



Safe Environments Programme

Contaminated Sites Division

Acceptable Risk in HH TRV Derivation: Accounting for Genetic Variability

Presented at: UBC Contaminated Sites Risk Assessment Symposium

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Health Canada, Sidney, BC

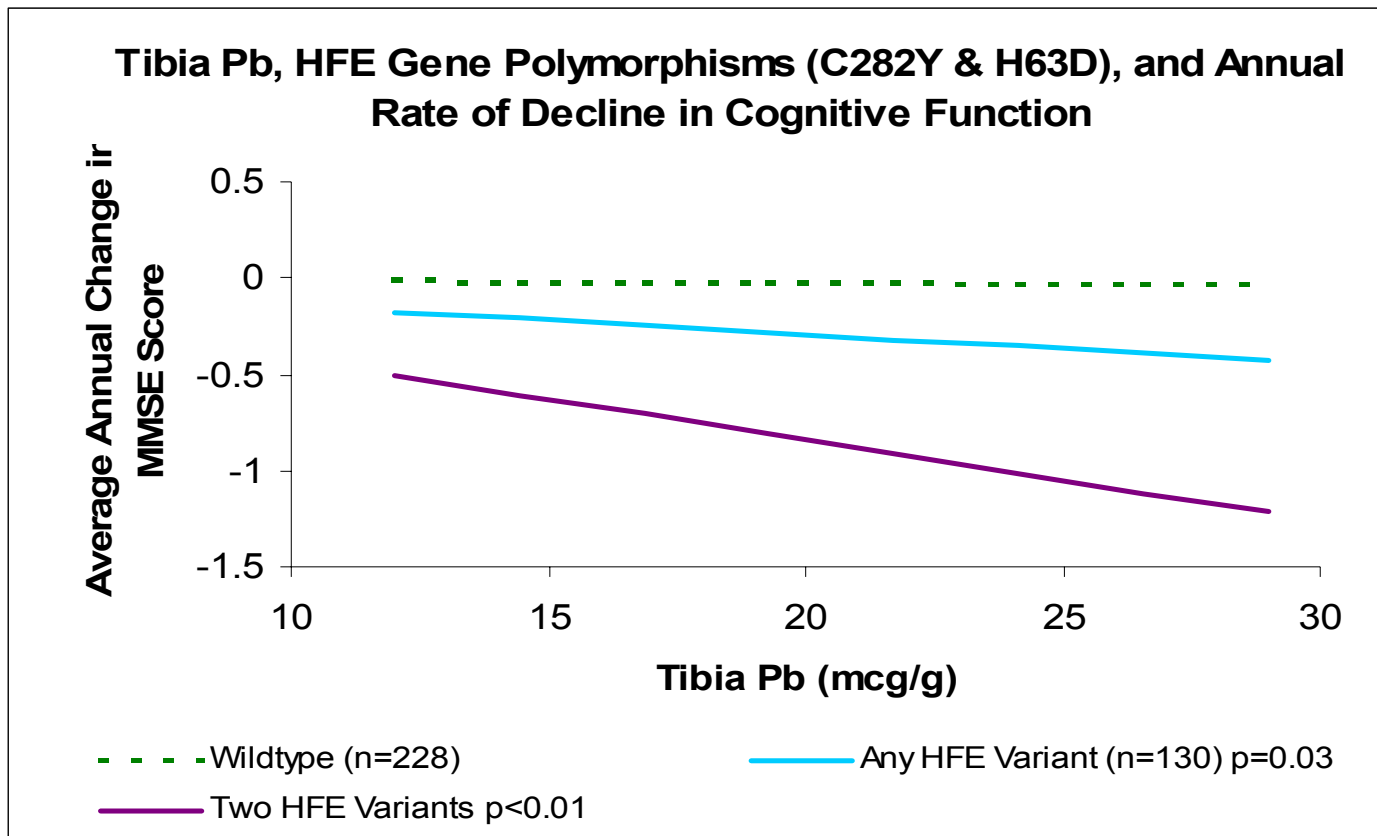




Key Questions

- Should acceptable levels of effects inherent in *Human Health* Toxicological Reference Values (TRVs) be protective of genetic variability?
- If so, what magnitude of uncertainty/adjustment factor should be applied to a point of departure (NOAEL or benchmark dose) to account for this uncertainty?

