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Inferring the 1985–2014 impact of mobile phone use on selected brain cancer subtypes using Bayesian structural time series and synthetic controls

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ABSTRACT

Background: Mobile phone use has been increasing rapidly in the past decades and, in parallel, so has the annual incidence of certain types of brain cancers. However, it remains unclear whether this correlation is coincidental or whether use of mobile phones may cause the development, promotion or progression of specific cancers. The 1985–2014 incidence of selected brain cancer subtypes in England were analyzed and compared to counterfactual 'synthetic control' timeseries.

Methods: Annual 1985–2014 incidence of malignant glioma, glioblastoma multiforme, and malignant neoplasms of the temporal and parietal lobes in England were modelled based on population-level covariates using Bayesian structural time series models assuming 5,10 and 15 year minimal latency periods. Post-latency counterfactual 'synthetic England' timeseries were nowcast based on covariate trends. The impact of mobile phone use was inferred from differences between measured and modelled time series.

Results: There is no evidence of an increase in malignant glioma, glioblastoma multiforme, or malignant neoplasms of the parietal lobe not predicted in the 'synthetic England' time series. Malignant neoplasms of the temporal lobe however, have increased faster than expected. A latency period of 10 years reflected the earliest latency period when this was measurable and related to mobile phone penetration rates, and indicated an additional increase of 35% (95% Credible Interval 9%:59%) during 2005–2014; corresponding to an additional 188 (95%CI 48–324) cases annually.

Conclusions: A causal factor, of which mobile phone use (and possibly other wireless equipment) is in agreement with the hypothesized temporal association, is related to an increased risk of developing malignant neoplasms in the temporal lobe.

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1. Introduction

Mobile phone use has been increasing in Western, developed societies (de Vocht et al., 2011; Khurana et al., 2009) as well as worldwide (Khurana et al., 2009), and in parallel the incidence of certain types of brain cancers has also been increasing in the previous decades (Dobes et al., 2011; Zada et al., 2012). Although it is not entirely clear what the cause of the latter is, the temporal correlation between brain cancer incidence rates and mobile phone use has not gone unnoticed. Mobile phones utilize (in England) radiofrequency (RF) radiation in the 900–1800 MHz (2G), 900–2100 MHz (3G) and more recently 800–1800/2600 MHz (4G) frequency bands, and consequently also expose people using their phones to RF (Cardis et al., 2011). It remains unclear whether the RF exposure from mobile phones could be genotoxic to humans (Banerjee et al., 2016; Liu et al., 2015). The World Health Organisation (WHO) International Agency for Research on Cancer (IARC) in 2011 declared, based on the scientific evidence available at the time, exposure of humans to RF (frequency range 30 kHz–300 GHz) as "possibly carcinogenic to humans" (Group 2B) (Baan and others, 2011). However, conflicting interpretations of the available evidence remain (Morgan et al., 2015; Peres, 2010; Repacholi et al., 2012), while susceptibility of subgroups such as children is being investigated (Sadetzki et al., 2014), and results from the large prospective cohort study COSMOS (Schuz et al., 2011) are not yet available.

Monitoring of brain tumour incidence trends has been identified as a high priority research area and can provide evidence of whether an "epidemic" in brain cancers as a result of the widespread use of mobile phones may be imminent (Samet et al., 2014; van Deventer et al., 2011). Moreover, these are important to estimate the magnitude of the impact of RF exposure from mobile phones on population health so that appropriate measures could be taken, if required.

Previous work in England did not provide any evidence of a noticeable change in brain cancer incidence rates in England between 1998 and 2007, nor for specific brain regions (de Vocht et al., 2011). These findings corroborated analyses from other countries (Chapman et al.,

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2016; Deltour et al., 2012; Deltour et al., 2009; Inskip et al., 2010; Kim et al., 2015). Similarly, although the incidence of tumours of the parotid gland and other tumours of the salivary gland have been increasing in England, these trends were not indicative of mobile phones being a causative factor (de Vocht, 2011). However, these studies have been criticized for their short follow-up which, in combination with an average latency period between exposure and clinical detection of the tumour of at least a decade, would prevent the detection of measureable changes (Kundi, 2011; Rothman, 2009). Nonetheless, a recent study in Australia covering 29 years again did not find evidence of increased brain cancer risk related to mobile phone use (Chapman et al., 2016), but this study did not look at specific brain cancer subtypes or locations, while other limitations were also highlighted (Bandara, 2016).

This study aims to analyse time series of specific brain cancer subtypes and locations covering the time period of 1985–2014 in England. More specifically, two specific hypotheses are addressed: (1) trends in histologically-defined brain cancers that have previously been linked to mobile phone exposure; malignant glioma (Corle et al., 2012) and glioblastoma multiforme (Grade IV astrocytoma) (Hardell et al., 2013), or GBM4, and (2) malignant neoplasms of the temporal and parietal lobes, which receive the highest exposures (Cardis et al., 2008; Ghanmi et al., 2014), and for which especially the temporal lobe has been highlighted as an important location of interest (Samet et al., 2014). Using Bayesian structural time series and a novel causal impact framework, these analyses further aim to infer the impact of mobile phone use on population health, if any, by not only evaluating the annual incidence trends of each outcome, but additionally compare it to the expected, counterfactual, time series (Pearl, 2009).

