

	Leukopenia	Normal	Leukocytosis	P value	Thrombocyto- penia	Normal	Thrombocytos is	P value
Number	7895	131364	3932		2312	139239	1640	
Male sex (%)	38.4	41.9	37.5	<0.001	68.6	41.5	13.4	<0.001
Age (years)	46.4 ± 12.4	44.3 ± 12.8	42.8 ± 11.3	<0.001	47.5 ± 14.4	44.4 ± 12.7	43.5 ± 11.7	<0.001
BMI (kg/m²)	24.4 ± 3.4	26.1 ± 4.3	27.2 ± 5.3	<0.001	25.9 ± 4.0	26.0 ± 4.3	26.8 ± 5.2	<0.001
Smoking				<0.001				<0.001
Current/former/ never	6.9/38.5/54.6	20.3/33.1/46.6	68.2/13.3/18.5		17.8/36.4/45.8	20.9/32.8/46.3	28.2/30.0/41.8	
Number of medications used	0 (0 – 1)	1 (0 – 2)	1 (0 – 3)	<0.001	0 (0 – 2)	1 (0 – 2)	1 (0 – 2)	<0.001
Alcohol use				<0.001				<0.001
Non/light/ moderate/heavy	19.6/51.9/ 21.7/6.8	21.3/50.2/ 20.4/8.1	28.3/43.0/ 18.0/3.6		19.2/48.4/ 21.4/2.2	21.3/50.2/ 20.4/8.1	35.2/46.5/ 13.2/5.2	
Anemia (%)	9.0	3.9	2.6	<0.001	4.5	4.0	18.3	<0.001
MCV (fL)	89.9 ± 4.5	89.8 ± 4.1	91.2 ± 4.6	<0.001	89.6 ± 4.5	89.9 ± 4.1	88.3 ± 6.7	<0.001
	Neutropenia	Normal	Neutrophilia	P value	Lymphopenia	Normal	Lymphocytosis	P value
Number	6756	13214	2020		473	134530	5887	
Male sex (%)	37.4	41.8	34.5	<0.001	48.4	41.8	34.8	<0.001
Age (years)	45.4 ± 13.8	44.4 ± 12.7	42.6 ± 10.6	<0.001	47.8 ± 12.0	44.5 ± 12.7	41.3 ± 14.0	<0.001
BMI (kg/m²)	24.3 ± 3.4	26.1 ± 4.3	26.7 ± 5.3	<0.001	25.1 ± 3.7	26.0 ± 4.3	26.8 ± 5.1	<0.001
Smoking				<0.001				<0.001
Current/former/ never	8.8/37.3/53.9	20.5/33.1/46.5	60.8/15.1/24.1		11.8/36.7/51.5	19.3/33.6/47.2	49.2/20.2/30.6	
Number of medications used	0 (0 – 1)	1 (0 – 2)	1 (0 – 2)	<0.001	0 (0 – 3)	1 (0 – 2)	1 (0 – 2)	<0.001
Alcohol use				<0.001				<0.001
Non/light/ moderate/heavy	17.3/52.6/ 22.5/7.6	21.5/50.1/ 20.3/8.1	27.7/45.7/ 17.6/9.0		21.6/50.7/ 19.7/8.1	21.3/50.3/ 20.4/8.0	23.0/48.3/ 19.0/9.6	

Anemia (%)	7.5	4.0	3.0	<0.001	9.1	4.3	2.3	<0.001
MCV (fL)	90.0 ± 4.3	89.8 ± 4.2	91.3 ± 4.6	<0.001	90.1 ± 4.9	89.8 ± 4.2	90.6 ± 4.2	<0.001
	Monocyto- penia	Normal	Monocytosis	P value		Normal	Basophilia	P value
Number	9713	129056	2121			140877	13	
Male sex (%)	25.9	42.3	62.5	<0.001		41.5	46.2	0.734
Age (years)	43.4 ± 11.8	44.5 ± 12.8	45.4 ± 13.4	<0.001		44.4 ± 12.7	52.4 ± 8.2	0.024
BMI (kg/m²)	24.8 ± 3.8	26.1 ± 4.3	26.8 ± 4.8	<0.001		26.0 ± 4.3	26.3 ± 7.1	0.567
Smoking				<0.001				0.066
Current/former/ never	9.7/36.4/53.9	20.8/32.9/46.3	54.3/22.1/23.6			20.5/33.0/46.5	38.5/46.2/15.4	
Number of medications used	1 (0 – 1)	1 (0 – 2)	1 (0 – 2)	<0.001		1 (0 – 2)	1 (0 – 2)	0.978
Alcohol use				<0.001				0.675
Non/light/ moderate/heavy	22.9/54.4/ 18.0/4.7	21.3/50.0/ 20.5/8.2	21.3/40.9/ 22.4/2.7			21.4/50.2 20.4/8.1	16.7/41.7/ 25.0/16.7	
Anemia (%)	6.4	2.0	2.9	<0.001		4.1	7.7	0.520
MCV (fL)	89.6 ± 4.2	89.8 ± 4.2	91.2 ± 4.4	<0.001		89.8 ± 4.2	90.5 ± 8.7	0.843
		Normal	Eosinophilia	P value	1st quintile	2nd-4th quintile	5th quintile	P value
Number		133329	7561		28201	84714	27975	
Male sex (%)		41.0	49.8	<0.001	40.4	42.7	39.0	<0.001
Age (years)		44.4 ± 12.7	44.0 ± 13.3	0.007	43.3 ± 14.4	44.4 ± 12.5	45.4 ± 11.7	<0.001
BMI (kg/m²)		26.0 ± 4.3	26.0 ± 4.3	0.545	25.3 ± 3.9	26.1 ± 4.3	26.4 ± 4.7	<0.001
Smoking								
Current/former/ never		9.9/33.2/46.9	30.9/29.1/40.1	<0.001	18.3/34.0/47.7	20.4/33.0/46.6	22.9/32.0/45.1	<0.001
Number of medications used		1 (0 – 2)	1 (0 – 2)	<0.001	1 (0 – 2)	1 (0 – 2)	1 (0 – 2)	<0.001
Alcohol use				<0.001				<0.001
Non/light/ moderate/heavy		21.4/50.4/ 17.8/51.4/	20.5/46.6/ 21.3/50.2/ 25.1/49.0/		17.8/51.4/ 21.3/50.2/ 25.1/49.0/	21.3/50.2/ 25.1/49.0/	25.1/49.0/ 25.1/49.0/	

moderate/heavy	20.2/7.9	22.6/10.3		21.6/8.8	20.4/8.0	18.5/7.4	
Anemia (%)	3.9	0.2	0.005	3.8	4.0	5.0	<0.001
MCV (fL)	89.8 ± 4.2	90.1 ± 4.2	<0.001	90.0 ± 4.0	89.8 ± 4.1	89.9 ± 4.5	<0.001

SDC, Table 1. Baseline characteristics for participants with and without peripheral blood cell count abnormalities. Data are given as mean ± SD, median (IQR) when not normally distributed, or percentage. BMI, body mass index; IQR, interquartile range; MCV, mean corpuscular volume; SD, standard deviation.

