

## ORIGINAL RESEARCH

## OUTCOMES AND QUALITY

# Neutrophil-to-Lymphocyte Ratio and Mortality in Cardiovascular Disease or Cancer



## A Population-Based Cohort Study

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## ABSTRACT

**BACKGROUND** Inflammation contributes to development and progression of cardiovascular disease (CVD) and cancer. Whether the neutrophil-to-lymphocyte ratio (NLR), routinely available from blood counts, predicts prognosis in the general population is uncertain.

**OBJECTIVES** The purpose of this study was to evaluate the association of NLR with mortality in people with and without CVD or cancer.

**METHODS** In this retrospective cohort study, we used National Health Service records from the Greater Glasgow & Clyde region for people aged >50 years in 2012. Participants were classified hierarchically into 5 exclusive groups: history of cancer, heart failure (HF, or dispensed loop diuretics), CVD, CV risk factors only, or none. Mortality was tracked until December 2019.

**RESULTS** We identified 223,388 people with NLR measured between 2014 and 2015: 106,973 (48%) with CV risk factors only, 14,490 (7%) with CVD, 23,009 (10%) with HF or dispensed loop diuretics, 8,677 (4%) with cancer, and 70,239 (31%) none of these features. Median NLR was lowest in the latter group (2.0 [1.5-2.7]) and highest in those with HF or dispensed loop diuretics (2.7 [1.9-3.9]) or cancer (2.7 [1.9-4.1]). Median follow-up was 5.0 years (IQR: 4.4-5.0). In models adjusted for age, sex, estimated glomerular filtration rate, and hemoglobin, the highest NLR quartile predicted higher mortality across all groups (HR [95% CI] 2.07 [1.98-2.17] for CV risk factors and 2.18 [2.02-2.36] for none; 1.87 [1.70-2.04] for CVD, 2.10 [1.98-2.24] for HF or loop diuretics, and 2.30 [2.10-2.52] for cancer).

**CONCLUSIONS** Higher NLR is associated with greater mortality in adults with and without CVD, HF or cancer, suggesting it could enhance population risk scores. (JACC Adv. 2026;5:102362) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

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**ABBREVIATIONS  
AND ACRONYMS****CRP** = C-reactive protein**CV** = cardiovascular**CVD** = cardiovascular disease**eGFR** = estimated glomerular filtration rate**EPRs** = electronic patient records**HF** = heart failure**LD** = loop diuretics**NHS** = National Health Service**NLR** = neutrophil-to-lymphocyte ratio

**C**ardiovascular disease (CVD) and cancer are common causes of disability, morbidity, and mortality worldwide and share many risk factors.<sup>1</sup> Smoking, reduced physical activity, and obesity increase the risk of developing both conditions. Cancer and CVD might also share biological mechanisms driving pathophysiology.<sup>2</sup> Immunoinflammatory responses are involved in the development of atherosclerosis, myocardial infarction, and progression to heart failure (HF),<sup>3,4</sup> as well as in different cancer types.<sup>5</sup> Inflammation-targeted therapies could potentially improve the outcome of many cardiovascular (CV) conditions, including HF<sup>6-8</sup> and inhibit cancer development or facilitate its regression.<sup>9</sup>

The neutrophil-to-lymphocyte ratio (NLR) is a simple, routinely available marker of a disturbed inflammatory state. A higher NLR is associated with worse outcomes in patients with myocardial infarction, diabetes, stroke, HF, and cancer.<sup>10</sup> However, the generalizability of these findings is limited, as they are usually based on cohorts of highly selected individuals who have been invited and consented to participate in multicenter research registries or trials, or from small, single-center, retrospectively collected samples of patients. Information on general populations is lacking. Therefore, we investigated the distribution and associations of NLR with mortality in middle aged or older adults with or without CV risk factors, overt CVD with or without HF or cancer.

**METHODS**

**DATA SOURCE.** We used routinely collected National Health Service (NHS) electronic patient records (EPRs) for Greater Glasgow & Clyde from January 1, 2012, to December 31, 2019. NHS Greater Glasgow & Clyde provides health care services to a population of approximately 1.2 million residents across Glasgow City, East Dunbartonshire, East Renfrewshire, Inverclyde, Renfrewshire, and West Dunbartonshire. It is the largest health board in Scotland and among the largest in the United Kingdom. Data were accessed through the NHS West of Scotland Safe-Haven, which is a trusted research environment where pseudonymized health records can be linked

for audit and research purposes.<sup>11</sup> Data comprise demographics, dispensing records from community but not hospital pharmacies, laboratory tests from both primary and secondary care, hospital admissions, including diagnostic and procedural codes, and death records, including certified cause of death. NLR was calculated from lymphocyte and neutrophil counts taken at the same time and date, dividing neutrophil by lymphocyte counts.

**STUDY POPULATION.** People aged >50 years on the 1st of January 2012 with an available EPRs were included. Using information acquired from the EPRs during 2012/13, patients were classified into one of 5 mutually exclusive groups in a hierarchical fashion (ie, patients belonging to a group could not belong to any subsequent group) based on hospital records and treatments dispensed in primary care during the 6 months prior to the index date. These 5 groups were: 1) cancer; 2) HF or treatment with a loop diuretic, a surrogate for a missed diagnosis of HF<sup>12</sup> (HF/LD); 3) established CVD, including ischemic heart disease, myocardial infarction, or stroke; 4) CV risk factors, which included a diagnosis of, or treatment for hypertension, diabetes, or hyperlipidemia; or 5) none of these (without CV risk factors) (Supplemental Figure 1, Supplemental Table 1).

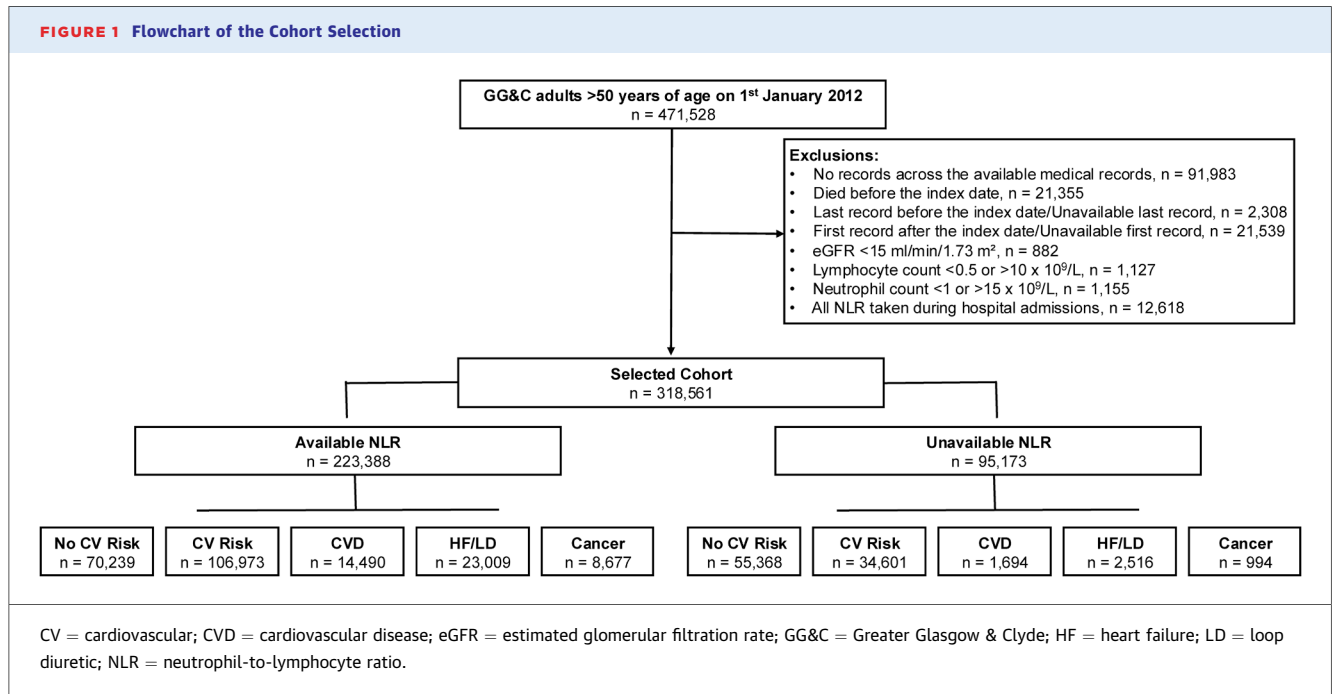
From January 1, 2014, to December 31, 2015, the first available NLR measurement taken in primary care was identified; blood tests taken during hospital admissions were excluded because such results might reflect transient acute illnesses. We also excluded those with end-stage renal disease, defined as an estimated glomerular filtration rate (eGFR) < 15 mL/min/1.73 m<sup>2</sup>, and those with extreme values for lymphocyte (<0.5 or >10 × 10<sup>9</sup> cells/L) or neutrophil (<1 or >15 × 10<sup>9</sup> cells/L) counts that might be due to hematological disorders (Figure 1). Furthermore, in a sensitivity analysis, we have excluded patients with a recorded history of malignant hematological cancer (Supplemental Table 2). Patients with a known blood cancer were otherwise included in the cancer cohort.

