Table 1. Adjusted time ratios for mesothelioma latency among British asbestos workers (1971–2005)

			Including year of first exposure			Excluding year of first exposure		
Characteristic	**No. of deaths**	**Person-years at risk**	**Time ratio**	**95% CI**	**LR test**	**Time ratio**	**95% CI**	**LR test**
Sex					$P=0.015$			$P=0.154$
Male	359	6427	1.00	Ref.		1.00	Ref.	
Female	8	169	1.12	1.01–1.25		1.08	0.96–1.23	
Main smoking status					$P=0.258$			$P=0.146$
Current	199	3684	1.00	Ref.		1.00	Ref.	
Former	103	1753	1.03	0.99–1.07		1.04	1.00–1.09	
Never	65	1159	1.01	0.97–1.06		1.02	0.97–1.07	
Main occupation					$P=0.483$			$P=0.034$
Manufacturing	121	2436	0.98	0.93–1.02		0.96	0.91–1.02	
Removal	117	1856	0.98	0.93–1.03		0.93	0.87–0.98	
Other	53	980	1.01	0.96–1.06		1.00	0.94–1.06	
Insulation	76	1324	1.00	Ref.		1.00	Ref.	
Year of first exposure					$P<0.001$			NA
1950–1959	220	3745	1.00	Ref.		NA	NA	
1960–1969	147	2851	0.86	0.83–0.90		NA	NA	
Age at first exposure (years)					$P<0.001$			$P<0.001$
<20	148	2599	1.00	Ref.		1.00	Ref.	
20–	112	2129	0.96	0.92–0.99		0.97	0.93–1.01	
30–	66	1171	0.91	0.87–0.96		0.90	0.85–0.95	
40–	30	535	0.80	0.74–0.86		0.77	0.71–0.84	
50+	11	162	0.84	0.76–0.92		0.77	0.69–0.86	
Duration of exposure (years)					$P=0.237$			$P=0.001$
<10	13	372	1.00	Ref.		1.00	Ref.	
10–	83	2048	1.09	1.00–1.19		1.13	1.02–1.25	
20–	155	2800	1.08	0.99–1.18		1.18	1.07–1.30	
30–	101	1302	1.11	1.01–1.23		1.27	1.15–1.42	
40+	15	75	1.08	0.97–1.21		1.21	1.07–1.38	
Mesothelioma type					$P=0.020$			$P=0.025$
Pleural	184	3450	1.00	Ref.		1.00	Ref.	
Peritoneal	80	1378	0.97	0.93–1.01		0.97	0.93–1.02	
Pleural + peritoneal	4	56	0.75	0.65–0.86		0.76	0.64–0.89	
Not specified	99	1712	0.98	0.94–1.02		0.96	0.92–1.00	

Abbreviations: CI = confidence interval; LR = likelihood ratio; NA = not applicable; Ref. = reference. The time ratios were estimated using multivariable generalised gamma accelerated failure-time models including only cases first exposed between 1950 and 1969 and using full follow-up (1971–2005).

This is not informative and was not the quantity of interest in this study, but rather the median latency for those who died with mesothelioma. I acknowledge that the median latency of 23 years estimated in the study (30 years after excluding deaths within 10 years of first occupational exposure) will be restricted by the duration of follow-up, and so would increase as follow-up continues.

Second, if individuals who died from other causes or were alive at the end of follow-up were included as censored observations, then the estimated latency becomes dependent on the mesothelioma incidence rate. For example, if the incidence rate of mesothelioma was greater than the 37 cases per 100 000 person-years observed among the cohort, then the predicted median latency among the cohort (that is, the estimated time at which 50% of the full cohort would have died with mesothelioma) would be shorter even if the median latency for the cases were the same. This could have a great impact when comparing groups with very different incidence rates, such as asbestos insulation workers and removal workers.

The methodology employed by the study is by no means perfect, and many of the limitations are discussed here, in previous comments and in the original paper. However, I believe that it was appropriate and remains valid. I would like to thank the commenters for their thoughtful and constructive remarks, which highlight the challenges involved when latency is the outcome of interest.