	Leukopenia		WBC in normal range		Leukocytosis	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
Physical functioning	92.0 ± 13.0	95.0 (90.0-100.0)	90.6 ± 14.2	95.0 (90.0-100.0)	85.2 ± 19.6	90.0 (80.0-100.0)
Social functioning	88.5 ± 17.3	100.0 (87.5-100.0)	87.7 ± 18.0	100.0 (75.0-100.0)	83.0 ± 21.7	87.5 (75.0-100.0)
Physical role functioning	87.1 ± 28.9	100.0 (100.0-100.0)	86.8 ± 29.2	100.0 (100.0-100.0)	80.2 ± 34.6	100.0 (75.0-100.0)
Emotional role functioning	91.6 ± 24.2	100.0 (100.0-100.0)	90.8 ± 29.2	100.0 (100.0-100.0)	86.0 ± 30.7	100.0 (100.0-100.0)
Mental health	80.2 ± 13.3	84.0 (72.0-88.0)	79.8 ± 13.7	84.0 (72.0-88.0)	76.6 ± 16.2	80.0 (68.0-88.0)
Vitality	69.6 ± 16.7	70.0 (60.0-80.0)	67.9 ± 17.0	70.0 (60.0-80.0)	62.6 ± 18.9	65.0 (50.0-75.0)
Bodily pain	85.6 ± 18.2	89.8 (77.6-100.0)	84.5 ± 19.0	89.8 (67.3-100.0)	79.8 ± 22.6	89.8 (67.3-100.0)
General health	74.3 ± 16.4	75.0 (65.0-85.0)	72.0 ± 16.6	75.0 (65.0-85.0)	65.2 ± 19.0	65.0 (55.0-80.0)
	Thrombocytopenia		Platelets in normal range		Thrombocytosis	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
Physical functioning	90.4 ± 14.4	95.0 (90.0-100.0)	90.6 ± 14.3	95.0 (90.0-100.0)	86.8 ± 18.1	95.0 (85.0-100.0)
Social functioning	88.9 ± 17.3	100.0 (87.5-100.0)	87.6 ± 18.0	100.0 (75.0-100.0)	84.1 ± 21.1	87.5 (75.0-100.0)
Physical role functioning	86.2 ± 30.2	100.0 (100.0-100.0)	86.7 ± 29.3	100.0 (100.0-100.0)	81.4 ± 33.8	100.0 (75.0-100.0)
Emotional role functioning	92.0 ± 23.5	100.0 (100.0-100.0)	90.8 ± 25.3	100.0 (100.0-100.0)	88.3 ± 28.5	100.0 (100.0-100.0)
Mental health	81.7 ± 13.3	84.0 (72.0-92.0)	79.7 ± 13.8	84.0 (72.0-88.0)	78.0 ± 14.9	80.0 (72.0-88.0)
Vitality	70.0 ± 17.1	73.3 (60.0-83.8)	67.9 ± 17.0	70.0 (60.0-80.0)	64.3 ± 18.3	65.0 (50.0-75.0)
Bodily pain	86.0 ± 18.4	100.0 (77.6-100.0)	84.5 ± 19.1	89.8 (67.3-100.0)	80.1 ± 22.1	89.8 (67.3-100.0)
General health	71.8 ± 17.0	75.0 (60.0-85.0)	72.0 ± 16.7	75.0 (65.0-85.0)	68.3 ± 19.0	70.0 (60.0-80.0)
	Neutropenia		Neutrophils in normal range		Neutrophilia	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
Physical functioning	92.3 ± 12.6	95.0 (90.0-100.0)	90.6 ± 14.3	95.0 (90.0-100.0)	86.2 ± 18.7	95.0 (80.0-100.0)
Social functioning	88.6 ± 17.1	100.0 (87.5-100.0)	87.6 ± 18.0	100.0 (75.0-100.0)	83.4 ± 21.6	87.5 (75.0-100.0)
Physical role functioning	88.1 ± 27.8	100.0 (100.0-100.0)	86.7 ± 29.3	100.0 (100.0-100.0)	81.3 ± 34.2	100.0 (75.0-100.0)
Emotional role functioning	91.9 ± 23.8	100.0 (100.0-100.0)	90.8 ± 25.3	100.0 (100.0-100.0)	86.2 ± 30.3	100.0 (100.0-100.0)
Mental health	80.3 ± 13.1	84.0 (72.0-88.0)	79.8 ± 13.7	84.0 (72.0-88.0)	76.8 ± 16.0	80.0 (68.0-88.0)
Vitality	69.9 ± 16.3	70.0 (60.0-80.0)	67.9 ± 17.0	70.0 (60.0-80.0)	63.2 ± 18.6	65.0 (50.0-75.0)
Bodily pain	85.7 ± 18.1	89.8 (77.6-100.0)	84.5 ± 19.1	89.8 (67.3-100.0)	80.7 ± 22.4	89.8 (67.3-100.0)
General health	74.5 ± 16.0	75.0 (65.0-85.0)	72.0 ± 16.7	75.0 (65.0-85.0)	66.6 ± 19.1	70.0 (55.0-80.0)