**PATIENTS CHARACTERISTICS.** Comorbidities and procedures were identified through the International Statistical Classification of Diseases and Related Health Problems, 10th Revision codes in any diagnostic or Office of Population Censuses and Surveys Classification of Interventions and Procedures

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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**FIGURE 1** Flowchart of the Cohort Selection



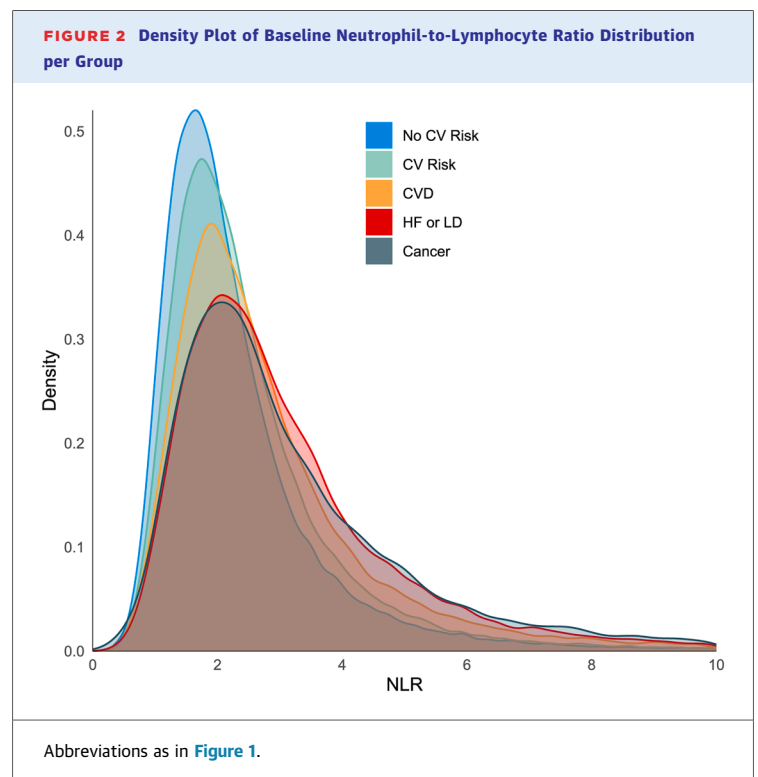
version 4 codes in any procedural position. Diagnostic code lists were derived from CALIBER phenotypes<sup>13</sup> and existing research literature.<sup>14,15</sup> Patients who did not have a diagnostic record for a particular disease were considered to be free of that condition. Baseline treatment and blood results were identified during a 6-month window before the index date. Medications dispensed were identified using the British National Formulary codes (Supplemental Table 3). Data sources and coding systems are described in supplementary materials. The eGFR was calculated using the Chronic Kidney Disease-Epidemiology Collaboration equation without any adjustment for ethnicity.<sup>16,17</sup>

**STUDY OUTCOMES.** We investigated the association between the first measurement of NLR in 2014/15 and 5-year all-cause mortality and cause of death. Cause of death was identified from National Records Scotland deaths records and classified as CV, cancer, infection, injury, or others (Supplemental Tables 4 and 5). These outcome measures have been assessed in prior studies using data from the same region and data sources.<sup>12,18</sup>

Individuals were followed up until the first outcome occurred, or until the date of the last available EPRs, whichever came first. The follow-up period concluded on December 31, 2019. To account for potential dropouts due to residential relocation or emigration, the date of the last available EPR was

considered the censoring date if it occurred before the end of the follow-up period. Individuals without any available EPRs after the index date were excluded (Figure 1).

**FIGURE 2** Density Plot of Baseline Neutrophil-to-Lymphocyte Ratio Distribution per Group



**TABLE 1** Baseline Demographics, Comorbidities, Blood Tests, and Medications of Cardiovascular Risk Free, Cardiovascular Risk, Cardiovascular Disease, and Heart Failure or Loop Diuretic Cohorts by Quartiles of Neutrophil-to-Lymphocyte Ratio

