Re: Response to questions raised 9/12/05 to SHL by the panel.

To: Dr. Genevieve Matanoski and panelists
From: Steven H. Lamm, MD, DTPH
Date: September 12, 2005

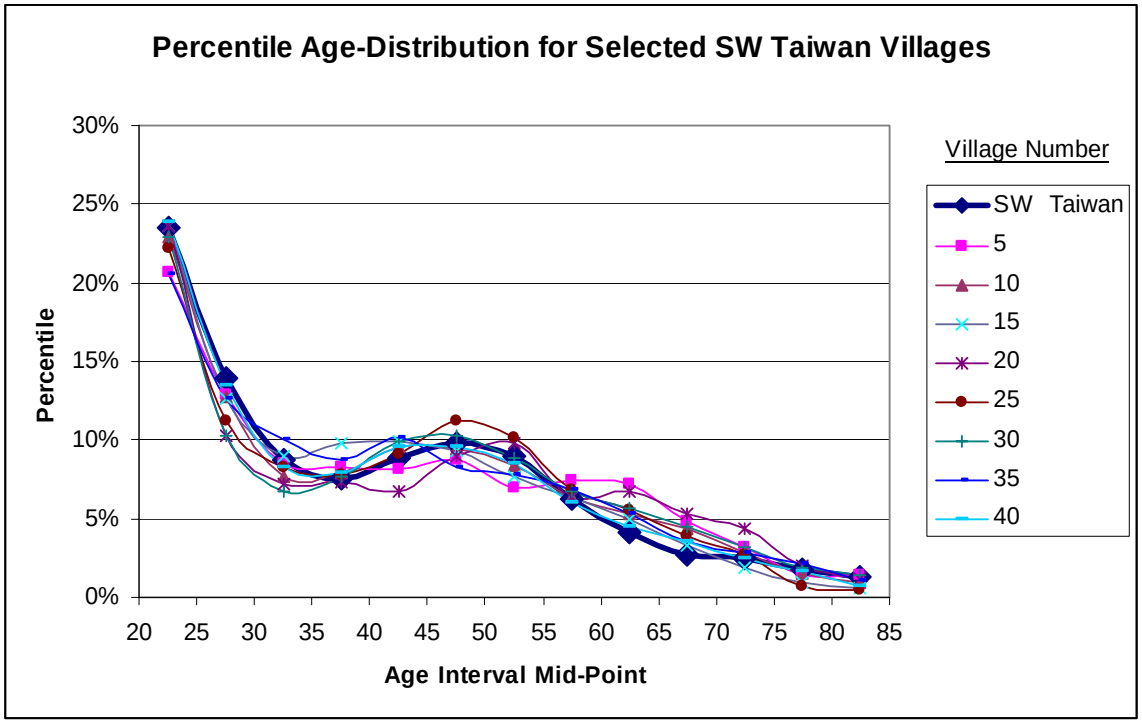
This is in response to the questions I was asked following my presentation:

Dr. Portier – Are your regressions different if you did a forward hierarchical analysis rather than a backward step wise regression?

For the most part, the differences were only 1 %. The exception is that for male bladder cancer, the R^2 for township is 5 %, where it did not previously appear. There should be a correction in my presentation in that for male lung cancer the R^2 for township should have been 12%.

Dr. Matanoski – You were concerned that the age-distributions of the various SW Taiwan villages were not reasonably similar.

Based on the data I had received from Dr. Ryan, I have constructed the graph below by calculating the percentile age-distribution of the reference SW Taiwan population and of each of the 42 villages. The graph below shows the comparison of the age-distribution for the reference population and for every fifth village in the NRC order. I suggest that these are probably representative of the full set. I am not struck with a great variation between the villages and the reference population in the age-distributions.



Dr. Hopenhayn – You had asked about the confidence range of the exposures in the township graph for low-dose villages (slide 13).

They are in ppm:

Township	Mean	St Dev
0	0.080	0.037
3	0.039	0.022
4	0.086	0.038
6	0.059	0.020

Dr. Heeringa – You have asked about the data contents of the Wu et al. study.

Both the Wu (1989) and Chen (1992) studies are of the 898,806 person-years of risk recorded for the residents of the 42 villages. The Chen (1992) analysis, however, is of the total population, while the Wu (1989) analysis is limited to the person-years of age 20 years or more. This difference eliminates about 50 % of the person-years and 12 % of these three cancers. It seems surprising to me that there would be 85 cancers (bladder, lung, and liver, combined) at ages < 20 years old, but that would need to be examined and compared as rates.