2. Methods

2.1. Data

National annual number of newly registered cases of the selected cancers for the years 1985–2014 were obtained from the Office of National Statistics (ONS). Pre-1995 incident cases were aggregated for malignant glioma (ICD-9 191.9; morphology codes M9380/3, M9400/3, M9382/3), malignant neoplasms of the temporal lobe (ICD-9 191.2), malignant neoplasms of the parietal lobe (191.3), and glioblastoma multiforme (GBM4) (ICD-9 191.9, morphology codes M9440/3, M9442/3, M9441/3), and from 1995 onwards cancers were aggregated as malignant glioma (ICD-10 C71.9; morphology codes M9380/3, M9400/3, M9382/3), malignant neoplasms of the temporal lobe (ICD-10 C71.2), malignant neoplasms of the parietal lobe (ICD-10 C71.3), and GBM4 (ICD-10 C71.9, morphology codes M8440/3, M9442/3, M9441/3). Although age-standardized incidence rates are available, here the actual numbers of newly diagnosed cases are used to enable a straightforward quantitative estimation of the population impact.

The number of cellular mobile phone subscriptions was obtained from the United Nations specialized agency for information and communication technologies (ITU) (de Vocht et al., 2011; ITU, 2016).

Data on covariates for the years 1985–2014 were obtained from ONS (ONS, 2016b), the Health Survey for England (HSCIC, 2015) and the Worldbank (Worldbank, 2016) and include incidence of all cancers (excluding non-melanoma skin cancer), annual population estimates, median age of the UK population, population prevalence of cigarette smokers and never smokers, urbanization rate, and a quality measure for coding of cancer cases coded as the percentage of status 3 records (record failed one or several vital validation checks on fields which are vital for inclusion in ONS tables). Covariate data were interpolated where they were not available for specific years. In addition, because of the transfer from ICD9 to ICD10 in 1995 a dichotomous variable for the years 1993–1997 to deal with some short-term disruption of the time series in that period was included.

2.2. Statistical methodology

To infer the impact of mobile phone use on the annual incidence of the selected brain cancers, Bayesian structural time series models are utilized (Scott and Varian, 2014). In short, the time series from 1985 up to an *a priori* specified point in time is modelled using other time series of covariates that may be correlated with the annual number of newly registered cases.

The specified time point referred to above generally refers to some intervention (Brodersen et al., 2015) or some event expected to change the time series (such as, for example, an armed conflict for which this methodology has been previously used (Abadie and Gardeazabal, 2003)), but here this is interpreted as the point in time at which, if mobile phone use were associated with increased brain cancer risk, this would be measurable in population-level data. This design can be thought of as a natural experiment, and therefore (as well as for ease of reference) this specified time point will be referred to as the 'cut-off'. In these analyses, three specific cut-offs were modelled relative to the year 1995, when mobile phone penetration in England reached about 10% (ITU, 2016); (1) the year 2000, which implies that increased risk would be observable five years later, and thus corresponding to a detectable latency period between exposure and clinically detectable tumours of five years, and subsequently (2) the year 2005 and (3) 2010, corresponding to ten and 15 year minimal latency periods, respectively. The 5–15 year minimal latency time at which an increased risk would be measurable would correspond to a peak latency period of up to several decades (Ahlbom and others, 2009). Based on previous research (Ahlbom and others, 2009; Cardis et al., 2011; Corle et al., 2012; Hardell et al., 2007; Khurana et al., 2009; Levis et al., 2011), *a priori* the hypothesis was that measurable effects, if any, would be observed for the implied 10-year latency. The 0 and 5 year latency periods were included as control analyses, but additionally would be informative in relation to the cut-off at 1995, which was about a decade after the introduction of mobile phones but, somewhat arbitrary, was thought to signify a point from effects could be measurable at population level because cell phone penetration had reached 10%.

Under the assumption that the relationship between the time series of the annual number of new cases and the time series of covariates (described above) that existed prior to the specified year remains constant in the period thereafter, the counterfactual 'post-cut-off' trend for the selected cancers is estimated from the time trends in the measured covariates by constructing a 'synthetic England' (Abadie et al., 2010; Abadie and Gardeazabal, 2003), which describes what would have happened had the intervention not happened (*i.e.* had mobile phones not been introduced). And finally, the (causal) impact of mobile phone use can then be estimated by comparing the time series in the counterfactual 'synthetic England' with the measured annual number of registered new cases in the period from the 'cut-off' to the year 2014.

The Bayesian structural time series model consists of a time series component that models the temporal trend in the data and a regression component that captures the impact of the 'intervention'. The time series component in turn consists of two equations, with an observation equation that links the observed data with an unobserved latent state and a transition equation that defines how the latent state evolves over time. The regression component is based on a set of external covariates that contribute to the prediction, and a Bayesian 'spike and slab prior', based on a Bernoulli prior, is used to estimate the effect size of each covariate in each MCMC iteration. The "spike" places positive probability mass at zero (*i.e.* a null effect) and the "slab" is a weakly informative Gaussian prior that describes a non-null effect. Prior standard deviations are modelled as inverse Gamma distributions. The post-cut-off time series is then estimated based on the weighted (through Bayesian model averaging of the predictors) pre-cut-off model coefficients to create the counterfactual 'synthetic England' (George and R.E., 1997; Scott and Varian, 2014). The framework outlined above is described in detail elsewhere (Brodersen et al., 2015; Scott and Varian,

2014), and the Bayesian structural time series are constructed using the *bsts* package in *R* (Scott, 2016), and subsequently used as input for the *CausalImpact R* package (Brodersen 2014–2016) to estimate the population (causal) impact.

