**Table S1. Comparison of the Baseline Characteristics of the Included versus Excluded Participants**

| Characteristic | All | Included | Excluded | $P^a$ |
|---|---|---|---|---|
| **Number** | 1846 | 1232 | 614 | |
| **Demographics** | | | | |
| Age, years | 57.6 ± 14.0 | 57.7 ± 13.8 | 57.5 ± 14.4 | 0.74 |
| Female sex | 1038 (56.2) | 699 (56.7) | 339 (55.2) | 0.55 |
| Black race | 1156 (62.6) | 801 (65.0) | 355 (57.8) | **0.004** |
| **Clinical Characteristics** | | | | |
| ICED score | 2.0 ± 0.8 | 2.0 ± 0.8 | 2.0 ± 0.8 | 0.19 |
| Diabetes | 823 (44.6) | 555 (45.0) | 268 (43.6) | 0.58 |
| Cardiac disease | 1479 (80.1) | 976 (79.2) | 503 (81.9) | 0.17 |
| Gastrointestinal disease | 678 (36.7) | 466 (37.8) | 212 (34.5) | 0.18 |
| Attributed cause of End-Stage Renal Disease | | | | 0.26 |
| Diabetes | 686 (37.2) | 463 (37.96) | 223 (36.3) | |
| Hypertension | 586 (31.7) | 397 (32.2) | 189 (30.8) | |
| Polycystic Kidney Disease | 58 (3.1) | 32 (2.6) | 26 (4.2) | |
| Other | 464 (25.1) | 316 (25.6) | 148 (24.1) | |
| **Dialysis Characteristics** | | | | |
| Years of prior dialysis | 3.7 ± 4.4 | 3.5 ± 4.2 | 4.2 ± 4.7 | **<0.001** |
| Residual kidney urea clearance > 0 | 607 (32.9) | 413 (33.5) | 194 (31.6) | 0.43 |
| Predialysis systolic blood pressure | 151.8 ± 22.1 | 152.4 ± 21.8 | 150.7 ± 22.8 | 0.12 |
| Target weight, Kg | 68.9 ± 14.6 | 69.7 ± 14.9 | 67.3 ± 14.1 | **<0.001** |
| Body Mass Index, Kg/m$^2$ | 25.5 ± 5.2 | 25.7 ± 5.3 | 25.0 ± 5.0 | **0.014** |
| Number of reuse of the dialyzer | 6.4 ± 5.3 | 6.5 ± 5.5 | 6.2 ± 4.8 | 0.21 |
| Relative volume removed, % | 4.1 ± 1.5 | 4.0 ± 1.4 | 4.1 ± 1.6 | 0.11 |
| High-dose group | 920 (49.8) | 613 (49.8) | 307 (50.0) | 0.96 |
| High-flux group | 921 (49.9) | 620 (50.3) | 301 (49.0) | 0.62 |
| **Predialysis Laboratory Tests** | | | | |
| Blood Urea Nitrogen, mg/dL | 56.7 ± 14.3 | 56.3 ± 14.5 | 57.5 ± 14.0 | 0.092 |
| Single-pool Kt/V | 1.6 ± 0.2 | 1.6 ± 0.2 | 1.6 ± 0.2 | 0.11 |
| Serum albumin, g/dL | 3.6 ± 0.4 | 3.6 ± 0.3 | 3.6 ± 0.4 | 0.85 |
| Serum β2-microglobulin, mg/L | 36.3 ± 13.5 | 35.6 ± 13.8 | 37.7 ± 12.6 | **0.003** |
| Equilibrated nPCR, g/kg/day | 1.0 ± 0.2 | 1.0 ± 0.2 | 1.0 ± 0.2 | 0.14 |
| **Dietary recall** | | | | |
| Total protein, g/kg ABW/day | 0.9 ± 0.3 | 0.9 ± 0.3 | 0.9 ± 0.3 | 0.48 |
| Fat % | 35.4 ± 7.8 | 35.6 ± 7.5 | 34.8 ± 8.5 | **0.04** |
| Carbohydrates % | 48.6 ± 9.4 | 48.3 ± 9.2 | 49.2 ± 9.8 | 0.057 |

*Note:* Values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation.
[a]*P* values were calculated from one-way ANOVA for continuous variables and Fisher's exact test for categorical variables.

