Supplementary methods

Blood and biochemical parameters

Blood samples were collected at baseline (2005-2010) in participants who had fasted overnight and had refrained from smoking for at least 6 h.

Hemochromocytometric analyses were performed on EDTA anticoagulated freshly collected blood by a cell counter (Coulter HMX, Beckman Coulter, IL, Milan, Italy) within 3 hours from venipuncture.

Quality control was performed by using three different levels of standards Abnormal 1 (Abn1) a pathologically high control, Abnormal 2 (Abn2) a pathologically low control and normal (Coulter HMX, Beckman Coulter). The coefficients of variability (CV) for Abn I, Abn II and normal standards were respectively 6.2%, 3.3%, and 3.0%, for white blood cells, 2.4%; 2.7% and 1.4%, for MPV; 7.6%, 4.4% and 4.1%, for Plt, 3.0%, 1.0% and 2.3% for PDW.

Lipids (total cholesterol, HDL-cholesterol, triglycerides) and blood glucose were assayed in serum samples by enzymatic reaction methods using an automatic analyzer (ILab 350, Instrumentation Laboratory, Milan, Italy) and quality control for lipids and glucose were obtained by two commercial standards SeraChem® 1 (for normal levels) and SeraChem® 2 (for pathological high levels); the CVs of these two commercial standards were respectively 4.9% and 5.2% for total blood cholesterol, 3.2% and 3.0% for HDL-cholesterol, 5.2% and 5.3% for triglycerides, 4.7% and 4.1% for blood glucose.

High-sensitivity C-reactive protein (hs-CRP) was measured in fresh serum samples by a particle-enhanced immune-turbidimetric assay (ILab 350, Instrumentation Laboratory, Milan, Italy). Quality control for hs-CRP was maintained using an in-house serum pool and a commercial laboratory standard; inter-day CVs for hs-CRP were 4.2% and 5.5%, respectively.

D-dimer levels were measured on fresh citrated plasma by an automated latex-enhanced immunoassay (HemosIL-IL, Milan, Italy). Quality control was maintained using an internal laboratory standard in-house plasma pool. Inter and intra-day variability coefficients were 5.4% and 7.6%, respectively.

Markers of renal function (Cystatin C, Creatinine), were measured subsequently on thawed samples stored in liquid nitrogen vapors at the Biological Bank of the Moli-sani Study (http://www.neuromed.it/biobanking-centre/) in the framework of the collaborative BiomarCaRE research project (EUFP7, HEALTH-F2-2011-278913) whose primary objective is to assess the value of established and emerging biomarkers for CVD risk prediction by using data from 23 cohorts across Europe.[1,2]

In a sub-sample of the cohort (n=14,335) fibrinogen levels were measured in citrated plasma samples by the Clauss method using the STA Liquid FIB reagent on the STA-R Max (Diagnostica Stago, France) according to the manufacturers' recommendations at the Department of Functional Coagulation, Synapse Research Institute, Maastricht, the Netherlands.[3] Both intra- and inter-assay CVs were 2.1% for samples within the normal range of fibrinogen specified to be 2-4 g/L in healthy subjects.

Covariate assessment

History of CVD (including angina, myocardial infarction, revascularization procedures, and cerebrovascular events), heart failure, atrial fibrillation, and cancer were self-reported with confirmation by medical records and drug therapy provided during the baseline visit. Current pharmacological treatment (*e.g.*, use of antiplatelet drugs, hormone replacement therapy, and oral contraceptives), and menopause status were also collected by direct interviews with the participants.

Systolic and diastolic blood pressure (BP) were measured by an automatic device (OMRON-HEM-705CP) three times on the non-dominant arm and the average of the last two values was taken as the BP. Measurements were made in a quiet room with a comfortable temperature with the participants lying down for at least 5 minutes. Hypertension was defined as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg or treatment for hypertension. Hypercholesterolemia was defined as total cholesterol ≥240 mg/dL or by the use of medication. Diabetes was defined as blood glucose ≥126 mg/dl or by use of pharmacological treatment.

Body mass index was calculated as kg/m^2 and then grouped into three categories: normal (≤25), overweight (>25 and <30), or obese (≥30). Subjects were classified as never-smokers, current smokers, or ex-smokers (quitting for at least 1 year). Leisure-time physical activity was expressed as daily energy expenditure in metabolic equivalent task hours (MET-h/d) for sport, walking, and gardening. Educational attainment was based on the highest qualification attained and categorized as low (up to

lower secondary school; approximately ≤8 years of study) or high (upper secondary education or higher; approximately ≥9 years of study). Household income was a three-level variable (≤40,000; >40,000 euros/year), with missing values collapsed into a non-respondent category. Urban or rural environments were defined based on the urbanization level as described by the European Institute of Statistics (EUROSTAT definition) and obtained by the tool 'Atlante Statistico dei Comuni' provided by the Italian National Institute of Statistics.[4] Food intake during the year before enrolment was assessed by the validated Italian EPIC food frequency questionnaire,[5] and adherence to the Mediterranean was defined according to the Mediterranean Diet Score.[6]