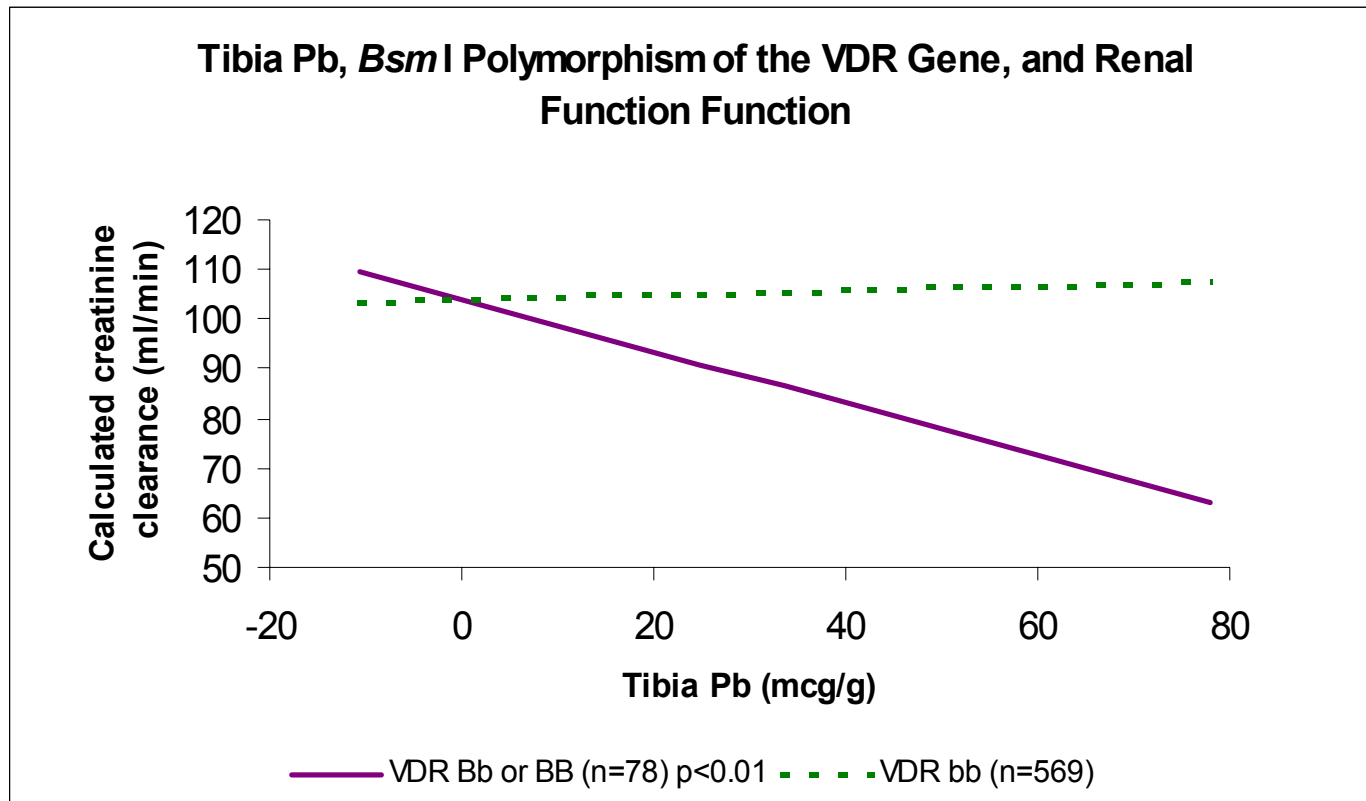
Pb, Cognitive Decline, & HFE Gene Polymorphisms



Wang, F. T., H. Hu, et al. (2007). "Modifying Effects of the HFE Polymorphisms on the Association between Lead Burden and Cognitive Decline." *Environ Health Perspect In Press*(doi:10.1289/ehp.9855).



