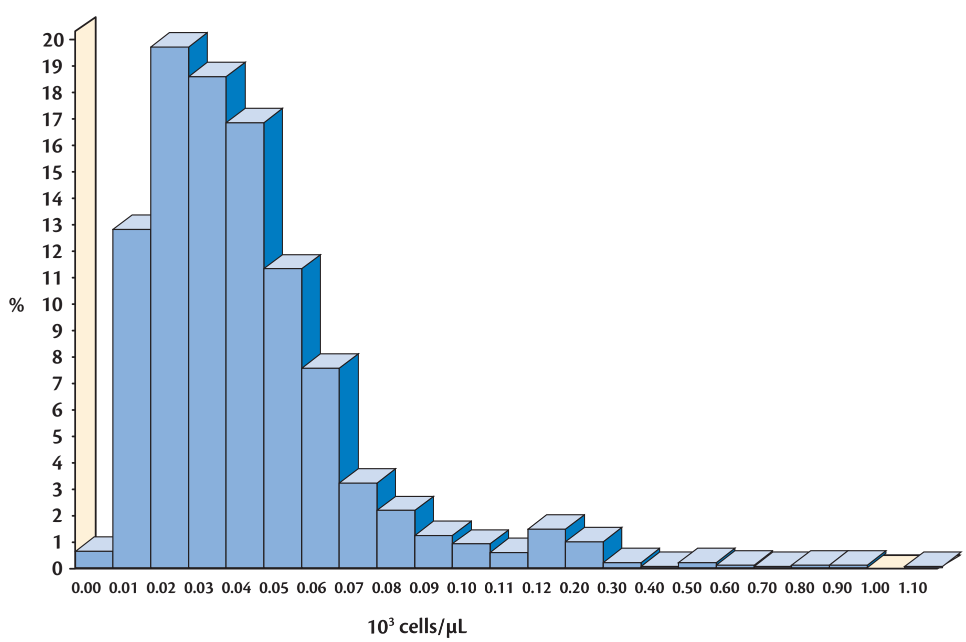


Figure 61: Frequency distribution of basophil counts by gender

Excludes two subjects with values 1.53 (female from Entebbe) and 1.89 (male from KNH)

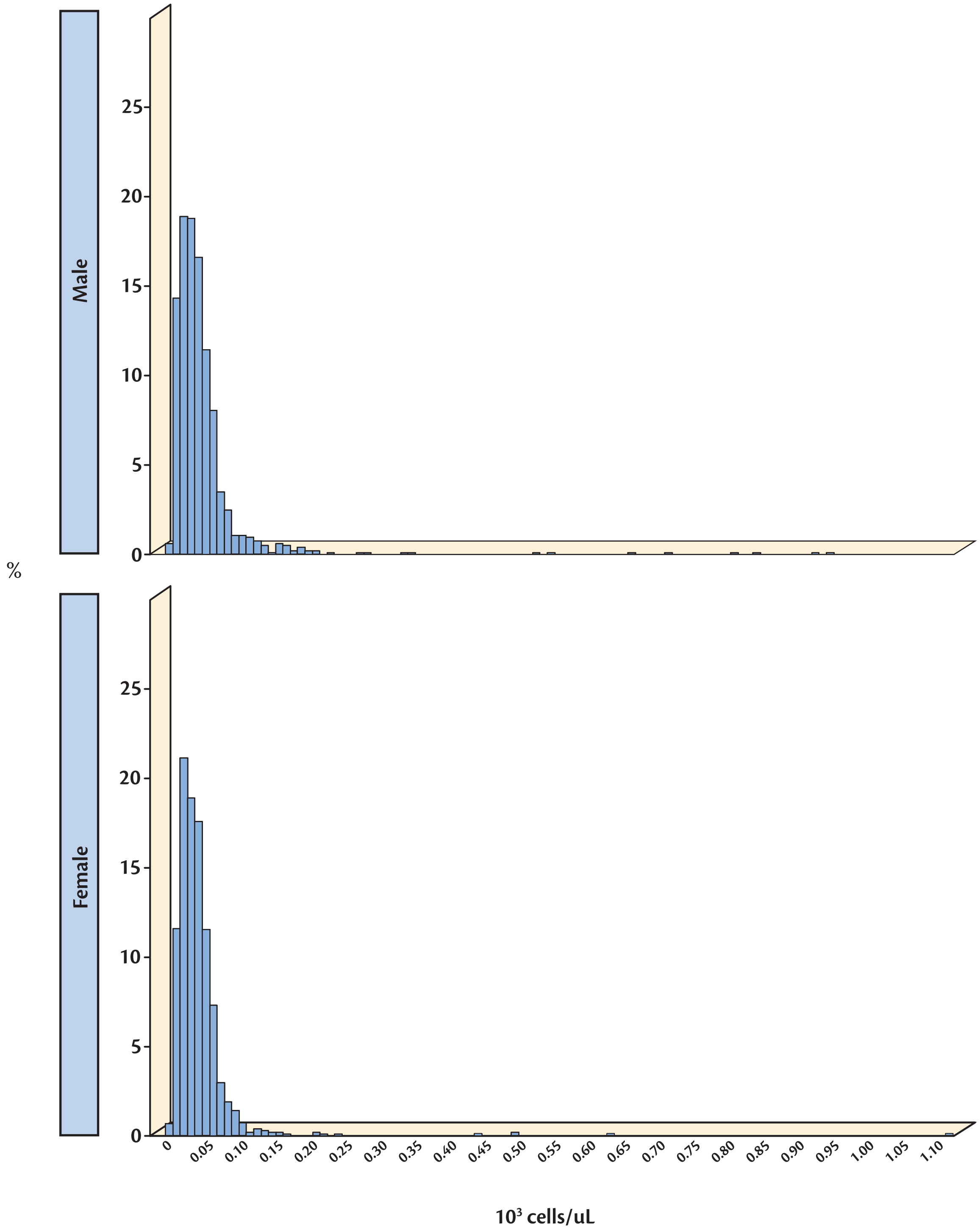


Figure 62: Frequency distribution of basophil counts by research center

Excludes two subjects with values 1.53 (female from Entebbe) and 1.89 (male from KNH)

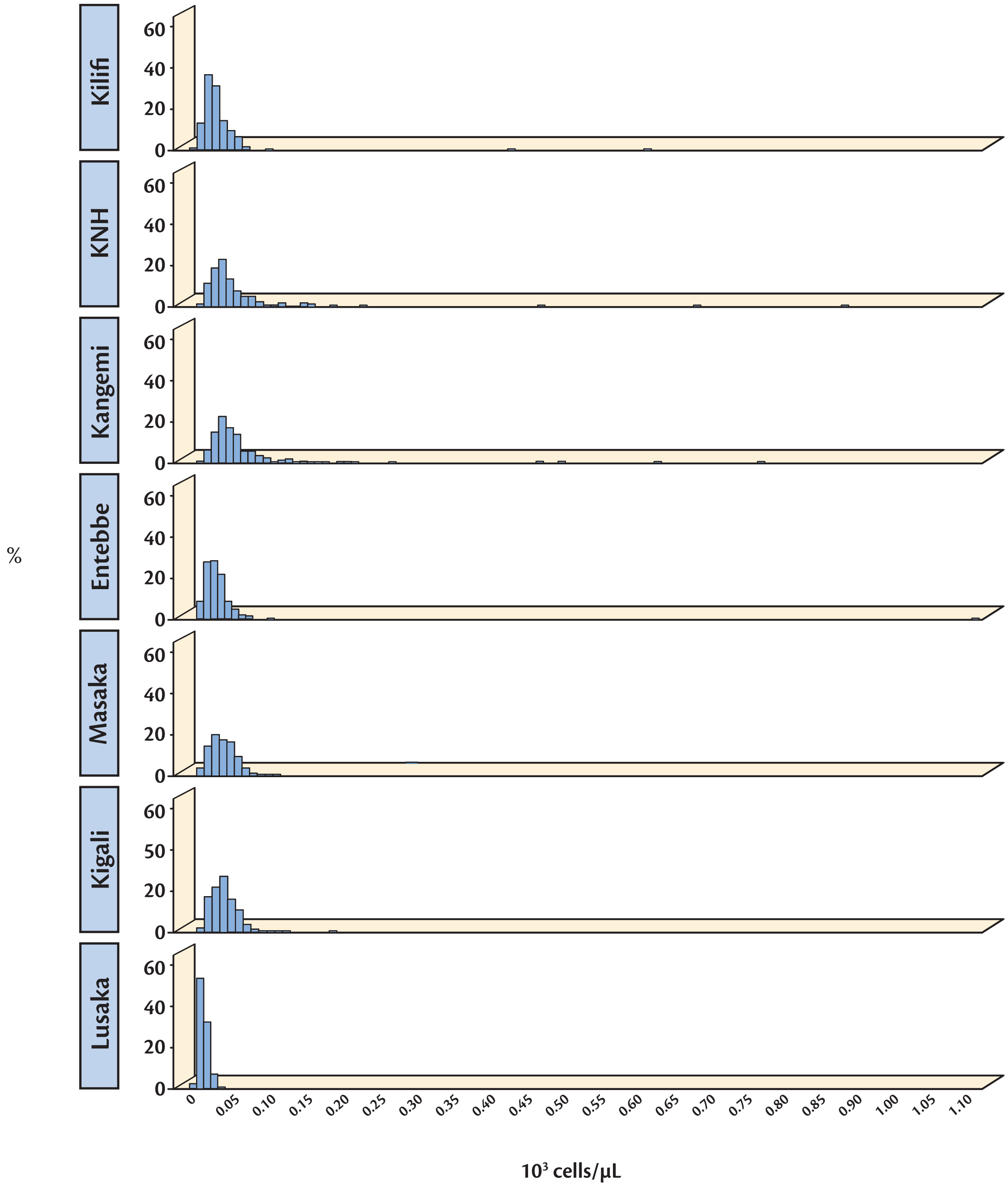


Table 42: Basophil counts distribution by research center and gender
Log transformation used, values are back-transformed (i.e., the geometric mean is shown)

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	0.026 (0.016)	0.030	0.007 to 0.092	0.01 to 0.06	0.01 to 0.60
	KNH	99	0.042 (0.022)	0.040	0.014 to 0.121	0.02 to 0.14	0.01 to 0.47
	Kangemi	176	0.050 (0.027)	0.050	0.017 to 0.145	0.02 to 0.15	0.01 to 0.47
	Entebbe	98	0.030 (0.022)	0.030	0.007 to 0.128	0.01 to 0.08	0.01 to 1.53
	Masaka	148	0.036 (0.020)	0.040	0.012 to 0.109	0.01 to 0.10	0.01 to 0.16
	Kigali	188	0.038 (0.015)	0.040	0.017 to 0.086	0.02 to 0.08	0.01 to 0.09
	Lusaka	184	0.015 (0.007)	0.020	0.006 to 0.040	0.01 to 0.03	0.01 to 0.20
	Total	1022	0.032 (0.021)	0.030	0.008 to 0.121	0.01 to 0.10	0.01 to 1.53
Male	Kilifi	167	0.027 (0.015)	0.030	0.009 to 0.080	0.01 to 0.06	0.01 to 0.10
	KNH	98	0.054 (0.045)	0.050	0.010 to 0.281	0.02 to 0.68	0.01 to 1.89
	Kangemi	186	0.052 (0.032)	0.050	0.015 to 0.180	0.02 to 0.22	0.01 to 0.77
	Entebbe	96	0.031 (0.016)	0.030	0.011 to 0.085	0.01 to 0.08	0.01 to 0.11
	Masaka	183	0.041 (0.025)	0.040	0.012 to 0.140	0.01 to 0.11	0.01 to 0.90
	Kigali	185	0.040 (0.025)	0.040	0.011 to 0.140	0.01 to 0.18	0.01 to 0.33
	Lusaka	168	0.012 (0.005)	0.010	0.006 to 0.027	0.01 to 0.03	0.01 to 0.03
	Total	1083	0.033 (0.025)	0.030	0.007 to 0.151	0.01 to 0.16	0.01 to 1.89
Total	Kilifi	296	0.027 (0.015)	0.030	0.008 to 0.085	0.01 to 0.06	0.01 to 0.60
	KNH	197	0.048 (0.033)	0.040	0.012 to 0.194	0.02 to 0.23	0.01 to 1.89
	Kangemi	362	0.051 (0.030)	0.050	0.016 to 0.162	0.02 to 0.18	0.01 to 0.77
	Entebbe	194	0.030 (0.019)	0.030	0.009 to 0.106	0.01 to 0.08	0.01 to 1.53
	Masaka	331	0.039 (0.023)	0.040	0.012 to 0.126	0.01 to 0.11	0.01 to 0.90
	Kigali	373	0.039 (0.021)	0.040	0.014 to 0.112	0.02 to 0.12	0.01 to 0.33
	Lusaka	352	0.014 (0.006)	0.010	0.006 to 0.034	0.01 to 0.03	0.01 to 0.20
	Total	2105	0.032 (0.023)	0.030	0.008 to 0.136	0.01 to 0.13	0.01 to 1.89

Research Center Comparisons

For both males and females there is a significant difference in basophil counts between Lusaka and the other centers combined (Table 43).

Table 43: Evaluation of basophil counts by research center

All Centers Combined	Kigali, KNH, Entebbe, Kangemi, Musaka, Kilifi		Lusaka		CLSI Guidelines Criteria	
Reference Interval	Consensus Interval	Mean (SD)	Reference Interval	Mean (SD)	Difference in Means>25% Ref. Interval	SD ratio > 1.5
Males						
0.01 to 0.16	0.01 to 0.17	-3.227 (0.663)	0.01 to 0.03	-4.361 (0.363)	Yes	Yes
		0.040 (0.026)*		0.013 (0.005)*		
Females						
0.01 to 0.10	0.01 to 0.12	-3.29 (0.58)	0.01 to 0.03	-4.171 (0.459)	Yes	No
		0.037 (0.022)*		0.015 (0.007)*		

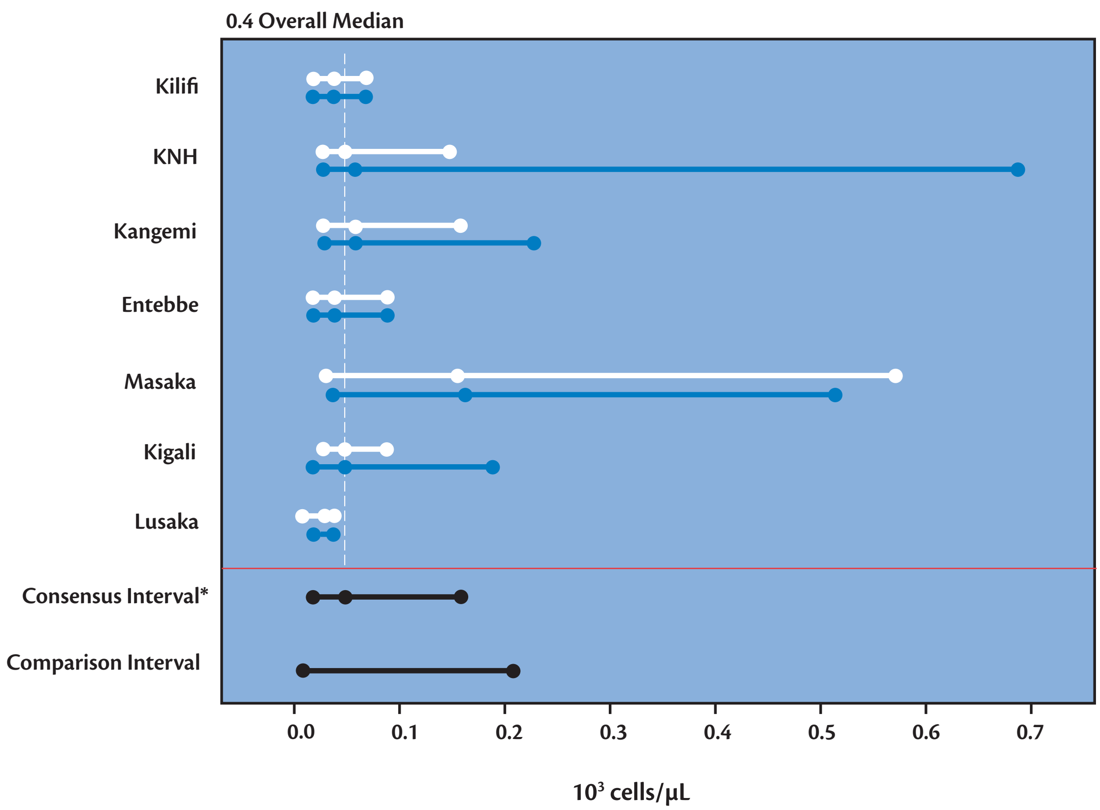
* Back-transformed from log estimates

Gender Comparisons

Excluding data from Lusaka, the difference between males and females in the remaining centers is not significant according to the CLSI guidelines.

Figure 63: Basophil counts 95% intervals and medians by research center and gender

*Consensus interval: 0.01 to 0.15**
Comparison interval: 0 to 0.2
White: Females, Blue: Males, Black: Overall



*Excludes data from Lusaka

Percent Basophils

Results

Table 44 shows the number of subjects with data included in the analysis. Figures 64, 65, and 66 show the percent basophils distribution overall, by gender and by research center, respectively. Table 45 shows the distribution of percent basophils by research center and gender, together with the stratified 95% reference intervals. Since the distribution of percent basophils is highly skewed to the left, log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 67. If any significant differences exist across center or gender, these will be presented in Table 46. The comparison and final estimated intervals are shown below.

Estimated Reference Intervals (%)

	Males	Females	Overall
Comparison interval:	*NA*	*NA*	*0 to 3.0*
Consensus interval:*	*0.3 to 2.8*	*0.4 to 1.4*	*0.4 to 2.5*

** Excludes data from Entebbe and Lusaka, and females from Kilifi.*

Table 44: Number of observations, percent basophils

	Male		Female		Total
	N	%	N	%	Data
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1083	51.45	1022	48.55	2105

Figure 64: Frequency distribution of percent basophils

Excludes two subjects with values 23.8% and 38.9% (both are females from Entebbe)

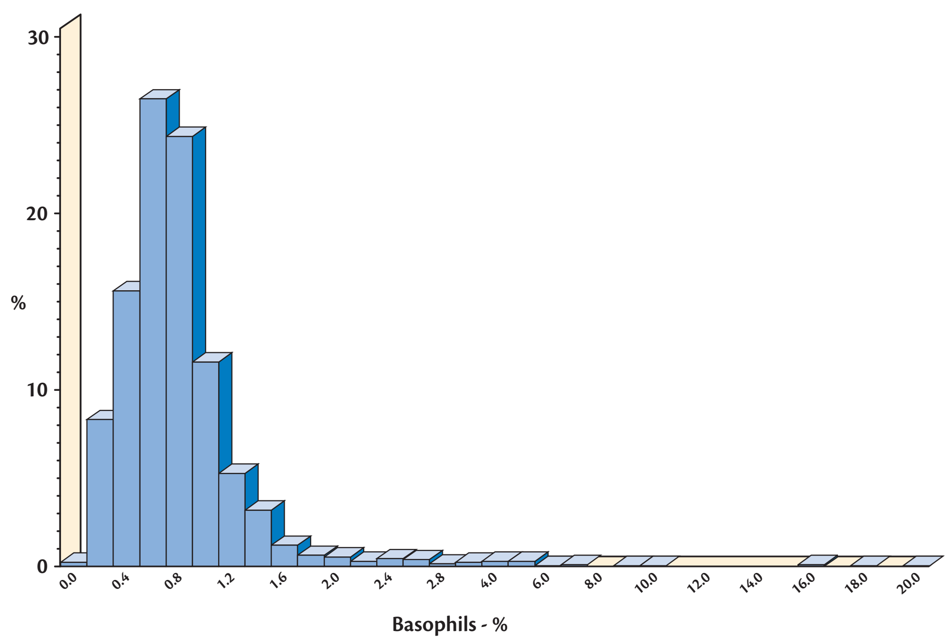


Figure 65: Frequency distribution of percent basophils by gender

Excludes two subjects with values 23.8% and 38.9% (both are females from Entebbe)

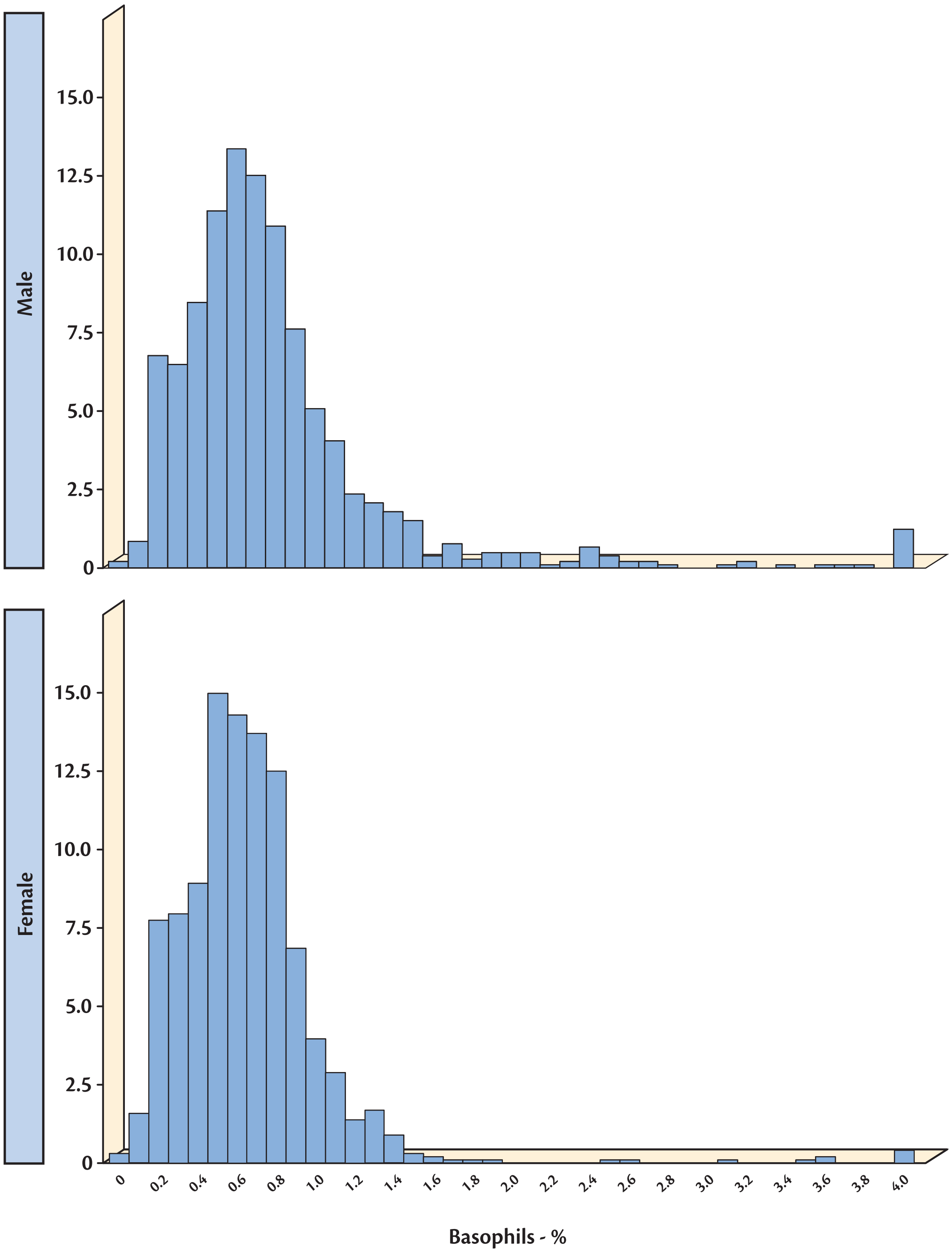


Figure 66: Frequency distribution of percent basophils by research center

Excludes two subjects with values 23.8% and 38.9% (both are females from Entebbe)

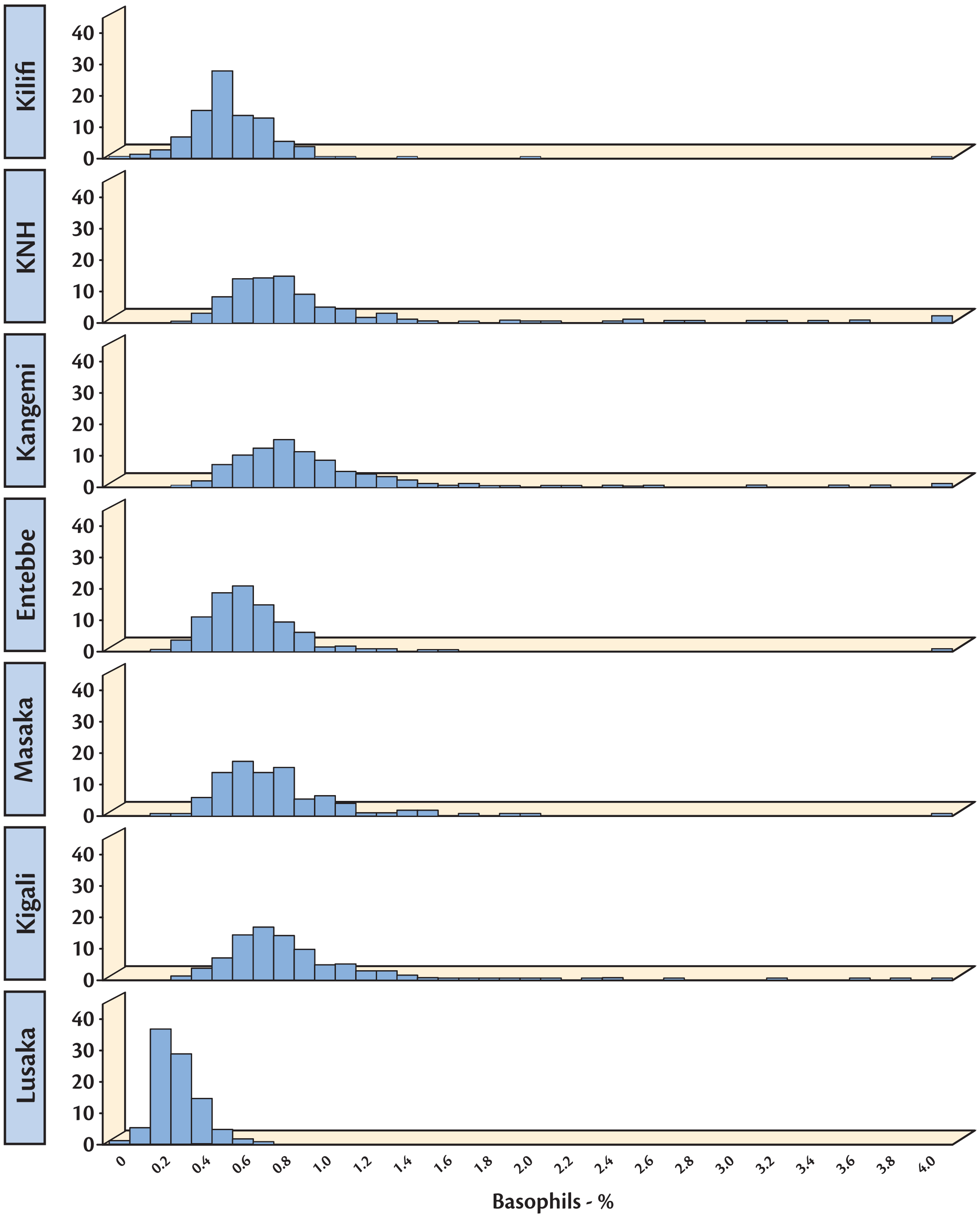


Table 45: Percent basophils distribution by research center and gender

Log transformation used, values are back-transformed (i.e., the geometric mean is shown)

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	0.48 (0.19)	0.50	0.22 to 1.05	0.20 to 0.90	0.10 to 0.90
	KNH	99	0.75 (0.33)	0.70	0.31 to 1.81	0.40 to 3.60	0.30 to 8.80
	Kangemi	176	0.83 (0.35)	0.80	0.36 to 1.91	0.40 to 2.50	0.30 to 9.60
	Entebbe	98	0.61 (0.40)	0.60	0.17 to 2.23	0.30 to 1.60	0.30 to 38.90
	Masaka	148	0.67 (0.21)	0.70	0.35 to 1.27	0.40 to 1.30	0.30 to 1.50
	Kigali	188	0.74 (0.22)	0.70	0.41 to 1.32	0.40 to 1.30	0.30 to 1.90
	Lusaka	184	0.24 (0.15)	0.30	0.07 to 0.86	0.10 to 0.50	0.01 to 0.60
	Total	1022	0.56 (0.36)	0.60	0.16 to 2.00	0.20 to 1.40	0.01 to 38.90
Male	Kilifi	167	0.52 (0.30)	0.50	0.16 to 1.63	0.20 to 1.10	0.01 to 5.00
	KNH	98	1.04 (0.70)	0.90	0.27 to 4.01	0.50 to 6.10	0.40 to 15.70
	Kangemi	186	0.96 (0.48)	0.90	0.35 to 2.63	0.50 to 3.70	0.40 to 18.10
	Entebbe	96	0.65 (0.22)	0.60	0.33 to 1.27	0.30 to 1.30	0.20 to 1.50
	Masaka	183	0.77 (0.35)	0.70	0.31 to 1.89	0.40 to 1.70	0.20 to 19.50
	Kigali	185	0.87 (0.45)	0.80	0.31 to 2.46	0.40 to 3.20	0.30 to 6.60
	Lusaka	168	0.26 (0.13)	0.30	0.10 to 0.69	0.10 to 0.60	0.01 to 0.70
	Total	1083	0.66 (0.45)	0.70	0.17 to 2.56	0.20 to 2.50	0.01 to 19.50
Total	Kilifi	296	0.50 (0.25)	0.50	0.18 to 1.37	0.20 to 0.90	0.01 to 5.00
	KNH	197	0.88 (0.52)	0.80	0.27 to 2.88	0.40 to 4.90	0.30 to 15.70
	Kangemi	362	0.89 (0.42)	0.80	0.35 to 2.28	0.50 to 2.60	0.30 to 18.10
	Entebbe	194	0.63 (0.32)	0.60	0.22 to 1.77	0.30 to 1.30	0.20 to 38.90
	Masaka	331	0.72 (0.29)	0.70	0.32 to 1.61	0.40 to 1.50	0.20 to 19.50
	Kigali	373	0.80 (0.34)	0.80	0.34 to 1.88	0.40 to 2.30	0.30 to 6.60
	Lusaka	352	0.25 (0.14)	0.30	0.08 to 0.78	0.10 to 0.50	0.01 to 0.70
	Total	2105	0.61 (0.40)	0.60	0.16 to 2.29	0.20 to 2.10	0.01 to 38.90

Research Center Comparisons

For males, the distribution of percent basophils at Lusaka differs significantly from the the other centers combined (Tables 45, 46). For females the distributions of percent basophils at Lusaka and Kilifi differ significantly from each other and from the other centers combined (Table 46) according to the CLSI guidelines (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment and either the magnitude of the difference is ≥25% of the overall interval or the Ratio of the two interval standard deviations is >1.5.)