	Lymphopenia		Lymphocytes in normal range		Lymphocytosis	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
Physical functioning	87.2 ± 18.3	95.0 (85.0-100.0)	90.7 ± 14.1	95.0 (90.0-100.0)	87.9 ± 16.8	95.0 (85.0-100.0)
Social functioning	84.5 ± 21.7	100.0 (75.0-100.0)	87.8 ± 17.9	100.0 (100.0-100.0)	84.9 ± 20.5	100.0 (75.0-100.0)
Physical role functioning	80.9 ± 34.9	100.0 (75.0-100.0)	86.8 ± 29.2	100.0 (100.0-100.0)	83.2 ± 32.5	100.0 (75.0-100.0)
Emotional role functioning	88.7 ± 28.3	100.0 (100.0-100.0)	90.9 ± 25.1	100.0 (100.0-100.0)	87.6 ± 29.1	100.0 (100.0-100.0)
Mental health	79.9 ± 13.4	84.0 (72.0-88.0)	79.8 ± 13.6	84.0 (72.0-88.0)	77.5 ± 15.5	80.0 (68.0-88.0)
Vitality	67.5 ± 18.9	70.0 (55.0-80.0)	68.1 ± 17.0	70.0 (60.0-80.0)	64.6 ± 18.3	65.0 (50.0-80.0)
Bodily pain	82.9 ± 21.3	89.8 (67.3-100.0)	84.6 ± 19.0	89.8 (67.3-100.0)	81.9 ± 21.1	89.8 (67.3-100.0)
General health	67.5 ± 21.3	75.0 (55.0-80.0)	72.2 ± 16.6	75.0 (65.0-85.0)	67.7 ± 18.2	70.0 (55.0-80.0)
	Monocytopenia		Monocytes in normal range		Monocytosis	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
Physical functioning	91.9 ± 13.0	95.0 (90.0-100.0)	90.6 ± 14.3	95.0 (90.0-100.0)	86.7 ± 18.4	95.0 (85.0-100.0)
Social functioning	87.5 ± 18.1	100.0 (75.0-100.0)	87.7 ± 18.0	100.0 (75.0-100.0)	85.8 ± 20.2	100.0 (75.0-100.0)
Physical role functioning	87.6 ± 28.4	100.0 (100.0-100.0)	86.6 ± 29.4	100.0 (100.0-100.0)	83.2 ± 32.4	100.0 (75.0-100.0)
Emotional role functioning	91.3 ± 25.0	100.0 (100.0-100.0)	90.8 ± 25.2	100.0 (100.0-100.0)	87.8 ± 28.9	100.0 (100.0-100.0)
Mental health	79.5 ± 13.4	84.0 (72.0-88.0)	80.0 ± 13.7	84.0 (72.0-88.0)	76.1 ± 15.5	84.0 (72.0-92.0)
Vitality	67.8 ± 16.7	70.0 (60.0-80.0)	67.9 ± 17.0	70.0 (60.0-80.0)	66.1 ± 18.3	70.0 (55.0-80.0)
Bodily pain	85.1 ± 18.3	89.8 (77.6-100.0)	84.4 ± 19.1	89.8 (67.3-100.0)	83.1 ± 20.9	89.8 (67.3-100.0)
General health	73.7 ± 16.3	75.0 (65.0-85.0)	71.9 ± 16.7	75.0 (65.0-85.0)	67.5 ± 18.1	70.0 (55.0-80.0)
	NLR lowest quintile		NLR 2nd to 4th quintile		NLR highest quintile	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
Physical functioning	91.6 ± 13.4	95.0 (90.0-100.0)	90.6 ± 14.3	95.0 (90.0-100.0)	89.1 ± 15.7	95.0 (85.0-100.0)
Social functioning	88.3 ± 17.6	100.0 (75.0-100.0)	87.5 ± 18.2	100.0 (75.0-100.0)	86.5 ± 18.8	100.0 (75.0-100.0)
Physical role functioning	87.9 ± 28.0	100.0 (100.0-100.0)	86.6 ± 29.4	100.0 (100.0-100.0)	84.7 ± 31.1	100.0 (100.0-100.0)
Emotional role functioning	91.3 ± 24.6	100.0 (100.0-100.0)	90.7 ± 25.4	100.0 (100.0-100.0)	89.6 ± 26.8	100.0 (100.0-100.0)
Mental health	79.8 ± 13.6	84.0 (72.0-88.0)	79.7 ± 13.8	84.0 (72.0-88.0)	79.2 ± 14.1	84.0 (72.0-88.0)
Vitality	68.8 ± 16.8	70.0 (60.0-80.0)	67.7 ± 17.1	70.0 (55.0-80.0)	66.8 ± 17.4	70.0 (55.0-80.0)
Bodily pain	85.1 ± 18.5	89.8 (77.6-100.0)	84.5 ± 19.2	89.8 (67.3-100.0)	83.3 ± 19.9	89.8 (67.3-100.0)
General health	72.9 ± 16.4	75.0 (65.0-85.0)	71.8 ± 16.7	75.0 (62.5-85.0)	70.7 ± 17.3	70.0 (60.0-85.0)

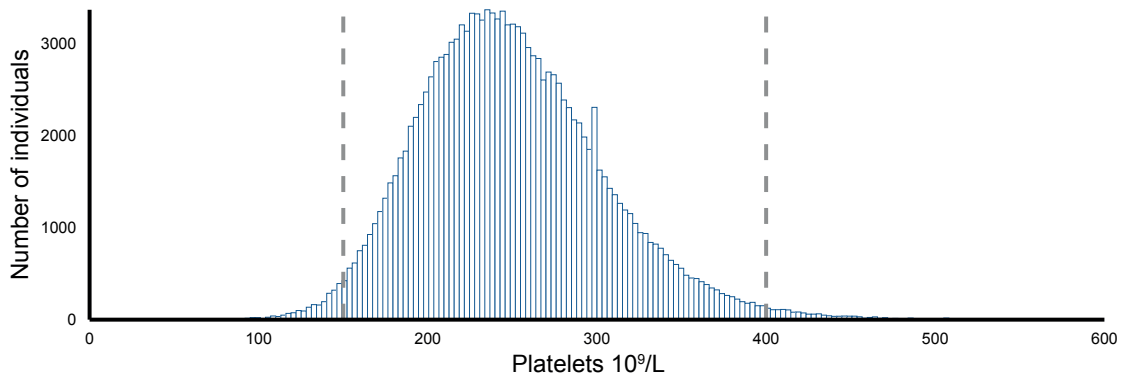
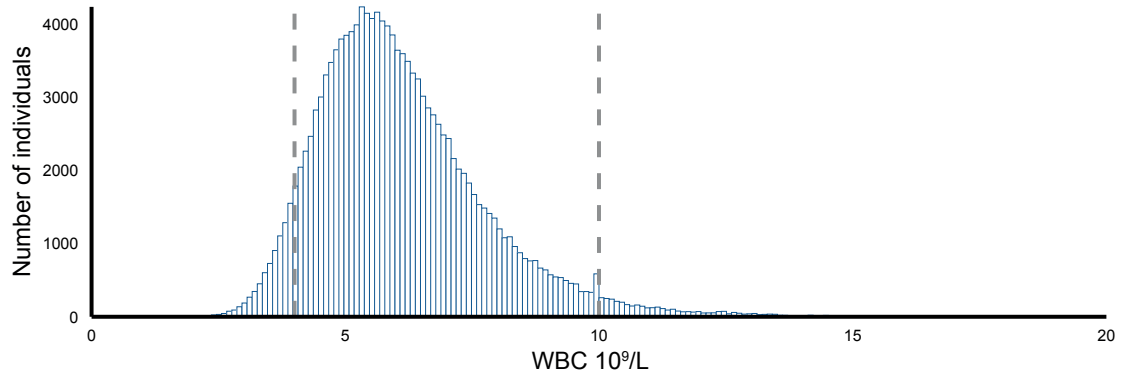
SDC, Table 2. Absolute scores for the different domains of the RAND-36 health survey, stratified according to differential blood cell count abnormality. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell.

