Role of Metabolic Genes in Blood Arsenic Concentrations of Jamaican Children with and without Autism Spectrum Disorder

---

Detailed description of General Linear Models used to obtain the results reported in Table 3 (based on 100 matched pairs)

General Linear Models that assessed unadjusted effects of various exposure variables in blood arsenic concentrations of children with and without ASD can be represented by the following linear regression equations:

Models: $E(Y_i | X_{1i}, X_{2i}, X_{12ij}) = \beta_0 + \beta_1 X_{1i} + \beta_{2k} X_{2ki} + \sum_{j=1}^{99} \beta_{3j} X_{3ij}$; *k=1, 2,..., 27 that represent various exposure variables*

$$i = 1, 2, \dots, 200 \ (number \ of \ children); \ j = 1, 2, \dots, 99 (number \ of \ dummy \ variables \ representing \ the \ 100 \ matched \ pairs);$$

$$Y_i = ln \ of \ blood \ arsenic \ concentrations \ of \ the \ i^{th} \ child;$$

$$X_{1i} = case \ status \ of \ the \ i^{th} \ child \ (ASD \ case = 1; \ TD \ control = 0);$$

$$X_{21i} = car \ ownership \ associated \ with \ family \ of \ the \ i^{th} \ child \ (\ No \ cars = 0; \ otherwise = 1);$$

$$X_{22i} = maternal \ age \ at \ child's \ birth \ associated \ with \ the \ i^{th} \ child \ ("maternal \ age \geq 35 \ years" = 1; \ otherwise = 0);$$

$$X_{23i} = parental \ levels \ of \ education \ associated \ with \ the \ i^{th} \ child \ (both \ parents \ had \ up \ to \ high \ school = 0; \ otherwise = 1);$$

$$X_{24i} = source \ of \ drinking \ water \ associated \ with \ the \ i^{th} \ child \ (piped \ water = 1; \ otherwise = 0);$$

$$X_{25i} = consumption \ of \ "yam, sweet \ potato, or \ dasheen" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{26i} = consumption \ of \ "carrot \ or \ pumpkin" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{27i} = consumption \ of \ "lettuce" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{28i} = consumption \ of \ "callaloo, broccoli, or \ pak \ choi" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{29i} = consumption \ of \ "cabbage" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{210i} = consumption \ of \ "string \ beans" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{211i} = consumption \ of \ "tomatoes" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{212i} = consumption \ of \ "ackee" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{213i} = consumption \ of \ "avocado" \ associated \ with \ the \ i^{th} \ child \ (No \ consumption = 0; \ otherwise = 1);$$

$$X_{214i} = high \ seafood \ consumption \ associated \ with \ the \ i^{th} \ child \ (more \ than \ 6 \ seafood \ meals \ per \ week = 1; \ otherwise = 0);$$

X_{215i} = *frequency of seafood consumption associated with the ith child = number of seafood meals consumed in a week;*

X_{216i} = *consumption of "salt water fish" associated with the ith child (No consumption = 0; otherwise = 1);*

X_{217i} = *consumption of "fresh water fish" associated with the ith child (No consumption = 0; otherwise = 1);*

X_{218i} = *consumption of "sardine, mackerel" associated with the ith child (No consumption = 0; otherwise = 1);*

X_{219i} = *consumption of "tuna" associated with the ith child (No consumption = 0; otherwise = 1);*

X_{220i} = *consumption of "salted fish" associated with the ith child (No consumption = 0; otherwise = 1);*

X_{221i} = *consumption of "shellfish" associated with the ith child (No consumption = 0; otherwise = 1);*

X_{222i} = *consumption of "shrimp" associated with the ith child (No consumption = 0; otherwise = 1);*

X_{223i} = *GSTM1 genotype associated with the ith child ("DD" = 0; "I/I" or "I/D" = 1);*

X_{224i} = *GSTT1 genotype associated with the ith child ("DD" = 0; "I/I" or "I/D" = 1);*

X_{225i} = *"GSTP1(Ile/Ile) genotype" associated with the ith child (GSTP1(Ile/Ile) genotype = 1; otherwise = 0);*

X_{226i} = *"GSTP1(Val/Val) genotype" associated with the ith child (GSTP1(Val/Val) genotype = 1; otherwise = 0);*

