McNally RJ, Wakeford R, James PW, Basta NO, Alston RD, Pearce MS, Elliott AT.

Reply to Comment on 'A geographical study of thyroid cancer incidence in north-west England following the Windscale nuclear reactor fire of 1957'.

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Response to Comments on the paper titled "A geographical study of thyroid cancer incidence in north-west England following the Windscale nuclear reactor fire of 1957"

We thank Drs Hunter and Haylock for their interest in our paper [1] reporting the results of a geographical study of thyroid cancer incidence in the two counties of north-west England most affected by ^{131}I contamination following the Windscale reactor accident at Sellafield in October 1957. This study was part of the work of the Committee on Medical Aspects of Radiation in the Environment (COMARE) for its Seventeenth Report [2]. To clarify a point arising from the first two sentences of the letter of Hunter and Haylock: the study analysed thyroid cancer registrations during 1974-2012 among those resident in Cumbria and Lancashire *at diagnosis* while less than 85 years of age, but we could not determine from routinely available data where affected individuals were living during the last quarter of 1957. We discussed in the paper inward and outward migration as a limitation of the geographical study [1].

As was made clear in the paper [1], the study focussed, *a priori*, upon those who were less than 20 years of age at the time of the accident (those born during 1939-1958) because evidence from previous studies demonstrates that those irradiated at a young age are at the highest risk of consequent thyroid cancer, and that this excess risk persists into later life [1]. Our primary finding, therefore, was the thyroid cancer registration rate in the more contaminated county (Cumbria) for this young age-at-exposure group. However, we believed that it was important to consider finer age groups (not least because of the prior evidence that the risk is greatest at the youngest ages at exposure [1]) and other periods of birth to provide some perspective for the primary result.

There is no doubt that the rate of thyroid cancer registrations during 1974-2012 for those born during 1939-1958 is ~30% higher for Cumbria compared to that for England (excluding Cumbria and Lancashire), and is ~10% lower

for Lancashire. The crucial question then is, how should these findings be interpreted? One aspect of interpretation is “statistical significance”. Our starting point was the assumption that Poisson processes were generating the rates, but it became apparent during the study that the distributions were overdispersed, as illustrated by the unusual temporal patterns of registration rate ratios presented in Figure 2 of our paper [1], patterns that differ between Cumbria and Lancashire. However, we kept to our original intention of principally presenting Poisson confidence intervals, but also presented in the Supplementary Material confidence intervals that incorporated a particular adjustment for extra-Poisson variation using a method proposed by Breslow [3]. While it may be argued that these “Breslow-adjusted” confidence intervals, all of which contained a rate ratio of unity, should perhaps have been those taking precedence in the paper, this would almost certainly have led to accusations of “massaging the data”. We did, however, emphasise in the paper the importance to interpretation of the finding of overdispersion, including in the Abstract [1].

Perhaps of greater importance to interpretation are the patterns of rate ratios found in the study. Thus, the rate ratio for Cumbrian registrations for those born during 1954-1958 (1.12, for those who were youngest at the time of the accident) was less than that for those born during 1929-1933 (1.44, for those in the study who were oldest at the time of the accident), while the ratio was greatest for those born during 1959-1963 (1.49, for those who were not exposed to ^{131}I from the accident). The equivalent rate ratios for Lancashire registrations were 1.05, 0.61 and 0.91, respectively. These patterns do not suggest that ^{131}I exposure from the Windscale accident was responsible for the raised rate ratio for Cumbrian registrations during 1974-2012 among those born during 1939-1958, 1.29, the primary finding. Rather, they suggest either problems with thyroid cancer registration data, the influence of major (non-radiation) risk factors for thyroid cancer, or both. We emphasised this in the paper [1]. We are most surprised that Hunter and Haylock believe that the Abstract of our paper implies that these patterns of rate ratios result from exposure to ^{131}I from the accident, because we believe that the Abstract clearly implies exactly the opposite.

As we made plain in the paper [1], the geographical study can be only a preliminary examination of the potential impact upon thyroid cancer risk of ^{131}I released during the Windscale accident. We are firmly of the opinion that more detailed investigations are required to better understand the unusual nature of the thyroid cancer registration patterns that we reported [1]. The COMARE Seventeenth Report [2] specifically recommends that such investigations should be conducted.

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References

[1] McNally R J Q, Wakeford R, James P W, Basta N E, Alston R D, Pearce M S, Elliott A T 2016 A geographical study of thyroid cancer incidence in north-west England following the Windscale nuclear reactor fire of 1957 *J. Radiol. Prot.* **36** 934-952

[2] Committee on Medical Aspects of Radiation in the Environment (COMARE) 2016 *COMARE Seventeenth Report. Further Consideration of the Incidence of Cancers Around the Nuclear Installations at Sellafield and Dounreay* (Chilton: Public Health England) (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/554981/COMARE_17th_Report.pdf)

[3] Breslow N E 1984 Extra-Poisson variation in log-linear models *Appl. Stat.* **33** 38–44