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**Response to letter from Alasdair Philips**


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We recently reported on brain tumour incidence time trends in 20 to 59 year old Australians, from 1982 to 2013, and analysed these in terms of mobile phone usage patterns and diagnostic improvements over that interval1. This was designed to determine whether claims that mobile phone use causes brain tumours, are consistent with the pattern of brain tumour incidence in Australia, and in particular to compare such incidence patterns with the results of the multinational Interphone case control study2. In summary, we reported that: 1/ Overall brain tumour incidence rates did not change over time; 2/ Increased glioblastoma incidence was seen during intervals that coincided with improvements in diagnostic technologies (CT, MRI); 3/ Decreased incidence of 'unspecified' tumours was seen during the same intervals; and 4/ No evidence of increased tumour incidence (including glioblastoma) related to mobile phone use was found (based on incidence rates seen during the period of substantial mobile phone use and on modelling using a range of hypothetical relative risks and latency periods).

Philips submitted a Letter to the Editor3 of BMJ Open, where he purports to show that there are 'significant flaws and unjustifiable conclusions' in the above paper. Although he may firmly hold this view, his letter does not provide any evidence of this, and we strongly disagree with his statement. We have addressed the substance of his letter below to hopefully obviate potential misunderstandings that his letter may generate.

1/ A substantial portion of the Letter is dedicated to describing aspects of a paper published by Philips and colleagues4. Philips does not relate that description to Karipidis et al. (2018)1, and as his restatement of his paper does not raise any issues that were not considered in our work, we do not comment on that here.

2/ There are a number of factual inaccuracies in Philips' letter.

For example, in relation to our report of an increased incidence in glioblastoma over the 1993-2002 period, he claims that Karipidis et al. concluded that it "was due to diagnostic improvements". If Philips was correct, we would agree that this would represent an oversimplification of the data. However, we have been very careful to appropriately interpret the results and the level of certainty the evidence provided from the analyses; indeed we stated that the elevated glioblastoma incidence from 1993 to 2002, with no significant increase from 2003 to 2013, was "most likely due to improved diagnosis from MRI" (p. 10). Further, in support of this we gave substantial reasons for why diagnostic improvements are a far more likely explanation than radiofrequency exposure from mobile phone use.

Similarly, Philips' letter says that "Karipidis et al incorrectly state that we did not analyse different time periods to investigate the impact of mobile phone use", and then goes on to show that different time periods were reported separately. However, our statement is correct in that, although some breakdown of time periods was given, these time periods do not

correspond to periods relevant for determining whether incidence changes were related to mobile phone use (such as intervals relating to diagnosis change or mobile phone usage patterns), and no data is provided to address the issue of mobile phone use. Indeed Philips et al. did not even claim to have addressed cancer incidence in terms of mobile phone use specifically, and Karipidis et al. has merely noted this.

3/ Philips asks how rapidly developing tumours can be misdiagnosed and recorded. This has been dealt with in our paper, which includes consideration of the fact that there is no increase in glioma overall, that the increase in glioblastoma is paralleled by a reduction in 'unspecified' tumours, that the increase in glioblastoma incidence occurs during a period of improved diagnosis and changes to the tumour classification scheme, and that it precedes the period of rapid mobile phone use. Further, Philips does not provide any argument for his apparent view that we are erroneous in our conclusion that the temporary rise in glioblastoma incidence is most likely due to improved diagnosis and classification.

4/ Philips states that changes in antenna position on different phones, and different communication technologies (e.g. 2G, 3G, 4G) "should have been discussed by Karipidis et al." However, Karipidis et al. states that we could not take changes in technology and patterns of individual use into account, as we had no representative data on the effects of such changes on individual exposure; and discussion could thus be no more than speculation.

5/ Philips' letter criticised our paper for assessing data for 20-59 year olds, rather than for all ages. Although Philips may see benefit in conducting a study quite different to ours, there are many benefits in the method that we used, and these were described in Karipidis et al. For example, our study was designed to compare cancer incidence with that that would be expected based on different interpretations of the Interphone2 results, and this is the age range used in the Interphone study (which in turn was chosen to "maximise the likelihood of exposure"5). Beyond that, more-general methodological considerations point to the appropriateness of this age range: 1/ As cases older than 60 would be more affected by the diagnostic issues described above, 60+ year olds were not included as their inclusion would reduce the chance of seeing mobile phone related changes to tumour incidence; 2/ As we wanted to test whether tumour onset latencies of > 10 years could explain observed tumour incidence rates, and as this would require cases < 20 years old to have substantial mobile phone usage before the age of 10 (which they do not), those < 20 were not suitable for the purposes of this study. The relatively small number of cases in the < 20 year age group (being far rarer than in adults), would also increase data instability, making it less likely to observe meaningful changes in tumour incidence.

6/ Philips criticises Karipidis et al. for using the World Health Organization's (WHO) world standard population to standardize our data, as he believes that a different method should have been sought. However the purpose of this standardisation is to ensure age-comparability of each year's data, and the WHO world population provides comparability with much of the international literature, which is very useful in addressing this issue. We do not believe that the use of other standards would change the time trends appreciably.

7/ It is noteworthy that Philips is the Technical Director of a company that derives income from selling devices which were "mainly designed by Alasdair Philips", "to protect people from the ever-increasing levels of Electromagnetic radiation, or electrosmog, in our environment" (https://emfields-solutions.com/aboutus.asp). Thus although he fails to declare any conflict of interest in relation to his letter, this activity would normally be seen as a direct

conflict of interest; whether radiofrequency exposure due to mobile phone use is seen as being related to cancer induction or promotion would have a tangible effect on whether people purchased devices to ‘protect’ themselves from such radiofrequency exposure.

In conclusion, Philips’ Letter to the Editor does not raise any cogent issues with Karipidis et al. Instead it provides a series of claims that Karipidis et al. is inadequate, but does not provide relevant argumentation in support of this. We maintain that the data presented in Karipidis et al. does not provide any indication of mobile phone-related increases in cancer incidence, but conversely that it does suggest that changes to glioblastoma diagnostic and classification practices in Australia are a more likely explanation for the reported increase in glioblastoma incidence rates in Australia.

References:

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Conflict of Interest:

The authors report no conflicts of interest.