Table 46: Evaluation of percent basophils by gender

46a. Males (Consensus includes Kigali, KNH, Kangemi, Masaka, and Kilifi)

Combined Interval	Lusaka Interval	Lusaka Mean (SD)	Entebbe Interval	Entebbe Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.10 to 1.10	0.10 to 0.60	-1.330(0.450)	0.30 to 1.30	-0.438(0.340)	Yes	No
		0.264(0.119)*		0.645(0.219)*		
* Back-transformed from log estimates						

Combined Interval	Consensus Interval	Consensus Mean (SD)	Lusaka Interval	Lusaka Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.20 to 2.60	0.30 to 2.80	-0.222(0.555)	0.10 to 0.60	-1.330(0.450)	Yes	No
		0.801(0.445)*		0.264(0.119)*		
* Back-transformed from log estimates						

Combined Interval	Consensus Interval	Consensus Mean (SD)	Entebbe Interval	Entebbe Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.30 to 2.70	0.30 to 2.80	-0.222(0.555)	0.30 to 1.30	-0.438(0.340)	No	Yes
		0.801(0.445)*		0.645(0.219)*		
* Back-transformed from log estimates						

46b. Females (Consensus includes Kigali, KNH, Kangemi, and Masaka)

Combined Interval	Lusaka Interval	Lusaka Mean (SD)	Entebbe Interval	Entebbe Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.10 to 0.90	0.10 to 0.50	-1.372(0.407)	0.30 to 1.60	-0.487(0.644)	Yes	Yes
		0.253(0.103)*		0.615(0.396)*		
* Back-transformed from log estimates						

Combined Interval	Lusaka Interval	Lusaka Mean (SD)	Kilifi Interval	Kilifi Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.10 to 0.80	0.10 to 0.50	-1.372(0.407)	0.20 to 0.90	-0.730(0.390)	Yes	No
		0.253(0.103)*		0.482(0.188)*		
* Back-transformed from log estimates						

Combined Interval	Entebbe Interval	Entebbe Mean (SD)	Kilifi Interval	Kilifi Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.20 to 1.00	0.30 to 1.60	-0.487(0.644)	0.20 to 0.90	-0.730(0.390)	No	Yes
		0.615(0.396)*		0.482(0.188)*		
* Back-transformed from log estimates						

Combined Interval	Consensus Interval	Consensus Mean (SD)	Lusaka Interval	Lusaka Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.20 to 1.40	0.40 to 1.40	-0.293(0.372)	0.10 to 0.50	-1.372(0.407)	Yes	No
		0.746(0.278)*		0.253(0.103)*		
* Back-transformed from log estimates						

Table 46: Evaluation of percent basophils by gender (continued)

46b. Females (Consensus includes Kigali, KNH, Kangemi, and Masaka) - continued

Combined Interval	Consensus Interval	Consensus Mean (SD)	Entebbe Interval	Entebbe Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.40 to 1.50	0.40 to 1.40	-0.293(0.372)	0.30 to 1.60	-0.487(0.644)	No	Yes
		0.746(0.278)*		0.615(0.396)*		
* Back-transformed from log estimates						

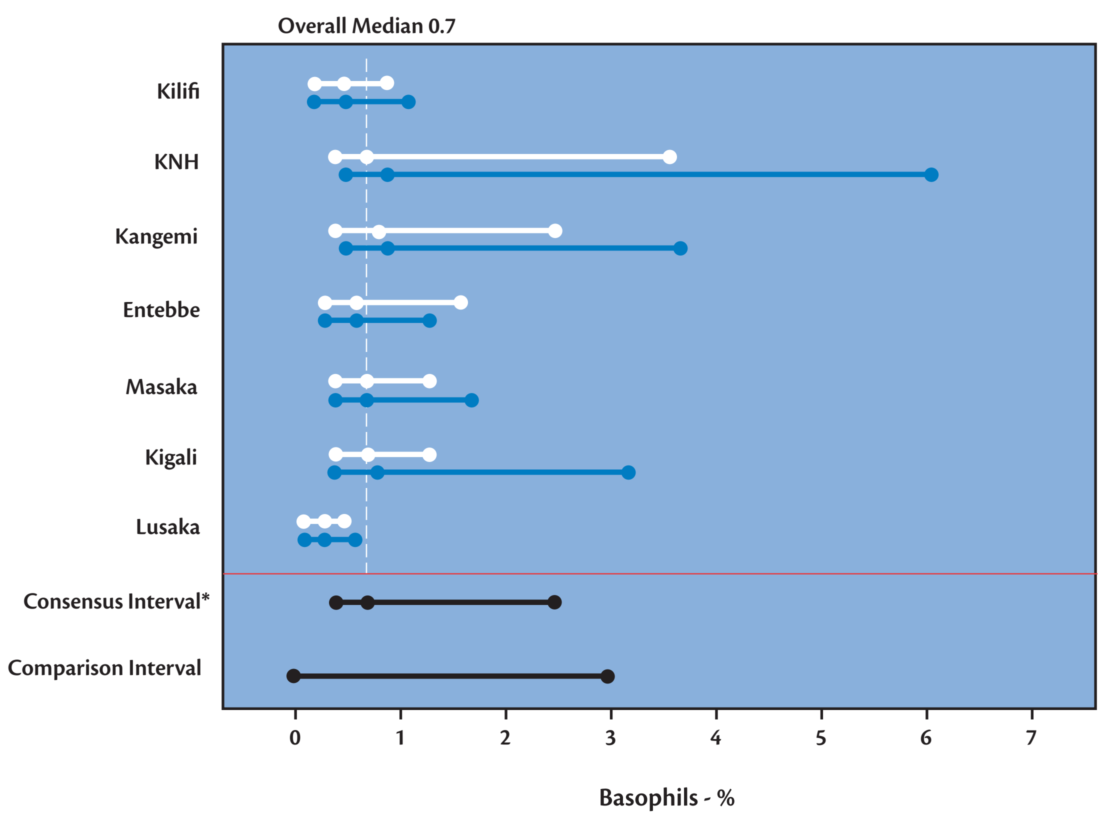
Combined Interval	Consensus Interval	Consensus Mean (SD)	Kilifi Interval	Kilifi Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.30 to 1.40	0.40 to 1.40	-0.293(0.372)	0.20 to 0.90	-0.730(0.390)	Yes	No
		0.746(0.278)*		0.482(0.188)*		
* Back-transformed from log estimates						

Gender Comparisons

Excluding all data from Entebbe and Lusaka and also females from Kilifi, the difference between males and females in the remaining data is not significant according to the CLSI guidelines.

Figure 67: Percent basophils 95% intervals and medians by research center and gender

*Consensus interval: 0.4 to 2.5**
Comparison interval: 0 to 3.0
White: Females, Blue: Males, Black: Overall



*Excludes data from Entebbe, Lusaka, and females from Kilifi

3.12. CD4 T Cell Counts

Results

Table 47 shows the number of subjects with data included in the analysis. Figures 68, 69, and 70 show the CD4 T cell counts distribution overall, by gender and by research center, respectively. All machines were calibrated to read results ≥ 2,000 cells/µl as 2,000 cells/µl. Table 48 shows the distribution of CD4 T cell counts by research center and gender, together with the stratified 95% reference intervals. Since the distribution of CD4 T cell counts is skewed to the left (see Figure 68), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 71. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (cells/µL)

Comparison interval: *518 to 1981*
All centers, consensus interval: *457 to 1628*

Table 47: Number of observations, CD4 T cell counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	180	55.21	146	44.79	326
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1080	51.43	1020	48.57	2100

Figure 68: Frequency distribution of CD4 T cell counts
Includes 8 values ≥ 2,000 cells/µl shown as 2,000 cells/µl

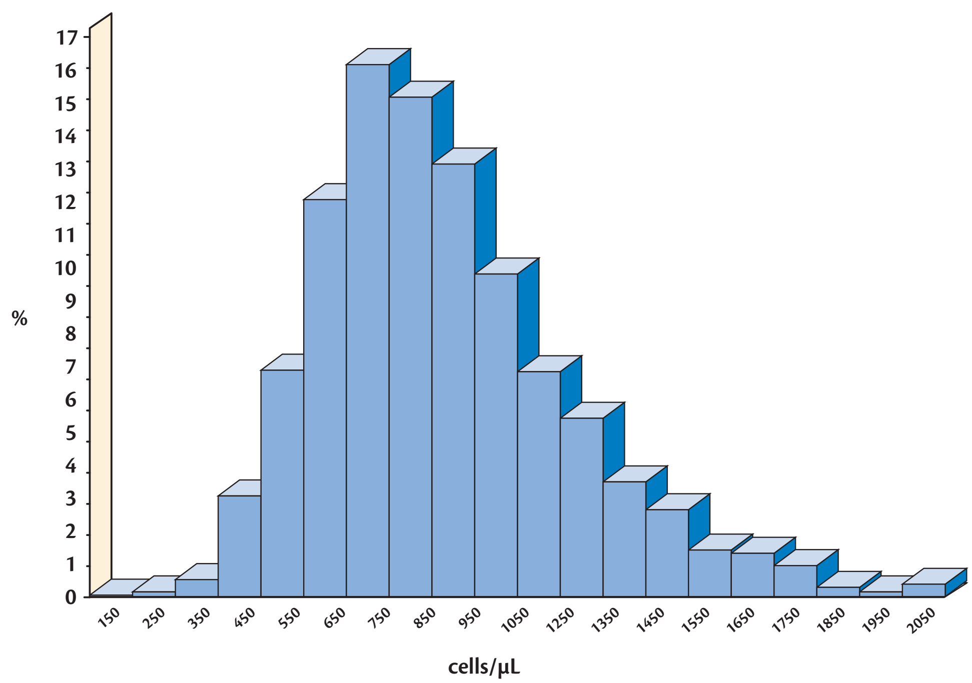


Figure 69: Frequency distribution of CD4 T cell counts by gender

Includes 8 values ≥ 2,000 cells/µl shown as 2,000 cells/µl

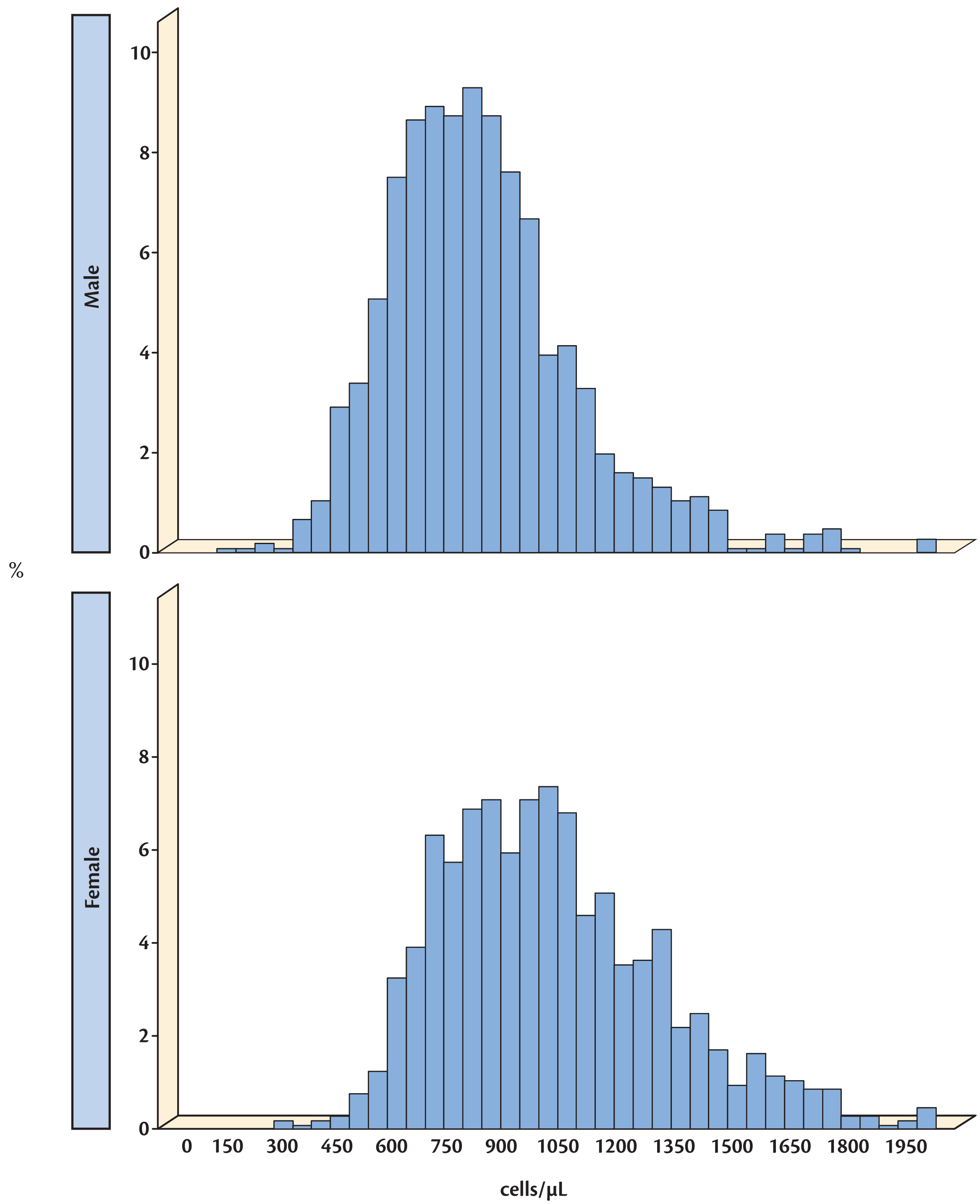


Figure 70: Frequency distribution of CD4 T cell counts by research center

Includes 8 values ≥ 2,000 cells/μl shown as 2,000 cells/μl

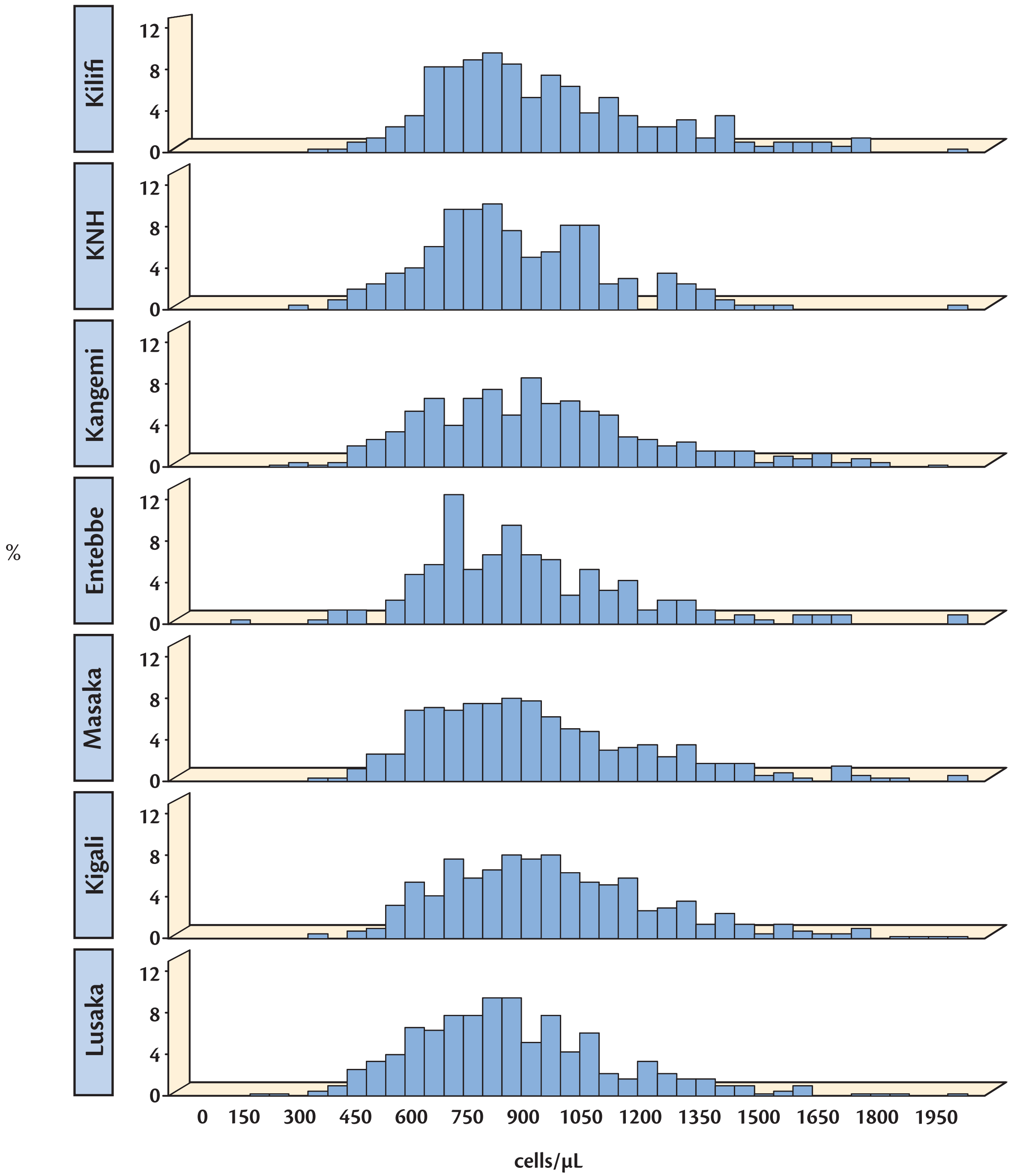


Table 48: CD4 T cell counts distribution by research center and gender

Includes 8 values ≥ 2,000 cells/µl shown as 2,000 cells/µl

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	994 (279.6)	989	566 to 1745	606 to 1702	508 to 2000
	KNH	99	955 (255.0)	992	560 to 1629	570 to 1449	309 to 1557
	Kangemi	176	1004 (298.0)	1005	555 to 1818	543 to 1730	302 to 1956
	Entebbe	98	942 (282.6)	908	517 to 1717	606 to 1690	408 to 2000
	Masaka	146	955 (309.2)	973	500 to 1825	508 to 1749	445 to 2000
	Kigali	188	1019 (285.8)	1006	581 to 1786	590 to 1762	520 to 2000
	Lusaka	184	925 (260.6)	917	527 to 1625	574 to 1589	326 to 1850
	Total	1020	973 (284.3)	976	542 to 1745	564 to 1703	302 to 2000
Male	Kilifi	167	834 (246.8)	806	461 to 1507	452 to 1533	367 to 1774
	KNH	98	731 (182.9)	730	444 to 1206	443 to 1124	419 to 2000
	Kangemi	186	770 (248.4)	784	404 to 1468	421 to 1426	259 to 1790
	Entebbe	96	778 (253.2)	808	406 to 1492	421 to 1293	160 to 1686
	Masaka	180	830 (241.4)	828	464 to 1485	492 to 1441	369 to 2000
	Kigali	185	832 (238.6)	834	469 to 1476	438 to 1381	354 to 1726
	Lusaka	168	725 (234.0)	740	380 to 1383	418 to 1417	215 to 2000
	Total	1080	789 (241.5)	791	428 to 1456	429 to 1430	160 to 2000
Total	Kilifi	296	900 (271.9)	875	492 to 1647	512 to 1661	367 to 2000
	KNH	197	836 (243.1)	831	468 to 1496	443 to 1423	309 to 2000
	Kangemi	362	876 (295.4)	896	446 to 1720	445 to 1662	259 to 1956
	Entebbe	194	857 (279.7)	851	446 to 1646	423 to 1674	160 to 2000
	Masaka	326	884 (277.0)	873	472 to 1654	502 to 1703	369 to 2000
	Kigali	373	921 (277.3)	925	505 to 1682	546 to 1677	354 to 2000
	Lusaka	352	823 (267.9)	825	430 to 1578	425 to 1553	215 to 2000
	Total	2100	874 (277.0)	870	463 to 1647	457 to 1628	160 to 2000

Research Center Comparisons

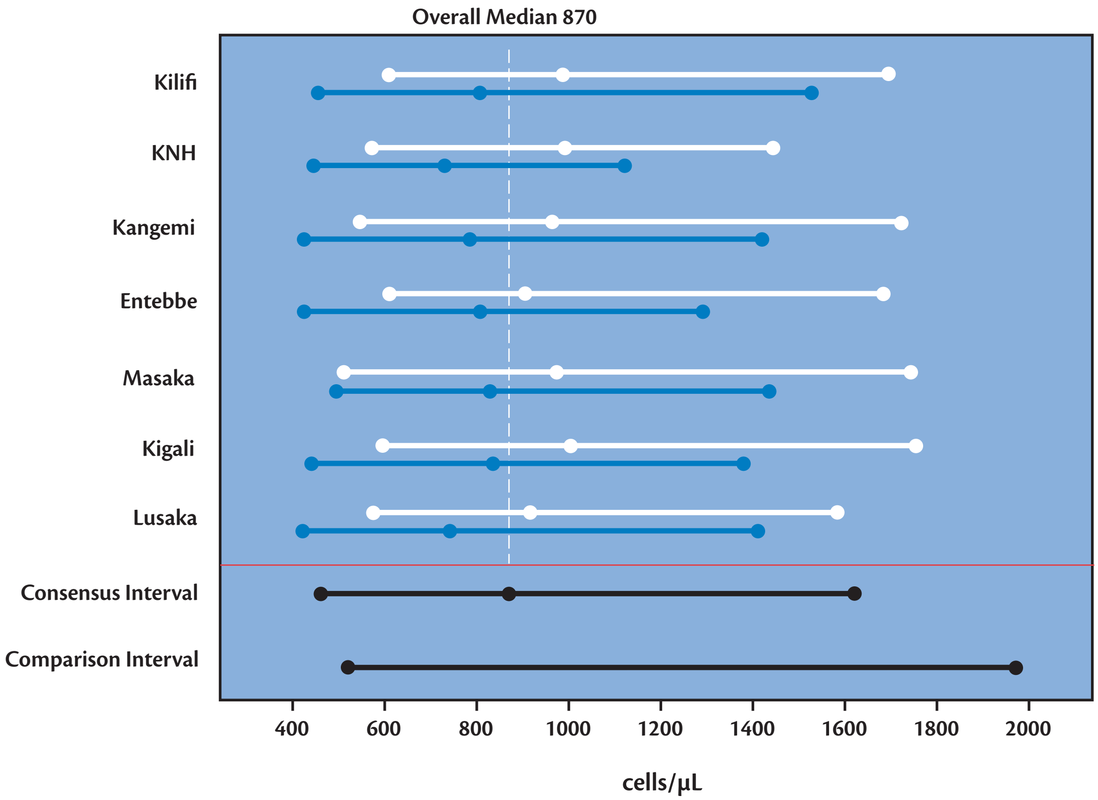
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 71: CD4 T cell counts 95% intervals and medians by research center and gender

Consensus interval: 457 to 1628
Comparison interval: 518 to 1981
White: Females, Blue: Males, Black: Overall



3.13. CD8 T Cell Counts

Results

Table 49 shows the number of subjects with data included in the analysis. Figures 72, 73, and 74 show the CD8 T cell counts distribution overall, by gender and by research center, respectively. Table 50 shows the distribution of CD8 T cell counts by research center and gender, together with the stratified 95% reference intervals. Since the distribution of CD8 T cell counts is skewed to the left (see Figure 72), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 75. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (cells/μL)

Comparison interval: *270 to 1335*
All centers, consensus interval: *230 to 1178*

Table 49: Number of observations, CD8 T cell counts

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	96	49.48	98	50.52	194
Masaka	180	55.21	146	44.79	326
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1080	51.43	1020	48.57	2100

Figure 72: Frequency distribution of CD8 T cell counts

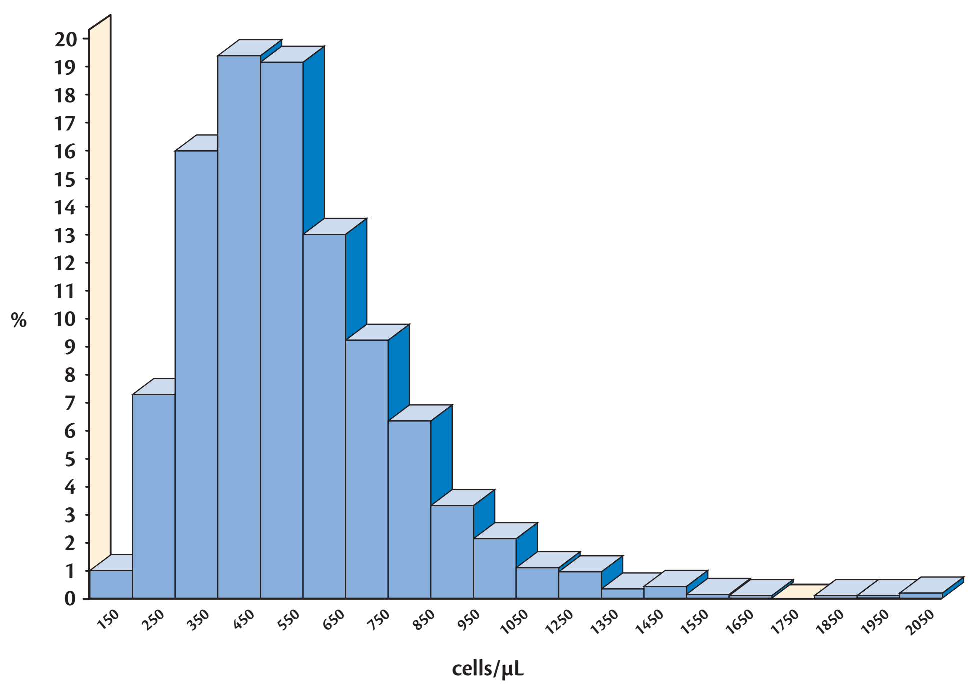


Figure 73: Frequency distribution of CD8 T cell counts by gender

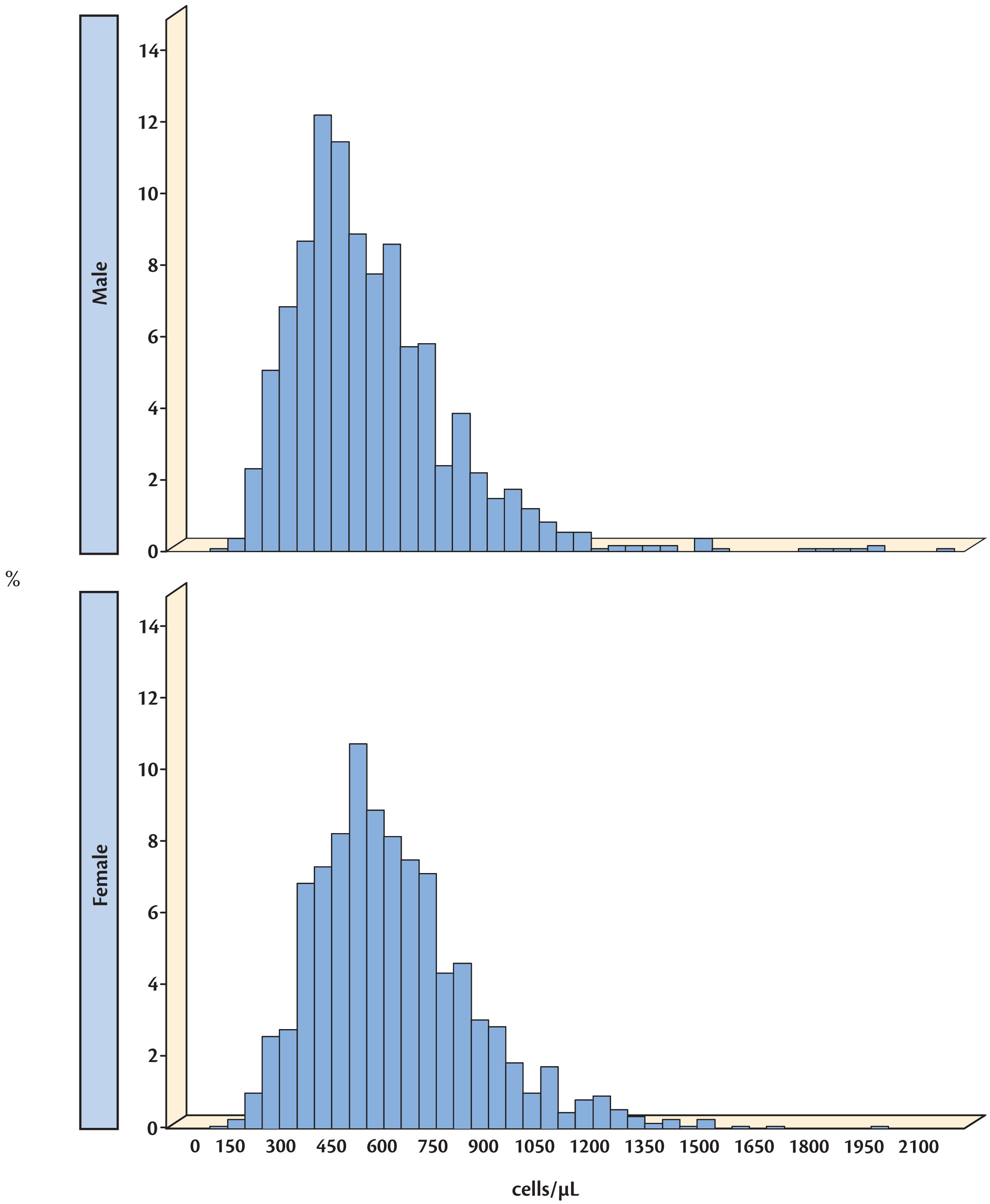


Figure 74: Frequency distribution of CD8 T cell counts by research center

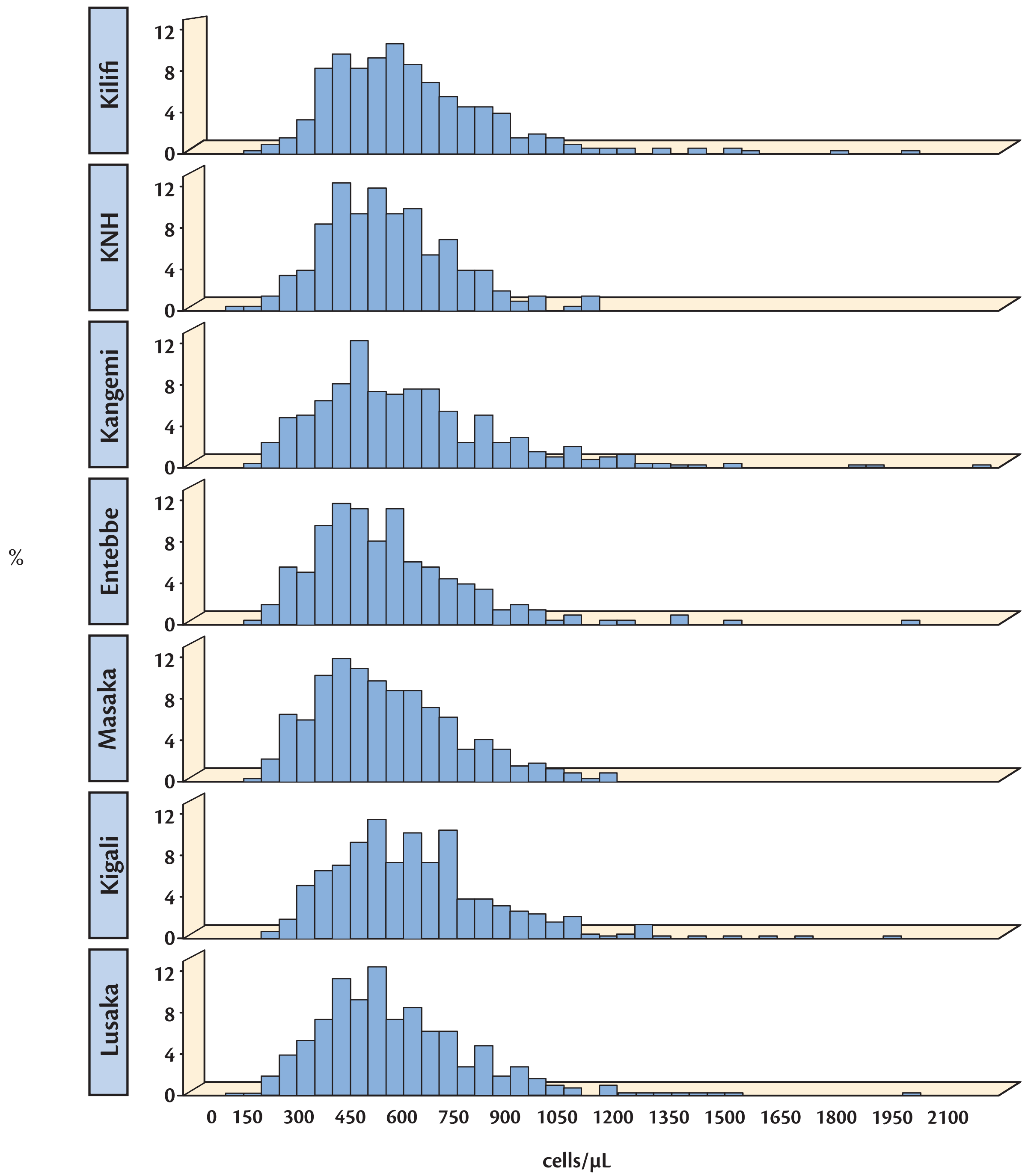


Table 50: CD8 T cell counts distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	585 (206.5)	580	289 to 1185	302 to 1209	226 to 1390
	KNH	99	540 (205.7)	567	252 to 1157	213 to 1084	94 to 1114
	Kangemi	176	582 (238.5)	593	257 to 1321	254 to 1235	186 to 1487
	Entebbe	98	513 (215.5)	531	221 to 1188	222 to 1184	158 to 1476
	Masaka	146	518 (198.2)	509	241 to 1113	247 to 1028	172 to 1164
	Kigali	188	621 (229.0)	628	297 to 1298	261 to 1249	218 to 1696
	Lusaka	184	559 (214.7)	540	260 to 1206	266 to 1357	213 to 2000
	Total	1020	565 (219.8)	568	259 to 1230	252 to 1211	94 to 2000
Male	Kilifi	167	542 (233.4)	534	229 to 1282	231 to 1512	152 to 2000
	KNH	98	464 (163.7)	472	229 to 940	234 to 913	179 to 956
	Kangemi	186	496 (240.1)	470	189 to 1306	204 to 1369	155 to 2178
	Entebbe	96	485 (194.6)	462	217 to 1082	249 to 1068	181 to 2000
	Masaka	180	477 (185.5)	489	219 to 1039	215 to 941	185 to 1169
	Kigali	185	523 (200.7)	518	243 to 1127	272 to 1255	211 to 1957
	Lusaka	168	474 (200.5)	470	203 to 1105	200 to 999	118 to 1257
	Total	1080	497 (207.6)	495	215 to 1146	222 to 1122	118 to 2178
Total	Kilifi	296	560 (224.1)	556	252 to 1247	251 to 1286	152 to 2000
	KNH	197	501 (187.3)	505	237 to 1058	213 to 956	94 to 1114
	Kangemi	362	536 (244.4)	531	216 to 1334	222 to 1252	155 to 2178
	Entebbe	194	499 (204.9)	495	219 to 1134	222 to 1184	158 to 2000
	Masaka	326	495 (191.9)	505	228 to 1075	226 to 992	172 to 1169
	Kigali	373	570 (219.8)	577	264 to 1233	272 to 1249	211 to 1957
	Lusaka	352	517 (212.4)	511	227 to 1176	224 to 1145	118 to 2000
	Total	2100	529 (216.3)	531	233 to 1198	230 to 1178	94 to 2178

Research Center Comparisons

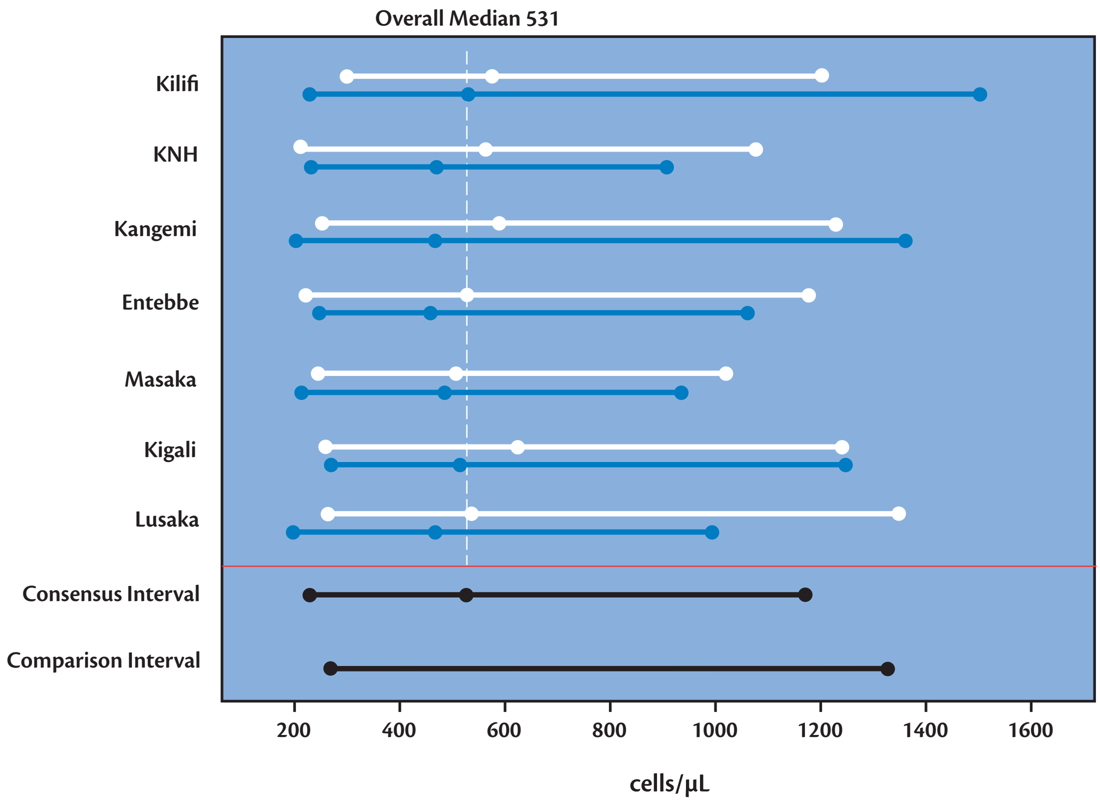
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 75: CD8 T cell counts 95% intervals and medians by research center and gender