Prior standard deviation was set at 20% of the sample standard deviation to allow the modelled time series to have enough "freedom" while at the same time retaining predictive power. Gaussian priors were set with mean to the incidence in the year 1985 and standard deviation to the pre-period standard deviation. Upper limits for the Gaussian and Inverse Gamma standard deviation priors were set to 150% of the observed standard deviation. Priors for the effects sizes were set to '0' (no effect) with the exception of the intercept which was set to the empirical intercept. Prior expected explained variance was set at 77% based on initial static regression with prior degrees of freedom set to pre-period years. Exploratory analyses indicated additional seasonal or first order autoregressive covariance components did not improve fit.

Convergence of the MCMC chains was assessed through inspection of the trace plots, Heidelberger-Welch tests, and Geweke diagnostic tests. Autocorrelation was evaluated using ACF/PACF autocorrelation plots and Durbin-Watson tests. Precision was estimated from mean absolute 1-step prediction errors and range.

Additional sensitivity analyses were conducted with stricter and less informative priors for the standard deviation, and were set to 10% and 50% of the sample standard deviation, respectively. Because the post-cut-off prediction period was shorter for longer pre-cut-off modelling periods, sensitivity analyses were conducted with post-cut off periods to be predicted restricted to 5 years for all analyses. And finally, to explore the likelihood mobile phone use may be the causal factors, the number of mobile phone subscriptions was included for latency periods up to 5 years from 1995 (or 15 years from 1985, respectively) by shifting the mobile phone subscription trend.

3. Results

Numbers of newly registered cases of gliomas and glioblastoma multiforme, as well as those of malignant tumours of the temporal and parietal lobes are shown in Fig. 1, and indicate that the annual number of new glioma cases in England has been decreasing since 1985, with the notable exception of the 1992–1997 period, while that for GBM4 increased annually until about 2005, after which it stabilized. In contrast, the annual number of newly registered cases of malignant neoplasms of the temporal and parietal lobes have been consistently increasing from 1985.

The temporal trends of the covariates (standardized for convenience) are shown in Fig. S1 in Online Supplementary Material (OSM) and show increased trends in all covariates but for the proportion of smokers in the population and the percentage of status 3 records. Inclusion probabilities of the covariates differs between the different models, and are shown in OSM (Table S1).

All diagnostics indicate acceptable convergence of MCMC chains after a maximum of 250,000 MCMC samples (OSM; Table S2). The prediction of the Bayesian structural time series models were relatively accurate with mean (absolute) 1-step prediction errors <10% in all but one of the models.

Table 1 shows the results of the Bayesian modelling for selected cancers for the different latency periods since 1995 (0,5, 10, and 15 years, respectively), and are shown graphically for the histological-based cancers in Fig. 2 and for the location-based cancers in Fig. 3. There is no evidence of an increase in the incidence of malignant glioma or GBM4 that was not predicted in the counterfactual 'synthetic England' time series, regardless of the latency period. Moreover, although the 95% credible intervals all include 0%, the point estimates for the effect sizes are almost exclusively negative; indicating that based on the counterfactual 'synthetic England' higher annual incidences were expected.

Similarly, although continuingly increasing since 1985, the annual incidence of malignant neoplasms of the parietal lobe is comparable to the expected trend observed in the counterfactual time series. There is some evidence that the increase in incidence that has been apparent since 1985 has been unexpectedly flattening off since about the year 2000 compared to the counterfactual time series, with the incidence being about 36% (95%CI −70%:−4%) lower than expected.

The annual incidence of malignant neoplasms of the temporal lobe however, has been increasing faster than expected, with a period of 10 years post-1995 reflecting the earliest latency period when this additional increase was measurable. Post-2005 an additional increase of 35% (95%CI 9%:59%) was evident compared to the counterfactual time series in the 'synthetic England'; corresponding to an average of an additional 188 (95%CI 48–324) cases of malignant neoplasms of the temporal lobe annually. Addition of mobile phone penetration in the models showed a reduction of 15% in the effect size for 5-year latency (Table 2), indicating observed increased incidence can, at least in part, by attributed to mobile phone use (Note that unfortunately longer latencies cannot be explored in these time series).

Sensitivity analyses using different priors show comparable results to those presented above (OSM Tables S3 and S4). The additional analyses with restricted 5-year 'nowcasting' periods confirmed the main results and indicated excess incidence of malignant neoplasms of the

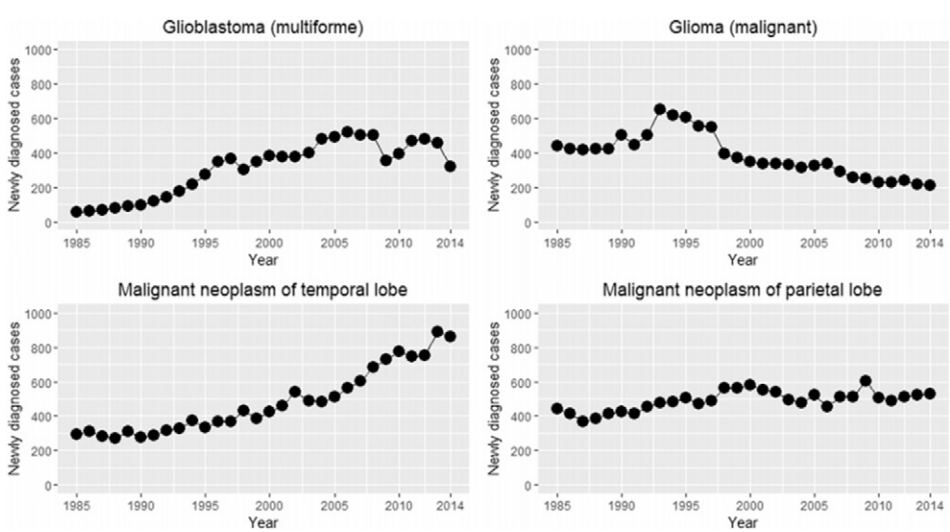

Fig. 1. 1985–2014 annual number of newly registered cases of glioblastoma multiforme, malignant glioma, and malignant neoplasms of the parietal and temporal lobes.

