Table S2: Association of ADMA and SDMA Quintiles and Outcomes in the HEMO Study

	Range, μM	N	Events	IR Per 1000 PY	Model 1 HR (95% CI)	P	Model 2 HR (95% CI)	P	Model 3 HR (95% CI)	P	Model 4 HR (95% CI)	P
Cardiac Death												
ADMA												
Quintile 1	0.43-0.744	255	33	44.1	Reference		Reference		Reference		Reference	
Quintile 2	0.745-0.841	254	39	61.0	1.39 (0.95-2.02)	0.09	1.42 (0.97-2.07)	0.07	1.23 (0.85-1.77)	0.3	1.23 (0.86-1.76)	0.3
Quintile 3	0.842-0.938	255	44	66.8	1.52 (0.98-2.34)	0.06	1.44 (0.88-2.34)	0.1	1.35 (0.83-2.20)	0.2	1.35 (0.83-2.18)	0.2
Quintile 4	0.939-1.06	254	38	60.3	1.37 (0.94-2.00)	0.1	1.38 (0.97-1.97)	0.08	1.19 (0.80-1.76)	0.4	1.18 (0.80-1.76)	0.4
Quintile 5	1.07-2.56	258	66	108.8	**2.56 (1.80-3.64)**	**<.001**	**2.66 (1.88-3.74)**	**<.001**	**2.12 (1.47-3.06)**	**<.001**	**2.10 (1.44-3.05)**	**<.001**
p-trend						**<.001**		**<.001**		**<.001**		**<.001**
SDMA												
Quintile 1	1.35-3.11	255	47	71.7	Reference		Reference		Reference		Reference	
Quintile 2	3.12-3.78	255	44	63.3	0.88 (0.56-1.37)	0.6	1.01 (0.66-1.56)	0.9	1.08 (0.76-1.53)	0.7	1.07 (0.76-1.52)	0.7
Quintile 3	3.79-4.41	256	53	86.6	1.21 (0.90-1.63)	0.2	**1.48 (1.10-1.99)**	**0.01**	**1.59 (1.18-2.14)**	**0.002**	**1.57 (1.16-2.12)**	**0.003**
Quintile 4	4.42-5.19	255	38	55.2	0.76 (0.54-1.07)	0.1	1.12 (0.79-1.57)	0.5	1.28 (0.82-2.00)	0.3	1.27 (0.82-1.97)	0.3
Quintile 5	5.2-12.8	255	38	60.2	0.83 (0.56-1.24)	0.4	1.27 (0.86-1.88)	0.2	1.47 (0.99-2.20)	0.06	1.44 (0.95-2.20)	0.09
p-trend						0.2		0.2		**0.03**		**0.05**
Sudden Cardiac Death												
ADMA												
Quintile 1	0.43-0.744	255	20	26.8	Reference		Reference		Reference		Reference	
Quintile 2	0.745-0.841	254	22	34.4	1.30 (0.81-2.09)	0.3	1.34 (0.84-2.15)	0.2	1.17 (0.78-1.74)	0.4	1.17 (0.79-1.74)	0.4
Quintile 3	0.842-0.938	255	23	34.9	1.33 (0.82-2.18)	0.2	1.28 (0.79-2.07)	0.3	1.17 (0.70-1.94)	0.5	1.17 (0.70-1.94)	0.5
Quintile 4	0.939-1.06	254	22	34.9	1.35 (0.88-2.05)	0.2	1.35 (0.90-2.03)	0.1	1.15 (0.76-1.74)	0.5	1.15 (0.75-1.75)	0.5
Quintile 5	1.07-2.56	258	39	64.3	**2.57 (1.89-3.50)**	**<.001**	**2.65 (2.05-3.43)**	**<.001**	**2.07 (1.49-2.89)**	**<.001**	**2.06 (1.46-2.90)**	**<.001**
p-trend						**<.001**		**<.001**		0.002		0.003
SDMA												
Quintile 1	1.35-3.11	255	28	42.7	Reference		Reference		Reference		Reference	
Quintile 2	3.12-3.78	255	25	36.0	0.85 (0.38-1.88)	0.7	0.97 (0.45-2.09)	0.9	1.04 (0.55-1.97)	0.9	1.04 (0.55-1.97)	0.9
Quintile 3	3.79-4.41	256	27	44.1	1.04 (0.60-1.81)	0.9	1.26 (0.72-2.22)	0.4	1.39 (0.82-2.37)	0.2	1.38 (0.80-2.37)	0.2
Quintile 4	4.42-5.19	255	24	34.8	0.83 (0.44-1.54)	0.5	1.16 (0.64-2.08)	0.6	1.36 (0.70-2.64)	0.4	1.36 (0.70-2.62)	0.4
Quintile 5	5.2-12.8	255	22	34.9	0.81 (0.42-1.55)	0.5	1.20 (0.63-2.29)	0.6	1.51 (0.82-2.76)	0.2	1.48 (0.80-2.76)	0.2
p-trend						0.5		0.4		0.1		0.1
First Cardiovascular Event or Any-Cause Death												
ADMA												
Quintile 1	0.43-0.744	241	105	186.1	Reference		Reference		Reference		Reference	
Quintile 2	0.745-0.841	234	125	276.0	**1.50 (1.23-1.82)**	**<.001**	**1.60 (1.30-1.97)**	**<.001**	**1.53 (1.24-1.88)**	**<.001**	**1.53 (1.25-1.88)**	**<.001**
Quintile 3	0.842-0.938	240	126	261.2	**1.41 (1.13-1.76)**	**0.003**	**1.37 (1.09-1.73)**	**0.007**	**1.35 (1.05-1.72)**	**0.02**	**1.35 (1.05-1.72)**	**0.02**
Quintile 4	0.939-1.06	236	150	338.7	**1.83 (1.48-2.25)**	**<.001**	**1.83 (1.46-2.29)**	**<.001**	**1.69 (1.35-2.10)**	**<.001**	**1.69 (1.36-2.10)**	**<.001**