X_{227i} = *"GSTP1(Ile/Val) genotype" associated with the ith child (GSTP1(Ile/Val) genotype = 1; otherwise = 0);*

$$X_{3ij} = \begin{cases} 1, \text{if the } i^{th} \text{ child in the } j^{th} \text{ matched pair is an ASD case} \\ 0, \text{if the } i^{th} \text{ child in the } j^{th} \text{ matched pair is a TD control} \end{cases} ;$$

$E(Y_i|X_{1i}, X_{2ki}, \ldots, , X_{3ij})$ *stands for mean ln blood arsenic concentrations given the X_{1i}, X_{2ki}, X_{3ij};*

$\beta_0, \beta_1, \beta_{2k}, \beta_{3j}$ *are regression coefficients associated with the General Linear Models.*

Detailed description of additive General Linear Models that are used to obtain the results reported in Table 4 (based on 65 matched pairs)

The univariable and final multivariable additive General Linear Models used that assessed possible association between blood arsenic concentrations and ASD status can be represented by the following linear regression equations:

For the univariable model: $E(Y_i \mid X_{1i}, X_{12ij}) = \beta_{10} + \beta_{11} X_{1i} + \sum_{j=1}^{64} \beta_{112j} X_{12ij}$;

For the final multivariable model: $E(Y_i \mid X_{1i}, X_{2i}, \ldots, X_{11i}, X_{12ij}) = \beta_{20} + \beta_{21} X_{1i} + \beta_{22} X_{2i} + \cdots + \beta_{211} X_{11i} + \sum_{j=1}^{64} \beta_{212j} X_{12ij}$;

$i = 1, 2, \ldots, 130$ (*number of children*); $j = 1, 2, \ldots, 64$ (*number of dummy variables representing the 65 matched pairs*);

$Y_i = ln$ *of blood arsenic concentrations of the ith child;*

$X_{1i} =$ *case status of the ith child (ASD case $= 1$; TD control $= 0$);*

$X_{2i} =$ *car ownership associated with family of the ith child (No cars $= 0$; otherwise $= 1$);*

$X_{3i} =$ *maternal age at child's birth associated with the ith child ("maternal age ≥ 35 years" $= 1$; otherwise $= 0$);*

$X_{4i} =$ *Parental levels of education associated with the ith child (both parents had up to high school $= 0$; otherwise $= 1$);*

$X_{5i} =$ *source of drinking water associated with the ith child (piped water $= 1$, otherwise $= 0$);*

$X_{6i} =$ *consumption of "yam, sweet potato, or dasheen" associated with the ith child (No consumption $= 0$; otherwise $= 1$);*

$X_{7i} =$ *consumption of "carrot or pumpkin" associated with the ith child (No consumption $= 0$; otherwise $= 1$);*

$X_{8i} =$ *consumption of "callaloo, broccoli, or pak choi" associated with the ith child (No consumption $= 0$; otherwise $= 1$);*

$X_{9i} =$ *consumption of "cabbage" associated with the ith child (No consumption $= 0$; otherwise $= 1$);*

$X_{10i} =$ *consumption of "avocado" associated with the ith child (No consumption $= 0$; otherwise $= 1$);*

$X_{11i} =$ *frequency of seafood consumption associated with the ith child $=$ number of seafood meals consumed in a week;*

$$X_{12ij} = \begin{cases} 1, \textit{if the } i^{th} \textit{ child in the } j^{th} \textit{ matched pair is an ASD case} \\ 0, \textit{if the } i^{th} \textit{ child in the } j^{th} \textit{ matched pair is a TD control} \end{cases} ;$$

$E(Y_{1i} \mid X_{1i}, X_{12ij})$ *stands for mean ln blood arsenic concentrations given X_{1i}, X_{12ij};*

$E(Y_{2i} \mid X_{1i}, X_{2i}, \ldots, X_{11i}, X_{12ij})$ *stands for mean ln blood arsenic concentrations given $X_{1i}, X_{2i}, \ldots, X_{11i}, X_{12ij}$;*

$\beta_{10}, \beta_{11}, \beta_{112j}$ *are regression coefficients associated with the univaribale model;*