	No CV Risk				CV Risk			
	Q1 ≤1.47 (n = 17,677)	Q2 1.48-1.96 (n = 17,552)	Q3 1.97-2.71 (n = 17,546)	Q4 >2.71 (n = 17,464)	Q1 ≤1.61 (n = 27,142)	Q2 1.62-2.16 (n = 26,577)	Q3 2.17-3.00 (n = 27,734)	Q4 >3.00 (n = 25,520)
Age, y	61 (57-67)	61 (57-68)	62 (57-70)	65 (59-74)	67 (60-74)	68 (61-76)	70 (62-78)	73 (65-80)
Women	11,577 (65%)	10,788 (61%)	9,977 (57%)	9,116 (52%)	16,177 (60%)	14,749 (55%)	14,646 (53%)	13,073 (51%)
DM	Excluded				4,303 (16%)	4,690 (18%)	5,168 (19%)	4,440 (17%)
IHD					Excluded			
MI								
AF/AFL								
PCI								
CABG								
Stroke								
HF								
COPD	234 (1%)	258 (2%)	338 (2%)	656 (4%)	470 (1%)	515 (2%)	689 (3%)	1,028 (4%)
Blood tests <sup>a</sup>								
Neutrophil count, 10 <sup>3</sup> /μL	2.8 (2.3-3.5)	3.6 (3.0-4.3)	4.2 (3.5-5.0)	5.5 (4.4-7.0)	3.2 (2.6-3.9)	4.0 (3.3-4.7)	4.6 (3.8-5.5)	5.8 (4.7-7.3)
Lymphocyte count, 10 <sup>3</sup> /μL	2.5 (2.0-3.0)	2.1 (1.8-2.5)	1.8 (1.5-2.2)	1.4 (1.1-1.8)	2.5 (2.1-3.1)	2.1 (1.8-2.5)	1.8 (1.5-2.2)	1.4 (1.1-1.7)
eGFR <sup>b</sup> , mL/min/1.73 m <sup>2</sup>	88 (79-95)	88 (78-95)	88 (77-95)	86 (75-95)	83 (72-92)	82 (69-91)	80 (67-90)	77 (61-88)
CRP, mg/dL	0.3 (0.1-0.4)	0.3 (0.1-0.5)	0.3 (0.2-0.7)	0.5 (0.3-2.0)	0.3 (0.2-0.5)	0.3 (0.2-0.6)	0.3 (0.3-0.8)	0.6 (0.3-2.0)
Hemoglobin (women), g/dL	13.5 (12.9-14.2)	13.6 (12.9-14.3)	13.6 (12.8-14.3)	13.4 (12.5-14.2)	13.5 (12.7-14.2)	13.4 (12.6-14.2)	13.3 (12.4-14.1)	13.1 (12.0-14.0)
Hemoglobin (men), g/dL	15.0 (14.2-15.7)	15.0 (14.2-15.7)	15.0 (14.1-15.8)	14.8 (13.7-15.6)	14.8 (13.9-15.6)	14.7 (13.8-15.6)	14.6 (13.6-15.5)	14.3 (13.1-15.3)
Medications <sup>a,c</sup>								
Loop diuretics	Excluded				Excluded			
Thiazides and related					7,144 (26%)	7,299 (27%)	7,754 (28%)	7,245 (28%)
ACEI/ARBs					13,230 (49%)	13,518 (51%)	14,421 (52%)	13,018 (51%)
Beta-blocker					8,082 (30%)	8,072 (30%)	8,645 (31%)	7,786 (31%)
MRA					121 (<1%)	125 (<1%)	199 (<1%)	232 (<1%)
Antiplatelet					9,677 (36%)	10,265 (39%)	11,489 (41%)	11,324 (44%)
Statins	Excluded				16,545 (61%)	16,643 (63%)	17,723 (64%)	15,954 (63%)
Oral anticoagulants					804 (3%)	852 (3%)	1,146 (4%)	1,380 (5%)
Insulin					562 (2%)	633 (2%)	796 (3%)	825 (3%)
Other hypoglycemics					3,936 (15%)	4,275 (16%)	4,699 (17%)	3,845 (15%)
PPI	5,121 (29%)	4,970 (28%)	5,110 (29%)	5,081 (29%)	11,346 (42%)	11,017 (41%)	11,719 (42%)	11,492 (45%)
Corticosteroids (inhaled)	1,313 (7%)	1,525 (9%)	1,689 (10%)	2,141 (12%)	2,606 (10%)	2,822 (11%)	3,255 (12%)	3,847 (15%)
Bronchodilators	1,759 (10%)	1,987 (11%)	2,179 (12%)	2,665 (15%)	3,641 (13%)	3,848 (14%)	4,356 (16%)	5,025 (20%)

Values are median (IQR) or; n (%). SI conversion factor: To convert C-reactive protein from mg/dL to mg/L, or hemoglobin from g/dL to g/L, multiply by 10. <sup>a</sup>Most recent blood tests and medication use in the last 6 months before the index date. <sup>b</sup>eGFR, estimated glomerular filtration rate using CKD-EPI equation. <sup>c</sup>Solely or in combination.

ACEI = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; AFL = atrial flutter; ARB = angiotensin receptor blocker; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; HF = heart failure; IHD = ischemic heart disease; LD = loop diuretic; MI = myocardial infarction; MRA = mineralocorticoid receptor antagonist; PCI = percutaneous coronary intervention; PPI = proton pump inhibitor.

Continued on the next page

**STATISTICAL ANALYSIS.** Categorical data are presented as numbers and percentages, and continuous data as median and IQR. We used Kaplan-Meier survival analysis and log-rank test to assess the difference in overall survival between diagnostic groups and between quartiles of NLR in each diagnostic group. Mortality rates were calculated as the number of deaths divided by total person-time at risk, expressed per 1,000 person-years. To address the association between NLR and all-cause mortality, we

used Cox proportional hazard model to estimate HRs and corresponding 95% CIs, initially adjusting for age and sex, then by adding eGFR and hemoglobin. NLR was modeled as quartiles, taking the first quartile as a reference group, or restricted cubic splines with 4 knots placed at 5th, 35th, 65th, and 95th percentiles, allowing for flexible dynamic of NLR accounting for nonlinearity.<sup>19</sup> Number of knots was chosen based on Akaike Information Criterion, where the models with the lowest Akaike Information Criterion were

TABLE 1 Continued

	CVD				HF/LD			
	Q1 ≤1.77 (n =3,657)	Q2 (1.78-2.41) (n =3,602)	Q3 (2.42-3.43) (n =3,618)	Q4 >3.43 (n =3,613)	Q1 ≤1.91 (n =5,758)	Q2 (1.92-2.67) (n =5,766)	Q3 (2.68-3.85) (n =5,758)	Q4 >3.85 (n =5,727)
Age, y	69 (61-77)	71 (63-79)	74 (66-81)	77 (69-84)	74 (65-81)	76 (68-83)	78 (70-84)	79 (72-86)
Women	1,779 (49%)	1,627 (45%)	1,651 (46%)	1,684 (47%)	3,960 (69%)	3,647 (63%)	3,511 (61%)	3,391 (59%)
DM	629 (17%)	667 (19%)	708 (20%)	690 (19%)	1,141 (20%)	1,376 (24%)	1,396 (24%)	1,488 (26%)
IHD	2,175 (59%)	2,045 (57%)	1,882 (52%)	1,706 (47%)	1,031 (18%)	1,134 (20%)	1,173 (20%)	1,300 (23%)
MI	993 (27%)	975 (27%)	873 (24%)	739 (20%)	555 (10%)	611 (11%)	610 (11%)	687 (12%)
AF/AFL	850 (23%)	861 (24%)	994 (27%)	1,213 (34%)	636 (11%)	757 (13%)	966 (17%)	1,232 (22%)
PCI	450 (12%)	493 (14%)	364 (10%)	252 (7.0%)	183 (3%)	195 (3%)	173 (3%)	167 (3%)
CABG	78 (2%)	86 (2%)	61 (2%)	59 (2%)	67 (1.2%)	61 (1.1%)	68 (1.2%)	41 (0.7%)
Stroke	786 (21%)	813 (23%)	886 (24%)	955 (26%)	222 (3.9%)	266 (4.6%)	293 (5.1%)	354 (6.2%)
HF	Excluded				788 (14%)	949 (16%)	1,010 (18%)	1,260 (22%)
COPD	537 (15%)	519 (14%)	597 (17%)	716 (20%)	519 (9.0%)	638 (11%)	760 (13%)	988 (17%)
Blood tests <sup>a</sup>								
Neutrophil count, 10 <sup>3</sup> /μL	3.5 (2.8-4.2)	4.2 (3.5-5.1)	4.8 (4.0-5.8)	6.3 (5.0-7.9)	3.6 (2.9-4.3)	4.4 (3.7-5.3)	5.1 (4.2-6.1)	6.4 (5.1-8.0)
Lymphocyte count, 10 <sup>3</sup> /μL	2.5 (2.1-3.1)	2.0 (1.7-2.5)	1.7 (1.4-2.0)	1.3 (1.0-1.6)	2.5 (2.0-3.0)	1.9 (1.6-2.3)	1.6 (1.3-1.9)	1.1 (0.9-1.4)
eGFR <sup>b</sup> , mL/min/1.73 m <sup>2</sup>	81 (67-91)	78 (64-90)	77 (61-88)	74 (57-85)	71 (55-84)	67 (50-81)	63 (45-79)	58 (40-76)
CRP, mg/dL	0.3 (0.2-0.5)	0.3 (0.3-0.8)	0.4 (0.3-1.0)	0.7 (0.3-2.5)	0.4 (0.3-0.8)	0.5 (0.3-1.1)	0.6 (0.3-1.6)	1.0 (0.4-2.9)
Hemoglobin (women), g/dL	13.1 (12.3-14.0)	13.1 (12.2-14.0)	12.8 (11.9-13.8)	12.7 (11.5-13.7)	13.1 (12.2-14.0)	12.9 (11.9-13.9)	12.7 (11.6-13.7)	12.4 (11.2-13.5)
Hemoglobin (men), g/dL	14.5 (13.4-15.3)	14.4 (13.4-15.3)	14.2 (12.9-15.2)	13.7 (12.4-14.9)	13.9 (12.7-15.1)	13.9 (12.7-15.0)	13.6 (12.3-14.9)	13.0 (11.7-14.3)
Medications <sup>a,c</sup>								
Loop diuretics	Excluded				5,428 (94%)	5,454 (95%)	5,454 (95%)	5,468 (95%)
Thiazides and related	428 (12%)	505 (14%)	524 (14%)	483 (13%)	341 (6%)	313 (5%)	335 (6%)	334 (6%)
ACEI/ARBs	1,851 (51%)	1,861 (52%)	1,852 (51%)	1,575 (44%)	3,240 (56%)	3,484 (60%)	3,358 (58%)	3,177 (55%)
Beta-blocker	1,914 (52%)	1,878 (52%)	1,762 (49%)	1,537 (43%)	2,602 (45%)	2,839 (49%)	2,820 (49%)	2,756 (48%)
MRA	32 (<1%)	41 (1%)	32 (<1%)	44 (1%)	399 (6.9%)	431 (7.5%)	491 (8.5%)	591 (10%)
Antiplatelet	2,575 (70%)	2,547 (71%)	2,474 (68%)	2,335 (65%)	2,944 (51%)	3,071 (53%)	3,090 (54%)	3,020 (53%)
Statins	2,716 (74%)	2,683 (74%)	2,639 (73%)	2,475 (69%)	3,676 (64%)	3,901 (68%)	3,844 (67%)	3,780 (66%)
Oral anticoagulants	501 (14%)	526 (15%)	570 (16%)	595 (16%)	918 (16%)	1,123 (19%)	1,262 (22%)	1,462 (26%)
Insulin	116 (3%)	113 (3%)	120 (3%)	125 (4%)	253 (4%)	331 (6%)	349 (6%)	419 (7%)
Other hypoglycemics	463 (13%)	485 (13%)	510 (14%)	469 (13%)	929 (16%)	1,131 (20%)	1,108 (19%)	1,106 (19%)
PPI	1,898 (52%)	1,824 (51%)	1,828 (51%)	1,824 (50%)	3,256 (57%)	3,204 (56%)	3,198 (56%)	3,339 (58%)
Corticosteroids (inhaled)	444 (12%)	466 (13%)	521 (14%)	596 (16%)	959 (17%)	1,051 (18%)	1,140 (20%)	1,367 (24%)
Bronchodilators	644 (18%)	636 (18%)	727 (20%)	809 (22%)	1,365 (24%)	1,462 (25%)	1,538 (27%)	1,784 (31%)