REFERENCES

Consonni D, Barone-Adesi F, Mensi C (2014) Comment on 'The latency period of mesothelioma among a cohort of British asbestos workers (1978–2005)': methodological problems with case-only survival analysis. *Br J Cancer* **111**: 1674.

Farioli A, Mattioli S, Curti S, Violante FS (2014) Comment on 'The latency period of mesothelioma among a cohort of British asbestos workers (1978–2005)': the effect of left censoring. *Br J Cancer* **111**: 2197–2198.

Frost G (2013) The latency period of mesothelioma among a cohort of British asbestos workers (1978–2005). *Br J Cancer* **109**: 1965–1973.

Mirabelli D, Zugna D (2014) Comment on 'The latency period of mesothelioma among a cohort of British asbestos workers (1978–2005)'. *Br J Cancer* **111**: 1675.

Peto J (1985) Some problems in dose-response estimation in cancer epidemiology. In *Methods for Estimating Risk of Chemical Injury: Human and Non-Human Biota and Ecosystems*, Vouk VB, Butler GC, Hoel DG, Peakall D (eds). pp 361–380. Wiley: New York, NY, USA.

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Comment on 'Residential distance at birth from overhead high-voltage powerlines: childhood cancer risk in Britain 1962–2008'

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Bunch *et al* (2014) studied the incidence of childhood leukaemia in relation to distance at birth from high-voltage powerlines over the period 1962–2008 and found that, for children born within 200 m, the relative risk fell from 4.5 (0.97–20.83) in the 1960s to 0.71 (0.49–1.03) in the 2000s.

The opening year of the study was the last in which there was insufficient capacity to meet the maximum demand for electricity (Department of Energy and Climate Change (DECC), 2013). The next decade saw a near doubling of demand which drove a frenzied programme of power station and power line construction, (National Grid Company, 2010) and, by the time that the 1973 oil crisis forced a slow down, a 50% margin of generating capacity over the peak demand had been established (Department of Energy and Climate Change (DECC), 2013).

Construction of the 400 kV supergrid did not begin until 1965 and it is noteworthy that Bunch *et al's* maximum relative risk of 4.5 (0.97–20.83)

relates to the period 1962–1999 when construction activity would have been intense. This activity was reliant on an influx (which included this author) of itinerant workers to the communities hosting the construction sites and the population mixing associated with this influx has been associated with the incidence of childhood leukaemia (Kinlen *et al,* 1995; Kinlen and Doll, 2004).

Kinlen *et al* studied the incidence of childhood leukaemia within 10 km of large, rural, construction sites and five of their chosen locations (Drax, West Burton, Longannet, Pembroke and Fawley) housed power stations and supported an on site construction work force of more than 2000 during the first decade of Bunch's study.

To quote from Kinlen's abstract:

> A 37% excess of leukaemia and non-Hodgkin's lymphoma at 0–14 years of age was recorded during construction and the following calendar year. The excesses were greater at times when construction workers and operating staff overlapped (72%), particularly in areas of relatively high social class. For several sites the excesses were similar or greater than those near the nuclear site of Sellafield (67%), which is distinctive in its large workforce with many construction workers.

The reader may object that Bunch *et al* were considering the impact of power lines, not power stations but all of the power stations under consideration were connected to the National Grid and powerlines would, necessarily, have run through the areas which Kinlen *et al* identified as having an elevated relative risk of childhood leukaemia.

He concluded that:

> Overall these findings provide further support for the hypothesis that rural population mixing is conducive to the transmission of the underlying infective agent(s) among susceptible people so as to increase the incidence of childhood leukaemia and non-Hodgkin's lymphoma.

The consumption of electricity in the UK grew by a factor of nearly three between 1962 and 2008 (Department of Energy and Climate Change (DECC), 2013), whilst Bunch *et al* show that the relative risk of leukaemia declined, from 4.5 to 0.71, over the same period. There can be little debate over their observation that magnetic fields cannot provide an explanation for their findings.