Patients included in the study versus those excluded were more likely to be Black (65% versus 58%; p=0.004) and had shorter duration of prior dialysis (3.5 years versus 4.2 years; p<0.001), lower target weight (69.7 kg versus 67.3 kg; p<0.001), higher BMI (25.7 kg/m$^2$ versus 25.0 kg/m$^2$; p=0.014) and lower serum β2-microglobulin (35.6 versus 37.7 mg/L; p=0.003).

# Table S2: Association of TMAO Quintiles and Outcomes in 1232 Patients of the HEMO Study stratified by Race.

| | Range, mmol/L | 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** | | | | | | | | | | | | |
| **White** | | | | | | | | | | | | |
| Quintile 1 | 6.42-56 | 89 | 15 | 73.0 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 80 | 12 | 65.6 | 0.90 (0.45-1.81) | 0.775 | 0.99 (0.46-2.13) | 0.979 | 1.06 (0.47-2.40) | 0.883 | 1.08 (0.48-2.47) | 0.849 |
| Quintile 3 | 77-100 | 85 | 17 | 91.4 | 1.24 (0.69-2.23) | 0.481 | 1.31 (0.72-2.38) | 0.383 | 1.36 (0.68-2.75) | 0.387 | 1.38 (0.69-2.76) | 0.368 |
| Quintile 4 | 101-134 | 99 | 29 | 141.6 | **1.94 (1.35-2.80)** | **<.001** | **2.01 (1.33-3.04)** | **<.001** | **2.18 (1.43-3.32)** | **<.001** | **2.18 (1.42-3.34)** | **<.001** |
| Quintile 5 | 135-468 | 78 | 23 | 136.5 | **1.82 (1.23-2.69)** | **0.003** | **1.90 (1.24-2.90)** | **0.003** | **1.80 (1.13-2.87)** | **0.014** | **1.78 (1.12-2.82)** | **0.015** |
| p-trend | | | | | | **<.001** | | **<.001** | | **<.001** | | **<.001** |
| **Black** | | | | | | | | | | | | |
| Quintile 1 | 2.25-56.2 | 157 | 22 | 52.0 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 168 | 34 | 76.0 | 1.46 (0.93-2.29) | 0.097 | **1.71 (1.06-2.77)** | **0.029** | **1.90 (1.29-2.78)** | **0.001** | **1.88 (1.30-2.74)** | **<.001** |
| Quintile 3 | 76.8-100 | 158 | 23 | 51.3 | 0.98 (0.57-1.68) | 0.935 | 1.07 (0.60-1.89) | 0.827 | 1.12 (0.63-1.97) | 0.702 | 1.11 (0.64-1.92) | 0.718 |
| Quintile 4 | 101-134 | 152 | 24 | 53.8 | 1.03 (0.62-1.73) | 0.904 | 1.15 (0.66-1.99) | 0.618 | 1.14 (0.72-1.79) | 0.577 | 1.13 (0.73-1.75) | 0.593 |
| Quintile 5 | 135-682 | 166 | 17 | 36.8 | 0.73 (0.49-1.09) | 0.121 | 0.78 (0.50-1.21) | 0.265 | 0.78 (0.51-1.18) | 0.238 | 0.78 (0.51-1.18) | 0.233 |
| p-trend | | | | | | **0.026** | | **0.047** | | **0.02** | | **0.019** |
| **Sudden Cardiac Death** | | | | | | | | | | | | |