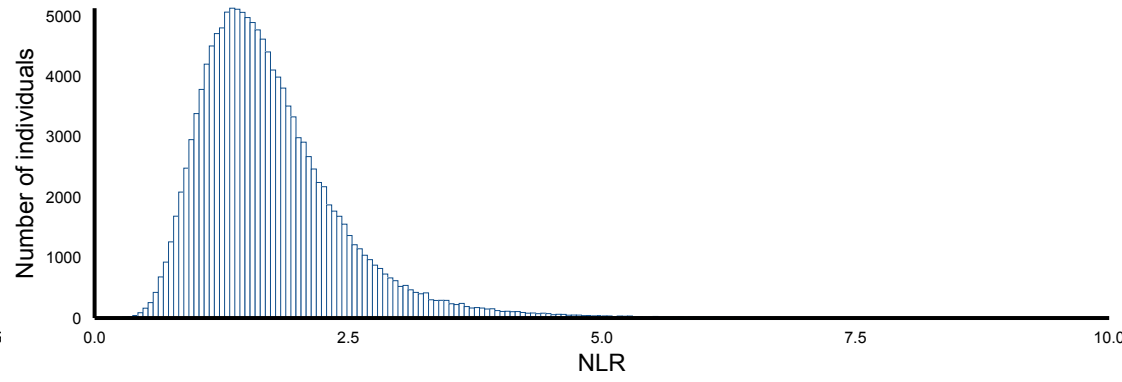
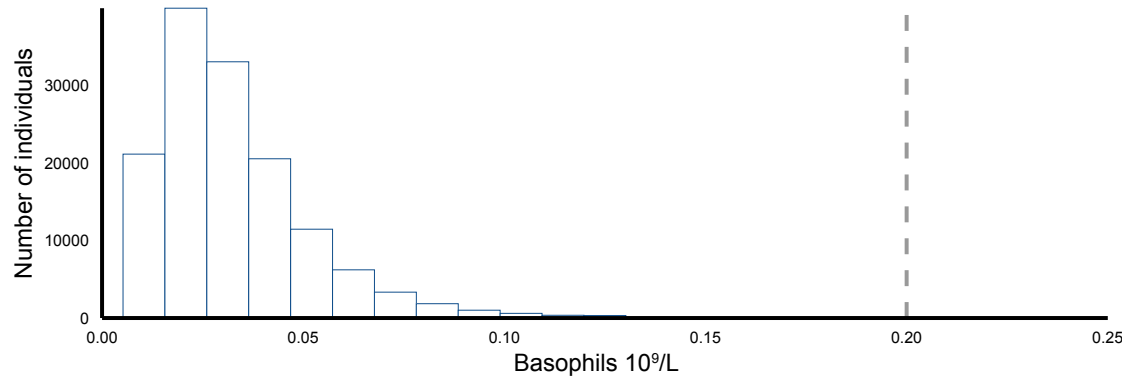
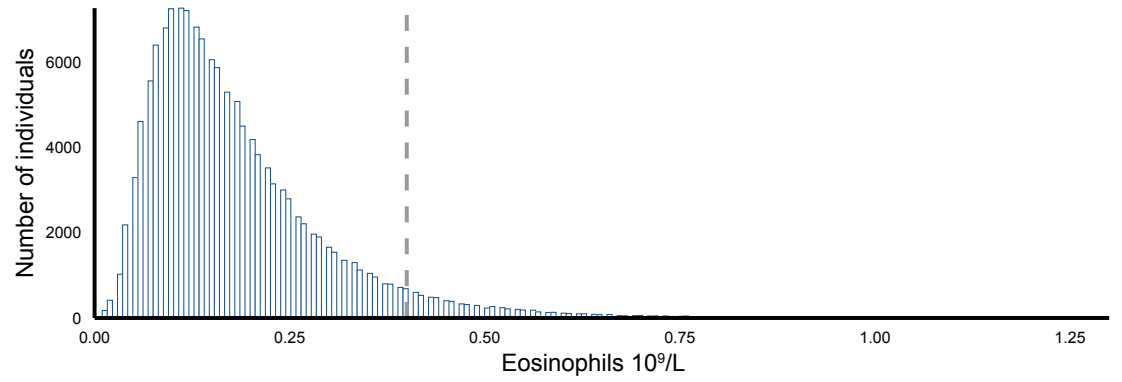
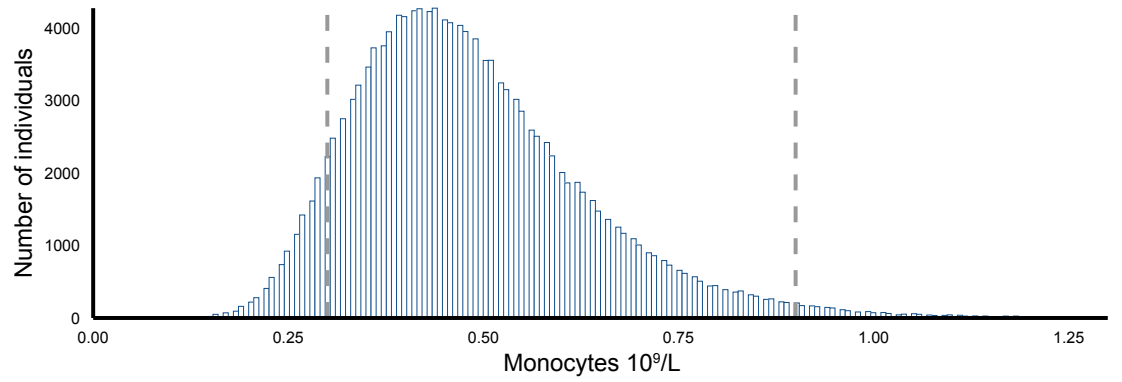
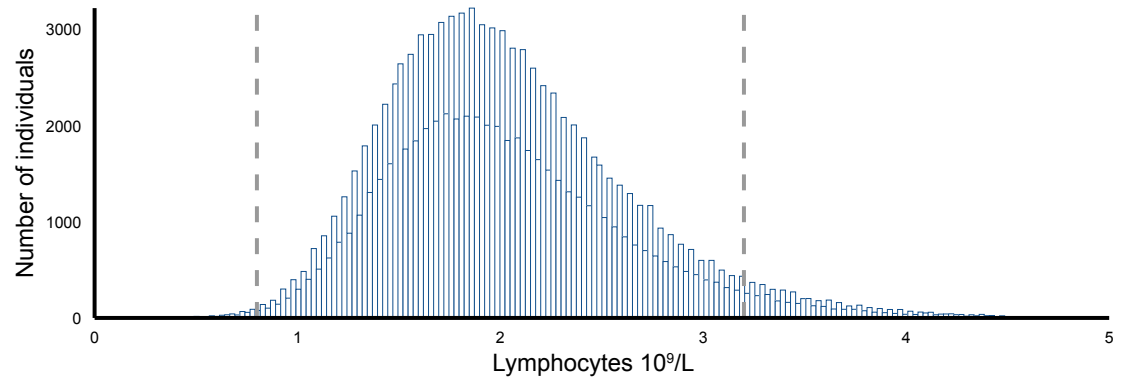
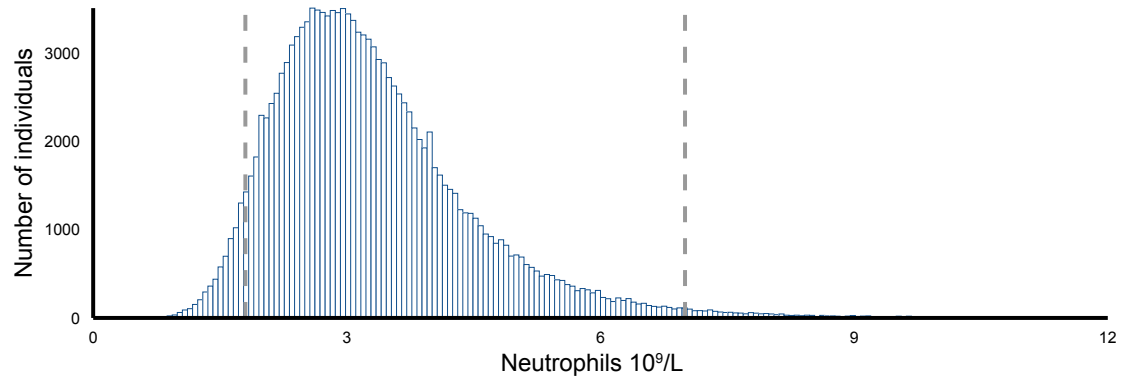
SDC, Figure 1. Distribution of white blood cell and platelet counts in the evaluable Lifelines cohort (n=143191). In order to improve visibility, figures were cropped at the extremes and a minor proportion of outliers in platelet count ($>600 \times 10^9/L$, n=52) and white blood cell count ($>20 \times 10^9/L$, n=34) were removed. WBC, white blood cell.