Consensus interval: 230 to 1178
Comparison interval: 270 to 1335
White: Females, Blue: Males, Black: Overall



4. CHEMISTRY

4.1. Creatinine

Results

Table 51 shows the number of subjects with data included in the analysis. Figures 76, 77, and 78 show the creatinine distribution overall, by gender and by research center, respectively. Table 52 shows the distribution of creatinine by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 79. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (µmol/L)

Comparison interval: *0 to 133*
All centers, consensus interval: *47 to 109*

Table 51: Number of observations, creatinine

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1081	51.40	1022	48.60	2103

Figure 76: Frequency distribution of creatinine

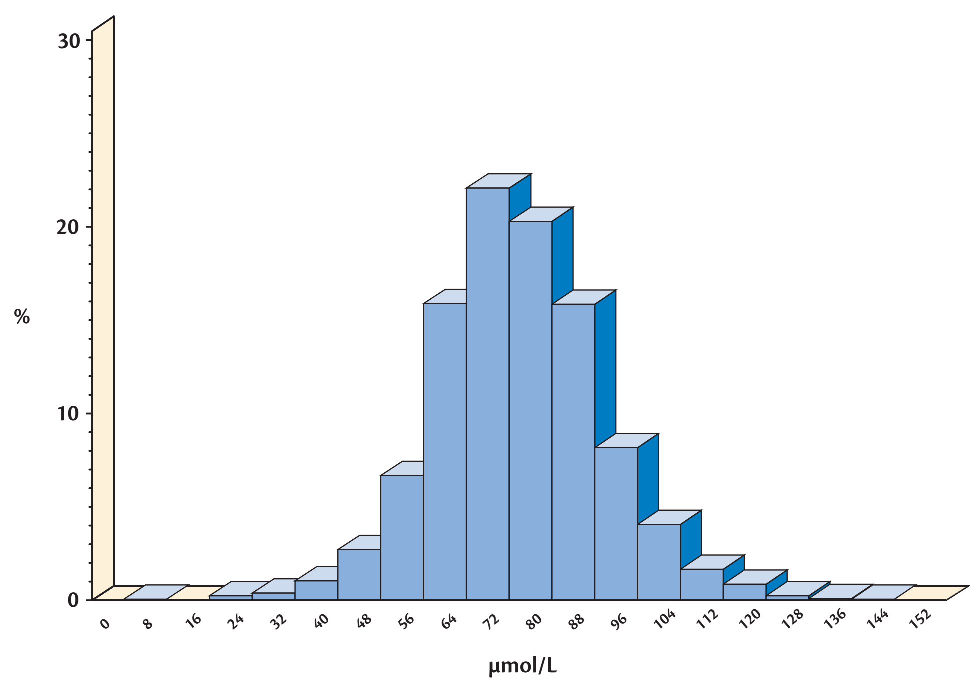


Figure 77: Frequency distribution of creatinine by gender

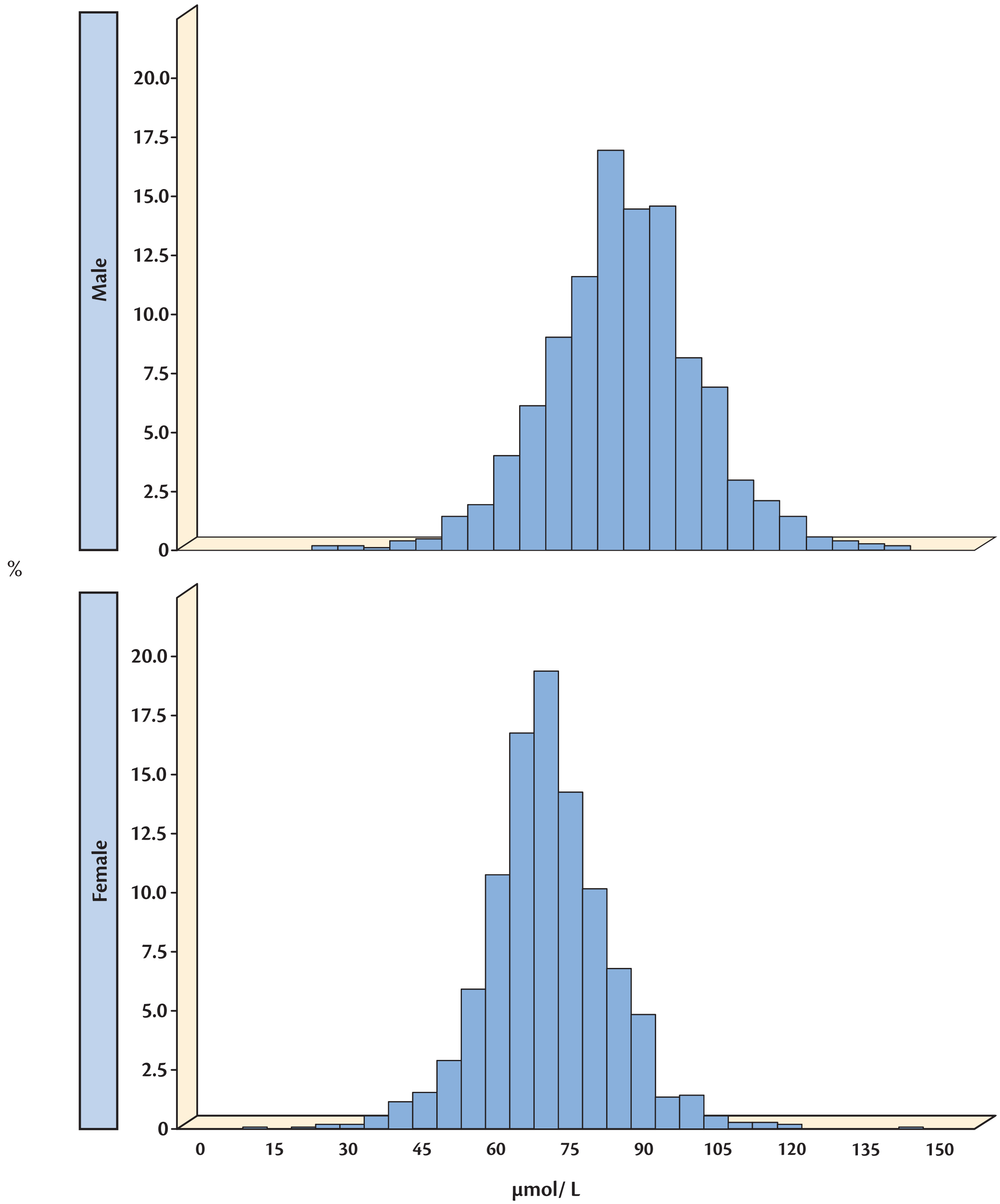


Figure 78: Frequency distribution of creatinine by research center

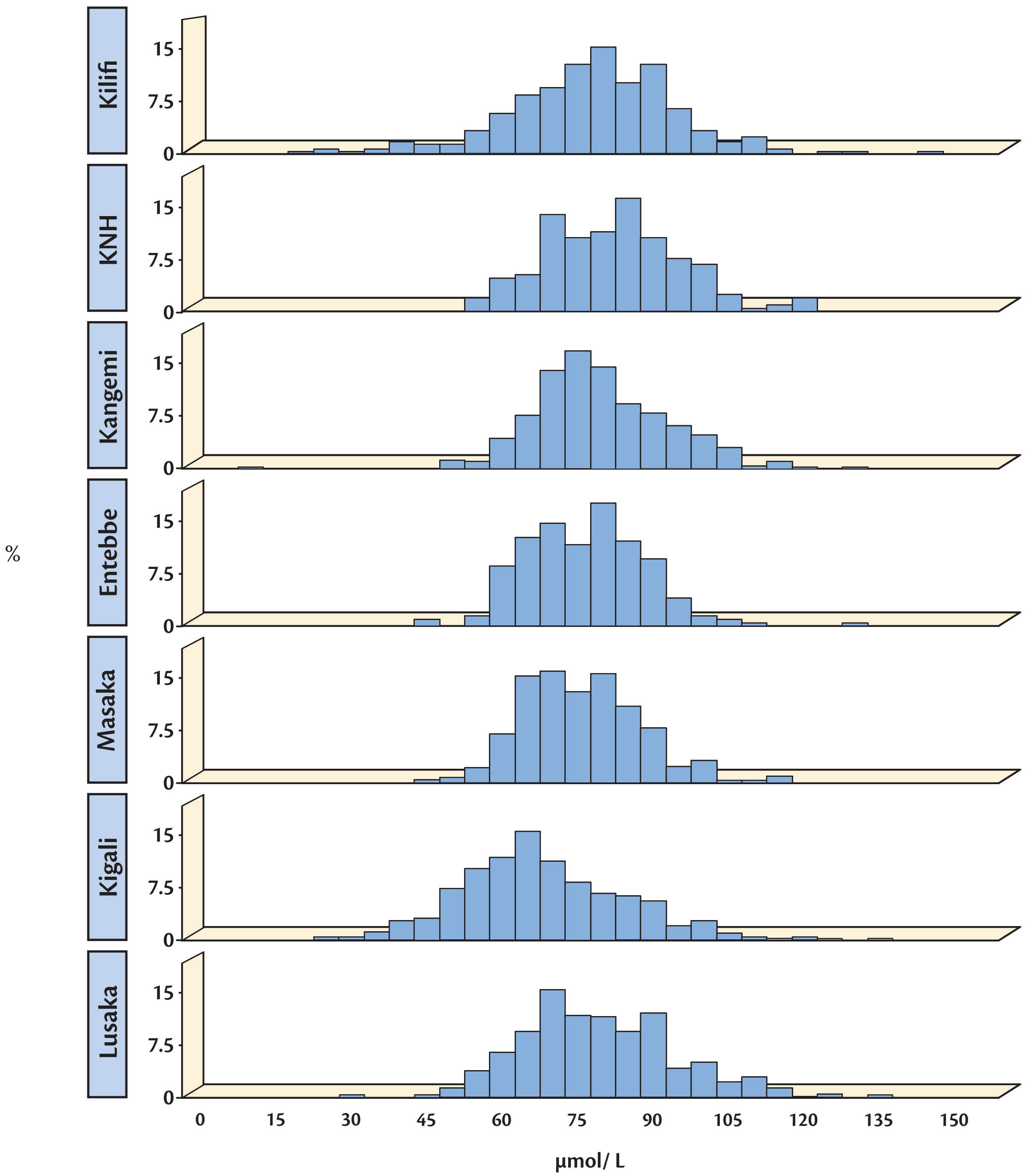


Table 52: Creatinine distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	70.3 (15.5)	71	39.3 to 101.4	37 to 92	20 to 144
	KNH	99	76.2 (12.4)	75	51.5 to 101.0	56 to 106	54 to 122
	Kangemi	176	74.2 (11.8)	73	50.5 to 97.9	53 to 100	10 to 114
	Entebbe	98	70.3 (9.8)	69.5	50.8 to 89.8	56 to 91	45 to 98
	Masaka	148	70.5 (11.8)	69	47.0 to 94.0	51 to 92	0 to 98
	Kigali	188	61.8 (13.8)	62	34.2 to 89.3	36 to 99	24 to 121
	Lusaka	184	72.3 (12.8)	71	46.8 to 97.9	50 to 105	31 to 113
	Total	1022	70.4 (13.5)	70	43.4 to 97.4	43 to 99	0 to 144
Male	Kilifi	167	83.6 (16.5)	85	50.7 to 116.6	44 to 111	24 to 129
	KNH	98	88.5 (12.2)	88	64.1 to 112.8	67 to 120	58 to 122
	Kangemi	186	84.4 (13.4)	83	57.6 to 111.2	61 to 116	49 to 128
	Entebbe	94	83.3 (10.4)	82	62.4 to 104.2	67 to 104	59 to 128
	Masaka	183	79.9 (12.3)	79	55.4 to 104.4	60 to 112	47 to 117
	Kigali	185	74.7 (17.7)	74	39.2 to 110.2	41 to 112	27 to 135
	Lusaka	168	87.0 (14.5)	85.5	57.9 to 116.1	59 to 117	50 to 134
	Total	1081	82.5 (15.0)	82	52.5 to 112.6	52 to 114	24 to 135
Total	Kilifi	296	77.8 (17.3)	79	43.1 to 112.5	38 to 111	20 to 144
	KNH	197	82.3 (13.7)	82	54.9 to 109.7	58 to 116	54 to 122
	Kangemi	362	79.4 (13.6)	78	52.2 to 106.7	57 to 107	10 to 128
	Entebbe	192	76.6 (12.0)	77	52.7 to 100.6	57 to 102	45 to 128
	Masaka	331	75.7 (12.9)	75	49.9 to 101.5	55 to 101	0 to 117
	Kigali	373	68.2 (17.1)	66	33.9 to 102.4	38 to 103	24 to 135
	Lusaka	352	79.3 (15.5)	78	48.4 to 110.3	53 to 113	31 to 134
	Total	2103	76.6 (15.5)	76	45.6 to 107.7	47 to 109	0 to 144

Research Center Comparisons

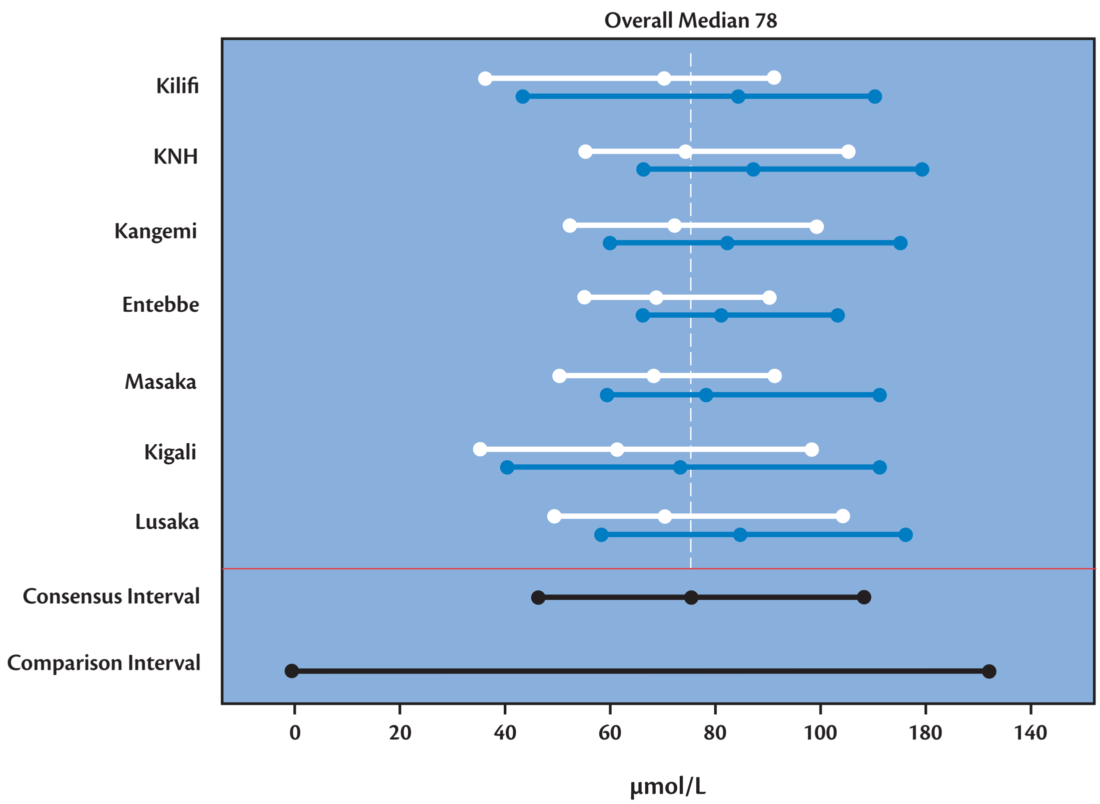
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 79: Creatinine 95% intervals and medians by research center and gender

Consensus interval: 47 to 109
Comparison interval: 0 to 133
White: Females, Blue: Males, Black: Overall



4.2. Aspartate Aminotransferase (AST)

Results

Table 53 shows the number of subjects with data included in the analysis. Figures 80, 81, and 82 show the AST (also referred to SGOT, serum glutamic-oxaloaetic transaminase) distribution overall, by gender and by research center, respectively. Table 54 shows the distribution of AST by research center and gender, together with the stratified 95% reference intervals. Since the distribution of AST is highly skewed to the left (Figure 80), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 82. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (IU/L)

Comparison interval: *0 to 35*
All centers, consensus interval: *14 to 60*

Table 53: Number of observations, AST

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1081	51.40	1022	48.60	2103

Figure 80: Frequency distribution of AST

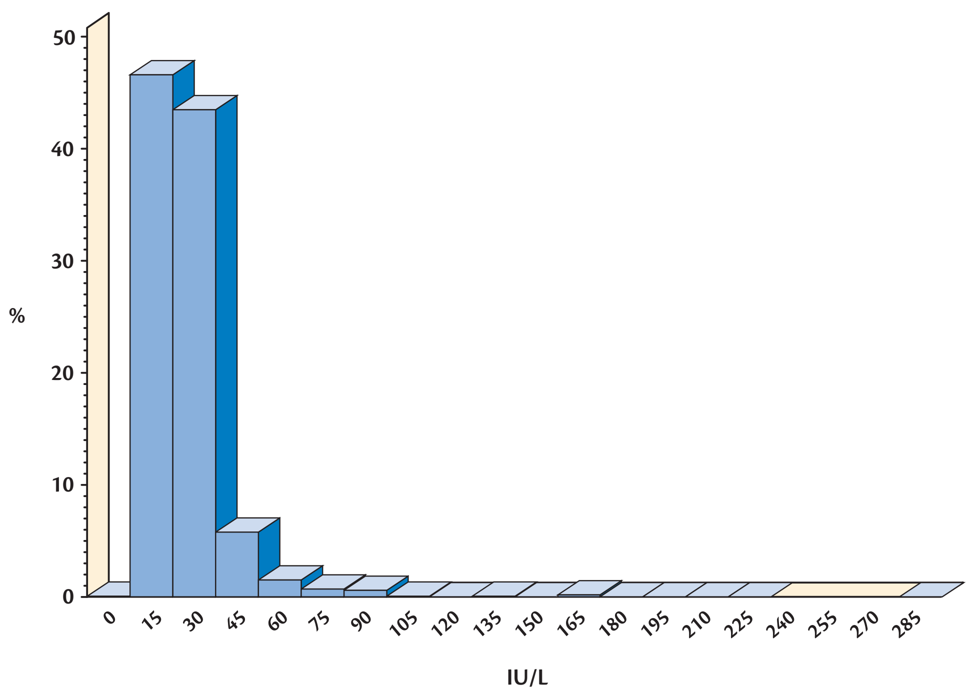
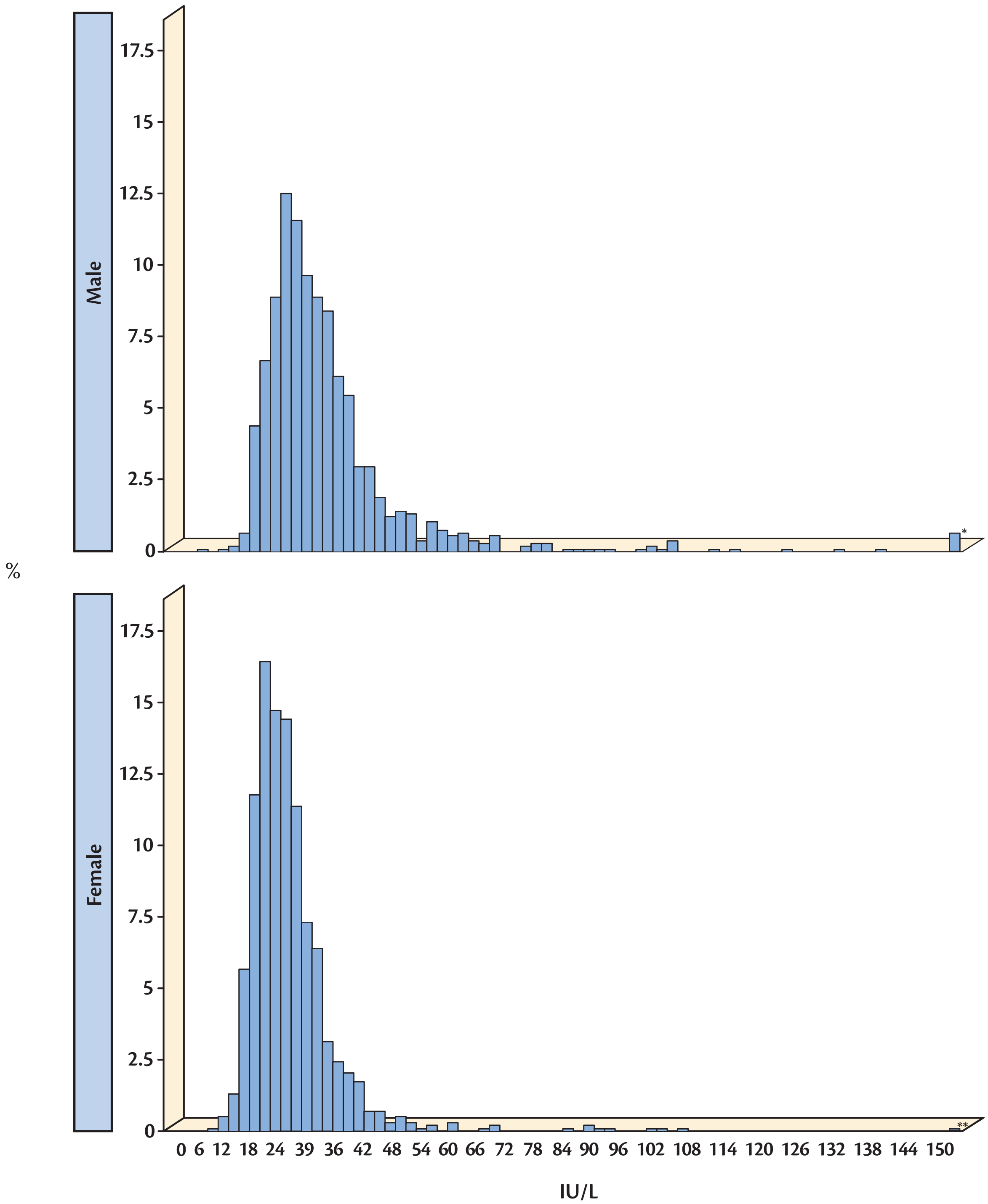


Figure 81: Frequency distribution of AST by gender



Final bar represents maximum values of: *152, 159, 164, 167, 168, 187, 197 IU/L
**283 IU/L

Figure 82: Frequency distribution of AST by research center

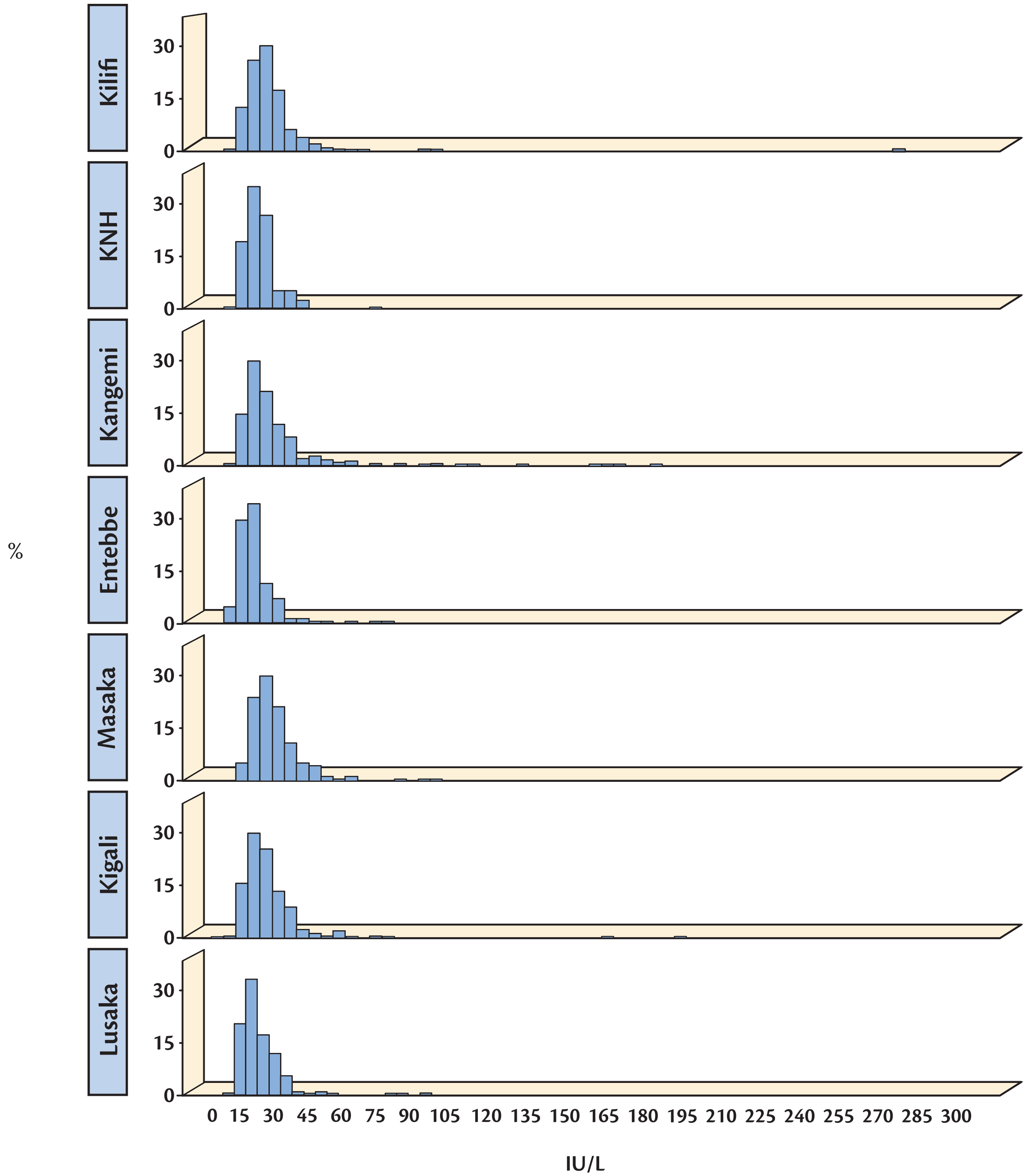


Table 54: AST distribution by research center and gender

Log transformation used, values are back-transformed (i.e., the geometric mean is shown)

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	23 (8.4)	23	11 to 48	13 to 40	11 to 283
	KNH	99	20 (4.8)	20	12 to 32	13 to 35	13 to 41
	Kangemi	176	21 (6.7)	21	11 to 40	13 to 41	11 to 97
	Entebbe	98	19 (5.2)	18	11 to 32	11 to 37	9 to 50
	Masaka	148	25 (7.3)	24	14 to 45	15 to 49	14 to 81
	Kigali	188	21 (6.5)	21	11 to 39	13 to 43	7 to 76
	Lusaka	184	20 (5.9)	19	11 to 36	13 to 33	9 to 93
	Total	1022	21 (6.7)	21	11 to 40	13 to 43	7 to 283
Male	Kilifi	167	27 (8.6)	26	14 to 51	16 to 54	15 to 95
	KNH	98	24 (6.3)	23	14 to 40	15 to 39	12 to 70
	Kangemi	186	30 (14.4)	27	12 to 78	16 to 128	15 to 187
	Entebbe	94	21 (7.5)	21	11 to 43	13 to 62	10 to 77
	Masaka	183	29 (8.9)	28	16 to 54	17 to 58	15 to 96
	Kigali	185	28 (10.4)	26	13 to 59	17 to 69	13 to 197
	Lusaka	168	27 (11.7)	26	11 to 64	15 to 94	6 to 152
	Total	1081	27 (10.5)	26	13 to 59	15 to 71	6 to 197
Total	Kilifi	296	25 (8.8)	24	12 to 51	15 to 53	11 to 283
	KNH	197	22 (5.8)	22	13 to 37	13 to 38	12 to 70
	Kangemi	362	26 (11.3)	23	11 to 62	14 to 90	11 to 187
	Entebbe	192	20 (6.5)	19	10 to 38	11 to 46	9 to 77
	Masaka	331	27 (8.4)	27	15 to 50	17 to 55	14 to 96
	Kigali	373	24 (9.0)	23	11 to 51	13 to 55	7 to 197
	Lusaka	352	23 (9.2)	21	10 to 51	14 to 79	6 to 152
	Total	2103	24 (9.0)	23	11 to 51	14 to 60	6 to 283

Research Center Comparisons

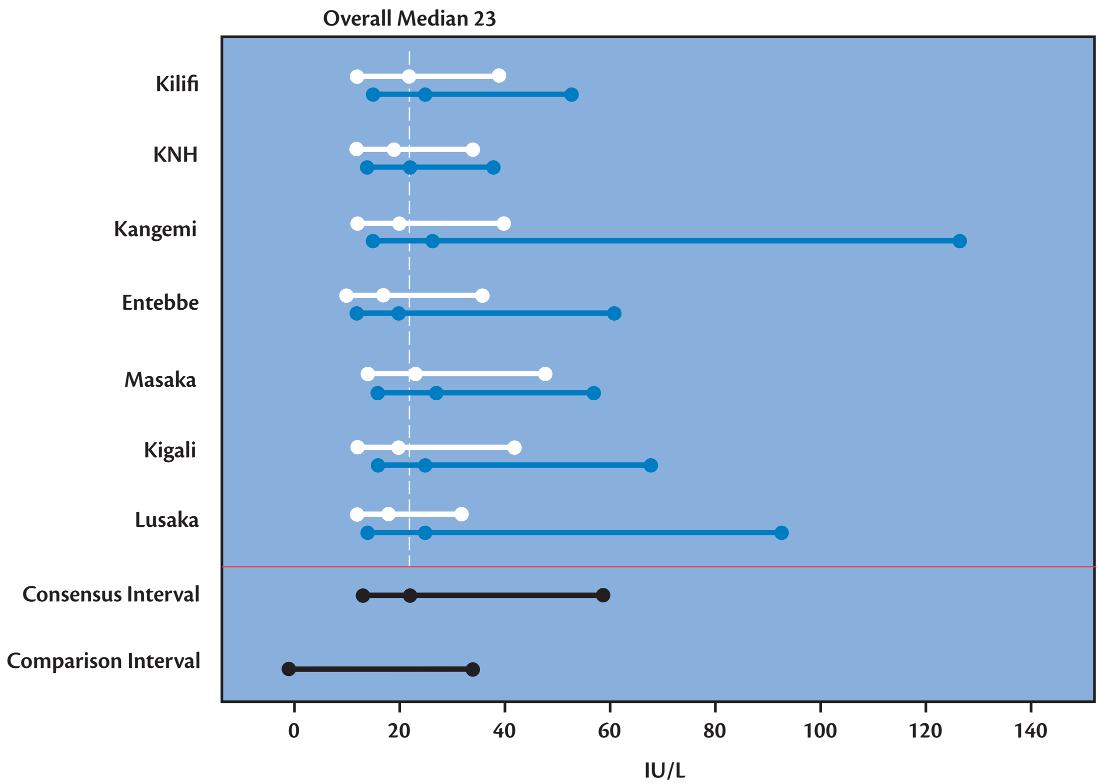
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 83: AST 95% intervals and medians by research center and gender

Consensus interval: 14 to 60
Comparison interval: 0 to 35
White: Females, Blue: Males, Black: Overall



4.3. Alanine Aminotransferase (ALT)

Results

Table 55 shows the number of subjects with data included in the analysis. Figures 84, 85, and 86 show the ALT (also referred to as SGPT, serum glutamate pyruvate transaminase) distribution overall, by gender and by research center, respectively. Table 56 shows the distribution of ALT by research center and gender, together with the stratified 95% reference intervals. Since the distribution of ALT is highly skewed to the left (Figure 84), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 87. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (IU/L)