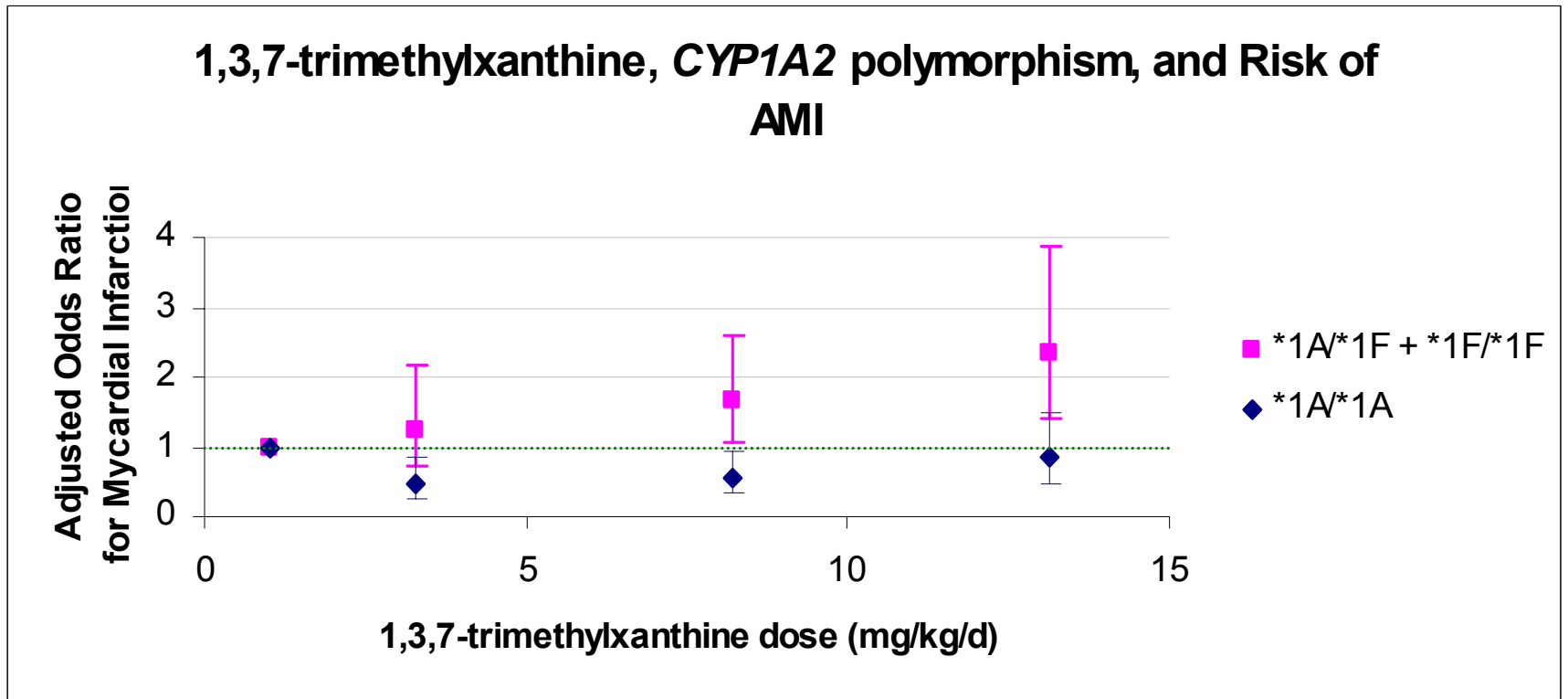
Pb, Renal Function, & VDR Gene Polymorphism



Weaver, V. M., B. K. Lee, et al. (2006). "Effect modification by delta-aminolevulinic acid dehydratase, vitamin D receptor, and nitric oxide synthase gene polymorphisms on associations between patella lead and renal function in lead workers." *Environ Res* **102**(1): 61-9.



CYP1A2 Polymorphism and Risk of Heart Attack



Cornelis, M. C., A. El-Sohemy, et al. (2006). "Coffee, *CYP1A2* Genotype, and Risk of Myocardial Infarction 10.1001/jama.295.10.1135." *JAMA* 295(10): 1135-1141.