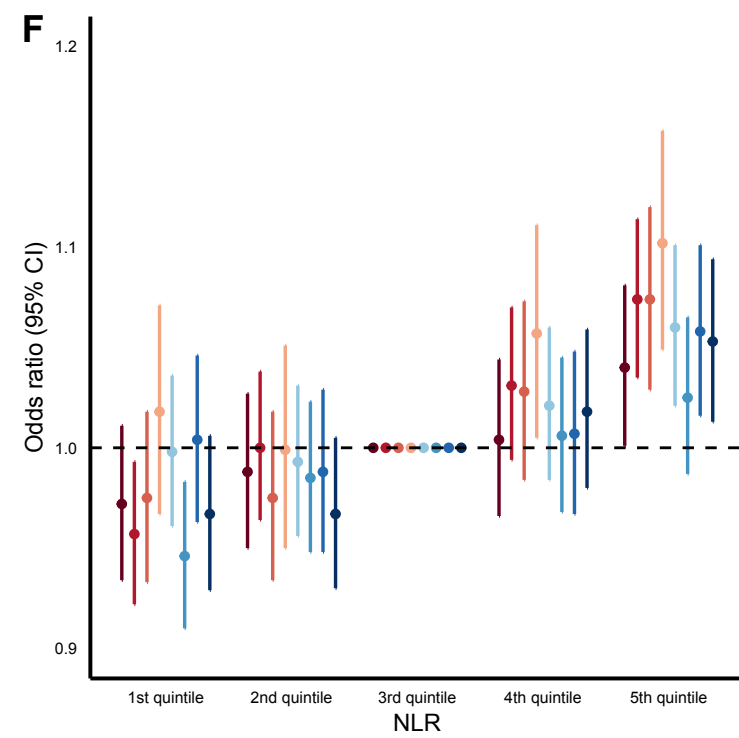
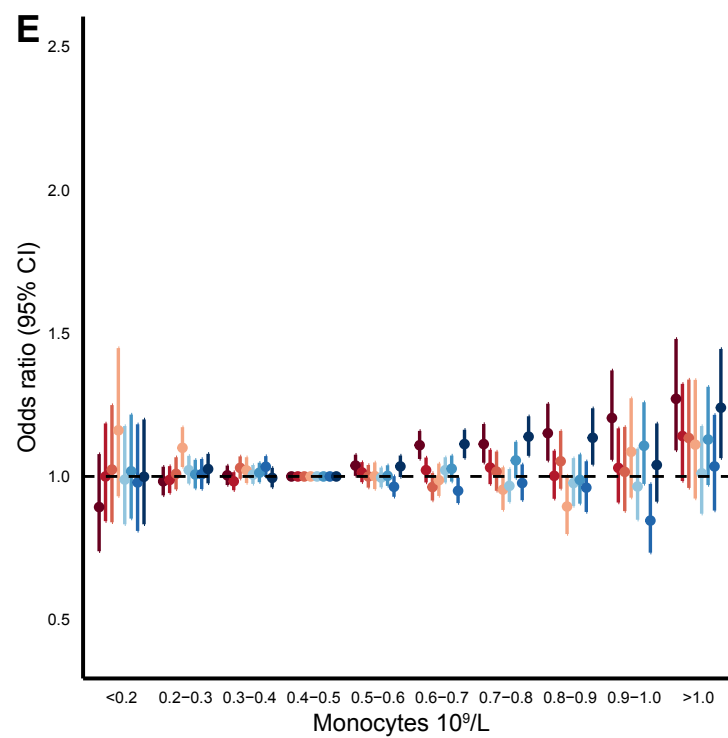
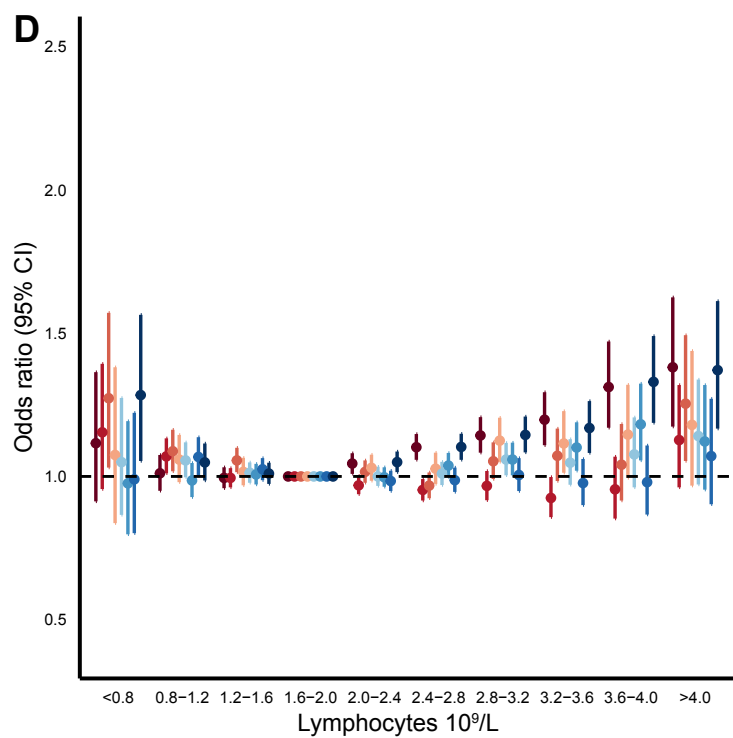
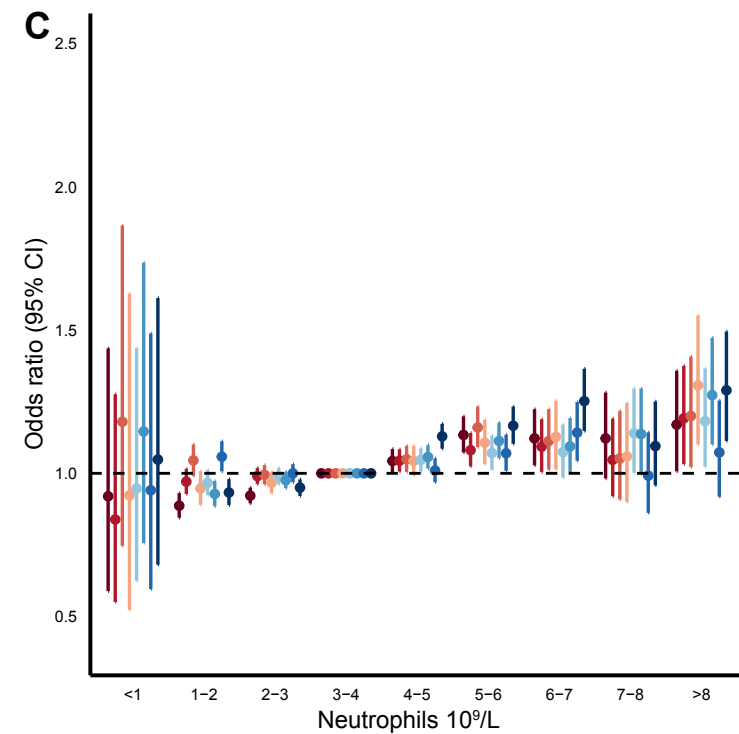
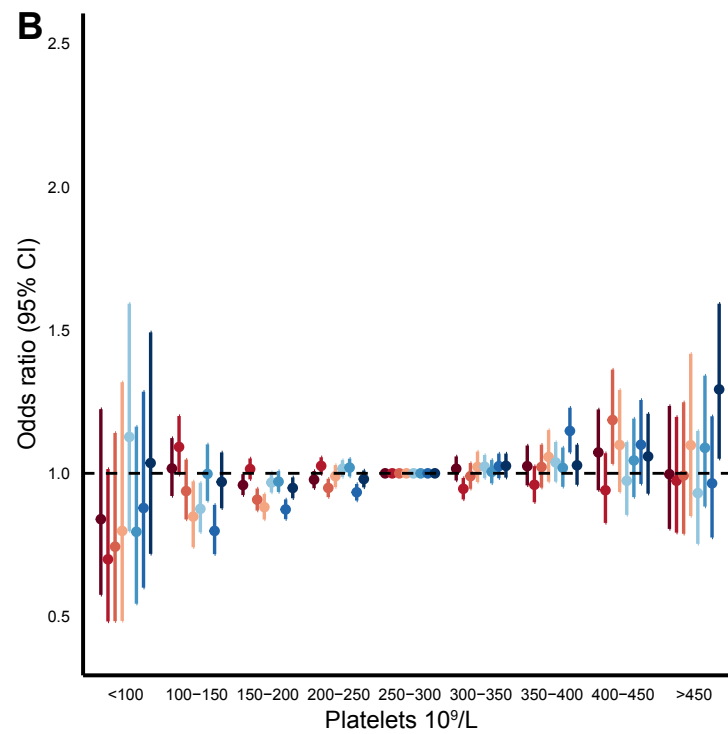
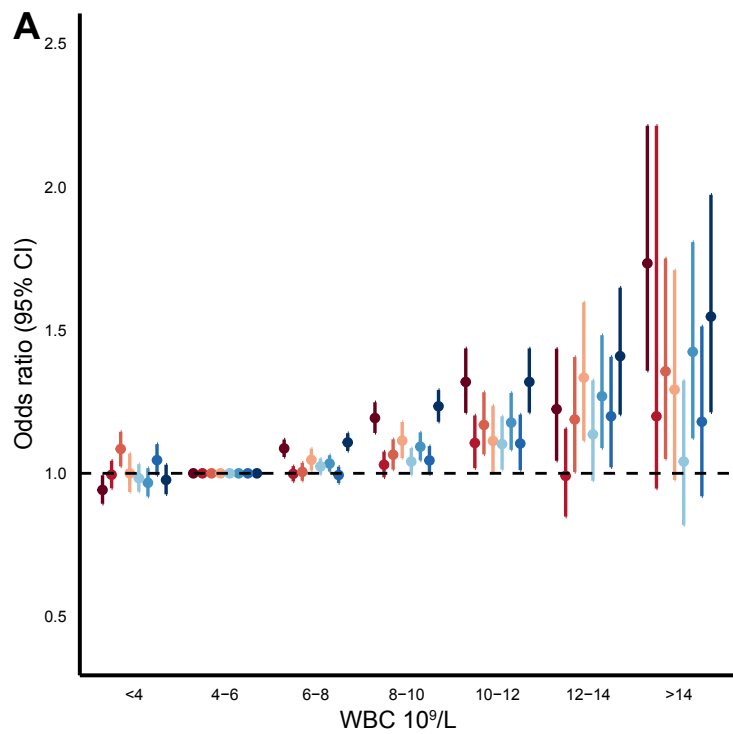
SDC, Figure 2. Distribution of differential white blood cell counts in the evaluable Lifelines cohort (n=140890). In order to improve visibility, figures were cropped at the extremes and a minor proportion of outliers in neutrophil count ($>12 \times 10^9/L$, n=57), lymphocyte count ($>5 \times 10^9/L$, n=3), monocyte count ($>1.3 \times 10^9/L$, n=67), eosinophil count ($>1.3 \times 10^9/L$, n=86), basophil count ($>0.25 \times 10^9/L$, n=8) and neutrophil to lymphocyte ratio (>10 , n=50) were removed. NLR, neutrophil to lymphocyte ratio.