Table 1
Inferred impact of mobile phone use (and possibly other wireless technology) on annual incidence of selected brain cancer subtypes.

	Implied lag (from 1995)	Absolute average effect (95%CI)	Absolute cumulative effect (95%CI)	Relative effect (95%CI)	Posterior probability of effect
Histology based					
Malignant glioma[a]	0 years	−449 (−1116, 355)	−8539 (−21,207,6749)	−58% (−145%,46%)	0.11
	5 years	−29 (−308, 330)	−403 (−4311, 4618)	−9.4 (−100%,108%)	0.37
	10 years	−63 (−221, 95)	−570 (−1993,854)	−20% (−71%, 30%)	0.21
	15 years	−15 (−147, 117)	−59 (−589, 469)	−6.2% (−62%, 50%)	0.41
Glioblastoma multiforme[b]	0 years	35 (−385, 547)	657 (−7307, 10,397)	9.1% (−101%, 144%)	0.42
	5 years	−69 (−549, 311)	−967 (−7691, 4361)	−14% (−108%, 61%)	0.39
	10 years	−120 (−364, 117)	−1080 (−3279, 1055)	−21% (−65%,21%)	0.16
	15 years	4.3 (−182, 191)	17.4 (−727, 765)	1% (−43%, 45%)	0.48
Location based					
Malignant neoplasms of the temporal lobe[c]	0 years	176 (−36, 446)	3352 (−677, 8471)	43% (−8.8%, 110%)	0.06
	5 years	30 (−194, 258)	415 (−2711, 3605)	4.8% (−31%, 42%)	0.42
	10 years	188 (48, 324)	1696 (436, 2918)	35% (8.9%, 59%)	0.01
	15 years	43 (−127, 213)	170 (−509, 851)	5.5% (−17%, 28%)	0.31
Malignant neoplasms of the parietal lobe[d]	0 years	−58 (−312, 226)	−1094 (−5926, 4302)	−10% (−54%, 39%)	0.31
	5 years	−290 (−565, −30)	−4066 (−7913, 423)	−36% (−70%, −3.7%)	0.01
	10 years	−37 (−148, 71)	−332 (−1332, 635)	−6.7% (−27%, 13%)	0.25
	15 years	−44 (−131,40)	−175 (−526, 161)	−7.9% (−24%, 7.2%)	0.16

[a] ICD-9 191.9 (morphology codes M9380/3, M9400/3, M9382/3), ICD-10 C71.9 (morphology codes M9380/3, M9400/3, M9382/3).
[b] ICD-9 191.9 (morphology codes M9440/3, M9442/3, M9441/3), ICD-10 C71.9 (morphology codes M8440/3, M9442/3, M9441/3).
[c] ICD-9 191.2, ICD-10 C71.2.
[d] ICD-9 191.3, ICD-10 C71.3.

temporal lobe for an implied latency until detectable results of 10 years only (although the number of new cases of malignant neoplasms of the parietal lobe was lower than expected from 2000 onwards was observed here as well, similar to the full analyses in Table 1) (OSM Table S5).

4. Discussion

This research aimed to assess whether the increased incidences of selected brain cancers observed since 1985 that have been previously reported as possibly associated with mobile phone use were indeed indicative of excess risks compared to their counterfactual time series. Comparison of the measured and modelled pre-cut-off data indicated that the measured time series were accurately modelled with absolute 1-step prediction of <10% (<5% in 50% of models) and, under the assumption that the correlations between the different covariates does not change post-latency period, implies that the counterfactual time series will have been of similar accuracy.

As such, although the number of newly registered cases of these selected brain tumours has generally been increasing since 1985 (with the exception of malignant glioma), for malignant glioma, GBM4 and malignant neoplasms of the parietal lobe these trends were consistent with

