independent of oestrogen pathways, such as metabolic dysfunction (Gangwisch et al, 2007) and chronic inflammation (Irwin et al, 2006).

Again, we thank Yang et al for this letter and are glad that more studies, such as the population-based case-control study in Jiujiang city mentioned by Yang et al, are using objective measures along with questionnaires to better assess both the quantity and quality of sleep in relation to breast cancer risk and other health outcomes.

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*Correspondence: Dr Q Xiao; E-mail: qian.xiao@nih.gov
Published online 21 April 2015
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BJC

Comment on ‘Possible pro-carcinogenic association of endotoxin on lung cancer among Shanghai women textile workers’

R Rylander* and R Jacobs

1BioFact Environmental Health Research Center, Lerum, Sweden and 2Environmental and Occupational Health Sciences, School of Public Health and Information Sciences, University of Louisville, Louisville, KY, USA

Sir,

In a recent article in this Journal, Checkoway et al (2014) suggest that the exposure to endotoxin in industrial environments is associated with an increase in the risk of lung cancer.

A number of studies over the past 50 years has demonstrated a decreased risk in different environments involving a high exposure to endotoxin such as cotton handling and farming (Rylander, 1992; Maestrangelo et al, 2005; Lenters et al, 2010). Plausible cellular mechanisms for this defence have been discussed. In the data now presented there are no significant differences in risk—all are within the 95% confidence limit—and no significance for trend in relation to exposure duration. The only observation, thoroughly discussed, is a small, non-significant increase in risk in a subgroup. It is difficult to understand how such data can be used as a support to challenge a previously well-established relationship.

More serious is the lack of control of possible confounding factors. It is well known that indoor air pollution from cooking fuels is a risk factor for lung cancer. Such exposures change over the years and are closely related to socio-economic factors. The problem is discussed but in the absence of data the discussion remains speculative. Diet modulates the risk of lung cancer but is not discussed (Seow et al, 2002; Rylander and Axelson, 2006). Finally, possible changes in endotoxin exposure over the years are not dealt with. Also in China, work hygiene standards have improved over the years since the measurements were made and could result in a change of exposure to endotoxin.

In view of the above, a correct conclusion from the material presented is that ‘no relation between endotoxin exposure and lung cancer risk could be detected’.

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*Correspondence: Professor R Rylander; E-mail: envhealth@biofact.se
Published online 20 November 2014
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BJC

Reply to Comment on: ‘Possible pro-carcinogenic association of endotoxin on lung cancer among Shanghai women textile workers’

H Checkoway*, 1 JI Lundin2, S Costello3, R M Ray4, W Li5, E A Eisen6, G Astrakianakis6, K Applebaum7, D L Gao8 and D B Thomas

1Department of Family and Preventive Medicine, University of California, San Diego, La Jolla, CA 92039, USA; 2Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA; 3Department of Environmental Health Sciences, University of California, Berkeley, CA, USA; 4Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA; 5Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA; 6School of Public Health and Information Sciences, University of Louisville, Louisville, KY, USA; 7Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, 98109, USA; 8Zhong Shan Hospital Cancer Center, Shanghai 2000030, China

Sir,

We appreciate the thoughtful comments by Rylander and Jacobs (2015) on our paper (Checkoway et al, 2014). The absence of an inverse exposure–response relation for endotoxin and lung cancer in the extended follow-up was somewhat unexpected in view of the reported consistent findings from numerous prior studies, including our initial follow-up of the
Response to ‘Are the studies on cancer risk from CT scans biased by indication? Elements of answer from a large-scale cohort study in France’

C R Muirhead* 1

1 Institute of Health & Society, Newcastle University, Baddiley-Clark Building, Richardson Road, Newcastle upon Tyne, NE2 4AX, UK

Sir,

The recent paper by Journy et al (2015) addresses an important issue regarding the interpretation of epidemiological studies of CT scans and cancer risk. It has been suggested that biased results reported in the studies in Northern England (Pearce et al, 2012) and Australia (Mathews et al, 2013) might reflect the early symptoms of undetected cancer, or of factors that predispose to cancer and which are the indications for the CT scans, rather than an effect of the CT scans per se (Walsh et al, 2014). The study of Journy et al based on a cohort of children who received CT scans at 23 radiology departments in France—benefits from the availability of information on predisposing factors for cancer. However, I have concerns that their findings could be misinterpreted.

Table 1 here combines the results from Table 5 and Supplementary Table 6 from the study by Journy et al. The authors have highlighted that – for each cancer type – the estimate of the excess relative risk (ERR) per 1 mGy cumulative organ dose is lower with adjustment for predisposing factors than without such an adjustment. At face value, this might suggest confounding by indication, reflecting higher cancer risk and potentially higher radiation doses from CT scanning among children with predisposing factors compared with children without such factors. However, Table 1 here also shows that – for each cancer type – the ERR among children without predisposing factors is at least as large as the unadjusted value for the cohort overall, whereas the ERR among children with predisposing factors is close to zero. This suggests that the difference between the unadjusted and adjusted values principally reflects modification of the ERR by predisposing factors, rather than confounding.

It is unclear from the study by Journy et al to what population the adjusted ERR estimates apply. Looking at Table 1, the adjusted estimates appear to be similar to a weighted average of the ERR estimates for those either with or without a predisposing factor, with weighting based on the numbers of cancer cases in each group. This would suggest that the adjusted estimates reflect the prevalence of predisposing factors among those children who developed cancer. However, from a public health perspective, it is more relevant to consider the prevalence of predisposing factors in the general population, rather than in the selected population.

We encourage analyses that consider temporal patterns of association in other endotoxin-exposed study populations, which can provide valuable insights into disease aetiology and pathogenesis.

*Correspondence: Professor H Checkoway; E-mail: hcheckoway@ucsd.edu
Published online 20 November 2014
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Table 1. Number of cases and associated risks of primary tumours of the CNS, leukaemia, and lymphoma

|                | CNS cancer | Leukaemia | Lymphoma |
|----------------|------------|-----------|----------|
| Cases          | IR         | ERR       | 95% CI   |
| All children   | 22 9.4     | 17 7.3    | 19 8.1   |
| Unadjusted for predisposing factors | 0.022 – 0.016, 0.061 | 0.057 – 0.079, 0.193 | 0.018 – 0.068, 0.104 |
| Adjusted for predisposing factors | 0.012 – 0.013, 0.037 | 0.047 – 0.065, 0.159 | 0.008 – 0.057, 0.073 |
| Children without a predisposing factor | 15 6.4 0.028 n.a. | 12 5.2 0.187 n.a. | 12 5.2 0.025 n.a. |
| Children with a predisposing factor | 7 56.5 0.005 n.a. | 5 128.0 – 0.012 n.a. | 7 160.3 – 0.005 n.a. |

Abbreviations: CNS = central nervous system; CI = confidence interval; ERR = excess relative risk; IR = incidence rate; n.a. = not available. The table provides the IR per 100 000 person-years, ERR related to cumulative organ dose (in mGy) from CT scans, for all children (without and with adjustment for predisposing factors), and separately for children with and without predisposing factors, with a 2-year exclusion period (based on Journy et al, 2015).

*Valid-based CI for the ERR.
*Factors predisposing specifically to cancer at the site specified.
*Listed as NG at Supplementary Table 6 of Journy et al.