Comparison interval:	*0 to 35*
All centers, consensus interval:	*8 to 61*

Table 55: Number of observations, ALT

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1081	51.40	1022	48.60	2103

Figure 84: Frequency distribution of ALT

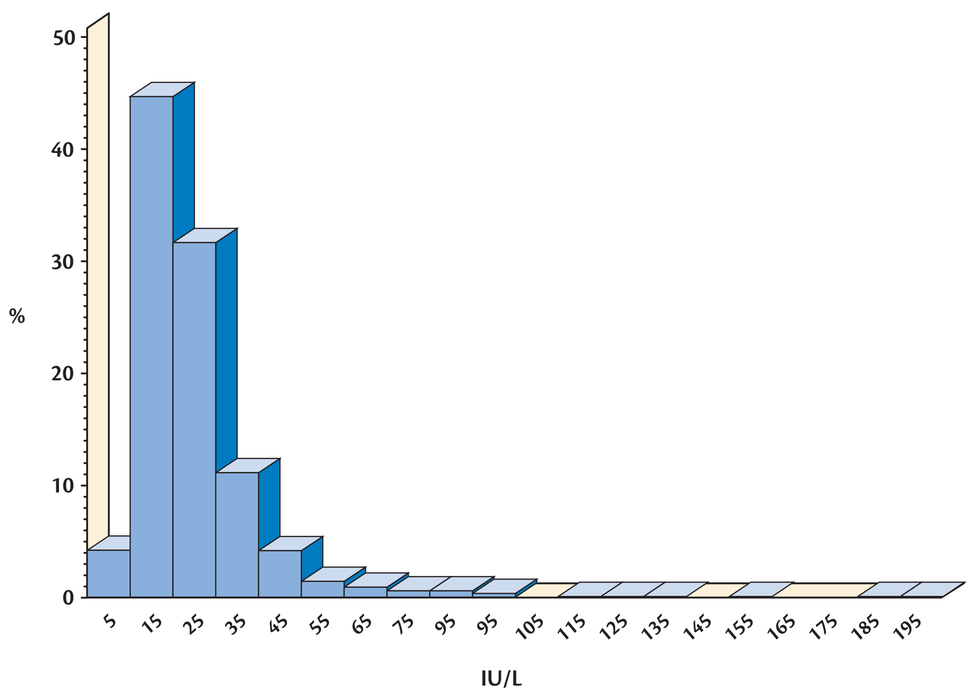


Figure 85: Frequency distribution of ALT by gender

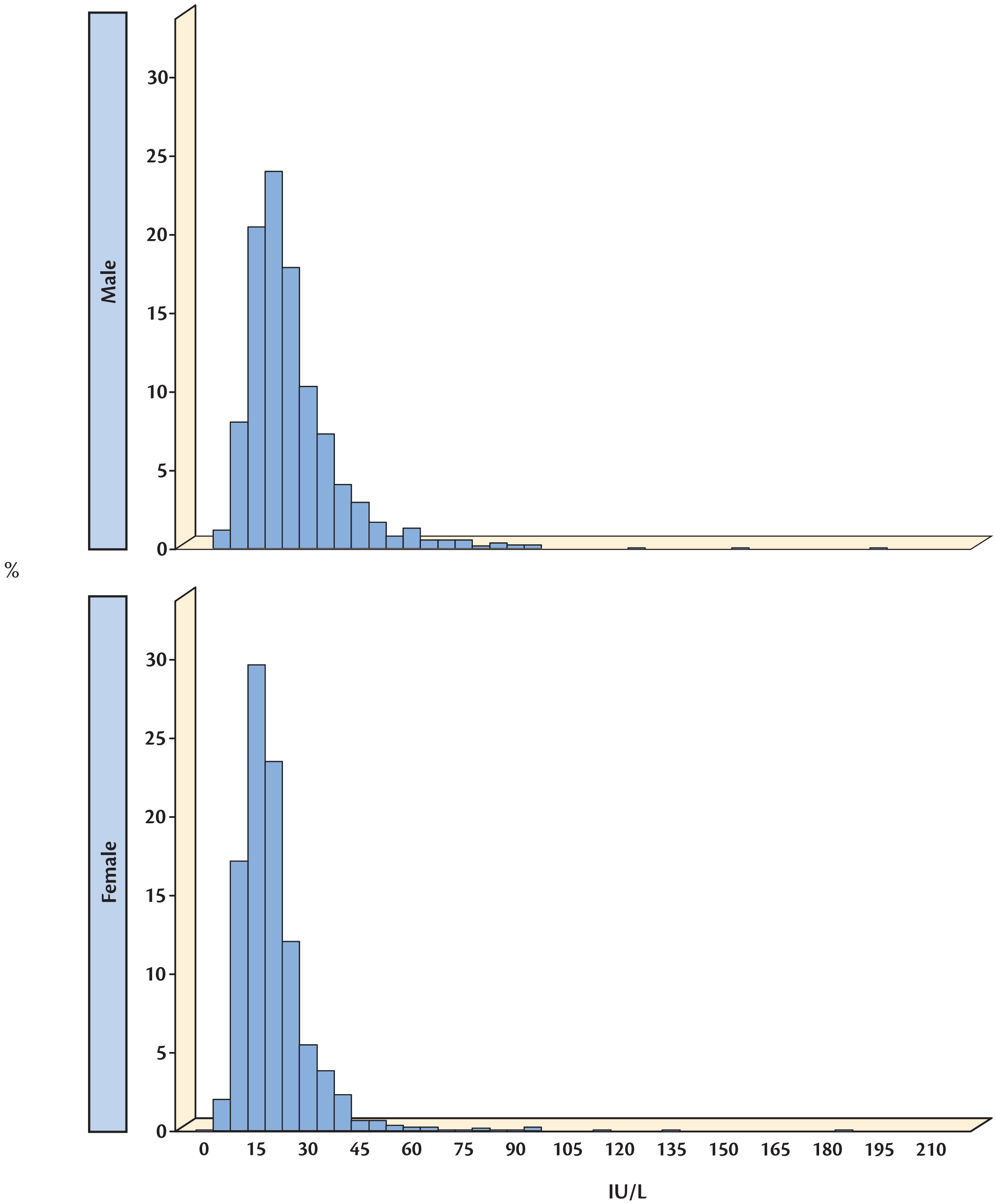


Figure 86: Frequency distribution of ALT by research center

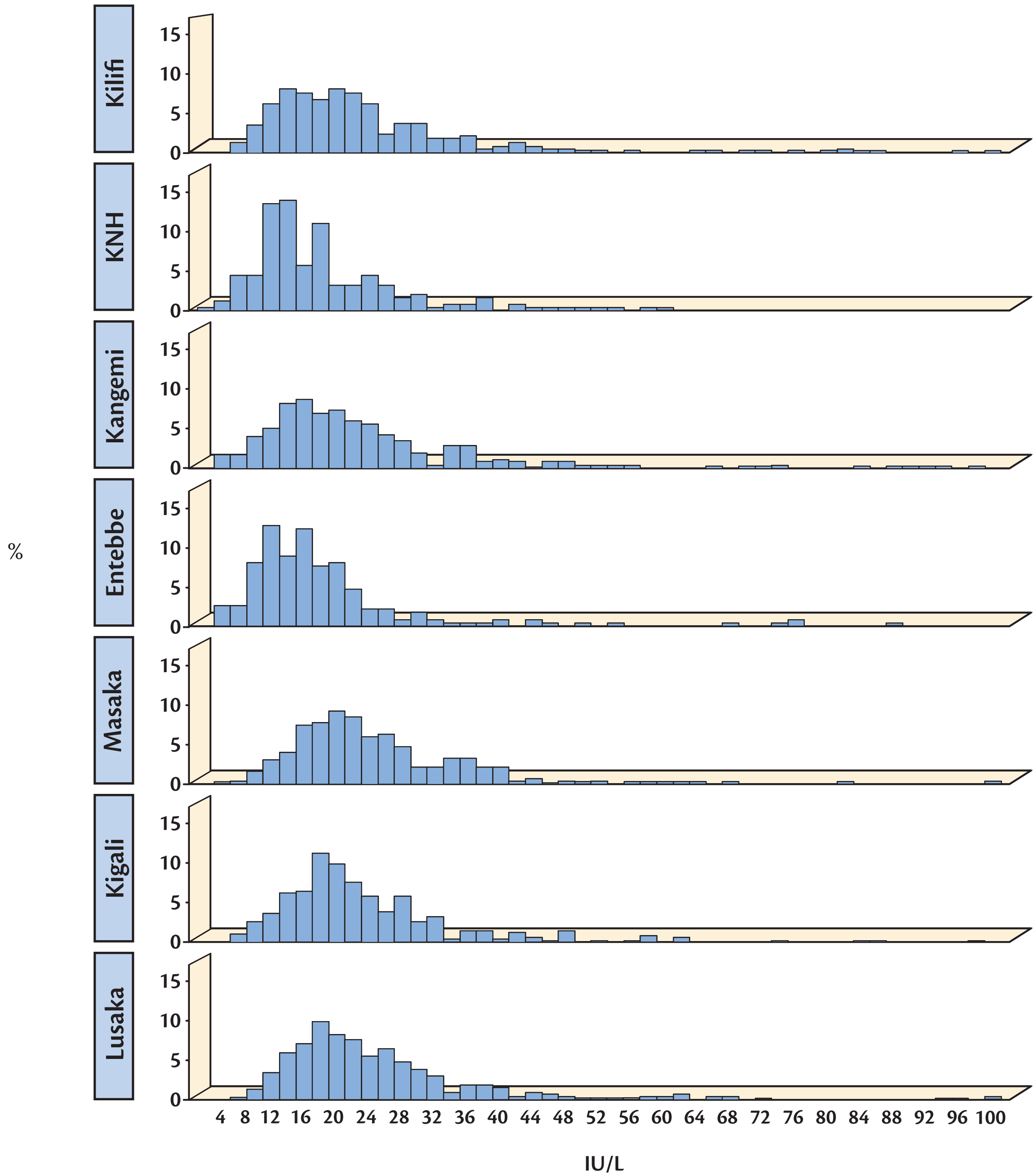


Table 56: ALT distribution by research center and gender

Log transformation used, values are back-transformed (i.e., the geometric mean is shown)

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	18 (8.1)	17	7 to 44	8 to 55	8 to 96
	KNH	99	14 (6.7)	13	6 to 37	6 to 38	4 to 43
	Kangemi	176	17 (8.1)	17	7 to 44	6 to 39	5 to 91
	Entebbe	98	14 (5.4)	14	7 to 31	7 to 40	5 to 54
	Masaka	148	22 (9.5)	20	9 to 52	10 to 59	8 to 114
	Kigali	188	19 (7.9)	19	8 to 44	8 to 48	7 to 97
	Lusaka	184	20 (8.9)	19	8 to 49	10 to 66	7 to 185
	Total	1022	18 (8.3)	18	7 to 45	8 to 48	4 to 185
Male	Kilifi	167	24 (11.4)	23	9 to 62	11 to 80	7 to 124
	KNH	98	18 (8.5)	17	7 to 46	8 to 54	7 to 59
	Kangemi	186	23 (12.4)	22	8 to 67	8 to 83	5 to 97
	Entebbe	94	18 (10.3)	17	6 to 56	6 to 75	5 to 88
	Masaka	183	23 (9.8)	24	10 to 54	11 to 49	6 to 197
	Kigali	185	24 (9.7)	22	10 to 54	9 to 58	9 to 83
	Lusaka	168	26 (10.7)	25	11 to 59	12 to 62	9 to 95
	Total	1081	23 (10.9)	22	9 to 59	9 to 67	5 to 197
Total	Kilifi	296	21 (10.2)	20	8 to 56	9 to 76	7 to 124
	KNH	197	16 (7.7)	15	6 to 42	7 to 49	4 to 59
	Kangemi	362	20 (10.6)	20	7 to 57	7 to 70	5 to 97
	Entebbe	192	16 (7.9)	15	6 to 43	6 to 67	5 to 88
	Masaka	331	23 (9.7)	22	10 to 53	10 to 56	6 to 197
	Kigali	373	21 (9.0)	20	9 to 50	9 to 58	7 to 97
	Lusaka	352	23 (10.1)	22	9 to 55	11 to 65	7 to 185
	Total	2103	20 (9.8)	20	8 to 53	8 to 61	4 to 197

Research Center Comparisons

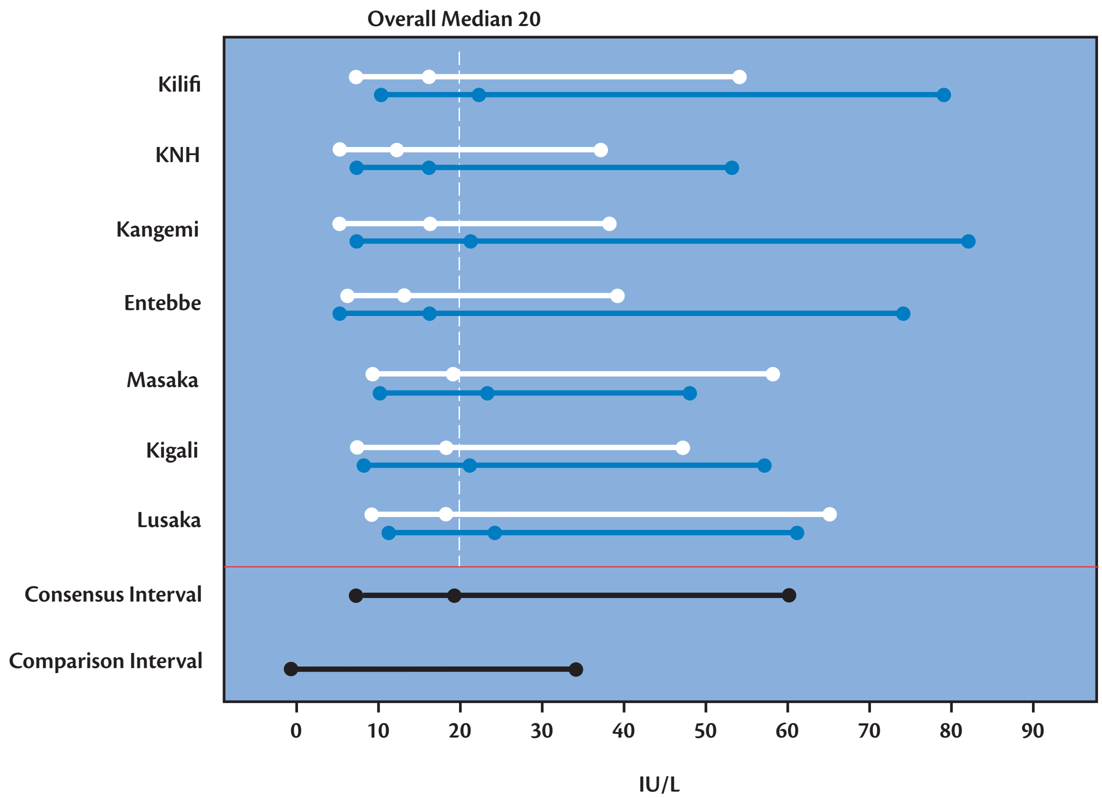
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 87: ALT 95% intervals and medians by research center and gender

Consensus interval: 8 to 61
Comparison interval 0 to 35
White: Females, Blue: Males, Black: Overall



4.4. Direct Bilirubin

Results

Table 57 shows the number of subjects with data included in the analysis. Figures 88, 89, and 90 show the direct bilirubin distribution overall, by gender and by research center, respectively. Table 58 shows the distribution of direct bilirubin by research center and gender, together with the stratified 95% reference intervals. Since the distribution of direct bilirubin is highly skewed to the left (Figure 88), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 91. Any significant differences that exist across center or gender are presented in Table 59. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (µmol/L)

Comparison interval: *1.7 to 5.1*
Consensus interval:* *0.4 to 8.8*
** Excludes females from Kilifi*

Table 57: Number of observations, direct bilirubin

	Male		Female		Total
	N	%	N	%	N
Kilifi	117	57.07	88	42.93	205
KNH	96	50.26	95	49.74	191
Kangemi	182	51.56	171	48.44	353
Entebbe	94	48.96	98	51.04	192
Masaka	183	55.45	147	44.55	330
Kigali	185	49.87	186	50.13	371
Lusaka	168	47.73	184	52.27	352
Total	1025	51.40	969	48.60	1994

Figure 88: Frequency distribution of direct bilirubin

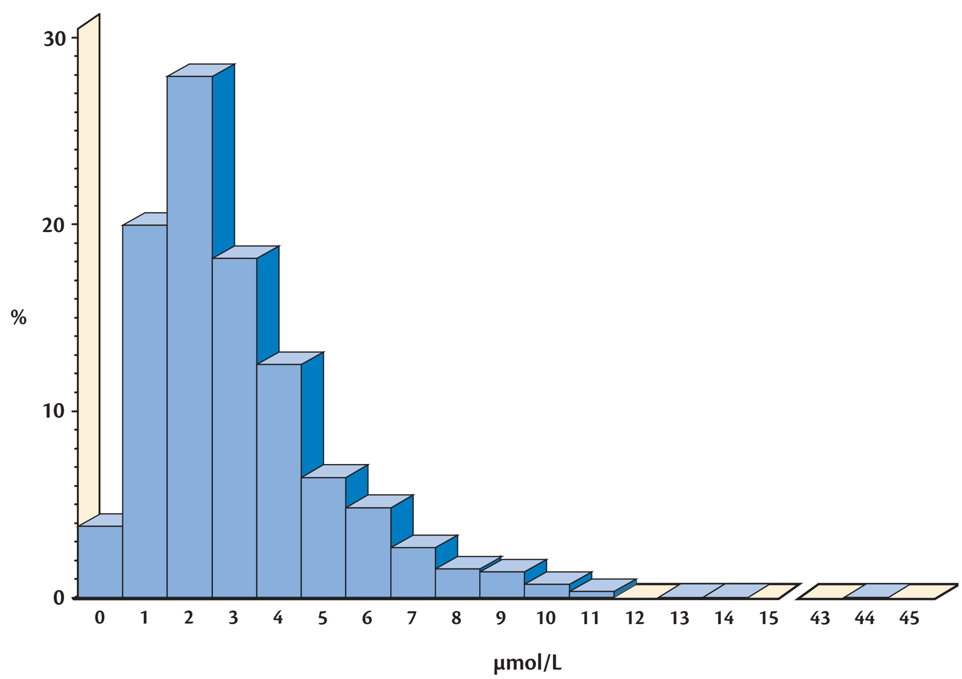


Figure 89: Frequency distribution of direct bilirubin by gender

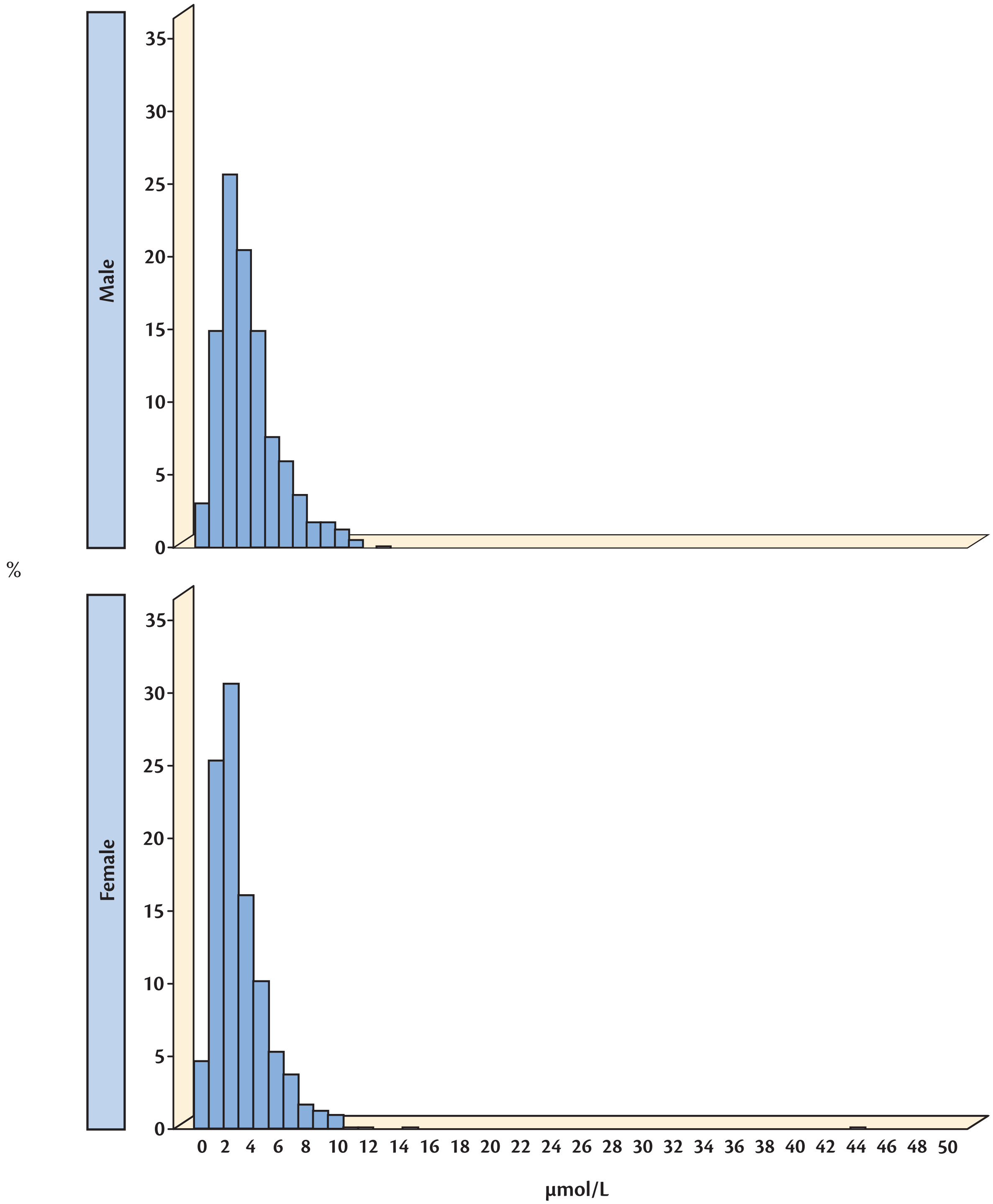


Figure 90: Frequency distribution of direct bilirubin by research center

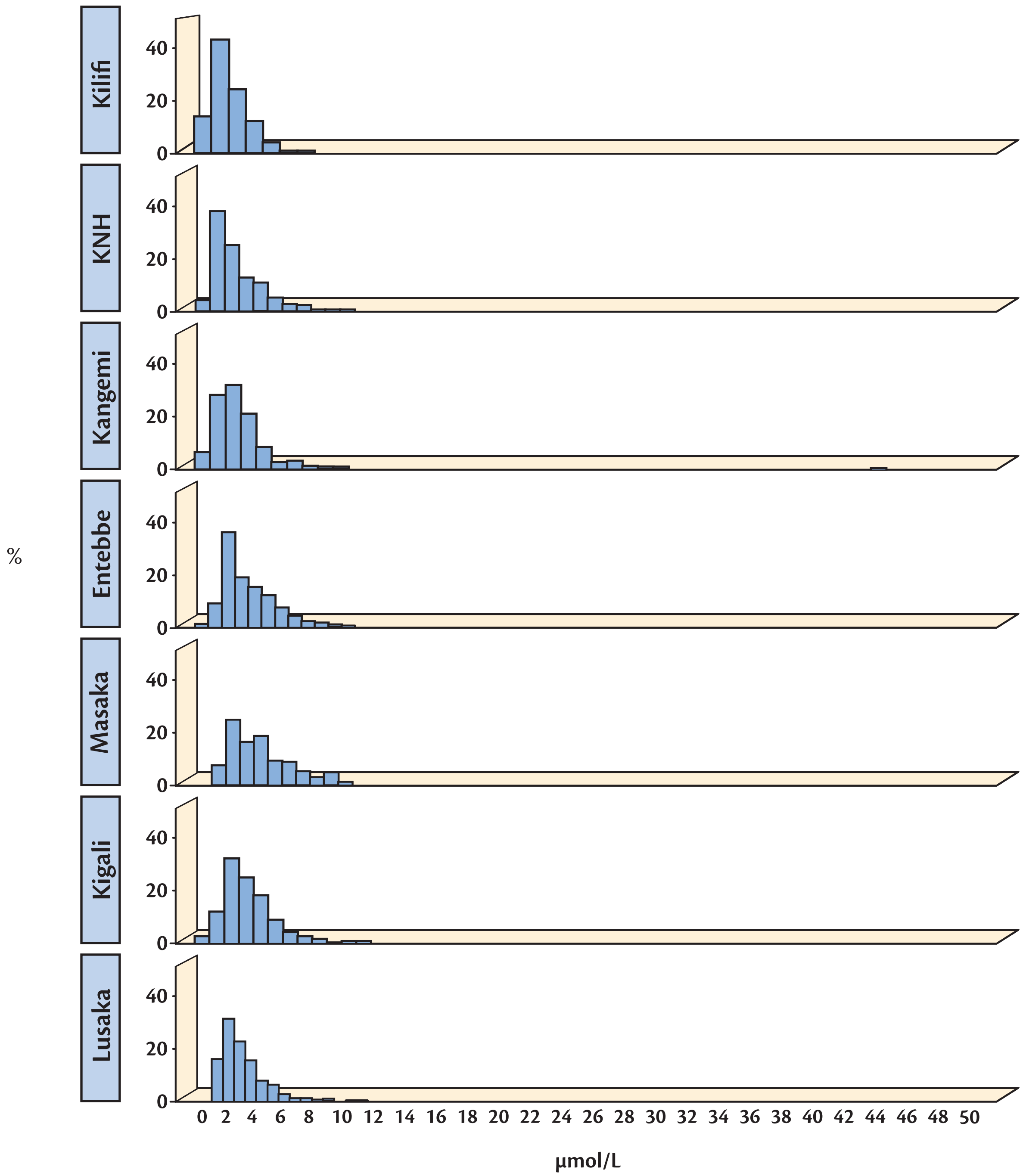


Table 58: Direct bilirubin distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	88	0.8 (0.7)	0.9	0.2 to 4.1	0.1 to 2.7	0.1 to 2.9
	KNH	95	1.4 (1.0)	1.4	0.3 to 6.2	0.3 to 6.2	0.3 to 7.6
	Kangemi	171	1.7 (1.3)	1.7	0.3 to 8.0	0.3 to 6.3	0.1 to 43.7
	Entebbe	98	2.5 (1.6)	2.4	0.7 to 9.0	0.6 to 7.5	0.3 to 9.0
	Masaka	147	3.0 (1.9)	3.2	0.8 to 10.7	0.8 to 9.2	0.6 to 10.1
	Kigali	186	2.2 (1.5)	2.3	0.6 to 8.8	0.4 to 6.6	0.1 to 10.8
	Lusaka	184	2.4 (1.6)	2.4	0.7 to 8.8	0.5 to 7.9	0.5 to 13.5
	Total	969	2.0 (1.6)	2.1	0.4 to 9.6	0.3 to 7.5	0.1 to 43.7
Male	Kilifi	117	1.4 (1.2)	1.6	0.2 to 7.8	0.1 to 5.2	0.1 to 5.9
	KNH	96	2.2 (1.7)	2.2	0.5 to 9.8	0.5 to 7.2	0.2 to 9.8
	Kangemi	182	1.9 (1.4)	2.0	0.4 to 8.8	0.3 to 6.5	0.1 to 8.1
	Entebbe	94	3.4 (2.2)	3.4	0.9 to 12.2	1.0 to 9.5	0.2 to 10.5
	Masaka	183	3.9 (2.3)	4.1	1.2 to 12.4	0.9 to 9.9	0.7 to 12.6
	Kigali	185	3.0 (2.1)	3.2	0.8 to 12.1	0.4 to 9.7	0.1 to 11.4
	Lusaka	168	3.2 (1.8)	3.2	1.1 to 10.0	1.1 to 10.0	0.8 to 12.7
	Total	1025	2.6 (2.0)	2.8	0.6 to 12.3	0.4 to 9.4	0.1 to 12.7
Total	Kilifi	205	1.1 (1.0)	1.2	0.2 to 6.3	0.1 to 4.3	0.1 to 5.9
	KNH	191	1.8 (1.4)	1.7	0.4 to 8.3	0.3 to 7.1	0.2 to 9.8
	Kangemi	353	1.8 (1.4)	1.9	0.4 to 8.4	0.3 to 6.5	0.1 to 43.7
	Entebbe	192	2.9 (1.9)	3.0	0.8 to 10.8	0.8 to 9.0	0.2 to 10.5
	Masaka	330	3.5 (2.1)	3.5	1.0 to 11.9	0.9 to 9.6	0.6 to 12.6
	Kigali	371	2.6 (1.8)	2.7	0.6 to 10.7	0.4 to 8.2	0.1 to 11.4
	Lusaka	352	2.8 (1.7)	2.7	0.8 to 9.7	0.8 to 9.4	0.5 to 13.5
	Total	1994	2.3 (1.8)	2.4	0.5 to 11.2	0.4 to 8.8	0.1 to 43.7

Research Center Comparisons

For females there is a significant difference in direct bilirubin between Kilifi and the other centers when considered together (Table 5) according to the CLSI guidelines (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment, and either the magnitude of the difference is ≥25% of the overall interv9al or the Ratio of the two interval standard deviations is >1.5.)

Table 59: Evaluation of direct bilirubin by gender and research center

Combined Interval	Consensus Interval	Consensus Mean (SD)	Kilifi Interval	Kilifi Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
0.30 to 7.50	0.40 to 7.60	0.77(0.73)	0.10 to 2.70	-0.20(0.80)	Yes	No
		2.17(1.58)*		0.82(0.66)*		

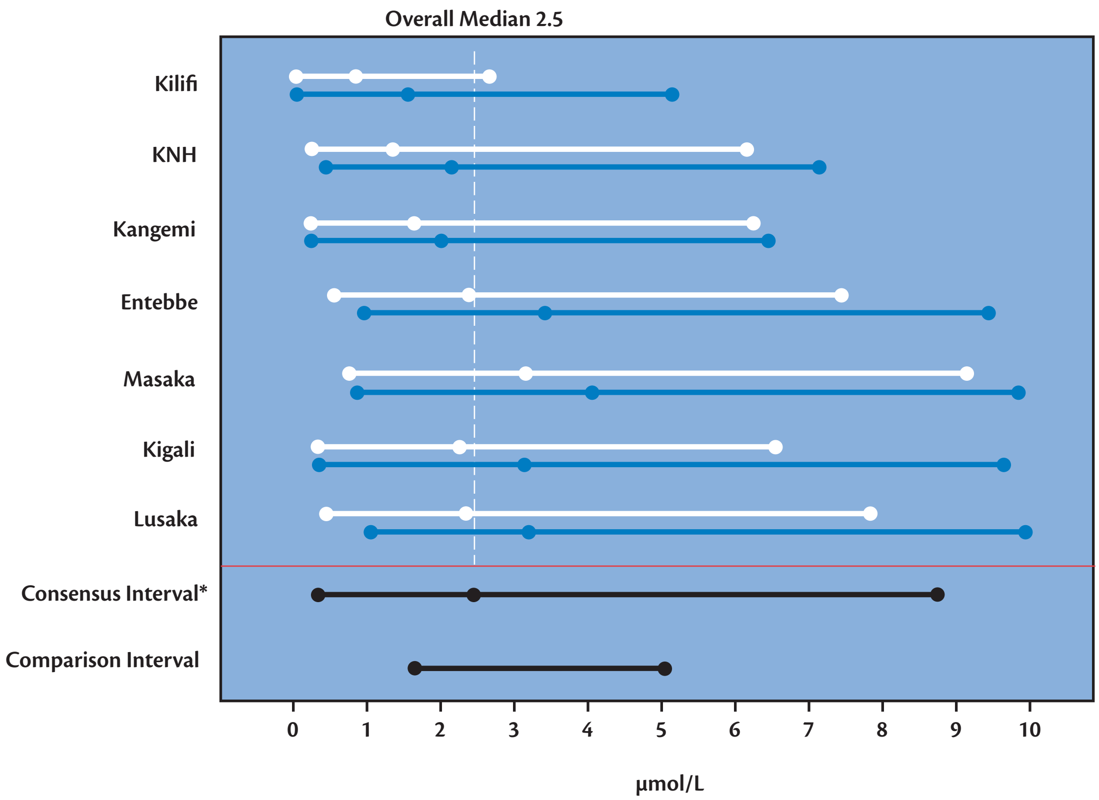
* Back-transformed from log estimates

Gender Comparisons

Excluding data from females at Kilifi, the difference between males and females in the remaining centers is not significant according to the CLSI guidelines.

