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Interpretation of Timetrends (1996–2017) of the Incidence of Selected Cancers in England in Relation to Mobile Phone Use as a Possible Risk Factor

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Radiofrequency (RF) radiation from mobile phones has been classified as possibly carcinogenic to humans (2b) by IARC. However, to date, the discussion on whether mobile phone use is a cancer risk factor has not been solved. In this context of continuing uncertainty, it is important to continue to monitor cancer incidence trends. Annual incidence rates and directly age-standardized rates of selected cancers by sex and 5-year age groups for 1996 to 2017 for England were obtained from the UK Office for National Statistics. Interpretation in light of mobile phone use as a contributing risk factor was conducted for cancers of the brain, parotid gland, thyroid, and colorectal cancer, which have all been hypothesized to be associated with RF exposure. Brain and parotid gland cancers were updated by an additional 10 years following a previous publication, and continue to provide little evidence of an association with mobile phone use. Although mobile phone use as a potential risk factor contributing to increased incidence of colorectal or thyroid cancer could not be excluded based on these ecological data, it is implausible that it is an important risk factor for either. In the absence of clarity from epidemiological studies, it remains important to continue to monitor trends. However, for the time being, and in agreement with data from other countries, there is little evidence of an association between mobile phone use and brain or parotid gland cancer, while the hypotheses of associations with thyroid or colorectal cancer are similarly weak. Bioelectromagnetics. 2021;42:609–615. © 2021 Bioelectromagnetics Society.

Keywords: **cancer; parotid; brain; colorectal; thyroid; ecological analyses; cell phones; mobile phones; RF; radiofrequency**

INTRODUCTION

The International Agency for Research on Cancer (IARC) has classified radiofrequency (RF) radiation as possibly carcinogenic to humans (Group 2b) [IARC, 2013]. Although the main sources of evidence for causal claims are epidemiological case-control and cohort studies, it is important to triangulate these data with evidence from mechanistic studies and studies in animals, as well as from epidemiological studies with other sources of potential bias and error. Ecological studies are generally considered weak study designs, but the coherence of trends in the incidence of various cancers hypothesized to be caused by mobile phones with findings from case-control and cohort studies puts boundaries on plausible results and would strengthen any causal claims. Moreover, the monitoring of national cancer incidence trends itself provides evidence for the public health impact of exposure to RF exposure from mobile phones, and continued monitoring has therefore been recommended [Van Deventer et al., 2011]. Indeed, with mobile phone penetration rates having rapidly increased from the early 1990s when they were introduced to over one mobile-cellular subscription per person in the UK from 2004–2005 [International Telecommunication Union ITU, 2021], important effects on cancer incidence, if these exist, should plausibly be observable in national data for some, or all, relevant cancers.

Due to the way mobile phones have been, and to some extent still are, used, brain cancers have

Conflicts of interest: FdV has previously conducted consulting for EPRI, not related to this work.

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generally been considered the main target. In agreement with data from other countries, in England, no noticeable increase in incidence was observed up to 2007 [De Vocht et al., 2011]. Cancer of the parotid gland was suspect for similar reasons as brain cancer, and while a relative increase was observed in England up to 2008, the gradual increase across the time period and sex differences in trends did not point to mobile phone use as an important factor [De Vocht, 2011]. This triangulates well with more recent data from Australia [Karipidis et al., 2021]. Incidence data from the Nordic countries for the period up to 2017 that indicated an increased incidence of thyroid cancer, especially in women, formed the basis to hypothesize a causal link with mobile phone use [Carlberg et al., 2020]. Also potentially of interest is a link between the carrying of mobile phones in back pockets and colorectal cancer. Although there is little evidence from human populations in the peer-reviewed literature, the possibility of such a link has been proposed based on recent trends of colorectal cancer, especially among young people [Davis et al., 2020] and some mechanistic data [Mokarram et al., 2017].