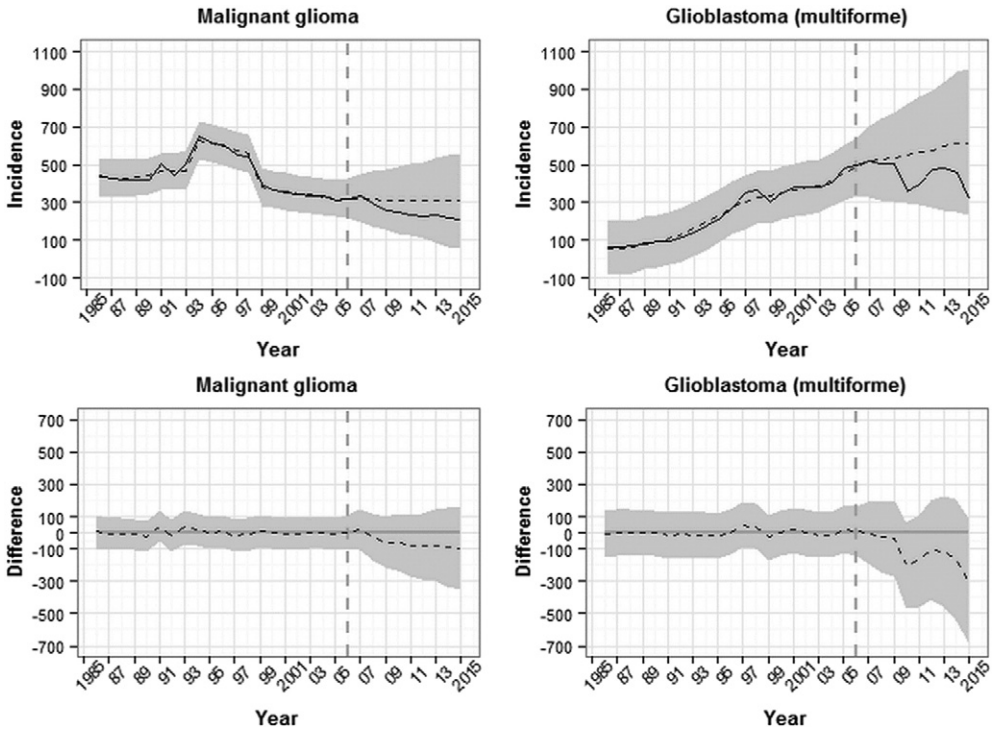

Fig. 2. Measured (solid) and modelled (dashed) incidence trends (top) and pointwise difference (bottom) for histology-based tumours; implied 10-year lag. Grey areas correspond to 95% Credible Intervals.

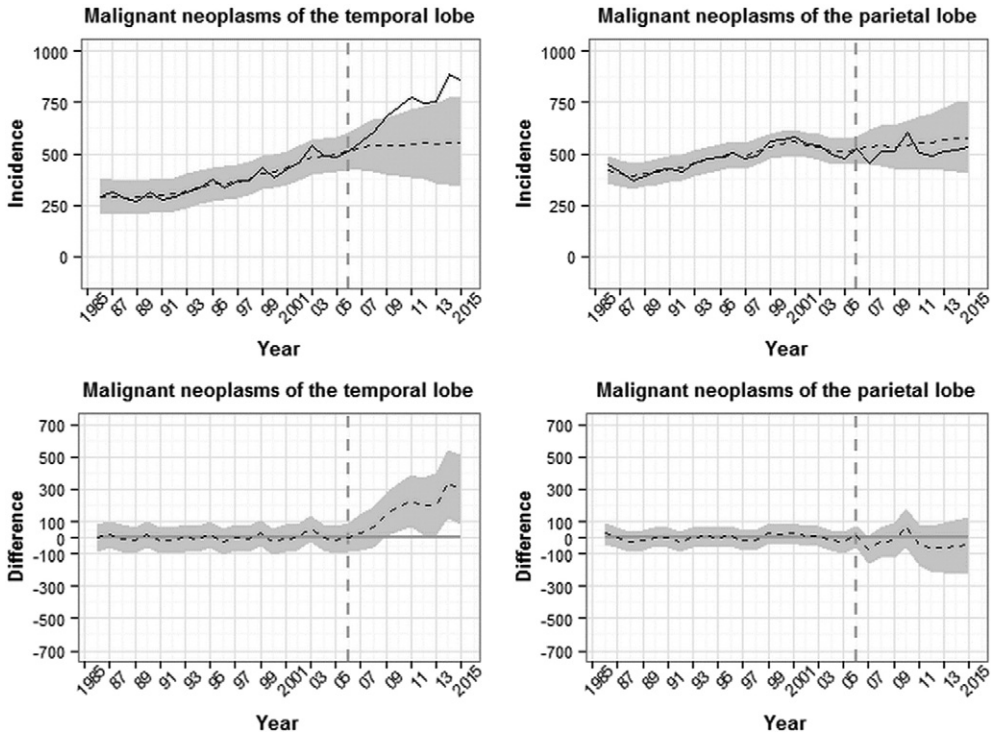

Fig. 3. Measured (solid) and modelled (dashed) incidence trends (top) and pointwise difference (bottom) for location-based brain tumours; implied 10-year lag. Grey areas correspond to 95% Credible Intervals.

what would be expected if there was no causal association between incidence and mobile phone use. It is likely that the generally observed negative effects are the results of under-reporting of more recent cases, since cancer registration in England can take up to five years after the end of a given year to reach 100% completeness (ONS, 2016a). With respect to gliomas, these findings are consistent with other incidence studies (Deltour et al., 2009; Little et al., 2012), the majority of results from cohort (Benson and others, 2013; Frei et al., 2011) and case-control studies (Corle et al., 2012), including Interphone (Interphone Study Group, 2010), but not with all (especially after at least a decade of use) (Coureau et al., 2014; Hardell and Carlberg, 2015; Hardell et al., 2013; Khurana et al., 2009). Increasing trends of GBM4 in the population have also been reported elsewhere (Dobes et al., 2011; Zada et al., 2012), but similarly there is little evidence of deviation from the counterfactual time series (at least in England). Similarly, the annual number of newly registered cases of malignant neoplasm of the parietal lobe has been increasing since 1985, which corresponds to the stable population rates also observed elsewhere (Zada et al., 2012), and which are comparable to their counterfactual time series. This does not point to mobile phone use as an important causative factor, which corroborates previous findings (de Vocht et al., 2011; Inskip et al., 2010).

