LETTER

Author's response to 'Re: Exposure to asbestos and the risk of colorectal cancer mortality: a systematic review and meta-analysis by Kwak *et al*'

We would like to thank Dr Boffetta for his comment on potential overlaps in the selection of cohorts. As we tried to keep the principle of examining all the available publications in the systematic review and avoiding the double count in the meta-analysis, we have re-examined the materials of the study again. Even though different aspects in the follow-ups of five cohorts were noted in the original review of 12 studies, we agree with Dr Boffetta that, on re-examination, there could be a potential of double counting. As for the Italian pool of asbestos worker cohorts,¹ which was included in the original review list of 310 full-text articles for eligibility assessment, we still find it ineligible, as it was a pooled study containing environmental exposures, and therefore did not satisfy the original inclusion criteria.²

Based on this re-examination, after excluding seven potentially overlapping studies (table 1 of the letter by Boffetta), we recalculated the pooled SMRs with only the most recent five cohorts kept in the analysis (table 1).^{3–7} The weight of the excluded seven cohorts was 15%. However, the overall results from the subgroup analysis were basically the same with only minor changes in the significance levels for some subgroups. Pooled standardised mortality ratio (SMR) of 'miscellaneous type of industry' has changed from a non-significant increase to a significant decrease; that of 'various type of industry' has gained significance; that of 'adequacy of follow-up in study quality' has lost significance. Forest plot of studies included in the meta-analysis was replotted in figure 1. The main results of the increased risk of colorectal cancer mortality in workers exposed to asbestos were almost the same in reanalysis as that of original analysis, and it remained statistically significant even after excluding seven potentially overlapping studies in the reanalysis.

Kyeongmin Kwak \odot , $^{\rm 1,2}$ Domyung Paek \odot , $^{\rm 1,3}$ Kyung Ehi Zoh \odot $^{\rm 1}$

Table 1	Recalculated pooled SMRs	of subgroup analysis
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		Heterogeneity		
	Studies (n)	Pooled SMR	l ² (%)	P value
Study area				
North America (USA and Canada)	13	1.08 (0.90–1.30)	73.0	< 0.001
Europe	22	1.21 (1.05–1.38)	34.0	0.061
Australia	1	1.45 (1.09–1.92)	-	-
Asia	3	1.43 (0.78–2.62)	0.0	0.704
Cohort size				
Small (<1500)	18	1.27 (1.10–1.47)	0.00	0.600
Large (≥1500)	21	1.09 (0.94–1.27)	76.4	<0.001
Type of industry				
Mining and milling	4	1.09 (0.72–1.65)	80.4	0.002
Insulation	4	1.49 (1.26–1.75)	4.0	0.373
Asbestos cement	8	1.06 (0.84–1.32)	23.6	0.241
Textile	10	1.19 (0.93–1.52)	49.7	0.037
Miscellaneous	7	0.86 (0.74–0.998)	0.0	0.808
Various	6	1.35 (1.24–1.47)	0.0	0.468
Follow-up duration				
Short (≤30 years)	17	1.07 (0.88–1.31)	46.5	0.019
Long (>30 years)	22	1.20 (1.04–1.38)	68.3	<0.001
Latency				
No latency	24	1.18 (1.03–1.36)	58.0	<0.001
Exist (5–20 years)	15	1.11 (0.91–1.37)	67.0	<0.001
Lung cancer SMR [*]				
Low (<2)	22	0.99 (0.85–1.16)	70.1	<0.001
High (≥2)	17	1.44 (1.29–1.60)	0.0	0.776
Smoking (ever) prevalence				
Data not available	23	1.20 (1.06–1.35)	43.3	0.015
Low (<75%)	9	1.00 (0.77–1.29)	40.4	0.098
High (≥75%)	7	1.25 (0.90–1.74)	77.2	<0.001
Smoking (current) prevalence				
Data not available	28	1.21 (1.07–1.37)	41.4	0.012
Low (<50%)	7	1.00 (0.75–1.34)	26.6	0.225
High (≥50%)	4	1.05 (0.72–1.53)	90.9	<0.001
Follow-up started year				
Early (1910–1965)	20	1.13 (0.97–1.32)	62.5	<0.001
Late (1966–2001)	19	1.19 (1.01–1.42)	58.7	0.001
Study quality				
Representativeness: representative	29	1.15 (1.02–1.30)	63.2	<0.001
Exposure measurement: formal	21	1.13 (0.97–1.33)	62.0	<0.001
Comparability of groups: standard	38	1.17 (1.04–1.31)	62.9	<0.001
Assessment of outcome: formal	39	1.16 (1.03–1.29)	62.4	<0.001
Adequacy of follow-up: virtually complete	23	1.15 (0.95–1.38)	35.0	0.051
Types of cancer				
Colon or intestine	15	1.18 (0.97–1.45)	70.0	<0.001
Rectum	14	1.17 (0.93–1.47)	34.7	0.097

SMR, standardised mortality ratio.