In this update, cancer incidence trends in England for cancers of the brain and parotid gland have been updated from previous work to 2017 and discussed in relation to mobile phone use for the first time for colorectal and thyroid cancer, and age-specific rates are explored.

MATERIALS AND METHODS

Cancer Registry data are freely available from the Office of National Statistics [ONS, 2021], and were submitted to ONS by the National Cancer Registration Service in Public Health England. Data are quality checked and serious errors are reported to be 0.1% or below, with the completeness of 98% or higher (although it can take up to 5 years to reach 100% completeness) [ONS, 2016]. Sex-specific annual cancer incidence rates were obtained for the whole population and for 5-year age strata, as well as the directly age-standardized rates (DAS rates) for the available years 1996–2017 and 1999–2017 for all other series for cancer of the brain (ICD-10 C71), cancer of the parotid gland (ICD-10 C07), cancer of the thyroid gland (ICD-10 C73), and cancer of the colon and rectum (ICD-10 C18-C20). Figures of population annual incidence rates and DAS rates are provided here, with age group-specific rates provided in Online Supplementary Material (OSM). Age group-specific rates are provided in 5-year groups from 15 to 84 years of age because of the low number of incidence cases in younger people and a change in the time series from 85+ years of age to 90+ (with an additional group of 85–89 years of age) from 2012. DAS rates were calculated relative to the "European Standard Population" (ESP) which is an artificial population to enable direct comparison between different countries. These have been provided for reference only because they are useful for comparison across countries, but for interpretation of national time trends, it is important that the EPS was updated in 2013 to better reflect the population structure. The new structure allocates a greater weight to the older population, and its implementation has resulted in an artificial increase in rates depending on specific cancer and sex [ONS, 2013]. For comparison and clarity, DAS rates recalculated based on the 2013 updated ESP for the complete time series are also provided. Time series are formally analyzed using log-rate regression models to determine linear in/decreases over time and additional mean changepoint analysis to identify sudden changes in the trends. Analyses were done in R (version 4.0.5; R Foundation for Statistical Computing, Vienna, Austria) base functions and the changepoint package (version 2.2.2) [Killick et al., 2014] using 0.05 to indicate statistical significance. Inferences regarding the plausibility of mobile phone use as a potential risk factor are based on temporal increases showing evidence of a change point rather than a gradual increase across the complete period and show comparable patterns across multiple age groups and sex. Isolated increases in a single 5-year age group but not in adjacent age groups are considered implausibly associated with a ubiquitous factor such as mobile phone use.

RESULTS

Although the DAS rates suggest an increase of 30% in the incidence rates of brain cancers in women and 34% in men from 1996 to 2017, especially resulting from a sharp increase around 2012, indicating the impact of the use of the revised ESP (as also illustrated by the recalculated ESP 2013 trends, which show little evidence of a significant increase), the corresponding population incidence trend is much lower and does not show evidence of a (statistically significant) changepoint (+19% and +18% for women and men over the time period, respectively) (Fig. 1). Age group-specific trends (OSM Fig. S1-14) show little evidence of a consistent increase in incidence in age groups, with statistically significant increases observed in men aged 30–34, 40–49, and 50–54 years, but women aged 25–29 only, with the exception of a steady increase over the period in the oldest

