CORRESPONDENCE

Table 1. Spearman rank correlation for various exposure metrics

	Regular use	Time since first use	Total duration of subscriptions	Total duration of calls	Total number of calls
Regular use	1				
Time since first use	0.80	1			
Total duration of subscriptions	0.85	0.94	1		
Total duration of calls	0.85	0.89	0.93	1	
Total number of calls	0.86	0.90	0.93	0.98	1

About half of our study participants were not regular mobile phone users, and they were considered in all analyses as the reference group. Among regular users, different aspects of mobile phone use, such as cumulative number of calls, cumulative duration of calls, and time since first mobile phone use are expected to be correlated with each other. Indeed, Spearman rank correlation coefficients between the various exposure metrics were 0.80 or higher (Table 1). Therefore, odds ratios (ORs) of all analyses fluctuate around the odds ratio for regular use (OR = 1.36, 95% confidence interval = 0.92 to 2.02). In the case of a causal association, however, one would expect to observe an exposure–response pattern; for example, an increase in the odds ratio with increasing duration of use or higher risk estimates for brain areas that receive the highest amount of exposure when using a mobile phone. We did not observe such a pattern in our study, so we concluded that the observed non-statistically significant increase in risk among regular uses most likely represents random variability. This interpretation is supported by the fact that brain tumor incidence rates in the Nordic Countries in the 5- to 19-year age group did not increase between 2000 and 2009 (see figure 1 in our response to Morgan et al.).

The use of various exposure metrics, which are related to each other, is common in epidemiological research, and it has also been done in previous brain tumor studies on mobile phone use among adults [eg, INTERPHONE Study Group, 2010 (1)]. In the absence of a known biological mechanism for carcinogenesis in the low exposure range of microwave radiation, such an approach helps to clarify which aspect, if any, of the exposure might be relevant for health. However, when using such an approach, one needs to carefully interpret the study results by focusing on the pattern of the risk estimates instead of highlighting single findings out of context. For a comprehensive discussion of the results of the CEFALO study in the light of the strengths and limitations, we refer to our article published in the Journal.

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Reference

1. INTERPHONE Study Group. Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. *Int J Epidemiol.* 2010;39(3): 675–694.

Notes

Response

The binomial test applied by Milham is based on the assumption that these events are not correlated and occur independently of each other. Obviously this is not the case for the various exposure metrics in our study, all of which reflect past mobile phone use. Consequently, the *P* values calculated by Milham are incorrect.