

Note to readers with disabilities: *EHP* strives to ensure that all journal content is accessible to all readers. However, some figures and Supplemental Material published in *EHP* articles may not conform to [508 standards](#) due to the complexity of the information being presented. If you need assistance accessing journal content, please contact ehp508@niehs.nih.gov. Our staff will work with you to assess and meet your accessibility needs within 3 working days.

Supplemental Material

Mercury Exposure, Blood Pressure, and Hypertension: A Systematic Review and Dose–response Meta-analysis

Xue Feng Hu, Kavita Singh, and Hing Man Chan

Table of Contents

Search in PubMed

Link to the PRISMA checklist

Figure S1. Funnel plots showing no publication bias for studies investigating association between mercury and hypertension (A), systolic blood pressure (B), and diastolic blood pressure (C).

Figure S2. Mercury exposure and systolic blood pressure, by mercury exposure level.

Figure S3. Mercury exposure and diastolic blood pressure, by mercury exposure level.

Figure S4. Mercury exposure and systolic blood pressure, by exposure group.

Figure S5. Mercury exposure and diastolic blood pressure, by exposure group.

Figure S6. Mercury exposure and systolic blood pressure, by mercury species.

Figure S7. Mercury exposure and diastolic blood pressure, by mercury species.

Figure S8. Mercury exposure and systolic blood pressure, by exposure biomarker.

Figure S9. Mercury exposure and diastolic blood pressure, by exposure biomarker.

Figure S10. Evaluation of dose response for mercury exposure and hypertension.

Figure S11. Evaluation of dose response for mercury exposure and systolic blood pressure.

References

Search in PubMed

(Mercury[MH] OR Mercury Poisoning[MH] OR mercury[title] OR Hg[title] OR "mercuric" OR methylmercury OR "methyl mercury" OR "quicksilver" OR "quecksilber" OR "mercurio" OR "liquid silver" OR "mercure" OR "kwik" OR "hydrargyrum" OR "colloidal mercury" OR dimethylmercury OR "dimethyl mercury" OR "7439-97-6" OR "22967-92-6" OR "593-74-8") AND (Cardiovascular Diseases[MH] OR "cardiovascular"[tiab] OR CVD[tiab] OR Heart OR Mortality OR "death" OR "deaths" OR Myocardial Infarction OR "myocardial infarctions" OR Stroke OR "strokes" OR Cerebrovascular Disorders OR "cerebrovascular" OR Peripheral Arterial Disease OR "peripheral arterial diseases" OR Peripheral Vascular Disease OR "peripheral vascular diseases" OR Hypertension OR Systolic OR "systole" OR "systoles" OR Diastolic OR "diastole" OR "diastoles" OR Atherosclerosis OR Arteriosclerosis OR Electrocardiography OR Heart Rate OR "heart rates" OR "heart rate variability" OR Ventricular Hypertrophy OR "ventricular mass" OR Heart Failure OR "heart failures" OR Cardiovascular Physiological Phenomena[MH] OR "cardiovascular system" OR Blood Circulation OR Hemodynamics OR Blood Pressure OR "pulse"[tiab] OR "pulse pressure" OR "Tunica Intima"[MH] OR "intima media thickness" OR "arterial wall thickness" OR (coronary AND calcification)) NOT ("animals"[MH] NOT ("humans"[MH] AND "animals"[MH]))

Figure captions

For Figure S2 to S9, the area of each square is proportional to the inverse of the variance of the estimated mean difference in systolic/diastolic blood pressure. Black diamonds represent point estimates of mean difference and horizontal lines represent 95% CIs. Arrowheads indicate that the upper limit of the 95% CI in that study exceeded the range specified. The open diamonds represent the combined mean difference for each subgroup and the overall mean difference for all studies. The solid line represents mean difference = 0. The dash line represents the point estimate of overall mean difference for all studies. The "metan" package in Stata only outputs p value up to 3 digit numbers for the heterogeneity tests. We reported in the text " $p < 0.0001$ " when the figures showed " $p = 0.000$ ". CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; * indicates mercury form was not described in the methods section and was assumed by authors of the present review.

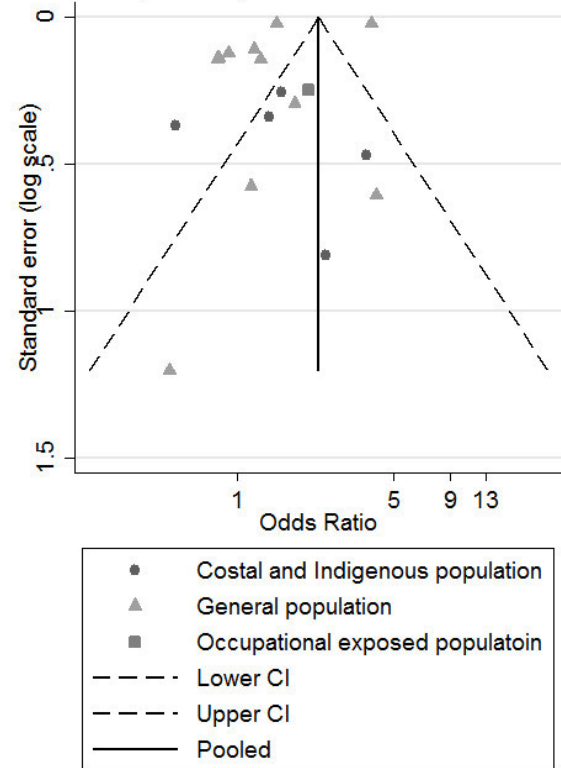
Figure S10, Evaluation of dose response for mercury exposure and hypertension. Black symbols indicate studies conducted in populations with low to moderate mercury exposure (hair mercury concentration $< 2 \mu\text{g/g}$ in the highest exposure category); blue symbols indicate studies conducted in populations with high mercury exposure (hair mercury concentration $\geq 2 \mu\text{g/g}$ in the highest exposure category). The size of each data point is inversely weighted based on the inverse of the variance of the estimated log OR.

Figure S11, Evaluation of dose response for mercury exposure and mean difference in systolic blood pressure. Data were modeled with fixed-effects restricted cubic spline models with 3 knots (at 15th, 50th, and 85th percentile) using (Crippa and Orsini 2016) method. The solid line represents the predicted nonlinear trend. Confidence intervals (not shown) were not reliable due to lack of data.