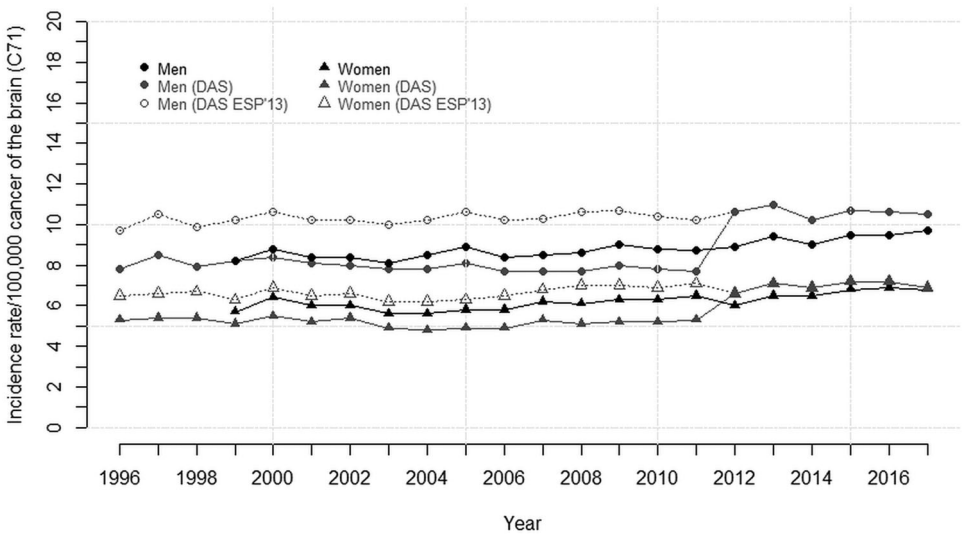

Fig. 1. 1996–2017 annual population incidence rates per 100,000 and directly age-standardized (DAS) rates (either based on original European Standard Population [ESP] or recalculated based on 2013 updated ESP) of malignant neoplasms of the brain (ICD-10 C71) by sex for England.

(80–84 years) group where a relative increase of 49% and 94% is observed in women and men ($P < 0.001$), respectively. Any trends were consistent over the period with no evidence of change points.

A steady increase ($P < 0.001$) from 0.4 to 0.6 incident cases per 100,000 women and 0.7 to 0.8 for men, respectively, over the 1996–2017 time period was observed for the incidence of cancer of the parotid gland, mainly in DAS rates as a result of the use of the revised ESP, as the 2013 ESP recalculated incidence trends show a comparable pattern to the non-standardized rates (Fig. 2). There was little consistent evidence of an increase in incidence in men, which was only observed in the age groups 65–69 and 80–84 year-olds ($P < 0.05$), while for women weak evidence of small increases ($P = 0.01$–0.10) were observed in age groups 35-39, 45–69, and 80–84 year-olds (OSM Fig. S15-28). Where trends were observed, these were stable across the complete time period with no indication of any changepoints.

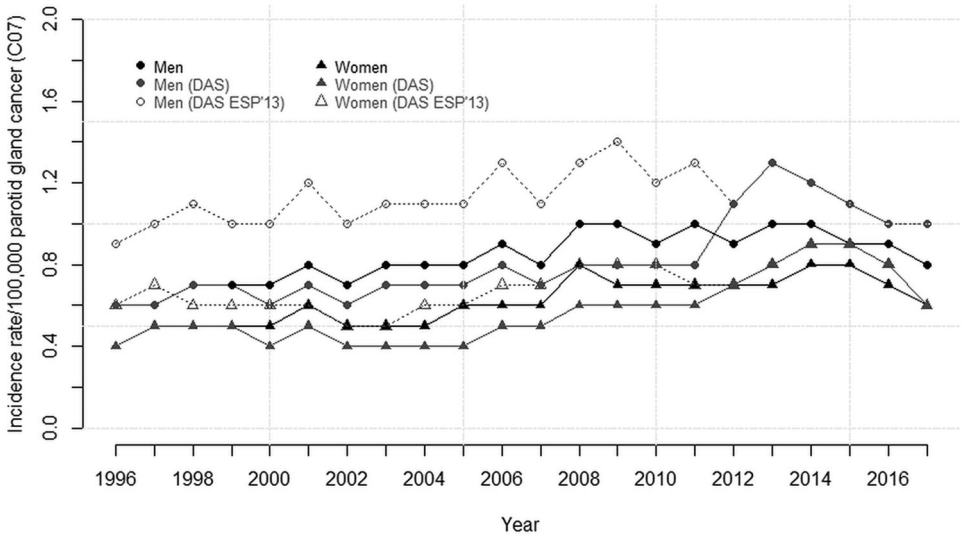

Fig. 2. 1996–2017 annual population incidence rates per 100,000 and directly age-standardized (DAS) rates (either based on original European Standard Population [ESP] or recalculated based on 2013 updated ESP) of malignant neoplasms of the parotid gland (ICD-10 C07) by sex for England.