| **White** | | | | | | | | | | | | |
| Quintile 1 | 6.42-56 | 89 | 6 | 29.2 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 80 | 5 | 27.3 | 0.94 (0.29-3.04) | 0.922 | 1.02 (0.32-3.27) | 0.977 | 1.09 (0.31-3.89) | 0.895 | 1.11 (0.30-4.07) | 0.879 |
| Quintile 3 | 77-100 | 85 | 9 | 48.4 | 1.63 (0.59-4.47) | 0.345 | 1.67 (0.62-4.49) | 0.312 | 1.74 (0.56-5.39) | 0.336 | 1.76 (0.56-5.53) | 0.333 |
| Quintile 4 | 101-134 | 99 | 19 | 92.8 | **3.12 (1.29-7.54)** | **0.011** | **3.22 (1.37-7.58)** | **0.007** | **3.29 (1.45-7.45)** | **0.004** | **3.30 (1.45-7.51)** | **0.004** |
| Quintile 5 | 135-468 | 78 | 15 | 89.0 | **2.98 (1.38-6.44)** | **0.005** | **3.03 (1.54-5.94)** | **0.001** | **2.79 (1.22-6.38)** | **0.015** | **2.76 (1.22-6.24)** | **0.014** |
| p-trend | | | | | | **<.001** | | **<.001** | | **<.001** | | **<.001** |
| **Black** | | | | | | | | | | | | |
| Quintile 1 | 2.25-56.2 | 157 | 13 | 30.7 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 168 | 15 | 33.5 | 1.13 (0.60-2.11) | 0.708 | 1.32 (0.69-2.52) | 0.398 | 1.46 (0.86-2.50) | 0.164 | 1.46 (0.86-2.47) | 0.164 |
| Quintile 3 | 76.8-100 | 158 | 16 | 35.7 | 1.17 (0.57-2.39) | 0.676 | 1.27 (0.60-2.73) | 0.533 | 1.36 (0.66-2.82) | 0.409 | 1.35 (0.66-2.75) | 0.406 |
| Quintile 4 | 101-134 | 152 | 16 | 35.9 | 1.20 (0.61-2.35) | 0.596 | 1.33 (0.65-2.73) | 0.435 | 1.33 (0.73-2.40) | 0.347 | 1.32 (0.74-2.35) | 0.344 |
| Quintile 5 | 135-682 | 166 | 10 | 21.6 | 0.73 (0.48-1.11) | 0.147 | 0.78 (0.51-1.21) | 0.269 | 0.80 (0.51-1.25) | 0.334 | 0.80 (0.51-1.25) | 0.331 |
| p-trend | | | | | | **0.05** | | 0.08 | | 0.08 | | 0.08 |
| **First Cardiovascular Event or Any-Cause Death** | | | | | | | | | | | | |
| **White** | | | | | | | | | | | | |
| Quintile 1 | 7.32-56 | 77 | 36 | 257.9 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 76 | 42 | 340.3 | **1.31 (1.00-1.70)** | **0.047** | **1.43 (1.00-2.03)** | **0.05** | **1.60 (1.19-2.16)** | **0.002** | **1.60 (1.19-2.14)** | **0.002** |
| Quintile 3 | 77-100 | 82 | 51 | 351.7 | 1.34 (0.96-1.86) | 0.084 | 1.37 (0.93-2.01) | 0.109 | 1.41 (1.00-1.99) | 0.051 | 1.40 (0.98-2.00) | 0.064 |
| Quintile 4 | 101-134 | 88 | 49 | 334.0 | 1.29 (0.94-1.75) | 0.112 | 1.28 (0.88-1.86) | 0.191 | **1.45 (1.02-2.08)** | **0.04** | **1.45 (1.01-2.08)** | **0.045** |

