

**Appendix** for the paper:

**Extreme Erythrocyte Macrocytic and Microcytic Percentages are Highly Predictive of Morbidity and Mortality**

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**Appendix Table 1A.** Baseline characteristics stratified by quartile categories of the percentage of macrocytic RBCs (%Macro, RBC volume >120 fL) and microcytic RBCs (%Micro, RBC volume <60 fL) among females (n=165,770). The means or percentages of all characteristics were significantly different ( $p<0.001$ ) across the %Macro/%Micro quartile categories by the chi-square test or ANOVA.

Characteristic	Quartile Category of %Macro/%Micro									
	LR1 <sup>A</sup>	LR2 <sup>B</sup>	3/3	1/4	2/4	3/4	4/1	4/2	4/3	4/4
Sample Size (n)	23,235	53,486	9,565	25,910	8,691	3,751	20,880	13,216	5,064	1,972
Age (years)	39.4±17	44.0±19	51.9±20	41.7±18	47.8±19	53.4±20	53.0±21	55.4±21	59.0±20	60.7±19
%Macro (%)	6.2±0.5	6.8±1.0	7.5±0.4	4.8±0.9	6.3±0.3	7.5±0.4	12.3±5.2	11.3±3.9	11.0±4.1	11.7±5.2
%Micro (%)	0.9±0.2	1.2±0.5	1.6±0.2	7.9±9.2	3.6±2.3	3.6±2.5	0.5±0.2	1.0±0.1	1.6±0.2	4.0±2.9
<i><u>CBC Parameters</u></i>										
RBC Count (10 <sup>6</sup> /μL)	4.3±0.4	4.5±0.4	4.7±0.5	4.5±0.5	4.8±0.5	4.7±0.6	4.2±0.5	4.4±0.5	4.4±0.7	4.3±0.9
Hemoglobin (g/dL)	13.2±1	13.5±1	13.8±1	11.9±2	13.4±2	13.3±2	13.6±2	13.7±2	13.4±2	12.4±2
Hematocrit (%)	38.4±4	39.7±4	41.3±4	36.2±4	40.3±4	40.3±5	40.6±4	40.9±4	40.3±5	38.2±7
WBC Count (10 <sup>9</sup> /L)	8.7±3.3	8.8±3.4	9.0±3.7	9.3±3.8	9.3±3.8	9.5±4.9	8.4±4.0	8.8±4.3	9.2±6.2	10.2±15.7
Platelet Count (10 <sup>9</sup> /L)	239±61	241±65	245±71	266±87	258±80	256±89	230±67	239±74	241±89	244±116
MCV (fL)	89.2±1	89.2±3	88.7±2	80.2±5	84.6±3	85.9±3	96.7±3	93.0±3	91.2±4	90.0±5
MCH (pg)	30.5±1	30.3±2	29.8±1	26.3±3	28.1±1	28.3±1	32.5±1	31.2±1	30.2±1	29.2±3

MCHC (g/dL)	34.2±1	34.0±2	33.5±1	32.8±2	33.2±1	32.9±1	33.6±1	33.5±1	33.1±1	32.5±3
RDW (%)	12.7±0.5	13.2±0.6	14.0±0.7	15.0±2	14.8±2	15.6±2	13.3±0.8	13.8±1	14.9±1	17.7±3
RDW-sd (fL)	41.4±2	42.9±2	45.1±3	43.6±4	45.4±4	48.6±6	46.7±4	46.5±5	49.2±6	57.6±10
MPV (fL)	10.18±1	10.31±1	10.43±1	10.15±1	10.34±1	10.38±1	10.33±1	10.39±1	10.41±1	10.34±1

*Diagnostic Outcomes: Morbidities and Medical History (see Appendix Table 9 for definitions)*

Metastatic Cancer	0.9%	1.2%	1.8%	1.5%	2.1%	3.2%	1.9%	2.1%	3.5%	8.4%
Acute MI	1.2%	1.9%	3.6%	2.4%	3.6%	4.6%	3.6%	4.2%	6.2%	7.7%
Diabetes	8.9%	12.0%	19.6%	17.7%	21.5%	26.7%	14.7%	17.8%	26.4%	30.9%
Pneumonia	5.2%	6.5%	10.7%	8.5%	10.9%	14.2%	10.5%	12.7%	17.7%	21.9%
Hypertensive HD	0.3%	0.3%	0.6%	0.4%	0.6%	0.7%	0.8%	0.7%	0.9%	1.6%
Angina	1.8%	2.9%	5.5%	3.3%	5.0%	6.9%	5.4%	6.3%	8.3%	9.6%
Cardioresp. Failure	4.8%	7.0%	13.4%	9.8%	14.0%	21.7%	14.1%	16.8%	24.7%	32.9%
Valvular HD	4.3%	5.7%	10.1%	6.1%	8.6%	12.2%	10.1%	13.1%	15.5%	18.7%
Arrhythmia	9.5%	12.4%	19.6%	13.1%	18.0%	24.9%	19.5%	22.9%	28.1%	32.6%
Hemi/Paraplegia, etc	2.7%	3.3%	4.4%	3.6%	4.7%	5.8%	5.0%	5.1%	7.0%	8.0%
Stroke	1.4%	2.1%	3.1%	1.9%	2.8%	4.3%	3.6%	3.9%	5.5%	5.5%
COPD	2.0%	3.1%	6.3%	3.9%	6.2%	9.7%	7.3%	8.5%	11.6%	15.1%
Fluid/Electrolyte Disord	22.5%	25.0%	33.9%	29.0%	33.5%	41.3%	33.3%	36.4%	44.5%	53.3%

Other Urinary Disorders	28.1%	29.5%	33.5%	31.3%	33.4%	37.0%	34.4%	36.0%	39.4%	41.6%
Decubitus/Skin Ulcer	1.1%	1.3%	2.7%	2.5%	3.1%	4.5%	2.9%	3.7%	5.8%	9.1%
Other GI Disorders	53.6%	57.5%	65.6%	57.7%	65.0%	70.2%	63.6%	66.3%	69.4%	74.4%
PUD, GI Hemorrhage	10.3%	12.2%	16.8%	13.8%	15.9%	20.2%	16.8%	18.0%	21.5%	28.4%
Severe Hematologic Dis	0.2%	0.4%	0.5%	0.6%	0.5%	1.0%	0.8%	0.8%	1.4%	3.5%
Nephritis	0.8%	1.0%	1.3%	1.3%	1.6%	1.9%	1.7%	1.6%	2.7%	2.9%
Dementia/Senility	4.6%	5.4%	7.8%	5.3%	7.1%	9.1%	9.2%	9.8%	11.4%	12.3%
Cancer	10.4%	14.0%	21.2%	12.9%	18.4%	23.9%	20.7%	23.4%	27.8%	32.7%
Liver/Biliary Disease	14.8%	17.5%	21.9%	19.3%	22.7%	25.6%	21.2%	22.5%	25.9%	31.6%
ESRD, Dialysis	0.2%	0.2%	0.3%	0.2%	0.4%	0.5%	0.8%	0.7%	1.0%	1.0%
Asthma	11.3%	12.5%	16.5%	14.4%	17.0%	18.7%	14.1%	15.8%	18.7%	19.7%
Anemia/Blood Disease	19.8%	21.4%	27.2%	34.6%	30.4%	39.7%	29.1%	30.7%	37.3%	56.3%
Drug/Alcohol Abuse	16.1%	16.4%	18.1%	17.3%	18.6%	22.0%	23.0%	20.4%	20.5%	24.2%
Major Psych Disorders	10.2%	10.5%	11.6%	11.5%	12.8%	14.6%	13.7%	12.9%	15.2%	15.8%
Depression	19.4%	20.9%	25.5%	22.7%	26.1%	30.3%	25.4%	26.8%	30.7%	33.7%
Other Psych Disorders	20.0%	20.7%	23.4%	22.0%	24.6%	28.7%	25.1%	25.1%	28.0%	30.5%
Fibrosis of Lung	1.3%	1.7%	3.2%	1.9%	3.1%	4.5%	3.4%	3.8%	5.5%	6.3%
Protein-Calorie Malnutr	1.1%	1.4%	2.4%	2.5%	2.7%	4.6%	3.4%	3.4%	5.3%	9.1%

CAD/Ischemic HD	3.5%	5.3%	10.0%	6.0%	9.1%	13.4%	10.7%	12.4%	17.0%	19.9%
Heart Failure	2.1%	3.4%	7.5%	5.3%	7.5%	14.2%	8.4%	10.8%	16.3%	23.7%
Revascularization	1.0%	1.4%	2.4%	1.6%	2.6%	3.1%	2.7%	2.8%	4.1%	4.6%
<i>Hospitalization</i>										
Inpatient	25.7%	27.9%	29.8%	35.1%	31.2%	35.3%	31.2%	30.6%	34.6%	41.8%
Outpatient	38.2%	36.6%	33.7%	27.6%	28.7%	29.4%	40.7%	35.0%	31.6%	32.2%
Emergency	36.1%	35.4%	36.5%	37.4%	40.1%	35.4%	28.0%	34.4%	33.8%	26.0%
Labor/Delivery	15.3%	16.8%	14.8%	20.4%	14.9%	12.6%	14.1%	12.8%	11.5%	7.6%

<sup>A</sup>LR1: combined group of %Macro/%Micro quartiles 1/1, 1/2, 2/1, and 2/2; <sup>B</sup>LR2: combined group of %Macro/%Micro quartiles 1/3, 3/1, 2/3, and 3/2.

CBC=complete blood count, WBC=white blood cell, MCV=mean corpuscular volume, MCH=mean corpuscular hemoglobin, MCHC=mean corpuscular hemoglobin concentration, RDW=red cell distribution width, RDW-sd=RDW-size distribution, MPV=mean platelet volume, MI=myocardial infarction, HD=heart disease, COPD=chronic obstructive pulmonary disease, GI=gastrointestinal, PUD=peptic ulcer disease, ESRD=end stage renal disease, CAD=coronary artery disease

**Appendix Table 1B.** Baseline characteristics stratified by %Macro/%Micro quartile categories among males (n=100,210). The means or percentages of all characteristics were significantly different ( $p < 0.001$ ) for both females and males across the %Macro/%Micro quartile categories (exception:  $*p = 0.006$ ) by the chi-square test or ANOVA.