SDC, Figure 3. Forest plots demonstrating the odds ratios for having a lower score than the (age- and sex-specific) 25th percentile cut-off per HRQoL subscale, according to different strata of blood cell counts. Logistic regression analyses included body mass index, smoking status, alcohol use, and number of medications, presence of anemia and mean corpuscular volume as covariates. The following ranges in peripheral blood cell counts were used as the reference group: white blood cell count $4-6 \times 10^9/L$; platelets $250-300 \times 10^9/L$; neutrophils $3-4 \times 10^9/L$; lymphocytes $1.6-2.0 \times 10^9/L$; monocytes $0.4-0.5 \times 10^9/L$; and NLR in the 3rd quintile. Circles indicate odds ratios for each domain, with horizontal lines corresponding to 95% confidence intervals. NLR, neutrophil to lymphocyte ratio; WBC, white blood cell.

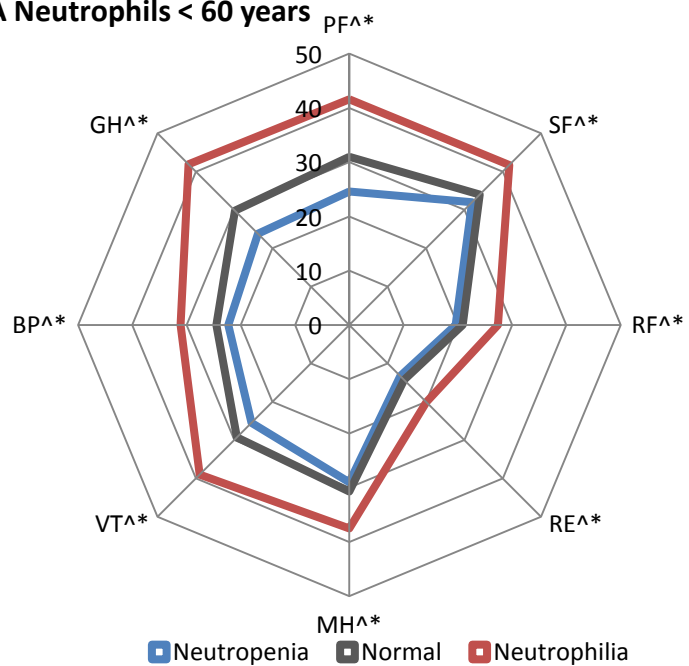
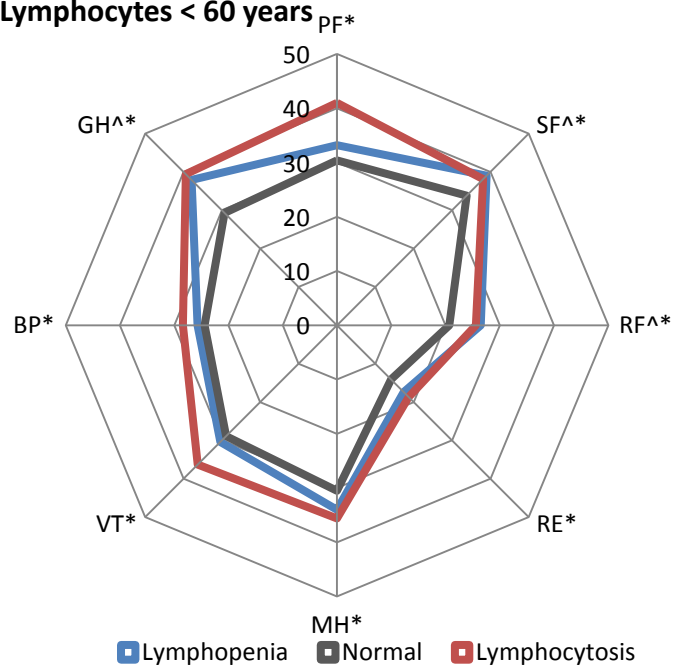
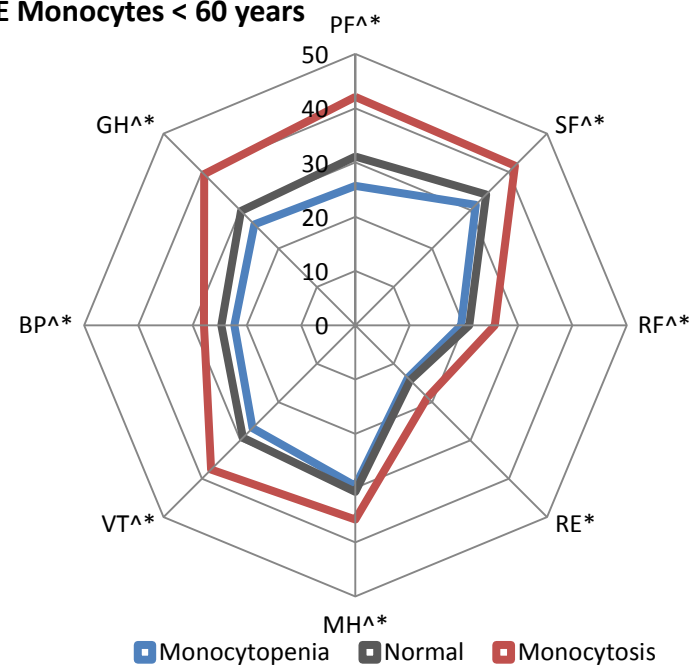
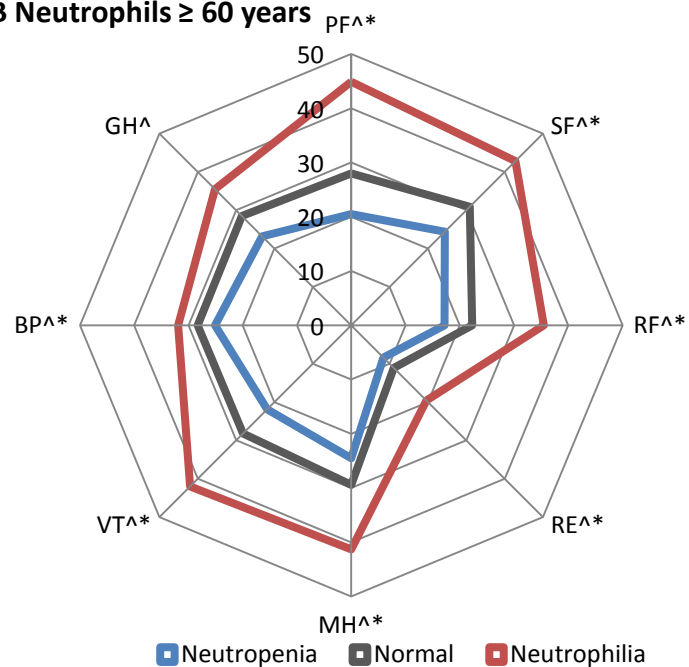
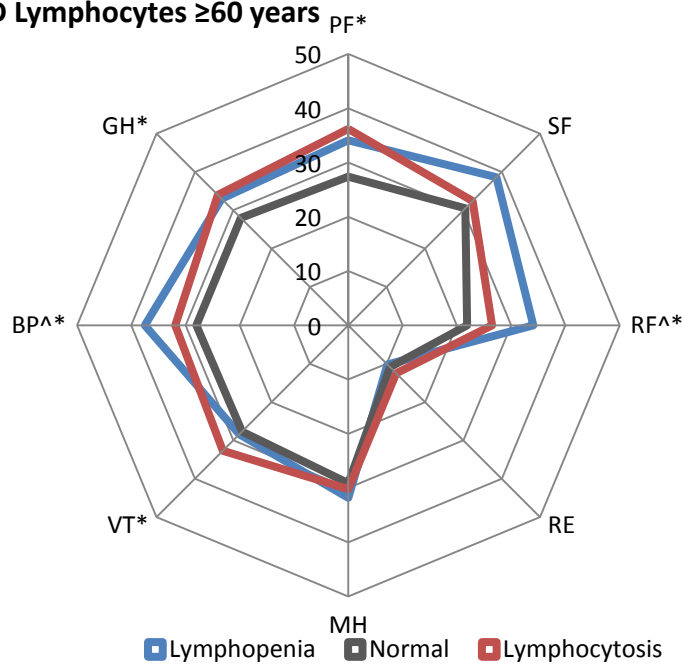
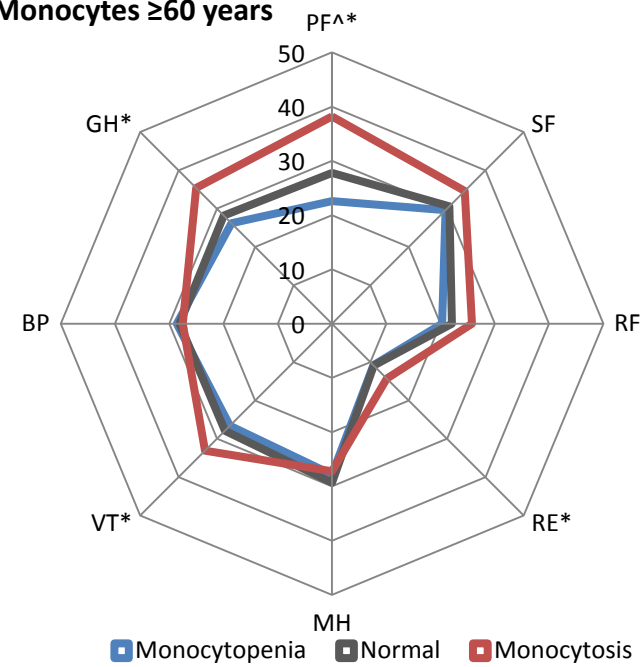
SDC, Figure 4. Percentage of individuals with a score below the age- and sex-specific cut-off value for the different domains of the RAND-36 health survey, stratified according to differential blood cell count abnormality and age group (<60 years and ≥ 60 years). A circumflex (^) indicates a significant difference in the proportion below the age- and sex-specific cut-off value for individuals with neutropenia, lymphopenia, monocytopenia or lowest NLR quintile, as compared to individuals with a normal blood cell count. An asterisk (*) indicates a significant difference in the proportion below the age- and sex-specific cut-off value for individuals with neutrophilia, lymphocytosis, monocytosis, eosinophilia or highest NLR quintile, as compared to individuals with a normal blood cell count. BP, bodily pain; GH, general health; MH, mental health; NLR, neutrophil to lymphocyte ratio; PF, physical functioning; RE, emotional role functioning; RF, physical role functioning; SF, social functioning; VT, vitality; WBC, white blood cell.