3

| | | | | | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Quintile 5 | 135-468 | 65 | 42 | 396.3 | **1.53 (1.01-2.32)** | **0.044** | **1.59 (1.07-2.35)** | **0.021** | 1.45 (0.98-2.15) | 0.064 | 1.45 (0.99-2.15) | 0.06 |
| p-trend | | | | | | 0.103 | | 0.052 | | 0.213 | | 0.193 |
| **Black** | | | | | | | | | | | | |
| Quintile 1 | 2.25-56.2 | 148 | 85 | 285.9 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 156 | 78 | 233.2 | 0.80 (0.54-1.20) | 0.279 | 0.93 (0.65-1.33) | 0.688 | 0.94 (0.69-1.27) | 0.674 | 0.94 (0.69-1.27) | 0.683 |
| Quintile 3 | 76.8-100 | 147 | 64 | 191.9 | **0.67 (0.47-0.96)** | **0.028** | 0.72 (0.50-1.03) | 0.072 | 0.73 (0.52-1.01) | 0.056 | 0.73 (0.53-1.00) | 0.053 |
| Quintile 4 | 101-134 | 147 | 85 | 257.2 | 0.88 (0.66-1.18) | 0.397 | 0.97 (0.73-1.29) | 0.838 | 0.97 (0.78-1.20) | 0.773 | 0.97 (0.79-1.20) | 0.79 |
| Quintile 5 | 135-682 | 162 | 94 | 288.3 | 0.99 (0.70-1.40) | 0.958 | 1.06 (0.77-1.45) | 0.726 | 1.02 (0.80-1.32) | 0.857 | 1.03 (0.80-1.31) | 0.842 |
| p-trend | | | | | | 0.431 | | 0.354 | | 0.44 | | 0.421 |
| **Any-Cause Death** | | | | | | | | | | | | |
| **White** | | | | | | | | | | | | |
| Quintile 1 | 6.42-56 | 89 | 40 | 194.7 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 80 | 34 | 185.8 | 0.97 (0.67-1.42) | 0.88 | 1.05 (0.69-1.59) | 0.819 | 1.28 (0.85-1.93) | 0.238 | 1.28 (0.84-1.95) | 0.241 |
| Quintile 3 | 77-100 | 85 | 48 | 258.0 | 1.37 (0.91-2.06) | 0.13 | 1.43 (0.93-2.21) | 0.106 | **1.65 (1.07-2.55)** | **0.023** | **1.65 (1.07-2.55)** | **0.023** |
| Quintile 4 | 101-134 | 99 | 50 | 244.1 | **1.34 (1.02-1.75)** | **0.034** | **1.36 (1.02-1.81)** | **0.038** | **1.70 (1.33-2.18)** | **<.001** | **1.70 (1.33-2.18)** | **<.001** |
| Quintile 5 | 135-468 | 78 | 45 | 267.1 | 1.40 (0.98-2.00) | 0.067 | **1.43 (1.01-2.02)** | **0.046** | **1.50 (1.03-2.20)** | **0.035** | **1.50 (1.03-2.18)** | **0.035** |
| p-trend | | | | | | **0.013** | | **0.007** | | **0.016** | | **0.018** |
| **Black** | | | | | | | | | | | | |
| Quintile 1 | 2.25-56.2 | 157 | 71 | 167.9 | Reference | | Reference | | Reference | | Reference | |
| Quintile 2 | 56.3-76.7 | 168 | 72 | 160.8 | 0.96 (0.68-1.35) | 0.807 | 1.08 (0.78-1.51) | 0.632 | 1.16 (0.87-1.54) | 0.313 | 1.16 (0.87-1.53) | 0.31 |
| Quintile 3 | 76.8-100 | 158 | 52 | 116.0 | 0.70 (0.47-1.04) | 0.075 | 0.75 (0.50-1.12) | 0.155 | 0.79 (0.51-1.21) | 0.276 | 0.79 (0.52-1.19) | 0.259 |
| Quintile 4 | 101-134 | 152 | 71 | 159.2 | 0.94 (0.70-1.25) | 0.651 | 1.03 (0.77-1.38) | 0.842 | 1.05 (0.79-1.39) | 0.749 | 1.04 (0.78-1.39) | 0.768 |
| Quintile 5 | 135-682 | 166 | 67 | 145.0 | 0.85 (0.65-1.11) | 0.239 | 0.89 (0.67-1.20) | 0.459 | 0.89 (0.66-1.21) | 0.456 | 0.89 (0.66-1.20) | 0.45 |
| p-trend | | | | | | 0.35 | | 0.474 | | 0.393 | | 0.393 |

*Abbreviation:* IR, Incidence Rate; HR, Hazard Ratio; CI, Confidence Interval; TMAO, trimethylamine N-oxide

HR represents increase in risk in each quintile compared with the first quintile.

Model 2 adjusted for age and sex

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).