Characteristic	LR1†	LR2‡	3/3	1/4	2/4	3/4	4/1	4/2	4/3	4/4
Sample Size	13,675	32,193	5,767	14,240	6,441	2,901	14,708	5,820	2,946	1,519
Age (years)	47.3±19	50.2±19	54.7±19	48.7±19	50.7±19	57.8±18	62.2±18	60.9±18	62.8±18	64.8±16
%Macro (%)	6.6±0.5	7.3±1.0	8.0±0.5	5.4±0.8	6.8±0.3	8.0±0.5	13.4±5.6	11.9±4.1	11.8±4.5	13.0±6.1
%Micro (%)	1.0±0.2	1.2±0.4	1.5±0.2	5.6±7.5	3.0±1.7	3.1±1.9	0.5±0.2	1.0±0.1	1.5±0.2	3.5±2.3
<i><u>CBC Parameters</u></i>										
RBC Count ( $10^6/\mu\text{L}$ )	4.7±0.5	4.9±0.5	5.1±0.6	4.9±0.7	5.3±0.6	5.2±0.8	4.5±0.6	4.8±0.7	4.8±0.9	4.4±1.2
Hemoglobin (g/dL)	14.6±2	15.1±2	15.5±2	13.7±2	15.3±2	15.0±2	14.8±2	15.0±2	14.7±3	13.2±3
Hematocrit (%)	41.8±4	43.5±4	45.3±4	40.1±6	44.7±4	44.3±6	43.6±5	44.2±6	43.5±7	40.1±10
WBC Count ( $10^9/\text{L}$ )	8.5±3.6	8.8±4.0	9.0±4.0	9.1±4.6	9.3±6.9	9.7±6.6	8.5±5.4	9.0±6.8	9.5±9.4	10.7±18.6
Platelet Count ( $10^9/\text{L}$ )	218±59	219±60	219±66	234±88	223±69	221±90	202±67	212±72	209±82	211±124
MCV (fL)	89.2±2	89.1±3	88.6±2	81.7±5	84.9±2	86.3±3	96.8±4	92.8±4	91.7±4	91.4±6
MCH (pg)	31.1±1	30.8±1	30.3±1	27.8±2	29.0±1	29.0±1	32.9±1	31.5±2	30.9±2	30.3±7
MCHC (g/dL)	34.8±1	34.6±2	34.2±1	34.0±2	34.2±1	33.7±1	34.0±1	34.0±2	33.7±2	33.1±6

RDW (%)	12.7±0.5	13.1±0.6	13.8±0.7	14.3±2	14.2±1	15.3±2	13.4±0.9	14.0±1	14.9±1	17.6±3
RDW-sd (fL)	41.2±2	42.5±3	44.4±3	42.3±5	43.9±5	47.8±6	47.3±4	47.2±5	49.7±7	58.0±10
MPV (fL)	10.07±1	10.21±1	10.35±1	10.02±1	10.25±1	10.32±1	10.29±1	10.31±1	10.37±1	10.35±1

*Diagnostic Outcomes: Morbidities and Medical History (see Appendix Table 9 for definitions)*

Metastatic Cancer	1.2%	1.0%	1.5%	2.3%	1.8%	3.3%	2.1%	2.4%	3.2%	8.6%
Acute MI	6.1%	7.4%	10.1%	8.2%	9.1%	13.2%	12.5%	11.4%	13.8%	14.5%
Diabetes	16.8%	18.1%	22.4%	27.2%	24.5%	32.6%	22.7%	24.4%	32.5%	37.6%
Pneumonia	7.5%	8.9%	12.0%	12.0%	11.7%	18.4%	15.0%	16.3%	20.5%	26.8%
Hypertensive HD	0.5%	0.7%	0.9%	0.7%	0.9%	1.0%	1.2%	1.3%	1.3%	2.0%
Angina	6.4%	8.3%	10.9%	9.1%	10.2%	16.1%	14.6%	14.3%	18.4%	20.3%
Cardioresp. Failure	8.5%	10.7%	15.8%	14.5%	15.8%	25.2%	19.6%	22.6%	29.2%	40.0%
Valvular HD	5.6%	6.8%	9.6%	8.5%	9.4%	14.7%	13.6%	13.7%	17.9%	21.5%
Arrhythmia	16.6%	19.7%	26.8%	21.5%	24.7%	33.8%	33.3%	32.9%	39.8%	45.8%
Hemi/Paraplegia, etc	5.1%	5.2%	6.6%	6.9%	6.8%	7.4%	7.5%	7.2%	8.7%	10.2%
Stroke	2.6%	3.2%	3.8%	3.6%	3.5%	4.8%	5.4%	5.8%	6.5%	5.3%
COPD	4.1%	5.5%	8.2%	6.9%	7.2%	13.9%	13.0%	13.3%	16.2%	22.0%
Fluid/Electrolyte Disord	24.6%	26.2%	31.7%	33.8%	32.5%	43.1%	36.7%	38.9%	45.0%	56.3%
Other Urinary Disorders	9.0%	10.1%	12.7%	11.8%	12.9%	17.2%	15.8%	18.2%	20.0%	22.4%

Decubitus/Skin Ulcer	2.0%	2.6%	3.7%	5.6%	4.5%	6.8%	4.2%	5.1%	7.1%	11.2%
Other GI Disorders	56.0%	59.2%	64.4%	61.4%	64.8%	70.1%	66.8%	69.4%	70.2%	76.2%
PUD, GI Hemorrhage	11.6%	12.9%	16.0%	17.0%	17.9%	23.1%	18.3%	20.1%	22.1%	29.8%
Severe Hematologic Dis	0.4%	0.4%	0.7%	0.7%	0.7%	1.1%	1.1%	1.0%	2.4%	5.3%
Nephritis	1.6%	1.6%	2.1%	3.2%	2.3%	3.5%	2.5%	2.7%	4.2%	6.0%
Dementia/Senility	5.8%	6.3%	7.4%	6.2%	6.4%	9.1%	10.7%	9.9%	10.6%	11.8%
Cancer	17.1%	20.4%	25.0%	20.5%	22.9%	30.5%	30.8%	31.7%	35.1%	41.1%
Liver/Biliary Disease	13.3%	15.2%	18.5%	18.3%	19.8%	25.5%	21.6%	23.1%	25.0%	32.8%
ESRD, Dialysis	0.5%	0.4%	0.5%	0.7%	0.7%	1.1%	1.2%	1.3%	2.0%	2.1%
Asthma	8.6%	9.6%	11.3%	10.6%	11.2%	12.9%	10.3%	11.3%	12.0%	13.2%
Anemia/Blood Disease	17.4%	17.7%	21.6%	29.4%	24.1%	32.4%	29.9%	29.7%	36.2%	54.6%
Drug/Alcohol Abuse	28.9%	27.2%	26.4%	28.1%	26.9%	30.0%	32.0%	29.1%	29.5%	31.5%
Major Psych Disorder	11.7%	11.4%	10.4%	12.0%	11.0%	12.4%	11.5%	11.0%	11.3%	13.6%*
Depression	15.2%	15.4%	16.3%	17.6%	17.4%	20.7%	17.1%	17.8%	20.3%	23.4%
Other Psych Disorders	17.7%	17.8%	18.1%	19.5%	19.4%	20.8%	18.4%	18.9%	19.6%	22.8%
Fibrosis of Lung	1.9%	2.3%	3.4%	3.0%	3.2%	5.4%	4.6%	5.0%	5.6%	8.1%
Protein-Calorie Malnutr	1.6%	1.8%	2.5%	4.0%	2.9%	4.7%	4.1%	4.0%	6.3%	11.8%
CAD/Ischemic HD	13.1%	15.8%	21.3%	17.4%	19.5%	28.9%	28.8%	28.1%	33.1%	39.8%



Heart Failure	4.6%	6.0%	10.0%	9.8%	11.4%	19.2%	14.8%	16.1%	23.3%	32.0%
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Revascularization	6.0%	7.5%	9.2%	7.5%	8.7%	12.3%	12.5%	10.7%	13.4%	14.0%
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*Hospitalization*

Inpatient	25.3%	23.3%	23.6%	30.5%	23.9%	29.2%	28.9%	25.7%	30.5%	40.4%
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Outpatient	32.2%	35.1%	35.2%	27.4%	31.2%	32.4%	38.4%	35.4%	33.9%	32.9%
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Emergency	42.4%	41.6%	41.1%	42.1%	44.8%	38.4%	32.7%	38.9%	35.6%	26.8%
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\*p=0.006; †LR1: combined group of %Macro/%Micro quartiles 1/1, 1/2, 2/1, and 2/2; ‡LR2: combined group of %Macro/%Micro quartiles 1/3, 3/1, 2/3, and 3/2.

**Appendix Table 2.** Baseline characteristics stratified by RDW quartile. Among females, RDW quartiles were RDW values  $\leq 12.8\%$ , 12.9%-13.4%, 13.5%-14.2%,  $\geq 14.3\%$ ; for males, RDW quartiles were RDW  $\leq 12.7\%$ , 12.8%-13.2%, 13.3%-13.9%,  $\geq 14.0\%$ . Except where noted, all comparisons across the RDW quartiles for females and males had  $p$ -trend $<0.001$  by the chi-square test or ANOVA.