¹Department of Environmental Health Sciences, Seoul National University Graduate School of Public Health, Seoul, Korea (the Republic of)

²Department of Occupational and Environmental Medicine, Korea University Ansan Hospital, Ansan, Gyeonggi-do, Korea (the Republic of) ³Institute of Health and Environment, Seoul National University, Seoul, Korea (the Republic of)

Correspondence to Kyung Ehi Zoh, Department of Environmental Health Sciences, Seoul National University Graduate School of Public Health, Seoul 08826, Korea (the Republic of); kezoh@snu.ac.kr

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Study	ES (95% CI)	% Weight					
Mancuso TF, et al. (1963)	1.42 (0.53, 3.81)	1.08					
Ohlson CG, et al. (1984)	0.72 (0.42, 1.24)	2.53					
Acheson ED, et al. (1984)	1.32 (0.67, 2.59)	1.92					
Peto J, et al. (1985) - Cohort I	1.45 (0.39, 5.45)	0.65					
Peto J, et al. (1985) - Cohort II	1.98 (0.65, 6.07)	0.87					
Peto J, et al. (1985) - Cohort III	0.78 (0.44, 1.39)	2.34					
Ohlson CG, et al. (1985)	1.86 (0.98, 3.52)	2.05					
Woitowitz HJ, et al. (1986) - Cohort I	0.79 (0.30, 2.10)	1.09					
Woitowitz HJ, et al. (1986) - Cohort II	2.15 (0.57, 8.05)	0.65					
Seidman H, et al. (1986)	1.85 (1.19, 2.87)	3.14					
Gardner MJ, et al. (1986)	0.71 (0.38, 1.34)	2.08					
Enterline PE, et al. (1987)	1.16 (0.75, 1.79)	3.20					
Hughes JM, et al. (1987)	0.90 (0.57, 1.41)	3.07					
Botta M, et al. (1991)	0.87 (0.53, 1.43)	2.79					
Selikoff IJ, et al. (1992)	1.37 (1.14, 1.65)	5.18					
Sanden A, et al. (1992)	1.10 (0.54, 2.25)	1.75					
McDonald JC, et al. (1980) (1993)	0.80 (0.68, 0.94)	5.34					
Rösler JA, et al. (1994)	0.96 (0.26, 3.60)	0.65					
Battista G, et al. (1999)	0.93 (0.38, 2.27)	1.27					
Germani, D. et al. (1999)	2.18 (1.15, 4.12)	2.06					
Szeszenia-Dabrowska N, et al. (2000)	1.75 (0.92, 3.31)	2.06					
Berry G, et al. (2000)	1.54 (1.11, 2.14)	3.98					
Wilczynska U, et al. (2005)	1.56 (1.10, 2.22)	3.80					
	0.69 (0.47, 1.02)	3.51					
	1.03 (0.66, 1.61)	5.00					
Dement 3, et al. (2009)	1.02 (0.09, 0.90)	5.24					
Loomic Date (2009)	1.50 (1.24, 1.45)	4.25					
Desch B et al (2010)	0.77 (0.34, 1.41)	4.20					
	1 12 (0 37 3 41)	0.88					
	1 30 (0 74 2 28)	2 42					
	1 18 (0 38 3 63)	0.86					
	1 94 (0 76 4 97)	1 16					
Van den Borre L., et al. (2015)	0.85 (0.23, 3.16)	0.66					
	1.40 (0.98, 2.01)	3.73					
Levin JL, et al. (2016)	1.95 (1.22, 3.11)	2.97					
Oddone E. et al. (2017)	0.92 (0.64, 1.32)	3.74					
Pira E, et al. (2017)	0.83 (0.47, 1.46)	2.39					
Reid A, et al. (2018)	1.45 (1.09, 1.92)	4.36					
Overall (I-squared = 62.4%, p = 0.000)	1.16 (1.03, 1.29)	100.00					
NOTE: Weights are from random effects analysis							
.05 .1 .2 .5 1 2 5 10 20							
*ES, effect size							
*Detailed references of included studies can be found in reference 2							

Figure 1 Revised forest plot of studies included in the meta-analysis of exposure asbestos and the risk of colorectal cancer mortality.



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ORCID iDs

Kyeongmin Kwak http://orcid.org/0000-0001-6296-8058

Domyung Paek http://orcid.org/0000-0003-4510-6362 Kyung Ehi Zoh http://orcid.org/0000-0002-2821-070X

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