Database Selection for Carcinogenic Risk Estimation

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Charge Section C2

Use of human epidemiological data from direct iAs exposure

A. *Does the Taiwanese dataset remain the most appropriate choice for estimating cancer risk in humans?*

B. *What is the rationale for the response*?

Answer

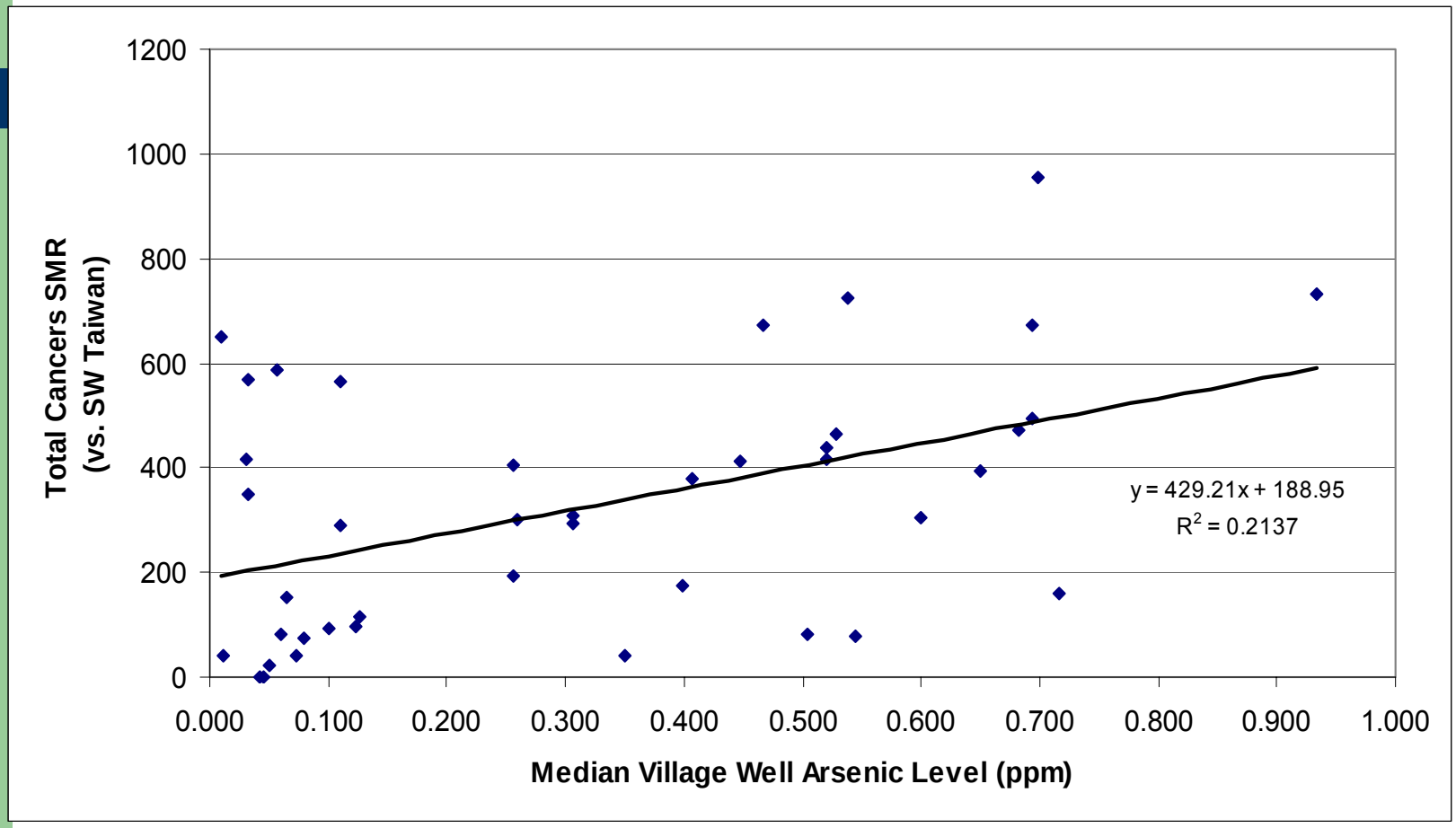
NO,

if it means the current SW dataset.