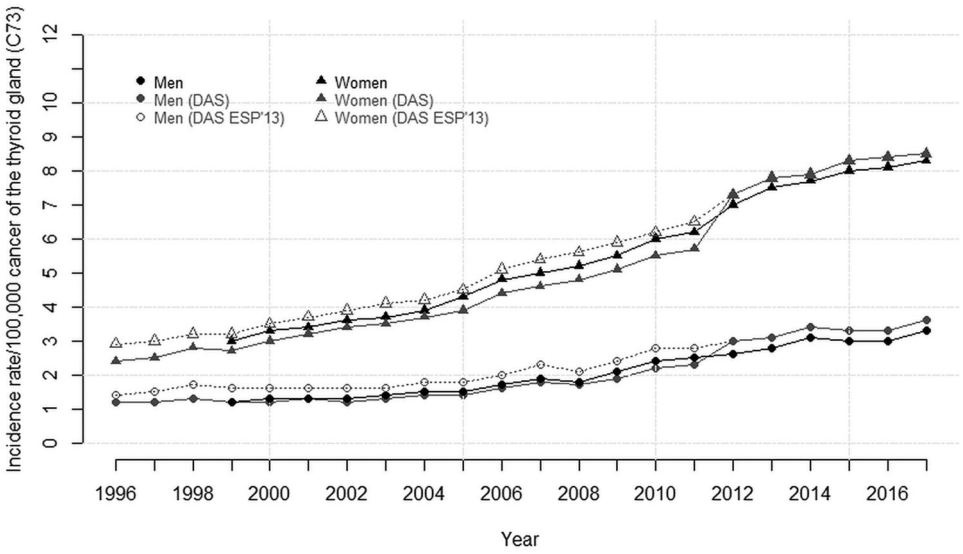

Fig. 3. 1996–2017 annual population incidence rates per 100,000 and directly age-standardized (DAS) rates (either based on original European Standard Population [ESP] or recalculated based on 2013 updated ESP) of malignant neoplasms of the thyroid gland (ICD-10 C73) by sex for England.

Cancer of the thyroid gland has increased steadily over time ($P < 0.001$), especially in women where the DAS rate has more than tripled from 1996 to 2017 from 2.7 incident cases to 8.5 per 100,000 women but also in men (from 1.2 to 3.6 incident cases per 100,000 men), with little differences between population rates and DAS rates (Fig. 3). This pattern is consistent in both sexes and across all age groups ($P < 0.001$), but an increasing incidence is especially prevalent in women aged 30–54 years with no evidence of any changepoints; ranging from 6% annually in the 30–34 year age group to 8% annually in the 45–49 year age group (OSM Fig. S29-42).

The incidence rates of colorectal cancer in England have been stable for women (+3% from 1999 to 2017; $P < 0.001$) and slightly increasing for

