







**YES! CELL PHONES DO CAUSE CANCER**

# Cellular Phone Use and Risk of Tumors: Systematic Review and Meta-Analysis

  
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# Abstract

We investigated whether cellular phone use was associated with increased risk of tumors using a meta-analysis of case-control studies. PubMed and EMBASE were searched from inception to July 2018. The primary outcome was the risk of tumors by cellular phone use, which was measured by pooling each odds ratio (OR) and its 95% confidence interval (CI). In a meta-analysis of 46 case-control studies, compared with never or rarely having used a cellular phone, regular use was not associated with tumor risk in the random-effects meta-analysis. However, in the subgroup meta-analysis by research group, there was a statistically significant positive association (harmful effect) in the Hardell et al. studies (OR, 1.15—95% CI, 1.00 to 1.33— n = 10), a statistically significant negative association (beneficial effect) in the INTERPHONE-related studies (case-control studies from 13 countries coordinated by the International Agency for Research on Cancer (IARC); (OR, 0.81—95% CI, 0.75 to 0.89—n = 9), and no statistically significant association in other research groups' studies. Further, cellular phone use with cumulative call time more than 1000 h statistically significantly increased the risk of tumors. This comprehensive meta-analysis of case-control studies found evidence that linked cellular phone use to increased tumor risk.

*Keywords:* [cellular phone](#); [electromagnetic field](#); [tumor](#); [case-control study](#); [meta-analysis](#)

# 1. Introduction

According to estimates from the International Telecommunication Union, the number of worldwide mobile cellular subscriptions increased from 68.0 per 100 inhabitants in 2009 to 108.0 per 100 inhabitants in 2019 [1]. With the increasing use of cellular phones, concerns have arisen over the carcinogenic effects of electromagnetic fields (EMFs) emitted from cellular phones [2]. Since 1999, observational epidemiologic studies, specifically case-control studies have reported inconsistent findings on the association between cellular phone use and tumor risk, and several meta-analyses [3,4,5,6] of case-control studies on this topic have been published before 2011.

Among these studies, Myung et al.'s meta-analysis [5] of 23 case-control studies concluded that mobile phone use was associated with an increased tumor risk in high quality studies and studies conducted by a specific research group, and that long-term mobile phone use of 10 or more years increased the risk of tumors regardless of methodological quality or research group. Similarly, Khurana et al. also reported that cellular phone use of 10 or more years doubled the risk of brain tumors in 11 epidemiologic studies [6].

Based on evaluation of the available literature including experimental animal studies and epidemiological studies in humans, in 2011, the World Health Organization (WHO)/International Agency for Research on Cancer (IARC) classified radiofrequency electromagnetic fields (RF-EMFs) associated with cellular phone use as possibly

carcinogenic to humans [7]. Recently, an advisory group of 29 scientists recommended that IARC prioritize a new review of the carcinogenicity of RF-EMF by 2024 due to mechanistic evidence of the carcinogenicity of cell phone radiation published since 2011 [8]. Although many case-control studies and several meta-analyses have been published regarding the association between cellular phone use and tumor risk, the findings remain inconsistent.

The purpose of this study was to evaluate the associations between cellular phone use and tumor risk using a systematic review and meta-analysis of case-control studies according to various factors including differences in response rates between cases and controls, use of blinding at interview for ascertainment of exposure, methodological quality, funding sources, type of case-control study, malignancy of tumor, and dose–response relationship.

## **2. Materials and Methods**

### **2.1. Literature Search**

We searched PubMed and EMBASE in July 2018, using common keywords related to cellular phones and tumors as follows: “cellular phone or mobile phone,” and “tumor or cancer”. We also located additional articles by reviewing the bibliographies of relevant articles.

### **2.2. Selection Criteria**

We selected articles based upon the following criteria: case-control studies; investigated the associations between cellular phone or mobile phone use (not cordless phones) and the risk of benign or malignant tumors; reported outcome measures with adjusted odds ratios (OR) with 95% confidence intervals (CIs); and peer-reviewed articles written in English. If data were duplicated or shared in more than one article, we selected only the article with the larger sample size.

### **2.3. Selection of Relevant Studies**

Two authors (Y.-J.C and Y.-R.L) independently reviewed the articles from the search and selected articles meeting the predetermined selection criteria. Disagreements between the two authors were resolved by discussion.