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Quintile 5	1.07-2.56	235	138	337.5	**1.82 (1.45-2.29)**	**<.001**	**1.89 (1.49-2.42)**	**<.001**	**1.74 (1.35-2.26)**	**<.001**	**1.75 (1.35-2.27)**	**<.001**
p-trend						**<.001**		**<.001**		**<.001**		**<.001**
SDMA												
Quintile 1	1.35-3.11	237	145	331.6	Reference		Reference		Reference		Reference	
Quintile 2	3.12-3.78	237	120	233.9	**0.69 (0.57-0.84)**	**<.001**	**0.77 (0.66-0.90)**	**0.001**	**0.78 (0.67-0.91)**	**0.002**	**0.78 (0.67-0.91)**	**0.002**
Quintile 3	3.79-4.41	242	154	357.5	1.06 (0.87-1.30)	0.6	**1.20 (1.01-1.43)**	**0.04**	1.14 (0.94-1.38)	0.2	1.14 (0.94-1.38)	0.2
Quintile 4	4.42-5.19	238	115	224.2	**0.66 (0.53-0.82)**	**<.001**	0.87 (0.70-1.08)	0.2	0.91 (0.75-1.10)	0.3	0.90 (0.74-1.10)	0.3
Quintile 5	5.2-12.8	232	110	240.6	**0.70 (0.51-0.94)**	**0.02**	0.96 (0.71-1.29)	0.8	0.99 (0.73-1.34)	0.9	1.00 (0.74-1.35)	0.9
p-trend						**0.02**		0.9		0.7		0.6
Any-Cause Death												
ADMA												
Quintile 1	0.43-0.744	255	87	116.4	Reference		Reference		Reference		Reference	
Quintile 2	0.745-0.841	254	113	176.8	**1.52 (1.26-1.84)**	**<.001**	**1.57 (1.28-1.93)**	**<.001**	**1.43 (1.17-1.73)**	**<.001**	**1.43 (1.17-1.73)**	**<.001**
Quintile 3	0.842-0.938	255	111	168.4	**1.40 (1.17-1.68)**	**<.001**	**1.35 (1.09-1.67)**	**0.006**	1.27 (0.98-1.63)	0.07	1.27 (0.98-1.63)	0.07
Quintile 4	0.939-1.06	254	127	201.6	**1.71 (1.36-2.15)**	**<.001**	**1.76 (1.42-2.16)**	**<.001**	**1.56 (1.20-2.04)**	**<.001**	**1.56 (1.20-2.04)**	**<.001**
Quintile 5	1.07-2.56	258	127	209.4	**1.77 (1.43-2.19)**	**<.001**	**1.86 (1.50-2.31)**	**<.001**	**1.56 (1.22-2.00)**	**<.001**	**1.56 (1.21-2.00)**	**<.001**
p-trend						**<.001**		**<.001**		**0.003**		**0.004**
SDMA												
Quintile 1	1.35-3.11	255	129	196.9	Reference		Reference		Reference		Reference	
Quintile 2	3.12-3.78	255	104	149.7	**0.73 (0.57-0.95)**	**0.02**	0.83 (0.66-1.06)	0.1	0.87 (0.69-1.10)	0.2	0.87 (0.69-1.10)	0.2
Quintile 3	3.79-4.41	256	133	217.2	1.08 (0.87-1.34)	0.5	**1.27 (1.04-1.56)**	**0.02**	**1.29 (1.03-1.62)**	**0.02**	**1.29 (1.03-1.62)**	**0.03**
Quintile 4	4.42-5.19	255	98	142.2	**0.68 (0.54-0.85)**	**<.001**	0.97 (0.81-1.16)	0.7	1.05 (0.83-1.32)	0.7	1.05 (0.83-1.32)	0.7
Quintile 5	5.2-12.8	255	101	160.1	0.77 (0.58-1.03)	0.07	1.13 (0.84-1.52)	0.4	1.24 (0.94-1.64)	0.1	1.24 (0.93-1.65)	0.1