considered.<sup>20</sup> In addition, cross-validation was used to assess model predictive value.<sup>21</sup> Proportional hazards assumption was checked by visual inspection of scaled Schoenfeld residuals, due to large sample size, and sufficiently met for all the variables. Two-tailed *P* values <0.05 were considered significant. All analyses were conducted with R software version 4.3.0. Packages are listed in supplementary materials.

## RESULTS

Of 318,561 people, 223,388 (70%) had a valid record of NLR in 2014/15. Of these, prior to 2014, 106,973 (48%)

had CV risk factors, 14,490 (7%) had CVD but without HF/LD, 23,009 (10%) had HF/LD, and 8,677 had cancer (4%); 70,239 (31%) had none of the above (Figure 1). Median NLR (IQR) increased with severity of disease, from 2.0 (1.5-2.7) in those free from risk factors or disease to 2.7 (1.9-3.9) in those with HF/LD, and 2.7 (1.9-4.1) in those with cancer (Figure 2, Supplemental Table 6).

Patients with HF/LD (23,009 out of 25,525) and cancer (8,677 out of 9,671) were highly likely to have an NLR available (~90%); the healthiest cohort (70,239 out of 125,607; 56%) was least likely to have an available measurement. Those in whom NLR was not measured during 2014/15 were generally younger

**TABLE 2** Baseline Demographics, Comorbidities, Lab Tests, and Medications of Cancer Cohort by Quartiles of Neutrophil-Lymphocyte Ratio

	Q1 ≤1.88 (n = 2,183)	Q2 (1.89-2.67) (n = 2,172)	Q3 (2.68-4.07) (n = 2,157)	Q4 >4.07 (n = 2,165)
Age, y	69 (63-77)	71 (64-78)	73 (65-79)	73 (66-80)
Women	1,158 (53%)	1,072 (49%)	975 (45%)	935 (43%)
DM	247 (11%)	275 (13%)	343 (16%)	319 (15%)
IHD	202 (9%)	206 (10%)	230 (11%)	278 (13%)
MI	83 (4%)	93 (4%)	94 (4%)	138 (6%)
AF/AFL	110 (5%)	111 (5%)	164 (8%)	200 (9%)
PCI	20 (<1%)	32 (2%)	21 (1%)	27 (1%)
CABG	9 (<1%)	<5 (<1%)	5 (<1%)	<5 (<1%)
Stroke	73 (3%)	80 (4%)	83 (4%)	94 (4%)
HF	54 (3%)	56 (3%)	89 (4%)	125 (6%)
COPD	173 (8%)	202 (9%)	249 (12%)	304 (14%)
Blood tests <sup>a</sup>				
Neutrophil count, 10 <sup>3</sup> /μL	3.2 (2.5-4.0)	4.1 (3.3-4.9)	4.8 (3.9-6.0)	6.2 (4.9-8.2)
Lymphocyte count, 10 <sup>3</sup> /μL	2.2 (1.8-2.8)	1.8 (1.5-2.2)	1.50 (1.2-1.8)	1.0 (0.8-1.3)
eGFR <sup>b</sup> , mL/min/1.73 m <sup>2</sup>	82 (68-91)	81 (66-90)	79 (62-90)	79 (59-91)
CRP, mg/dL	0.4 (0.3-0.9)	0.4 (0.3-1.1)	0.6 (0.3-1.9)	1.4 (0.4-5.1)
Hemoglobin (women), g/dL	13.0 (11.9-13.8)	12.9 (11.9-13.8)	12.7 (11.6-13.6)	12.3 (11.0-13.4)
Hemoglobin (men), g/dL	13.8 (12.6-14.9)	14.0 (12.7-15.0)	13.8 (12.3-14.9)	13.0 (11.5-14.3)
Medications <sup>a,c</sup>				
Loop diuretics	203 (9%)	236 (11%)	271 (13%)	411 (19%)
Thiazides and related	280 (13%)	313 (14%)	314 (15%)	279 (13%)
ACEI/ARBs	707 (32%)	667 (31%)	731 (34%)	733 (34%)
Beta-blocker	529 (24%)	549 (25%)	520 (24%)	585 (27%)
MRA	16 (<1%)	25 (1%)	34 (2%)	47 (2%)
Antiplatelet	641 (29%)	713 (33%)	744 (34%)	744 (34%)
Statins	835 (38%)	912 (42%)	985 (46%)	965 (45%)
Oral anticoagulants	108 (5%)	111 (5%)	141 (7%)	186 (9%)
Insulin	38 (2%)	45 (2%)	66 (3%)	68 (3%)
Other hypoglycemics	196 (9%)	219 (10%)	264 (12%)	234 (11%)
PPI	1,026 (47%)	992 (46%)	1,063 (49%)	1,216 (56%)
Corticosteroids (inhaled)	203 (9%)	261 (12%)	302 (14%)	353 (16%)
Bronchodilators	321 (15%)	368 (17%)	397 (18%)	490 (23%)

Values are median (IQR) or; n (%) for categorical variables. SI conversion factor: To convert C-reactive protein from mg/dL to mg/L, or hemoglobin from g/dL to g/L, multiply by 10. <sup>a</sup>Most recent blood tests and medication use in the last 6 months before the index date. <sup>b</sup>eGFR, estimated glomerular filtration rate using CKD-EPI equation. <sup>c</sup>Solely or in combination.