References

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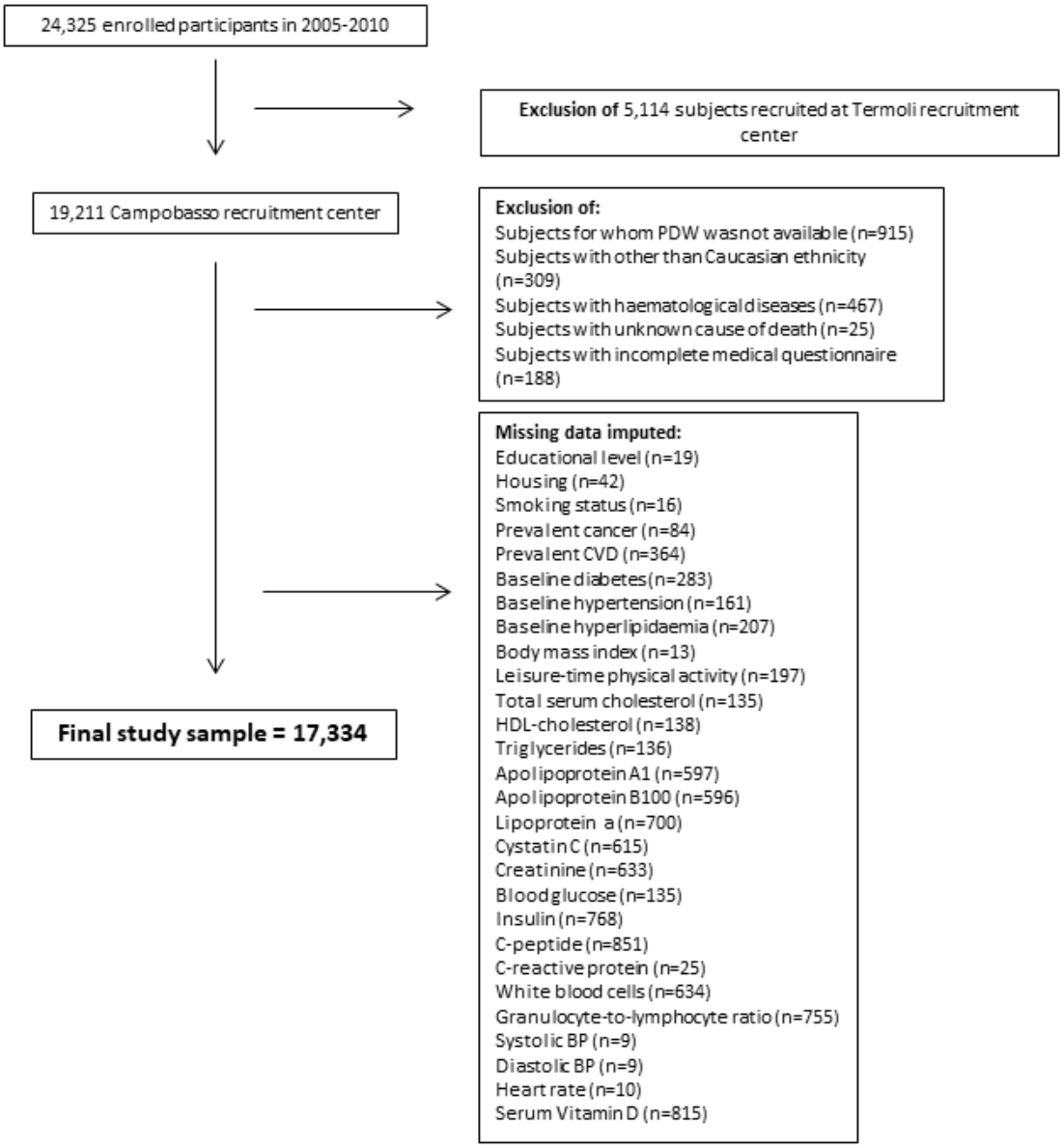
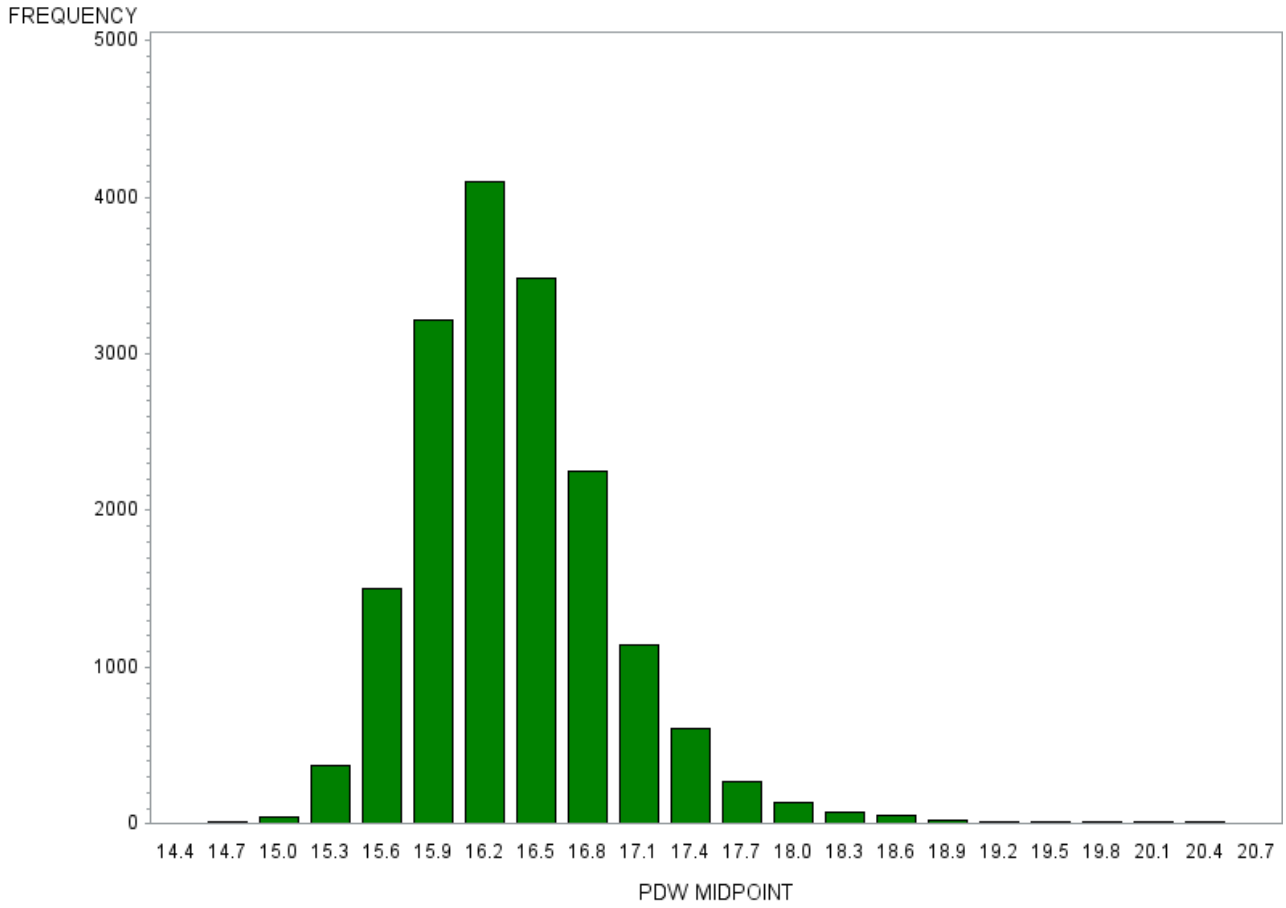
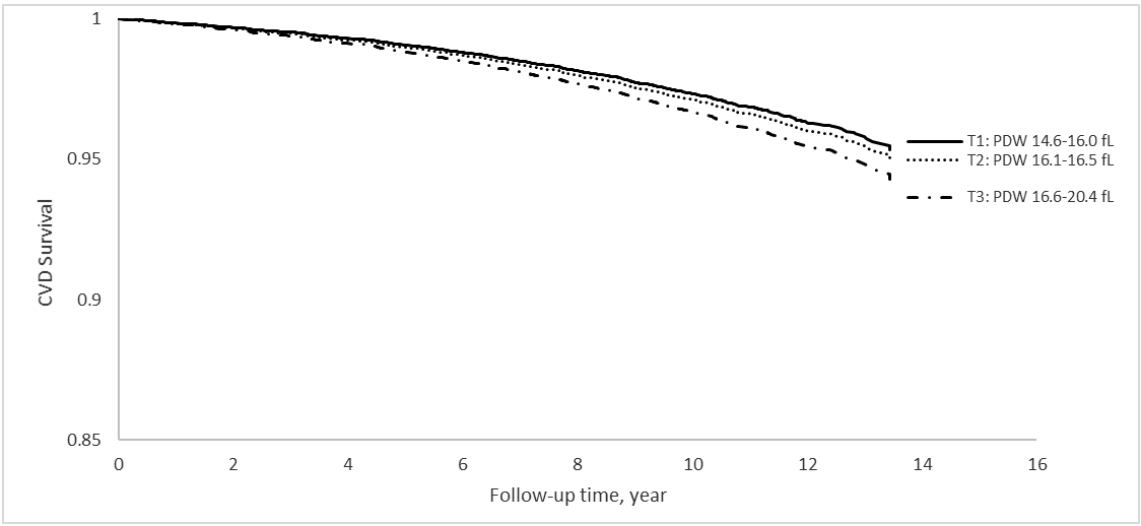
6. Ghaffari S, Parvizian N, Pourafkari L, et al. Prognostic value of platelet indices in patients with acute pulmonary thromboembolism. J Cardiovasc Thorac Res 2020;12:56-62.