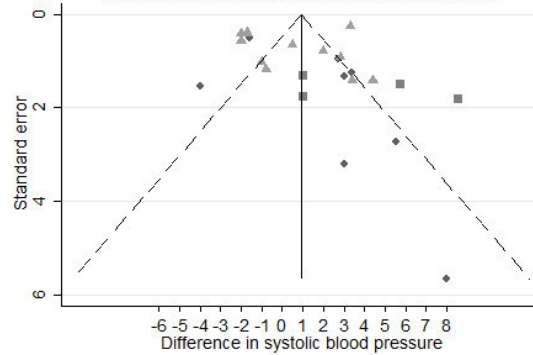
Link to the PRISMA checklist

www.prisma-statement.org

A Funnel plot with pseudo 95% confidence limits



B Funnel plot with pseudo 95% confidence limits



C Funnel plot with pseudo 95% confidence limits

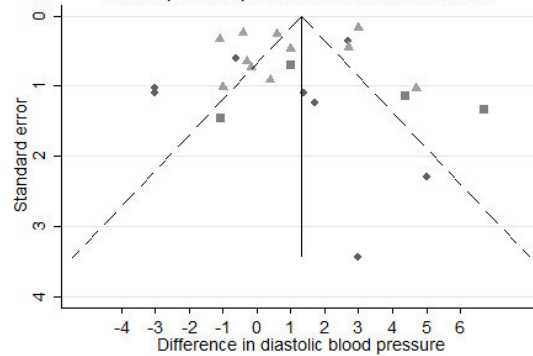


Figure S1 Funnel plots

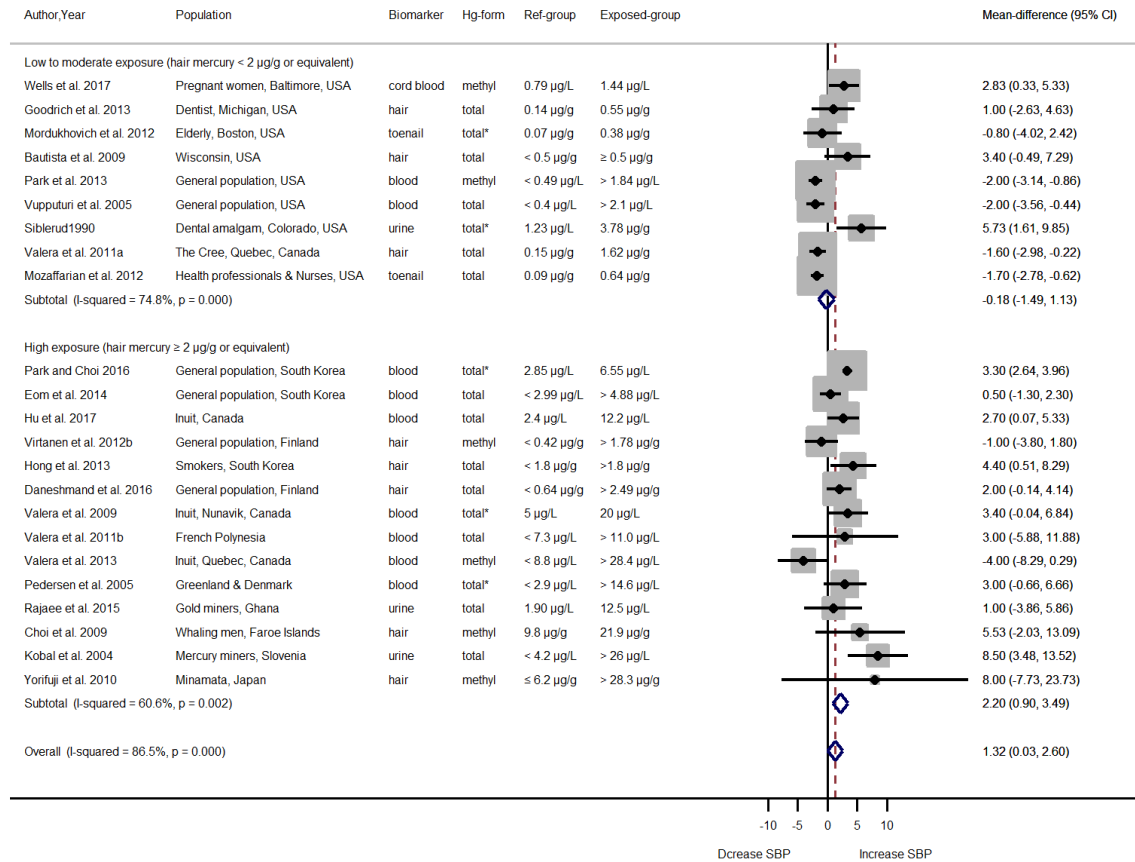


Figure S2. Mercury exposure and systolic blood pressure, by mercury exposure level