Figure 91: Direct bilirubin 95% intervals and medians by research center and gender

*Consensus interval: 0.4 to 8.8**
Comparison interval: 1.7 to 5.1
White: Females, Blue: Males, Black: Overall



*Excludes females from Kilifi

4.5. Total Bilirubin

Results

Table 60 shows the number of subjects with data included in the analysis. Figures 92, 93, and 94 show the total bilirubin distribution overall, by gender and by research center, respectively. Table 61 shows the distribution of total bilirubin by research center and gender, together with the stratified 95% reference intervals. Since the distribution of total bilirubin is highly skewed to the left (Figure 92), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 95. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (µmol/L)

Comparison interval: *5.1 to 17.0*
All centers, consensus interval: *3.9 to 37.0*

Table 60: Number of observations, total bilirubin

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	182	55.15	148	44.85	330
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1080	51.38	1022	48.62	2102

Figure 92: Frequency distribution of total bilirubin

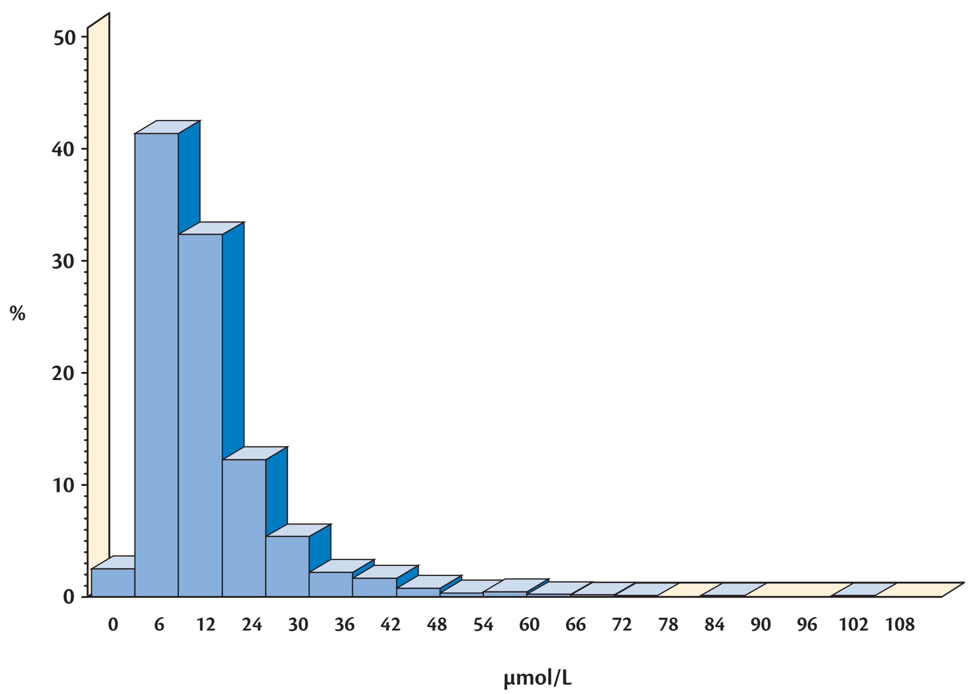


Figure 93: Frequency distribution of total bilirubin by gender

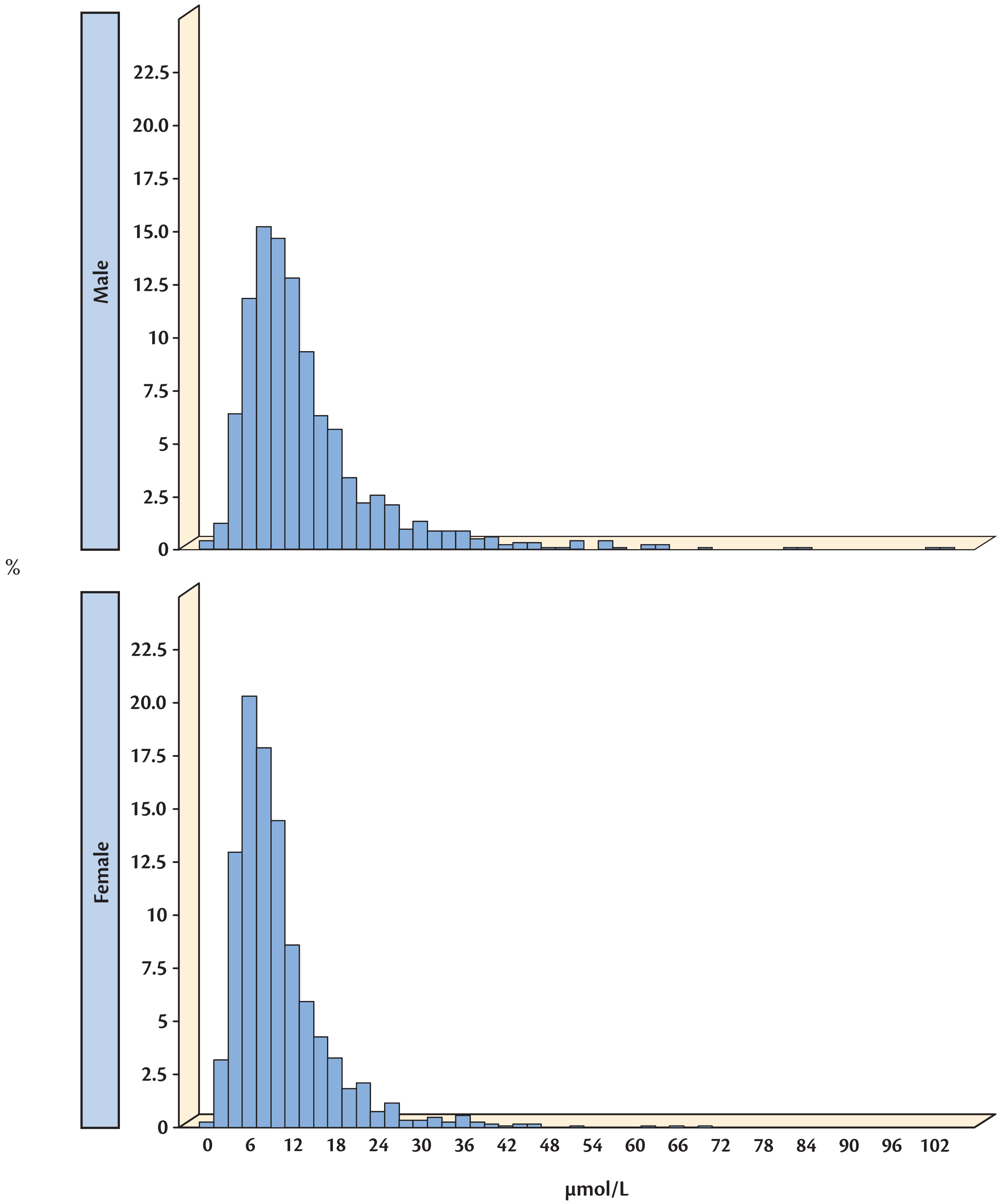


Figure 94: Frequency distribution of total bilirubin by research center

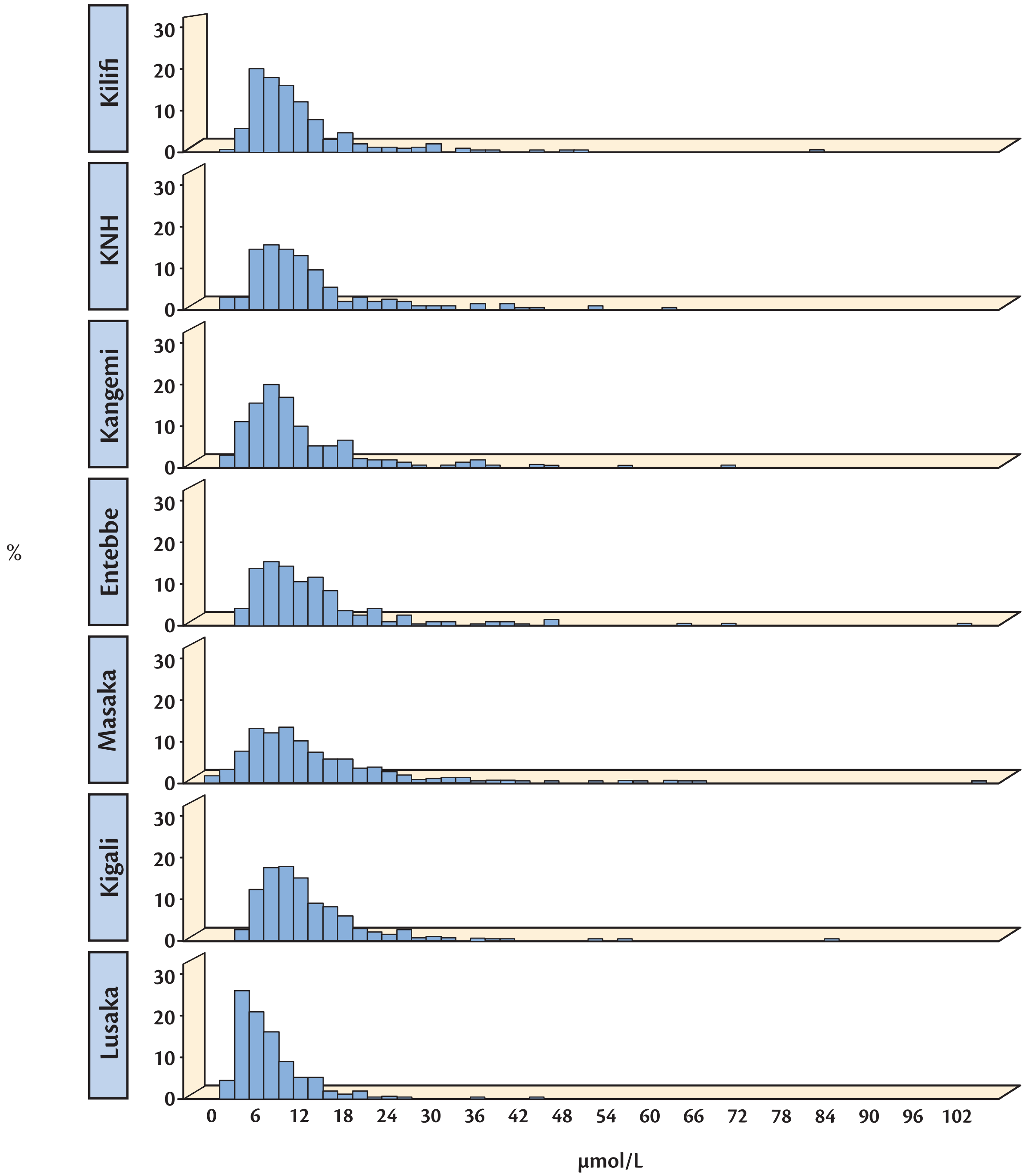


Table 61: Total bilirubin distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	8.2 (3.8)	7.7	3.2 to 20.9	3.9 to 22.3	3.5 to 29.4
	KNH	99	8.6 (5.0)	8.8	2.7 to 27.8	2.4 to 31.9	1.6 to 41.4
	Kangemi	176	8.9 (5.9)	9.0	2.4 to 33.7	2.6 to 35.3	0.2 to 43.7
	Entebbe	98	10.5 (6.2)	9.8	3.2 to 34.0	4.3 to 46.8	3.6 to 70.6
	Masaka	148	9.3 (7.7)	9.2	1.8 to 49.1	1.2 to 40.6	0.2 to 66.6
	Kigali	188	9.8 (4.3)	9.3	4.0 to 23.8	4.3 to 25.2	3.8 to 36.4
	Lusaka	184	6.2 (3.5)	5.7	2.0 to 19.0	2.3 to 18.0	1.5 to 43.8
	Total	1022	8.6 (5.3)	8.5	2.5 to 29.8	2.7 to 31.5	0.2 to 70.6
Male	Kilifi	167	11.9 (6.5)	11.0	4.0 to 35.5	5.2 to 38.2	2.7 to 81.9
	KNH	98	13.8 (9.1)	13.5	3.7 to 51.2	5.4 to 51.5	0.4 to 62.7
	Kangemi	186	10.2 (6.6)	9.9	2.8 to 37.2	2.7 to 37.2	1.1 to 69.7
	Entebbe	94	14.0 (8.0)	13.3	4.5 to 43.8	5.2 to 46.5	4.0 to 101.8
	Masaka	182	11.9 (10.1)	12.5	2.2 to 64.9	2.1 to 56.9	0.2 to 103.8
	Kigali	185	13.6 (6.3)	13.1	5.4 to 34.5	5.7 to 38.2	4.5 to 84.1
	Lusaka	168	7.6 (3.9)	7.1	2.7 to 21.2	3.3 to 23.0	1.9 to 36.6
	Total	1080	11.3 (7.4)	11.1	3.1 to 41.8	3.6 to 41.9	0.2 to 103.8
Total	Kilifi	296	10.1 (5.5)	9.5	3.4 to 30.1	4.0 to 33.2	2.7 to 81.9
	KNH	197	10.9 (7.2)	10.9	2.9 to 41.0	2.9 to 41.4	0.4 to 62.7
	Kangemi	362	9.5 (6.3)	9.4	2.6 to 35.6	2.7 to 35.8	0.2 to 69.7
	Entebbe	192	12.1 (7.2)	11.6	3.7 to 39.8	4.3 to 46.8	3.6 to 101.8
	Masaka	330	10.7 (9.0)	10.9	2.0 to 58.1	1.8 to 52.5	0.2 to 103.8
	Kigali	373	11.5 (5.6)	11.2	4.4 to 30.3	4.8 to 31.5	3.8 to 84.1
	Lusaka	352	6.8 (3.7)	6.6	2.3 to 20.3	2.5 to 20.7	1.5 to 43.8
	Total	2102	9.9 (6.5)	9.8	2.7 to 36.5	2.9 to 37.0	0.2 to 103.8

Research Center Comparisons

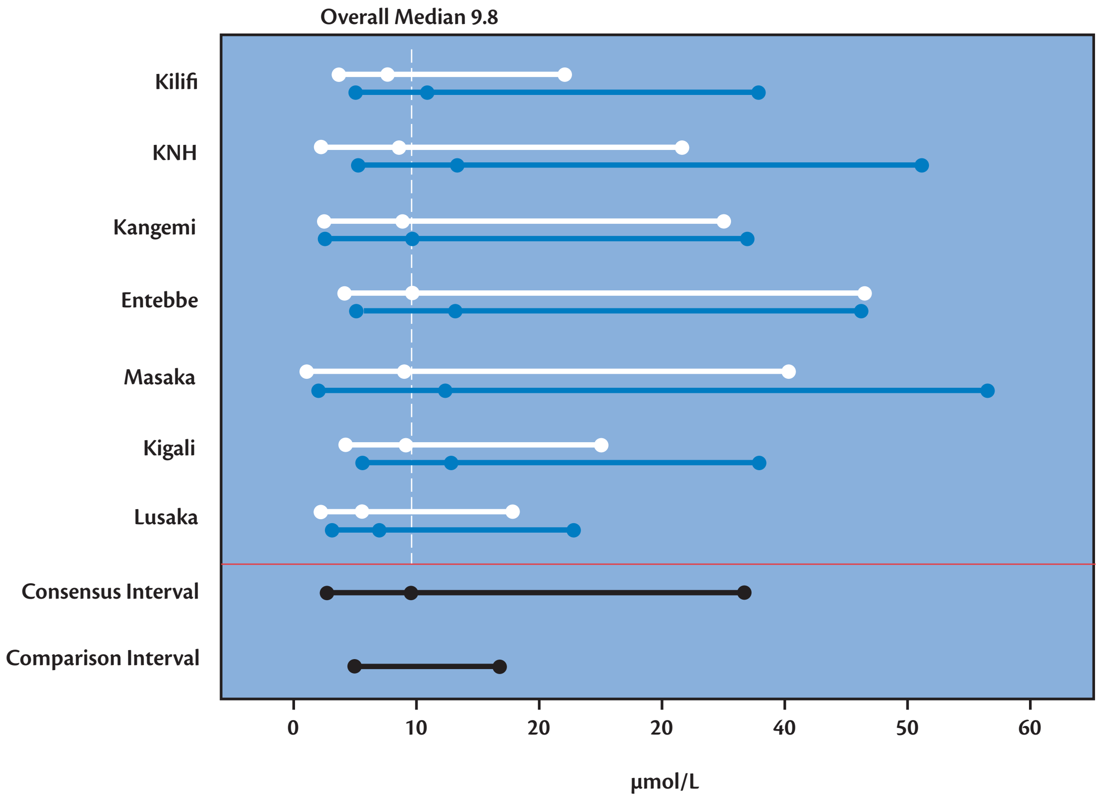
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 95: Total bilirubin 95% intervals and medians by research center and gender

Consensus interval: 3.9 to 37.0
Comparison interval: 5.1 to 17.0
White: Females, Blue: Males, Black: Overall



4.6. Albumin

Results

Table 62 shows the number of subjects with data included in the analysis. Figures 96, 97, and 98 show the albumin distribution overall, by gender and by research center, respectively. Table 63 shows the distribution of albumin by research center and gender, together with the stratified 95% reference intervals. The same quantiles and median values are shown in Figure 99. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (g/L)

Comparison interval:	*35 to 55*
All centers, consensus interval:	*35 to 52*

Table 62: Number of observations, albumin

	Male		Female		Total
	N	%	N	%	N
Kilifi	**167**	**56.42**	**129**	**43.58**	**296**
KNH	**98**	**49.75**	**99**	**50.25**	**197**
Kangemi	**186**	**51.38**	**176**	**48.62**	**362**
Entebbe	**94**	**48.96**	**98**	**51.04**	**192**
Masaka	**183**	**55.29**	**148**	**44.71**	**331**
Kigali	**185**	**49.60**	**188**	**50.40**	**373**
Lusaka	**168**	**47.73**	**184**	**52.27**	**352**
Total	**1081**	**51.40**	**1022**	**48.60**	**2103**

Figure 96: Frequency distribution of albumin

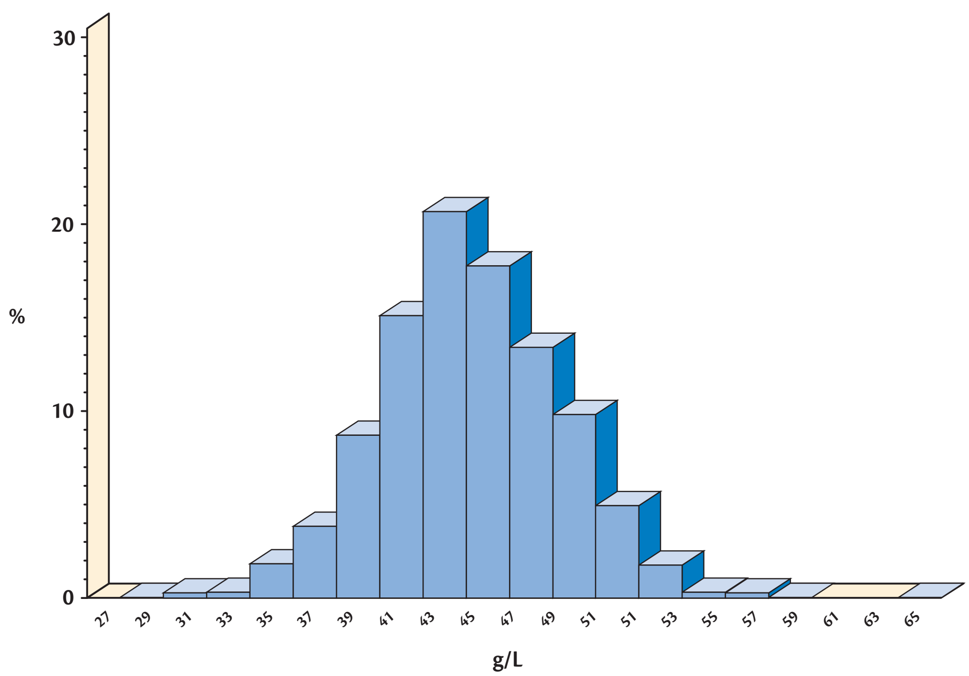


Figure 97: Frequency distribution of albumin by gender

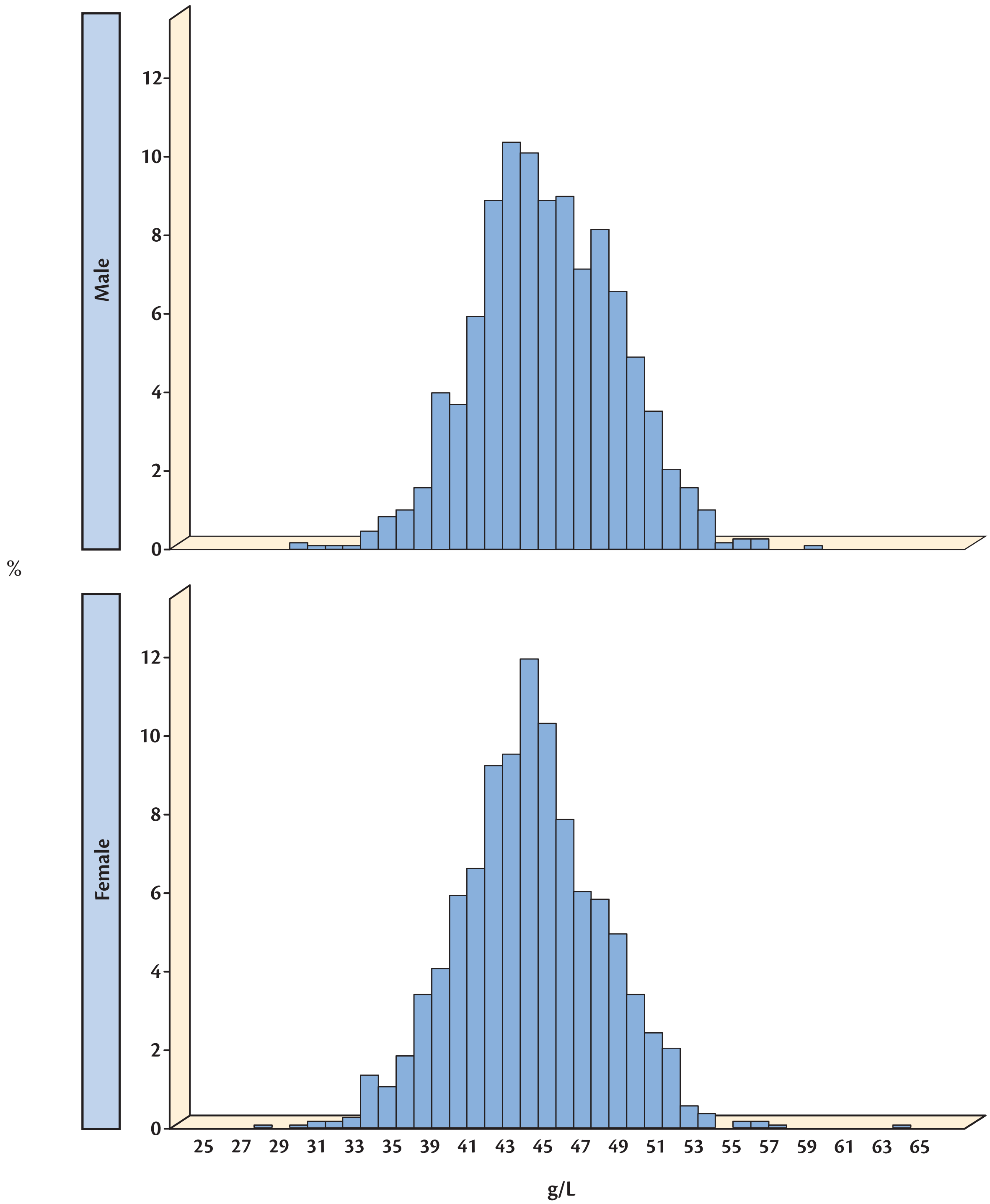


Figure 98: Frequency distribution of albumin by research center

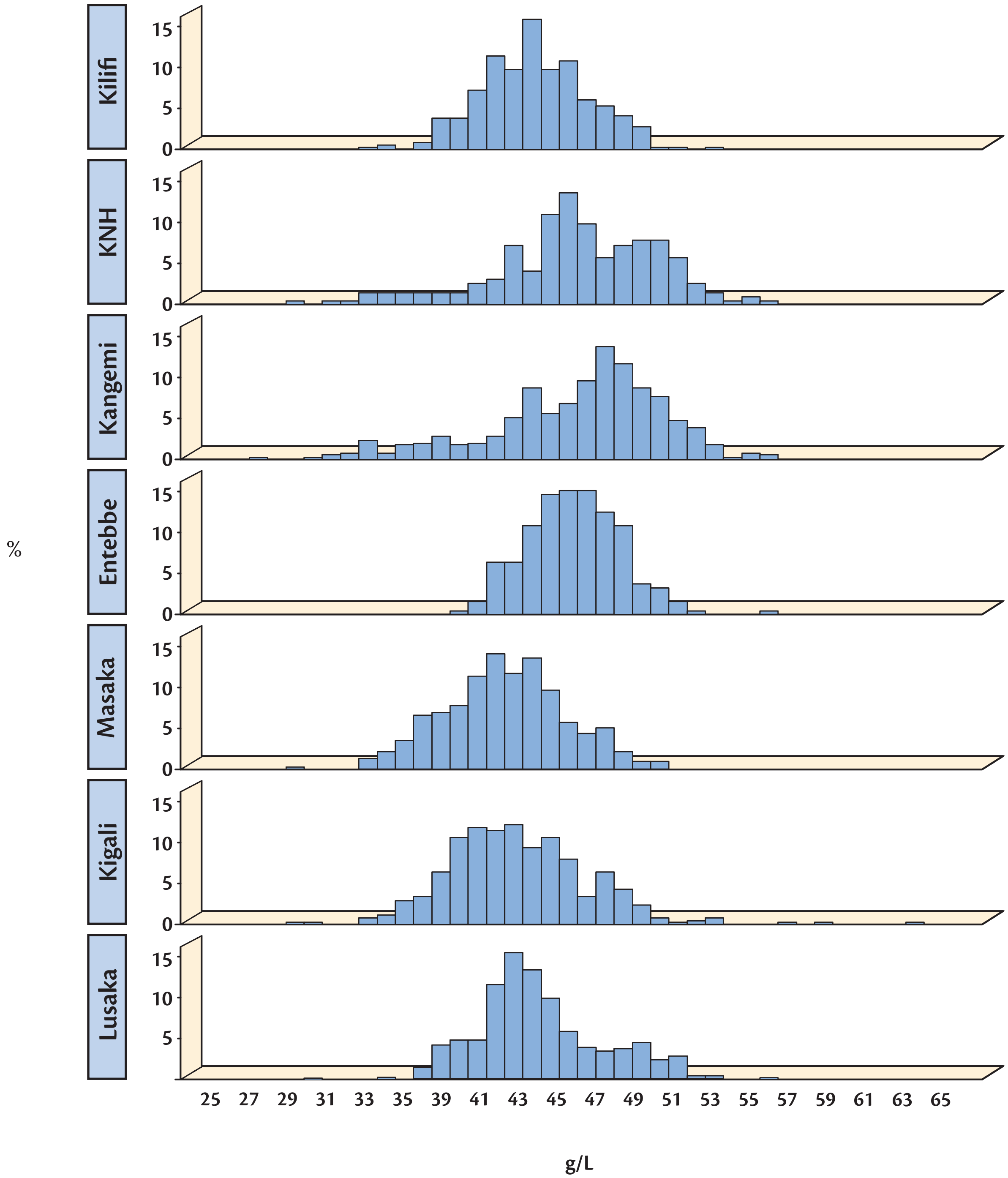


Table 63: Albumin distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	42.6 (3.0)	43	36.6 to 48.6	37 to 49	34 to 53
	KNH	99	44.7 (4.7)	45	35.4 to 54.1	34 to 52	30 to 56
	Kangemi	176	43.9 (4.9)	45	34.2 to 53.6	33 to 51	28 to 55
	Entebbe	98	45.3 (2.8)	45	39.8 to 50.9	41 to 51	39 to 56
	Masaka	148	40.8 (3.4)	41	33.9 to 47.7	34 to 47	34 to 50
	Kigali	188	41.9 (4.2)	41	33.6 to 50.2	35 to 52	31 to 64
	Lusaka	184	43.6 (3.5)	43	36.6 to 50.6	38 to 51	37 to 53
	Total	1022	43.1 (4.1)	43	34.8 to 51.3	35 to 51	28 to 64
Male	Kilifi	167	43.6 (2.9)	43	37.7 to 49.4	38 to 49	35 to 51
	KNH	98	45.9 (4.7)	46	36.6 to 55.2	34 to 53	32 to 55
	Kangemi	186	46.8 (4.4)	47	38.0 to 55.7	35 to 54	33 to 56
	Entebbe	94	45.2 (2.5)	45	40.2 to 50.3	41 to 50	40 to 51
	Masaka	183	42.1 (3.2)	42	35.6 to 48.5	36 to 48	30 to 50
	Kigali	185	42.8 (3.9)	42	35.0 to 50.5	36 to 50	30 to 59
	Lusaka	168	43.2 (3.7)	43	35.8 to 50.6	37 to 51	31 to 56
	Total	1081	44.0 (4.1)	44	35.9 to 52.2	36 to 52	30 to 59
Total	Kilifi	296	43.2 (3.0)	43	37.2 to 49.2	38 to 49	34 to 53
	KNH	197	45.3 (4.7)	45	35.9 to 54.7	34 to 53	30 to 56
	Kangemi	362	45.4 (4.9)	46	35.7 to 55.1	34 to 53	28 to 56
	Entebbe	192	45.3 (2.7)	45	40.0 to 50.6	41 to 51	39 to 56
	Masaka	331	41.5 (3.4)	41	34.8 to 48.3	35 to 48	30 to 50
	Kigali	373	42.3 (4.0)	42	34.2 to 50.4	36 to 50	30 to 64
	Lusaka	352	43.4 (3.6)	43	36.2 to 50.6	38 to 51	31 to 56
	Total	2103	43.6 (4.1)	43	35.3 to 51.8	35 to 52	28 to 64

Research Center Comparisons

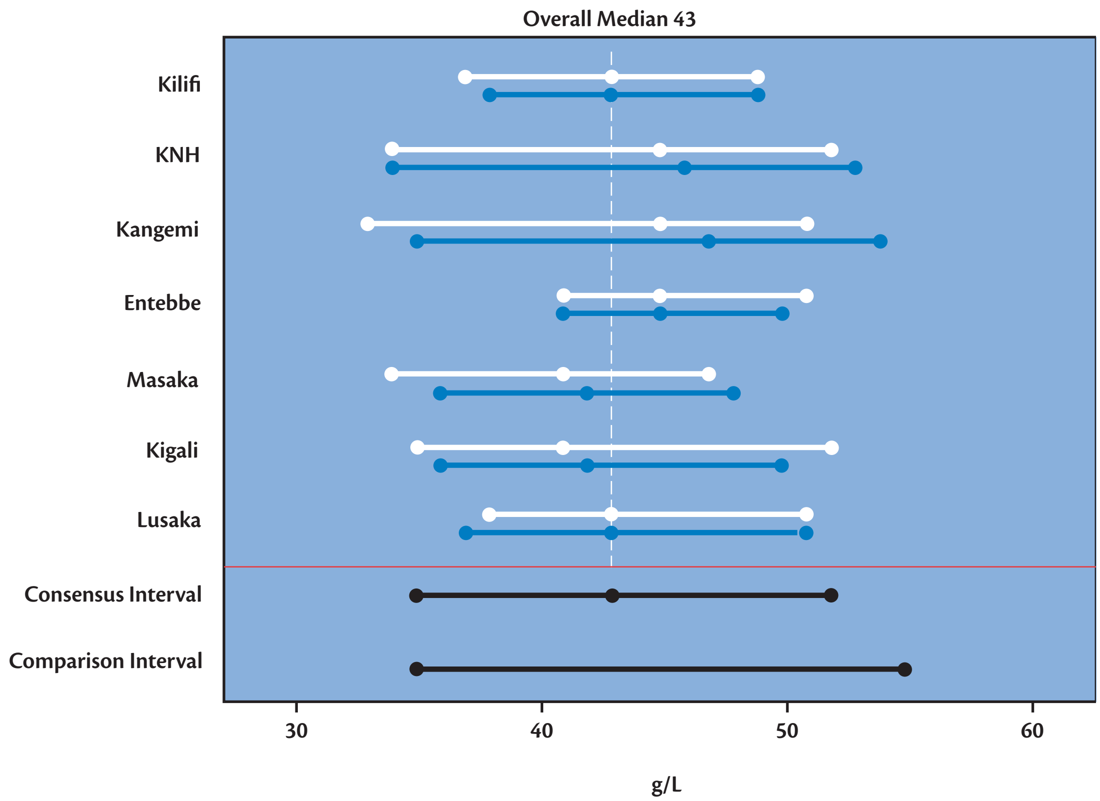
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 99: Albumin 95% intervals and medians by research center and gender

Consensus interval: 35 to 52
Comparison interval: 35 to 55
White: Females, Blue: Males, Black: Overall



4.7. Immunoglobulin Gamma (IgG)

Results

Table 64 shows the number of subjects with data included in the analysis. Figures 100, 101, and 102 show the IgG distribution overall, by gender and by research center, respectively. Table 65 shows the distribution of IgG by research center and gender, together with the stratified 95% reference intervals. The same intervals and median values are shown in Figure 103, by research center and gender. Any significant differences that exist across center are presented in Table 66. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (mg/dL)

Comparison interval: *614 to 1295*
Consensus interval:* *759 to 2776*
** All data except for males from Masaka.*

Table 64: Number of observations, IgG

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.52	175	48.48	361
Entebbe	94	48.96	98	51.04	192
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1081	51.43	1021	48.57	2102