Bunch *et al* did not consider the relatively short term impact of the influx of powerline and power station construction workers but rather suggest that the result may be due to the *'changing population characteristics of people living near powerlines.'* Power stations are nodes on the powerline network and, of course, the lines are remote from them for much of their length. The authors mention *'changes to the types of houses built near powerlines or the characteristics of people living in them'* as possible causes of their findings. These changes would have taken time but the maximum relative risk of leukaemia was found in the early years of the study when the influx of contractors would have been at its height.

Kinlen's data show that mixing can enhance the risk of leukaemia in the relatively short term (1970–75 at Drax Phase 1, 1968–73 at Longannet, 1966–68 at West Burton). His cases were drawn from the same registry as Bunch's and it would be of great interest to locate the totality of Bunch *et al's* exposed cases with respect to the power stations as well as the powerlines.

REFERENCES

Bunch KJ, Keegan TJ, Swanson J, Murphy MFG (2014) Residential distance at birth from overhead high-voltage powerlines: childhood cancer risk in Britain 1962–2008. *Br J Cancer* **110**: 1402–1408.

Department of Energy and Climate Change (DECC) (2013) *60th Anniversary Digest of United Kingdom Energy Statistics*, pp 42–44. Stationery Office: Norwich.

Kinlen LJ, Dickson M, Stiller CA (1995) Childhood leukaemia and non-Hodgkin's lymphoma near large rural construction sites, with a comparison with Sellafield nuclear site. *BMJ* **310**: 763–768.

Kinlen L, Doll R (2004) Population mixing and childhood leukaemia: Fallon and other US clusters. *BJC* **91**: 1–3.

National Grid Company (2010) National Grid 75th Anniversary Timeline www.nationalgrid75.com/.

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Comment on 'The NQO1 polymorphism C609T (Pro187Ser) and cancer susceptibility: a comprehensive meta-analysis'

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Sir,

I read the article by Lajin and Alachkar (2013) with great interest, which appeared in your journal as *Br J Cancer*. The study aimed to evaluate the impact of the NQO1 gene polymorphism with cancer risk. Although the study provides preliminary evidence to consider NQO1 polymorphism as a risk factor for cancer; however, after careful reading of the article, a few important issues came out that must be addressed for further actions.

First, it appears that the authors somehow missed the statistical power in this study. Sample sizes remain a major issue in genetic case–control studies analysing the association of polymorphism with disease susceptibility. The authors did neither mention the statistical power of individual studies nor their overall meta-analysis. Hence, the study should obtain an adequate statistical power (80%) to estimate significant association accurately, which remains a primary criterion to perform such studies, especially from the venous blood of study subjects. Underpowered studies usually lead to false-positive associations and misinterpretations (Hattersley and McCarthy, 2005). The authors also failed to mention the incidence rate of various cancers in the said study. The individual studies recruited in the present meta-analysis achieved the required statistical power is questionable and did not discuss in the text.

Second, the authors mention the sample size of Malik *et al* as 107 gastric cancer cases and 195 controls (Malik *et al*, 2011). But the exact number of gastric cancer cases is 108 in the study by Malik *et al.* All these points suggest a thorough examination of the association observed in the said study, and must be clarified before concluding that NQO1 gene polymorphism is a potential marker of cancer.

REFERENCES

Hattersley AT, McCarthy MI (2005) What makes a good genetic association study? *Lancet* **366**: 1315–1323.

Lajin B, Alachkar A (2013) The NQO1 polymorphism C609T (Pro187Ser) and cancer susceptibility: a comprehensive meta-analysis. *Br J Cancer* **109**(5): 1325–1337.

Malik MA, Zargar SA, Mittal B (2011) Role of NQO1 609C4T and NQO2-3423G4A polymorphisms in susceptibility to gastric cancer in Kashmir valley. *DNA Cell Biol* **30**(5): 297–303.

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