Characteristic	Females: RDW Quartile				Males: RDW Quartile			
	1	2	3	4	1	2	3	4
Sample Size (n)	39,869	43,942	41,920	40,039	23,882	24,796	25,544	25,988
Age (years)	41 $\pm$ 17	45 $\pm$ 19	49 $\pm$ 21	52 $\pm$ 21	43 $\pm$ 17	50 $\pm$ 18	56 $\pm$ 18	63 $\pm$ 17
Macrocytic RBCs (%)	7.5 $\pm$ 2.7	7.6 $\pm$ 2.7	7.8 $\pm$ 3.1	7.8 $\pm$ 4.9	7.6 $\pm$ 2.6	7.9 $\pm$ 2.6	8.4 $\pm$ 3.3	9.4 $\pm$ 5.5
Microcytic RBCs (%)	0.9 $\pm$ 0.5	1.2 $\pm$ 0.8	1.7 $\pm$ 1.3	5.7 $\pm$ 8.1	1.1 $\pm$ 0.6	1.3 $\pm$ 0.8	1.5 $\pm$ 1.1	3.7 $\pm$ 6.0
<i><u>CBC Parameters</u></i>								
RBC Count ( $10^6/\mu\text{L}$ )	4.5 $\pm$ 0.4	4.5 $\pm$ 0.5	4.4 $\pm$ 0.5	4.4 $\pm$ 0.6	5.0 $\pm$ 0.5	4.9 $\pm$ 0.5	4.9 $\pm$ 0.6	4.6 $\pm$ 0.8
Hemoglobin (HGB) (g/dL)	13.9 $\pm$ 1	13.6 $\pm$ 1	13.2 $\pm$ 1	12.2 $\pm$ 2	15.5 $\pm$ 1	15.2 $\pm$ 2	14.9 $\pm$ 2	13.6 $\pm$ 2
Hematocrit (%)	40.4 $\pm$ 3	40.0 $\pm$ 4	39.5 $\pm$ 4	37.4 $\pm$ 5	44.1 $\pm$ 4	44.0 $\pm$ 4	43.4 $\pm$ 5	40.6 $\pm$ 7
WBC Count ( $10^9/\text{L}$ )	8.4 $\pm$ 3.3	8.8 $\pm$ 3.4	9.1 $\pm$ 3.6	9.3 $\pm$ 5.1	8.5 $\pm$ 3.6	8.7 $\pm$ 3.7	8.8 $\pm$ 4.1	9.3 $\pm$ 8.4
Platelet Count ( $10^9/\text{L}$ )	245 $\pm$ 60	241 $\pm$ 65	240 $\pm$ 71	253 $\pm$ 93	221 $\pm$ 57	220 $\pm$ 59	216 $\pm$ 65	215 $\pm$ 93
Mean Corpuscular Volume (fL)	90.1 $\pm$ 4	89.8 $\pm$ 4	89.2 $\pm$ 5	85.9 $\pm$ 8	88.9 $\pm$ 4	89.1 $\pm$ 4	89.6 $\pm$ 5	88.9 $\pm$ 7
Mean Corpuscular HGB (pg)	30.9 $\pm$ 2	30.4 $\pm$ 2	29.9 $\pm$ 2	28.0 $\pm$ 3	31.2 $\pm$ 1	30.9 $\pm$ 2	30.6 $\pm$ 2	29.6 $\pm$ 3

Mean Corpusc HGB Conc (g/dL)	34.4±2	33.9±1	33.6±1	32.6±2	35.1±1	34.6±1	34.2±1	33.3±2
Red Cell Distribution Width (%)	12.5	13.1	13.8	15.7	12.4	13.0	13.6	15.3
RDW-size distribution (fL)	40.9±2	43.0±2	44.8±3	48.7±6	40.1±2	42.2±2	44.3±3	49.3±6
Mean Platelet Volume (fL)	10.20±0.9	10.31±0.9	10.38±0.9	10.28±1.0	10.15±0.8	10.21±0.8	10.23±0.9	10.22±0.9

Morbidities and Medical History

Metastatic Cancer	0.8%	1.2%	1.6%	3.0%	0.7%	0.9%	1.5%	3.8%
Acute MI	1.1%	2.0%	2.9%	4.8%	4.0%	6.8%	10.3%	14.6%
Diabetes	9.4%	12.4%	16.0%	23.3%	13.0%	16.9%	23.0%	34.4%
Pneumonia	5.6%	6.9%	8.9%	13.9%	6.4%	8.3%	11.6%	20.0%
Hypertensive HD	0.3%	0.3%	0.5%	0.8%	0.3%	0.5%	0.9%	1.5%
Angina	1.8%	3.2%	4.5%	6.5%	4.3%	7.4%	11.4%	17.8%
Cardioresp. Failure	5.1%	7.4%	11.3%	19.3%	6.5%	9.7%	14.7%	28.0%
Valvular HD	4.5%	5.9%	8.3%	12.2%	3.9%	6.2%	9.5%	17.3%
Arrhythmia	10.0%	12.9%	16.7%	22.8%	13.0%	18.1%	25.9%	39.5%
Hemi/Paraplegia, etc	2.7%	3.3%	4.2%	5.8%	3.7%	5.1%	6.3%	9.8%
Stroke	1.4%	2.1%	2.9%	3.9%	1.9%	2.8%	4.2%	6.3%
COPD	2.3%	3.5%	5.3%	8.8%	3.0%	5.0%	8.2%	15.7%
Fluid/Electrolyte Disord	24.9%	25.6%	29.4%	38.3%	22.7%	25.1%	31.1%	46.3%

Other Urinary Disorders	29.4%	29.7%	32.0%	36.2%	6.9%	9.4%	13.3%	19.8%
Decubitus/Skin Ulcer	1.0%	1.3%	2.3%	4.8%	1.4%	2.2%	3.5%	8.3%
Other GI Disorders	56.9%	58.4%	60.7%	65.0%	53.4%	58.6%	65.0%	71.5%
PUD, GI Hemorrhage	11.2%	12.7%	14.4%	19.3%	10.2%	12.4%	15.9%	24.2%
Severe Hematologic Disord	0.3%	0.4%	0.5%	1.2%	0.3%	0.3%	0.6%	1.8%
Nephritis	0.7%	1.0%	1.3%	2.2%	1.0%	1.3%	2.1%	4.7%
Dementia/Senility	4.7%	5.9%	7.2%	9.0%	4.8%	5.9%	7.7%	11.1%
Cancer	11.7%	15.0%	17.7%	21.3%	13.4%	19.9%	26.3%	34.0%
Liver/Biliary Disease	16.4%	18.0%	19.7%	23.7%	11.6%	15.0%	19.1%	26.1%
ESRD, Dialysis	0.1%	0.3%	0.3%	0.8%	0.2%	0.4%	0.6%	1.8%
Asthma	11.9%	12.7%	14.7%	16.6%	8.7%	9.4%	10.3%	12.4%
Anemia/Blood Disease	18.8%	21.6%	26.7%	41.6%	12.6%	16.4%	23.4%	42.2%
Drug/Alcohol Abuse	18.9%	17.2%	17.0%	19.8%*	27.9%	27.5%	28.3%	30.1%
Major Psych Disorders	11.3%	10.7%	11.2%	13.8%	11.3%	10.8%	11.3%	12.6%
Depression	20.9%	21.5%	23.1%	27.5%	14.1%	14.6%	16.9%	20.7%
Other Psych Disorders	22.1%	20.9%	22.0%	25.5%	16.8%	17.4%	18.6%	21.1%
Fibrosis of Lung	1.3%	1.9%	2.6%	4.0%	1.4%	2.2%	3.3%	5.8%
Protein-Calorie Malnutr	1.1%	1.4%	2.2%	4.8%	1.0%	1.5%	2.7%	6.7%

CAD/Ischemic HD	3.4%	5.6%	8.5%	13.0%	8.4%	14.3%	22.3%	34.2%
Heart Failure	1.9%	3.4%	6.1%	12.9%	2.5%	5.0%	9.4%	22.6%
Number of Diagnoses	3.1±3.1	3.5±3.4	4.0±3.9	5.3±4.6	2.9±2.8	3.6±3.3	4.6±3.8	6.7±4.6
Revascularization	0.8%	1.4%	2.2%	3.4%	3.7%	6.7%	10.0%	14.3%

Hospitalization

Inpatient Hospitalization	17.3%	27.1%	35.5%	40.8%	18.6%	21.8%	26.7%	37.3%
Outpatient Exam/Procedure	39.5%	37.0%	33.0%	29.8%	32.6%	34.4%	34.9%	32.8%†
Emergency Visit	43.3%	35.9%	31.5%	29.3%	48.8%	43.8%	38.5%	29.9%
Labor/Delivery	7.5%	15.9%	21.4%	18.4%	-----	-----	-----	-----

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\*p-trend=0.003; †p-trend=0.50.

**Appendix Table 3.** Association of the RBC size dispersion variables with the mean number of morbidities in univariable and multiple variable ANOVA models for females (n=165,770) and males (n=100,210).

Variable	Females, mean number of morbidities (95% CI)			Males, mean number of morbidities (95% CI)		
	Univariable	Trivariable <sup>A</sup>	Multivariable <sup>B</sup>	Univariable	Trivariable <sup>A</sup>	Multivariable <sup>B</sup>
<b>Quartile Categories of the Percentage of Macrocytic RBCs (%Macro, &gt;120 fL) and Microcytic RBCs (%Micro, &lt;60 fL)</b>						
LR1 <sup>C</sup>	2.94 (2.89,2.99)	3.56 (3.51,3.61)	4.74 (4.63,4.86)	3.44 (3.37,3.50)	4.68 (4.62,4.75)	5.00 (4.87,5.13)
LR2 <sup>D</sup>	3.37 (3.33,3.40) <sup>E</sup>	3.72 (3.68,3.75) <sup>E</sup>	4.75 (4.64,4.86) <sup>F</sup>	3.76 (3.71,3.80) <sup>E</sup>	4.37 (4.33,4.41) <sup>E</sup>	4.83 (4.71,4.95) <sup>E</sup>
3/3	4.50 (4.42,4.57) <sup>E</sup>	4.18 (4.10,4.25) <sup>E</sup>	4.85 (4.73,4.98) <sup>E</sup>	4.53 (4.43,4.62) <sup>E</sup>	4.00 (3.90,4.09) <sup>E</sup>	4.59 (4.46,4.73) <sup>E</sup>
1/4	3.84 (3.80,3.89) <sup>E</sup>	3.91 (3.86,3.97) <sup>E</sup>	5.09 (4.97,5.21) <sup>E</sup>	4.52 (4.46,4.58) <sup>E</sup>	4.73 (4.66,4.80)	5.32 (5.19,5.45) <sup>E</sup>
2/4	4.52 (4.44,4.60) <sup>E</sup>	4.21 (4.13,4.29) <sup>E</sup>	5.13 (5.00,5.26) <sup>E</sup>	4.58 (4.49,4.67) <sup>E</sup>	4.28 (4.19,4.37) <sup>E</sup>	4.99 (4.84,5.13)
3/4	5.61 (5.49,5.73) <sup>E</sup>	4.73 (4.60,4.85) <sup>E</sup>	5.43 (5.28,5.59) <sup>E</sup>	6.03 (5.89,6.17) <sup>E</sup>	4.46 (4.33,4.60) <sup>F</sup>	5.13 (4.96,5.30) <sup>F</sup>
4/1	4.58 (4.53,4.63) <sup>E</sup>	4.05 (3.99,4.11) <sup>E</sup>	4.85 (4.73,4.97) <sup>E</sup>	5.42 (5.35,5.48) <sup>E</sup>	4.38 (4.31,4.44) <sup>E</sup>	4.66 (4.54,4.79) <sup>E</sup>
4/2	4.96 (4.89,5.02) <sup>E</sup>	4.48 (4.42,4.55) <sup>E</sup>	4.95 (4.83,5.07) <sup>E</sup>	5.58 (5.48,5.68) <sup>E</sup>	4.40 (4.30,4.49) <sup>E</sup>	4.75 (4.60,4.89) <sup>E</sup>
4/3	6.01 (5.90,6.11) <sup>E</sup>	5.16 (5.05,5.26) <sup>E</sup>	5.44 (5.30,5.59) <sup>E</sup>	6.49 (6.35,6.63) <sup>E</sup>	4.68 (4.55,4.81)	5.09 (4.92,5.26)
4/4	7.23 (7.06,7.39) <sup>E</sup>	5.86 (5.67,6.02) <sup>E</sup>	6.19 (6.00,6.38) <sup>E</sup>	8.00 (7.81,8.20) <sup>E</sup>	5.45 (5.26,5.63) <sup>E</sup>	5.96 (5.75,6.17) <sup>E</sup>
<b>RDW Quartile</b>						
1	3.14 (3.10,3.18)	4.41 (4.35,4.48)	5.10 (4.98,5.22)	2.91 (2.86,2.96)	4.10 (4.02,4.17)	4.76 (4.63,4.90)
2	3.46 (3.43,3.50) <sup>E</sup>	4.33 (4.28,4.38) <sup>F</sup>	5.01 (4.89,5.12) <sup>E</sup>	3.58 (3.53,3.62) <sup>E</sup>	4.23 (4.17,4.29) <sup>E</sup>	4.77 (4.64,4.90)
3	4.03 (3.99,4.06) <sup>E</sup>	4.26 (4.21,4.30) <sup>F</sup>	5.04 (4.93,5.15) <sup>E</sup>	4.59 (4.55,4.64) <sup>E</sup>	4.49 (4.44,4.55) <sup>E</sup>	4.92 (4.80,5.04) <sup>E</sup>