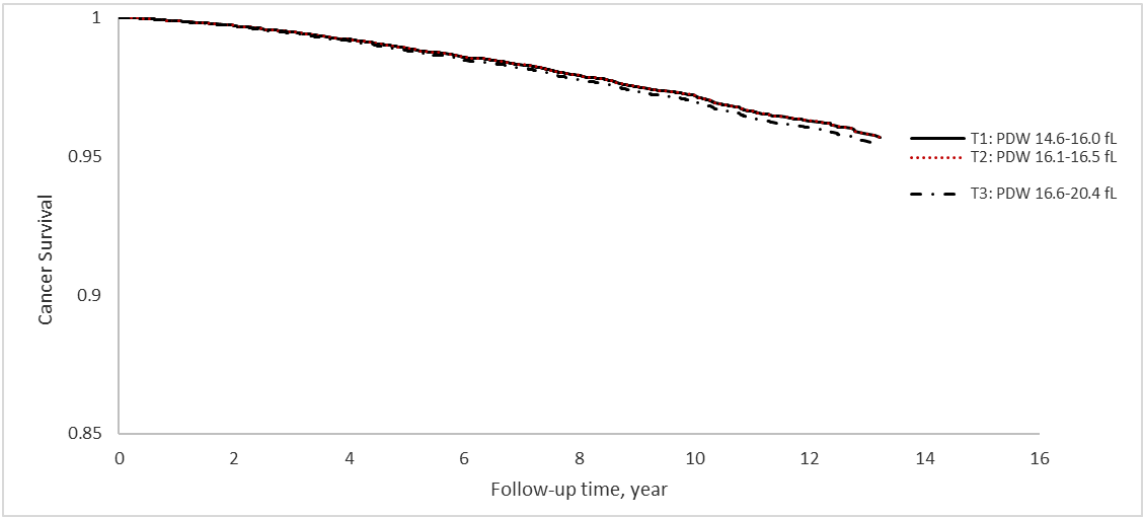


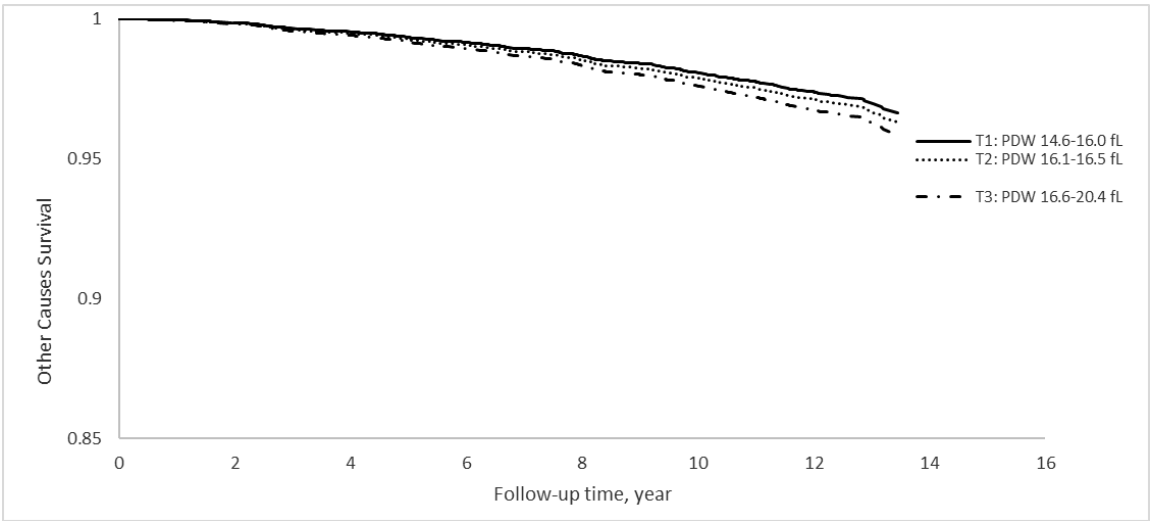
Supplementary Figure S1. Flow chart of selection of the studied population among Moli-sani participants. The groups of eliminated participants (out of the 24,325 recruited at baseline) are overlaid. The final study sample cannot be calculated as a subtraction of the sum of eliminated groups out of the recruited subjects at baseline.



Supplementary Figure S2. Platelet distribution width (fL) distribution in the Moli-sani cohort.







Supplementary Figure S3. Multivariable survival estimates for cardiovascular disease (panel A, P=0.058), cancer (panel B, P=0.73) and other-cause (panel C, P=0.19) mortality according to platelet distribution width tertiles. Multivariable survival curves were obtained from the multivariable model adjusted for age, sex, hematocrit; systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, Cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio, platelet count, mean platelet volume, white blood cell count by using the first imputed dataset. The other imputed datasets are similar and thus omitted.

Supplementary Table S1. Hazard ratios (95% confidence intervals) for all-cause, cardiovascular, cancer and other-cause mortality, according to platelet distribution width tertiles (17,334).

