

1Supplement to

2**Pregnancy associated plasma protein-A as a**  
3**cardiovascular risk marker in patients with stable**  
4**coronary heart disease during 10 years follow-up – a**  
5**CLARICOR trial sub-study**

6 Supplementary tables referenced in the main text are presented below.

7 **Table S1.** Logistic regression analyses of risk associated with elevated PAPP-A  $\geq 4$  mIU/L

Outcome	Variable	Discovery cohort	Replication cohort
Composite outcome	Odds ratio	1.46	1.13
	95% CI	1.06-1.99	0.82-1.56
	p-value	0.019	0.45
All-cause mortality	Odds ratio	1.66	1.64
	95% CI	1.22-2.26	1.18-2.27
	p-value	0.001	0.003

8 Shown are results from logistic regression models for the outcomes that violated the proportional hazard  
9 assumption for age at entry. Adjustment was for established risk factors and co-morbidities, standard  
10 biochemical predictors and treatments as shown in Supplementary Table 1, including age at entry. The  
11 composite outcome was defined as AMI, unstable angina pectoris, cerebrovascular disease, or death due to any  
12 cause. Abbreviations: PAPP-A, pregnancy-associated plasma protein A.

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Table S2. Risk of specific outcomes associated with elevated PAPP-A

Outcome	Variable	Discovery cohort		Replication cohort	
		Model A	Model B	Model A	Model B
Acute myocardial infarction	Hazard ratio	1.19	1.15	0.93	0.87
	95% CI	0.92-1.56	0.88-1.50	0.68-1.26	0.64-1.18
	p-value	0.19	0.32	0.65	0.37
Unstable angina pectoris	Hazard ratio	1.13	1.13	0.85	0.81
	95% CI	0.83-1.54	0.83-1.54	0.60-1.21	0.57-1.17
	p-value	0.43	0.44	0.36	0.27
Cerebrovascular disease	Hazard ratio	1.22	1.19	0.99	0.90
	95% CI	0.89-1.70	0.87-1.66	0.71-1.38	0.64-1.25
	p-value	0.22	0.27	0.96	0.52
Cardiovascular mortality	Hazard ratio	1.28	1.24	1.48	1.27
	95% CI	0.97-1.70	0.93-1.65	1.14-1.92	0.97-1.65
	p-value	0.079	0.14	0.003	0.084
Non-cardiovascular mortality	Hazard ratio	1.62	1.57	1.29	1.23
	95% CI	1.27-2.08	1.22-2.03	0.99-1.70	0.93-1.61
	p-value	<0.001	<0.001	0.062	0.14
All-cause* mortality	Hazard ratio	1.85	1.49	1.77	1.37
	95% CI	1.54-2.22	1.23-1.80	1.47-2.12	1.14-1.66
	p-value	<0.001	<0.001	<0.001	0.001

15 Results from Cox proportional hazards models are shown. Elevated PAPP-A was defined as baseline values  
 16  $\geq 4$  mIU/L and using those with PAPP-A  $<4$  mIU/L as referents. Model A was adjusted for age at entry and  
 17 sex. Model B was adjusted for established risk factors and co-morbidities, standard biochemical predictors and  
 18 treatments as shown in Supplementary Table 1. \* Proportional hazards assumption was violated for age at  
 19 entry. Abbreviations: PAPP-A, pregnancy-associated plasma protein A.

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22 **Table S3.** The role of elevated PAPP-A when used in combination with ‘standard predictors’ in the  
 23 prediction of outcome status

Type of predictions	Standard predictors	PAPP-A added to ‘standard predictors’
<b>Composite outcome</b>		
<b>True favorable predictions, N (%)</b>	2910 (48.7)	2906 (48.7)
<b>True unfavorable predictions, N (%)</b>	1174 (19.7)	1164 (19.5)
<b>Total number of true predictions, N (%)</b>	4084 (68.4)	4070 (68.2)
<b>All-cause mortality</b>		
<b>True favorable predictions, N (%)</b>	4585 (76.8)	4584 (76.8)
<b>True unfavorable predictions, N (%)</b>	392 (6.57)	405 (6.78)
<b>Total number of true predictions, N (%)</b>	4977 (83.4)	4989 (83.6)

24 Correct predictions of status of status of composite outcome (AMI, UAP, CVD, death) not experienced by  
 25 patient (favorable status) versus experienced by patient (unfavorable status) and for the outcomes death  
 26 (favorable status alive versus unfavorable status not alive) and correct predictions, in 2199 placebo patients.  
 27 Predictions of status was made at 3 years, at 6 years, and at 9 years following randomization. In all, for the  
 28 composite outcome 5972 predictions were made and for all-cause mortality 5971 predictions were made. The  
 29 first model includes the standard predictors listed in **appendix A** as covariates and the second model includes  
 30 the standard predictors plus binary PAPP-A as covariables.



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