

Supplementary Table 1: Baseline characteristics of included patients by inflammatory status (left) and excluded patients (right).

Characteristics	INCLUDED				EXCLUDED	
	Overall	Inflammation	No Inflammation	Inflamed vs. non-Inflamed	Overall	Excluded vs. Included
	(N=5904)	(N=3231)	(N=2673)	P-value	(N=4696)	P-value
BMI, mean (SD), kg/m ²	25.9 (5.2)	25.8 (5.3)	26.0 (4.9)	0.2506	25.9 (5.4)	0.9617
Serum CRP, median (Q1-Q3), mg/L	7.9 (3.1,19.6)	18.0 (10.8,34.7)	3.6 (1.6,6.0)	NA	10.0 (3.7,30.0)	<0.0001
Serum albumin, mean (SD), g/L	37.4 (4.9)	35.2 (5.1)	40.0 (2.9)	NA	35.7 (5.7)	<0.0001
Patient renal diagnosis classification (Model 1)						
Hypertension/vascular, No. (%)	1014 (17.2)	555 (17.2)	459 (17.2)	0.9954	649 (13.8)	<0.0001
Glomerulonephritis, No. (%)	526 (8.9)	262 (8.1)	264 (9.9)	0.0176	448 (9.5)	0.2641
Diabetic nephropathy, No. (%)	1549 (26.2)	870 (26.9)	679 (25.4)	0.1850	910 (19.4)	<0.0001
Tubulo-interstitial nephropathy, No. (%)	680 (11.5)	401 (12.4)	279 (10.4)	0.0181	450 (9.6)	0.0013
Polycystic kidney disease, No. (%)	315 (5.3)	119 (3.7)	196 (7.3)	<0.0001	233 (5.0)	0.3880
Unknown renal diagnosis, No. (%)	1820 (30.8)	1024 (31.7)	796 (29.8)	0.1130	2006 (42.7)	<0.0001
Demographics and medical history (Model 1)						
Age, mean (SD), years	64.6 (14.6)	66.9 (13.4)	61.9 (15.4)	<0.0001	64.2 (15.3)	0.1564
Sex, male, No. (%)	3559 (60.3)	1954 (60.5)	1605 (60.0)	0.7358	2818 (60.0)	0.7758
Cohort entry-year 2007, No. (%)	1220 (20.7)	646 (20.0)	574 (21.5)	0.1621	826 (17.6)	<0.0001
Cohort entry-year 2008, No. (%)	2024 (34.3)	1049 (32.5)	975 (36.5)	0.0012	1622 (34.5)	0.7810
Cohort entry-year 2009, No. (%)	2660 (45.1)	1536 (47.5)	1124 (42.1)	<0.0001	2248 (47.9)	0.0039
Western Europe No. (%)	3328 (56.4)	1749 (54.1)	1579 (59.1)	0.0001	3324 (70.8)	<0.0001