## Table S3: Sub-group Analyses for the Association between TMAO and Outcomes in 1232 patients of the HEMO Study.

| Strata (N) | Cardiac Death HR (95% CI) | P[1] | Sudden Cardiac Death HR (95% CI) | P[1] | First Cardiovascular Event or Any-Cause Death HR (95% CI) | P[1] | Any-Cause Death HR (95% CI) | P[1] |
|---|---|---|---|---|---|---|---|---|
| Entire Sample Overall | 1.09 (0.96-1.24) | | **1.16 (1.01-1.35)** | | 1.05 (0.98-1.14) | | 1.06 (0.98-1.14) | |
| Age < 59 years (616) | 0.98 (0.81-1.19) | 0.34 | 1.02 (0.77-1.34) | 0.30 | 1.07 (0.95-1.20) | 0.78 | 1.04 (0.93-1.17) | 0.78 |
| Age ≥ 59 years (616) | 1.17 (0.94-1.45) | | 1.26 (1.01-1.57) | | 1.05 (0.95-1.15) | | 1.07 (0.96-1.18) | |
| Male (533) | 1.14 (0.97-1.33) | 0.63 | 1.26 (0.91-1.75) | 0.54 | 1.08 (0.91-1.28) | 0.72 | 1.08 (0.94-1.24) | 0.75 |
| Female (699) | 1.06 (0.87-1.29) | | 1.10 (0.93-1.32) | | 1.04 (0.96-1.13) | | 1.04 (0.90-1.20) | |
| White (431) | **1.45 (1.24-1.69)** | **<.001** | **1.70 (1.34-2.15)** | **<.001** | 1.15 (1.01-1.32) | 0.09 | **1.22 (1.09-1.36)** | **0.02** |
| Black (801) | 0.90 (0.77-1.06) | | 0.92 (0.78-1.08) | | 1.01 (0.93-1.10) | | 0.97 (0.85-1.10) | |
| Diabetes = No (677) | **1.25 (1.05-1.49)** | **0.03** | 1.27 (1.00-1.61) | 0.37 | 1.09 (0.96-1.25) | 0.32 | 1.09 (0.98-1.21) | 0.48 |
| Diabetes = Yes (555) | 0.94 (0.77-1.14) | | 1.07 (0.84-1.36) | | 0.99 (0.88-1.10) | | 1.01 (0.89-1.16) | |
| Cardiac Disease = No (256) | 1.46 (0.92-2.33) | 0.22 | 2.32 (0.95-5.66) | 0.12 | 1.23 (1.01-1.49) | 0.13 | **1.30 (1.05-1.61)** | **0.04** |
| Cardiac Disease = Yes (976) | 1.05 (0.91-1.21) | | 1.09 (0.93-1.29) | | 1.02 (0.93-1.11) | | 1.01 (0.95-1.09) | |
| GI Disease = No (766) | 1.17 (0.97-1.42) | 0.26 | 1.25 (0.99-1.58) | 0.40 | 1.06 (0.95-1.18) | 0.78 | 1.11 (1.00-1.24) | 0.22 |
| GI Disease = Yes (466) | 1.00 (0.84-1.21) | | 1.08 (0.86-1.35) | | 1.03 (0.90-1.18) | | 0.99 (0.88-1.12) | |
| BMI < 18 kg/m$^2$ (39) | 1.54 (0.90-2.63) | 0.16 | 1.83 (1.10-3.04) | 0.06 | 1.02 (0.62-1.68) | 0.89 | 1.31 (0.88-1.96) | 0.27 |
| BMI 18 to 25 kg/m$^2$ (597) | 1.14 (0.95-1.36) | | 1.17 (0.89-1.54) | | 1.09 (0.92-1.29) | | 1.12 (1.00-1.24) | |
| BMI > 25 kg/m$^2$ (596) | 1.01 (0.86-1.19) | | 1.11 (0.92-1.34) | | 1.03 (0.90-1.17) | | 0.97 (0.85-1.11) | |
| Albumin < 3.6 g/dL (556) | 1.23 (1.00-1.51) | 0.07 | 1.27 (1.04-1.56) | 0.31 | 1.08 (0.99-1.18) | 0.54 | 1.08 (0.98-1.20) | 0.41 |
| Albumin ≥ 3.6 g/dL (670) | 0.92 (0.75-1.13) | | 1.03 (0.76-1.40) | | 1.02 (0.89-1.18) | | 1.01 (0.90-1.14) | |
| Standard Kt/V$_{UREA}$ (619) | 1.12 (0.92-1.37) | 0.61 | 1.30 (0.97-1.75) | 0.33 | **1.20 (1.05-1.38)** | **0.03** | 1.10 (0.98-1.23) | 0.53 |
| High Kt/V$_{UREA}$ (613) | 1.06 (0.93-1.21) | | 1.05 (0.86-1.30) | | 0.94 (0.82-1.07) | | 1.02 (0.87-1.19) | |
| Low-Flux (612) | 1.04 (0.90-1.19) | 0.29 | 1.01 (0.86-1.20) | 0.07 | 1.11 (1.00-1.23) | 0.37 | 1.07 (1.00-1.15) | 0.72 |
| High-Flux (620) | 1.17 (0.96-1.42) | | 1.35 (1.06-1.73) | | 1.02 (0.90-1.16) | | 1.04 (0.91-1.20) | |
| RKF = No (819) | 1.04 (0.89-1.22) | 0.44 | 1.08 (0.88-1.31) | 0.31 | 1.05 (0.96-1.15) | 0.77 | 1.02 (0.91-1.14) | 0.27 |
| RKF = Yes (412) | 1.21 (0.89-1.64) | | 1.42 (0.92-2.18) | | 1.07 (0.97-1.18) | | 1.15 (0.99-1.34) | |

*Abbreviation:* HR, Hazard Ratio; CI, Confidence Interval; TMAO, trimethylamine N-oxide; GI, Gastrointestinal; BMI, Body Mass Index; RKF, Residual Kidney Function

HR represents increase in risk per 2-fold increase in TMAO concentrations. Modeled as natural log transformed TMAO/natural log of 2.

