

## 1. Supplemental Methods

### 1.1. Outcome Measurements

In a sensitivity analysis, we examined the relationships using three additional equations that use serum creatinine to estimate GFR. The original Bedside-Schwartz formula used to calculate eGFR and used as the main method of measuring eGFR was calculated using the following formula:

$$eGFR = 0.413 \times \frac{\text{Height (cm)}}{\text{Serum Creatinine (mg/dL)}} \quad (1)$$

as recommended in conjunction with this laboratory method [1]. The CKiD under 25 eGFR measurement was calculated using the following formula:

$$eGFR = K \left( \frac{\text{Height (cm)}}{\text{Serum Creatinine (mg/dL)}} \right) \quad (2)$$

as recently recommended in conjunction with this laboratory method [2]. This calculation takes into account age and sex of individuals up until age 25 years. The Gao quadratic eGFR equation was calculated using the following formula:

$$eGFR = 0.68 \times \frac{\text{Height (cm)}}{\text{Serum Creatinine (mg/dL)}} - 0.0008 \times \left( \frac{\text{Height (cm)}}{\text{Serum Creatinine (mg/dL)}} \right)^2 + 0.48 \times \text{age} - (21.53 \text{ for males and } 25.68 \text{ for females}) \quad (3)$$

as recommended in conjunction with this laboratory method [3]. The Full Age Spectrum eGFR equation was calculated using the following formula:

$$eGFR = \frac{107.3}{\text{Serum Creatinine (mg/dL)}^Q} \quad (4)$$

where

$$Q = 3.94 - (13.4 \times \text{height}) + (17.6 \times \text{height}^2) - (9.84 \times \text{height}^3) + (2.04 \times \text{height}^4) \quad (5)$$

as recently recommended in conjunction with this laboratory method [4,5].

**Table S1.** Comparison of adjusted<sup>1</sup> effect estimates of blood Mn (log<sub>10</sub> µg/L) concentrations with eGFR using four serum-creatinine based eGFR formulae, and **stratified by sex or race/ethnicity**.

|                       | Creatinine-Based<br>Bedside Schwartz<br>eGFR equation |              |             | CKiD under 25 eGFR<br>equation |              |             | Gao Quadratic eGFR<br>equation |              |             | Full Age Spectrum<br>eGFR equation |              |             |
|-----------------------|-------------------------------------------------------|--------------|-------------|--------------------------------|--------------|-------------|--------------------------------|--------------|-------------|------------------------------------|--------------|-------------|
|                       | β                                                     | 95%<br>CI    | P-<br>value | β                              | 95% CI       | P-<br>value | β                              | 95%<br>CI    | P-<br>value | β                                  | 95%<br>CI    | P-<br>value |
| <b>Main Model</b>     |                                                       |              |             |                                |              |             |                                |              |             |                                    |              |             |
| Unadjusted            | 23.2                                                  | (14.4, 32.0) | <0.001      | 9.56                           | (1.9, 17.2)  | 0.01        | 12.5                           | (7.3, 17.7)  | <0.001      | 14.9                               | (5.0, 24.8)  | 0.004       |
| Adjusted              | 5.8                                                   | (-1.6, 13.2) | 0.1         | 5.9                            | (-1.4, 13.3) | 0.1         | 3.9                            | (-0.7, 8.4)  | 0.1         | 6.8                                | (-2.5, 16.2) | 0.1         |
| <b>Sex</b>            |                                                       |              |             |                                |              |             |                                |              |             |                                    |              |             |
| Females               | 3.2                                                   | (-8.0, 14.4) | 0.6         | 3.1                            | (-7.4, 13.7) | 0.5         | 2.0                            | (-5.4, 9.4)  | 0.6         | 4.9                                | (-9.0, 18.9) | 0.5         |
| Males                 | 5.7                                                   | (-5.9, 17.3) | 0.3         | 7.6                            | (-4.9, 20.0) | 0.2         | 3.4                            | (-3.7, 10.5) | 0.3         | 7.0                                | (-5.1, 19.2) | 0.2         |
| <b>Race/Ethnicity</b> |                                                       |              |             |                                |              |             |                                |              |             |                                    |              |             |
| Mexican American      | 5.7                                                   | (-8.9, 20.4) | 0.4         | 7.4                            | (-8.3, 23.1) | 0.3         | 5.6                            | (-4.7, 15.9) | 0.3         | 8.8                                | (-8.5, 26.2) | 0.3         |

|                    |       |               |       |      |               |      |      |               |      |      |               |      |
|--------------------|-------|---------------|-------|------|---------------|------|------|---------------|------|------|---------------|------|
| Other Hispanic     | 29.4  | (-0.4, 59.3)  | 0.053 | 26.5 | (-4.3, 57.3)  | 0.09 | 20.6 | (5.9, 35.4)   | 0.01 | 21.7 | (-8.0, 51.3)  | 0.1  |
| Non-Hispanic White | -1.99 | (-12.8, 8.9)  | 0.7   | -1.8 | (-12.0, 8.4)  | 0.7  | -1.5 | (-8.9, 5.9)   | 0.7  | 1.7  | (-11.8, 15.2) | 0.8  |
| Non-Hispanic Black | 14.5  | (0.4, 28.7)   | 0.04  | 14.3 | (1.0, 27.7)   | 0.03 | 11.0 | (2.0, 20.0)   | 0.02 | 17.8 | (-2.9, 38.4)  | 0.08 |
| Non-Hispanic Asian | 15.9  | (-33.6, 65.4) | 0.5   | 14.0 | (-33.3, 61.2) | 0.5  | -1.5 | (-18.0, 14.9) | 0.8  | 1.9  | (-51.9, 55.8) | 0.9  |
| Other Race         | 28.4  | (6.8, 50.1)   | 0.01  | 27.3 | (6.7, 47.8)   | 0.01 | 19.1 | (4.9, 33.2)   | 0.01 | 21.3 | (0.001, 42.6) | 0.05 |

<sup>1</sup> Models were adjusted for age, sex, BMI z-score, race/ethnicity, and PIR.

CI: confidence interval; eGFR: estimated glomerular filtration rate

**Table S2.** Adjusted associations of urine Mn (log<sub>10</sub> µg Mn/g creatinine) and eGFR using survey weighted linear regression, **stratified by sex or race/ethnicity**. Urine Mn levels were creatinine-adjusted in all models.

|                                   | eGFR |              |         |
|-----------------------------------|------|--------------|---------|
|                                   | β    | 95% CI       | p-value |
| <b>Sex<sup>1</sup></b>            |      |              |         |
| Females                           | 15.4 | (7.9, 22.9)  | 0.0002  |
| Males                             | 15.4 | (8.6, 22.3)  | <.0001  |
| <b>Race/Ethnicity<sup>2</sup></b> |      |              |         |
| Mexican American                  | 10.9 | (1.8, 20.0)  | 0.02    |
| Other Hispanic                    | 35.8 | (23.4, 48.2) | <.0001  |
| Non-Hispanic White                | 14.7 | (6.2, 23.2)  | 0.0014  |
| Non-Hispanic Black                | 17.4 | (8.3, 26.6)  | 0.0005  |
| Non-Hispanic Asian                | 7.7  | (-6.3, 21.7) | 0.3     |
| Other Race                        | 20.9 | (7.3, 34.6)  | 0.004   |

<sup>1</sup> Models were adjusted for BMI z-score, race/ethnicity, and PIR.

<sup>2</sup> Models were adjusted for sex, BMI z-score, and PIR.

CI: confidence interval; eGFR: estimated glomerular filtration rate

## References

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