

Individual comments from SAB Member, Dr. Stanley Young, on lead and cardiovascular effects, May 13, 2020.

Several public speakers raised the question of a possible lead effect on cardiovascular disease. I examined data from Chowdhury et al. 2018, their Figure 3, my Table 1.

The standard method of meta-analysis is to compute a weighted average of the risk ratios, RR, along with its standard error. In Chowdhury that analysis indicated statistical significance. That result is in error based on the following analysis. First the RRs differ one from another by more than is expected by chance, $I^2=67.6\%$. There is study to study heterogeneity.

A p-value was computed for each study. If nothing is going on, these p-values should be uniformly space between 0 and 1. If the p-values are first ranked from smallest to largest, then plotted against the integers 1, 2, ..., 10, again if nothing is going on they should fall roughly on a 45-degree line. In this case we see a hockey stick figure, bilinear. There are 4 p-values below 0.05 and 6 above. We have a mixture. Four studies support an effect, and six do not. It makes no sense to average over a mixture. See Young and Kindzierski 2019 a and b.

The claimed cardiovascular disease effect is inconsistent, a mixture of significant and non-significant studies. The claim of an effect is therefore not supported.

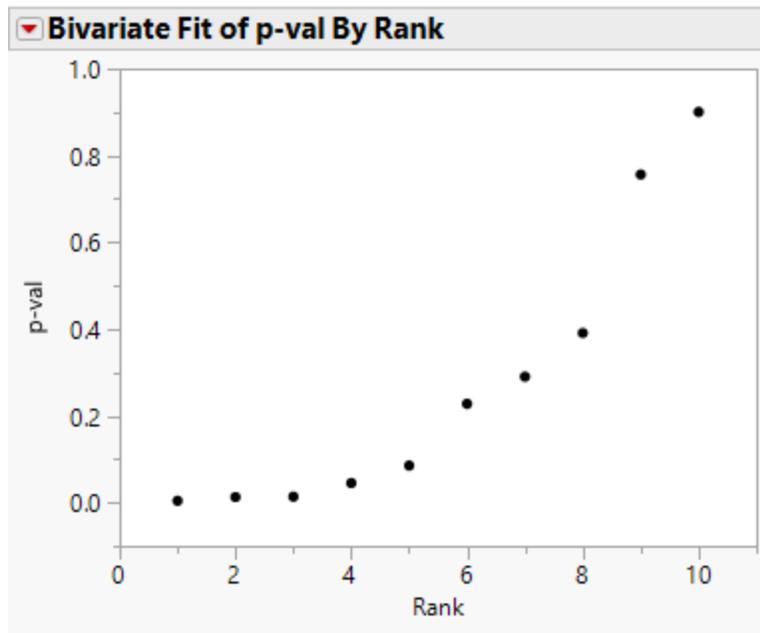
Stan Young

Table 1. Data from Chowdhury Figure 3

	RosID	Ref	RR	CLlow	CLhigh	SE95	Z95	p-val	Rank
1	1	SOF	2.23	0.99	4.99	1.0204	1.2054	0.228049	6
2	2	Glostrup Population Studies	1.11	0.61	2	0.3546	0.3102	0.756397	9
3	3	Zutphen study	1.05	0.53	2.1	0.4005	0.1248	0.900650	10
4	4	VA-NAS	0.69	0.32	1.47	0.2934	-1.0567	0.290651	7
5	5	BRHS	1.21	0.82	1.78	0.2449	0.8575	0.391169	8
6	6	NHANES II	1.25	1	1.57	0.1454	1.7193	0.085560	5
7	7	ABLES	1.64	1.21	2.22	0.2577	2.4840	0.012993	2
8	8	McElvenny (2015)	4.09	2.48	6.74	1.0867	2.8434	0.004464	1
9	9	NHANES III	1.24	1.03	1.5	0.1199	2.0017	0.045317	4
10	10	NHANES III	1.47	1.14	1.89	0.1913	2.4565	0.014028	3

Chi-square test of heterogeneity: $P=0.001$, $I^2=67.6\%$

Figure 1. P-value plot.



4 stat sig and 6 non-significant

The points on the “45-degree” imply that 6 studies are essentially random.

References

Chowdhury, R., Ramond, A., O’Keeffe, L. M., Shahzad, S., Kunutsor, S., Muka, T., ... Di Angelantonio, E. 2018. Environmental toxic metal contaminants and risk of cardiovascular disease: systematic review and meta-analysis. *BMJ*, 362, k3310.

<https://doi.org/10.1136/bmj.k3310>

Young S.S., Kindzierski K.B. 2019a. Combined background information for meta-analysis evaluation. <https://arxiv.org/abs/1808.04408>

Young S.S., Kindzierski K.B. 2019b. Evaluation of a meta-analysis of air quality and heart attacks, a case study, *Critical Reviews in Toxicology*, doi: [10.1080/10408444.2019.1576587](https://doi.org/10.1080/10408444.2019.1576587)