Non-smoker, No. (%)	2352 (39.8)	1253 (38.8)	1099 (41.1)	0.0682	1670 (35.6)	<0.0001
Former smoker, No. (%)	1101 (18.6)	674 (20.9)	427 (16.0)	<0.0001	670 (14.3)	<0.0001
Current smoker, No. (%)	481 (8.1)	260 (8.0)	221 (8.3)	0.7575	295 (6.3)	0.0003
Missing smoking data, No. (%)	1970 (33.4)	1044 (32.3)	926 (34.6)	0.0587	2061 (43.9)	<0.0001
Diabetes ^a , No. (%)	2233 (37.8)	1260 (39.0)	973 (36.4)	0.0406	1479 (31.5)	<0.0001
Cardiovascular disease ^a , No. (%)	2185 (37.0)	1266 (39.2)	919 (34.4)	0.0001	1387 (29.5)	<0.0001
Cancer ^a , No. (%)	519 (8.8)	346 (10.7)	173 (6.5)	<0.0001	366 (7.8)	0.0653
Modifiable factors added in Model 2						
Hospitalization ^b , No. (%)	1285 (21.8)	910 (28.2)	375 (14.0)	<0.0001	1231 (26.2)	<0.0001
Catheter use ^c , No. (%)	2606 (44.1)	1663 (51.5)	943 (35.3)	<0.0001	2432 (51.8)	<0.0001
Kt/V, mean (SD)	1.28 (0.63)	1.27 (0.29)	1.30 (0.88)	0.1346	1.26 (0.29)	0.0038
Mean blood flow, mean (SD), ml/min	304 (152)	301 (199)	306 (62)	0.2389	298 (89)	0.0302
Systolic blood pressure ^d , mean (SD), mmHg	137 (17)	136 (18)	137 (17)	0.0333	137 (19)	0.2305
Additional Laboratory parameters						
Hemoglobin, mean (SD), g/L	108 (14)	105 (14)	111 (13)	<0.0001	105 (15)	<0.0001
Serum creatinine, mean (SD), μmol/L	562 (184)	539 (174)	589 (192)	<0.0001	570 (200)	0.0325
Serum cholesterol, mean (SD), mmol/L	4.39 (1.10)	4.35 (1.15)	4.43 (1.04)	0.0108	4.28 (1.15)	0.0001
Serum LDL-cholesterol, mean (SD), mmol/L	2.49 (0.91)	2.50 (0.93)	2.47 (0.88)	0.2156	2.45 (0.94)	0.1481
Serum calcium, mean (SD), mmol/L	2.18 (0.17)	2.16 (0.17)	2.21 (0.16)	<0.0001	2.19 (0.19)	0.1234
Serum phosphate, mean (SD), mmol/L	1.53 (0.40)	1.49 (0.41)	1.57 (0.39)	<0.0001	1.48 (0.47)	<0.0001
Serum intact PTH, median (Q1-Q3), ng/L	216 (121,362)	207 (114,343)	224 (128,385)	<0.0001	214 (116,372)	0.9076
Serum ferritin, median (Q1-Q3), μg/L	562 (308,976)	637 (346,1076)	489 (270,856)	<0.0001	574 (315,995)	0.3470

Abbreviations; BMI; body mass index, CRP; C-reactive protein, NA; not applicable, LDL; low-density cholesterol, PTH; parathyroid hormone

^a; prior to end of baseline

^b; during the baseline period

^c; during first 3 months, missing data in 958 patients

^d; pre-dialysis value

Supplementary Table 2: All cause, cardiovascular and non-cardiovascular mortality rates per 100 person-years in included patients by inflammatory status and excluded patients.

Event	Included			Excluded (N=4696)
	Overall (N=5904)	Inflammation (N=3231)	No Inflammation (N=2673)	
<i>All-cause mortality</i>				
Event patients	1929	1334	595	1531
PY (sum)	16513.49	8446.96	8066.52	9802.47
PY (median [Q1, Q3])	3.01 [1.27,4.06]	2.64 [1.08,3.90]	3.30 [1.61,4.27]	1.69 [0.36,3.64]
Rate [95% CI]	11.68 [11.17-12.21]	15.79 [14.96-16.66]	7.38 [6.80-7.99]	15.62 [14.85-16.42]
<i>CV mortality</i>				
Patients	822	550	272	585
PY (sum)	16513.49	8446.96	8066.52	9802.47
PY (median [Q1, Q3])	3.01 [1.27,4.06]	2.64 [1.08,3.90]	3.30 [1.61,4.27]	1.69 [0.36,3.64]
Rate [95% CI]	4.98 [4.64-5.33]	6.51 [5.98-7.08]	3.37 [2.98-3.8]	5.97 [5.49-6.47]
<i>Non-CV mortality</i>				
Patients	1107	784	323	946
PY (sum)	16513.49	8446.96	8066.52	9802.47
PY (median [Q1, Q3])	3.01 [1.27,4.06]	2.64 [1.08,3.90]	3.30 [1.61,4.27]	1.69 [0.36,3.64]
Rate [95% CI]	6.70 [6.31-7.11]	9.28 [8.64-9.95]	4.00 [3.58-4.47]	9.65 [9.05-10.29]

Abbreviations; PY; person years, Q1; quintile 1, Q3; quintile 3, CI; confidence interval

Supplementary Table 3: All-cause mortality by baseline BMI-Inflammation: Cox proportional hazards analysis