4	5.26 (5.23,5.30) <sup>E</sup>	4.54 (4.49,4.60) <sup>F</sup>	5.42 (5.30,5.54) <sup>F</sup>	6.67 (6.62,6.71) <sup>E</sup>	5.35 (5.29,5.42) <sup>E</sup>	5.67 (5.54,5.80) <sup>E</sup>
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***RDW-sd Quartile***

1	2.97 (2.93,3.00)	3.55 (3.49,3.60)	4.95 (4.83,5.07)	2.70 (2.66,2.75)	3.07 (3.00,3.13)	4.27 (4.14,4.40)
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2	3.32 (3.28,3.36) <sup>E</sup>	3.90 (3.85,3.95) <sup>E</sup>	4.89 (4.77,5.00) <sup>E</sup>	3.52 (3.48,3.56) <sup>E</sup>	3.81 (3.76,3.87) <sup>E</sup>	4.57 (4.44,4.69) <sup>E</sup>
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3	3.87 (3.84,3.91) <sup>E</sup>	4.35 (4.30,4.39) <sup>E</sup>	4.96 (4.85,5.08) <sup>F</sup>	4.74 (4.70,4.78) <sup>E</sup>	4.82 (4.77,4.88) <sup>E</sup>	5.06 (4.94,5.19) <sup>E</sup>
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4	5.72 (5.69,5.76) <sup>E</sup>	5.75 (5.69,5.80) <sup>E</sup>	5.77 (5.65,5.89) <sup>E</sup>	6.97 (6.93,7.02) <sup>E</sup>	6.47 (6.39,6.55) <sup>E</sup>	6.23 (6.10,6.36) <sup>E</sup>
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<sup>A</sup>Trivariable model data are the predicted mean from analysis of variance entering RDW quartiles, RDW-sd quartiles, and quartile categories of %Macro/%Micro; <sup>B</sup>Multivariable model results are the predicted means from analysis of variance evaluations adding age to the trivariable models; <sup>C</sup>LR1: combined group of %Macro/%Micro quartiles 1/1, 1/2, 2/1, and 2/2; <sup>D</sup>LR2: combined group of %Macro/%Micro quartiles 1/3, 3/1, 2/3, and 3/2; <sup>E</sup>p<0.001 vs. quartile 1 or LR1; <sup>F</sup>p<0.05 vs. quartile 1 or LR1.

**Appendix Table 4.** Hazard ratios and 95% confidence intervals from Cox regression for the association with all-cause mortality of the RBC size dispersion variables among males (n=100,210). For corresponding results among females, please see Table 1 (main text).

<b>Macro/Microcytic</b>	<b>Absolute</b>	<b>Univariable</b>	<b>Age-adjusted</b>	<b>Age, CBC<sup>A</sup></b>	<b>Fully Adjusted<sup>A</sup></b>	<b>Sample</b>
<b>Quartile Combination</b>	<b>Mortality Risk</b>	<b>HR (95% CI)</b>	<b>HR (95% CI)</b>	<b>HR (95% CI)</b>	<b>HR (95% CI)</b>	<b>Size (n)</b>
<b>Quartile Categories of %Macro/%Micro</b>						
LR1 <sup>D</sup>	1.2%	1.0 (referent)	1.0 (referent)	1.0 (referent)	1.0 (referent)	13,675
LR2 <sup>E</sup>	1.6%	1.31 (1.09, 1.56) <sup>E</sup>	1.14 (0.96, 1.36)	1.13 (0.94, 1.36)	1.17 (0.97, 1.40)	32,193
3/3	2.5%	2.07 (1.65, 2.59) <sup>D</sup>	1.50 (1.20, 1.88) <sup>D</sup>	1.26 (0.99, 1.60)	1.25 (0.98, 1.60)	5,767
1/4	3.3%	2.61 (2.18, 3.13) <sup>D</sup>	2.51 (2.10, 3.00) <sup>D</sup>	1.62 (1.31, 2.01) <sup>D</sup>	1.44 (1.17, 1.76) <sup>D</sup>	14,240
2/4	3.1%	2.54 (2.06, 3.12) <sup>D</sup>	2.24 (1.82, 2.76) <sup>D</sup>	1.83 (1.45, 2.31) <sup>D</sup>	1.62 (1.29, 2.04) <sup>D</sup>	6,441
3/4	6.2%	5.09 (4.11, 6.31) <sup>D</sup>	3.31 (2.67, 4.11) <sup>D</sup>	2.19 (1.73, 2.78) <sup>D</sup>	1.76 (1.38, 2.24) <sup>D</sup>	2,901
4/1	4.4%	3.76 (3.17, 4.47) <sup>D</sup>	1.98 (1.66, 2.35) <sup>D</sup>	1.31 (1.08, 1.60) <sup>E</sup>	1.35 (1.12, 1.63) <sup>E</sup>	14,708
4/2	5.6%	4.70 (3.89, 5.67) <sup>D</sup>	2.58 (2.13, 3.11) <sup>D</sup>	1.63 (1.32, 2.02) <sup>D</sup>	1.63 (1.32, 2.01) <sup>D</sup>	5,820
4/3	8.3%	7.07 (5.80, 8.63) <sup>D</sup>	3.70 (3.03, 4.52) <sup>D</sup>	1.90 (1.52, 2.38) <sup>D</sup>	1.74 (1.39, 2.17) <sup>D</sup>	2,946
4/4	15.9%	13.63 (11.11, 16.71) <sup>D</sup>	6.73 (5.48, 8.27) <sup>D</sup>	2.51 (2.00, 3.14) <sup>D</sup>	2.17 (1.72, 2.73) <sup>D</sup>	1,519
<b>RDW Quartile</b>						
1	0.8%	1.0 (referent)	1.0 (referent)	1.0 (referent)	1.0 (referent)	23,882
2	1.3%	1.57 (1.32, 1.88) <sup>D</sup>	1.53 (1.28, 1.82) <sup>D</sup>	1.16 (0.97, 1.38)	0.97 (0.80, 1.17)	24,796



3	2.2%	2.73 (2.32, 3.20) <sup>D</sup>	2.39 (2.03, 2.81) <sup>D</sup>	1.43 (1.21, 1.69) <sup>D</sup>	0.95 (0.78, 1.16)	25,544
4	7.8%	9.55 (8.25,11.05) <sup>D</sup>	6.09 (5.24, 7.07) <sup>D</sup>	3.02 (2.58, 3.52) <sup>D</sup>	1.23 (0.99, 1.52)	25,988
<b><i>RDW-sd Quartile</i></b>						
1	0.6%	1.0 (referent)	1.0 (referent)	1.0 (referent)	1.0 (referent)	25,119
2	1.2%	2.01 (1.65, 2.46) <sup>D</sup>	1.31 (1.07, 1.60) <sup>E</sup>	1.11 (0.90, 1.38)	1.17 (0.94, 1.44)	24,887
3	2.4%	4.12 (3.43, 4.95) <sup>D</sup>	1.92 (1.60, 2.31) <sup>D</sup>	1.25 (1.002,1.56) <sup>E</sup>	1.23 (0.99, 1.54)	25,438
4	8.4%	15.12 (12.75,17.92) <sup>D</sup>	5.51 (4.61, 6.57) <sup>D</sup>	1.77 (1.39, 2.27) <sup>D</sup>	1.41 (1.10, 1.80) <sup>E</sup>	24,766

<sup>A</sup>Adjustments for traditional CBC components included the RDW, red blood cell count, white blood cell count, platelet count, mean corpuscular volume, mean corpuscular hemoglobin concentration, and mean platelet volume (hemoglobin, hematocrit, and mean corpuscular hemoglobin were collinear with other CBC components and thus excluded from analyses), while full adjustment included age, all three RBC dispersion variables, other CBC components, and the 38 morbidities and health system encounter types listed in Appendix Table 1; <sup>B</sup>LR1: combined group of %Macro/%Micro quartiles 1/1, 1/2, 2/1, and 2/2; <sup>C</sup>LR2: combined group of %Macro/%Micro quartiles 1/3, 3/1, 2/3, and 3/2; <sup>D</sup> p<0.001; <sup>E</sup> p<0.05.