	PDW tertiles			P trend	Continuous (for every SD increase of PDW)	P value
	T1	T2	T3			
PDW, fL range	14.6-16.0	16.1-16.5	16.6-20.4			
N	5,145	6,477	5,712			
Person-years	58,587.0	73,282.4	63,652.0			
All-cause mortality						
N of events	351	543	641			
Crude model	ref.	1.24 (1.08-1.42)	1.69 (1.48-1.92)	<.0001	1.19 (1.14-1.25)	<.0001
Model 1	ref.	1.07 (0.93-1.23)	1.24 (1.08-1.41)	0.0009	1.06 (1.02-1.12)	0.011
Model 2	ref.	1.06 (0.93-1.22)	1.21 (1.06-1.39)	0.0030	1.05 (1.01-1.11)	0.029
Model 3	ref.	1.06 (0.92-1.21)	1.20 (1.04-1.37)	0.0066	1.05 (1.00-1.10)	0.051
Cardiovascular mortality						
N of events	127	201	251			
Crude model	ref.	1.27 (1.01-1.58)	1.83 (1.48-2.26)	<.0001	1.22 (1.13-1.31)	<.0001
Model 1	ref.	1.08 (0.87-1.35)	1.31 (1.06-1.63)	0.0088	1.08 (1.00-1.17)	0.053
Model 2	ref.	1.08 (0.86-1.35)	1.25 (1.00-1.55)	0.039	1.06 (0.98-1.14)	0.16
Model 3	ref.	1.10 (0.88-1.37)	1.29 (1.03-1.62)	0.019	1.07 (0.99-1.16)	0.10
Cancer mortality						
N of events	140	203	218			
Crude model	ref.	1.16 (0.94-1.44)	1.44 (1.16-1.78)	0.0006	1.12 (1.04-1.21)	0.0030
Model 1	ref.	1.01 (0.82-1.26)	1.09 (0.88-1.35)	0.41	1.01 (0.93-1.10)	0.74
Model 2	ref.	1.00 (0.81-1.25)	1.08 (0.87-1.35)	0.43	1.01 (0.93-1.10)	0.79
Model 3	ref.	1.00 (0.80-1.24)	1.07 (0.86-1.34)	0.50	1.01 (0.93-1.10)	0.86
Other-cause mortality						
N of events	84	139	172			
Crude model	ref.	1.32 (1.01-1.74)	1.89 (1.46-2.46)	<.0001	1.25 (1.14-1.36)	<.0001
Model 1	ref.	1.15 (0.88-1.51)	1.38 (1.06-1.80)	0.014	1.11 (1.01-1.22)	0.024
Model 2	ref.	1.16 (0.88-1.52)	1.40 (1.07-1.83)	0.011	1.12 (1.02-1.22)	0.020
Model 3	ref.	1.11 (0.85-1.47)	1.27 (0.97-1.68)	0.075	1.08 (0.98-1.19)	0.11

Model 1, adjusted for age, sex, haematocrit; Model 2, Model 1 further adjusted for systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, Cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio; Model 3, Model 2 further adjusted for platelet count, mean platelet volume, white blood cell count. SD, standard deviation; PDW, platelet distribution width.

Supplementary Table S2. Hazard ratios (95% confidence intervals) for all-cause, cardiovascular and cancer mortality, according to platelet distribution width tertiles excluding subjects with missing value for plasmatic fibrinogen (n=14,335).

	PDW tertiles			P trend	Continuous (for every SD increase of PDW)	P value
	T1	T2	T3			
All-cause mortality						
Model 3	ref.	1.07 (0.91-1.24)	1.26 (1.08-1.46)	0.0022	1.07 (1.02-1.13)	0.013
Model 4	ref.	1.06 (0.91-1.23)	1.25 (1.07-1.46)	0.0026	1.07 (1.02-1.13)	0.012
Cardiovascular mortality						
Model 3	ref.	1.15 (0.90-1.47)	1.34 (1.05-1.73)	0.017	1.07 (0.98-1.16)	0.16
Model 4	ref.	1.14 (0.89-1.46)	1.34 (1.04-1.72)	0.020	1.07 (0.98-1.16)	0.16
Cancer mortality						
Model 3	ref.	0.97 (0.75-1.26)	1.16 (0.89-1.49)	0.22	1.07 (0.97-1.17)	0.19
Model 4	ref.	0.97 (0.75-1.25)	1.15 (0.89-1.49)	0.22	1.07 (0.98-1.16)	0.16
Other cause mortality						
Model 3	ref.	1.12 (0.83-1.52)	1.31 (0.97-1.78)	0.070	1.09 (0.98-1.21)	0.098
Model 4	ref.	1.12 (0.82-1.51)	1.31 (0.97-1.77)	0.072	1.09 (0.98-1.21)	0.096

Model 3, adjusted for age, sex, hematocrit, systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, Cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio for platelet count, mean platelet volume, white blood cell count. Model 4, Model 3 plus fibrinogen. SD, standard deviation; PDW, platelet distribution width.

Supplementary Table S3. Sensitivity analyses for the association of platelet distribution width with all-cause and cause specific mortality considering a case complete approach (n=15,868).