### **2.4. Assessment of Methodological Quality**

We evaluated the methodological quality of the case-control studies based on the Newcastle-Ottawa Scale (NOS) [9] and the National Heart, Lung, and Blood Institute (NHLBI) quality assessment tool of case-control studies [10]. A star system of the NOS ranging from 0 to 9 is composed of three subscales: selection of study groups, comparability, and exposure. The NHLBI quality assessment tool consists of 12 questions answered with yes, no, or other (cannot determine, not applicable, or not reported). Two authors (Y.-J.C and Y.-R.L) independently assigned a score for each study, and disagreements were resolved by discussion. We considered a study awarded a number of stars or “yes” more than the mean of all the included studies as a high-quality study because standard criteria have not been established.

## **2.5. Main and Subgroup Analyses**

We investigated the associations between cellular phone use (used vs. never or rarely used) and tumor risk by using adjusted data for the main analysis. When an individual study reported data on both analog and digital phones, the data on digital phones were selected. We also conducted subgroup meta-analyses by research group: Hardell et al. studies (Hardell studies), the INTERPHONE-related studies (INTERPHONE case-control studies in 13 countries coordinated by the International Agency for Research on Cancer [IARC]), and studies by other groups. Additionally, for each research group, we conducted subgroup meta-analyses by various factors as follows: difference in response rates between cases and controls (smaller difference vs. larger difference, by difference in response rates of 14.5%, which was an average difference in response rates



between cases and controls in all studies), use of blinding at interview for ascertainment of exposure (used vs. not used or no description), methodological quality by the NOS (high vs. low, by average score), funding sources (cellular phone industry funding vs. not funded), type of case-control study (hospital-based vs. population-based), and malignancy of tumor (malignant vs. benign). In order to evaluate an exposure–response relationship, we also performed subgroup meta-analyses by time since first use or latency (<5 vs. 5–9 vs. ≥10 years), cumulative or lifetime use (<5 vs. 5–9 vs. ≥10 years), cumulative call time (<300 vs. 300–1000 vs. ≥1000 h), and cumulative number of calls (<1000 vs. 1000–7000 vs. >7000). Latency refers to the length of time between the beginning of regular cellular phone use and the diagnosis of tumor occurrence. When multiple ORs with 95% CI were presented within each category of time or number of calls, a longer time or a higher number of calls was used for the analysis.

## **2.6. Statistical Analysis**

To compute a pooled OR with its 95% CI, we used adjusted data from individual studies. A random-effects model meta-analysis on the basis of the DerSimonian and Laird method [11] was used in the current study because individual trials were carried out in the different populations. We also used a chi-square test to evaluate any differences in response rates between the case and control groups. We tested heterogeneity across the studies using Higgins  $I^2$ , which represents the percentage of total variation within studies meta-analyzed [12].  $I^2$  was calculated as below:

$$I^2 = 100\% \times (Q - df)/Q,$$


(1)

where  $Q$  is Cochran's heterogeneity statistics, and  $df$  represents the degrees of freedom. Negative values of  $I^2$  are set to zero, and  $I^2$  lies between 0% (no observed heterogeneity) and 100% (maximal heterogeneity). We estimated publication bias using Begg's funnel plot and Egger's test. When there is publication bias, Begg's funnel plot exhibits asymmetry, or the  $p$ -value  $< 0.05$  by Egger's test. The Stata SE version 14.0 software package was used for statistical analysis (StataCorp, College Station, TX, USA).

# 3. Results

## 3.1. Study Selection

[Figure 1](#) shows a flow diagram for the selection process of relevant studies. We identified a total of 425 articles from three core databases with 219 articles from PubMed, 203 articles from EMBASE, and 3 articles from hand-search. After excluding 118 duplicate articles and 200 articles that did not satisfy the pre-determined selection criteria by reviewing those titles and abstracts, the full texts of the remaining 107 articles were assessed for the final selection. After reviewing the full texts, 61 articles were excluded for the following reasons: not relevant studies (n = 24), letters, comments, or correspondence (n = 18), shared an identical population (n = 12), insufficient data (n = 5), and cohort studies (n = 2). The remaining 46 case-control studies (13–58) were included in the final analysis.

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**Figure 1.** Study selection.