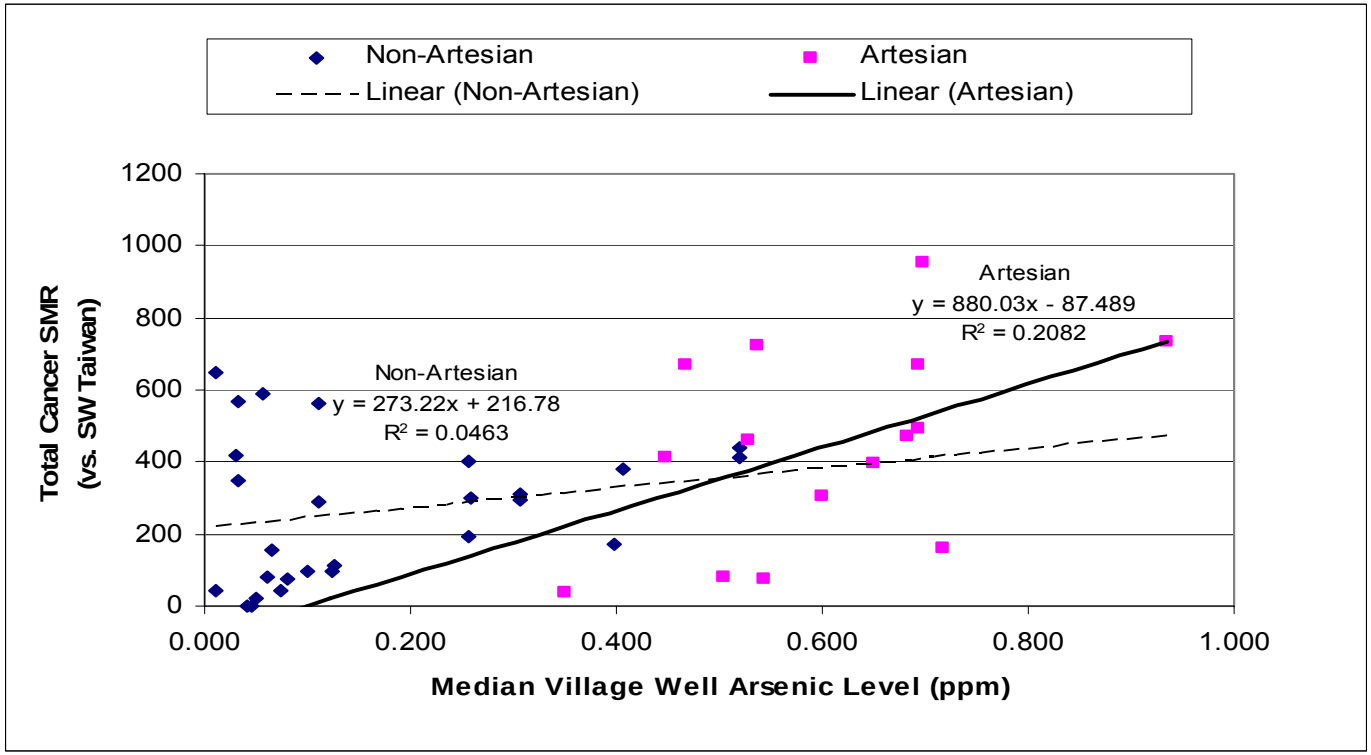
Rationale

- Problems with Current SW Taiwanese Dataset
  - The dataset is incomplete, lacking the variables previously shown to be significant.
  - Township carries almost as much weight as median arsenic as an explanatory variable.
  - More recently published studies have fewer internal problems than does the SW Taiwan dataset.