Abbreviations as in [Table 1](#).

and less likely to have comorbidities; in other words, they had a lower risk profile ([Supplemental Table 7](#)).

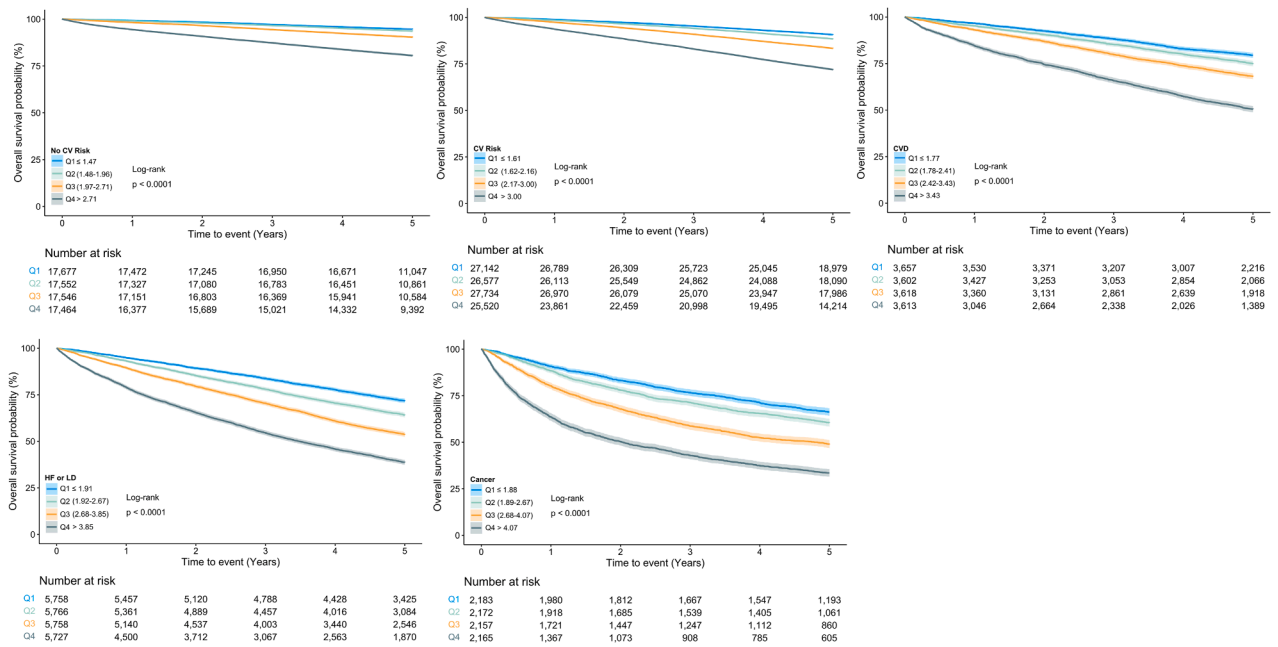
[Tables 1 and 2](#) illustrate baseline characteristics of each cohort, divided by quartiles of NLR.

Across all CV diagnostic and cancer groups, those in the highest quartile of NLR were more likely to be older and to be men and to have lower hemoglobin and eGFR than those in the lowest quartile. There was also a substantial increase in C-reactive protein (CRP) levels among those in the highest NLR quartile. However, CRP was missing for >60% of the population ([Supplemental Table 6](#)).

During a median follow-up of 5.0 years IQR (4.4-5.0), 42,099 (19%) people died. Compared to others, patients with cancer had the highest all-cause mortality, followed by those with HF/LD ([Supplemental Figure 2](#)). For all cohorts ([Figure 3](#)), patients in the highest quartile of NLR had the highest probability of mortality. In full adjusted Cox proportional hazard models, NLR was associated with a higher mortality across all groups ([Figure 4, Table 3](#)).

In a sensitivity analysis that excluded 799 people (9% of the total cancer population) with a history of hematological malignancies, findings did not

**FIGURE 3** Kaplan-Meier Estimates of 5-Year Survival by Quartiles of Neutrophil-to-Lymphocyte Ratio



Abbreviations as in Figure 1.

substantially change: compared to the lowest quartile, patients with cancer in the highest NLR quartile had a greater risk of death (HR [95% CI]; 2.46 [2.23-2.71], when the model was adjusted for age, sex, eGFR, and hemoglobin) (Supplemental Figure 3).

Patients with HF or CVD were more likely to die of CV causes compared to other diagnostic groups. For patients without cancer, those in the highest quartile of NLR had more deaths due to infection, and less due to cancer, compared to the lowest quartile. Most patients with cancer on the index date died of cancer, particularly those in the highest quartile of NLR (Supplemental Figure 4).

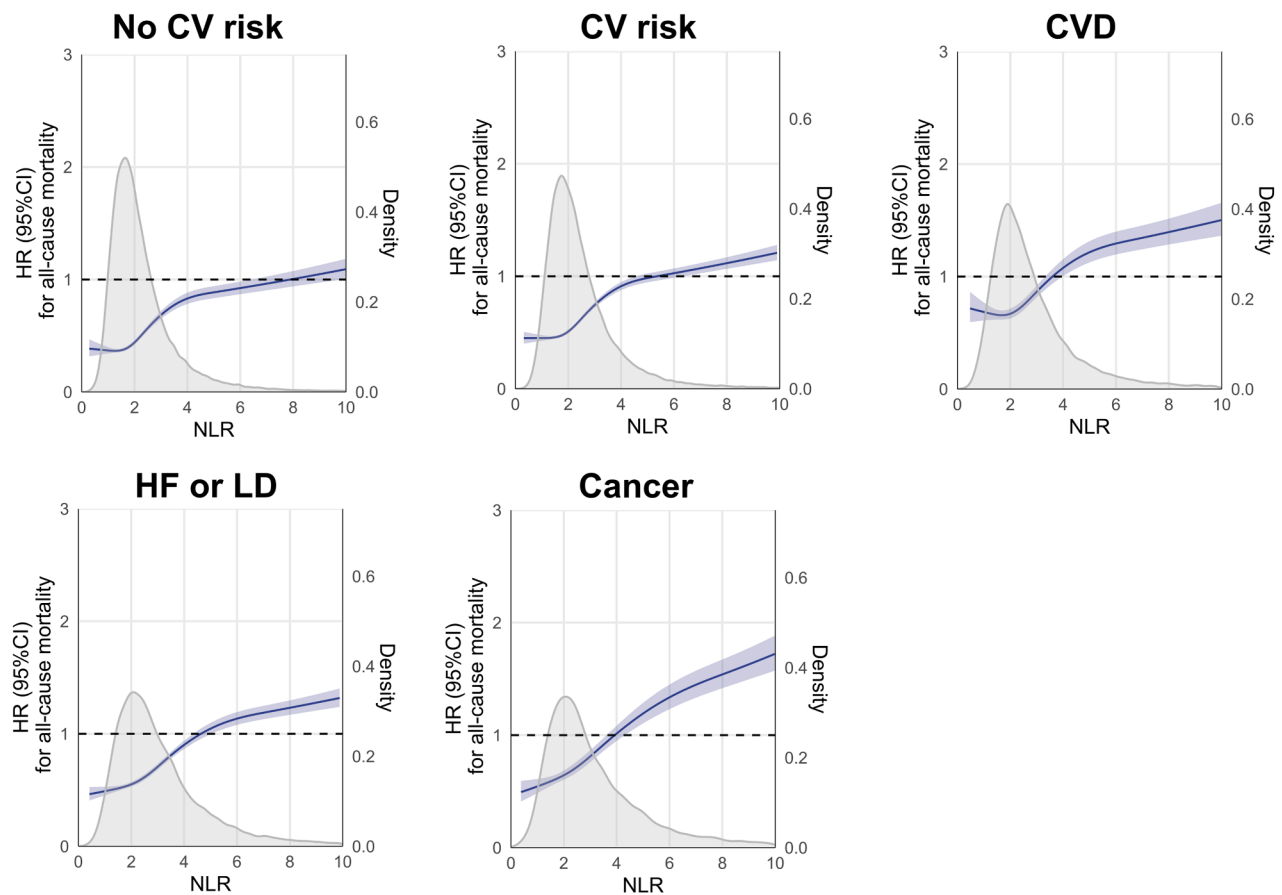
## DISCUSSION

This analysis shows that NLR, a routinely measured, readily available, blood marker that can easily be obtained from EPRs (Central Illustration), might be used to stratify mortality risk for a broad range of patients at risk or with CVD or cancer.