## 3.2. General Characteristics of Studies and Participants

General characteristics of the case-control studies included in the meta-analysis are shown in [Table 1](#). The 46 case-control studies involved a total of 66,075 participants with 24,717 cases and 41,358 controls. For studies reporting gender, 53.9% of study participants were women. A total of 37 studies were hospital-based case-control

studies, while nine studies were population-based case-control studies. The included studies were conducted in the following countries: Sweden (n = 24), Denmark (n = 9), United Kingdom (n = 8), Finland (n = 7), Norway (n = 6), Germany (n = 5), US (n = 4), Israel (n = 3), Japan (n = 2), Italy (n = 2), New Zealand (n = 2), France (n = 2), Brazil (n = 1), China (n = 1), South Korea (n = 1), and Thailand (n = 1). The most common type of tumor in the included studies was brain tumor (34 out of 46 studies, 74%), and the next most common ones were head and neck cancer such as parotid gland tumor (5/46, 12%), hematologic malignancies such as leukemia and non-Hodgkin's lymphoma (4/46, 8.7%), melanoma (2/46, 4.3%), and testicular cancer (1/46, 2.2%).

**Table 1.** General characteristics of studies included in the meta-analysis (n = 46).

 Table

The studies were classified by research group, i.e., Hardell studies (n = 11), INTERPHONE studies (n = 19), and studies conducted by other groups (n = 16). As shown in [Table S1](#) and [Table S2](#), the NOS scores ranged between 4 and 8 (average score, 6.4), and the NHLBI quality assessment scores ranged between 6 and 10 (average score, 8.3). We considered studies with an NOS score of  $\geq 7$  stars or an NHLBI quality assessment score of  $\geq 9$  points as having high quality and the remaining studies as having low quality.

The Hardell studies were not funded by the cellular phone industry. Most had high scores of  $\geq 7$  stars in the NOS and high scores of  $\geq 9$  points in the NHLBI quality assessment; most reported high response rates ( $>70\%$ ) with smaller differences in response rates ( $<14.5\%$ ) between the case group and the control group; and all

were population-based case-control studies ([Table 2](#), [Table S1](#), and [Table S2](#)). All of the INTERPHONE studies were partly funded by the cellular phone industry (precisely, supported by funding from the International Union against Cancer, which received funds from the Mobile Manufacturers' Forum and Global System for Mobile Communications Association) except for the INTERPHONE-Japan studies. Most had low scores of <7 stars and low scores of <9 points, showed low response rates (<70%), and had larger differences in response rates (>14.5%) between the case group and the control group. All were population-based case-control studies ([Table 2](#), [Table S1](#), and [Table S2](#)).

**Table 2.** Use of cellular phones and risk of tumors in subgroup meta-analysis of case-control studies.


 Table

No study conducted by the other groups was funded by the cellular phone industry. Most of these studies had low response rates and mainly larger differences in response rates between the case group and the control group ([Table 2](#)).

### 3.3. Overall Use of Cellular Phone and Risk of Tumors

As shown in [Figure 2](#), as compared with never or none, the overall use of cellular phones was not associated with tumor risk in a random-effects meta-analysis of all 36 studies (OR, 0.99; 95% CI, 0.91 to 1.07;  $I^2 = 47.4$ ). Of the 46 studies, several [[24](#),[25](#),[26](#),[27](#),[28](#),[29](#),[30](#),[32](#),[33](#),[34](#),[35](#),[36](#)] were excluded from the main analysis but included in the subgroup meta-analysis because study subjects overlapped with the INTERPHONE study published in 2010

[40] and 2011 [41] (which reported pooled results from all 13 countries).

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**Figure 2.** Cellular phone use and risk of tumors in a random-effects subgroup meta-analysis of case-control studies by research groups (n = 36). OR—odds ratio; CI—confidence interval. \*—2010 and 2011 The INTERPHONE Study Group studies involved 13 countries. In the subgroup meta-analysis by research group, cellular phone use was associated with marginally increased tumor risk in the Hardell studies (OR, 1.15 (95% CI, 1.00 to 1.33; n = 10;  $I^2 = 40.1\%$ ), whereas it was associated with decreased tumor risk in the INTERPHONE studies (OR, 0.81; 95% CI, 0.75 to 0.88; n = 9;  $I^2 = 1.3\%$ ). In the studies conducted by other groups, there was no statistically significant association between the cellular phone use and tumor risk (OR, 1.02; 95% CI, 0.92 to 1.13; n = 17;  $I^2 = 8.1\%$ ). Publication bias was not observed overall (Begg's funnel plot was symmetric; Egger's test, p for bias = 0.07). In addition, there was no publication bias in the subgroup meta-analysis by research group (Egger's test, p for bias = 0.36 in the Hardell studies, 0.57 in the INTERPHONE studies, and 0.68 in studies by other groups, respectively).