	PDW tertiles			P trend	Continuous (for every SD increase of PDW)	P value
	T1	T2	T3			
PDW, fL range	14.6-16.0	16.1-16.5	16.6-20.4			
N	4,717	5,937	5,214			
Person-years	53,718.0	67,346.8	58,294.2			
All-cause mortality						
N of events	310	470	544			
HR (95% CI)	ref.	1.04 (0.90-1.20)	1.16 (1.00-1.34)	0.034	1.03 (0.98-1.09)	0.24
Cardiovascular mortality						
N of events	113	166	207			
HR (95% CI)	ref.	1.02 (0.80-1.29)	1.21 (0.95-1.54)	0.093	1.04 (0.96-1.14)	0.33
Cancer mortality						
N of events	124	179	195			
HR (95% CI)	ref.	1.00 (0.80-1.26)	1.10 (0.87-1.39)	0.39	1.01 (0.93-1.10)	0.82
Other-cause mortality						
N of events	73	125	142			
HR (95% CI)	ref.	1.15 (0.86-1.55)	1.20 (0.89-1.61)	0.24	1.04 (0.94-1.16)	0.45

Model adjusted for age, sex, hematocrit, systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, Cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio, platelet count, mean platelet volume, white blood cell count. SD, standard deviation; PDW, platelet distribution width; HR, hazard ratio; CI, confidence interval.

Supplementary Table S4. Sensitivity analyses for the association of platelet distribution width with all-cause mortality excluding early deaths (follow-up >2 years, n=17,198).

	PDW tertiles			P trend	Continuous (for every SD increase of PDW)	P value
	T1	T2	T3			
PDW, fL range	14.6-16.0	16.1-16.5	16.6-20.4			
N	5,117	6,432	5,649			
Person-years	58,554.9	73,231.4	63,581.4			
All-cause mortality						
N of events	323	498	578			
HR (95% CI)	ref.	1.05 (0.91-1.21)	1.19 (1.03-1.37)	0.014	1.04 (0.98-1.09)	0.19
Cardiovascular mortality						
N of events	121	183	216			
HR (95% CI)	ref.	1.04 (0.82-1.32)	1.19 (0.94-1.51)	0.11	1.05 (0.96-1.14)	0.28
Cancer mortality						
N of events	127	185	199			
HR (95% CI)	ref.	1.00 (0.79-1.25)	1.08 (0.85-1.36)	0.49	1.01 (0.93-1.10)	0.82
		Other-causes mortality				
N of events	75	130	163			
HR (95% CI)	ref.	1.17 (0.88-1.56)	1.37 (1.03-1.83)	0.029	1.08 (0.98-1.19)	0.14

Model adjusted for age, sex, hematocrit, systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, Cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio, platelet count, mean platelet volume, white blood cell count. SD, standard deviation; PDW, platelet distribution width; HR, hazard ratio; CI, confidence interval.

Supplementary Table S5. Subgroup analyses for the association of platelet distribution width with all-cause mortality.

	N of events/ n of subjects	PDW tertiles			P trend	P interaction
		T1	T2	T3		
Age						0.028
<65 years	411/13,176	Ref.	0.93 (0.73-1.19)	0.93 (0.72-1.20)	0.61	
≥65 years	1,124/4,158	Ref.	1.13 (0.96-1.34)	1.34 (1.14-1.58)	0.0003	
Gender						0.70
Men	987/8,395	Ref.	1.04 (0.87-1.25)	1.19 (1.00-1.42)	0.031	
Women	548/8,939	Ref.	1.08 (0.88-1.33)	1.23 (0.99-1.53)	0.068	
Diabetes						0.29
Yes	333/1,695	Ref.	1.29 (0.91-1.82)	1.45 (1.03-2.04)	0.037	
No	1,202/15,639	Ref.	1.03 (0.89-1.19)	1.15 (0.99-1.33)	0.063	
Hypercholesterolemia						0.53
Yes	535/6,013	Ref.	1.10 (0.87-1.38)	1.21 (0.96-1.53)	0.098	
No	1,000/11,321	Ref.	1.04 (0.87-1.23)	1.18 (1.00-1.40)	0.039	
Smoking habits						0.79
No smoking	658/8,708	Ref.	1.13 (0.95-1.38)	1.20 (0.98-1.47)	0.081	
Current smoking	298/3,956	Ref.	0.91 (0.67-1.23)	1.02 (0.75-1.39)	0.81	
Former smoking	579/4,670	Ref.	1.10 (0.86-1.40)	1.33 (1.05-1.68)	0.0091	
WH-ratio						0.30
Abnormal (F: ≥0.85; M: ≥0.90)	1,363/13,611	Ref.	1.09 (0.94-1.26)	1.28 (1.10-1.48)	0.0006	
Normal	172/3,723	Ref.	1.07 (0.74-1.56)	1.12 (0.75-1.65)	0.58	
History of CVD						0.53
Yes	275/908	Ref.	1.26 (0.89-1.79)	1.46 (1.03-2.06)	0.032	
No	1,260/16,426	Ref.	1.02 (0.88-1.19)	1.15 (0.99-1.34)	0.047	
History of cancer						0.88
Yes	140/543	Ref.	0.80 (0.50-1.29)	1.36 (0.87-2.12)	0.10	
No	1,395/16,791	Ref.	1.09 (0.94-1.26)	1.19 (1.03-1.37)	0.017	

