use, OR = 5.30, 95% CI = 2.12–13.23, $P < .001$; and for use exclusively in urban areas, OR = 8.20, 95% CI = 1.37–49.07.[24]

In conclusion, the authors' statement that the "evidence published since the IARC monograph in 2011 does not support an association between cellular phone use and the risk of glioma in adults[1]" requires revision.

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References

1. Ostrom QT, Bauchet L, Davis FG, et al. The epidemiology of glioma in adults: a "state of the science" review. *Neuro Oncol*. 2014;16(7):896–913.
2. Deltour I, Auvinen A, Feychting M, et al. Mobile phone use and incidence of glioma in the Nordic countries 1979–2008: consistency check. *Epidemiology*. 2012;23(2):301–307.
3. Little MP, Rajaraman P, Curtis RE, et al. Mobile phone use and glioma risk: comparison of epidemiological study results with incidence trends in the United States. *BMJ*. 2012;344:e1147.
4. Barchana M, Margaliot M, Liphshitz I. Changes in brain glioma incidence and laterality correlates with use of mobile phones—a nationwide population based study in Israel. *Asian Pac J Cancer Prev*. 2012;13(11):5857–5863.
5. Frei P, Poulsen AH, Johansen C, et al. Use of mobile phones and risk of brain tumours: update of Danish cohort study. *BMJ*. 2011;343:d6387.
6. Benson VS, Pirie K, Schüz J, et al. Mobile phone use and risk of brain neoplasms and other cancers: prospective study. *Int J Epidemiol*. 2013;42(3):792–802.
7. Hardell L, Carlberg M, Söderqvist F, et al. Case-control study of the association between malignant brain tumours diagnosed between 2007 and 2009 and mobile and cordless phone use. *Int J Oncol*. 2013;43(6):1833–1845.
8. Clegg LX, Feuer EJ, Midthune DN, et al. Impact of reporting delay and reporting error on cancer incidence rates and trends. *J Natl Cancer Inst*. 2002;94(20):1537–1545.
9. Coons SW, Johnson PC, Scheithauer BW, et al. Improving diagnostic accuracy and interobserver concordance in the classification and grading of primary gliomas. *Cancer*. 1997;79(7):1381–1393.
10. Danish Strategic Research Council (grant number 2064-04-0010). http://www.thecosmosproject.org/funding.php. Accessed 12 December 2014.
11. CTIA's Semi-Annual Wireless Industry Survey Results: December 1985–December 2008. 2009 CTIA–The Wireless Association.
12. Ostrom QT, Gittleman H, Farah P, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2006–2010. *Neuro Oncol*. 2013;15(Suppl 2):ii1–i56.
13. Cardis E, Deltour I, Mann S, et al. Distribution of RF energy emitted by mobile phones in anatomical structures of the brain. *Phys Med Biol*. 2008;53:2771–2783.
14. Zada G, Bond AE, Wang YP, et al. Incidence trends in the anatomic location of primary malignant brain tumors in the United States: 1992–2006. *World Neurosurg*. 2012;77(3–4):518–524.
15. Dobes M, Shadbolt B, Khurana VG, et al. A multicenter study of primary brain tumor incidence in Australia (2000–2008). *Neuro Oncol*. 2011;13(7):783–790.
16. Dobes M, Khurana VG, Shadbolt B, et al. Increasing incidence of glioblastoma multiforme and meningioma, and decreasing incidence of Schwannoma (2000–2008): findings of a multicenter Australian study. *Surg Neurol Int*. 2011;2:176. Epub 2011 Dec 13.
17. Cancerregisteret. 2012. http://www.ssi.dk/Aktuelt/Nyheder/2013/~/media/Indhold/DK%20-%20dansk/Sundhedsdata%20og%20it/NSF/Registre/Cancerregisteret/Cancerregisteret%202012.ashx. Accessed 12 December 2014.
18. Kundi M. Failure to detect a link between mobile phone use and brain tumours in a large Danish cohort study: but findings may be due to bias. *Evid Based Med*. 2012;17(5):165–166.
19. Hardell L, Carlberg M. Using the Hill viewpoints from 1965 for evaluating strengths of evidence of the risk for brain tumors associated with use of mobile and cordless phones. *Rev Environ Health*. 2013;28(2–3):97–106.
20. Hardell L, Carlberg M, Hansson Mild K. Use of cellular telephones and brain tumour risk in urban and rural areas. *Occup Environ Med*. 2005;62(6):390–395.
21. Hardell L, Carlberg M, Mild KH. Pooled analysis of two case-control studies on use of cellular and cordless telephones and the risk of malignant brain tumours diagnosed in 1997–2003. *Int J Oncol*. 2006;28:509–518.
22. Hardell L, Carlberg M, Hansson Mild K. Pooled analysis of two case control studies on the use of cellular and cordless telephones and the risk of benign brain tumors diagnosed during 1997–2003. *Int Arch Occup Environ Health*. 2006;28:509–518.
23. 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.
24. Coureau G, Bouvier G, Lebailly P, et al. Mobile phone use and brain tumours in the CERENAT case-control study. *Occup Environ Med*. 2014;71(7):514–522.

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Reply to Letter

Response to "The epidemiology of glioma in adults: a 'state of the science' review"

Mr. Morgan's letter gives us the opportunity to clarify a number of points from our review, but we also need to correct one error.