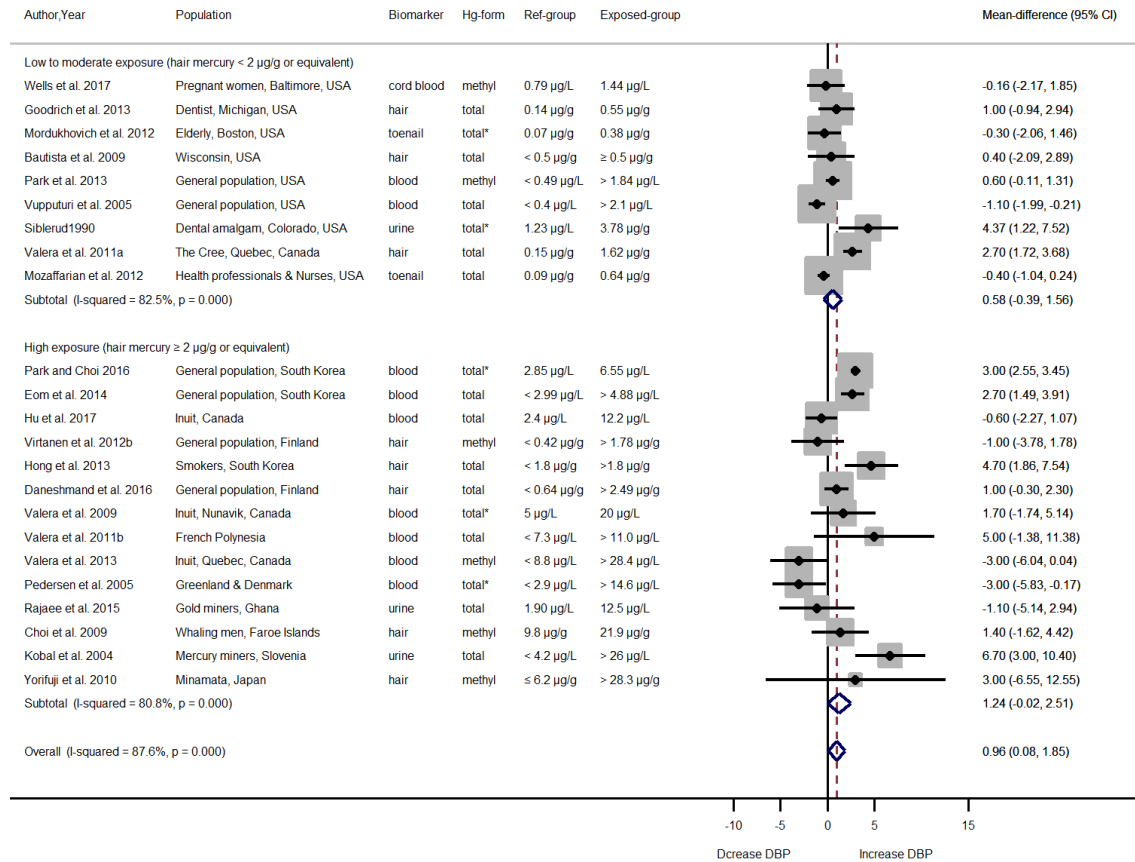


Figure S3. Mercury exposure and diastolic blood pressure, by mercury exposure level