Bladder and Lung Cancer SMRs (combined) for all 42 Villages by Median Village Well Arsenic Level



Bladder and Lung Cancer SMRs (combined) for all 42 Villages by Median Village Well Arsenic Level and Water Source



Available Data [NRC, 1999; Table A-10]+

Village	**0**-G	
Wells	**5**	
Arsenic (ppm)	0.010; 0.010; 0.030; 0.259; **0.770**	
Median	**0.030**	
	Male	Female
Person Years	5,388	4,861
Cancer Deaths		
Bladder	3	2
Lung*	4	5
Liver*	3	3

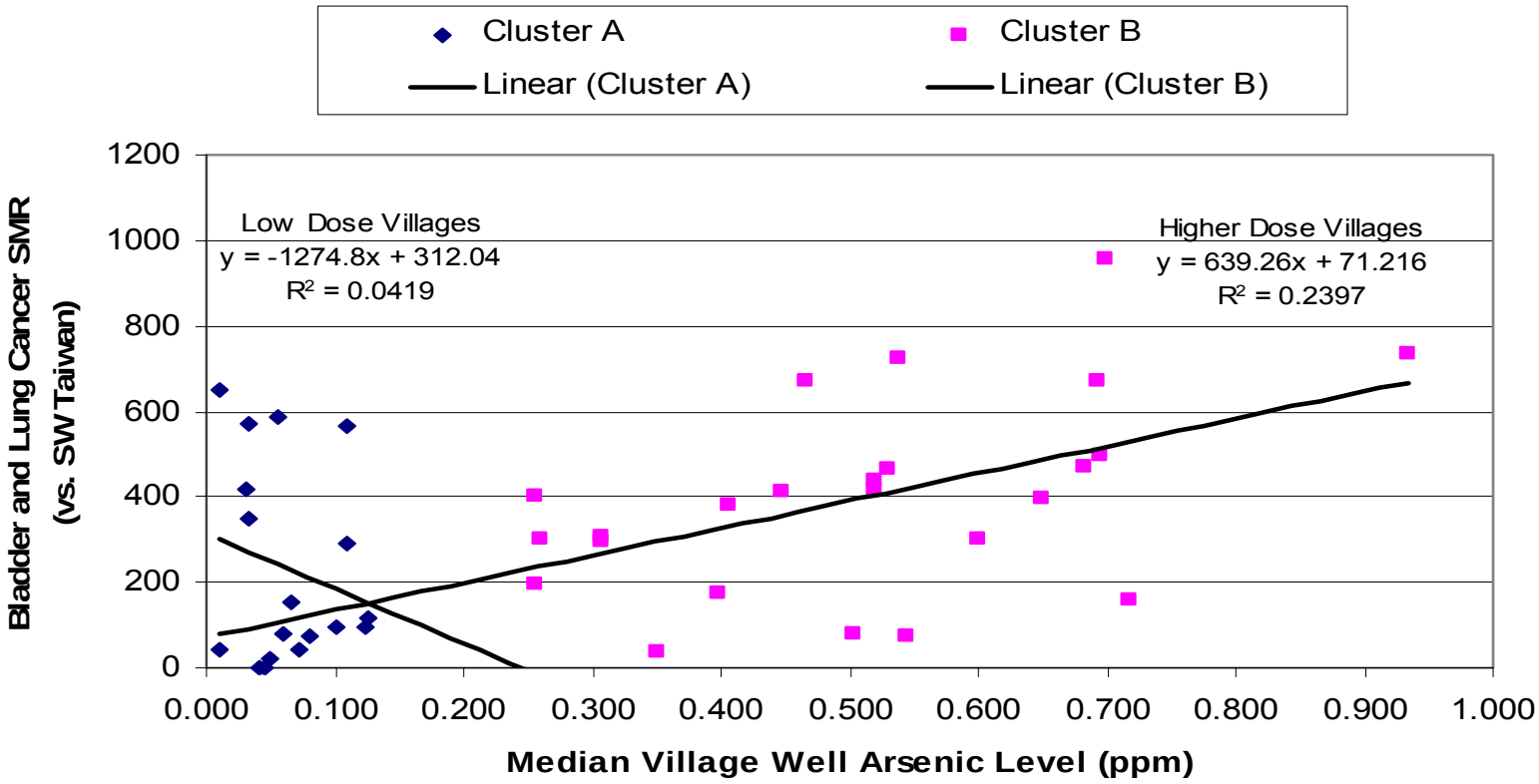
* Corrected