**Appendix Table 5.** Measures of predictive value and predictive improvement.

<b>Metric</b>	<b>Females (n=165,770)</b>	<b>Males (n=100,210)</b>
<b><i>C-statistic (*p&lt;0.001 vs. c=0.50)</i></b>		
RDW alone	0.717*	0.730*
RDW-sd alone	0.755*	0.754*
%Macro/%Micro alone	0.702*	0.678*
RDW and RDW-sd	0.768*	0.770*
RDW and %Macro/%Micro	0.758*	0.759*
RDW-sd, %Macro/%Micro (no RDW)	0.776*	0.773*
RDW, RDW-sd, and %Macro/%Micro	0.778*	0.779*
RDW, RDW-sd, %Macro/%Micro, age	0.869*	0.815*
<b><i>Net Reclassification Improvement Index (compared to RDW alone; *p&lt;0.001 by the Z-test)</i></b>		
RDW alone (referent)	-----	-----
RDW-sd alone	0.111*	0.075*
%Macro/%Micro alone	-0.069*	-0.212*
RDW and RDW-sd	0.111*	0.075*
RDW and %Macro/%Micro	0.032*	0.045*

RDW-sd, %Macro/%Micro (no RDW)	0.034*	0.081*
RDW, RDW-sd, and %Macro/%Micro	0.099*	0.082*
RDW, RDW-sd, %Macro/%Micro, age	0.310*	0.159*

***Change in the -2 Log Likelihood (compared to RDW alone in Cox regression, all are  $p < 0.001$  except RDW-sd: +2.28) in three columns for the following sets of variables: 1) the variables indicated, 2) the variables indicated and other variables in Appendix Table 1 except age (unless explicitly noted), and 3) the variables indicated, all other variables, and age (i.e., all column 3 results are age-adjusted)***

	<u>Column 1, 2, 3</u>	<u>Column 1, 2, 3</u>
RDW alone (referent)	0, 0, 0	0, 0, 0
RDW-sd alone	-858, +2.28, +39.5	-501, +4.13, +41.6
%Macro/%Micro alone	+158, +81.9, +3.85	+963, +85.6, +33.2
RDW and RDW-sd	-1028, -70.7, -30.0	-743, -41.7, -13.5
RDW and %Macro/%Micro	-875, -79.6, -85.0	-407, -60.4, -70.5
RDW-sd, %Macro/%Micro (no RDW)	-1230, -128, -95.4	-770, -88.0, -68.9
RDW, RDW-sd, and %Macro/%Micro	-1323, -148, -112	-893, -101, -80.2
RDW, RDW-sd, %Macro/%Micro, age	-4129, -947, -112	-1896, -430, -80.2

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**Appendix Table 6.** Hazard ratios and 95% confidence intervals (CI) from Cox regression among subjects whose RDW was in the sex-specific 4<sup>th</sup> quartile, both for RDW-sd quartiles and for quartile categories of the percentage of macrocytic RBCs (%Macro, RBC volume >120 fL) and microcytic RBCs (%Micro, RBC volume <60 fL). Due to the very small sample size in quartile 1 of the original sex-specific RDW-sd quartiles (females: n=1,664; males: n=600), RDW-sd quartiles were re-derived for analyses in this table. Further, due to the small sample sizes in the LR1\* %Macro/%Micro quartile category, it was combined with the LR2<sup>†</sup> category to form the reference group for analyses in this table.

<b>Variable</b>	<b>Absolute Mortality Risk</b>	<b>Age, CBC Adjusted‡ HR (95% CI)</b>	<b>Fully Adjusted‡ HR (95% CI)</b>	<b>Sample Size (n)</b>
<b>A) Females (n=40,039)</b>				
<b>Quartile Categories of %Macro/%Micro</b>				
LR1* and LR2 <sup>†</sup>	2.4%	1.0 (referent)	1.0 (referent)	2,445
3/3	2.8%	1.06 (0.76, 1.47)	1.04 (0.75, 1.45)	3,272
1/4	2.2%	1.70 (1.25, 2.31)§	1.50 (1.10, 2.03)	14,910
2/4	2.9%	1.55 (1.14, 2.12)	1.35 (0.99, 1.85)	5,291
3/4	5.5%	1.90 (1.39, 2.60)§	1.69 (1.24, 2.32)§	3,105
4/1	7.3%	0.75 (0.53, 1.07)	0.79 (0.55, 1.13)	1,913
4/2	7.7%	1.19 (0.88, 1.62)	1.21 (0.89, 1.65)	3,788
4/3	7.2%	1.15 (0.85, 1.57)	1.11 (0.81, 1.52)	3,404
4/4	12.1%	1.88 (1.37, 2.56)§	1.69 (1.24, 2.32)§	1,911

**RDW-sd Quartile**

1	1.1%	1.0 (referent)	1.0 (referent)	10,094
2	2.0%	1.12 (0.88, 1.43)	1.01 (0.79, 1.29)	9,908
3	3.7%	1.37 (1.08, 1.73)	1.15 (0.91, 1.46)	9,914
4	10.2%	2.54 (2.00, 3.22)§	1.78 (1.40, 2.26)§	10,121

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**B) Males (n=25,988)****Quartile Categories of %Macro/%Micro**

LR1* and LR2†	5.8%	1.0 (referent)	1.0 (referent)	2,382
3/3	5.0%	1.07 (0.83, 1.39)	1.11 (0.86, 1.44)	2,217
1/4	6.1%	1.34 (1.06, 1.68)	1.25 (0.99, 1.57)	6,242
2/4	5.7%	1.45 (1.14, 1.83)	1.36 (1.07, 1.73)	3,197
3/4	7.6%	1.44 (1.12, 1.83)	1.34 (1.05, 1.71)	2,300
4/1	9.8%	0.92 (0.72, 1.18)	1.03 (0.80, 1.31)	3,102
4/2	9.7%	1.26 (0.998, 1.58)	1.31 (1.04, 1.65)	2,827
4/3	10.4%	1.30 (1.02, 1.64)	1.29 (1.02, 1.64)	2,241
4/4	16.0%	1.59 (1.25, 2.03)§	1.53 (1.20, 1.95)§	1,480

**RDW-sd Quartile**

1	3.1%	1.0 (referent)	1.0 (referent)	6,500
2	4.8%	1.17 (0.96, 1.41)	1.03 (0.85, 1.25)	6,440
3	7.5%	1.45 (1.20, 1.75)§	1.16 (0.96, 1.40)	6,569
4	15.8%	2.23 (1.83, 2.73)§	1.58 (1.29, 1.94)§	6,479

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\*LR1: combined group of %Macro/%Micro quartiles 1/1, 1/2, 2/1, and 2/2; †LR2: combined group of %Macro/%Micro quartiles 1/3, 3/1, 2/3, and 3/2; ‡Adjustment for CBC here included red blood cell count, white blood cell count, platelet count, mean corpuscular volume, mean corpuscular hemoglobin concentration, and mean platelet volume (RDW was not included since analyses were performed in the 4<sup>th</sup> quartile of RDW), and the 38 morbidities and health system encounter types listed in Appendix Table 1; §p<0.001; ||p<0.05.

**Appendix Table 7.** Hazard ratios and 95% CI from Cox regression among females for RDW quartile 4 (n=40,039; deaths: 1,711) vs. 1 (n=39,869; deaths: 187) and the macrocytic (%Macro, RBC volume >120 fL)/microcytic (%Micro, RBC volume <60 fL) quartile categories 3/4 (n=3,752; deaths: 176), 4/3 (n=5,066; deaths: 272), and 4/4 (n=1,973; deaths: 235) vs. the combined low-risk set (LR1) of 1/1, 1/2, 2/1, 2/2 (n=23,243; deaths: 129), both overall and in clinical diagnostic group substrata. Multivariable adjustments included age and components of the complete blood count (RDW-sd and morbidities were not adjusted for herein).

Diagnosis	RDW Quartile			
	4 vs. 1	Quartile Categories of %Macro/%Micro		
Group	4 vs. 1	3/4 vs. LR1	4/3 vs. LR1	4/4 vs. LR1
All patients	2.45 (2.04, 2.94)*	2.34 (1.81, 3.04)*	1.39 (1.09, 1.77)†	2.55 (1.99, 3.26)*
Metastatic Cancer	1.12 (0.62, 2.03)	1.97 (0.89, 4.37)	1.42 (0.66, 3.04)	2.69 (1.29, 5.59)†
Acute MI	1.98 (1.17, 3.36)†	1.44 (0.72, 2.89)	0.69 (0.36, 1.33)	0.97 (0.49, 1.92)
Diabetes	1.95 (1.43, 2.66)*	1.89 (1.26, 2.84)†	1.04 (0.71, 1.54)	1.74 (1.17, 2.59)†
Pneumonia	1.73 (1.23, 2.44)†	1.79 (1.13, 2.84)†	0.81 (0.53, 1.24)	1.64 (1.06, 2.55)†
Hypertensive HD	1.47 (0.44, 4.87)	6.22 (0.55, 70.06)	3.17 (0.31, 32.53)	10.48 (1.09, 100.90)†
Angina	1.48 (0.92, 2.39)	1.24 (0.64, 2.43)	0.77 (0.42, 1.39)	0.83 (0.42, 1.65)
Cardioresp. Failure	1.67 (1.27, 2.18)*	1.68 (1.15, 2.46)†	1.06 (0.74, 1.51)	1.74 (1.21, 1.04)†
Valvular HD	1.87 (1.28, 2.73)†	1.44 (0.86, 2.43)	1.07 (0.67, 1.72)	2.23 (1.39, 3.58)*
Arrhythmia	1.75 (1.33, 2.28)*	1.68 (1.17, 2.40)†	1.10 (0.79, 1.53)	1.88 (1.33, 2.65)*
Hemi/Paraplegia, etc	1.64 (0.999, 2.69)	1.75 (0.90, 3.42)	1.07 (0.58, 1.97)	1.72 (0.89, 3.32)