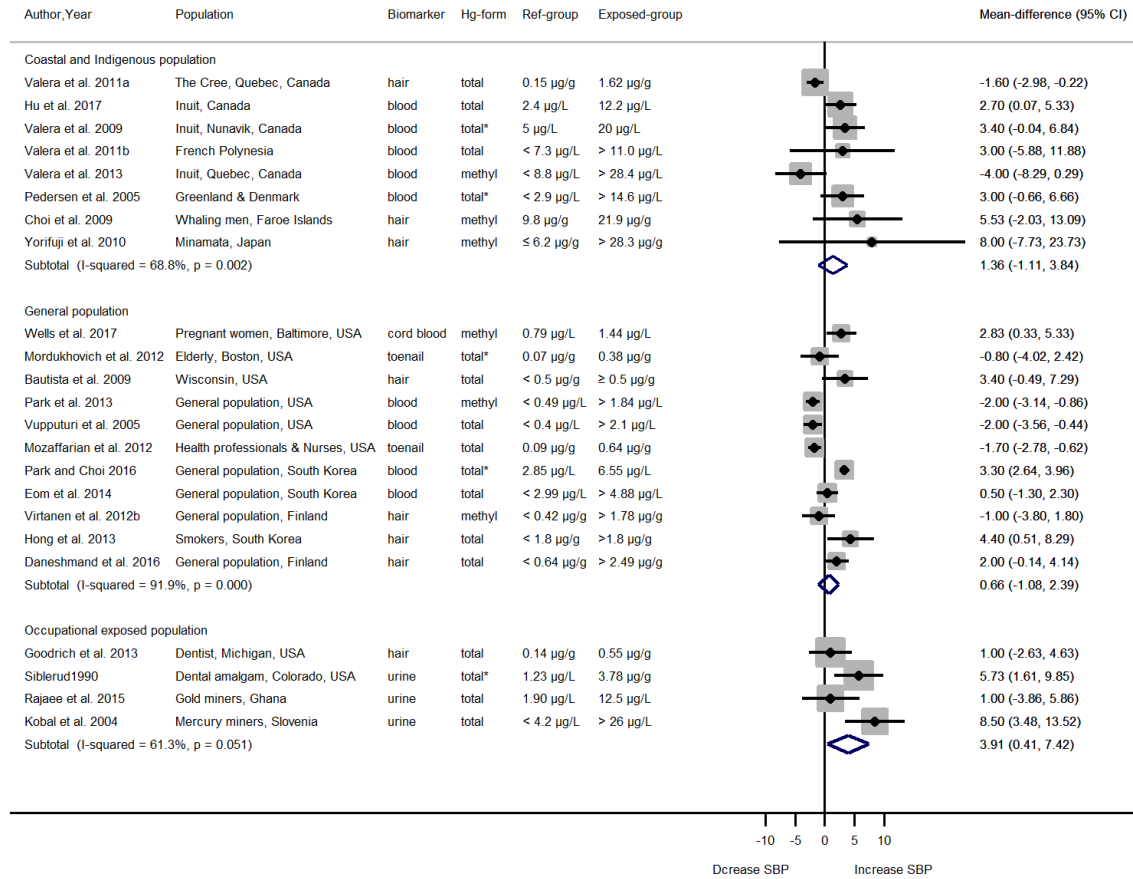


Figure S4. Mercury exposure and systolic blood pressure, by exposure group

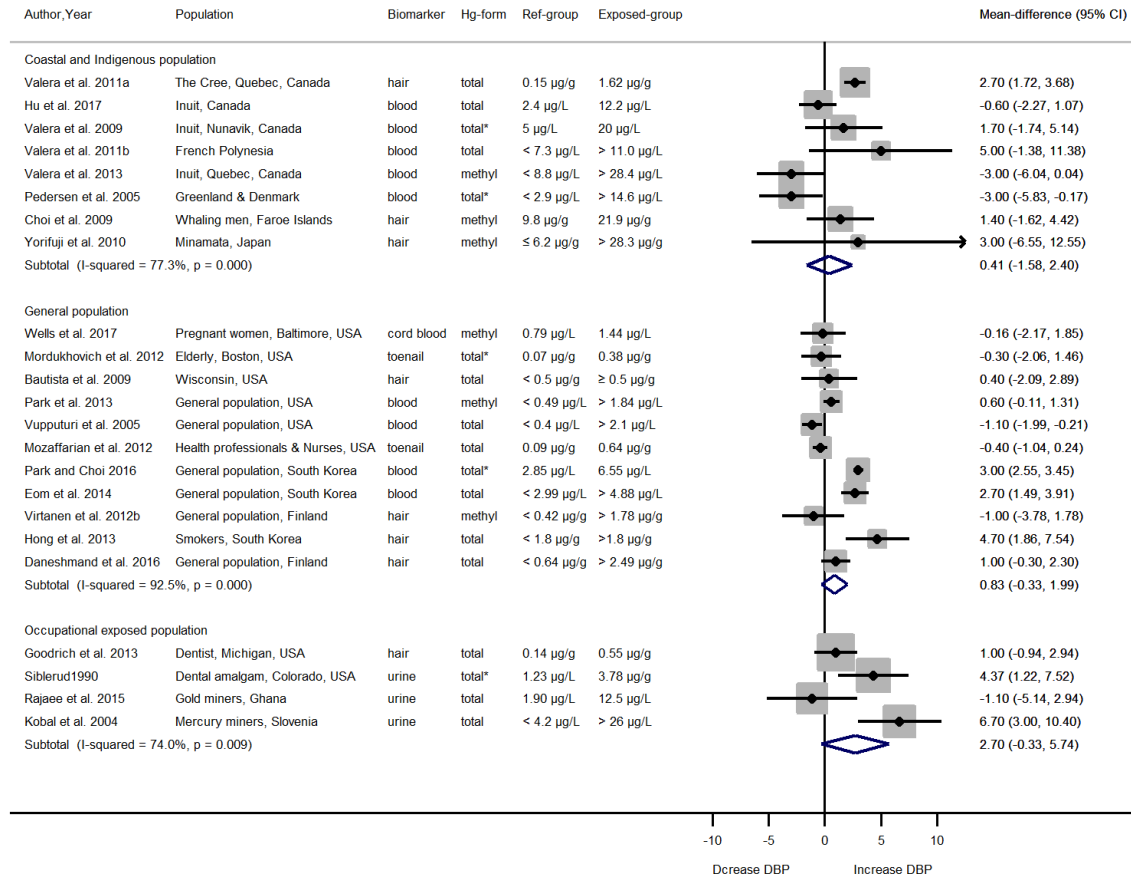


Figure S5. Mercury exposure and diastolic blood pressure, by exposure group