Model 4 adjusted for age, sex, 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, relative volume removed on dialysis and residual kidney function (urinary stdKt/V$_{UREA}$ calculated from urinary urea clearance).

[1] P-interactions between groups for the subgroup analyses.

# Table S4. Baseline Characteristics of 1232 Hemodialysis Patients by Quintiles of TMAO
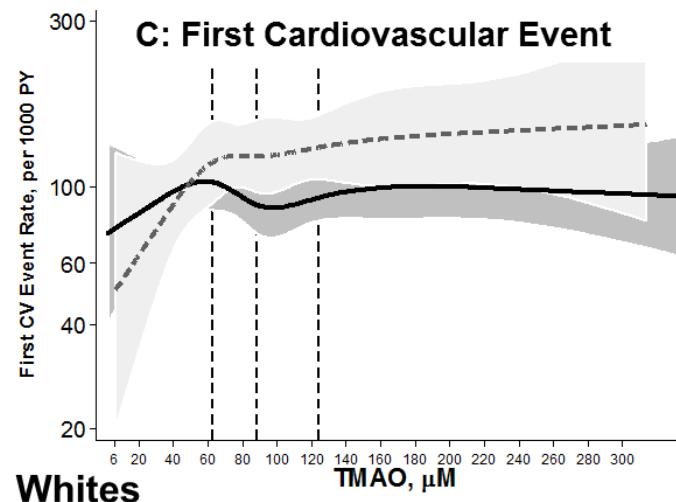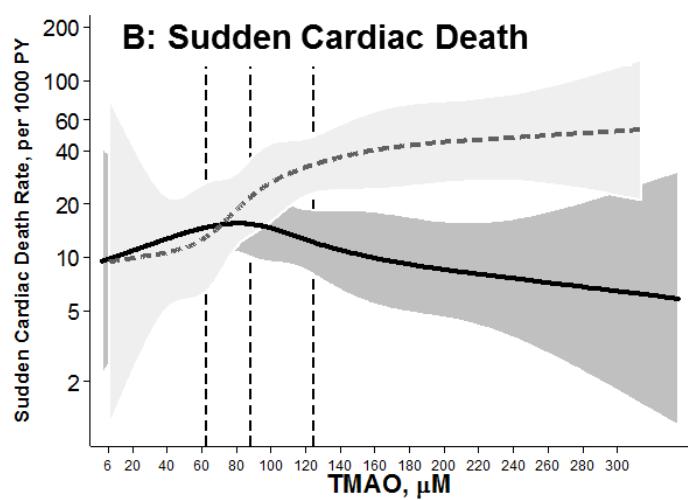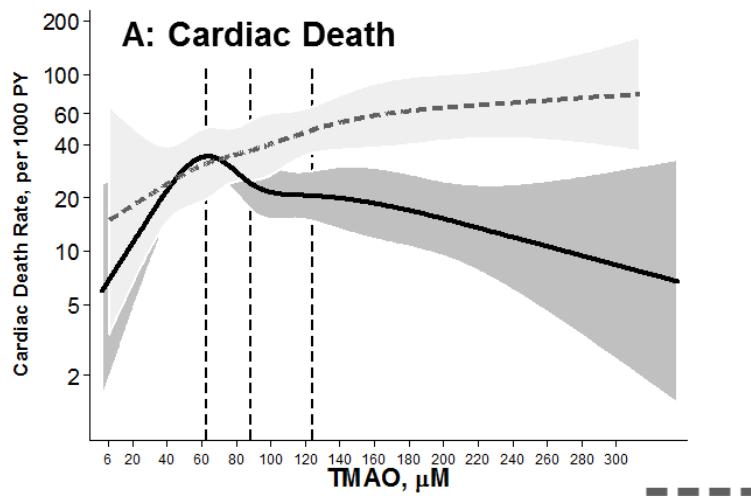
| Characteristic | Overall | By Quintiles of TMAO, µM | | | | | |
|---|---|---|---|---|---|---|---|
| | | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | |
| | | < 56.3 | 56.3 - 76.7 | 76.8 - 100 | 101 - 135 | ≥ 135 | p-trend |
| N | 1232 | 246 | 248 | 243 | 251 | 244 | |
| **Trimethylamine Oxide (µM)** | | | | | | | |
| Mean ± SD | 101.9 ± 63.9 | | | | | | |
| Median [25th to 75th percentiles] | 88 [62-124] | | | | | | |
| **Demographics** | | | | | | | |
| Age, years | 57.7 ± 13.8 | 57.9 ± 14.7 | 55.7 ± 14.4 | 58.6 ± 13.6 | 57.6 ± 14.0 | 58.7 ± 12.2 | 0.18 |
| Female sex | 699 (56.7) | 154 (62.6) | 137 (55.2) | 133 (54.7) | 142 (56.6) | 133 (54.5) | 0.18 |
| Black race | 801 (65.0) | 157 (63.8) | 168 (67.7) | 158 (65.0) | 152 (60.6) | 166 (68.0) | 0.64 |
| **Clinical Characteristics** | | | | | | | |
| ICED score | 2.0 ± 0.8 | 1.9 ± 0.9 | 1.9 ± 0.8 | 2.0 ± 0.9 | 2.0 ± 0.8 | 2.0 ± 0.8 | 0.058 |
| Diabetes | 555 (45.0) | 92 (37.4) | 107 (43.1) | 117 (48.1) | 112 (44.6) | 127 (52.0) | **0.002** |
| Cardiac disease | 976 (79.2) | 189 (76.8) | 196 (79.0) | 194 (79.8) | 203 (80.9) | 194 (79.5) | 0.49 |
| Gastrointestinal disease | 466 (37.8) | 94 (38.2) | 79 (31.9) | 94 (38.7) | 98 (39.0) | 101 (41.4) | 0.15 |