First, the letter incorrectly stated the funding source of the study by Deltour et al,[1] which was entirely funded by the Danish Strategic Research Council, under grant 2064-04-0010.

Second, in the section entitled "Nonionizing Radiation: Cellular Phones," we focus on articles written since the publication of the International Agency for Research on Cancer (IARC) monograph[3,4] which reviewed studies published before 2011. In recent studies since 2011, effect sizes are null, very small or very big, highlighting the complexity of brain tumor research (especially with respect to rapidly changing cellular phone technology.).

Third, the interpretation of malignant brain tumor incidence rates is straightforward as long as they remain stable over time. Explanations of changes, however, can only be tentative. We respectfully disagree that data completeness affects the results of the studies presented for assessing general incidence trends of malignant brain tumors. For example, the Nordic cancer registries are considered models of completeness, with 93%–98% complete population ascertainment for malignant tumors in people younger than 70. A recent analysis of cancer registry data covering ~98% of the US population from 2000–2010 showed decreased incidence of malignant brain tumors along with decreased incidence of some glioma subtypes.[5] This data, together with the other incidence studies,[1] suggests longer induction periods than currently investigated, lower risks than reported from some case-control studies, or the absence of any association. Decreases in incidence rates, as well as increases, may be a reflection of improved classification of tumors, evolution of medical practices, improved access to imaging or other technological changes, among numerous other factors, together with potential changes in other etiological factors. Some studies using cancer registry data showed an increase in glioma incidence from approximately 1975–1985, likely an artifact of increased detection from increased use of CT scans and MRIs over that period and improvements in cancer registration. All of these factors would have the greatest effect on reported incidence of nonmalignant tumors, while the majority of gliomas are malignant tumors.

Fourth, one of the major weaknesses of cellular phone studies has been the lack of accurate and complete measurement of use.[6] Although many investigations have compared self-reported use to information from cellular phone records to assess the magnitude of the reporting errors,[2,7,8] Hardell and colleagues have not provided information on the potential role of recall errors in their studies. Recall bias may cause cases to artificially report higher past usage than controls, which could result in a false association between cellular phone use and brain tumors. Many of these studies have also been plagued with low participation rates, time delay in recruiting controls versus cases, and other methodological issues which may affect results. Several studies currently underway–such as COSMOS,[2] MOBI-Kids,[9] and GERoNiMO[10]–may resolve some of the methodological issues that have complicated the interpretation of previous results, by recruiting a very large cohort with prospective recording of phone use via cell phone operators, by using sophisticated phone apps to record number and duration of calls, laterality, hands-free/speaker phone use, etc., or by looking at this exposure in combination with other environmental exposures and incorporating biological mechanisms. Regardless of these improvements, accurate and complete exposure assessment for cellular phone use will likely remain very challenging for several reasons. Types of phones available vary significantly by time and location. There is significant variability in how phones are used (holding phone to head, side phone is used on, using speaker phone, or ear buds) between and within users, and these use patterns may vary over time. In summary, exposure assessment for cellular phone use is extremely complex, due to difficultly identifying dose (total, duration, or other measures) and the rapid changes in cellular phone technology.

The recent evidence, with all of the weaknesses noted above, does not strengthen the evidence for an association between cellular phone use and occurrence of brain tumors.

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References

1. Deltour I, Auvinen A, Feychting M, et al. Mobile phone use and incidence of glioma in the Nordic countries 1979–2008: consistency check. *Epidemiology*. 2012;23(2):301–307.
2. Schuz J, Elliott P, Auvinen A, et al. An international prospective cohort study of mobile phone users and health (Cosmos): design considerations and enrolment. *Cancer Epidemiol*. 2011;35(1):37–43.
3. Baan R, Grosse Y, Lauby-Secretan B, et al. Carcinogenicity of radiofrequency electromagnetic fields. *Lancet Oncol*. 2011;12(7):624–626.
4. Samet JM, Straif K, Schuz J, et al. Commentary: mobile phones and cancer: next steps after the 2011 IARC review. *Epidemiology*. 2014;25(1):23–27.
5. Gittleman HR, Ostrom QT, Rouse CD, et al. Trends in central nervous system tumor incidence relative to other common cancers in adults, adolescents, and children in the United States, 2000 to 2010. *Cancer*. 2014;121(1):102–112.
6. Swerdlow AJ, Feychting M, Green AC, et al. International Commission for Non-Ionizing Radiation Protection Standing Committee on

Epidemiology. Mobile phones, brain tumors, and the interphone study: where are we now? *Environ. Health Perspect*. 2011;119(11): 1534–1538.

7. Vrijheid M, Armstrong BK, Bedard D, et al. Recall bias in the assessment of exposure to mobile phones. *J Expo Sci Environ Epidemiol*. 2009;19(4):369–381.
8. Aydin D, Feychting M, Schuz J, et al. Mobile phone use and brain tumors in children and adolescents: a multicenter case-control study. *J Natl Cancer Inst*. 2011;103(16):1264–1276.
9. Sadetzki S, Langer CE, Bruchim R, et al. The MOBI-Kids Study Protocol: Challenges in Assessing Childhood and Adolescent Exposure to Electromagnetic Fields from Wireless Telecommunication Technologies and Possible Association with Brain Tumor Risk. *Frontiers in Public Health*. 2014;2(124).
10. Langer CE, Grellier J, Turner MC, et al. Mobile phones and cancer: next steps. *Epidemiology*. 2014;25(4):616–617.

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