+Also age-gender distributions for person-years and death in each village and in reference population – Morales (2000)

Significant Explanatory Variables

Variable	p-Value
Township (Chen 1985)	0.02
Blackfoot Disease Prevalence (Chen 1985)	
Artesian Aquifer Dependency (Chen 1985)	0.01
Arsenic Strata (Wu 1989; Chen 1992)	0.02
Arsenic Median (Morales 2000)	0.01
Well Multiplicity (Lamm 2005)	0.01

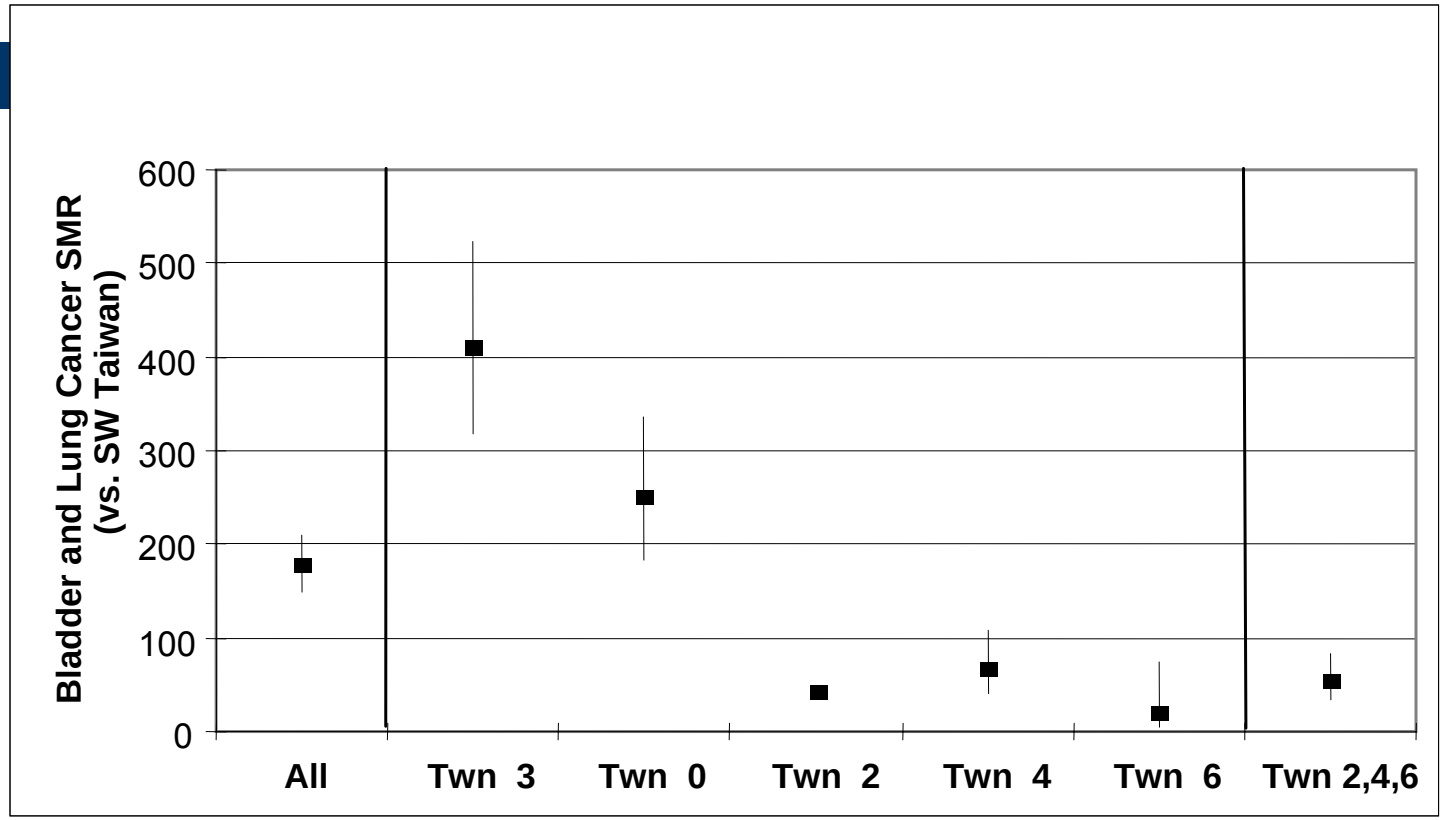
Bladder and Lung Cancer SMRs (combined) for all 42 Villages by Median Village Well Arsenic Level and Strata