Older age was associated with higher values of NLR. This might just reflect a higher burden of comorbidities and disease in older people. Age might depress neutrophil function, but it has little effect on their numbers.<sup>22,23</sup> However, aging is associated with

a decline in circulating lymphocytes,<sup>24,25</sup> and consequently an increase in NLR. Thus, a higher NLR might reflect both a greater disease burden and the effects of age on the immune system. As expected, we found that a higher NLR was directly associated with another marker of inflammation, CRP. Heightened inflammation may cause coronary and systemic vascular damage,<sup>9</sup> impair cardiac function, or promote tumor development and progression leading to worse clinical outcomes.<sup>26,27</sup> Anti-inflammatory therapy with canakinumab, or colchicine but not methotrexate has been successful in reducing the risk of CV events in individuals with a previous myocardial infarction, associated with reductions in CRP.<sup>6,28-31</sup> Canakinumab reduced NLR but methotrexate lowered the lymphocyte count and therefore increased NLR.<sup>32</sup> Finally, modulation of the immune system through immune checkpoint inhibitors has modified the history of disease of many types of cancers.<sup>33</sup> NLR has been suggested as a biomarker for tumor response to immune checkpoint inhibitors, with decrease in NLR after therapy associated with better patient outcomes.<sup>34,35</sup>

Our findings agree with, and expand on, those from other large-scale population studies, suggesting that higher NLR predicts a higher mortality.<sup>36,37</sup>

**FIGURE 4** Association Between Baseline Neutrophil-to-Lymphocyte Ratio and 5-Year All-Cause Mortality

Shading indicates 95% CI; and solid lines, HRs adjusted for age, sex, eGFR, and hemoglobin. Density plot showing the distribution of NLR in each group. Survival associations were assessed with restricted cubic splines with knots at 5th, 35th, 65th, and 95th percentiles of neutrophil-lymphocyte ratio distribution. Abbreviations as in Figure 1.

Interestingly, the association between NLR and mortality persists even among individuals apparently free of risk factors for CVD. For this group, those in the highest quartile of NLR had a 1-year mortality of almost 10%, suggesting the presence of undiagnosed severe disease. These findings support those from a population-based, prospective cohort study in an older community-dwelling population from the Netherlands ( $n = 8,715$ ), of whom  $<10\%$  had a history of CVD or cancer. In that cohort (mean age 66 years), participants in the highest quartile of NLR had a greater risk of death compared to the lowest quartile.<sup>38</sup> In another study that combined 2 Dutch cohorts ( $n = 14,433$ ), of younger (mean age 47.3 years) and healthier people, NLR did not associate with all-cause mortality.<sup>39</sup>

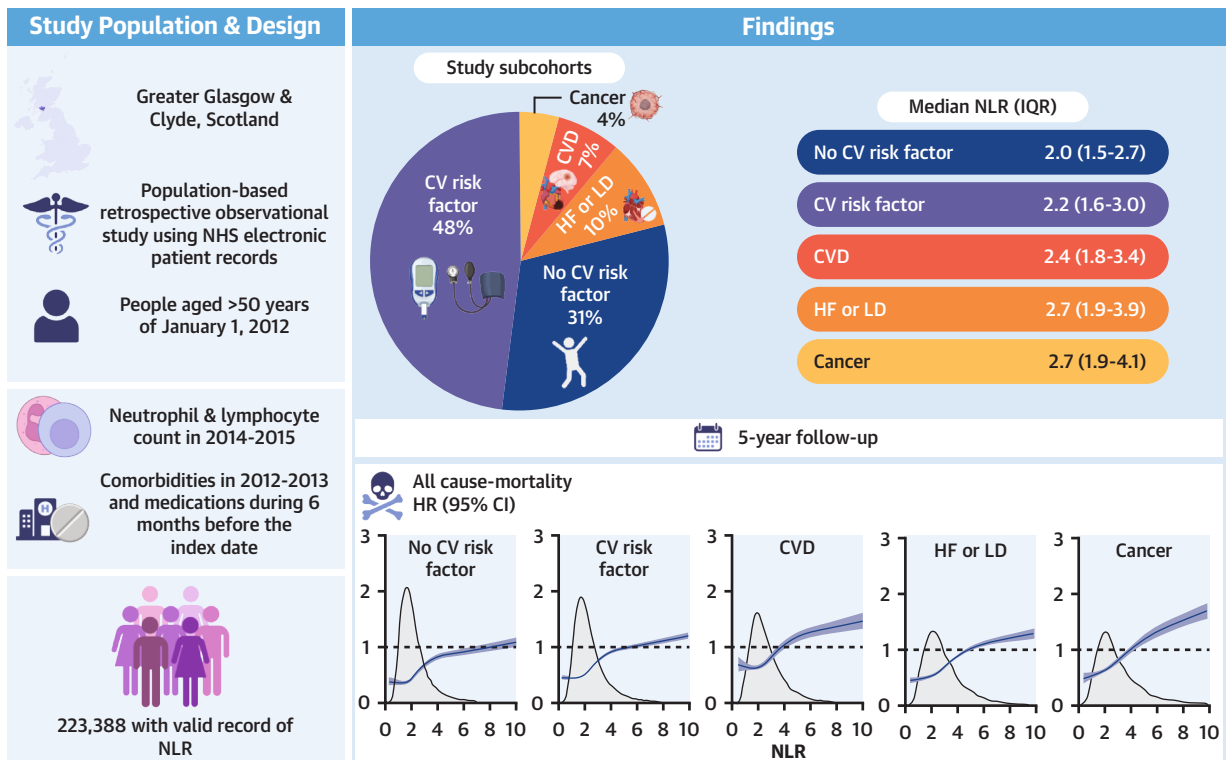
Overall, our findings suggest that the integration of NLR into routine clinical practice could enhance

the early identification of high-risk patients with or at risk of a range of different diseases in primary and secondary care. One of the strengths of our study is the use of large, routinely collected population-level data, which enhances the generalizability of our findings.

However, further research is warranted to elucidate the underlying mechanisms of these associations, and to refine the clinical applications of NLR in various clinical contexts.

**STUDY LIMITATIONS.** The observational nature of this study precludes causal inferences. Unlike registries and clinical trials, our data were derived from EPRs of people who had some reason for having a blood test. Additionally, missing or inaccurately recorded information in the EPRs could lead to misclassification of patient characteristics or

**CENTRAL ILLUSTRATION Association Between NLR and All-Cause Mortality in Different Diagnostic Groups**



Morsy MI, et al. JACC Adv. 2026;5(1):102362.