Figure 100: Frequency distribution of IgG

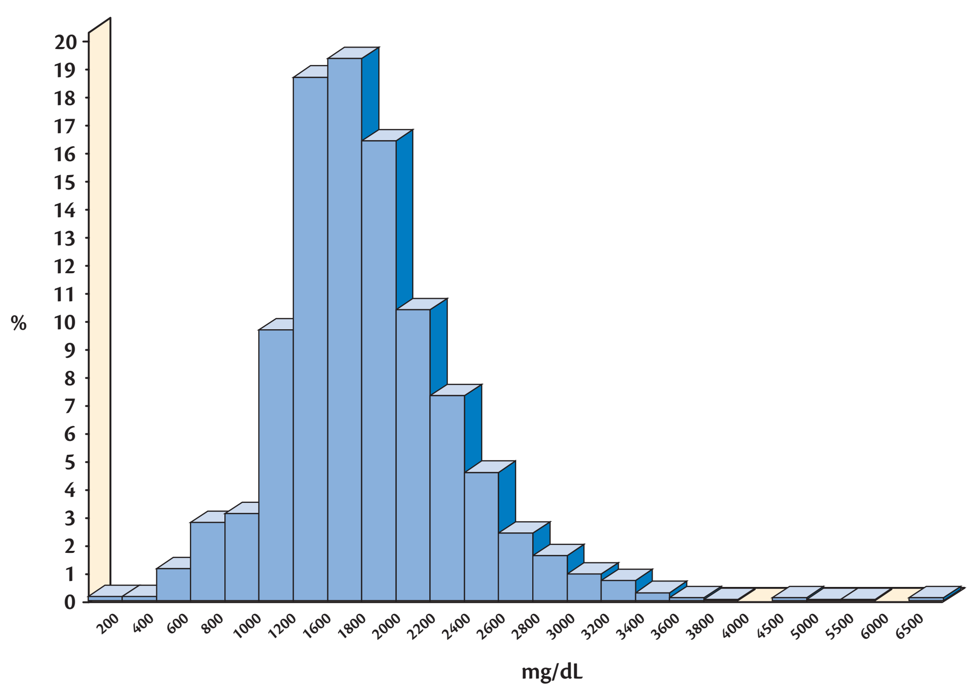


Figure 101: Frequency distribution of IgG by gender

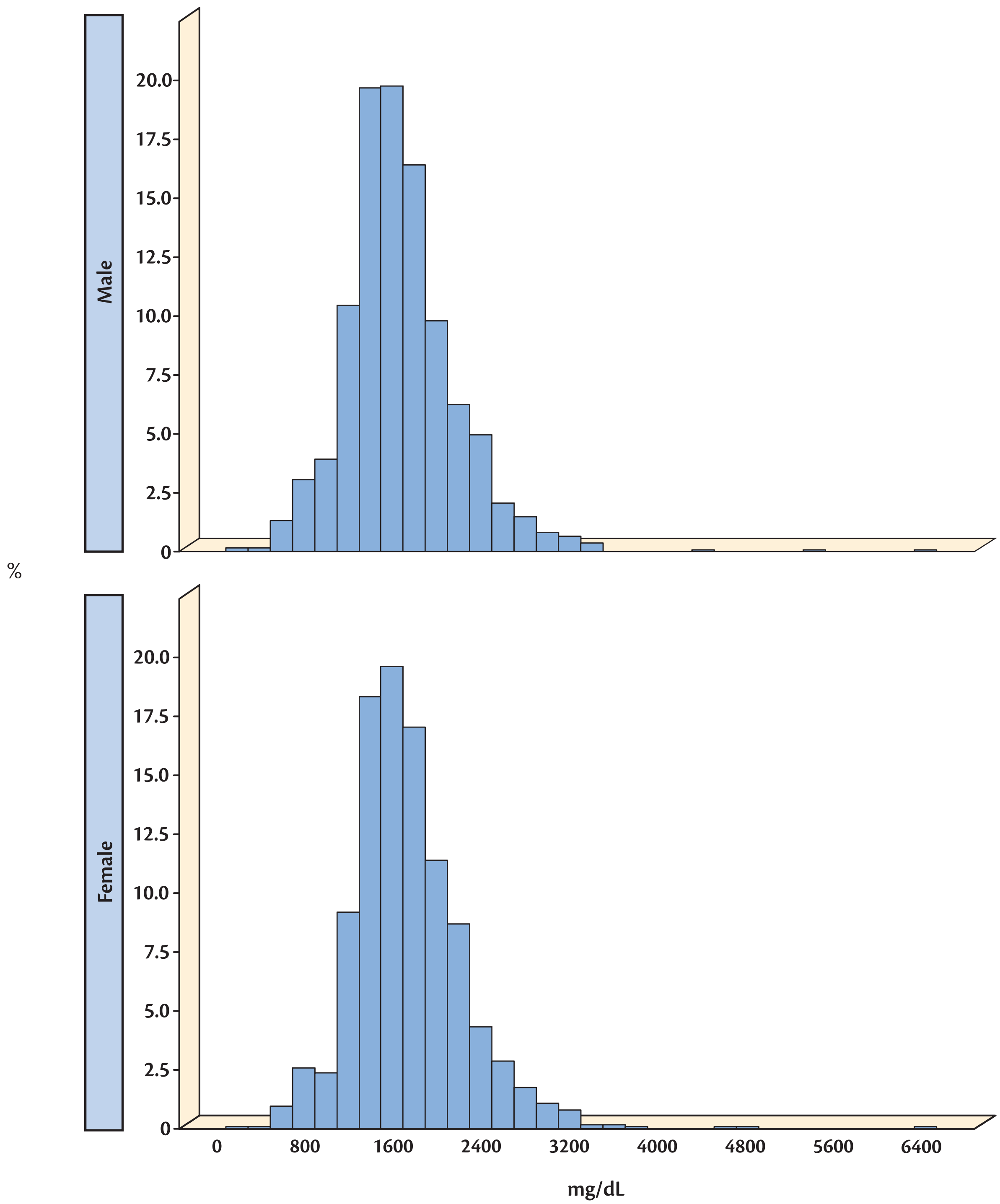


Figure 102: Frequency distribution of IgG by research center

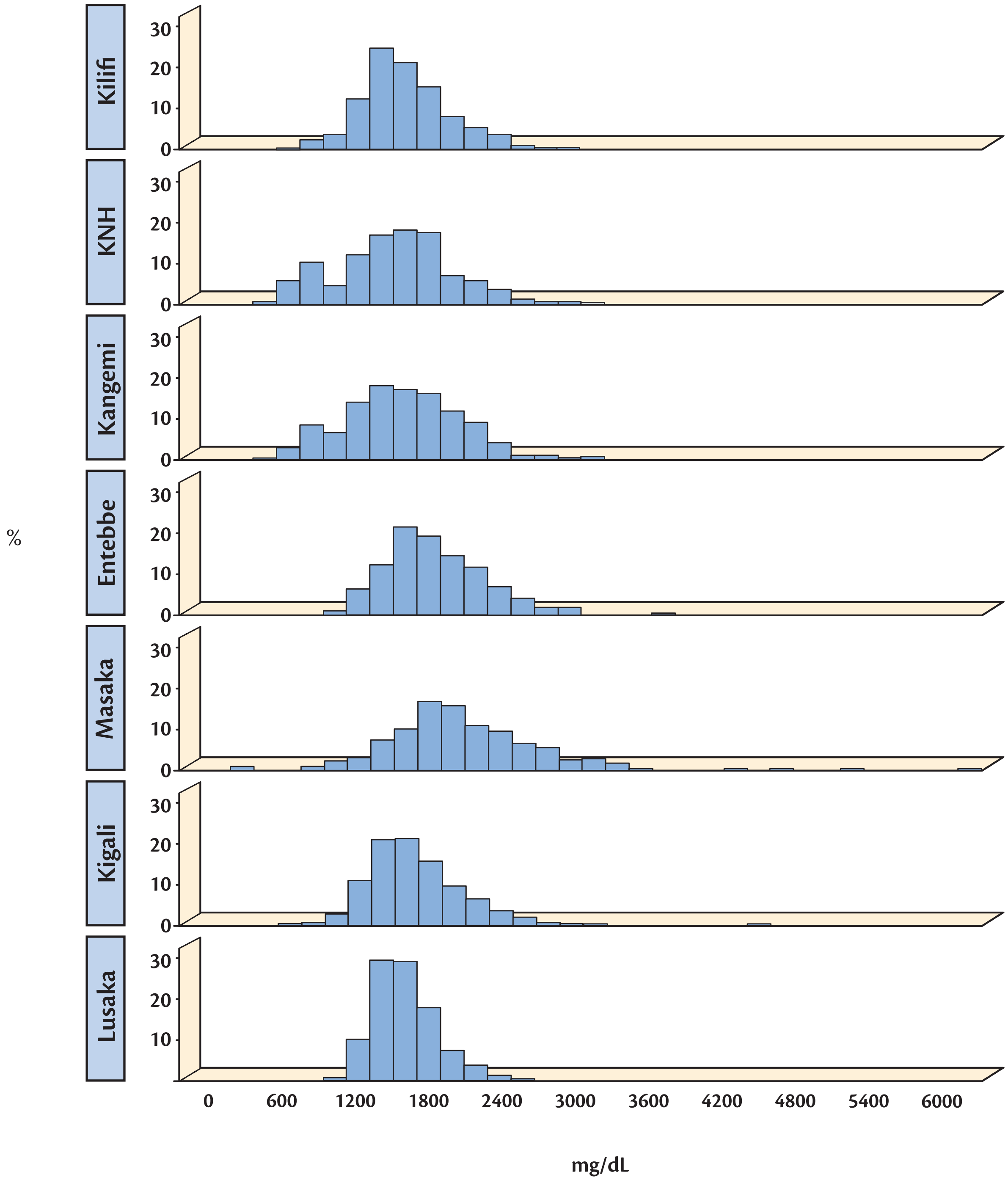


Table 65: IgG distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	1612.7 (391.1)	1566	830.5 to 2394.9	1038 to 2560	707 to 3044
	KNH	99	1599.6 (576.3)	1630	447.0 to 2752.2	623 to 2810	466 to 3032
	Kangemi	175	1643.9 (506.6)	1641	630.7 to 2657.1	746 to 2777	631 to 3242
	Entebbe	98	1813.6 (408.0)	1722	997.6 to 2629.5	1270 to 2780	1148 to 3754
	Masaka	148	2150.7 (611.7)	2061.5	927.3 to 3374.0	1092 to 3473	100 to 4843
	Kigali	188	1706.2 (436.4)	1659.5	833.4 to 2579.1	1034 to 2509	709 to 4641
	Lusaka	184	1626.4 (299.7)	1576	1027.1 to 2225.7	1194 to 2343	909 to 2690
	Total	1021	1733.7 (498.7)	1666	736.3 to 2731.1	792 to 2895	100 to 4843
Male	Kilifi	167	1591.2 (370.8)	1554	849.6 to 2332.8	864 to 2384	565 to 2717
	KNH	98	1445.6 (484.3)	1464.5	476.9 to 2414.2	630 to 2394	429 to 3213
	Kangemi	186	1528.4 (499.9)	1488	528.6 to 2528.2	643 to 2529	453 to 3060
	Entebbe	94	1919.1 (454.5)	1826	1010.1 to 2828.0	1115 to 2944	1085 to 3095
	Masaka	183	2027.6 (731.1)	1951	565.4 to 3489.7	891 to 3427	120 to 6499
	Kigali	185	1645.3 (428.5)	1599	788.4 to 2502.3	993 to 2771	618 to 3247
	Lusaka	168	1575.0 (239.0)	1541	1097.1 to 2053.0	1193 to 2138	1037 to 2538
	Total	1081	1676.3 (520.1)	1616	636.2 to 2716.5	756 to 2804	120 to 6499
Total	Kilifi	296	1600.6 (379.3)	1555.5	842.0 to 2359.1	885 to 2391	565 to 3044
	KNH	197	1523.0 (536.8)	1528	449.5 to 2596.5	623 to 2776	429 to 3213
	Kangemi	361	1584.4 (505.8)	1574	572.8 to 2595.9	669 to 2674	453 to 3242
	Entebbe	192	1865.2 (433.5)	1773.5	998.3 to 2732.2	1167 to 2915	1085 to 3754
	Masaka	331	2082.6 (682.1)	1997	718.5 to 3446.7	990 to 3427	100 to 6499
	Kigali	373	1676.0 (433.0)	1624	810.1 to 2542.0	1023 to 2593	618 to 4641
	Lusaka	352	1601.9 (273.2)	1558	1055.4 to 2148.3	1193 to 2222	909 to 2690
	Total	2102	1704.2 (510.5)	1643	683.2 to 2725.2	774 to 2833	100 to 6499

Research Center Comparisons

For males there is a significant difference in IgG between Masaka and the other centers taken together (Table 66) according to the CLSI guidelines (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment and either the magnitude of the difference is ≥25% of the overall interval or the Ratio of the two interval standard deviations is >1.5.)

Table 66: Evaluation of IgG by research center and gender

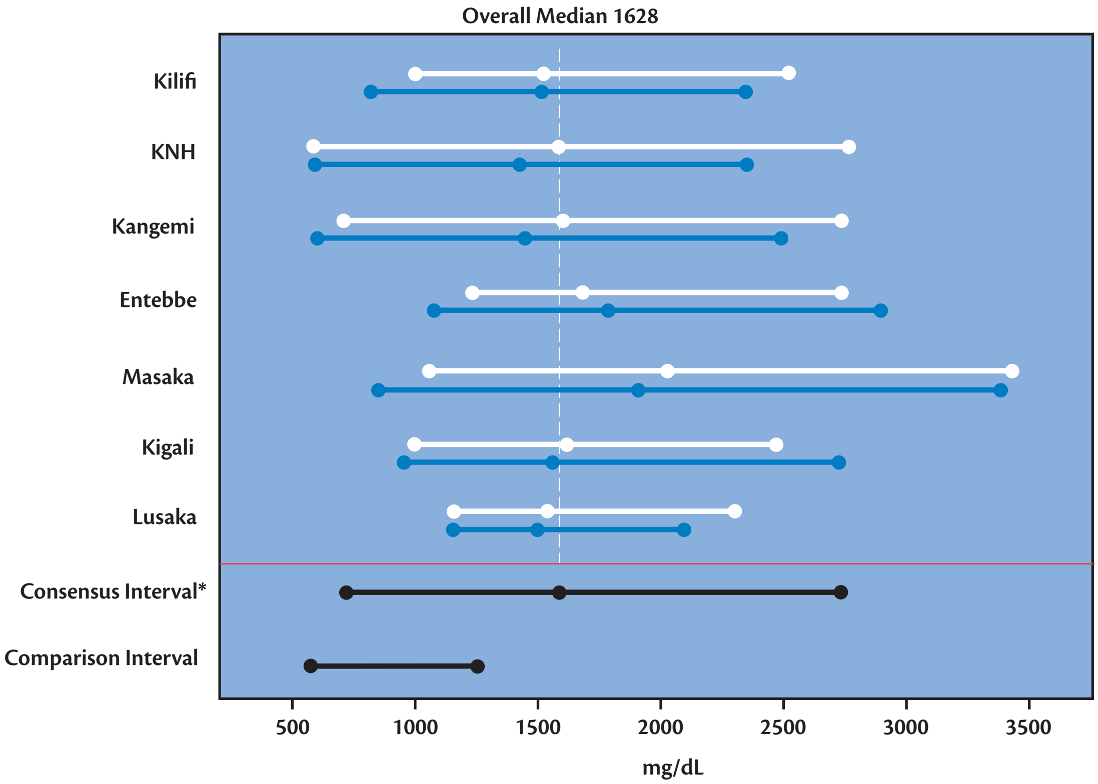
Combined Interval	Consensus Interval	Consensus Mean (SD)	Masaka Interval	Masaka Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
756 to 2804	724 to 2593	1605(432)	891 to 3427	2028(731)	No	Yes

Gender Comparisons

Excluding data from males at Masaka, the difference between males and females in the remaining centers is not significant according to the CLSI guidelines.

Figure 103: IgG 95% intervals and medians by research center and gender

*Consensus Interval: 759 to 2776**
Comparison Interval: 614 to 1295
White: Females, Blue: Males, Black: Overall



*Excludes males from Masaka

4.8. Amylase

Results

Table 67 shows the number of subjects with data included in the analysis. Figures 104, 105, and 106 show the amylase distribution overall, by gender and by research center, respectively. Table 68 shows the distribution of amylase by research center and gender, together with the stratified 95% reference intervals. Since the distribution of amylase is skewed to the left (Figure 104), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 107. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (IU/L)

Comparison interval: *60 to 180*
All centers, consensus interval: *35 to 159*

Table 67: Number of observations, amylase

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1081	51.40	1022	48.60	2103

Figure 104: Frequency distribution of amylase

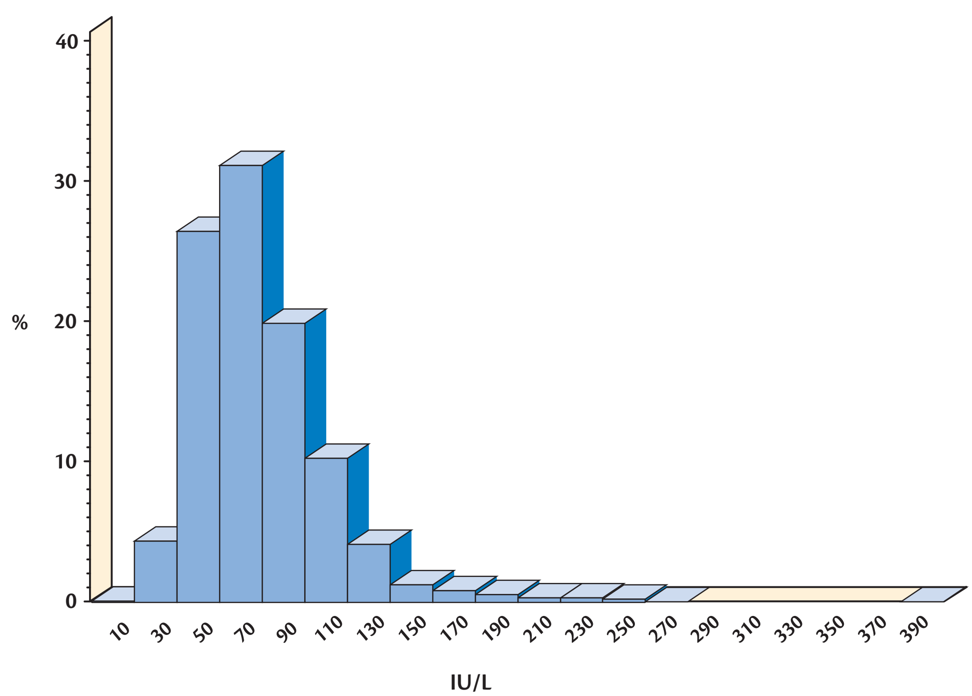


Figure 105: Frequency distribution of amylase by gender

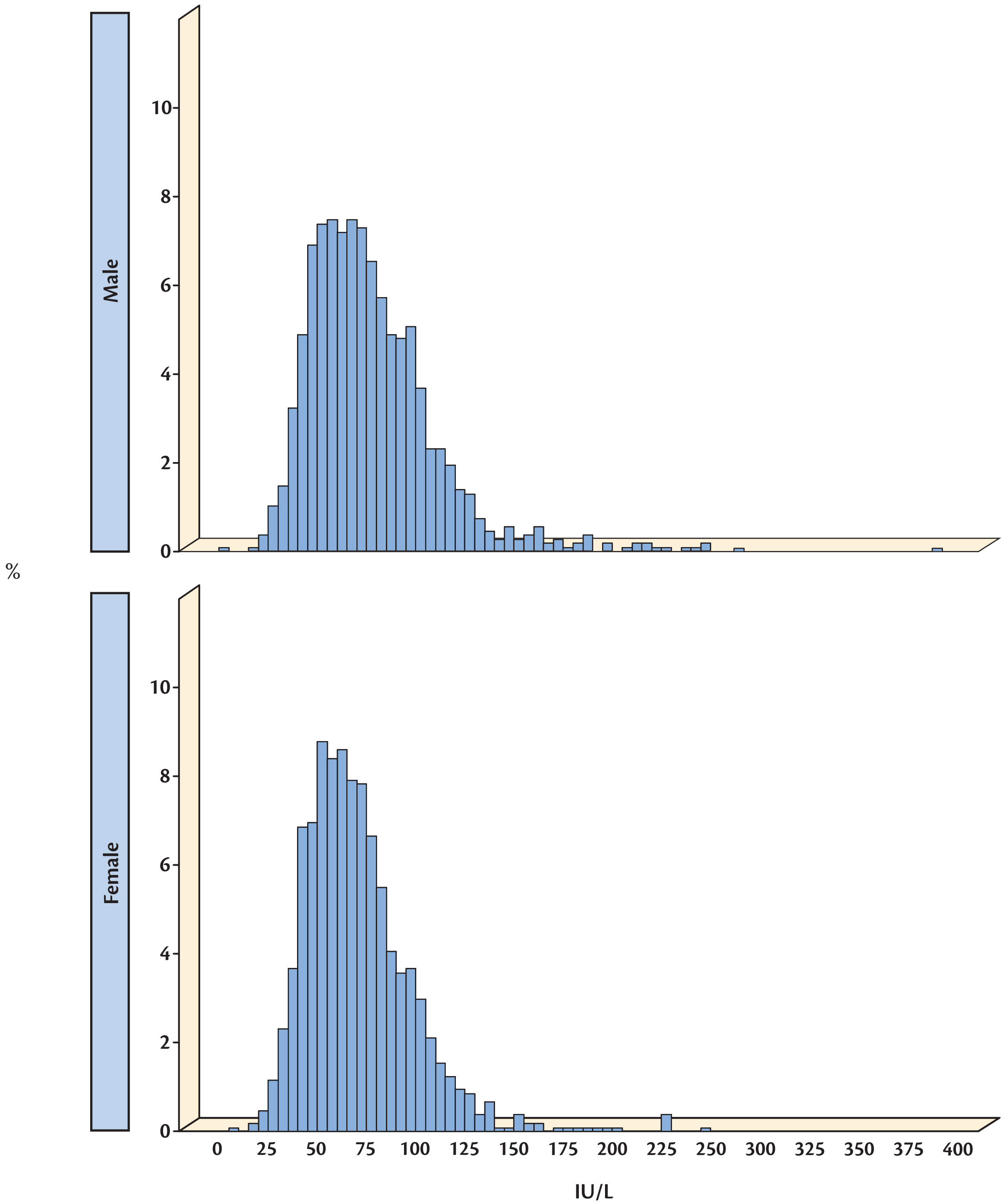


Figure 106: Frequency distribution of amylase by research center

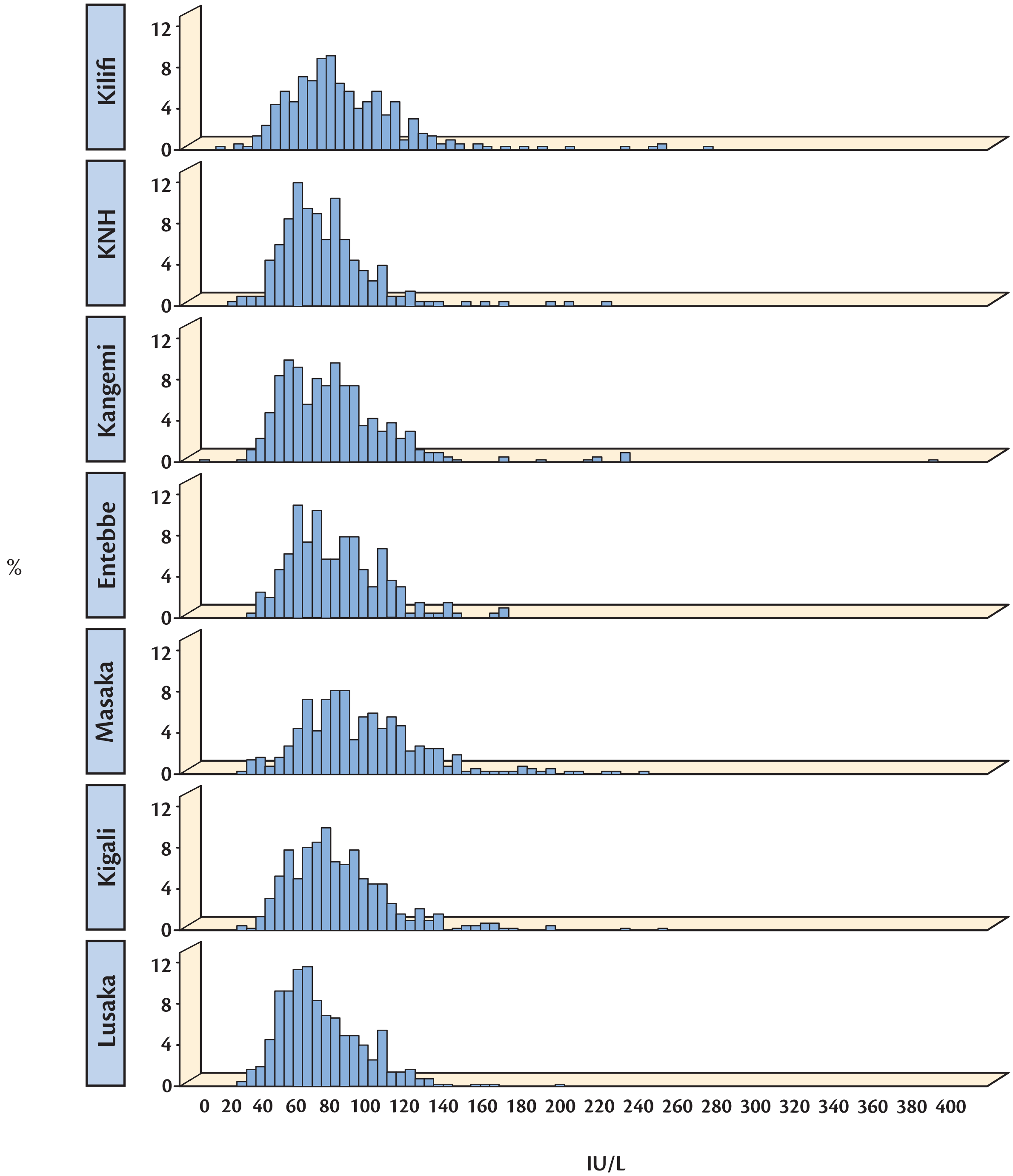


Table 68: Amylase distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	67.7 (29.4)	68	28 to 161	28 to 138	10 to 248
	KNH	99	62.6 (20.0)	60	33 to 118	32 to 123	27 to 188
	Kangemi	176	69.0 (25.2)	69	33 to 143	34 to 125	29 to 231
	Entebbe	98	70.6 (24.1)	73	36 to 140	35 to 140	29 to 167
	Masaka	148	81.5 (29.2)	80	40 to 167	34 to 174	26 to 203
	Kigali	188	70.8 (24.2)	69	36 to 140	34 to 144	25 to 229
	Lusaka	184	61.7 (19.9)	60	32 to 118	31 to 114	23 to 196
	Total	1022	68.9 (25.2)	69	33 to 143	33 to 140	10 to 248
Male	Kilifi	167	75.9 (31.4)	77	33 to 173	33 to 185	26 to 277
	KNH	98	70.5 (26.1)	68	34 to 148	38 to 166	21 to 219
	Kangemi	186	70.0 (30.8)	73	29 to 169	34 to 212	6 to 386
	Entebbe	94	73.4 (23.4)	71	39 to 139	42 to 135	33 to 167
	Masaka	183	85.8 (33.8)	89	39 to 189	34 to 189	28 to 240
	Kigali	185	75.7 (27.7)	74	36 to 158	40 to 166	29 to 252
	Lusaka	168	68.3 (23.2)	67	35 to 135	35 to 124	24 to 160
	Total	1081	74.4 (29.1)	74	34 to 163	37 to 167	6 to 386
Total	Kilifi	296	72.2 (30.7)	71	31 to 169	32 to 175	10 to 277
	KNH	197	66.4 (23.2)	65	33 to 134	32 to 154	21 to 219
	Kangemi	362	69.5 (28.1)	70	31 to 156	34 to 164	6 to 386
	Entebbe	192	71.9 (23.8)	72	37 to 139	36 to 136	29 to 167
	Masaka	331	83.9 (31.8)	83	39 to 179	34 to 181	26 to 240
	Kigali	373	73.2 (26.0)	72	36 to 149	40 to 155	25 to 252
	Lusaka	352	64.7 (21.7)	63	33 to 126	33 to 123	23 to 196
	Total	2103	71.7 (27.3)	71	33 to 154	35 to 159	6 to 386

Research Center Comparisons

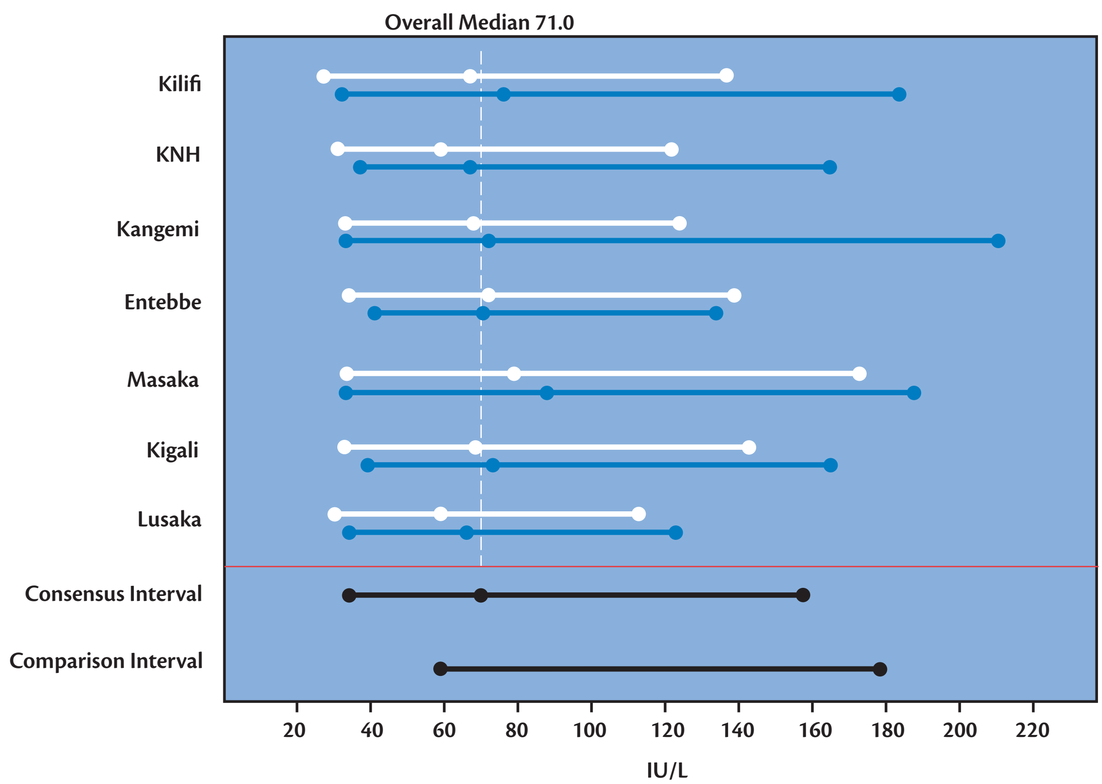
The differences between centers are not significant.

Gender Comparisons

The differences between males and females are not significant.

Figure 107: Amylase 95% intervals and medians by research center and gender

Consensus interval: 35 to 159
Comparison interval: 60 to 180
White: Females, Blue: Males, Black: Overall



4.9. Creatine Phosphokinase (CPK)

Results

Table 69 shows the number of subjects with data included in the analysis. Figures 108, 109, and 110 show the CPK distribution overall, by gender and by research center, respectively. Table 70 shows the distribution of CPK by research center and gender, together with the stratified 95% reference intervals. Since the distribution of CPK is highly skewed to the left (Figure 108), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 111. Any significant differences that exist across center or gender are presented in Table 71. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (IU/L)

	Males	Females	Overall
Comparison interval:	*60 to 400*	*0 to 150*	*NA*
All centers, consensus interval:	*60 to 709*	*49 to 354*	*53 to 552*

Table 69: Number of observations, CPK

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	182	55.15	148	44.85	330
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1080	51.38	1022	48.62	2102