Stroke	1.99 (1.19, 3.34)†	0.93 (0.48, 1.83)	0.73 (0.40, 1.32)	0.80 (0.39, 1.63)
COPD	1.49 (0.99, 2.23)	2.12 (1.18, 3.82)†	1.17 (0.67, 2.04)	1.79 (1.003, 3.21)†
Fluid/Electrolyte Dis	2.28 (1.82, 2.85)*	2.02 (1.48, 2.74)*	1.23 (0.93, 1.64)	2.15 (1.61, 2.88)*
Other Urinary Tract Dis	2.32 (1.79, 3.02)*	2.12 (1.48, 3.03)*	1.33 (0.95, 1.85)	2.48 (1.76, 3.47)*
Decubitus/Skin Ulcer	1.86 (1.01, 3.44)†	1.64 (0.83, 3.23)	0.83 (0.44, 1.56)	1.67 (0.89, 3.13)
Other GI Disorders	2.49 (2.02, 3.07)*	2.31 (1.74, 3.09)*	1.31 (0.999, 1.71)	2.32 (1.76, 3.06)*
PUD, GI Hemorrhage	2.59 (1.84, 3.66)*	1.69 (1.07, 2.68)†	1.06 (0.69, 1.61)	1.77 (1.15, 2.73)†
Severe Hematologic Dis	2.32 (0.25, 21.37)	5.91 (0.53, 66.01)	2.03 (0.20, 20.33)	0.81 (0.07, 8.80)
Nephritis	1.08 (0.47, 2.48)	4.77 (1.72, 13.26)†	1.62 (0.63, 4.16)	1.62 (0.58, 4.55)
Dementia	1.83 (1.27, 2.63)†	1.27 (0.78, 2.08)	0.87 (0.56, 1.36)	1.17 (0.72, 1.92)
Cancer	2.36 (1.72, 3.23)*	2.70 (1.74, 4.17)*	1.59 (1.06, 2.40)†	2.63 (1.74, 3.99)*
Liver/Biliary Disease	2.91 (2.10, 4.02)*	2.20 (1.42, 3.40)*	1.31 (0.67, 1.97)	2.46 (1.64, 3.69)*
ESRD, Dialysis	0.80 (0.24, 2.69)	2.57 (0.56, 11.92)	0.67 (0.17, 2.70)	0.88 (0.19, 4.21)
Asthma	1.87 (1.25, 2.78)†	1.97 (1.07, 3.62)†	1.20 (0.68, 2.10)	2.31 (1.29, 4.12)†
Anemia	2.03 (1.59, 2.59)*	2.21 (1.58, 3.09)*	1.34 (0.98, 1.84)	2.13 (1.55, 2.93)*
Drug/Alcohol Abuse	2.57 (1.83, 3.61)*	1.82 (1.11, 2.98)†	1.24 (0.79, 1.97)	1.62 (0.99, 2.64)
Major Psychological Dis	2.05 (1.39, 3.03)*	1.55 (0.88, 2.75)	1.33 (0.80, 2.20)	1.20 (0.68, 2.12)
Depression	2.02 (1.51, 2.71)*	1.77 (1.18, 2.65)†	1.16 (0.80, 1.69)	1.91 (1.29, 2.83)†



Other Psychological Dis	1.93 (1.44, 2.57)*	1.64 (1.08, 2.49)†	1.20 (0.82, 1.76)	2.23 (1.51, 3.31)*
Fibrosis of Lung	1.56 (0.84, 2.91)	1.60 (0.68, 3.76)	1.04 (0.47, 2.27)	1.17 (0.50, 2.74)
Protein-Calorie Malnutr	1.76 (1.04, 2.99)†	1.45 (0.77, 2.76)	1.03 (0.57, 1.87)	1.43 (0.78, 2.60)
CAD	1.67 (1.19, 2.33)†	1.64 (1.04, 2.56)†	0.97 (0.64, 1.48)	1.72 (1.12, 2.65)†
Heart Failure	1.61 (1.13, 2.29)†	1.32 (0.85, 2.05)	0.82 (0.54, 1.23)	1.48 (0.98, 2.23)

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\*p<0.001, †p<0.05.

**Appendix Table 8.** Hazard ratios and 95% CI from Cox regression among males for RDW quartile 4 (n=25,988; deaths: 2,029) vs. 1 (n=23,882; deaths: 198) and the macrocytic (%Macro, RBC volume >120 fL)/microcytic (%Micro, RBC volume <60 fL) quartile categories 3/4 (n=2,902; deaths: 179), 4/3 (n=2,947; deaths: 245), and 4/4 (n=1,519; deaths: 241) vs. the combined low-risk set (LR1) of 1/1, 1/2, 2/1, 2/2 (n=13,678; deaths: 163), both overall and in clinical diagnostic group substrata. Multivariable adjustments included age and components of the complete blood count (RDW-sd and morbidities were not adjusted for herein).

Diagnosis	RDW Quartile	Quartile Categories of %Macro/%Micro		
		4 vs. 1	3/4 vs. LR1	4/3 vs. LR1
All patients	2.16 (1.81, 2.57)*	2.19 (1.73, 2.78)*	1.90 (1.52, 2.38)*	2.51 (2.00, 3.14)*
Metastatic Cancer	1.04 (0.55, 1.97)	2.71 (1.24, 5.95)†	1.45 (0.63, 3.34)	1.99 (0.92, 4.29)
Acute MI	1.14 (0.79, 1.64)	2.38 (1.45, 3.92)*	1.75 (1.08, 2.83)†	3.51 (2.18, 5.64)*
Diabetes	1.43 (1.09, 1.88)†	1.73 (1.22, 2.44)†	1.82 (1.32, 2.50)*	2.38 (1.71, 3.32)*
Pneumonia	1.99 (1.39, 2.85)*	1.84 (1.19, 2.85)†	1.82 (1.20, 2.74)†	1.87 (1.23, 2.85)†
Hypertensive HD	1.63 (0.41, 6.49)	1.12 (0.21, 6.01)	0.92 (0.17, 4.85)	3.01 (0.71, 12.79)
Angina	1.13 (0.80, 1.60)	2.43 (1.49, 3.95)*	2.06 (1.29, 3.28)†	3.30 (2.07, 5.25)*
Cardioresp. Failure	1.27 (0.98, 1.65)	1.74 (1.23, 2.46)†	1.50 (1.08, 2.07)†	2.36 (1.71, 3.25)*
Valvular HD	2.14 (1.36, 3.36)*	2.16 (1.30, 3.59)†	1.83 (1.12, 2.99)†	2.58 (1.58, 4.20)*
Arrhythmia	1.35 (1.07, 1.72)†	2.24 (1.63, 3.08)*	2.00 (1.48, 2.71)*	2.68 (1.98, 3.63)*
Hemi/Paraplegia, etc	1.48 (0.96, 2.28)	1.69 (0.93, 3.08)	1.98 (1.16, 3.39)†	2.89 (1.65, 5.08)*

Stroke	1.41 (0.91, 2.19)	0.84 (0.41, 1.72)	1.08 (0.60, 1.94)	1.39 (0.68, 2.82)
COPD	1.50 (1.03, 2.17)†	1.37 (0.83, 2.24)	1.18 (0.74, 1.89)	1.94 (1.22, 3.08)†
Fluid/Electrolyte Dis	1.69 (1.36, 2.10)*	1.74 (1.32, 2.31)*	1.56 (1.20, 2.03)*	1.95 (1.49, 2.55)*
Other Urinary Tract Dis	1.48 (1.06, 2.07)†	1.78 (1.16, 2.75)†	1.64 (1.10, 2.45)†	1.95 (1.29, 2.94)†
Decubitus/Skin Ulcer	1.44 (0.81, 2.55)	1.86 (0.97, 3.57)	2.04 (1.10, 3.79)†	2.12 (1.14, 3.94)†
Other GI Disorders	2.15 (1.75, 2.64)*	2.10 (1.61, 2.75)*	1.80 (1.40, 2.33)*	2.36 (1.82, 3.06)*
PUD, GI Hemorrhage	2.45 (1.69, 3.54)*	2.06 (1.34, 3.17)†	1.76 (1.16, 2.66)†	2.19 (1.45, 3.32)*
Severe Hematologic Dis	1.75 (0.37, 8.26)	4.39 (0.76, 25.56)	1.84 (0.35, 9.67)	2.02 (0.39, 10.59)
Nephritis	1.88 (0.78, 4.51)	1.17 (0.52, 2.65)	2.09 (1.02, 4.29)†	2.55 (1.24, 5.24)†
Dementia	1.59 (1.10, 2.30)†	1.70 (1.03, 2.81)†	1.58 (1.001, 2.51)†	1.89 (1.16, 3.08)†
Cancer	1.74 (1.31, 2.31)*	2.52 (1.74, 3.65)*	1.99 (1.40, 2.83)*	2.80 (1.96, 3.99)*
Liver/Biliary Disease	2.05 (1.48, 2.84)*	1.97 (1.28, 3.04)†	1.67 (1.11, 2.53)†	2.73 (1.82, 4.10)*
ESRD, Dialysis	0.55 (0.17, 1.79)	1.33 (0.37, 4.78)	2.03 (0.67, 6.19)	2.04 (0.63, 6.59)
Asthma	2.09 (1.26, 3.44)†	1.80 (0.82, 3.95)	2.72 (1.33, 5.58)†	3.27 (1.59, 6.70)†
Anemia	1.76 (1.36, 2.28)*	1.77 (1.28, 2.44)*	1.69 (1.25, 2.28)*	2.24 (1.67, 3.00)*
Drug/Alcohol Abuse	2.21 (1.66, 2.96)*	2.30 (1.50, 3.54)*	1.72 (1.14, 2.59)†	2.88 (1.92, 4.31)*
Major Psychological Dis	1.51 (0.99, 2.30)	2.73 (1.40, 5.34)†	3.04 (1.60, 5.77)*	4.31 (2.28, 8.16)*
Depression	1.58 (1.12, 2.23)†	1.83 (1.13, 2.95)†	1.98 (1.26, 3.10)†	1.99 (1.25, 3.19)†

Other Psychological Dis	1.56 (1.12, 2.17)†	2.36 (1.45, 3.84)*	2.20 (1.38, 3.49)*	2.56 (1.59, 4.13)*
Fibrosis of Lung	1.30 (0.67, 2.53)	2.32 (1.05, 5.13)†	1.85 (0.86, 3.99)	2.08 (0.95, 4.55)
Protein-Calorie Malnutr	1.32 (0.78, 2.24)	1.69 (0.91, 3.11)	1.49 (0.84, 2.62)	1.48 (0.83, 2.62)
CAD	1.27 (0.98, 1.65)	2.08 (1.46, 2.95)*	1.98 (1.43, 2.74)*	2.84 (2.05, 3.94)*
Heart Failure	1.22 (0.87, 1.72)	1.70 (1.12, 2.56)†	1.75 (1.19, 2.57)†	2.29 (1.55, 3.38)*

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\*p<0.001, †p<0.05.

