

S. H. Lamm Comments for SAB Arsenic Teleconference (11/22/2010)

Thank you for the opportunity to speak briefly on the data analysis in this report. I have been interested in this issue for over fifteen years, having published research from southwest Taiwan, from Inner Mongolia, and from the United States. I have submitted multiple reports, letters, and analyses to the EPA and the SAB in these proceedings.

There are others who will discuss with you the issues of linearity vs non-linearity; single study, weight of evidence, or meta-analysis; and process and procedure. One topic of particular interest to me is the comparison of the analytic results from the ecological studies in SW Taiwan and the US, but I will hold that for another day. While all of these topics are important, I will narrow my attention at present to a more limited question that the SAB has asked of the EPA – *What is the dose-response relationship between bladder and lung cancer and arsenic ingestion based on the data from the SW Taiwan study including the SW regional data as a reference population and in the exposure range relevant to the US population?*

The primary questions that I raise are (1) What are reliable methodologies?, and (2) What are the relevant and reliable data for testing which hypothesis?

There are two major problems in the EPA analysis that we have addressed –

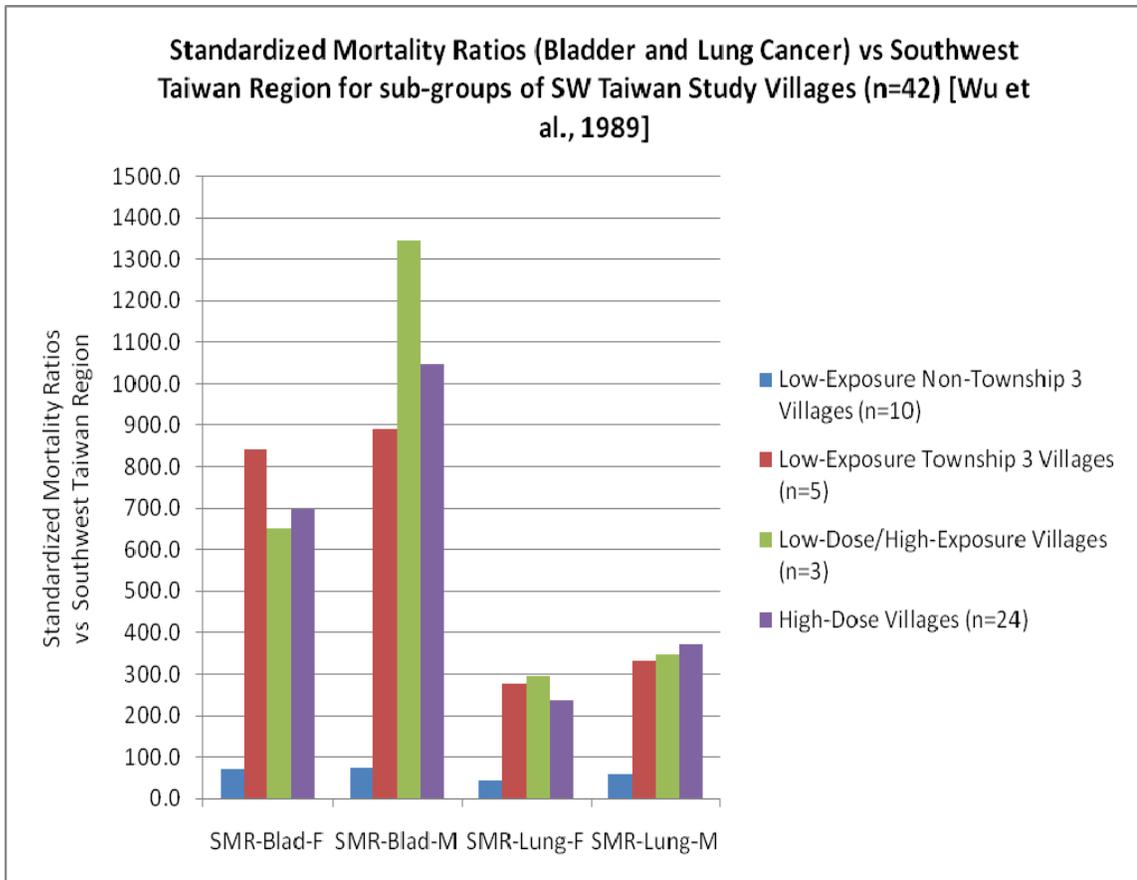
- (1) Use of the southwestern Taiwan population as an additional study village (rather than as a reference population) overwhelms the analysis, making it insensitive to the critical low-exposure village data. 98% of information in the analysis is in that single data point. As EPA's own sensitivity analysis (Table 5-10) showed, its inclusion accounts for up to 88% of the estimated risk. This has increased the risk up to 8 fold.
- (2) The data are "dirty" or confounded, both because of misclassification of villages with high arsenic levels (> 500 ug/L) as low-dose villages and because of some additional analytic factor various proposed as fluorescent or humic substance, artesian water source, or Township3. These issues have been well discussed in the published literature but are uncited in the Toxicological Review or cast off as "arbitrary." See Brown and Chen (1995) and Brown (HERA, Jan 2007). See Lamm et al., particularly (EHP, July 2007).

As I have said, the source of this second factor is not known. Recall that Blackfoot disease is unique to this arsenic exposure area and found nowhere else in the world. It might be a misclassification due to sampling as the deep wells previously used by the villagers may not have been open at the time of the sampling. Nonetheless, this geographic heterogeneity is clear and its solution should be a target of arsenic research.