Model	BMI quintile	Hazard Ratio [95% Confidence Interval]	
		Inflammation Present	Inflammation Absent
0	1	3.13 [2.52-3.89]	1.13 [0.86-1.48]
	2	2.63 [2.11-3.29]	1.19 [0.92-1.54]
	3	2.31 [1.85-2.89]	1.05 [0.81-1.36]
	4	2.32 [1.86-2.90]	1.19 [0.93-1.53]
	5	1.79 [1.42-2.25]	1
1	1	2.88 [2.31-3.59]	1.32 [1.01-1.74]
	2	2.19 [1.74-2.74]	1.21 [0.94-1.57]
	3	2.05 [1.63-2.57]	1.02 [0.79-1.33]
	4	1.90 [1.52-2.37]	1.12 [0.87-1.44]
	5	1.59 [1.26-2.00]	1
2	1	2.68 [2.14-3.35]	1.34 [1.02-1.77]
	2	2.07 [1.65-2.60]	1.22 [0.94-1.59]
	3	1.96 [1.56-2.46]	1.03 [0.79-1.34]
	4	1.80 [1.44-2.26]	1.17 [0.91-1.50]
	5	1.50 [1.19-1.89]	1

Model 0: non-adjusted.

Model 1: adjusted for demographics and medical history: age, gender, region (western or eastern Europe), dialysis vintage, smoking status, CKD etiology, diabetes, CVD and cancer history.

Model 2: Model 1 plus adjustment for modifiable factors: hospitalization, catheter use, Kt/V, actual blood flow and systolic blood pressure.

Supplementary Table 4: A sensitivity Cox proportional hazards analysis (unadjusted time-updated all-cause mortality) where inflammation was defined by CRP ≥ 10 mg/L or serum albumin ≤ 35 g/L alone.