Figure 108: Frequency distribution of CPK

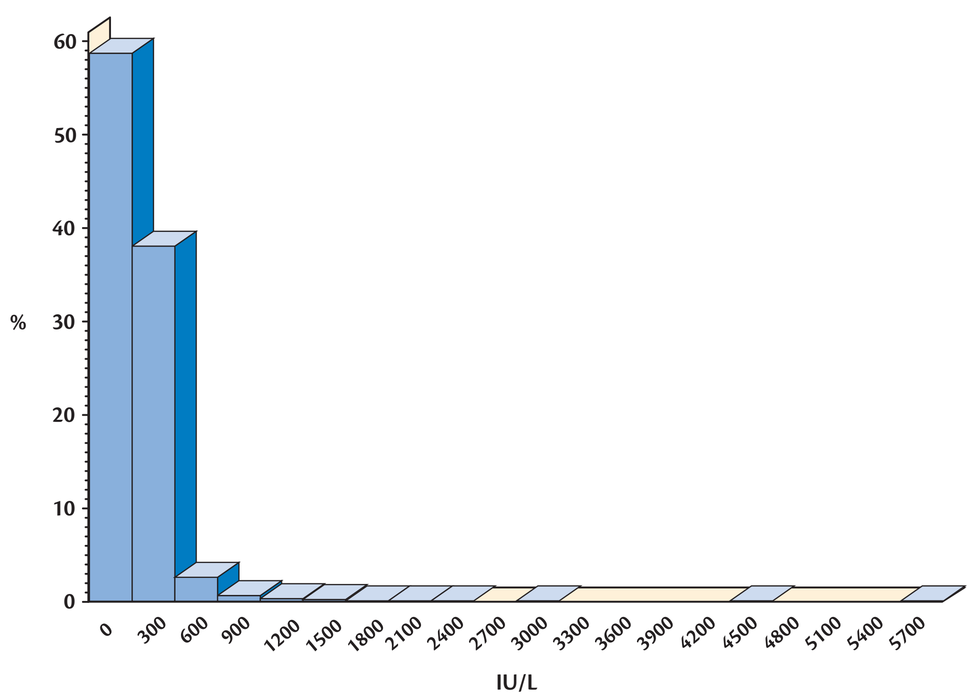


Figure 109: Frequency distribution of CPK by gender

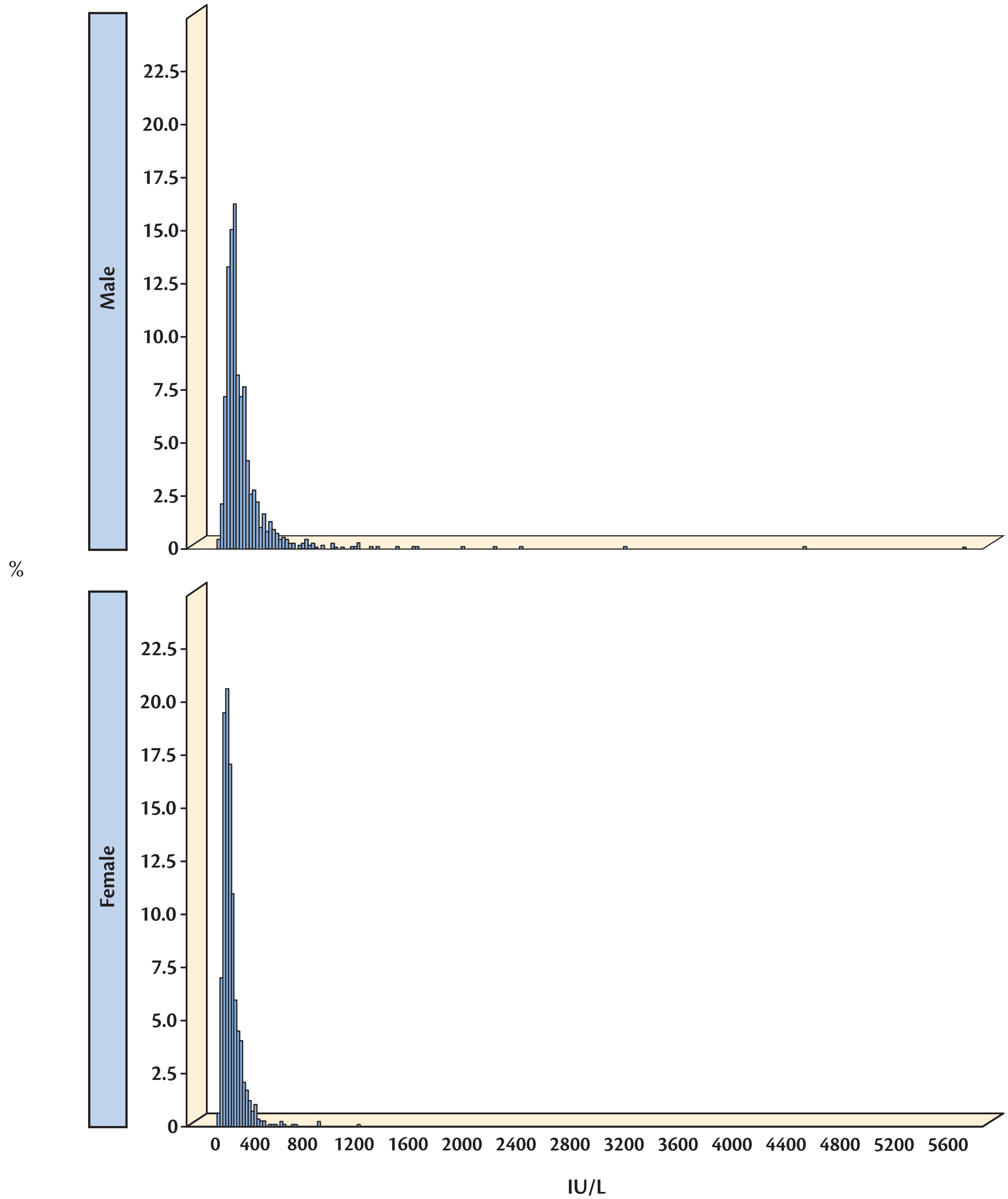


Figure 110: Frequency distribution of CPK by research center

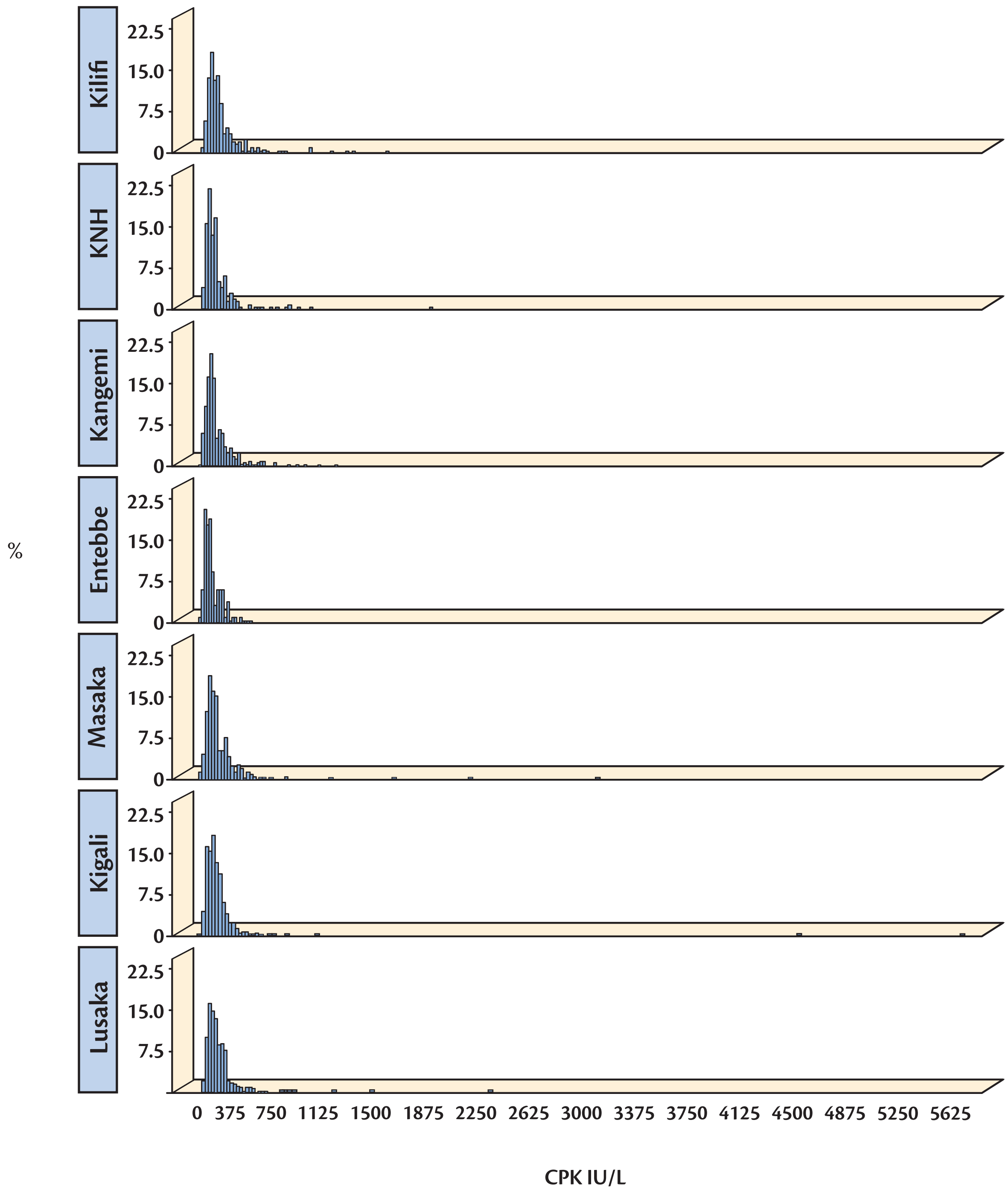


Table 70: CPK distribution by research center and gender

Log transformation used, values are back-transformed (i.e., the geometric mean is shown)

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	110.7 (64.8)	104	34 to 357	42 to 433	14 to 1256
	KNH	99	110.7 (48.0)	105	46 to 264	55 to 300	41 to 503
	Kangemi	175	122.7 (65.0)	123	43 to 354	45 to 372	33 to 889
	Entebbe	98	117.3 (63.4)	110	40 to 346	40 to 356	37 to 384
	Masaka	148	121.8 (65.9)	117	41 to 360	43 to 396	23 to 571
	Kigali	188	116.0 (53.8)	116	46 to 293	53 to 321	48 to 402
	Lusaka	184	130.3 (59.6)	124	52 to 325	57 to 342	43 to 684
	Total	1021	119.3 (60.7)	116	43 to 330	49 to 354	14 to 1256
Male	Kilifi	166	179.0 (115.0)	159	50 to 647	57 to 903	45 to 1524
	KNH	98	179.4 (119.1)	150	48 to 677	65 to 833	48 to 1905
	Kangemi	186	184.6 (111.1)	162	55 to 615	67 to 711	52 to 1259
	Entebbe	94	141.3 (81.5)	134	45 to 448	52 to 487	21 to 514
	Masaka	183	162.5 (105.9)	153	44 to 598	48 to 696	18 to 3142
	Kigali	185	156.1 (97.1)	151	45 to 542	66 to 576	16 to 5747
	Lusaka	168	183.9 (105.5)	173	58 to 579	76 to 737	54 to 2361
	Total	1080	170.1 (106.2)	156	49 to 593	60 to 709	16 to 5747
Total	Kilifi	295	145.1 (96.0)	137	39 to 545	50 to 709	14 to 1524
	KNH	197	140.8 (85.7)	132	42 to 476	55 to 755	41 to 1905
	Kangemi	361	151.4 (91.3)	138	45 to 506	53 to 589	33 to 1259
	Entebbe	192	128.5 (72.6)	120	42 to 398	44 to 436	21 to 514
	Masaka	331	142.9 (88.7)	137	41 to 494	48 to 454	18 to 3142
	Kigali	373	134.4 (76.2)	131	43 to 418	55 to 422	16 to 5747
	Lusaka	352	153.5 (83.5)	146	52 to 456	66 to 539	43 to 2361
	Total	2101	143.2 (85.6)	135	43 to 473	53 to 552	14 to 5747

Research Center Comparisons

The differences between centers are not significant.

Gender Comparisons

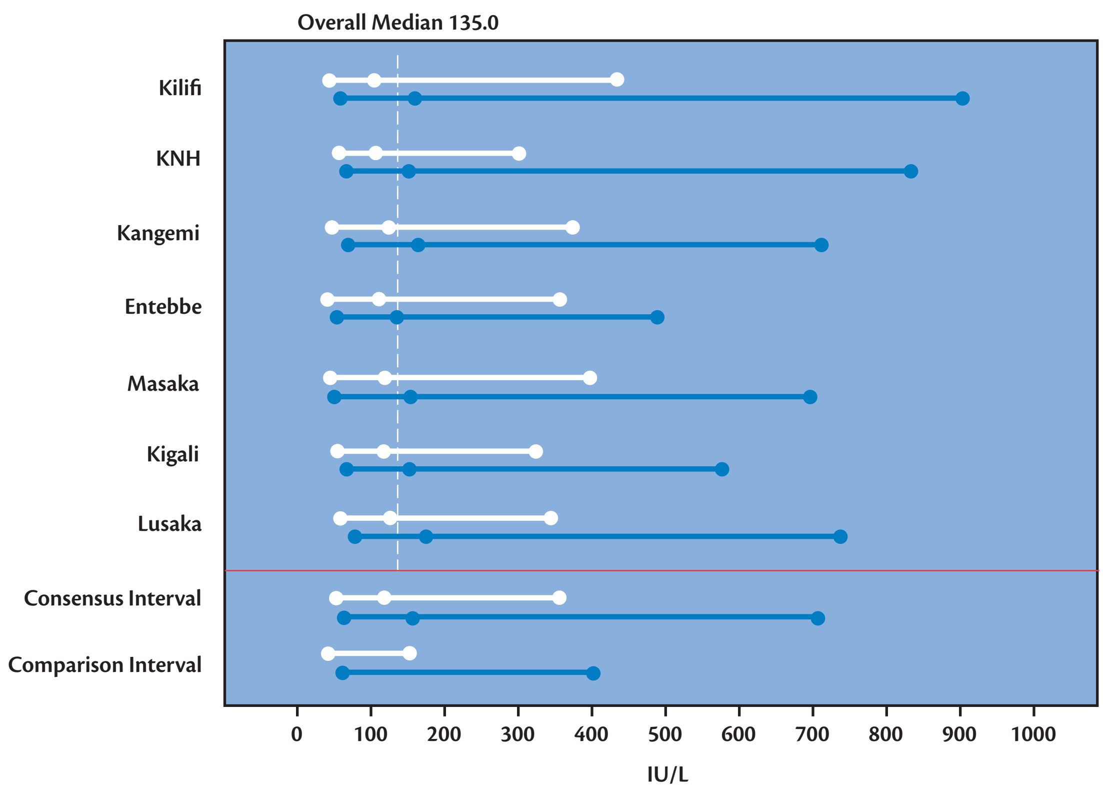
The differences between males and females are not significant. Although the upper limits do vary by gender (Table 70, Figure 111), the CLSI guidelines only recommend stratifying analyte intervals based on mean values. P values not shown.

Table 71: Evaluation of CPK by gender

Difference>25% of Combined Interval			Limits			Mean (SD)	
Means	Lower Limits	Upper Limits	Overall	Males	Females	Males	Females
No	No	Yes	4.0 to 6.3	4.1 to 6.6	3.9 to 5.9	5.14 (0.62)	4.78 (0.51)

Figure 111: CPK 95% intervals and medians by research center and gender

Reference interval (Males): 60 to 400
Reference interval (Females): 40 to 150
African interval (Males): 60 to 709
African interval (Females): 40 to 354
White: Females, Blue: Males



4.10. Lactate Dehydrogenase (LDH)

Results

Table 72 shows the number of subjects with data included in the analysis. Figures 112, 113, and 114 show the LDH distribution overall, by gender and by research center, respectively. Table 73 shows the distribution of LDH by research center and gender, together with the stratified 95% reference intervals. Since the distribution of LDH is highly skewed to the left (Figure 112), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 115. Any significant differences that exist across center or gender are presented in Table 74. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (IU/L)

Comparison interval: *100 to 190*
Consensus interval:* *214 to 528*
** Excludes Masaka and males from KNH*

Table 72: Number of observations, LDH

	Male		Female		Total
	N	%	N	%	N
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	183	55.29	148	44.71	331
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1081	51.40	1022	48.60	2103

Figure 112: Frequency distribution of LDH

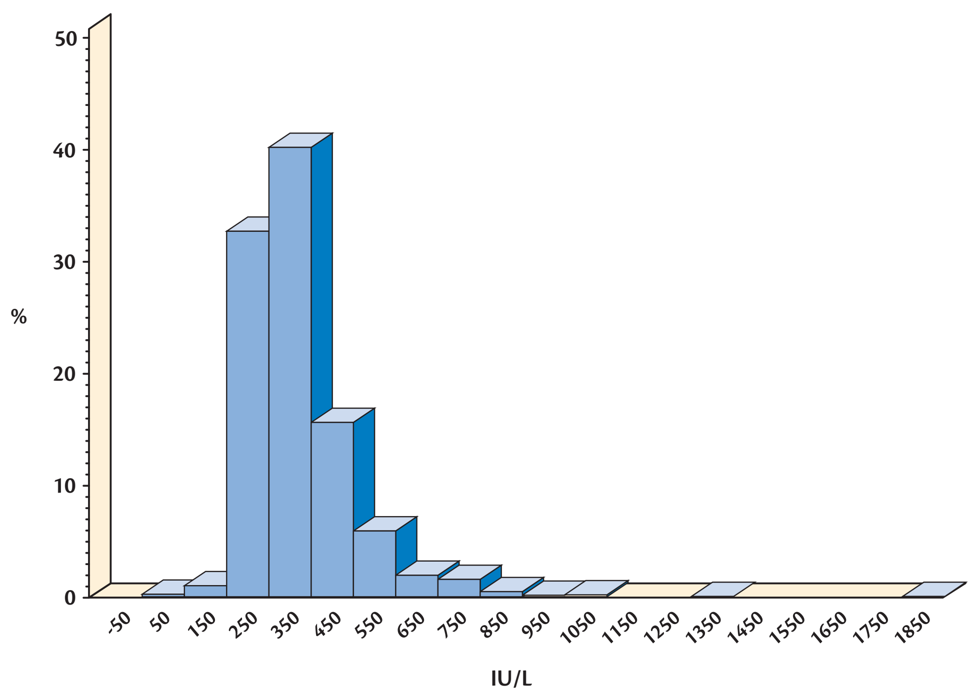


Figure 113: Frequency distribution of LDH by gender

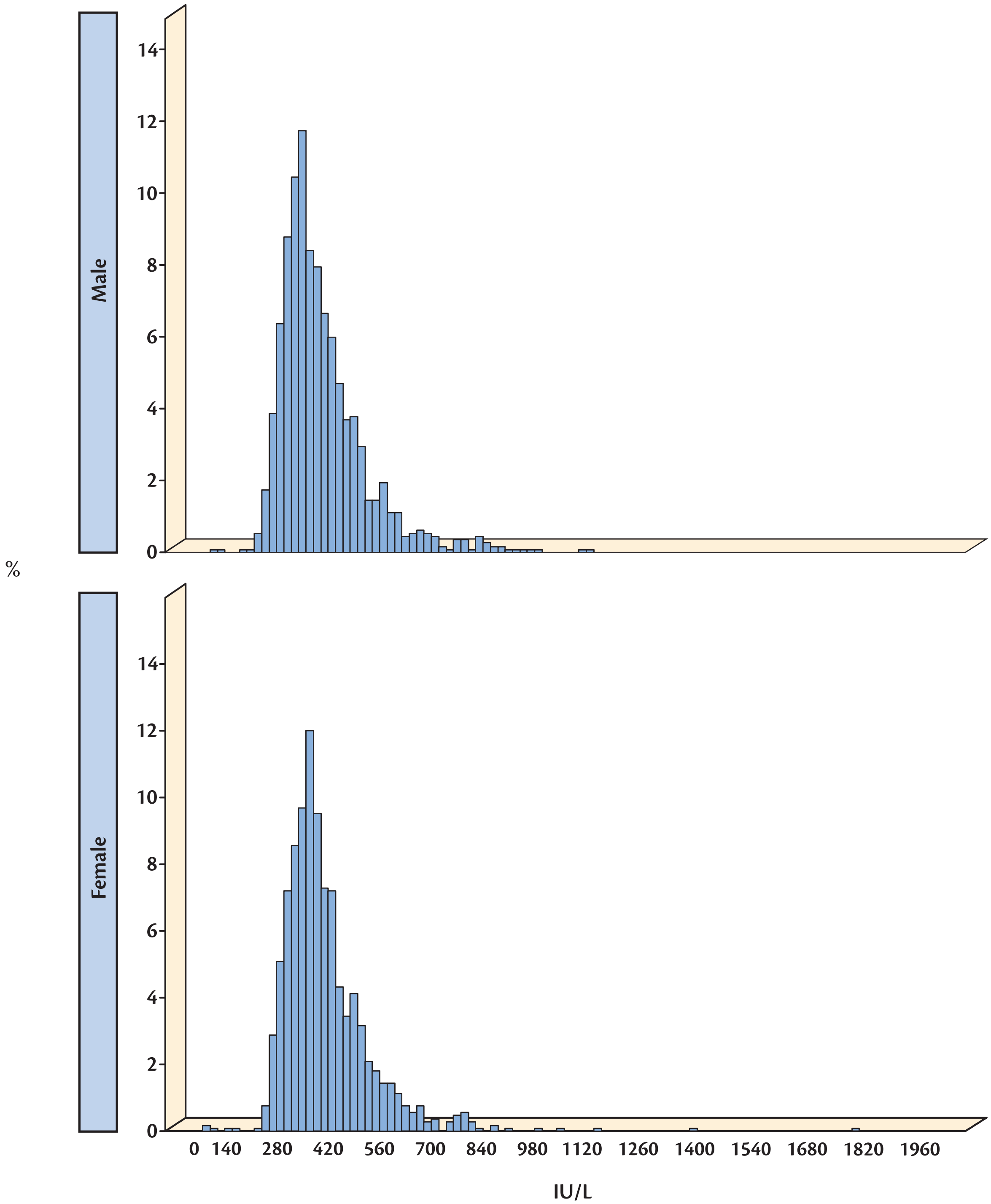


Figure 114: Frequency distribution of LDH by research center

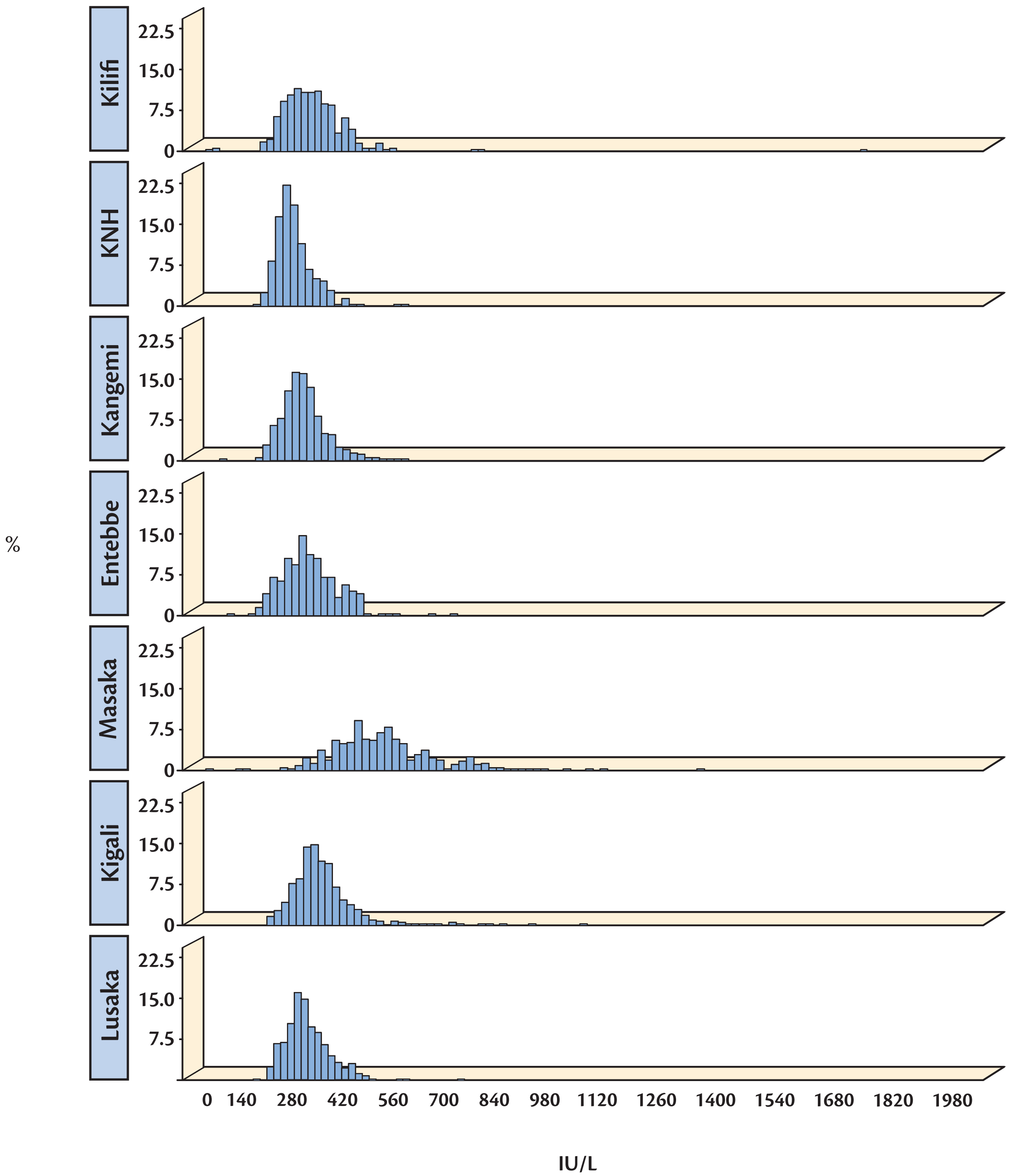


Table 73: LDH distribution by research center and gender

Log transformation used, values are back-transformed (i.e., the geometric mean is shown)

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	334.8 (128.7)	342	155 to 722	194 to 565	32 to 1802
	KNH	99	293.2 (55.0)	281	202 to 427	228 to 453	215 to 578
	Kangemi	176	304.4 (60.1)	302	205 to 452	210 to 464	192 to 572
	Entebbe	98	321.8 (83.3)	325	192 to 540	215 to 478	101 to 651
	Masaka	148	484.0 (171.2)	498	239 to 982	278 to 825	40 to 1367
	Kigali	188	360.7 (79.8)	348	232 to 561	243 to 641	222 to 853
	Lusaka	184	330.2 (61.0)	324	228 to 478	230 to 488	186 to 521
	Total	1022	345.5 (104.4)	334	189 to 632	217 to 652	32 to 1802
Male	Kilifi	167	327.6 (87.5)	331	192 to 559	214 to 506	54 to 834
	KNH	98	265.0 (42.1)	263	193 to 364	197 to 397	179 to 424
	Kangemi	186	289.7 (62.0)	288	189 to 444	197 to 443	80 to 510
	Entebbe	94	302.5 (81.7)	305	176 to 519	182 to 541	150 to 722
	Masaka	183	489.0 (134.8)	483	282 to 849	296 to 854	132 to 1050
	Kigali	185	352.6 (85.5)	348	217 to 573	237 to 725	225 to 1086
	Lusaka	168	315.6 (66.6)	303	207 to 481	228 to 466	214 to 770
	Total	1081	336.7 (102.0)	324	184 to 617	209 to 691	54 to 1086
Total	Kilifi	296	330.7 (106.8)	333	173 to 631	209 to 536	32 to 1802
	KNH	197	278.8 (50.4)	271	194 to 400	203 to 424	179 to 578
	Kangemi	362	296.7 (61.5)	296	196 to 449	204 to 463	80 to 572
	Entebbe	192	312.2 (82.9)	313	184 to 531	186 to 528	101 to 722
	Masaka	331	486.8 (152.1)	494	261 to 909	295 to 826	40 to 1367
	Kigali	373	356.7 (82.7)	348	224 to 567	240 to 652	222 to 1086
	Lusaka	352	323.2 (64.2)	317	217 to 481	229 to 484	186 to 770
	Total	2103	340.9 (103.2)	330	186 to 625	213 to 678	32 to 1802

Research Center Comparisons

For males, estimated reference intervals for Masaka and KNH are significantly different from the other sites combined. For females, the estimated reference interval for Masaka is significantly different from the other centers combined (Tables 74, 75) according to the CLSI guidelines (i.e., the difference between the two means is statistically significant ($p<0.05$) using ANOVA with Tukey adjustment and either the magnitude of the difference is ≥25% of the overall interval or the ratio of the two interval standard deviations is >1.5.)

Table 74: Evaluation of LDH by research center and gender

74a. Males

Combined Interval	KNH Interval	KNH Mean (SD)	Masaka Interval	Masaka Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
210 to 794	197 to 397	5.58(0.16)	296 to 854	6.19(0.28)	Yes	Yes
		265(42)*		489(135)*		
* Back-transformed from log estimates						

Combined Interval	Consensus Interval	Consensus Mean (SD)	Masaka Interval	Masaka Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
213 to 725	207 to 510	5.76(0.25)	296 to 854	6.19(0.28)	Yes	No
		318(79)*		489(135)*		
* Back-transformed from log estimates						

Combined Interval	Consensus Interval	Consensus Mean (SD)	KNH Interval	KNH Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
207 to 506	207 to 510	5.76(0.25)	197 to 397	5.58(0.16)	No	Yes
		318(79)*		265(42)*		
* Back-transformed from log estimates						

74b. Females

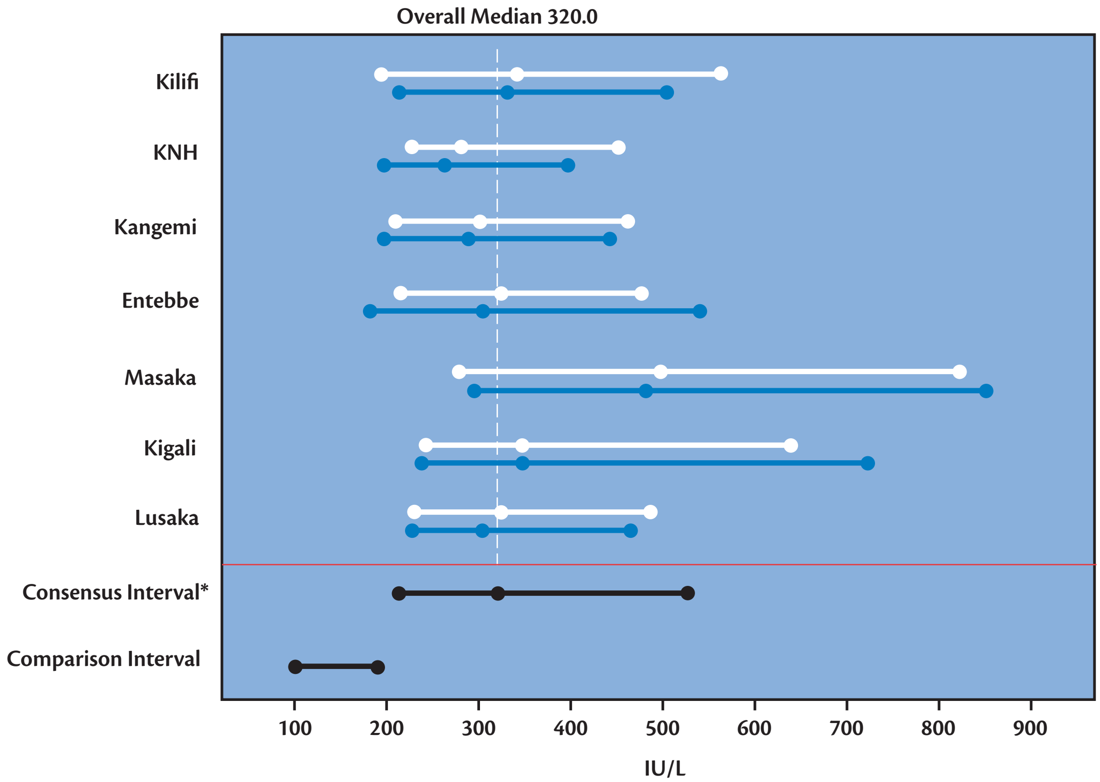
Combined Interval	Consensus Interval	Consensus Mean (SD)	Masaka Interval	Masaka Mean (SD)	Difference in Means>25% Ref. Interval	SD Ratio > 1.5
217 to 652	217 to 536	5.79(0.25)	278 to 825	6.18(0.35)	Yes	No
		326(82)*	278 to 825	484(171)*		
* Back-transformed from log estimates						

Gender Comparisons

The difference between males and females, excluding data from Masaka and males from KNH, is not significant. The difference between males and females at Masaka is not significant.

Figure 115: LDH 95% intervals and medians by research center and gender

*Consensus interval: 214 to 528**
Comparison interval: 100 to 190
White: Females, Blue: Males, Black: Overall



*Excludes Masaka and males from KNH

4.11. Alkaline Phosphatase (ALP)

Results

Table 75 shows the number of subjects with data included in the analysis. Figures 116, 117, and 118 show the ALP distribution overall, by gender and by research center, respectively. Table 76 shows the distribution of ALP by research center and gender, together with the stratified 95% reference intervals. Since the distribution of ALP is skewed to the left (see Figure 116), the log transformed values were used. Note that this has no effect on the interval estimates. The same quantiles and median values are shown in Figure 119. The comparison and final estimated consensus intervals are shown below.

Note that due to regional reagent availability during the study, two buffers were used in measuring this analyte (Table 77). The research center and gender analyses were done stratified by buffer type used. The reference for the ALP US-derived comparison interval does not report which buffer was used (Kratz et al. 2004).