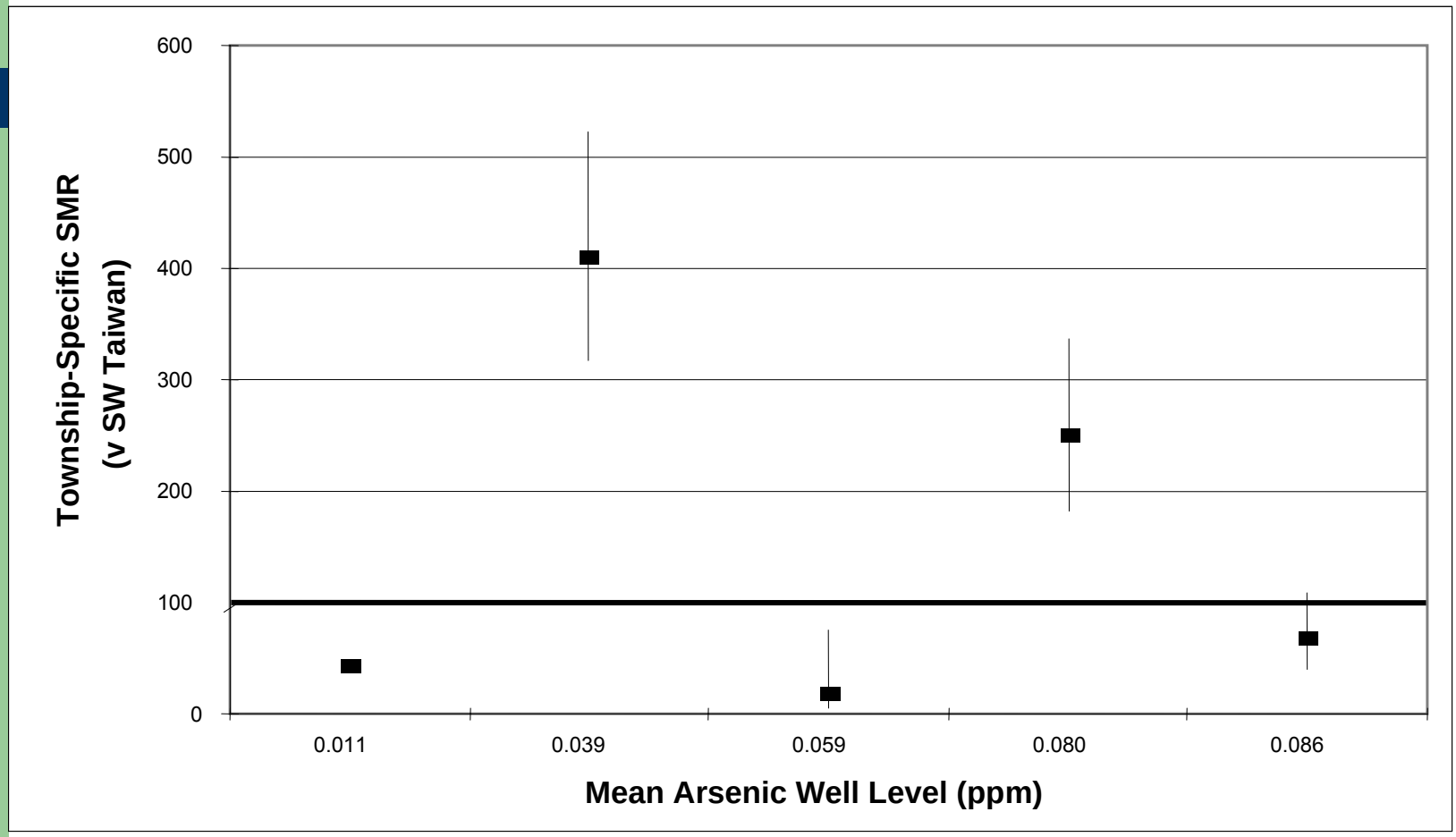
Bladder and Lung Cancer SMR
ANOVA Results for Independent Variables: Township, Water Source, Multiple Wells and Strata