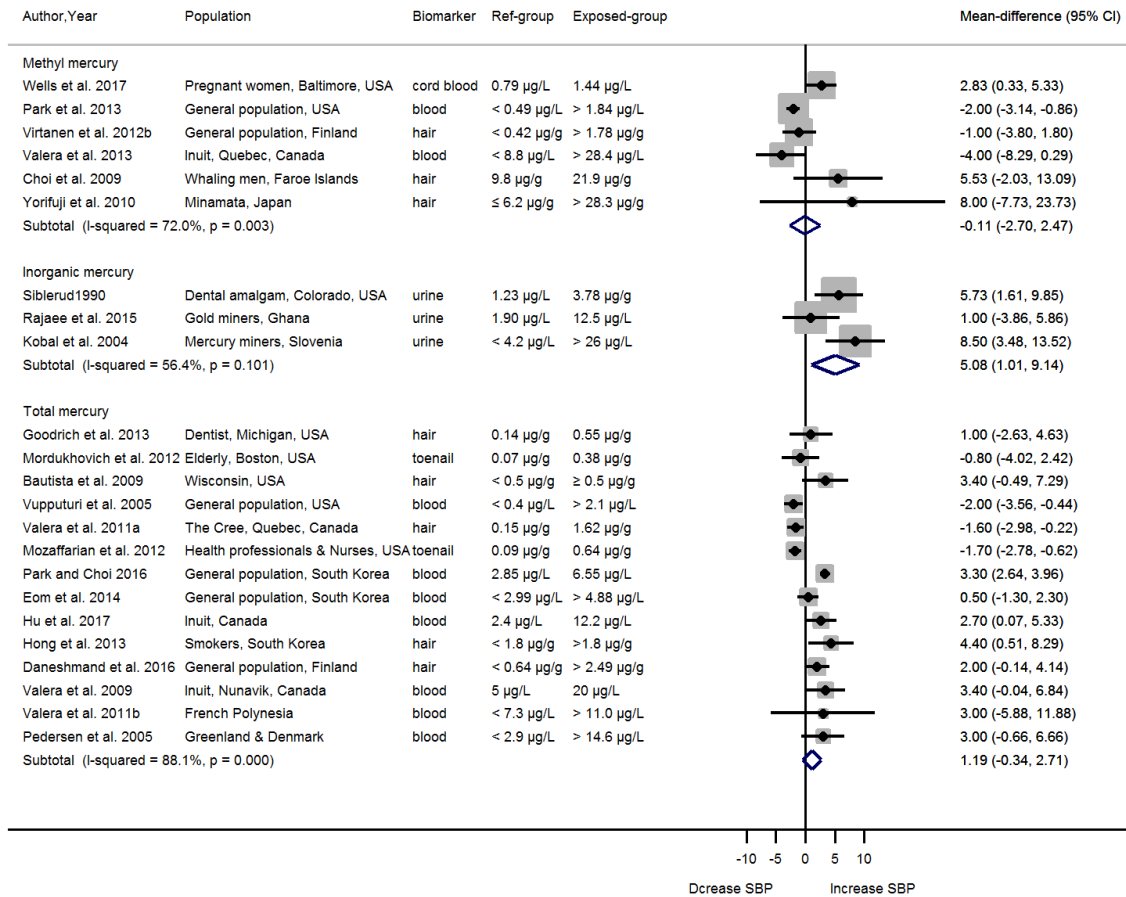


Figure S6. Mercury exposure and systolic blood pressure, by mercury species

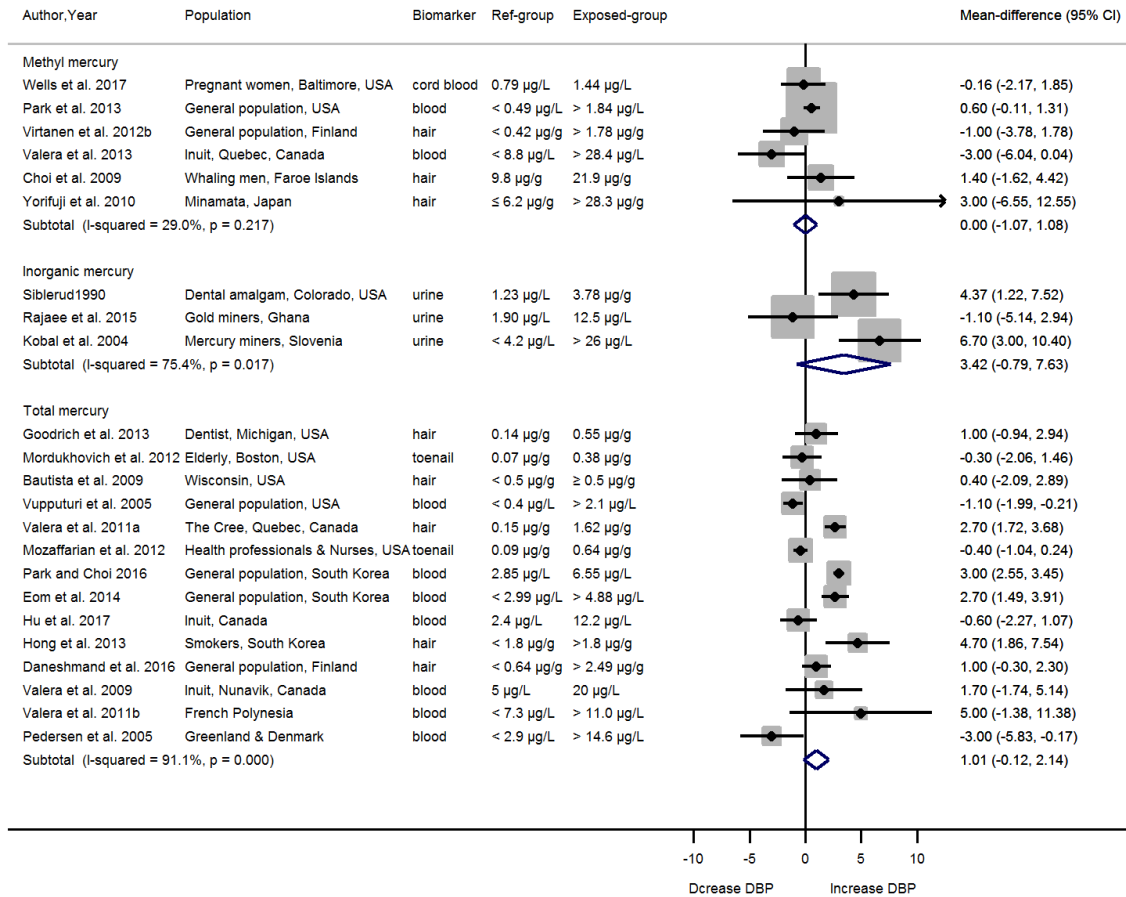


Figure S7. Mercury exposure and diastolic blood pressure, by mercury species