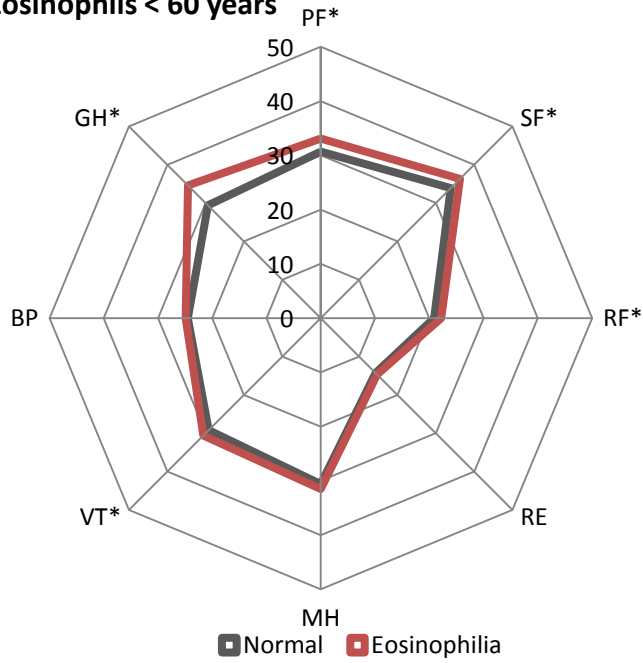




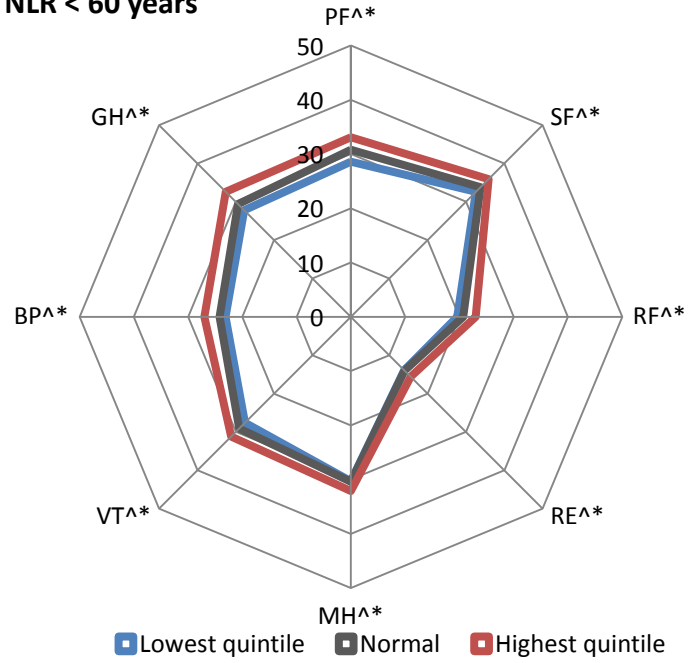
● Physical functioning
 ● Social functioning
 ● Physical role functioning
 ● Emotional role functioning
 ● Mental health
 ● Vitality
 ● Bodily pain
 ● General health

A Neutrophils < 60 years**C Lymphocytes < 60 years****E Monocytes < 60 years****B Neutrophils ≥ 60 years****D Lymphocytes ≥ 60 years****F Monocytes ≥ 60 years**

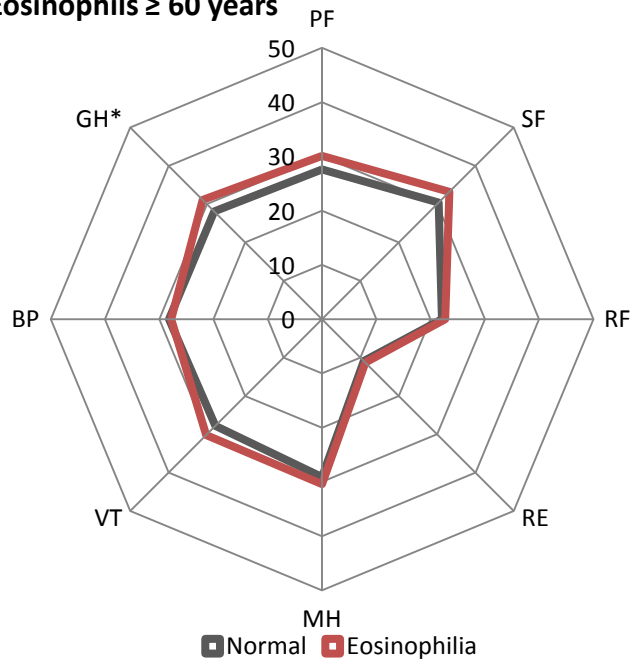
G Eosinophils < 60 years



I NLR < 60 years



H Eosinophils ≥ 60 years



J NLR ≥ 60 years