In contrast, these analyses do indicate that the observed increase in incidence of malignant neoplasms in the temporal lobe, which has been reported previously (de Vocht et al., 2011; Zada et al., 2012), was in excess to its expected counterfactual trend. The optimal implied latency period to when this was measurable in population data was 10 years (or about 20 years since the introduction of mobile phones in society). Although these analyses are not able to specifically and unambiguously link this excess incidence to mobile phone use, this finding is consistent with the *a priori* hypothesis if such a causal association would exist; both in terms of received exposure compared to other areas of the brain (Cardis et al., 2008; Ghanmi et al., 2014) and of expected latency period (Corle et al., 2012; Khurana et al., 2009; Myung et al., 2009). Moreover, inclusion of mobile phone subscriptions as a putative factor already (despite the data limitation that does not enable optimal assessment with 10 year latency) nearly halves the effect size, which is similarly consistent with what would be expected in the case of a causal association. This finding is in agreement with the Interphone results, which also indicate a slightly increased risk for gliomas in the temporal lobe, although this did not reach statistical significance (Interphone Study Group, 2010), and with findings from Hardell and Carlberg (Hardell and Carlberg, 2015). The increased incidence in malignant neoplasms in the temporal lobe, in excess of what was expected, was not previously observed in England (de Vocht et al., 2011) or elsewhere (Deltour et al., 2009; Inskip et al., 2010; Kim et al., 2015), which may have been the result of insufficient latency time to observe an effect in the earlier studies (Kundi, 2011) and/or as a result of the more sophisticated statistical methodology used here.

Table 2
Inclusion of mobile phone penetration rates with selected latencies for malignant neoplasms of the temporal lobe.

Implied lag (from 1995) for penetration rate	Absolute average effect (95%CI)	Absolute cumulative effect (95%CI)	Relative effect (95%CI)	Posterior probability of effect
Not included	188 (48, 324)	1696 (436, 2918)	35% (8.9%, 59%)	0.01
0 years	1913 (58, 325)	1739 (524, 2922)	36% (11%, 60%)	0.00
5 years	121 (−597, 799)	1085 (−5376, 7190)	20.0% (−97%, 130%)	0.42
10 years	No information on effect in pre-intervention time period			

These analyses indicate excess brain cancer risk is observed in the lobes where most of the electromagnetic energy is absorbed (depending on side of the head where the phone is held when calling) (Cardis et al., 2008), which has been observed previously (Barchana et al., 2012; Khurana et al., 2009). As such, it does not specifically exclude a specific association with gliomas (if these occur in the temporal lobe), which was reported in Interphone (Interphone Study Group, 2010), and of which about one in three occur in the temporal lobe (Larjavaara et al., 2007). A stronger causal argument could have been made if these analyses could have been stratified by laterality, with ipsilateral RF exposure having been linked to increased cerebral blood flow (Huber et al., 2005) and glucose metabolism (Volkow et al., 2011), as well as to increased risk of glioma in the temporal lobe (Barchana et al., 2012; Hardell and Carlberg, 2015), although not in all studies (Hartikka et al., 2009; Larjavaara et al., 2011), but this was not possible.

The analyses further indicate that the excess incidence in new cases of malignant neoplasms of the temporal lobe declines again when a 15-year latency is modelled. There are several possible explanations for this, which are not mutually exclusive. It may be possible that the positive finding for 10-year latency is a chance finding, although in this case it is surprising the non-null finding is observed exactly where hypothesized. Alternatively, this may be the result of reduced exposure as a result of technological advances that resulted in greatly reduced output power of the phones and/or the changed use of mobiles that resulted in less actual calling time (Cardis et al., 2011). It has also been speculated that such a pattern may be the result of an adaptive response of cells to RF exposure (Vijayalaxmi and Prihoda, 2014). And finally, this could be a methodological artefact resulting from the inclusion of the years 2005–2010, which were previously part of the post-effect period but now included in the pre-effect period, and thereby may have artificially (and erroneously) inflated the model coefficients in the pre-effect period.

An important limitation of this methodology is that the inference about a (causal) effect relies on the assumption that the relationship between covariates and the incidence time series prior to the cut-off remains stable through the post-period. Here, the 'synthetic England' counterfactual time series was comprehensively estimated based on set of covariates aimed at capturing temporal changes in population size, total cancer incidence, the aging population, smoking, urbanization, and quality of cancer registration. Although minor changes in any of these correlations will occur over a 20-year time period, it seems unlikely that a sudden and substantial difference occurs at the same time point that the intervention was modelled. In fact, if this were the case we would expect similar effects to occur across all selected cancers (unless this would be an artefact very specific to temporal lobe cancers). Nonetheless, this cannot be excluded either.

As highlighted above, this study does not have the ability to specifically link incidence to mobile (or cordless) phone use, but infers this association by *a priori* defining a time point when this association would be measurable in population data. As such, this leaves open the possibility of another causal (environmental) factor; for example ionising radiation exposure (Smoll et al., 2016) and air pollution (Poulsen et al., 2016) have been mentioned, but it seems unlikely effects would be limited to the temporal lobe only. Alternatively, the observed effect may be the result of diagnostic bias as a result of the increased volume and quality of neuroimaging in the last two decades (Zada et al., 2012), although this would be expected to have occurred in all selected cancers. Nonetheless, if in the absence of another probable cause, mobile (and cordless) phone use were the causal agent, then this modelling is based on an inferred exposure metric that includes a wide range of RF frequency bands since it necessarily includes the use of mobile phones (irrespective of its generation), cordless phones, and other wireless equipment. Although not very specific (as well as inferred instead of measured), this integration of all RF exposures in one metric can also be regarded as beneficial. In contrast to the individual-level case-control studies, it is not subject to problems of recall bias and resulting exposure measurement error, and potential issues in the selection of study participants (Ahlbom and others, 2009; Corle et al., 2012; Morgan et al., 2015; Myung et al., 2009).