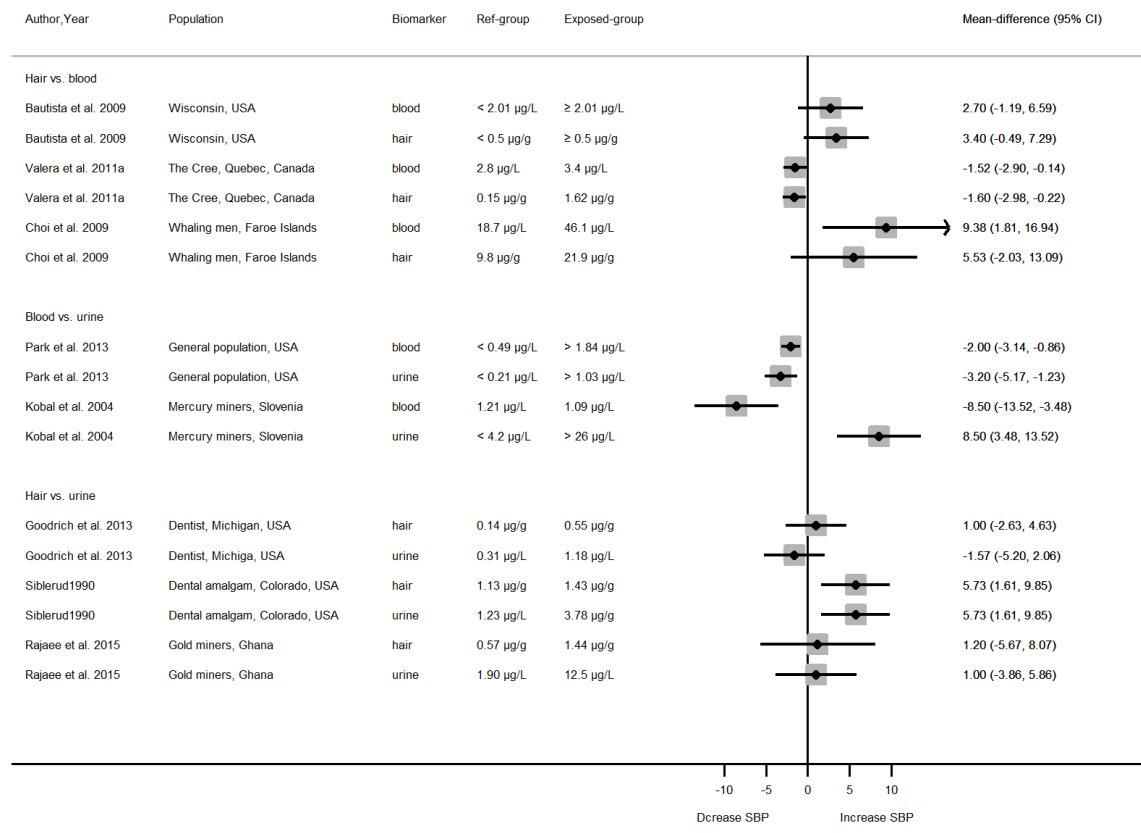


Figure S8. Mercury exposure and systolic blood pressure, by exposure biomarker

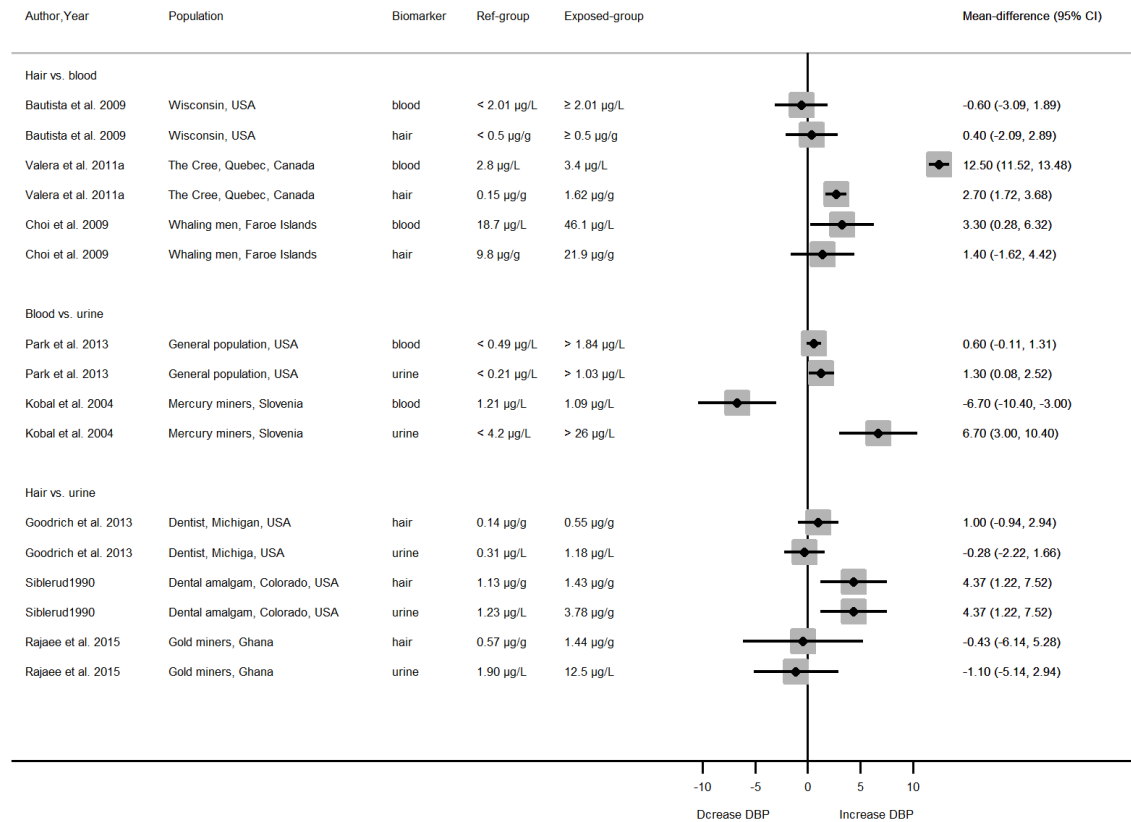


Figure S9. Mercury exposure and diastolic blood pressure, by exposure biomarker