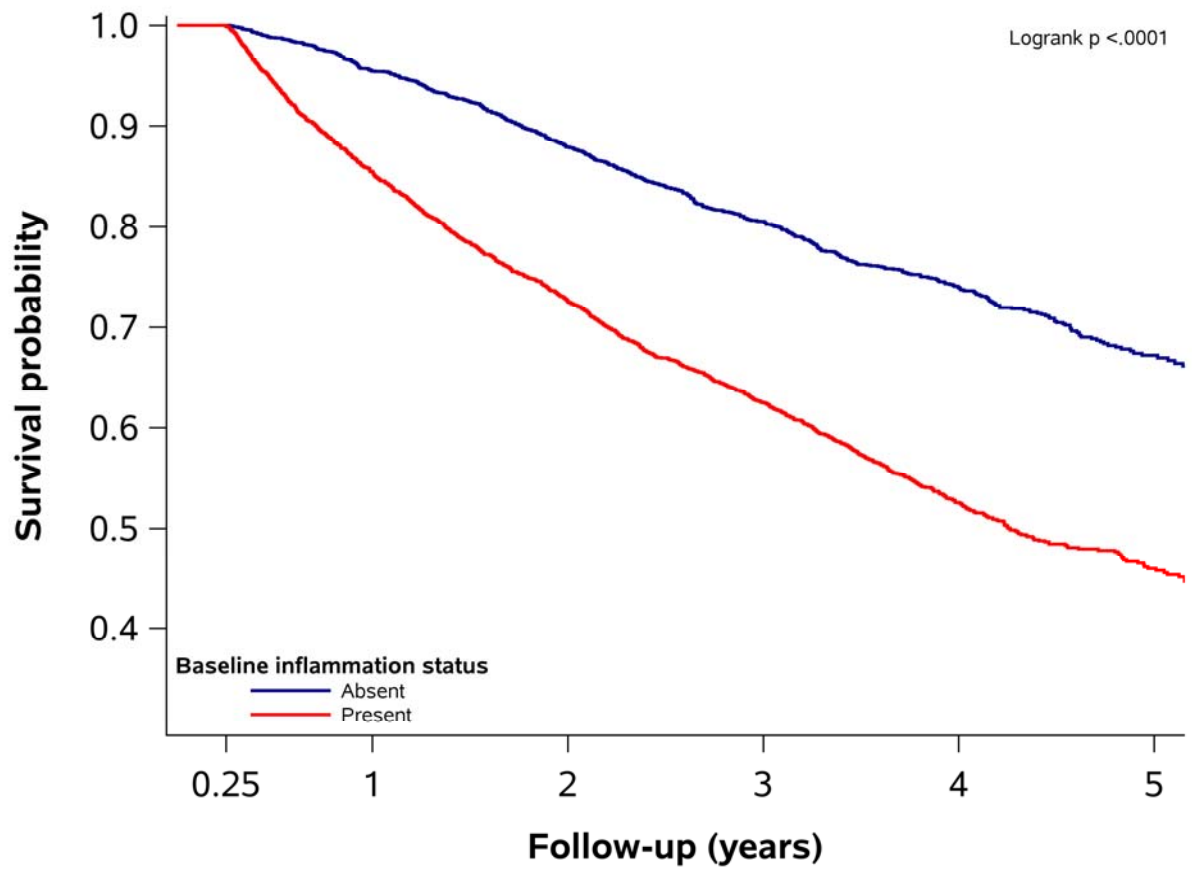
BMI quintile	Hazard Ratios [95% Confidence Intervals]					
	Main analysis			Sensitivity analysis		
	CRP & serum albumin		CRP alone		Serum albumin alone	
	Inflammation present	Inflammation absent	Inflammation present	Inflammation absent	Inflammation present	Inflammation absent
1	10.83 [8.22-14.26]	1.51 [1.06-2.14]	9.65 [7.57-12.29]	2.13 [1.62-2.79]	10.52 [8.64-12.81]	2.02 [1.62-2.52]
2	7.21 [5.43-9.57]	0.95 [0.66-1.39]	6.67 [5.19-8.59]	1.15 [0.85-1.56]	7.39 [5.95-9.17]	1.31 [1.04-1.66]
3	5.03 [3.76-6.72]	1.04 [0.73-1.49]	4.42 [3.40-5.75]	1.10 [0.82-1.48]	5.31 [4.19-6.73]	1.33 [1.06-1.66]
4	3.67 [2.72-4.95]	0.97 [0.68-1.40]	3.13 [2.38-4.10]	0.93 [0.68-1.27]	4.28 [3.32-5.52]	1.09 [0.87-1.38]
5	2.96 [2.19-4.01]	1	2.47 [1.88-3.26]	1	3.58 [2.75-4.67]	1

Supplementary Table 5: Cause-specific non-cardiovascular deaths based on ICD-10 codes among the inflamed and non-inflamed patient groups.

BMI quintile	Cause of death	Inflammation status		Total
		Present	Absent	
1	Cancer	31 (16.4)	4 (7.1)	35
	Infections	36 (19.0)	8 (14.3)	44
	Other	57 (30.2)	22 (39.3)	79
	Missing/invalid	65 (34.4)	22 (39.3)	87
2	Cancer	21 (13.0)	10 (14.3)	31
	Infections	39 (24.1)	10 (14.3)	49
	Other	45 (27.8)	21 (30.0)	66
	Missing/invalid	57 (35.2)	29 (41.4)	86
3	Cancer	26 (19.3)	8 (11.4)	34
	Infections	25 (18.5)	11 (15.7)	36
	Other	38 (28.1)	27 (38.6)	65
	Missing/invalid	46 (34.1)	24 (34.3)	70
4	Cancer	17 (9.9)	8 (11.6)	25
	Infections	32 (18.7)	20 (29.0)	52
	Other	61 (35.7)	15 (21.7)	76
	Missing/invalid	61 (35.7)	26 (37.7)	87
5	Cancer	13 (10.2)	4 (6.9)	17
	Infections	28 (22.0)	13 (22.4)	41
	Other	50 (39.4)	26 (44.8)	76
	Missing/invalid	36 (28.3)	15 (25.9)	51
Total		784	323	1107