The previous analyses of the English brain cancer incidence trends (de Vocht et al., 2011), but by extension those from other countries published at the time, were criticized for their short follow-up which, in combination with a lag between exposure and clinical detection of the tumour of at least a decade, would prevent measureable changes (Kundi, 2011). There remains the possibility that still not enough time has elapsed for increased risks for gliomas, GBM4 or malignant neoplasm of the parietal lobe to be detectable. However, the maximum 15-year latency period since 1995 (or 25 years since 1985 when, roughly, the first mobile phones made their appearance) corresponds to several decades when maximum impact would be expected (Ahlbom and others, 2009). Therefore, it seems unlikely that the absence of increased glioma and GBM4 risk can be attributed to this. Increased risks for asbestos exposure for example, with a maximum latency time of 30–40 years could be observed 5–15 years post-exposure (Walker, 1984) and similarly evidence of atomic bomb survivors indicated that whereas the maximum latency of solid tumours is about 50–60 years, excess mortality risk could be observed after about a decade (Furukawa et al., 2009). The observed increased incidence of cancers in the temporal lobe with an implied 10-year latency as such, is consistent with the hypothesis as well as with the latency distributions for solid cancers observed for asbestos and ionising radiation.

An finally, because of the aggregated level of these analyses the observed effects, or absence thereof, may be subject to the ecological fallacy (Greenland and Morgenstern, 1989), and/or may only be observable in specific susceptible subgroups in population such as children (Aydin et al., 2012), while also these analyses did not include all possible brain cancer subtypes and locations, including for example vestibular schwannoma (Morgan et al., 2015).

The statistical methodology here was used to retrospectively compare the predicted, counterfactual, time series with the measured annual incidence up to 2014, which enables inference of the (causal) impact. This, or similar, methodologies are beginning to be used to 'nowcast' trends in health data into the near future (Donker et al., 2011), and similarly would be useful to continuously monitor and predict whether an "epidemic" in brain cancers as a result of the widespread use of mobile phones may be imminent and what its population impact may be.

In summary, these analyses indicate that a causal factor, of which mobile phone use (and possibly other wireless equipment) is in agreement with the hypothesized spatial and temporal associations, is related to an increased risk of developing a malignant neoplasm in the temporal lobe. More specifically, if the calculated population impact is interpreted as a causal effect and is completely contributed to mobile phone use, then the population impact is an additional 188 cases annually in England; corresponding to about 1700 cases (range 436 to 2918) in the period 2005–2014 that would not have occurred otherwise. For reference, this corresponds to 0.02%–0.12% of new cancers during this period. If the relative effect is interpreted as a population relative risk, then a very moderate 1.35 (95%CI 1.09:1.59) is observed after a minimum 10-year latency.

Competing financial interests

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.envint.2016.10.019.

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Update

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Corrigendum

Corrigendum to "Inferring the 1985–2014 impact of mobile phone use on selected brain cancer subtypes using Bayesian structural time series and synthetic controls" [Environ. Int. (2016), 97, 100-107]

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The author regrets that, due to a misunderstanding between the author and the data provider, the incorrect data were used for malignant glioma and glioblastoma (multiforme).

As a result, the 1985–2014 trends shown in Fig. 1 and results of the statistical analyses shown in Table 1 and Fig. 2 are incorrect. This had no significant impact on the results of study, the interpretation of the results, or on the conclusions in the paper, which remain unchanged; i.e. there is no evidence of a causal association between mobile phone use and the incidence of malignant glioma and glioblastoma (multiforme). The corrected results are shown in Figs. 1 and 2 and Table 1 below.

The author would like to apologise for any inconvenience caused.

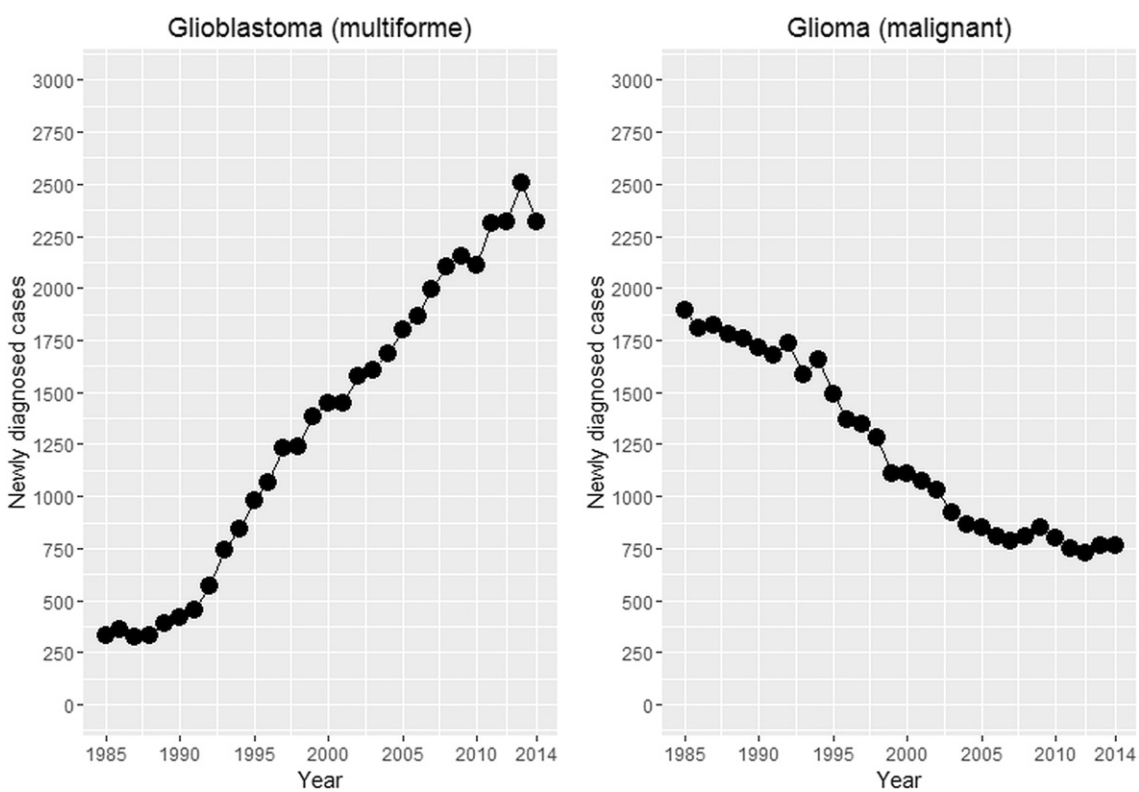

Fig. 1. 1985–2014 annual number of newly registered cases of malignant glioma and glioblastoma multiforme.