Created in BioRender. Maffia, P. (2025, <https://BioRender.com/ucz89qr>). NHS = National Health Service; other abbreviations as in Figure 1.

outcomes, potentially biasing our results. Although we excluded blood tests performed during hospitalizations and those that suggested possible undiagnosed hematological cancers, other potential confounders such as concurrent infections, medications, and/or other undiagnosed or diagnosed conditions requiring long-term monitoring might have influenced NLR and affected our results. Importantly, smoking, blood pressure and body mass index might influence NLR and prognosis,<sup>40</sup> but this information is not captured in the EPRs to which we had access. Additionally, NLR was measured at a single time point; longitudinal changes in NLR were not assessed.

**CONCLUSIONS**

NLR is a simple, widely available blood marker. Higher values of NLR are associated with greater age, higher blood CRP, a higher prevalence of CV and non-CV comorbidities and cancer, and a greater

risk of death. Further studies should be done to elucidate the mechanisms linking NLR with adverse outcomes, to determine the value of adding it to CV risk scores, and to explore its potential as a therapeutic target.

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**TABLE 3 Associations With 5-Year All-Cause Mortality in Patients With or Without Cardiovascular Risk Factors/Disease or Cancer by Quartiles of NLR at Baseline**

Group, NLR quartile	Model 1			Model 2		
	No. of Events/ No. of Patients	Rate per 1,000 Person-Years (95% CI)	HR (95% CI)	No. of Events/ No. of Patients	Rate per 1,000 Person-Years (95% CI)	HR (95% CI)
<b>No CV risk</b>						
Q1 ≤1.47	910/17,677	10.97 (10.27-11.71)	Reference	826/15,664	11.25 (10.50-12.04)	Reference
Q2 (1.48-1.96)	1,077/17,552	13.12 (12.35-13.92)	1.10 (1.01-1.20)	960/15,558	13.2 (12.37-14.06)	1.10 (1.00-1.21)
Q3 (1.97-2.71)	1,620/17,546	20.12 (19.15-21.12)	1.47 (1.35-1.59)	1,446/15,691	20.08 (19.05-21.14)	1.41 (1.29-1.54)
Q4 >2.71	3,281/17,464	43.77 (42.29-45.30)	2.40 (2.22-2.58)	2,974/15,736	44.09 (42.52-45.70)	2.18 (2.02-2.36)
<b>CV risk</b>						
Q1 ≤1.61	2,453/27,142	19.26 (18.51-20.04)	Reference	2,351/25,863	19.38 (18.60-20.18)	Reference
Q2 (1.62-2.16)	2,993/26,577	24.26 (23.40-25.15)	1.13 (1.07-1.19)	2,865/25,413	24.29 (23.41-25.19)	1.12 (1.06-1.18)
Q3 (2.17-3.00)	4,503/27,734	35.93 (34.89-36.99)	1.47 (1.40-1.54)	4,306/26,620	35.77 (34.71-36.85)	1.42 (1.35-1.49)
Q4 >3.00	6,996/25,520	65.46 (63.94-67.02)	2.23 (2.13-2.33)	6,694/24,509	65.15 (63.6-66.73)	2.07 (1.98-2.17)
<b>CVD</b>						
Q1 ≤1.77	734/3,657	45.57 (42.33-48.99)	Reference	692/3,444	45.63 (42.29-49.16)	Reference
Q2 (1.78-2.41)	880/3,602	56.97 (53.27-60.86)	1.12 (1.01-1.23)	829/3,411	56.57 (52.79-60.56)	1.11 (1.01-1.23)
Q3 (2.42-3.43)	1,127/3,618	76.24 (71.86-80.83)	1.29 (1.18-1.42)	1,053/3,408	75.42 (70.93-80.12)	1.26 (1.14-1.39)
Q4 >3.43	1,747/3,613	138.92 (132.48-145.59)	2.02 (1.85-2.20)	1,625/3,396	136.64 (130.07-143.44)	1.87 (1.70-2.04)
<b>HF/LD</b>						
Q1 ≤1.91	1,595/5,758	65.24 (62.08-68.52)	Reference	1,532/5,550	64.96 (61.75-68.29)	Reference
Q2 (1.92-2.67)	2,034/5,766	87.66 (83.89-91.55)	1.17 (1.10-1.25)	1,964/5,565	87.65 (83.82-91.61)	1.15 (1.08-1.23)
Q3 (2.68-3.85)	2,617/5,758	122.94 (118.27-127.74)	1.53 (1.44-1.63)	2,531/5,574	122.75 (118.01-127.63)	1.47 (1.38-1.57)
Q4 >3.85	3,451/5,727	196.65 (190.15-203.33)	2.30 (2.17-2.44)	3,316/5,523	195.36 (188.76-202.12)	2.10 (1.98-2.24)
<b>Cancer</b>						
Q1 ≤1.88	728/2,183	83.44 (77.49-89.73)	Reference	701/2,083	84.42 (78.29-90.91)	Reference
Q2 (1.89-2.67)	846/2,172	103.68 (96.81-110.91)	1.17 (1.06-1.30)	819/2,091	104.34 (97.31-111.73)	1.20 (1.08-1.32)
Q3 (2.68-4.07)	1,087/2,157	154.46 (145.41-163.92)	1.65 (1.50-1.81)	1,037/2,065	153.66 (144.45-163.30)	1.59 (1.44-1.75)
Q4 >4.07	1,420/2,165	262.12 (248.66-276.11)	2.61 (2.39-2.86)	1,373/2,082	264.92 (251.09-279.31)	2.30 (2.10-2.52)

Model 1: adjusted for age and sex. Model 2: adjusted for age, sex, eGFR, and hemoglobin.  
NLR = neutrophil-to-lymphocyte ratio; other abbreviations as in Table 1.