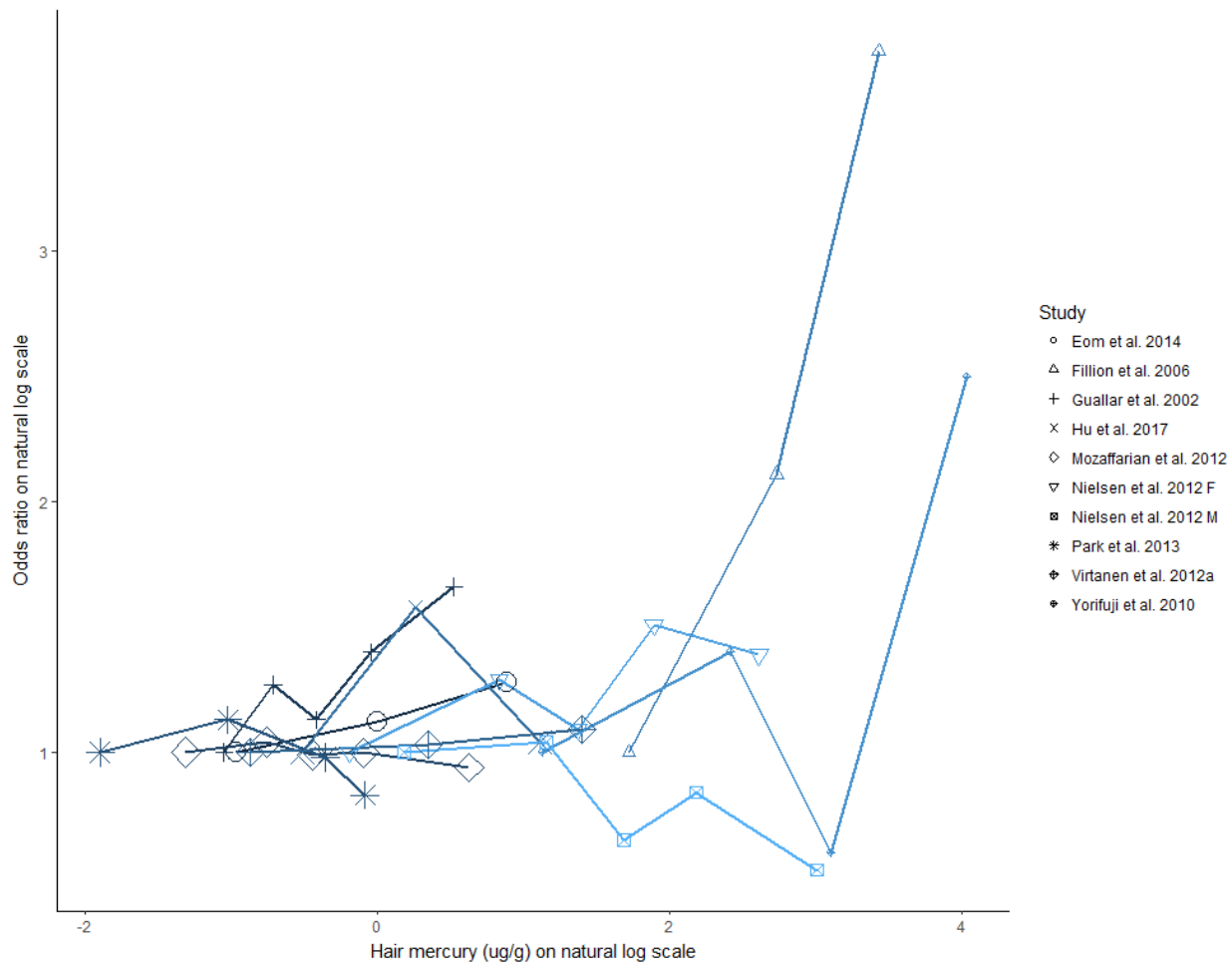


Figure S10. Evaluation of dose response for mercury exposure and hypertension

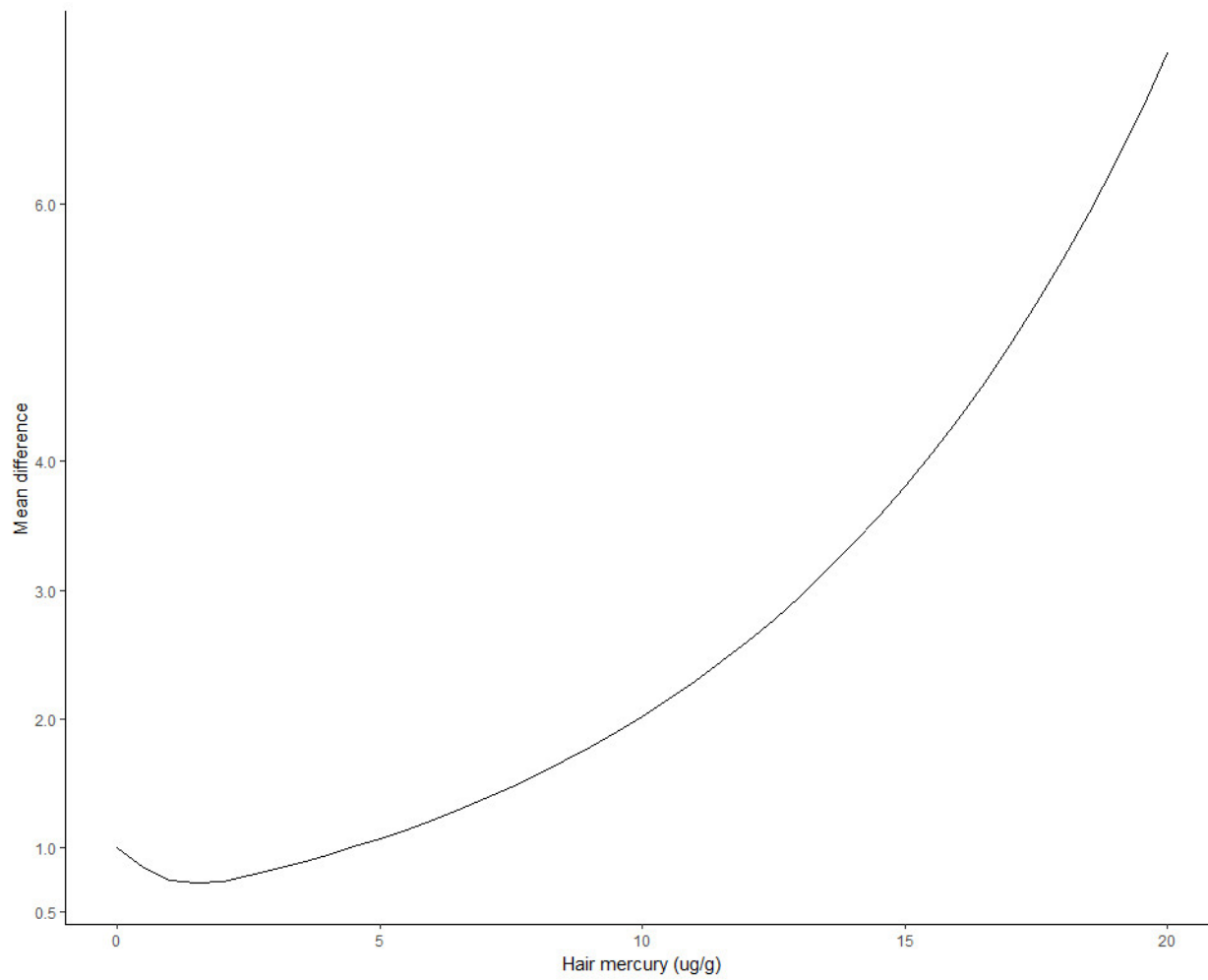


Figure S11 Evaluation of dose response for mercury exposure and systolic blood pressure

