Supplemental Material

Associations between Arsenic Species in Exfoliated Urothelial Cells and Prevalence of Diabetes among Residents of Chihuahua, Mexico

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**Table S1.** Basic characteristics of participants included in the present study and in the entire Chihuahua cohort

| Characteristics                          | Present study | Chihuahua cohort |
|-----------------------------------------|---------------|------------------|
| All subjects (N)                        | 374           | 1163             |
| Females (%)                             | 67.4          | 67.0             |
| Age, years (range, mean ± SD)           | 18–90         | 18–90            |
|                                         | 49.2 ± 15.6*  | 45.7 ± 15.8      |
| As in water, ppb (range, median)        | 0.01–275      | < LOD–420a       |
|                                         | 48.7          | 47.4             |
| Sum of As species in urine, ppb (range, median) | 0.5–492 | 0.5–375b |
|                                         | 53.5          | 53.2             |
| BMI > 30 (%)                             | 41            | 40               |
| Diabetic subjects (%)                   | 17.6          | 17.3             |

*a*To date, As concentrations were determined only in 876 samples of drinking water. *b*To date, concentrations of As species were determined only in 939 samples of urine. *c*Diabetes is classified by FPG ≥ 126 mg/dL or 2HPG ≥ 200 mg/dL, or self-reported doctor’s diagnosis or use of anti-diabetic medication (based on the questionnaire data).

*Difference between the present study and the Chihuahua cohort is statistically significant (p < 0.05).*
Figure S1. Associations between the log_{10}-transformed concentrations of As species in EUC and log_{10}-transformed As species in urine (not adjusted for creatinine): A, iAs^{III} in EUC vs. iAs^{III-V} in urine; B, iAs^{V} in EUC vs. iAs^{III-V} in urine; C, MAs^{III} in EUC vs. MAs^{III-V} in urine; D, MAs^{V} in EUC vs. MAs^{III-V} in urine; E, DMAs^{III} in EUC vs. DMAs^{III-V} in urine; DMAs^{V} in EUC vs. DMAs^{III-V} in urine; G, sum of As^{III} species in EUC vs. sum of As^{III-V} species in urine; H sum of As^{V} species in EUC vs. sum of As^{III-V} species in urine; Slope (β) and correlation coefficient (r^2) determined by linear regression analysis are shown. All slopes are significantly different from 0 (p < 0.001).
Table S2. Associations between the log_{10}-transformed concentrations of As species in EUC and log_{10}-transformed As species in urine after adjustment for urinary creatinine.

| As species in urine | As species in EUC | $\beta \pm SE$ | $r^2$ |
|---------------------|-------------------|----------------|------|
| iAs^{III+V}         | iAs^{III}         | $0.70 \pm 0.048$ | 0.36 |
| iAs^{III+V}         | iAs^{V}           | $0.33 \pm 0.073$ | 0.05 |
| MAs^{III+V}         | MAs^{III}         | $0.87 \pm 0.054$ | 0.41 |
| MAs^{III+V}         | MAs^{V}           | $0.79 \pm 0.094$ | 0.16 |
| DMAs^{III+V}        | DMAs^{III}        | $0.64 \pm 0.073$ | 0.17 |
| DMAs^{III+V}        | DMAs^{V}          | $0.52 \pm 0.103$ | 0.06 |
| Sum of As^{III+V} species | Sum of As^{III} species | $0.96 \pm 0.056$ | 0.44 |
| Sum of As^{III+V} species | Sum of As^{III} species | $0.53 \pm 0.090$ | 0.09 |

Slope ($\beta$), standard error (SE) and correlation coefficient ($r^2$) determined by linear regression analysis are shown. All slopes are significantly different from 0 ($p<0.001$).
Figure S2. Associations between the log-transformed EUC count and As content (log-transformed sum of As species) for EUC samples obtained from male (A) and female (B) study participants. Slope ($\beta$) and correlation coefficient ($r^2$) determined by linear regression analysis are shown. Both slopes are significantly different from 0 ($p < 0.05$).
Table S3. Associations of diabetes with As species in EUC and urine.