Multiplicative interaction between PDW (modelled as tertiles) and the designed effect modifier (sex, age classes, smoking habit, diabetes, hypercholesterolemia, history of CVD, history of cancer) in relation to all-cause mortality was tested with cross-product terms. Multivariable hazard ratios adjusted for age, sex, hematocrit, platelet count, mean platelet volume, white blood cell count, systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio. WH-ratio, waist-hip ratio; CVD, cardiovascular disease; PDW, platelet distribution width.

Supplementary Table S6. Subgroup analyses for the association of platelet distribution width with cardiovascular disease mortality.

	N of events/ n of subjects	PDW tertiles			P trend	P interaction
		T1	T2	T3		
Age						0.80
<65 years	96/13,176	Ref.	1.43 (0.84-2.45)	1.25 (0.71-2.20)	0.52	
≥65 years	483/4,158	Ref.	1.04 (0.81-1.34)	1.33 (1.04-1.70)	0.014	
Gender						0.52
Men	364/8,395	Ref.	1.12 (0.82-1.51)	1.26 (0.93-1.69)	0.11	
Women	215/8,939	Ref.	1.04 (0.74-1.46)	1.39 (0.98-1.97)	0.061	
Diabetes						0.72
Yes	131/1,695	Ref.	1.62 (0.88-2.96)	1.78 (0.97-3.25)	0.087	
No	448/15,639	Ref.	1.02 (0.80-1.31)	1.22 (0.95-1.56)	0.098	
Hypercholesterolemia						0.62
Yes	215/6,013	Ref.	1.15 (0.80-1.66)	1.34 (0.93-1.94)	0.11	
No	364/11,321	Ref.	1.04 (0.78-1.40)	1.24 (0.93-1.65)	0.11	
Smoking habits						0.93
No smoking	268/8,708	Ref.	1.12 (0.81-1.53)	1.30 (0.95-1.79)	0.10	
Current smoking	87/3,956	Ref.	1.03 (0.59-1.82)	0.97 (0.53-1.75)	0.88	
Former smoking	224/4,670	Ref.	1.07 (0.72-1.59)	1.41 (0.96-2.07)	0.044	
WH-ratio						0.57
Abnormal (F: ≥0.85; M: ≥0.90;	529/13,611	Ref.	1.12 (0.88-1.42)	1.38 (1.09-1.75)	0.0048	
Normal	50/3,723	Ref.	1.10 (0.53-2.24)	0.96 (0.47-2.07)	0.91	
History of CVD						0.50
Yes	146/908	Ref.	1.06 (0.66-1.72)	1.42 (0.90-2.25)	0.096	
No	433/16,426	Ref.	1.09 (0.84-1.42)	1.26 (0.97-1.62)	0.078	
History of cancer						0.29
Yes	32/543	Ref.	0.44 (0.16-1.25)	0.74 (0.26-2.12)	0.55	
No	547/16,791	Ref.	1.16 (0.91-1.46)	1.32 (1.05-1.67)	0.017	

Multiplicative interaction between PDW (modelled as tertiles) and the designed effect modifier (sex, age classes, smoking habit, diabetes, hypercholesterolemia, history of CVD, history of cancer) in relation to CVD mortality was tested with cross-product terms. Multivariable hazard ratios adjusted for age, sex, hematocrit, platelet count, mean platelet volume, white blood cell count, systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, cystatin C, Mediterranean Diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio. WH-ratio, waist-hip ratio; CVD, cardiovascular disease; PDW, platelet distribution width.

Supplementary Table S7. Subgroup analyses for the association of platelet distribution width with cancer mortality.