Chen 1992 Cancers All Ages)

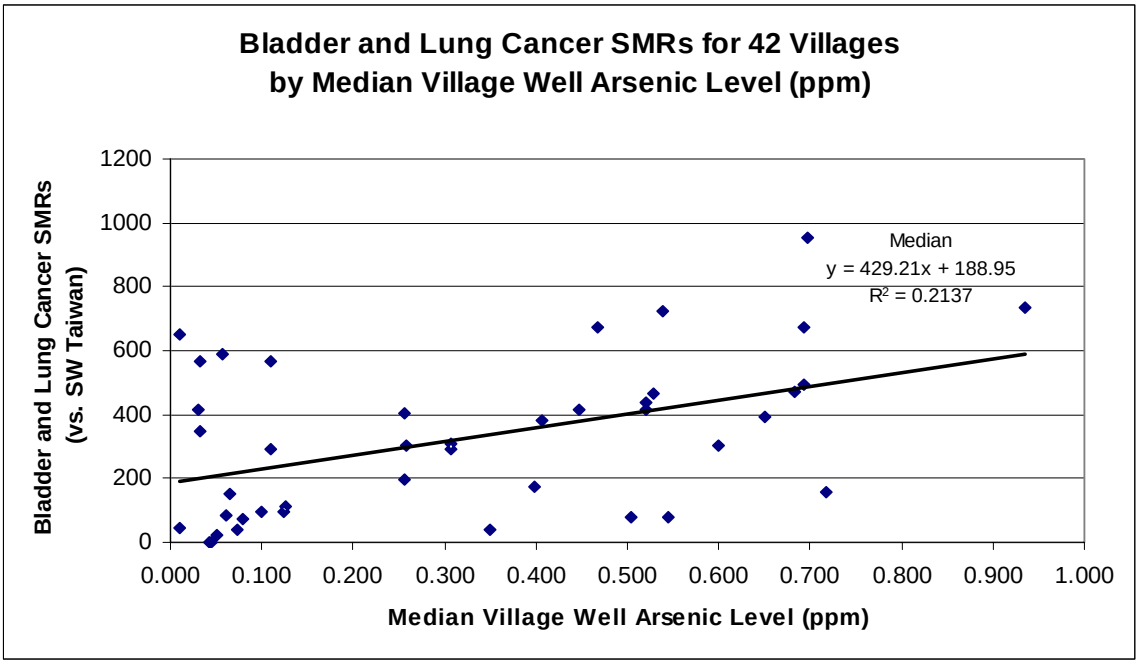
	PYs at Risk	Liver	Lung	Bladder	Total
Male	467,173	140	169	97	406
Female	461,633	62	135	105	302
Sum	928,806	202	304	202	708

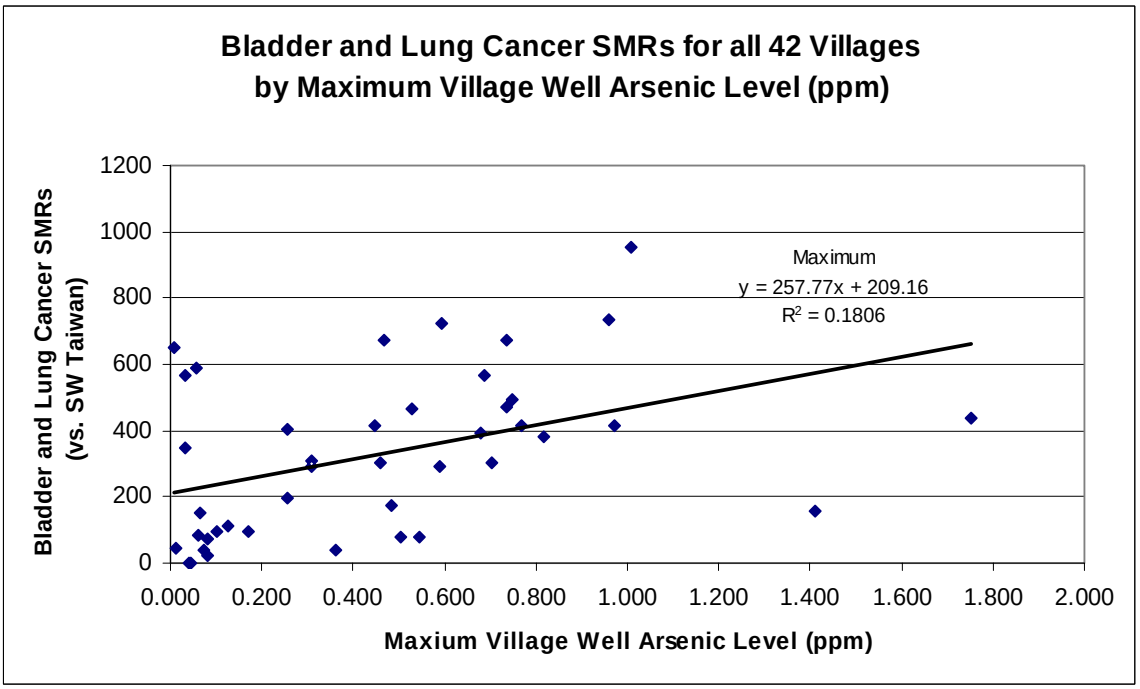
Wu 1989 Cancers (Age 20 +)