p-trend						0.06		0.2		**0.04**		0.05
First Infection-Related Hospitalization or Any-Cause Death												
ADMA												
Quintile 1	0.43-0.744	246	119	219.4	Reference		Reference		Reference		Reference	
Quintile 2	0.745-0.841	240	134	300.4	**1.38 (1.16-1.63)**	**<.001**	**1.40 (1.18-1.67)**	**<.001**	**1.30 (1.09-1.55)**	**0.003**	**1.30 (1.09-1.55)**	**0.003**
Quintile 3	0.842-0.938	239	129	280.1	1.25 (0.99-1.56)	0.06	1.23 (0.96-1.58)	0.1	1.22 (0.95-1.56)	0.1	1.22 (0.95-1.55)	0.1
Quintile 4	0.939-1.06	230	143	336.9	**1.53 (1.19-1.97)**	**<.001**	**1.54 (1.19-1.99)**	**0.001**	**1.42 (1.10-1.83)**	**0.007**	**1.41 (1.10-1.82)**	**0.007**
Quintile 5	1.07-2.56	228	138	354.0	**1.60 (1.31-1.96)**	**<.001**	**1.63 (1.33-2.00)**	**<.001**	**1.46 (1.20-1.79)**	**<.001**	**1.46 (1.19-1.78)**	**<.001**
p-trend						**<.001**		**<.001**		**0.001**		**0.001**
SDMA												
Quintile 1	1.35-3.11	240	145	337.4	Reference		Reference		Reference		Reference	
Quintile 2	3.12-3.78	233	126	259.9	**0.76 (0.58-1.00)**	**0.05**	0.83 (0.66-1.05)	0.1	0.84 (0.69-1.02)	0.08	0.84 (0.70-1.02)	0.09
Quintile 3	3.79-4.41	246	151	345.5	1.01 (0.87-1.19)	0.9	1.10 (0.96-1.27)	0.2	1.09 (0.92-1.28)	0.3	1.09 (0.92-1.28)	0.3
Quintile 4	4.42-5.19	226	117	245.9	**0.71 (0.60-0.85)**	**<.001**	0.86 (0.72-1.03)	0.1	0.90 (0.74-1.10)	0.3	0.90 (0.74-1.11)	0.3
Quintile 5	5.2-12.8	238	124	284.6	0.82 (0.67-1.01)	0.06	1.00 (0.83-1.20)	0.9	1.06 (0.88-1.28)	0.5	1.06 (0.87-1.28)	0.6
p-trend						0.1		0.8		0.4		0.4

Abbreviation: IR, Incidence Rate; HR, Hazard Ratio; CI, Confidence Interval; ADMA, Asymmetric Dimethylarginine; SDMA, Symmetric Dimethylarginine
HR represents increase in risk per 2-fold increase in ADMA or SDMA concentrations. Modeled as natural log transformed variable/natural log of 2.

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Model 1 was unadjusted.

Model 2 adjusted for age, sex and race.

Model 3 adjusted for variables in Model 2 + Index of Coexisting Disease (ICED) severity score, cause of end-stage renal disease, body mass index (categorized as <18, 18 to 25 and >25 kg/m2), systolic blood pressure (categorized as <130, 130-160 and >160 mm Hg), albumin, and relative volume removed on dialysis

Model 4 adjusted for variables in Model 3 + residual kidney function (urinary $stdKt/V_{UREA}$ calculated from urinary urea clearance).