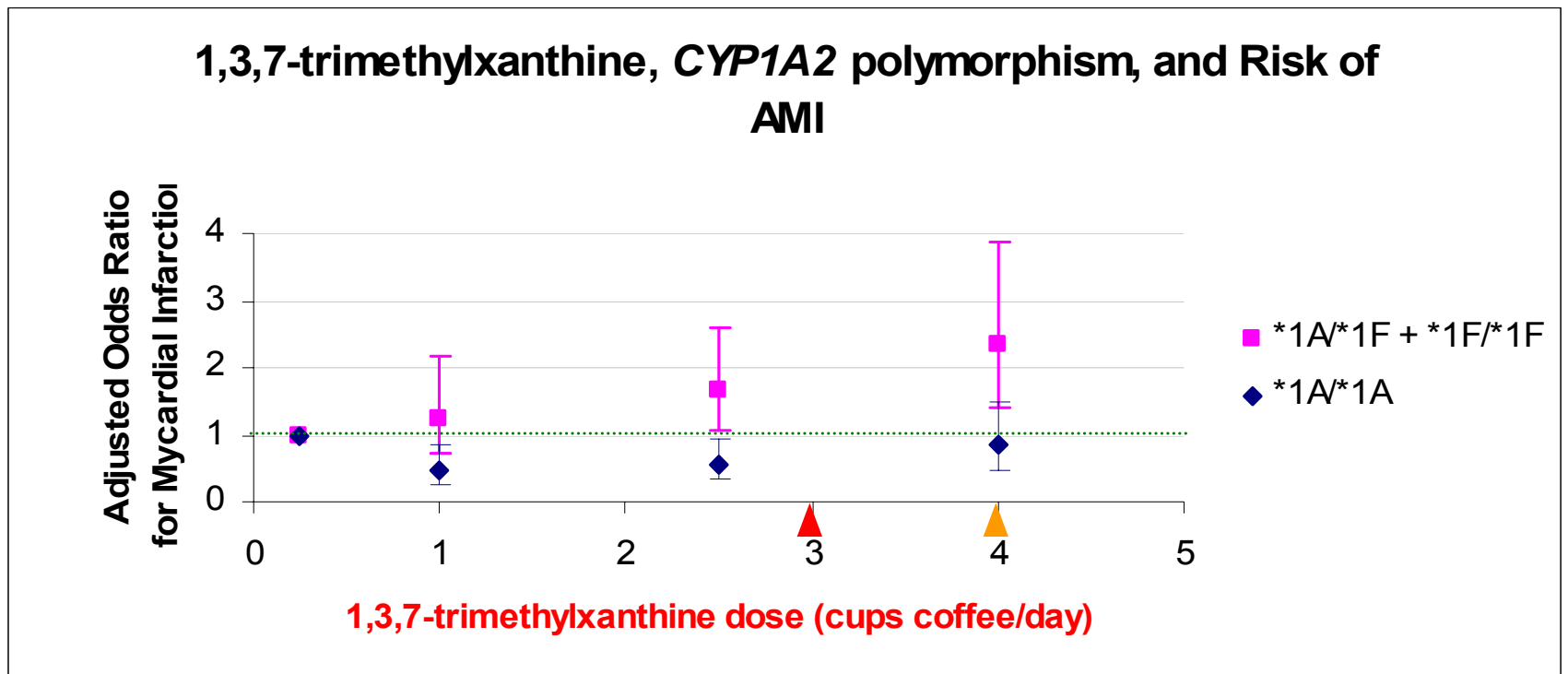


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Conclusions

- Genetic variability adds noise to the dose-response relationship – making it difficult to identify and characterize.
- Genetic variability places some subpopulations at greater risk of adverse toxic effects.

Discussion

- Should acceptable levels of effects inherent in *Human Health* Toxicological Reference Values (TRVs) be protective of genetic variability?
- If so, what magnitude of uncertainty/adjustment factor should be applied to a point of departure (NOAEL or benchmark dose) to account for this uncertainty?

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