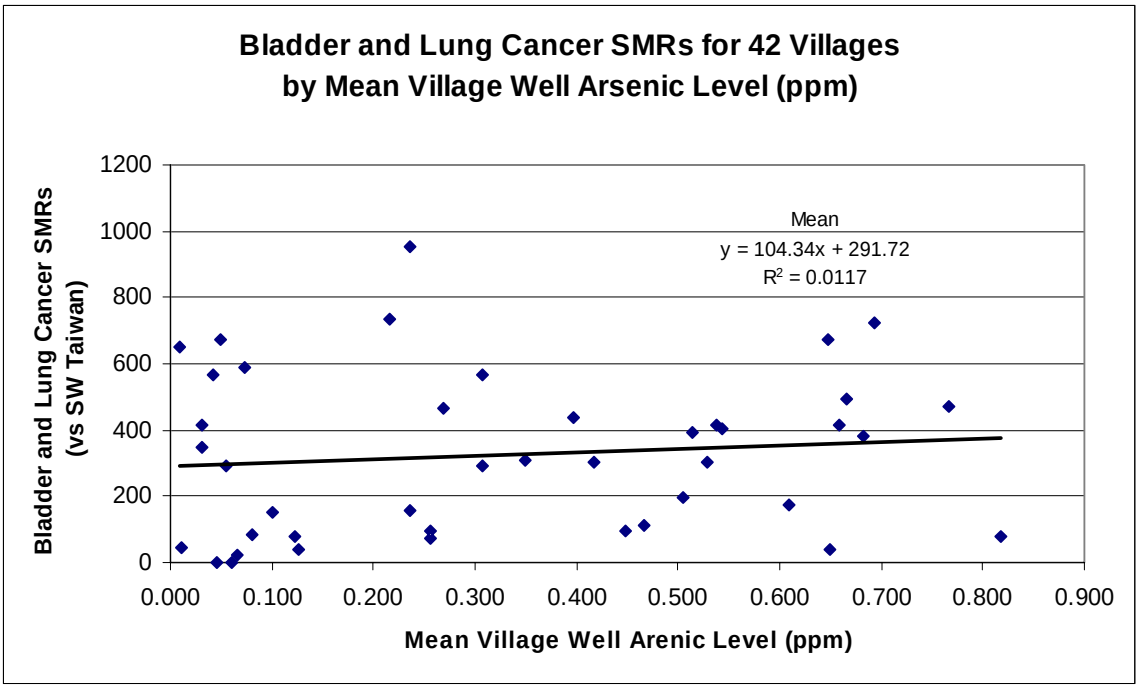
	PYs at Risk	Liver	Lung	Bladder	Total
Male	248,728	123	147	85	355
Female	230,048	51	121	96	268
Sum	478,776	174	268	181	623

The question had been raised as how representative the median was for the villages. I present below summary graphs based on the median village well arsenic level (ppm), the maximum village well arsenic level (ppm), and the mean village well arsenic level (ppm).

You will note that the median village well arsenic levels and the maximum village well arsenic levels provide similar explanatory power, but the slope for the maximum is only 60 % that of the median. It is unclear why the median is a more appropriate measure of the risk than the maximum. If the answer is that it is a measure of central tendency, then the observation that the mean village well arsenic level has almost no explanatory power is disturbing. I present this as an additional source of uncertainty that makes problematic the use of the median as the measure of risk in the analysis of the SW Taiwan dataset.


Bladder and Lung Cancer SMRs for 42 Villages
by Median Village Well Arsenic Level (ppm)
Bladder and Lung Cancer SMRs
(vs. SW Taiwan)
1200
1000
800
600
400
200
0
0.000
0.100
0.200
0.300
0.400
0.500
0.600
0.700
0.800
0.900
1.000
Median
y = 429.21x + 188.95
R2 = 0.2137
Median Village Well Arsenic Level (ppm)


Bladder and Lung Cancer SMRs for all 42 Villages
by Maximum Village Well Arsenic Level (ppm)
Bladder and Lung Cancer SMRs
(vs. SW Taiwan)
1200
1000
800
600
400
200
0
0.000
0.200
0.400
0.600
0.800
1.000
1.200
1.400
1.600
1.800
2.000
Maximum
y = 257.77x + 209.16
R2 = 0.1806
Maxium Village Well Arsenic Level (ppm)



I hope these responses are useful to you in examining the variety of sources of uncertainty that make the use of the SW Taiwan dataset troubling. There are a number of other study bases now available that may provide a risk estimate with less intrinsic uncertainty than the SW Taiwan dataset presented.

Cordially,

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