Estimated Reference Intervals (IU/L)

Comparison interval: *30 to 120*
Consensus interval (DEA): *106 to 382*
Consensus interval (AMP): *48 to 164*

Table 75: Number of observations, ALP

Buffer	Center	Male		Female		Total
		N	%	N	%	N
DEA	KNH	98	49.75	99	50.25	197
	Kangemi	186	51.38	176	48.62	362
	Entebbe	94	48.96	98	51.04	192
	Masaka	183	55.29	148	44.71	331
	Total	561	51.85	521	48.15	1082
AMP	Kilifi	167	56.42	129	43.58	296
	Kigali	185	49.60	188	50.40	373
	Lusaka	168	47.73	184	52.27	352
	Total	520	50.93	501	49.07	1021

Figure 116: Frequency distribution of ALP by buffer used

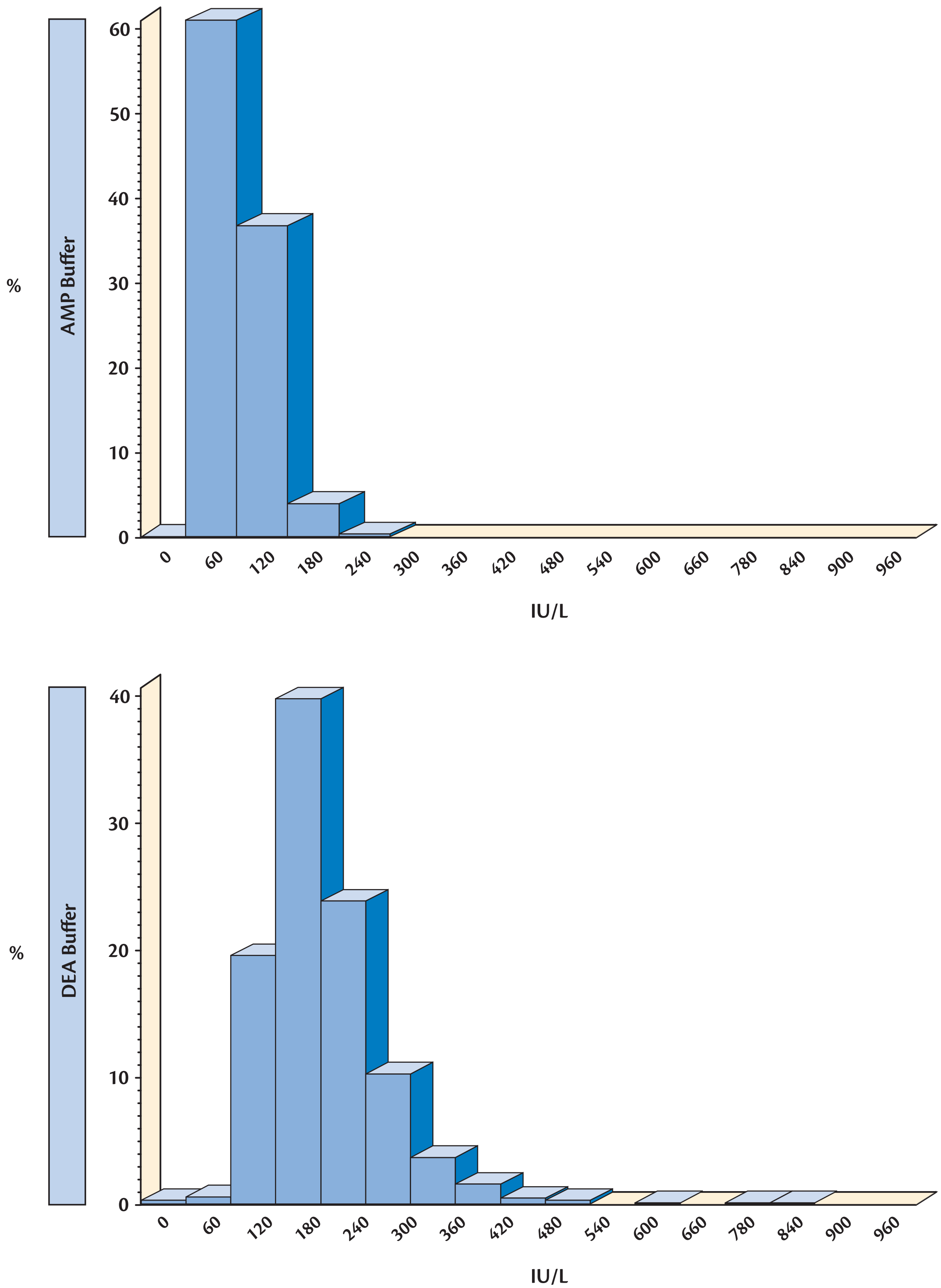


Figure 117: Frequency distribution of ALP by gender and buffer used (AMP Buffer)

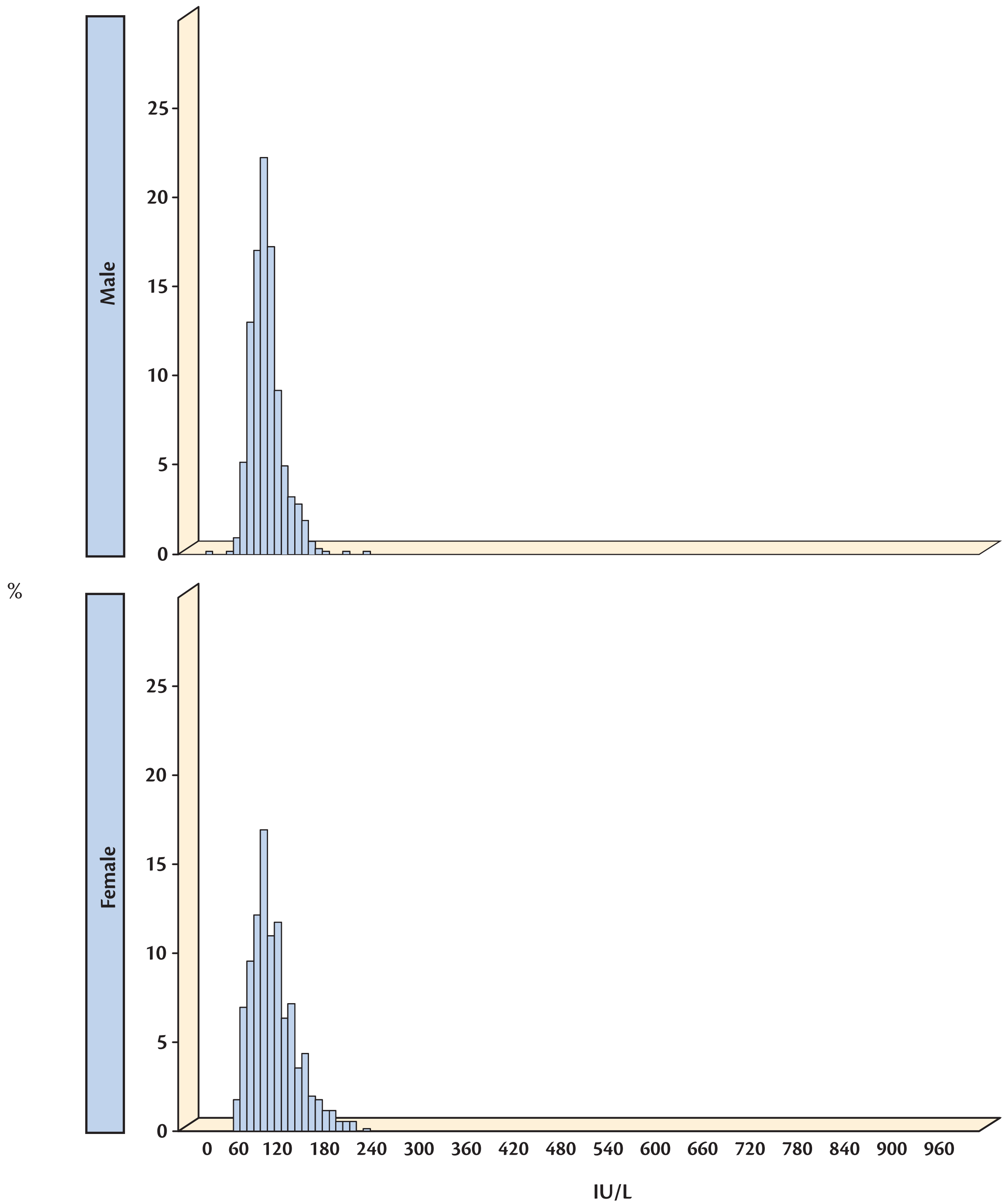


Figure 117: Frequency distribution of ALP by gender and buffer used (DEA Buffer)

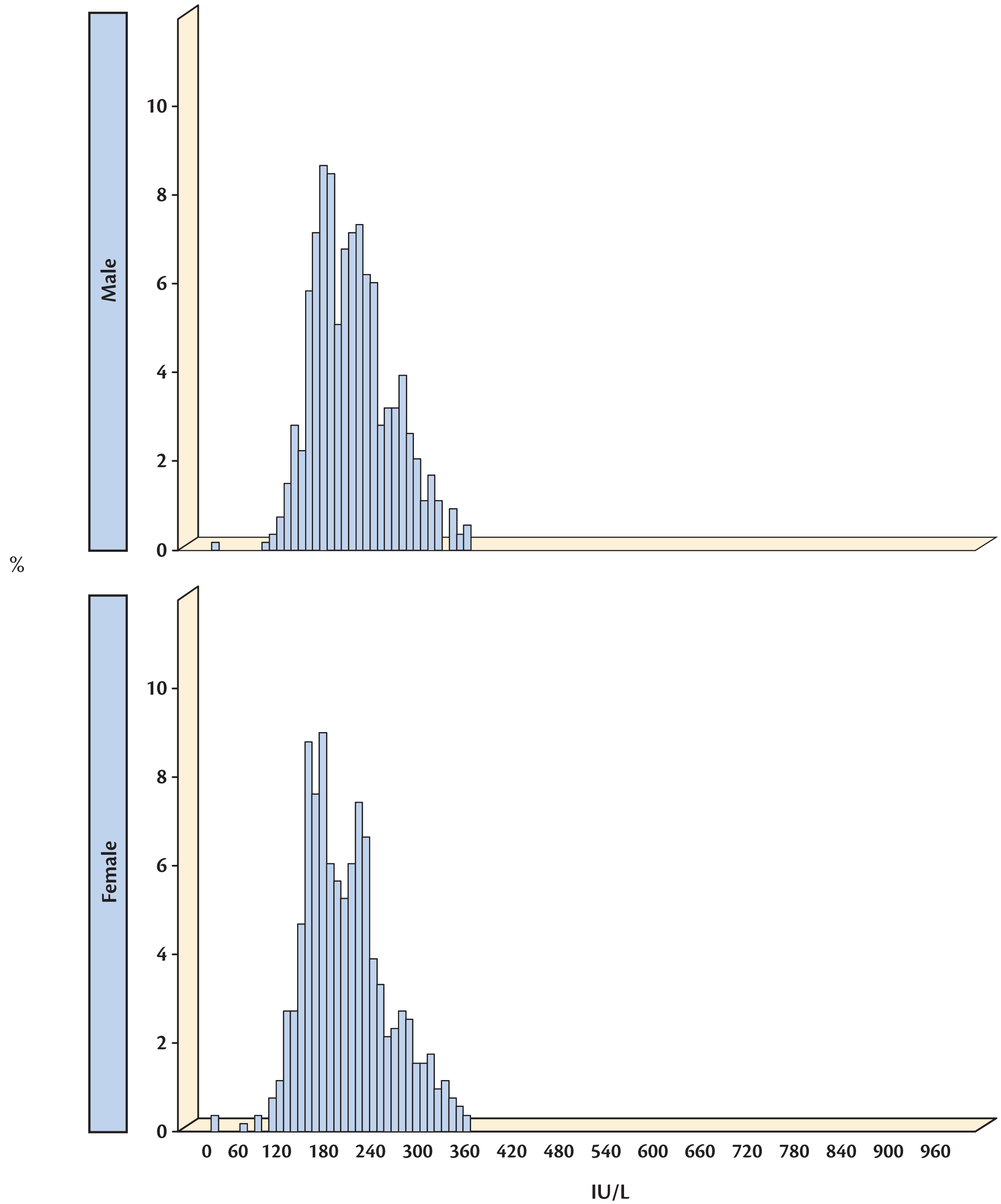


Figure 118: Frequency distribution of ALP by research center and buffer used

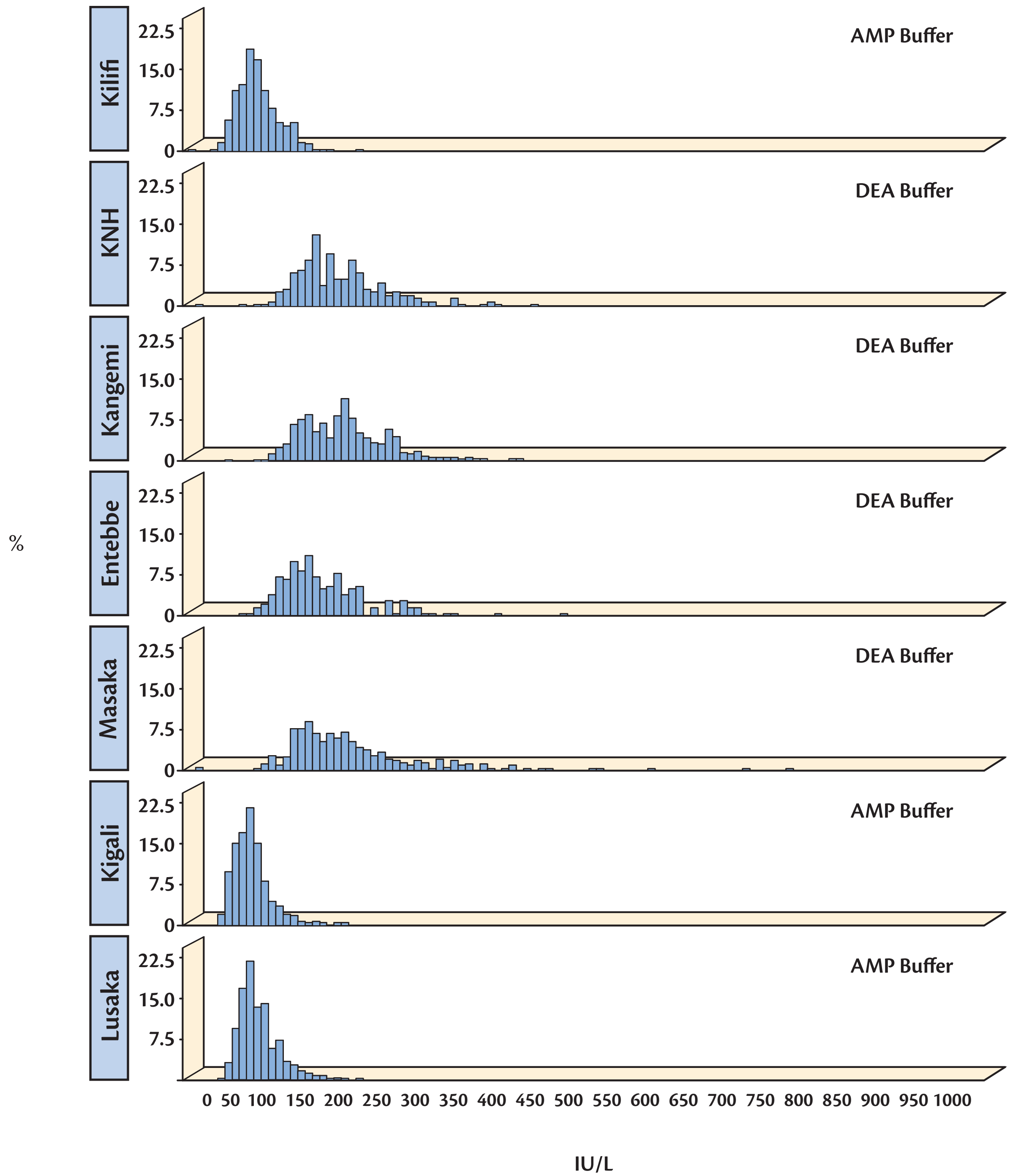


Table 76: ALP distribution by research center and gender, DEA buffer

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	KNH	99	189.4 (61.2)	187	99 to 361	103 to 360	67 to 424
	Kangemi	176	189.9 (54.4)	192	107 to 337	111 to 334	54 to 396
	Entebbe	98	164.8 (55.1)	155	84 to 322	92 to 316	70 to 353
	Masaka	148	199.2 (79.7)	202	89 to 444	106 to 428	13 to 491
	Total	521	187.3 (64.3)	188	94 to 372	103 to 353	13 to 491
Male	KNH	98	206.1 (58.7)	204	117 to 364	121 to 406	110 to 467
	Kangemi	186	209.9 (58.8)	208	120 to 368	123 to 378	94 to 451
	Entebbe	94	178.8 (55.6)	172	96 to 333	106 to 361	84 to 510
	Masaka	183	204.4 (93.2)	193	82 to 509	105 to 550	8 to 821
	Total	561	201.9 (71.9)	199	99 to 412	114 to 406	8 to 821
Total	KNH	197	197.5 (60.6)	192	107 to 365	110 to 395	67 to 467
	Kangemi	362	199.9 (57.4)	204	112 to 355	120 to 349	54 to 451
	Entebbe	192	171.5 (55.7)	166	90 to 328	92 to 327	70 to 510
	Masaka	331	202.0 (87.2)	198	85 to 479	106 to 442	8 to 821
	Total	1082	194.7 (68.5)	194	96 to 394	106 to 382	8 to 821

Table 77: ALP distribution by research center and gender, AMP buffer

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	86.2 (29.9)	82	43 to 173	46 to 169	41 to 226
	Kigali	188	86.0 (30.2)	86	43 to 174	43 to 187	39 to 210
	Lusaka	184	92.6 (30.5)	93	48 to 179	51 to 179	40 to 207
	Total	501	88.4 (30.3)	87	45 to 176	46 to 179	39 to 226
Male	Kilifi	167	84.8 (35.0)	89	37 to 194	44 to 143	2 to 153
	Kigali	185	72.7 (17.1)	74	45 to 117	47 to 122	36 to 171
	Lusaka	168	84.5 (19.8)	83	53 to 135	58 to 148	54 to 228
	Total	520	80.2 (25.0)	81	43 to 150	48 to 138	2 to 228
Total	Kilifi	296	85.4 (32.9)	88	40 to 185	45 to 156	2 to 226
	Kigali	373	79.1 (24.6)	79	42 to 147	45 to 170	36 to 210
	Lusaka	352	88.6 (25.8)	85	50 to 159	53 to 167	40 to 228
	Total	1021	84.1 (27.9)	83	43 to 163	48 to 164	2 to 228

Research Center Comparisons

The differences between centers within each buffer type are not significant.

Gender Comparisons

The differences between males and females within each buffer type are not significant.

Figure 119: ALP (DEA buffer) 95% intervals and medians by research center and gender

Consensus interval: 106 to 382
Comparison interval: 30 to 120
White: Females, Blue: Males, Black: Overall

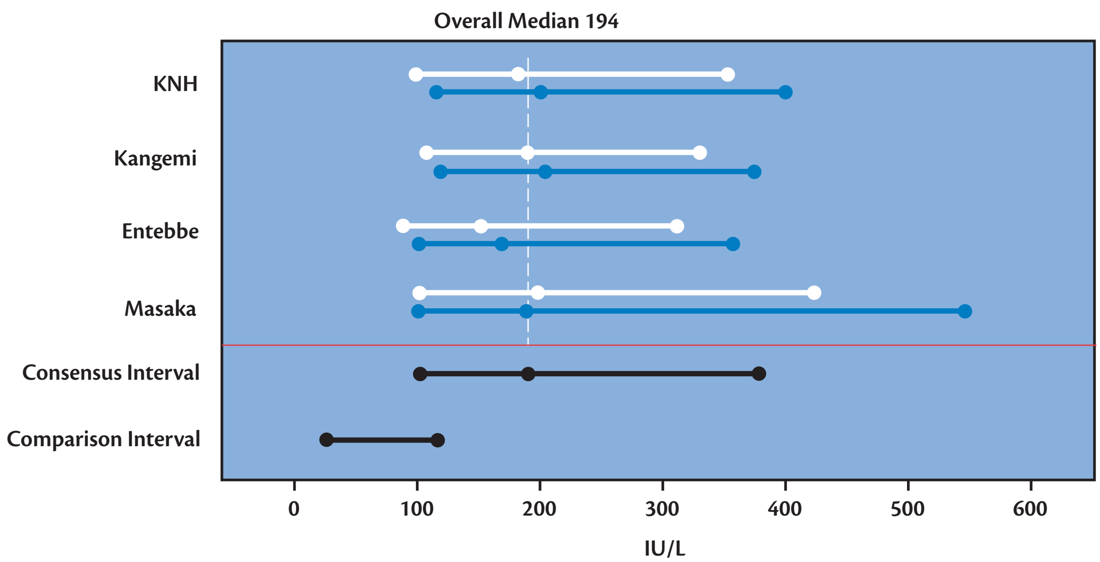
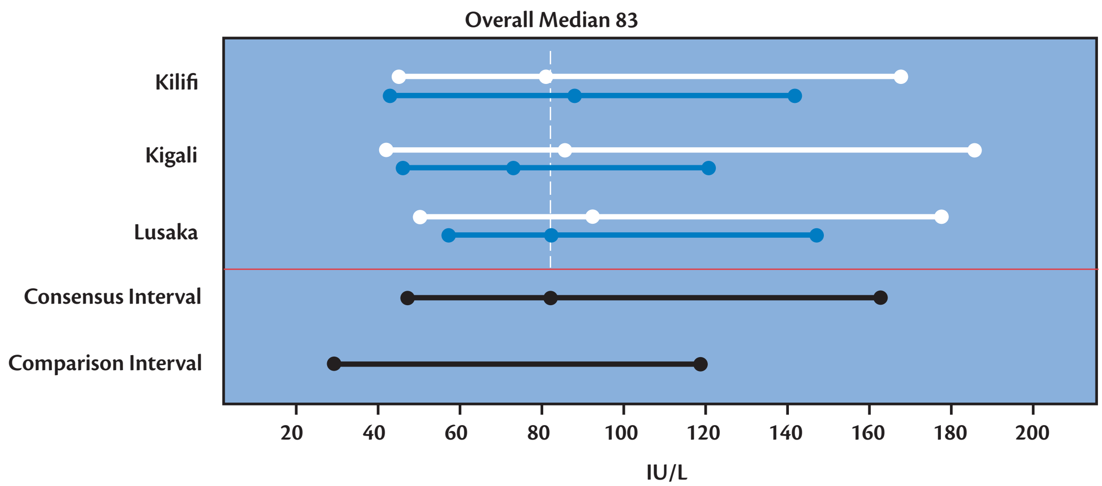


Figure 120: ALP (AMP buffer) 95% intervals and medians by research center and gender

Consensus interval: 48 to 164
Comparison interval: 30 to 120
White: Females, Blue: Males, Black: Overall



4.12. Total Protein

Results

Table 78 shows the number of subjects with data included in the analysis. Figures 121, 122, and 123 show the total protein distribution overall, by gender and by research center, respectively. Table 79 is the distribution of total protein by research center and gender, together with the stratified 95% reference intervals. The same quantiles and median values are shown in Figure 124. The comparison and final estimated consensus intervals are shown below.

Estimated Reference Intervals (g/L)

Comparison interval: *55 to 80*
All centers, consensus interval: *58 to 88*

Table 78: Number of observations, total protein

	Male		Female		Total
	N	%	N	%	Data
Kilifi	167	56.42	129	43.58	296
KNH	98	49.75	99	50.25	197
Kangemi	186	51.38	176	48.62	362
Entebbe	94	48.96	98	51.04	192
Masaka	125	51.87	116	48.13	241*
Kigali	185	49.60	188	50.40	373
Lusaka	168	47.73	184	52.27	352
Total	1023	50.82	990	49.18	2013

* Excludes 90 values collected from Nov-Dec 2005

Figure 121: Frequency distribution of total protein

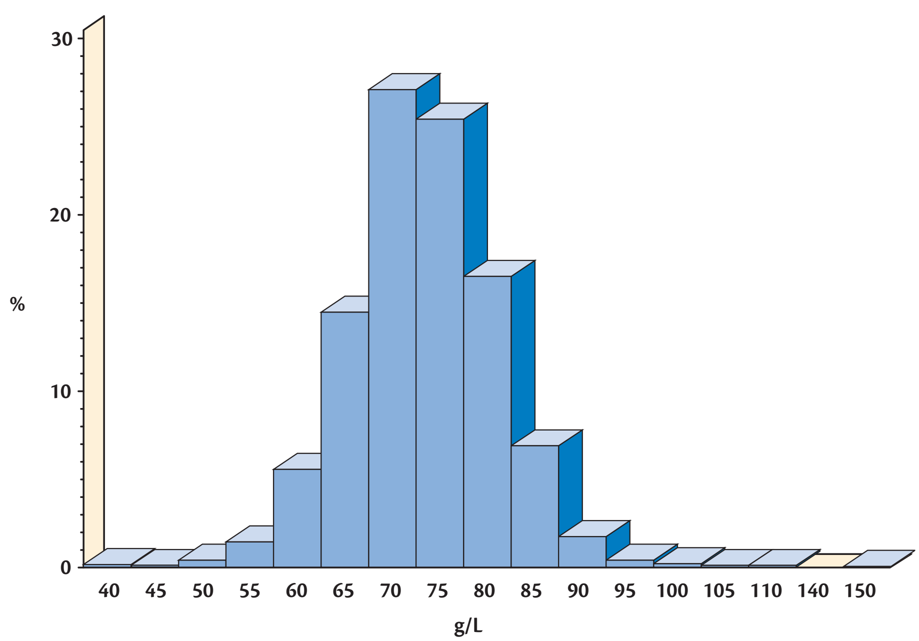


Figure 122: Frequency distribution of total protein by gender

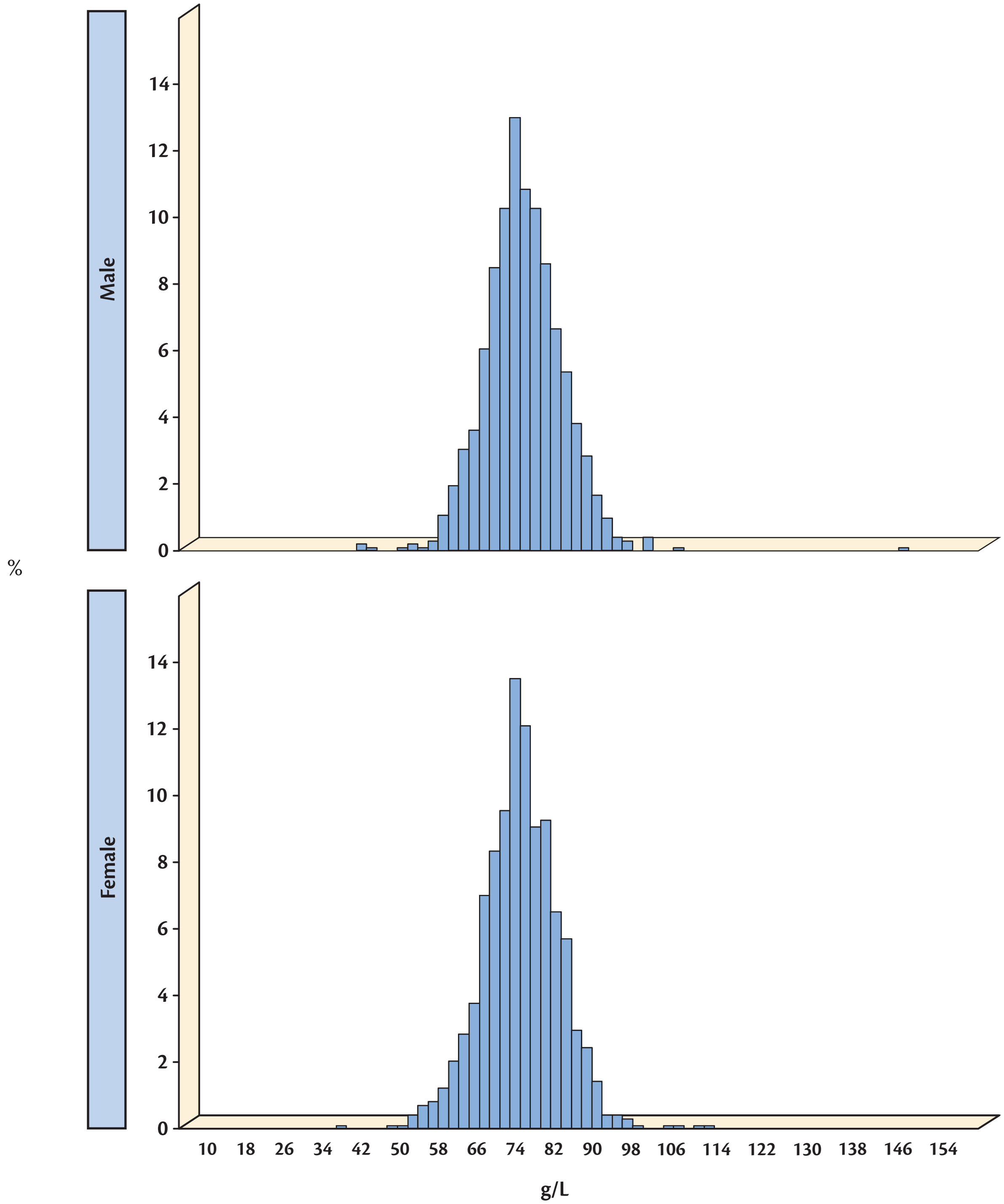


Figure 123: Frequency distribution of total protein by research center

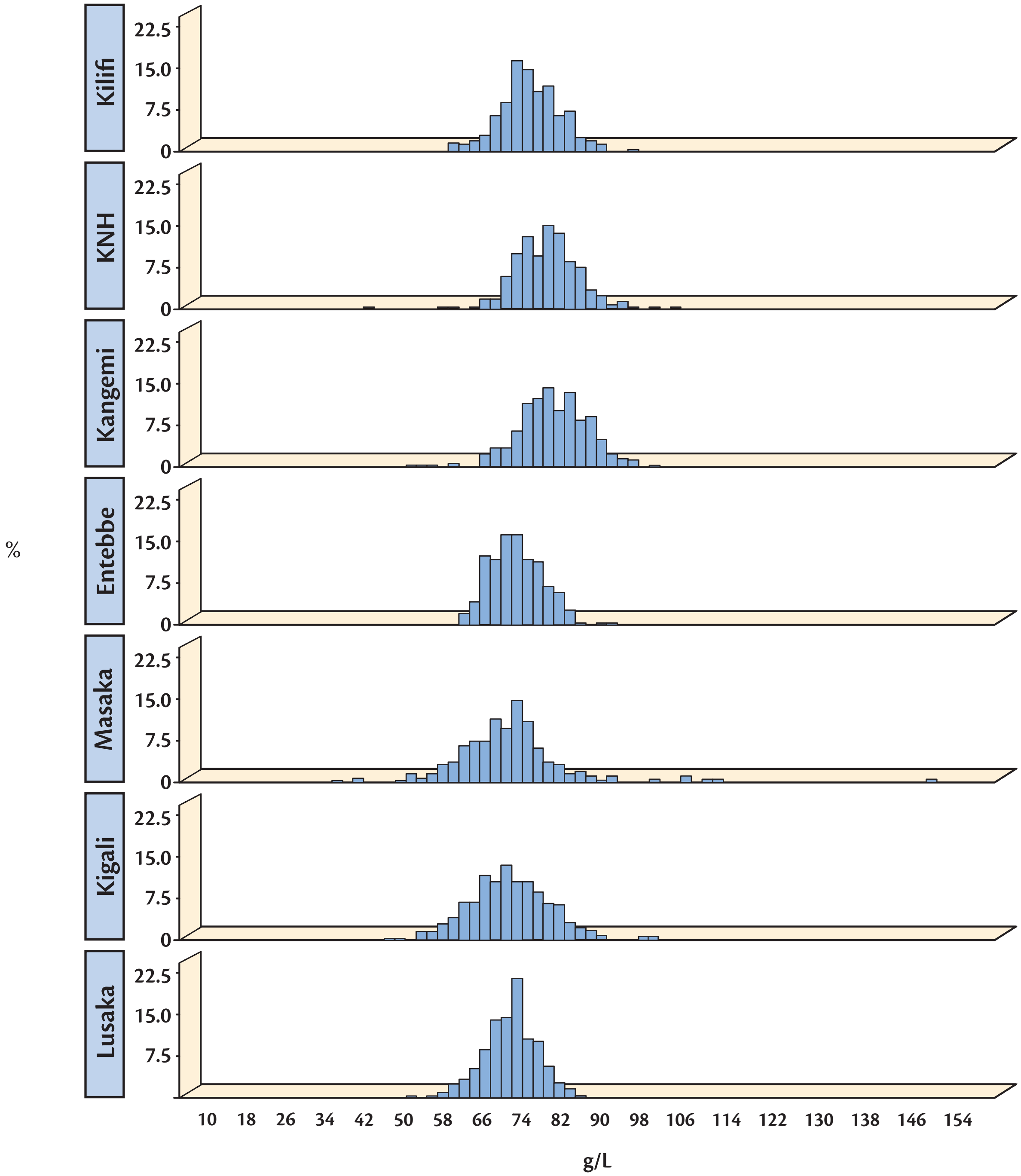


Table 79: Total protein distribution by research center and gender

Gender	Center	Sample Size	Mean (SD)	Median	Mean +/- 2SD	95% Interval	Min-Max
Female	Kilifi	129	73.9 (5.7)	74	62.5 to 85.3	63 to 85	59 to 93
	KNH	99	77.3 (6.6)	77	64.2 to 90.4	65 to 92	57 to 101
	Kangemi	176	77.5 (6.8)	78	64.0 to 91.1	65 to 90	52 to 94
	Entebbe	98	70.7 (4.9)	70	60.9 to 80.5	62 to 81	62 to 87
	Masaka	116	69.1 (9.9)	68	49.3 to 88.8	51 to 104	38 to 109
	Kigali	188	70.4 (7.9)	70	54.6 to 86.3	54 to 86	47 to 96
	Lusaka	184	70.4 (5.5)	71	59.4 to 81.3	59 to 81	52 to 83
	Total	990	72.7 (7.6)	73	57.4 to 87.9	58 to 87	38 to 109
Male	Kilifi	167	74.2 (5.8)	74	62.6 to 85.7	62 to 86	59 to 88
	KNH	98	76.8 (7.0)	77	62.9 to 90.7	67 to 92	43 to 97
	Kangemi	186	79.1 (6.5)	79.5	66.1 to 92.0	67 to 92	59 to 98
	Entebbe	94	72.5 (5.2)	72	62.0 to 82.9	64 to 82	61 to 90
	Masaka	125	70.5 (11.5)	70	47.5 to 93.5	52 to 89	41 to 148
	Kigali	185	69.8 (7.2)	69	55.4 to 84.2	57 to 84	50 to 98
	Lusaka	168	70.2 (4.9)	70.5	60.3 to 80.0	59 to 79	56 to 82
	Total	1023	73.3 (7.9)	73	57.6 to 89.0	59 to 88	41 to 148
Total	Kilifi	296	74.0 (5.7)	74	62.6 to 85.5	62 to 86	59 to 93
	KNH	197	77.1 (6.7)	77	63.6 to 90.5	65 to 92	43 to 101
	Kangemi	362	78.3 (6.7)	78	65.0 to 91.6	66 to 91	52 to 98
	Entebbe	192	71.6 (5.1)	71	61.3 to 81.8	63 to 82	61 to 90
	Masaka	241	69.8 (10.7)	70	48.3 to 91.3	52 to 89	38 to 148
	Kigali	373	70.1 (7.6)	70	55.0 to 85.3	56 to 85	47 to 98
	Lusaka	352	70.3 (5.2)	71	59.9 to 80.7	59 to 80	52 to 83
	Total	2013	73.0 (7.7)	73	57.5 to 88.5	58 to 88	38 to 148

Research Center Comparisons

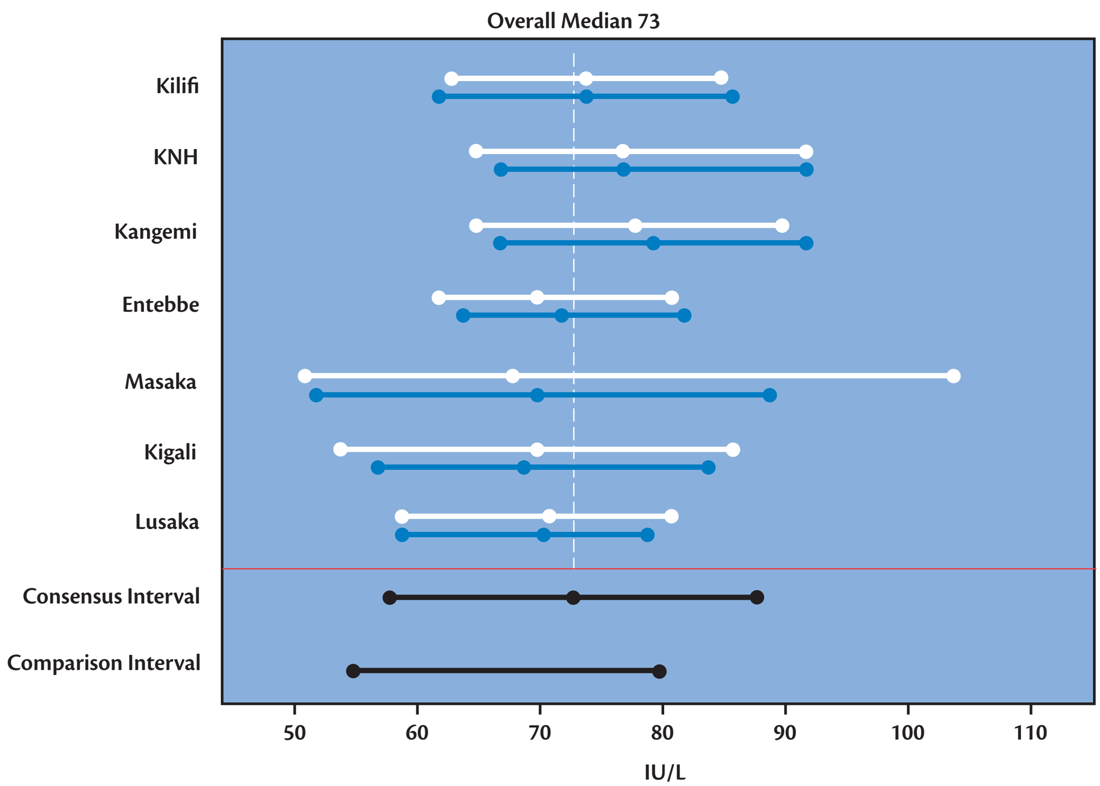
No significant differences were found between centers.

Gender Comparisons

The difference between males and females is not significant.

Figure 124: Total protein 95% intervals and medians by research center and gender

Consensus interval: 58 to 88
Comparison interval: 55 to 80
White: Females, Blue: Males, Black: Overall



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