All Villages (n=42)	P Value	
Township	**0.02**	
Artesian Aquifer Dependency	**0.01**	
Multiple Wells vs. Single Well	**0.01**	
Strata (Low, Medium, High)	**0.01**	
Strata (Low Dose, Higher dose)	**0.02**	
Low-Dose Villages (n = 18)	**P Value**	**Grouping**
Township	**0.01**	**0,3 v 4,6**
Artesian Aquifer Exposure	0.11	-
Multiple Wells vs. Single Well	0.21	-

Bladder and Lung Cancer (Combined) SMR by Township for Low-Dose Villages



Bladder and Lung Cancer (Combined) SMR by Mean Village Arsenic for Low-Dose Villages



Analytic Methodologies

- Historical Analysis
- Graphic Analysis
- Analysis of Variance (ANOVA)
  - Univariate and Grouping
- Multivariate Regression
- Step-wise Multivariate Regression

Explanatory Power (incremental R^2) for Significant Variables in Step-wise Multiple Regression Analysis for All 42 Villages [Grouped Cancers]

Outcome	Arsenic Median	Township	Multiple Wells
Bladder and Lung	**21%**	**18%**	
Bladder	18%	10%	
Lung	19%	19%	
Male	16%	12%	
Female	22%	19%	

Explanatory Power (incremental R^2) for Significant Variables in Step-wise and Hierarchical Multiple Regression Analysis for All 42 Villages [Individual Cancers]

Outcome	Arsenic Median	Township	Multiple Wells
Bladder and Lung	**21%**	**18%**	
Male Bladder	18%	5%	
Female Bladder	14%	11%	
Male Lung	14%	12%	
Female Lung		9%	26%

Interpretation

- Township as an explanatory variable probably reflects an effect related to Blackfoot Disease prevalence.
- Multiple wells as an explanatory variable suggests that the median is an inadequate estimate of the arsenic exposure.
- The SW Taiwan dataset as previously analyzed is incomplete, lacking significant explanatory variables and having unexplainable associations.

Alternative Datasets

- Ecological (Community data)
  - All 243 Taiwan township study (Guo, 2000)
  - US Counties (Lamm, 2004)
- Epidemiological (Individual data)
  - SW Taiwan* (Chen, 2004) *Different from EPA (NRC) dataset.
  - NE Taiwan (Chiou, 2001; Chen, 2004)
  - Case-control studies (Multiple)

Recommendations:

- Epidemiological study datasets trump ecological study datasets.
- Focus on NE Taiwan data (epi and low dose).
- Give weight to all the studies and examine the sources of outcome variability in each.