| Attributed cause of End-Stage Renal Disease | | | | | | | 0.12 |
| Diabetes | 463 (37.96) | 78 (31.7) | 90 (36.3) | 98 (40.3) | 97 (38.6) | 100 (41.0) | |
| Hypertension | 397 (32.2) | 85 (34.6) | 78 (31.5) | 74 (30.5) | 79 (31.5) | 81 (33.2) | |
| Polycystic Kidney Disease | 32 (2.6) | 9 (3.7) | 7 (2.8) | 2 (0.8) | 8 (3.2) | 6 (2.5) | |
| Other | 316 (25.6) | 70 (28.5) | 68 (27.4) | 66 (27.2) | 60 (23.9) | 52 (21.3) | |
| Residual kidney urea clearance > 0 | 413 (33.5) | 84 (34.1) | 97 (39.1) | 83 (34.2) | 78 (31.1) | 71 (29.1) | 0.053 |
| **Dialysis Characteristics** [a] | | | | | | | |
| Years of prior dialysis | 3.5 ± 4.2 | 3.8 ± 4.7 | 3.2 ± 3.7 | 3.0 ± 3.9 | 3.7 ± 4.3 | 3.7 ± 4.1 | 0.51 |
| Predialysis systolic blood pressure, mm Hg [a] | 152.2 ± 25.7 | 152.3 ± 25.8 | 152.9 ± 27.7 | 151.6 ± 25.9 | 152.8 ± 25.0 | 151.4 ± 24.3 | 0.66 |
| Postdialysis Weight, Kg | 70.3 ± 15.2 | 67.3 ± 13.5 | 69.8 ± 14.4 | 72.0 ± 14.4 | 71.4 ± 16.6 | 71.0 ± 16.5 | **0.016** |
| Body Mass Index, Kg/m$^2$ | 25.8 ± 5.4 | 25.1 ± 4.9 | 25.6 ± 5.1 | 26.5 ± 5.5 | 26.0 ± 5.6 | 25.9 ± 5.9 | 0.17 |
| Relative volume removed, % | 4.1 ± 1.7 | 3.9 ± 1.7 | 4.1 ± 1.6 | 4.1 ± 1.7 | 4.1 ± 1.7 | 4.1 ± 1.7 | 0.39 |
| High-dose group | 613 (49.8) | 141 (57.3) | 126 (50.8) | 126 (51.9) | 117 (46.6) | 103 (42.2) | **<0.001** |
| High-flux group | 620 (50.3) | 131 (53.3) | 116 (46.8) | 116 (47.7) | 129 (51.4) | 128 (52.5) | 0.63 |
| **Predialysis Laboratory Tests** [a] | | | | | | | |
| Blood Urea Nitrogen, mg/dL | 59.4 ± 18.7 | 50.3 ± 17.9 | 57.5 ± 17.4 | 60.5 ± 16.3 | 64.3 ± 18.3 | 64.5 ± 19.6 | **<0.001** |