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## REFERENCES

1. Wilcox NS, Amit U, Reibel JB, Berlin E, Howell K, Ky B. Cardiovascular disease and cancer: shared risk factors and mechanisms. *Nat Rev Cardiol.* 2024. <https://doi.org/10.1038/s41569-024-01017-x>
2. Libby P, Kobold S. Inflammation: a common contributor to cancer, aging, and cardiovascular diseases-expanding the concept of cardiology. *Cardiovasc Res.* 2019;115:824-829. <https://doi.org/10.1093/cvr/cvz058>
3. Libby P, Loscalzo J, Ridker PM, et al. Inflammation, immunity, and infection in atherothrombosis: JACC review topic of the week. *J Am Coll Cardiol.* 2018;72:2071-2081. <https://doi.org/10.1016/j.jacc.2018.08.1043>
4. Guzik TJ, Nosalski R, Maffia P, Drummond GR. Immune and inflammatory mechanisms in hypertension. *Nat Rev Cardiol.* 2024;21:396-416. <https://doi.org/10.1038/s41569-023-00964-1>
5. Hiam-Galvez KJ, Allen BM, Spitzer MH. Systemic immunity in cancer. *Nat Rev Cancer.* 2021;21:345-359. <https://doi.org/10.1038/s41568-021-00347-z>
6. Nelson K, Fuster V, Ridker PM. Low-dose colchicine for secondary prevention of coronary artery disease: JACC review topic of the week. *J Am Coll Cardiol.* 2023;82:648-660. <https://doi.org/10.1016/j.jacc.2023.05.055>
7. Pugliese NR, Pellicori P, Filidei F, et al. Inflammatory pathways in heart failure with preserved left ventricular ejection fraction: implications for future interventions. *Cardiovasc Res.* 2023;118:3536-3555. <https://doi.org/10.1093/cvr/cvac133>
8. Shoaran M, Maffia P. Tackling inflammation in atherosclerosis. *Nat Rev Cardiol.* 2024;21:442. <https://doi.org/10.1038/s41569-024-01007-z>
9. Engelen SE, Robinson AJB, Zurke YX, Monaco C. Therapeutic strategies targeting inflammation and immunity in atherosclerosis: how to proceed? *Nat Rev Cardiol.* 2022;19:522-542. <https://doi.org/10.1038/s41569-021-00668-4>
10. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to lymphocyte ratio: an emerging marker of the relationships between the immune system and diseases. *Int J Mol Sci.* 2022;23. <https://doi.org/10.3390/ijms23073636>
11. NHS Research Scotland. Data safe haven. Accessed October 14, 2025. <https://www.nhsresearchscotland.org.uk/research-in-scotland/data/safe-havens>
12. Friday JM, Cleland JG, Pellicori P, et al. Loop diuretic utilisation with or without heart failure: impact on prognosis. *Eur Heart J.* 2024. <https://doi.org/10.1093/eurheartj/ehae345>
13. Denaxas SC, George J, Herrett E, et al. Data resource profile: cardiovascular disease research using linked bespoke studies and electronic health records (CALIBER). *Int J Epidemiol.* 2012;41:1625-1638. <https://doi.org/10.1093/ije/dys188>
14. Reeves D, Springate DA, Ashcroft DM, et al. Can analyses of electronic patient records be independently and externally validated? The effect of statins on the mortality of patients with ischaemic heart disease: a cohort study with nested case-control analysis. *BMJ Open.* 2014;4:e004952. <https://doi.org/10.1136/bmjopen-2014-004952>
15. Conrad N, Judge A, Tran J, et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. *Lancet.* 2018;391:572-580. [https://doi.org/10.1016/S0140-6736\(17\)32520-5](https://doi.org/10.1016/S0140-6736(17)32520-5)
16. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: recommendations of the NKF-ASN task force on reassessing the inclusion of race in diagnosing kidney disease. *Am J Kidney Dis.* 2022;79:268-288.e261. <https://doi.org/10.1053/j.ajkd.2021.08.003>
17. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009;150:604-612. <https://doi.org/10.7326/0003-4819-150-9-200905050-00006>
18. Graham FJ, Friday JM, Pellicori P, Greenlaw N, Cleland JG. Assessment of haemoglobin and serum markers of iron deficiency in people with cardiovascular disease. *Heart.* 2023;109:1294-1301. <https://doi.org/10.1136/heartjnl-2022-322145>
19. Harrell FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis, 2nd Edition.* Cham: Springer Cham; 2015. <https://doi.org/10.1007/978-3-319-19425-7>
20. Atkinson AC. A note on the generalized information criterion for choice of a model. *Biometrika.* 1980;67:413-418. <https://doi.org/10.1093/biomet/67.2.413>
21. Vanhouwelingen JC, LeCessie S. Predictive value of statistical-models. *Statistics in Medicine.* 1990;9:1303-1325. <https://doi.org/10.1002/sim.4780091109>
22. Van Avondt K, Strecker JK, Tulotta C, Minnerup J, Schulz C, Soehlein O. Neutrophils in aging and aging-related pathologies. *Immunol Rev.* 2023;314:357-375. <https://doi.org/10.1111/imr.13153>
23. Valiathan R, Ashman M, Asthana D. Effects of ageing on the immune system: infants to elderly. *Scand J Immunol.* 2016;83:255-266. <https://doi.org/10.1111/sji.12413>
24. Mittelbrunn M, Kroemer G. Hallmarks of T cell aging. *Nat Immunol.* 2021;22:687-698. <https://doi.org/10.1038/s41590-021-00927-z>
25. Goronzy JJ, Weyand CM. Mechanisms underlying T cell ageing. *Nat Rev Immunol.* 2019;19:573-583. <https://doi.org/10.1038/s41577-019-0180-1>
26. Coussens LM, Werb Z. Inflammation and cancer. *Nature.* 2002;420:860-867. <https://doi.org/10.1038/nature01322>
27. Greten FR, Grivennikov SI. Inflammation and cancer: triggers, mechanisms, and consequences. *Immunity.* 2019;51:27-41. <https://doi.org/10.1016/j.immuni.2019.06.025>
28. Ridker PM, Everett BM, Thuren T, et al. Anti-inflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med.* 2017;377:1119-1131. <https://doi.org/10.1056/NEJMoa1707914>
29. Ridker PM, Everett BM, Pradhan A, et al. Low-dose methotrexate for the prevention of atherosclerotic events. *N Engl J Med.* 2019;380:752-762. <https://doi.org/10.1056/NEJMoa1809798>
30. Ridker PM, MacFadyen JG, Everett BM, et al. Relationship of C-reactive protein reduction to cardiovascular event reduction following treatment with canakinumab: a secondary analysis from the CANTOS randomised controlled trial. *Lancet.* 2018;391:319-328. [https://doi.org/10.1016/S0140-6736\(17\)32814-3](https://doi.org/10.1016/S0140-6736(17)32814-3)
31. Fiolet ATL, Opstal TSJ, Mosterd A, et al. Efficacy and safety of low-dose colchicine in patients with coronary disease: a systematic review and meta-analysis of randomized trials. *Eur Heart J.* 2021;42:2765-2775. <https://doi.org/10.1093/eurheartj/ehab115>
32. Adamstein NH, MacFadyen JG, Rose LM, et al. The neutrophil-lymphocyte ratio and incident atherosclerotic events: analyses from five contemporary randomized trials. *Eur Heart J.* 2021;42:896-903. <https://doi.org/10.1093/eurheartj/ehaa1034>
33. Robert C. A decade of immune-checkpoint inhibitors in cancer therapy. *Nat Commun.* 2020;11:3801. <https://doi.org/10.1038/s41467-020-17670-y>
34. Valero C, Lee M, Hoen D, et al. Pretreatment neutrophil-to-lymphocyte ratio and mutational burden as biomarkers of tumor response to immune checkpoint inhibitors. *Nat Commun.* 2021;12:729. <https://doi.org/10.1038/s41467-021-20935-9>
35. Cassidy MR, Wolchok RE, Zheng J, et al. Neutrophil to lymphocyte ratio is associated with outcome during Ipilimumab treatment. *EBioMedicine.* 2017;18:56-61. <https://doi.org/10.1016/j.ebiom.2017.03.029>
36. Larsen MK, Skov V, Kjaer L, et al. Neutrophil-to-lymphocyte ratio and all-cause mortality with and without myeloproliferative neoplasms-a Danish longitudinal study. *Blood Cancer J.* 2024;14:28. <https://doi.org/10.1038/s41408-024-00994-z>
37. Song M, Graubard BI, Rabkin CS, Engels EA. Neutrophil-to-lymphocyte ratio and mortality in the United States general population. *Sci Rep.* 2021;11:464. <https://doi.org/10.1038/s41598-020-79431-7>

38. Fest J, Rüter TR, Groot Koerkamp B, et al. The neutrophil-to-lymphocyte ratio is associated with mortality in the general population: the rotterdam study. *Eur J Epidemiol*. 2019;34:463-470. <https://doi.org/10.1007/s10654-018-0472-y>
39. Abete I, Lu Y, Lassale C, Verschuren M, van der Schouw Y, Bueno-de-Mesquita B. White cell counts in relation to mortality in a general population of cohort study in the Netherlands: a mediating effect or not? *BMJ Open*. 2019;9:e030949. <https://doi.org/10.1136/bmjopen-2019-030949>
40. Furutate R, Ishii T, Motegi T, et al. The neutrophil to lymphocyte ratio is related to disease severity and exacerbation in patients with chronic obstructive pulmonary disease. *Intern Med*. 2016;55:223-229. <https://doi.org/10.2169/internalmedicine.55.5772>

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**KEY WORDS** cardiovascular disease, cancer, epidemiology, heart failure, mortality, neutrophil-to-lymphocyte ratio

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**APPENDIX** For supplemental tables and figures, please see the online version of this paper.