| As species                      | MODEL 1<sup>a</sup>     | MODEL 1<sup>a</sup>     | MODEL 2<sup>b</sup>     | MODEL 2<sup>b</sup>     |
|---------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
|                                 | OR (95% CI)<sup>c</sup> | p                       | OR (95% CI)<sup>c</sup> | p                       |
| **EUC**                         |                         |                         |                         |                         |
| iAs<sub>III</sub>               | 1.57 (1.19, 2.07)       | < 0.01                  | 1.75 (1.29, 2.39)       | < 0.01                  |
| MAs<sub>III</sub>               | 1.63 (1.24, 2.15)       | < 0.01                  | 2.02 (1.48, 2.77)       | < 0.01                  |
| DMAs<sub>III</sub>              | 1.31 (0.96, 1.84)       | 0.09                    | 1.49 (1.04, 2.13)       | 0.03                    |
| iAs<sub>V</sub>                 | 1.23 (0.90, 1.67)       | 0.20                    | 1.41 (1.00, 1.98)       | 0.05                    |
| MAs<sub>V</sub>                 | 1.09 (0.79, 1.50)       | 0.61                    | 1.26 (0.89, 1.78)       | 0.20                    |
| DMAs<sub>V</sub>                | 0.97 (0.71, 1.33)       | 0.85                    | 0.99 (0.70, 1.38)       | 0.94                    |
| iAs<sub>III+V</sub>             | 1.38 (1.03, 1.84)       | 0.03                    | 1.53 (1.11, 2.11)       | < 0.01                  |
| MAs<sub>III+V</sub>             | 1.33 (0.99, 1.78)       | 0.06                    | 1.54 (1.12, 2.11)       | < 0.01                  |
| DMAs<sub>III+V</sub>            | 1.06 (0.77, 1.47)       | 0.70                    | 1.12 (0.80, 1.58)       | 0.50                    |
| Sum of As species<sup>d</sup>   | 1.24 (0.91, 1.68)       | 0.17                    | 1.41 (1.01, 1.97)       | 0.04                    |
| MAs/iAs                        | 1.06 (0.83, 1.36)       | 0.63                    | 1.09 (0.83, 1.42)       | 0.54                    |
| DMAs/MAAs                      | 0.62 (0.47, 0.83)       | < 0.01                  | 0.53 (0.38, 0.73)       | < 0.01                  |
| DMAs/iAs                       | 0.72 (0.55, 0.96)       | 0.02                    | 0.65 (0.48, 0.89)       | 0.01                    |
| (DMAs+MAAs)/iAs                | 0.77 (0.56, 1.04)       | 0.08                    | 0.78 (0.56, 1.05)       | 0.09                    |
| **Urine (unadjusted)**          |                         |                         |                         |                         |
| iAs<sub>III+V</sub>             | 1.18 (0.91, 1.53)       | 0.22                    | 1.34 (1.00, 1.79)       | 0.05                    |
| MAs<sub>III+V</sub>             | 1.13 (0.87, 1.46)       | 0.36                    | 1.23 (0.93, 1.63)       | 0.14                    |
| DMAs<sub>III+V</sub>            | 1.24 (0.96, 1.60)       | 0.10                    | 1.34 (1.02, 1.76)       | 0.04                    |
| Sum of As species               | 1.19 (0.93, 1.54)       | 0.17                    | 1.31 (0.99, 1.72)       | 0.06                    |
| MAs/iAs                        | 0.86 (0.67, 1.11)       | 0.25                    | 0.77 (0.58, 1.02)       | 0.07                    |
| DMAs/MAAs                      | 1.37 (1.03, 1.84)       | 0.03                    | 1.38 (1.00, 1.89)       | 0.05                    |
| DMAs/iAs                       | 1.12 (0.86, 1.46)       | 0.38                    | 1.05 (0.79, 1.40)       | 0.74                    |
| (DMAs+MAAs)/iAs                | 0.99 (0.75, 1.30)       | 0.95                    | 1.02 (0.77, 1.34)       | 0.91                    |
| Creatinine                     | 1.01 (0.78, 1.31)       | 0.93                    | 1.00 (0.75, 1.32)       | 0.98                    |
| Specific gravity               | 1.32 (1.01, 1.71)       | 0.07                    | 1.42 (1.07, 1.89)       | 0.02                    |
| **Urine (creatinine adjusted)** |                         |                         |                         |                         |
| iAs<sub>III+V</sub>             | 1.19 (0.92, 1.54)       | 0.19                    | 1.38 (1.04, 1.83)       | 0.03                    |
| MAs<sub>III+V</sub>             | 1.17 (0.91, 1.51)       | 0.23                    | 1.35 (1.01, 1.79)       | 0.04                    |
| DMAs<sub>III+V</sub>            | 1.26 (0.98, 1.62)       | 0.08                    | 1.39 (1.05, 1.84)       | 0.02                    |
| Sum of As species               | 1.24 (0.96, 1.60)       | 0.10                    | 1.39 (1.05, 1.84)       | 0.02                    |
| **Urine (specific gravity adjusted)** |                     |                         |                         |                         |
| iAs<sub>III+V</sub>             | 0.98 (0.76, 1.27)       | 0.87                    | 1.08 (0.81, 1.42)       | 0.61                    |
| MAs<sub>III+V</sub>             | 0.94 (0.73, 1.22)       | 0.65                    | 0.99 (0.75, 1.30)       | 0.92                    |
| DMAs<sub>III+V</sub>            | 1.04 (0.81, 1.33)       | 0.78                    | 1.10 (0.84, 1.44)       | 0.51                    |
| Sum of As species               | 1.00 (0.78, 1.29)       | 0.99                    | 1.04 (0.79, 1.36)       | 0.79                    |
aModel 1: Diabetes classified by either FPG $\geq 126$ mg/dL, 2HPG $\geq 200$ mg/dL, self-reported doctor’s diagnosis or use of medication to treat diabetes. bModel 2: Diabetes classified only by FPG $\geq 126$ mg/dL or 2HPG $\geq 200$ mg/dL. cOdds ratio (OR) and 95% confidence interval (CI) are standardized to an increment of one inter-quartile range (IQR) and adjusted for age, sex, and BMI (IQRs are listed in Table 2). dSum of As species = iAs\(^V\) + iAs\(^{III}\) + MAs\(^V\) + MAs\(^{III}\) + DMAs\(^V\) + DMAs\(^{III}\).