References

- Bautista LE, Stein JH, Morgan BJ, Stanton N, Young T, Nieto FJ. 2009. Association of blood and hair mercury with blood pressure and vascular reactivity. *WJ* 108:250–252; doi:10.1038/nbt.3121.ChIP-nexus.
- Choi AL, Weihe P, Budtz-Jørgensen E, Jørgensen PJ, Salonen JT, Tuomainen TP, et al. 2009. Methylmercury exposure and adverse cardiovascular effects in Faroese Whaling men. *Environ. Health Perspect.* 117:367–372; doi:10.1289/ehp.11608.
- Daneshmand R, Kurl S, Tuomainen T-P, Virtanen JK. 2016. Associations of serum n-3 and n-6 PUFA and hair mercury with the risk of incident stroke in men: the Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD). *Br. J. Nutr.* 115:1851–1859; doi:10.1017/S0007114516000982.
- Eom S-Y, Choi S-H, Ahn S-J, Kim D-K, Kim D-W, Lim J-A, et al. 2014. Reference levels of blood mercury and association with metabolic syndrome in Korean adults. *Int. Arch. Occup. Environ. Health* 87:501–513; doi:10.1007/s00420-013-0891-8.
- Fillion M, Mergler D, Passos CJS, Larribe F, Lemire M, Guimarães JRD. 2006. A preliminary study of mercury exposure and blood pressure in the Brazilian Amazon. *Environ. Heal.* 5:29; doi:10.1186/1476-069X-5-Received.
- Goodrich JM, Wang Y, Gillespie B, Werner R, Franzblau A, Basu N. 2013. Methylmercury and elemental mercury differentially associate with blood pressure among dental professionals. *Int. J. Hyg. Environ. Health* 216:195–201; doi:10.1016/j.ijheh.2012.03.001.
- Guallar E, Sanz-Gallardo I, Van't Veer P, Bode P, Aro A, Gomez-Aracena J, et al. 2002. Mercury, fish oils, and the risk of myocardial infarction. *N. Engl. J. Med.* 347: 1747–1754.
- Hong D, Cho SH, Park SJ, Kim SY, Park SB. 2013. Hair mercury level in smokers and its influence on blood pressure and lipid metabolism. *Environ. Toxicol. Pharmacol.* 36:103–107; doi:10.1016/j.etap.2013.03.007.
- Hu XF, Eccles K, Chan HM. 2017. High selenium exposure lower the odds ratios for hypertension, stroke, and myocardial infarction associated with mercury exposure among Inuit in Canada. *Environ. Int.* 102:200–206; doi:10.1016/j.envint.2017.03.002.
- Kobal AB, Horvat M, Prezelj M, Briški AS, Kršnik M, Dizdarevič T, et al. 2004. The impact of long-term past exposure to elemental mercury on antioxidative capacity and lipid peroxidation in mercury miners. *J. Trace Elem. Med. Biol.* 17:261–274; doi:10.1016/S0946-672X(04)80028-2.
- Lee B-K, Kim Y. 2013. Blood cadmium, mercury, and lead and metabolic syndrome in South Korea: 2005-2010 Korean National Health and Nutrition Examination Survey. *Am. J. Ind. Med.* 56:682–92; doi:10.1002/ajim.22107.
- Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(6): e1000097. doi:10.1371/journal.pmed1000097. Available at: <http://prisma-statement.org/prismastatement/Checklist.aspx>
- Mordukhovich I, Wright RO, Hu H, Amarasiriwardena C, Baccarelli A, Litonjua A, et al. 2012. Associations of toenail arsenic, cadmium, mercury, manganese, and lead with blood pressure in the Normative Aging Study. *Environ. Health Perspect.* 120: 98–104.
- Mozaffarian D, Shi P, Morris JS, Grandjean P, Siscovick DS, Spiegelman D, et al. 2012. Mercury exposure and risk of hypertension in US men and women in 2 prospective cohorts. *Hypertension* 60:645–652; doi:10.1161/HYPERTENSIONAHA.112.196154.
- Nielsen ABS, Davidsen M, Bjerregaard P. 2012. The association between blood pressure and whole blood methylmercury in a cross-sectional study among Inuit in Greenland. *Environ. Heal.* 11:44; doi:10.1186/1476-069X-11-44.
- Park S, Choi N-K. 2016. Associations of blood heavy metal levels with intraocular pressure. *Ann. Epidemiol.* 26:546–550; doi:10.1016/j.annepidem.2016.07.002.
- Park SK, Lee S, Basu N, Franzblau A. 2013. Associations of blood and urinary mercury with hypertension in U.S. adults: the NHANES 2003-2006. *Environ. Res.* 123:25–32; doi:10.1016/j.envres.2013.02.003.
- Pedersen EB, Jørgensen ME, Pedersen MB, Siggaard C, Sørensen TB, Mulvad G, et al. 2005. Relationship between mercury in blood and 24-h ambulatory blood pressure in Greenlanders and Danes. *Am. J. Hypertens.* 18:612–618; doi:10.1016/j.amjhyper.2004.11.022.
- Rajae M, Sánchez BN, Renne EP, Basu N. 2015. An investigation of organic and inorganic mercury exposure and blood pressure in a small-scale gold mining community in Ghana. *Int. J. Environ. Res. Public Health* 12:10020–10038; doi:10.3390/ijerph120810020.
- Saudny H, Leggee D, Egeland G. 2012. Design and methods of the Adult Inuit Health Survey 2007-2008. *Int. J. Circumpolar Health* 71:1–9;

doi:10.3402/ijch.v71i0.19752.

- Shiue I. 2014. Higher urinary heavy metal, arsenic, and phthalate concentrations in people with high blood pressure: US NHANES, 2009-2010. *Blood Press.* 23:363–369; doi:10.3109/08037051.2014.925228.
- Siblerud RL. 1990. The relationship between mercury from dental amalgam and the cardiovascular system. *Sci. Total Environ.* 99: 23–35.
- Valera B, Dewailly E, Poirier P. 2011a. Impact of mercury exposure on blood pressure and cardiac autonomic activity among Cree adults (James Bay, Quebec, Canada). *Environ. Res.* 111:1265–1270; doi:10.1016/j.envres.2011.09.001.
- Valera B, Dewailly É, Poirier P. 2013. Association between methylmercury and cardiovascular risk factors in a native population of Quebec (Canada): A retrospective evaluation. *Environ. Res.* 120:102–108; doi:10.1016/j.envres.2012.08.002.
- Valera B, Dewailly É, Poirier P. 2009. Environmental mercury exposure and blood pressure among Nunavik inuit adults. *Hypertension* 54:981–986; doi:10.1161/HYPERTENSIONAHA.109.135046.
- Valera B, Dewailly E, Poirier P, Counil E, Suhas E. 2011b. Influence of mercury exposure on blood pressure, resting heart rate and heart rate variability in French Polynesians: a cross-sectional study. *Environ. Heal.* 10:99; doi:10.1186/1476-069X-10-99.
- Virtanen JK, Laukkanen JA, Mursu J, Voutilainen S, Tuomainen TP. 2012a. Serum long-chain n-3 polyunsaturated fatty acids, mercury, and risk of sudden cardiac death in men: a prospective population-based study. *PLoS One* 7:e41046; doi:10.1371/journal.pone.0041046.
- Virtanen JK, Nyantika AN, Kauhanen J, Voutilainen S, Tuomainen TP. 2012b. Serum long-chain n-3 polyunsaturated fatty acids, methylmercury and blood pressure in an older population. *Hypertens. Res.* 35:1000–1004; doi:10.1038/hr.2012.80.
- Vupputuri S, Longnecker MP, Daniels JL, Guo X, Sandler DP. 2005. Blood mercury level and blood pressure among US women: Results from the National Health and Nutrition Examination Survey 1999-2000. *Environ. Res.* 97:195–200; doi:10.1016/j.envres.2004.05.001.
- Wells EM, Herbstman JB, Hong Y, Hibbeln JR, Halden RU, Witter FR, et al. 2017. Methyl mercury , but not inorganic mercury , associated with higher blood pressure during pregnancy. *Environ. Res.* 154:247–252; doi:10.1016/j.envres.2017.01.013.
- Yorifuji T, Tsuda T, Kashima S, Takao S, Harada M. 2010. Long-term exposure to methylmercury and its effects on hypertension in Minamata. *Environ. Res.* 110:40–46; doi:10.1016/j.envres.2009.10.011.