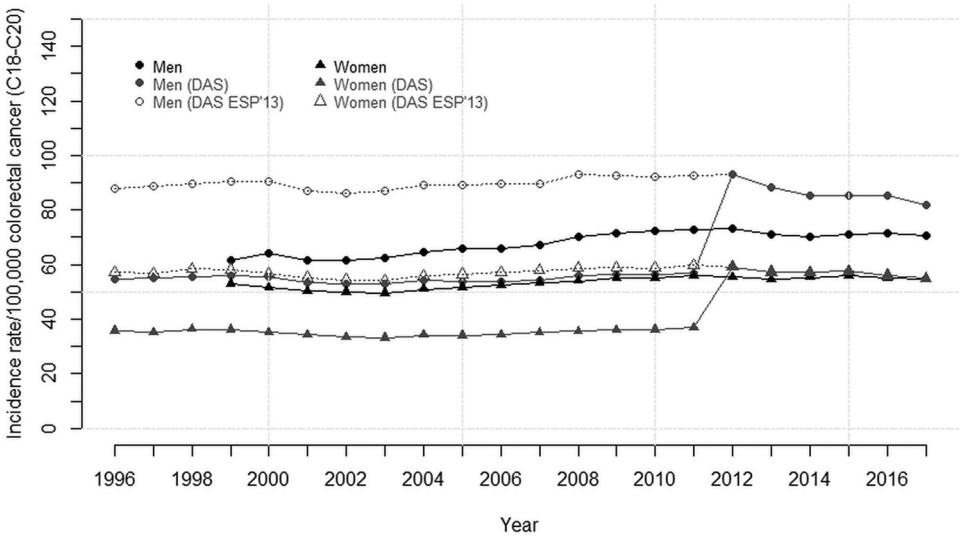

Fig. 4. 1996–2017 annual population incidence rates per 100,000 and directly age-standardized (DAS) rates (either based on original European Standard Population [ESP] or recalculated based on 2013 updated ESP) of colorectal malignant neoplasms (ICD-10 C18-C20) by sex for England.

men (+15% from 1999 to 2017; $P < 0.001$) (Fig. 4). The appearance of a sudden increase in rates of 60% (men) and 57% (women) from 2013 in the corresponding DAS rates is entirely consistent with the specific change in colorectal cancer incidence as a result of the change to the updated ESP [ONS, 2013], and indeed this is illustrated by the 2013 ESP recalculated incidence trends. Age group-specific rates show a clear pattern of increasing incidence by age, but with stable incidence rates of colorectal cancer for men aged 45 years or older and women aged 60 years or older (OSM Fig. S43-56). In younger age groups, a clear increase in incidence can be observed, especially in the groups of 25–34 year-olds describing annual increases of 7% in both sexes ($P < 0.001$), with some indication of plateauing of this pattern in those 29 years or younger.

DISCUSSION

Given the continuing ambiguity around whether RF radiation is a human carcinogen, despite its 10–20 years of ubiquitous societal presence, the monitoring of incidence trends of cancer hypothesized to be associated with mobile phone use continues to be important, especially where these can be triangulated with data from other epidemiological study designs. Mobile phone use itself has rapidly increased from the introduction of mobile phones with just over one million subscriptions in the UK in 1990 to just over seven million at the start of the cancer data in this study (1996), to over 43 million in 2000, and 79 million in 2017 [World Bank, 2021].