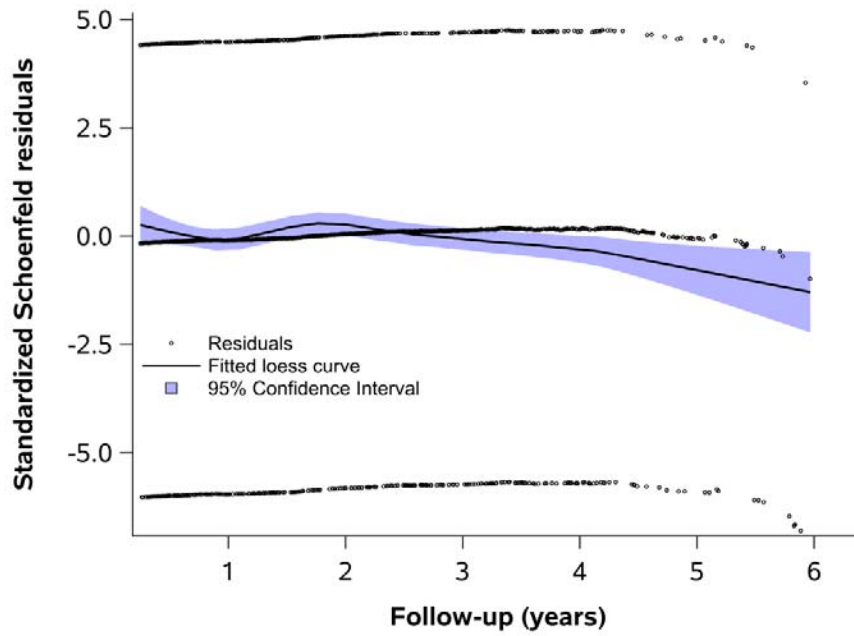
Abbreviation; ICD; international classification of diseases

Supplementary Figure 1:

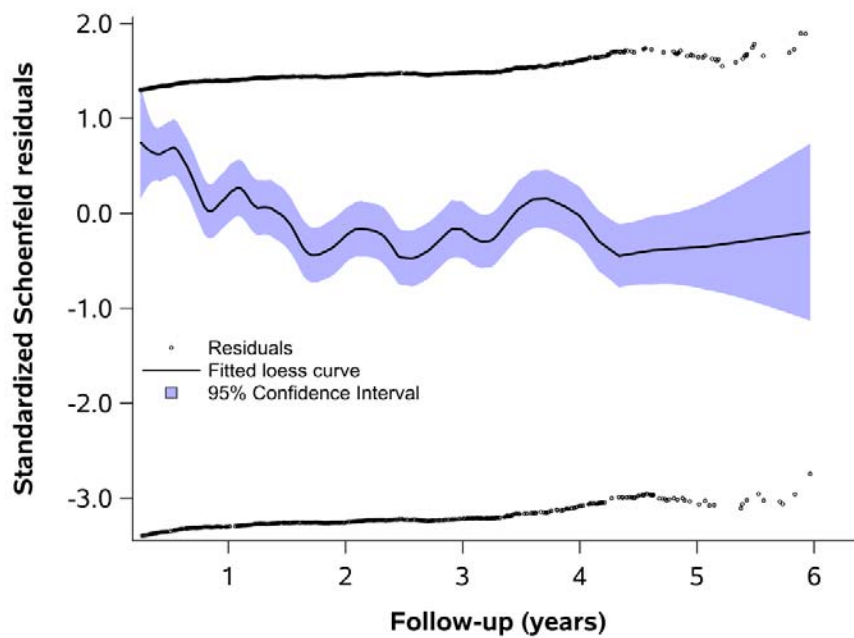


Supplementary Figure 2:

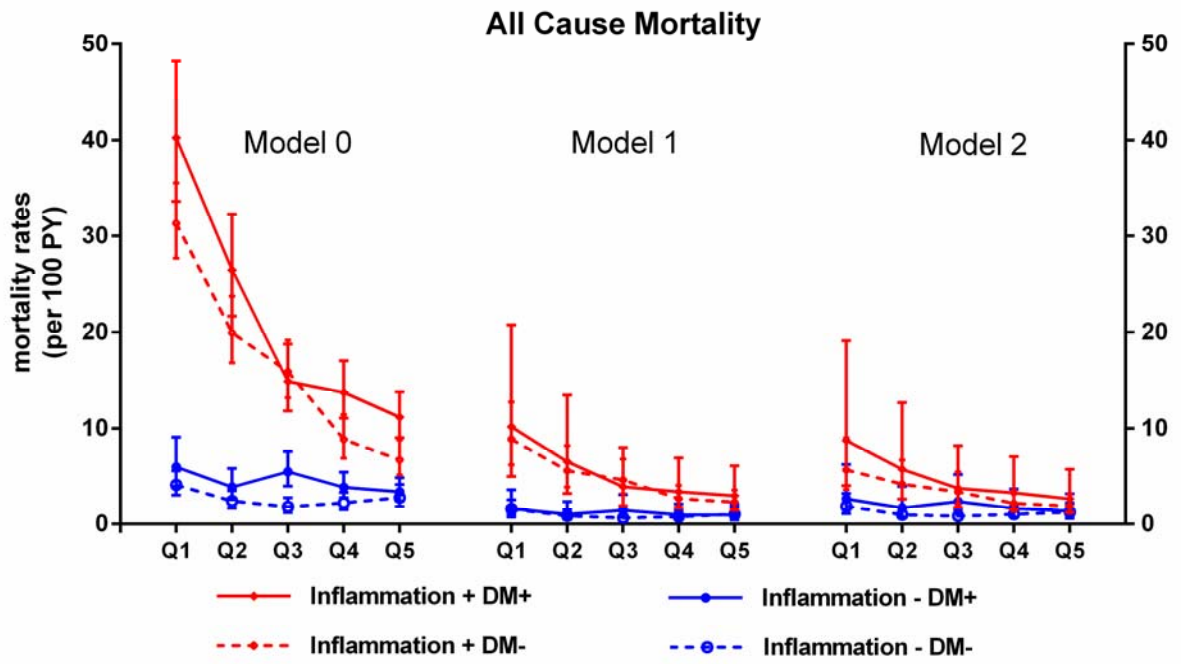
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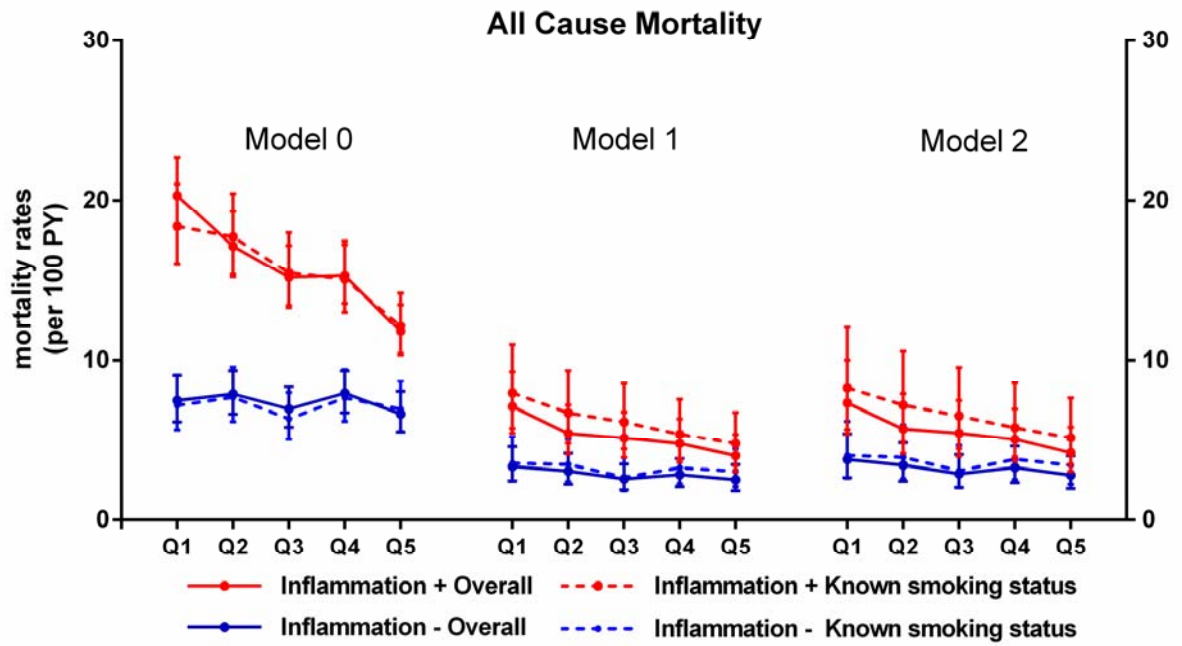
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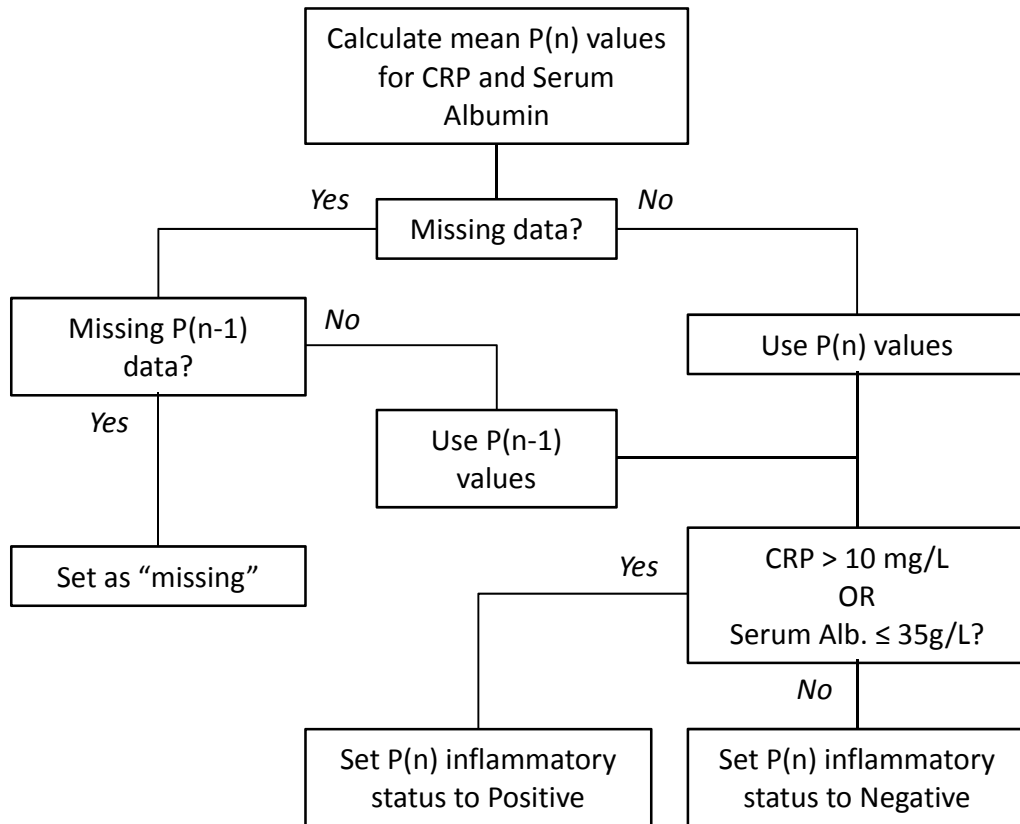
Supplementary Figure 3:



Supplementary Figure 4:



Supplementary Figure 5:



Legend to Supplemental Figures:

Figure 1: Kaplan Meier curves showing all-cause mortality by basal inflammation status.

Figure 2: Proportional hazards assumption for BMI (top) and inflammation (bottom).

Figure 3: All-cause mortality with and without the presence of diabetes mellitus in an unadjusted model (Model 0), following adjustment for demographics and medical history (Model 1) and following additional adjustment for modifiable factors (Model 2).

Figure 4: All-cause mortality with and without known smoking status in an unadjusted model (Model 0), following adjustment for demographics and medical history (Model 1) and following additional adjustment for modifiable factors (Model 2).

Figure 5: Algorithm to allocate inflammation status for time-updated analyses in case of missing data.

Supplementary appendix: ARO Research Initiative Study Collaborators and Sponsors.

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