$\beta_{20}, \beta_{21}, \ldots, \beta_{211}, \beta_{212j}$ *are regression coefficients associated with the final multivaribale model.*

Detailed description of additive General Linear Models used to obtain the results reported in Table 4 (based on 100 matched pairs)

The univariable and final multivariable additive General Linear Models used that assessed possible association between blood arsenic concentrations and ASD status can be represented by the following linear regression equations:

For the univariable model: $E(Y_i \mid X_{1i}, X_{12ij}) = \beta_{10} + \beta_{11} X_{1i} + \sum_{j=1}^{99} \beta_{112j} X_{12ij}$;

For the final multivariable model: $E(Y_i \mid X_{1i}, X_{2i}, \dots, X_{11i}, X_{12ij}) = \beta_{20} + \beta_{21} X_{1i} + \beta_{22} X_{2i} + \cdots + \beta_{211} X_{11i} + \sum_{j=1}^{99} \beta_{212j} X_{12ij}$;

$i = 1, 2, \dots, 200 \ (number\ of\ children);\ j = 1, 2, \dots, 99 (number\ of\ dummy\ variables\ representing\ the\ 100\ matched\ pairs);$

$Y_i = ln\ of\ blood\ arsenic\ concentrations\ of\ the\ i^{th}\ child;$

$X_{1i} = case\ status\ of\ the\ i^{th}\ child\ (ASD\ case\ = 1;\ TD\ control = 0);$

$X_{2i} = car\ ownership\ associated\ with\ family\ of\ the\ i^{th}\ child\ (\ No\ cars = 0;\ otherwise = 1);$

$X_{3i} = maternal\ age\ at\ child's\ birth\ associated\ with\ the\ i^{th}\ child\ ("maternal\ age \geq 35\ years" = 1;\ otherwise\ = 0);$

$X_{4i} = Parental\ levels\ of\ education\ associated\ with\ the\ i^{th}\ child\ (both\ parents\ had\ up\ to\ high\ school\ = 0;\ otherwise = 1);$

$X_{5i} = source\ of\ drinking\ water\ associated\ with\ the\ i^{th}\ child\ (piped\ water = 1,\ otherwise = 0);$

$X_{6i} = consumption\ of\ "yam, sweet\ potato, or\ dasheen"\ associated\ with\ the\ i^{th}\ child\ (No\ consumption = 0;\ otherwise = 1);$

$X_{7i} = consumption\ of\ "carrot\ or\ pumpkin"\ associated\ with\ the\ i^{th}\ child\ (No\ consumption = 0;\ otherwise = 1);$

$X_{8i} = consumption\ of\ "callaloo, broccoli, or\ pak\ choi"\ associated\ with\ the\ i^{th}\ child\ (No\ consumption = 0;\ otherwise = 1);$

$X_{9i} = consumption\ of\ "cabbage"\ associated\ with\ the\ i^{th}\ child\ (No\ consumption = 0;\ otherwise = 1);$

$X_{10i} = consumption\ of\ "avocado"\ associated\ with\ the\ i^{th}\ child\ (No\ consumption = 0;\ otherwise = 1);$

$X_{11i} = frequency\ of\ seafood\ consumption\ associated\ with\ the\ i^{th}\ child = number\ of\ seafood\ meals\ consumed\ in\ a\ week;$

$$X_{12ij} = \begin{cases} 1, if\ the\ i^{th}\ child\ in\ the\ j^{th}\ matched\ pair\ is\ an\ ASD\ case \\ 0, if\ the\ i^{th}\ child\ in\ the\ j^{th}\ matched\ pair\ is\ a\ TD\ control \end{cases} ;$$

$E(Y_{1i} \mid X_{1i}, X_{12ij})\ stands\ for\ mean\ ln\ of\ blood\ arsenic\ concentrations\ given\ X_{1i}, X_{12ij};$

$E(Y_{2i} \mid X_{1i}, X_{2i}, \dots, X_{12ij})\ stands\ for\ mean\ ln\ of\ blood\ arsenic\ concentrations\ given\ X_{1i}, X_{2i}, \dots, X_{11i}, X_{12ij};$

$\beta_{10}, \beta_{11}, \beta_{112j}\ are\ regression\ coefficients\ associated\ with\ the\ univaribale\ model;$