The extension of the incidence rates of brain cancers by another decade from 2007 [De Vocht et al., 2011] to 2017 has not changed the inference that because rates are relatively stable with no evidence of any changepoints in the log-rates, there is little evidence of an impact of mobile phone use. Age group-specific rates similarly provide little evidence of increasing risk. It has been suggested that brain cancer is too broad a category to expect observable risks because mobile phone use would be a causal factor for glioma specifically. The most recent published update is from Canada (up to 2015) and provides little evidence of an increase in glioma incidence that could be related to mobile phone use [Villeneuve et al., 2021]. More specifically, glioblastoma multiforme, an aggressive glioma subtype, has been reported to have been increasing; however, detailed evaluation of age group-specific incidence trends in England using causal inference methods provided evidence that it was unlikely that mobile phone use was an important risk factor [de Vocht, 2019]. Incidence of cancer of the parotid gland has slightly increased over the time period overall, but stable age group-specific trends show that this is the result of demographic changes with little impact from an exogenous factor such as mobile phone use. This additional decade of data compared to the previous assessment incidence trends in England [De Vocht, 2011] does not change the original overall inference of an absence of association. This also corroborates recent observations based on data up to 2016 from Australia [Karipidis et al., 2021]. The incidence of cancer of the thyroid gland in England has gradually increased over the previous 20 years, especially in women and especially in those aged 30–54. The gradual increase over the time period and the large difference between men and women, with only a minor excess, if at all, in the incidence of men aged 20–40, does not suggest that mobile phone use is an important risk factor. Nonetheless, although the increase in thyroid cancer incidence can for a large part be ascribed to enhanced detection or overdiagnosis [Vaccarella et al., 2016], modifiable risk factors might also partially contribute to observed trends and have been hypothesized to include obesity and excess weight [Kitahara and Sosa, 2020], ionizing radiation (including, specifically, the Windscale reactor accident of 1957 [Wakeford, 2007]), and possibly other environmental factors including organochlorines, pesticides, and others [Fiore et al., 2019]. RF is generally not considered as a likely risk factor (with the exception of Carlberg et al., [2020]), but based on these ecological data alone, the possibility of mobile phone use as a minor contributing factor cannot be excluded. Age group-specific patterns of colorectal cancer show that increasing incidence almost exclusively occurs in the under-40s, with little difference between sexes. Observed spatial and temporal patterns worldwide are generally considered to result from a variety of factors including primarily lifestyle-related factors linked to "westernization" including alcohol consumption, poor diet, obesity, physical inactivity, and smoking [Arnold et al., 2017]. Differences in these factors comprehensively explain a large proportion of observed patterns but do not exclude mobile phone use as a potential, relatively minor, contributing factor. This hypothesis is based on the prolonged time people carry mobile phones in their back pockets, and although in theory, this may contribute to colorectal cancer in adults aged 20–25 years or older, it is implausible that an increasing risk would be observed in adolescents aged 20 years or younger. In addition, the absence of increasing risk in people aged 40+ and observed differences between sexes in these groups also do not support this

hypothesis. More broadly, global differences between countries over time, including an observed decline in the incidence in young people in highly developed countries of Italy, Austria, and Lithuania [Siegel et al., 2019], would further weaken the plausibility of this hypothesis.

Ecological data are generally considered weak epidemiological evidence to infer causality, and the presented data provide little evidence to confirm or refute mobile phone use or RF radiation as a cancer hazard. It does, however, provide relevant information regarding population cancer risks, especially where triangulated with information from other study designs; it provides boundaries on the plausibility of results from the latter [Deltour et al., 2012]. It has further been pointed out that the results of mobile phone use on incidence trends may not be observable in national data because only a very small proportion of the population may be susceptible, or insufficient time has elapsed since the introduction of mobile phones for incidence to rise [Kundi, 2011]. Although the former may be true, this further strengthens the argument that RF exposure from mobile phones would be of relatively limited public health importance with respect to cancer (although it would be important to identify such vulnerable groups if these exist), while the latter is becoming increasingly implausible with time progressing; note, for example, that asbestos has an average induction period of several decades, but was already observable in national data after 10–14 years [Walker, 1984].

An important strength of national cancer incidence trends lies in their triangulation with evidence from other epidemiological study designs, and these data provide further indication that results from several important case-control studies were likely biased away from the Null—an inference in line with others [Deltour et al., 2012; Röösli et al., 2019; Villeneuve et al., 2021]—but does not exclude a small-moderate excess risk in a small subgroup of susceptible individuals with high mobile phone usage [de Vocht and Röösli, 2021].

In summary, updated incidence trends of cancers of the brain and parotid gland in England continue to provide little evidence that exposure to RF radiation from mobile phones is an important risk factor; if it is one at all. Patterns of thyroid and colorectal cancer incidence, more recently hypothesized to be associated with mobile phone use, similarly provide little evidence that mobile phone use is an important risk factor. However, temporal patterns to some extent coincide with mobile phone usage trends (plus latency), so based on these data alone a relatively minor contributions of RF exposure from mobile phones cannot be excluded. As an important contribution to the triangulation of evidence, monitoring the temporal patterns of these cancers continues to be worthwhile. And finally, with the introduction of 5G, it is worth also continuing to monitor other cancers hypothesized to possibly be associated with higher frequencies, mostly notably ocular and skin cancers [Simkó and Mattsson, 2019].

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