	N of events/ n of subjects	PDW tertiles			P trend	P interaction
		T1	T2	T3		
Age						0.020
<65 years	219/13,176	Ref.	0.77 (0.55-1.06)	0.77 (0.55-1.08)	0.14	
≥65 years	342/4,158	Ref.	1.24 (0.92-1.67)	1.37 (1.01-1.85)	0.046	
Gender						0.87
Men	366/8,395	Ref.	1.02 (0.77-1.36)	1.10 (0.83-1.46)	0.48	
Women	195/8,939	Ref.	0.98 (0.70-1.37)	1.07 (0.75-1.54)	0.72	
Diabetes						0.67
Yes	104/1,695	Ref.	0.97 (0.54-1.73)	1.07 (0.61-1.87)	0.74	
No	457/15,639	Ref.	1.02 (0.80-1.29)	1.06 (0.83-1.36)	0.61	
Hypercholesterolemia						0.22
Yes	191/6,013	Ref.	0.97 (0.66-1.41)	1.19 (0.81-1.74)	0.32	
No	370/11,321	Ref.	1.00 (0.77-1.31)	1.01 (0.77-1.33)	0.94	
Smoking habits						0.75
No smoking	217/8,708	Ref.	0.98 (0.70-1.38)	1.03 (0.70-1.46)	0.87	
Current smoking	144/3,956	Ref.	0.84 (0.55-1.27)	0.89(0.58-1.36)	0.62	
Former smoking	200/4,670	Ref.	1.23 (0.82-1.84)	1.38 (0.92-2.04)	0.13	
WH-ratio						0.91
Abnormal (F: ≥0.85; M: ≥0.90)	486/13,611	Ref.	0.99 (0.79-1.26)	1.09 (0.86-1.39)	0.41	
Normal	75/3,723	Ref.	1.25 (0.72-2.20)	1.29 (0.71-2.35)	0.40	
History of CVD						0.70
Yes	66/908	Ref.	1.72 (0.85-3.49)	1.57 (0.77 - 3.22)	0.28	
No	495/16,426	Ref.	0.94 (0.75-1.19)	1.02 (0.81-1.29)	0.79	
History of cancer						0.51
Yes	84/543	Ref.	0.82 (1.44-1.50)	1.45 (0.82-2.54)	0.12	
No	477/16,791	Ref.	1.02 (0.81-1.29)	1.02 (0.80-1.30)	0.87	

Multiplicative interaction between PDW (modelled as tertiles) and the designed effect modifier (sex, age classes, smoking habit, diabetes, hypercholesterolemia, history of CVD, history of cancer) in relation to cancer mortality was tested with cross-product terms. Multivariable hazard ratios adjusted for age, sex, hematocrit, platelet count, mean platelet volume, white blood cell count, systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio. WH-ratio, waist-hip ratio; CVD, cardiovascular disease; PDW, platelet distribution width.

Supplementary Table S8. Subgroup analyses for the association of platelet distribution width with other-cause mortality

	N of events/ n of subjects	PDW tertiles			P trend	P interaction
		T1	T2	T3		
Age						0.76
<65 years	96/13,176	Ref.	1.00 (0.59-1.71)	1.12 (0.66-1.91)	0.65	
≥65 years	299/4,158	Ref.	1.17 (0.85-1.62)	1.34 (0.97-1.85)	0.068	
Gender						0.71
Men	257/8,395	Ref.	0.99 (0.69-1.43)	1.28 (0.90-1.82)	0.087	
Women	138/8,939	Ref.	1.28 (0.85-1.94)	1.16 (0.74-1.83)	0.51	
Diabetes						0.36
Yes	98/1,695	Ref.	1.36 (0.70-2.65)	1.70 (0.89-3.24)	0.093	
No	297/15,639	Ref.	1.08 (0.79-1.47)	1.18 (0.87-1.61)	0.28	
Hypercholesterolemia						0.38
Yes	129/6,013	Ref.	1.24 (0.78-1.96)	1.08 (0.67-1.74)	0.82	
No	266/11,321	Ref.	1.10 (0.78-1.56)	1.38 (0.98-1.94)	0.045	
Smoking habits						0.92
No smoking	173/8,708	Ref.	1.34 (0.91-1.99)	1.27 (0.84-1.91)	0.29	
Current smoking	67/3,956	Ref.	0.97 (0.48-1.93)	1.46 (0.75-2.83)	0.20	
Former smoking	155/4,670	Ref.	0.96 (0.60-1.53)	1.17 (0.75-1.82)	0.38	
WH-ratio						0.22
Abnormal (F: ≥0.85; M: ≥0.90)	348/13,611	Ref.	1.22 (0.90-1.65)	1.44 (1.07-1.94)	0.015	
Normal	47/3,723	Ref.	0.76 (0.36-1.58)	0.90 (0.43-1.88)	0.78	
History of CVD						
Yes	63/908	Ref.	1.38 (0.66-2.90)	1.42 (0.66-3.05)	0.41	0.85
No	332/16,426	Ref.	1.08 (0.80-1.45)	1.25 (0.93-1.68)	0.12	
History of cancer						
Yes	24/543	Ref.	1.82 (0.32-10.3)	3.41 (0.62-18.6)	0.10	0.34
No	371/16,791	Ref.	1.11 (0.83-1.47)	1.25 (0.94-1.65)	0.11	

Multiplicative interaction between PDW (modelled as tertiles) and the designed effect modifier (sex, age classes, smoking habit, diabetes, hypercholesterolemia, history of CVD, history of cancer) in relation to other-cause mortality was tested with cross-product terms. Multivariable hazard ratios adjusted for age, sex, hematocrit, platelet count, mean platelet volume, white blood cell count, systolic blood pressure, atrial fibrillation, liver disease, hypercholesterolemia, Cystatin C, Mediterranean diet score, physical activity/leisure time, smoking, diabetes, waist-to-hip ratio. WH-ratio, waist-hip ratio; CVD, cardiovascular disease; PDW, platelet distribution width.