$\beta_{20}, \beta_{21}, \dots, \beta_{211}, \beta_{12j}\ are\ regression\ coefficients\ associated\ with\ the\ final\ multivaribale\ model.$

Detailed description of General Linear Models used to obtain the results reported in Table 5 (based on 100 matched pairs)

General Linear Models that assessed unadjusted and adjusted effects of *GSTP1* in blood arsenic concentrations of children with and without ASD can be represented by the following linear regression equations:

For the unadjusted model: $E(Y_i | X_{1i}, X_{2i}, X_{12ij}) = \beta_{10} + \beta_{11} X_{1i} + \beta_{12} X_{2i} + \beta_{13} X_{1i} * X_{2i} + \sum_{j=1}^{99} \beta_{113j} X_{13ij}$;

For the final adjusted model: $E(Y_i | X_{1i}, X_{2i}, \dots, X_{11i}, X_{12ij}) = \beta_{20} + \beta_{21} X_{1i} + \beta_{22} X_{2i} + \dots + \beta_{212} X_{12i} + \beta_{13} X_{1i} * X_{2i} + \sum_{j=1}^{99} \beta_{213j} X_{13ij}$;

$i = 1, 2, \dots, 200$ (*number of children*); $j = 1, 2, \dots, 99$(*number of dummy variables representing the 99 matched pairs*);

$Y_i = ln$ *of blood arsenic concentrations of the* i^{th} *child*;

$X_{1i} = $ *case status of the* i^{th} *child* (*ASD case* $= 1$; *TD control* $= 0$);

$X_{2i} = GSTP1$ *genotype associated with the* i^{th} *child* (*GSTP1 is categorized into 2 levels*);

$X_{3i} = $ *car ownership associated with family of the* i^{th} *child* (*No cars* $= 0$; *otherwise* $= 1$);

$X_{4i} = $ *maternal age at child's birth associated with the* i^{th} *child* ("*maternal age* ≥ 35 *years*" $= 1$; *otherwise* $= 0$);

$X_{5i} = $ *Parental levels of education associated with the* i^{th} *child* (*both parent up to high schhol* $= 0$; *otherwise* $= 1$);

$X_{6i} = $ *source of drinking water associated with the* i^{th} *child* (*piped water* $= 1$, *otherwise* $= 0$);

$X_{7i} = $ *consumption of "yam, sweet potato, or dasheen" associated with the* i^{th} *child* (*No consumption* $= 0$; *otherwise* $= 1$);

$X_{8i} = $ *consumption of "carrot or pumpkin" associated with the* i^{th} *child* (*No consumption* $= 0$; *otherwise* $= 1$);

$X_{9i} = $ *consumption of "callaloo, broccoli, or pak choi" associated with the* i^{th} *child* (*No consumption* $= 0$; *otherwise* $= 1$;

$X_{10i} = $ *consumption of "cabbage" associated with the* i^{th} *child* (*No consumption* $= 0$; *otherwise* $= 1$);

$X_{11i} = $ *consumption of "avocado" associated with the* i^{th} *child* (*No consumption* $= 0$; *otherwise* $= 1$);

$X_{12i} = $ *frequency of seafood consumption associated with the* i^{th} *child* $=$ *number of seafood meals consumed in a week*;

$$X_{13ij} = \begin{cases} 1, if\ the\ i^{th}\ child\ in\ the\ j^{th}\ matched\ pair\ is\ an\ ASD\ case \\ 0, if\ the\ i^{th}\ child\ in\ the\ j^{th}\ matched\ pair\ is\ a\ control \end{cases} ;$$

$E(Y_{1i}\mid X_{1i}, X_{13ij})$ *stands for mean ln of blood arsenic concentrations given* X_{1i}, X_{13ij};

$E(Y_{2i}\mid X_{1i}, X_{2i}, \ldots, , X_{13ij})$ *stands for mean ln of blood arsenic concentrations given the* $X_{1i}, X_{2i}, \ldots, X_{12i}, X_{13ij}$;

$\beta_{10}, \beta_{11}, \beta_{12}, \beta_{113j}$ *are regression coefficients associated with the univaribale model;*

$\beta_{20}, \beta_{21}, \ldots, \beta_{212}, \beta_{213j}$ *are regression coefficients associated with the final multivaribale model.*