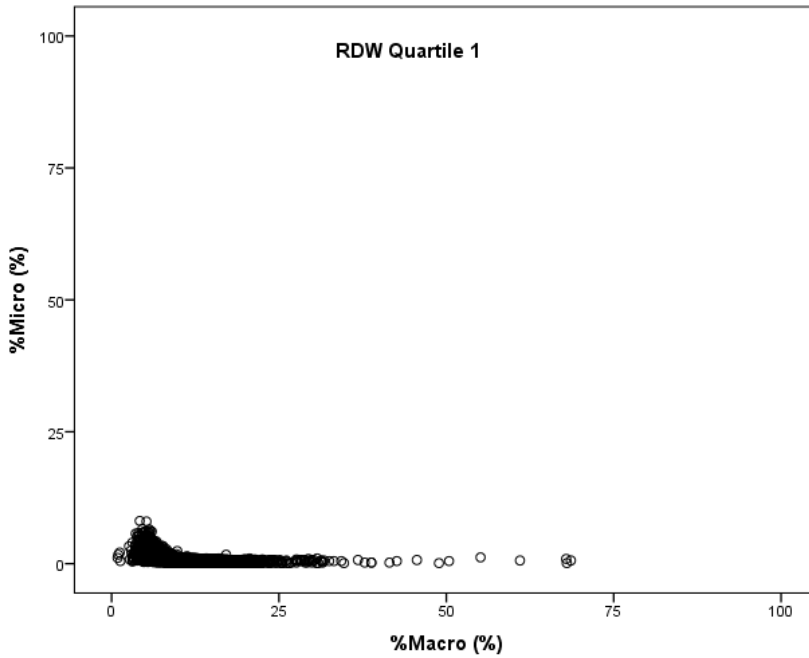
**Appendix Table 9.** Please see accompanying spreadsheet.

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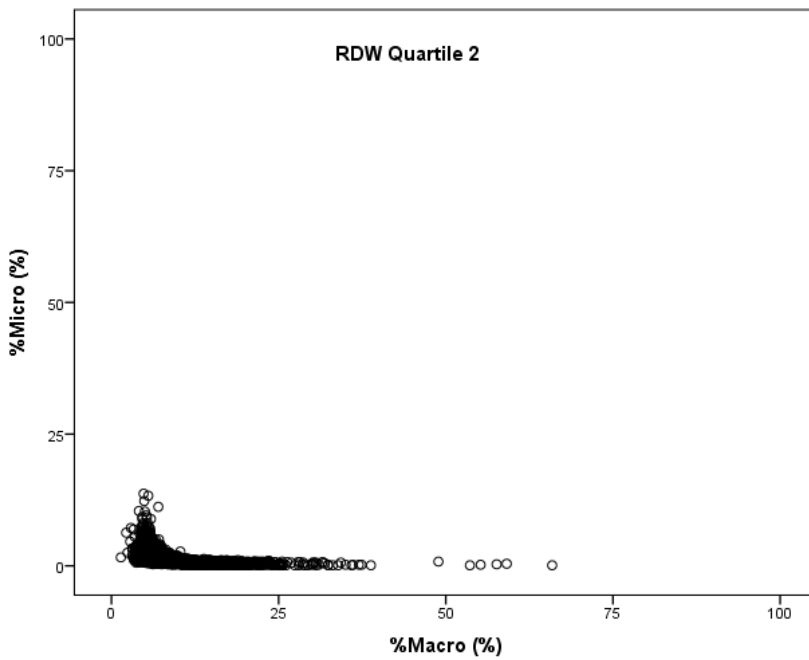
**Appendix Figure 1.** Scatterplots for males (n=100,210) of the percentage of RBCs that are macrocytic (%Macro, RBC volume >120 fL) and microcytic (%Micro, RBC volume <60 fL) in: A) RDW quartile 1 (n=23,882); B) RDW quartile 2 (n=24,796); C) RDW quartile 3 (n=25,544); and D) RDW quartile 4 (n=25,988).

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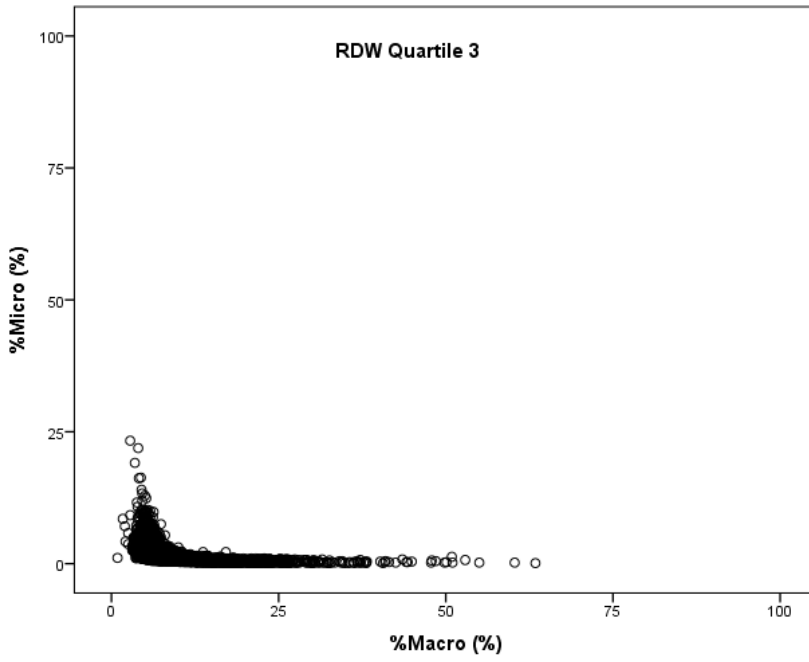
A)



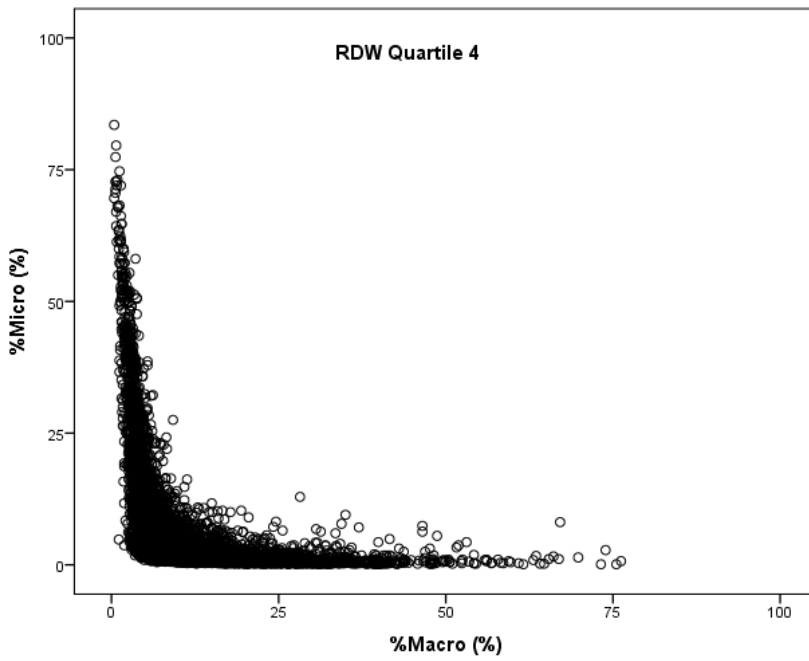
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C)



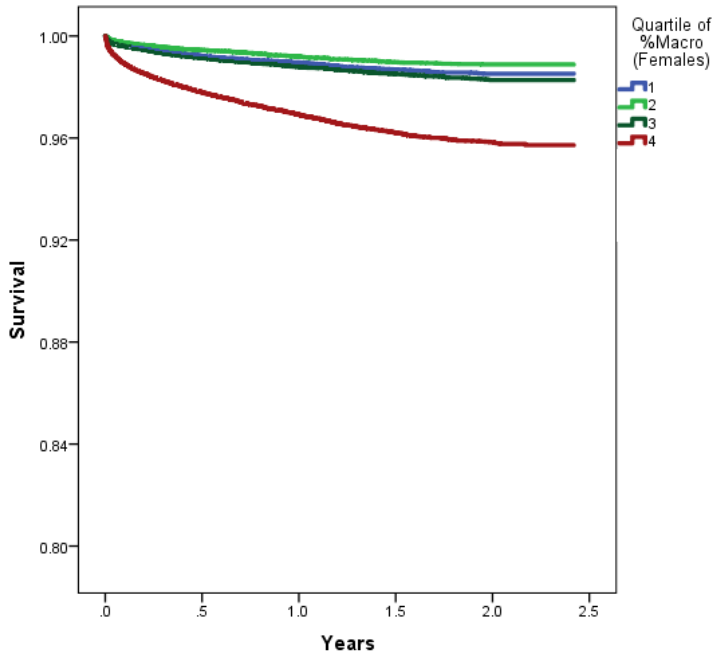
D)



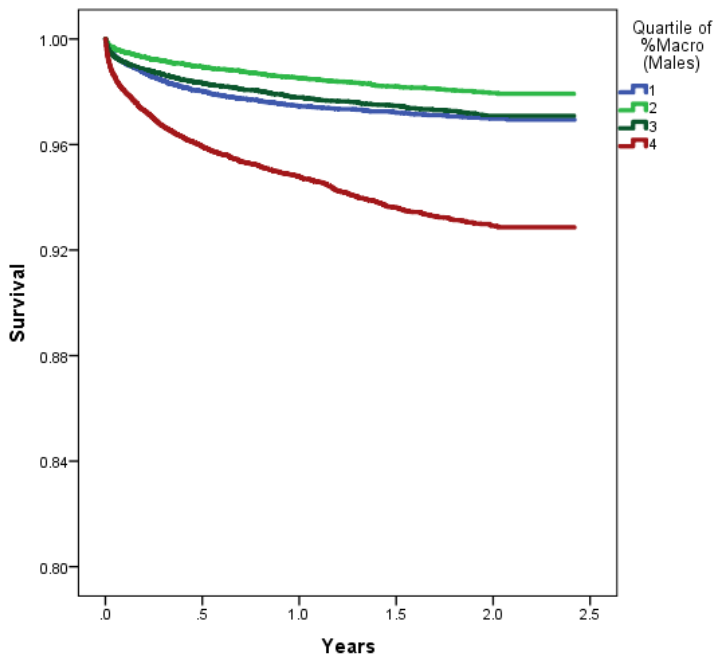
**Appendix Figure 2.** Kaplan-Meier survival curves among the primary study population (n=165,770 females, n=100,210 males) based on: A) %Macro (RBC volume >120 fL) for females, B) %Macro for males, C) %Micro (RBC volume <60 fL) for females where the first three quartiles overlap closely, and D) %Micro for males.