| Single-pool Kt/V | 1.5 ± 0.3 | 1.5 ± 0.3 | 1.5 ± 0.3 | 1.5 ± 0.3 | 1.5 ± 0.2 | 1.5 ± 0.3 | **0.011** |
| Serum albumin, g/dL | 3.6 ± 0.4 | 3.5 ± 0.4 | 3.6 ± 0.4 | 3.6 ± 0.4 | 3.6 ± 0.4 | 3.6 ± 0.3 | 0.26 |
| Serum β2-microglobulin, mg/L | 36.7 ± 14.3 | 34.6 ± 14.7 | 36.8 ± 14.7 | 36.3 ± 14.4 | 38.9 ± 14.9 | 36.9 ± 12.5 | 0.079 |
| enPCR, g/kg/day | 1.0 ± 0.3 | 0.9 ± 0.3 | 1.0 ± 0.3 | 1.0 ± 0.2 | 1.1 ± 0.3 | 1.1 ± 0.3 | **<0.001** |
| **Dietary recall at Baseline** | | | | | | | |
| Total protein, g/kg-ABW/day | 0.9 ± 0.3 | 0.9 ± 0.3 | 0.9 ± 0.4 | 0.9 ± 0.4 | 0.9 ± 0.3 | 1.0 ± 0.4 | 0.75 |
| Fat% | 35.6 ± 7.5 | 35.5 ± 7.7 | 36.0 ± 8.0 | 35.7 ± 7.1 | 35.2 ± 7.3 | 35.8 ± 7.4 | 0.96 |
| Carbohydrates% | 48.3 ± 9.2 | 48.8 ± 9.2 | 47.9 ± 10.0 | 47.7 ± 9.0 | 49.0 ± 8.8 | 48.2 ± 9.2 | 0.99 |
| **Dietary recall at Year 1** | | | | | | | |
| Total protein, g/kg-ABW/day | 0.9 ± 0.4 | 0.9 ± 0.4 | 1.0 ± 0.4 | 0.9 ± 0.3 | 0.9 ± 0.4 | 1.0 ± 0.4 | 0.57 |
| Fat% | 36.5 ± 7.8 | 36.4 ± 8.2 | 37.3 ± 7.2 | 36.7 ± 7.4 | 35.8 ± 8.0 | 36.6 ± 8.1 | 0.69 |
| Carbohydrates% | 47.2 ± 9.3 | 47.9 ± 10.0 | 46.4 ± 9.0 | 47.0 ± 8.1 | 48.0 ± 10.1 | 46.6 ± 8.9 | 0.52 |
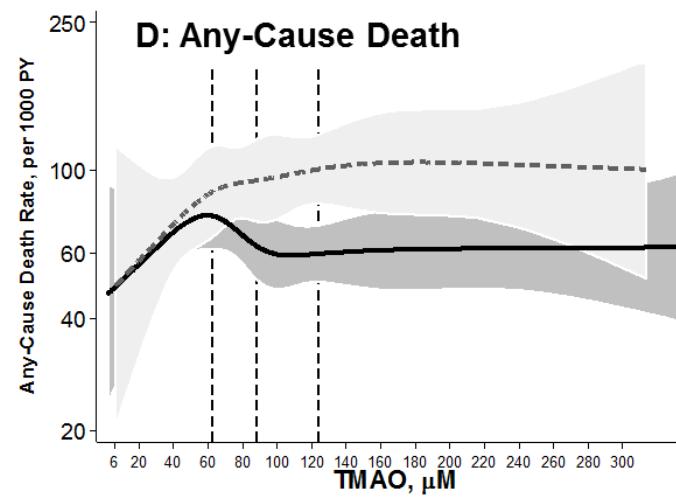
Note: Values for categorical variables are given as number (percentage); values for continuous variables are given as mean ± standard deviation.
Abbreviations: SD, Standard Deviation; ICED, Index of Coexistent Disease; enPCR, equilibrated normalized protein catabolic rate; ABW, adjusted body weight

[a] Data from the same date as the TMAO sample.

**Figure S1: Age and Sex Adjusted Incident Rates of Outcomes in 1232 Hemodialysis Patients of the HEMO Study**

**Figure S2: Fully Adjusted Association of TMAO with Outcomes in the HEMO Study**