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Table 1
Inferred impact of mobile phone use (and possibly other wireless technology) on annual incidence of selected brain cancer subtypes.

Histology based	Implied lag (from 1995)	Absolute average effect (95%CI)	Absolute cumulative effect (95%CI)	Relative effect (95%)	Posterior probability of effect
Malignant Glioma[a]	0 years	−387 (−1224, 313)	−7347 (−23,261, 5948)	−29% (−92%, 23%)	0.144
	5 years	312 (−585, 1413)	4375 (−8187, 19,780)	59% (−111%, 267%)	0.318
	10 years	102 (−448, 668)	922 (−4034, 6011)	15% (−66%, 98%)	0.362
	15 years	−10 (−465, 444)	−40 (−1859, 1775)	−1.3% (−61%, 58%)	0.484
Glioblastoma multiforme[b]	0 years	430 (−11,042, 2323)	8179 (−19,806, 44,138)	31% (−76%, 170%)	0.315
	5 years	−324 (−2072, 1054)	−4540 (−29,006, 14,762)	−14% (−90%, 46%)	0.395
	10 years	127 (−728, 950)	1142 (−6551, 8550)	6.2% (−35%, 46%)	0.377
	15 years	123 (−602, 847)	490 (−2408, 3387)	5.5% (−27%, 38%)	0.368

[a] ICD 9 site codes 191.0–191.9 (morphology codes M9380/3, M9382/3, M9400/3), ICD 10 site codes C71.0–C71.9 (morphology codes M9380/3, M9382/3, M9400/3).
[b] ICD 9 site codes 191.0–191.9 (morphology codes M9440/3, M9441/3, M9442/3,), ICD 10 site codes C71.0–C71.9 (morphology codes M9440/3, M9441/3, M9442/3).

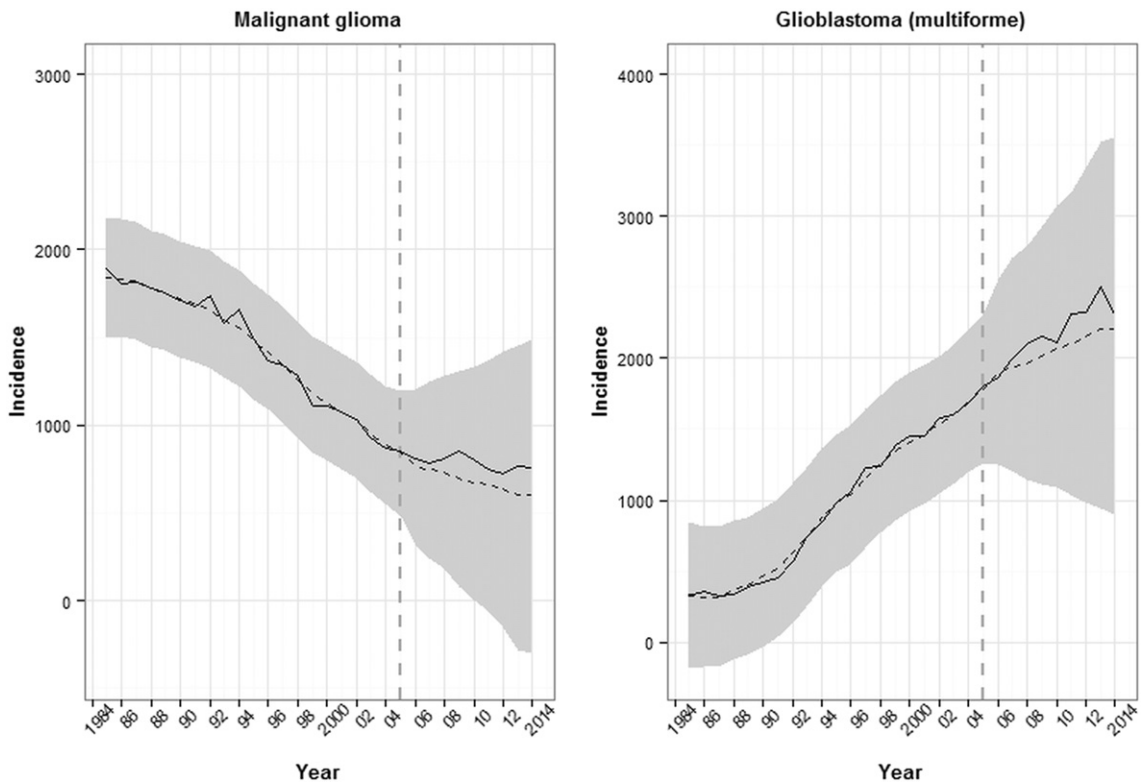

Fig. 2. Measured (solid) and modelled (dashed) incidence trends (top) for and malignant glioma and glioblastoma multiforme; implied 10-year lag. Grey areas correspond to 95% Credible Intervals.