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A)

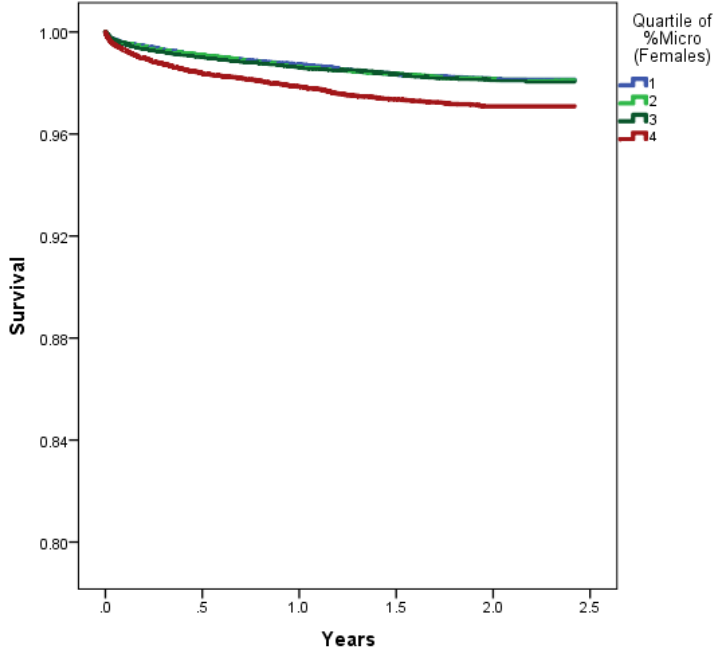


B)

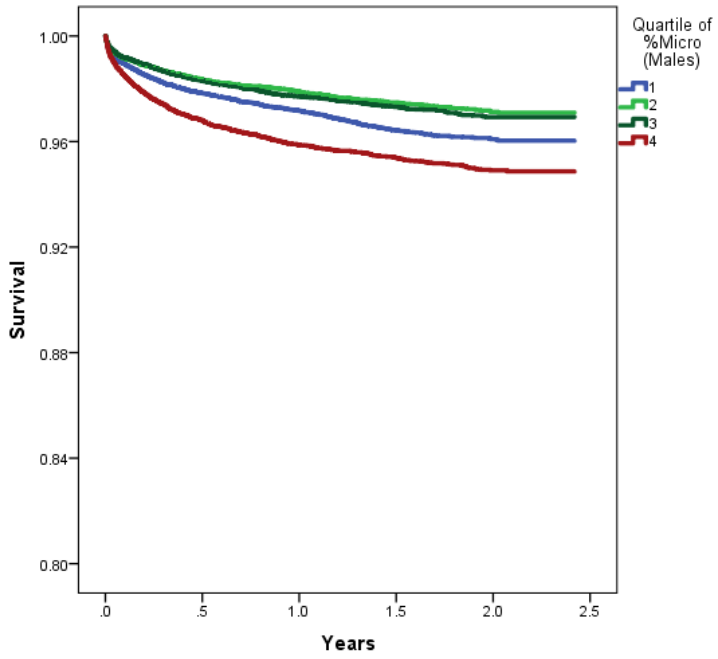




C)

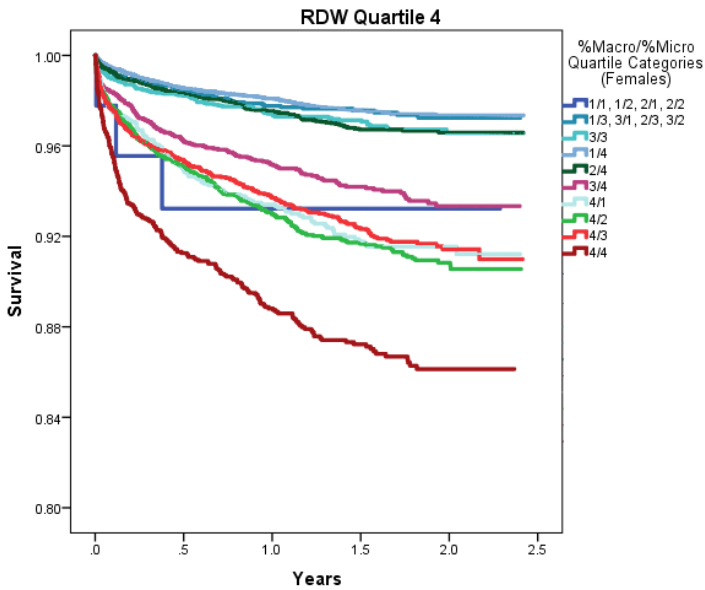


D)

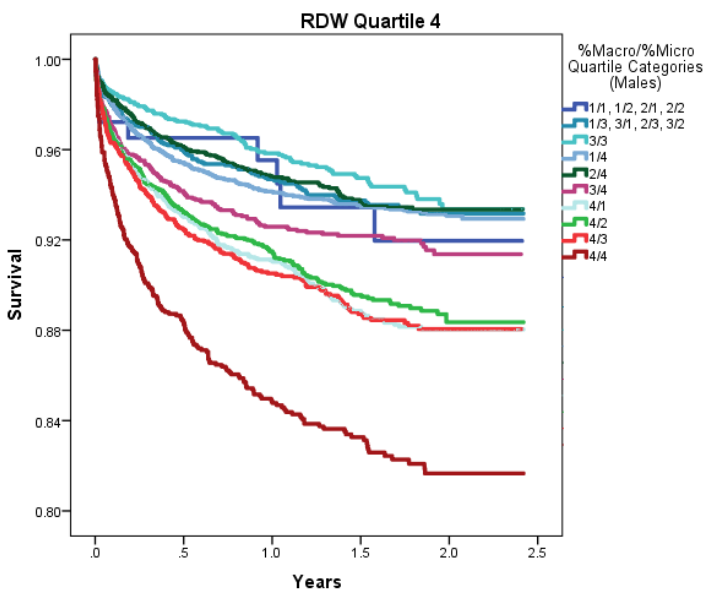


**Appendix Figure 3.** Kaplan-Meier survival curves in the 4<sup>th</sup> quartile of RDW among females (n=40,039) and males (n=25,988) demonstrate substantial ability of %Macro (RBC volume >120 fL) and %Micro (RBC volume <60 fL) quartile categories to stratify mortality risk among: A) females\*, and B) males\*, and for RDW-sd quartiles† to do the same for: C) females, and D) males (despite the high RDW).

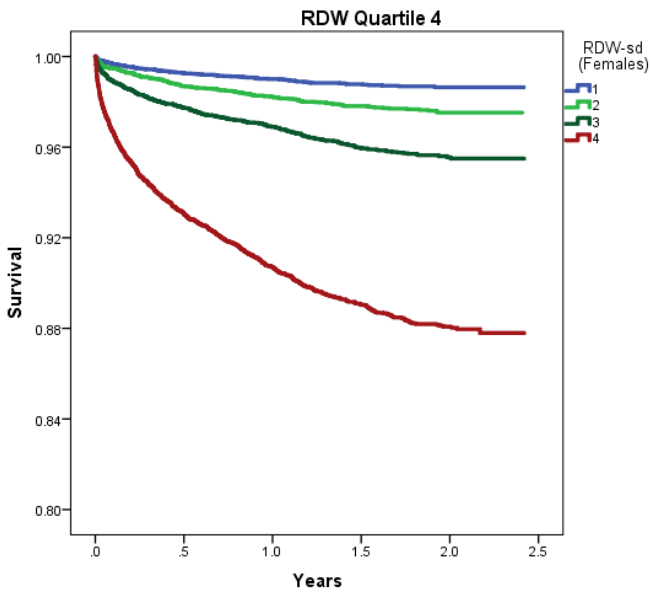
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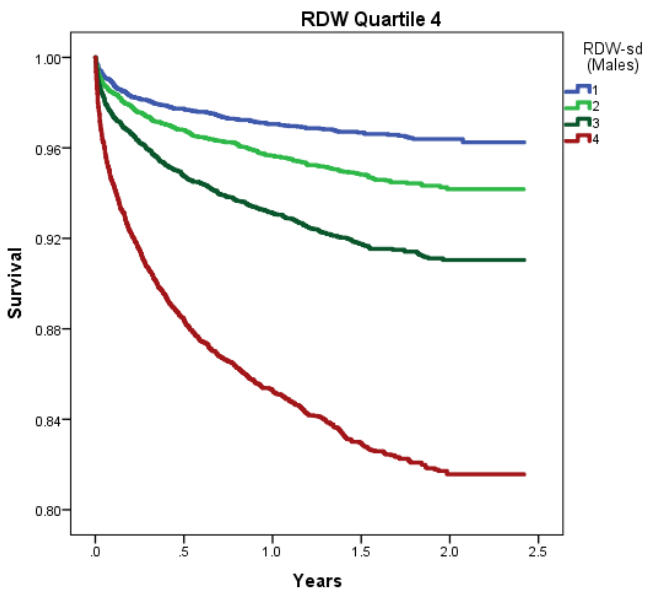
B)



C)



D)



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\*Category 1/1, 1/2, 2/1, 2/2 is LR1, and category 1/3, 3/1, 2/3, 3/2 is LR2; †Due to the small sample size in quartile 1 of the original sex-specific RDW-sd quartiles (females: n=1,664; males: n=600), RDW-sd quartiles were re-derived for the survival curves presented in this figure.