We have submitted to the SAB graphic analyses exploring this heterogeneity among the low-dose villages. These demonstrate that both the low-dose villages with high arsenic levels (> 500 ug/L) and those in Township 3 demonstrate the cancer risk behavior of the high dose villages, not that of the low-exposure villages.

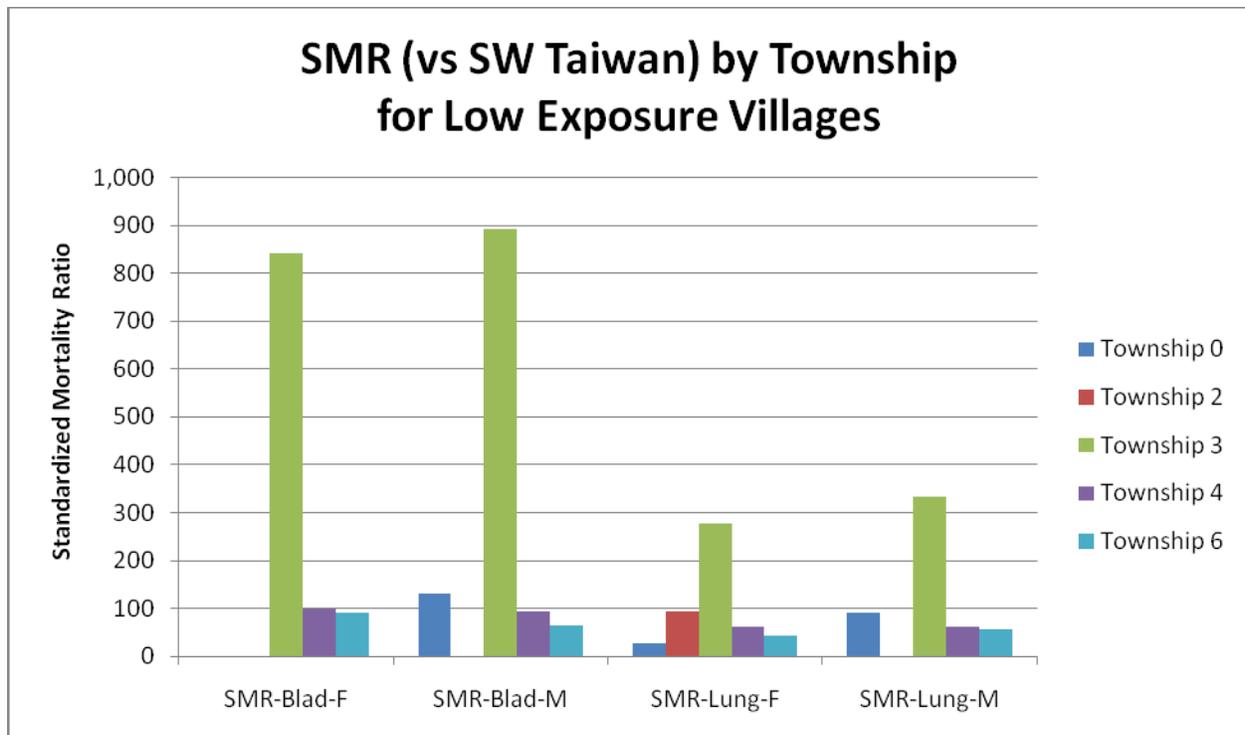
The bladder cancer risks in the Township 3 and high exposure villages is about 10 times greater than those in the low exposure villages, and the lung cancer risks are about 5 times greater. It is WRONG to include their data in the analysis of the dose-response in the low-exposure villages.

S. H. Lamm Comments for SAB Arsenic Teleconference (11/22/2010)



Similarly, we have compared the SMRs for the low-exposure villages by township and found that the risks in Township 3 do not behave like those in the other townships, all of which behave similarly. The bladder cancer mortality is about 10 times greater in the Township 3 low exposure villages than in the other low exposure villages; the lung cancer mortality is 5 times greater; and the bladder and lung cancer mortality is 6 times greater.

Certainly a clear presentation of geographic heterogeneity. The data and some graphic analyses underlying these calculations were submitted to the SAB last week and additional graphic presentation were submitted today. I hope that the panelists will have an opportunity to review those figures as well as the letter from Prof. Wilson prior to concluding their deliberations.



Further, the analysis above demonstrates the far greater risk of cancers in the confounded data. Only 27 of the 441 bladder and lung cancer deaths in the study villages (6%) occurred among residents of the 10 low-exposure villages. It is visually apparent that inclusion of data from the Township 3 villages or from the low-dose/High-Exposure villages might have a profound effect on the risk assessment for villages with low level arsenic exposure. It is unlikely that a study with 27 cancers in the exposure range of interest can have the same level of utility presumed for a study with 441 such cases.

We propose :

- (1) that the EPA discuss the heterogeneity in the underlying data and its source;
- (2) that the examination for the dose-response for low-level arsenic exposure be conducted on the data from the ten low-exposure villages outside of Township 3;
- (3) that the results of that analysis be included in a meta-analysis of data from similar exposure levels in other studies, including that of northeast Taiwan and of the United States;
- (4) that a “reality check” be conducted to assess the real world likelihood of the validity of the estimate; and
- (5) that a research goal should be the ascertaining of the reasons for the geographic heterogeneity in cancer risk in the southwest Tawian study.

Thank you,

Steven H. Lamm, MD
Jun Lu, PhD
Shayan Robbins, BA

November 22, 2010