### **3.4. Use of Cellular Phones and Risk of Tumors in Subgroup Meta-analysis By Various Factors**

[Table 2](#) shows the findings of the subgroup meta-analyses by various factors. Cellular phone use was statistically significantly associated with increased tumor risk in studies that used blinding at interview (OR, 1.16; 95% CI, 1.01 to 1.34; n = 10;  $I^2 = 39.4\%$ ). In

addition, cellular phone use had a marginally statistically significant association with increased tumor risk in studies with high methodological quality (OR, 1.11; 95% CI, 1.00 to 1.22;  $n = 17$ ;  $I^2 = 20.1\%$ , based on the NOS score; OR, 1.09; 95% CI, 0.99 to 1.20;  $n = 20$ ;  $I^2 = 29.3$ , based on the NHLBI quality assessment tool). In contrast, cellular phone use had statistically significant associations with reduced tumor risk in studies that did not use blinding at interview, or were rated as having low methodological quality. Both the NOS score and NHLBI quality assessment tool showed similar findings in methodological quality scores: most Hardell studies were rated high quality, while most INTERPHONE studies were rated low quality.

Similarly, subgroup meta-analyses by funding source revealed a non-significant increased risk of tumors by cellular phone use in studies not funded by the cellular phone industry (OR, 1.07; 95% CI, 0.98 to 1.17;  $n = 28$ ;  $I^2 = 21.9\%$ ), whereas a statistically significantly decreased risk of tumors was observed in studies partly funded by the cellular phone industry (OR, 0.81; 95% CI, 0.74 to 0.89;  $n = 8$ ;  $I^2 = 0\%$ ), all of which were INTERPHONE studies.

Cellular phone use was not statistically significantly associated with tumor risk in the subgroup meta-analysis by type of case-control study. In the subgroup meta-analysis by type of tumor, a significantly decreased risk of benign tumors was observed (OR, 0.86; 95% CI, 0.77 to 0.95;  $n = 14$ ;  $I^2 = 21.9$ ), while no significant association was observed for malignant tumors. This decreased risk of benign tumors was only found in INTERPHONE studies, not in Hardell et al. studies and studies by other groups.

### 3.5. Exposure–Response Relationship Between Use of Cellular Phones and Risk of Tumors

[Table 3](#) shows an exposure-response relationship between cellular phone use and tumor risk. In the subgroup meta-analysis by time since first use or latency, overall the risk of tumors by cellular phone use non-significantly increased from an OR of 0.97 to 1.29 as latency increased from less than 5 years to 10 or more years. This finding was observed in each subgroup meta-analysis by research group. Especially, statistically significant increased tumor risk was observed for latency of 10 or more years in the Hardell studies (OR, 1.62; 1.03 to 2.57;  $n = 5$ ;  $I^2 = 39.9\%$ ). Similarly, the use of cellular phones non-significantly increased the risk of tumors as the cumulative or lifetime use in years and the cumulative number of calls increased in all studies and in each study group. Remarkably, in the subgroup meta-analysis of all studies by cumulative call time, cellular phone use greater than 1000 h statistically significantly increased the risk of tumors (OR, 1.60; 1.12 to 2.30;  $n = 8$ ;  $I^2 = 74.5\%$ ). Interestingly, the use of cellular phones overall and in the Hardell studies (OR, 3.65; 1.69 to 7.85;  $n = 2$ , especially in the Hardell studies) non significantly increased the risk of tumors with cumulative call time of 300–1000 h and more than 1000 h, while it decreased the risk of tumors in most subgroup meta-analyses of the INTERPHONE studies.

**Table 3.** Exposure–response relationship between use of cellular phones and risk of tumors.

Table



### **3.6. Use of Cellular Phones and Risk of Tumors in Subgroup Meta-analysis By Type of Tumor**

[Table S3](#) shows the findings from the subgroup meta-analyses by type of tumor. There was no statistically significant association between cellular phone use and tumor risk in most subgroup meta-analyses. Increased tumor risk was found for malignant brain tumors only in the Hardell studies (OR, 1.35; 95% CI, 1.06 to 1.73;  $n = 5$ ;  $I^2 = 53.9\%$ ).

## 4. Discussion

In this comprehensive systematic review and meta-analysis, we found statistically significant differences in the findings for the association between cellular phone use and tumor risk which varied by research group. Namely, there was a statistically significant increased association by 15% in the Hardell studies, a statistically significant decreased association by 19% in the INTERPHONE studies (multi-national case-control studies coordinated by the IARC), and no significant association in the other research groups' studies. Importantly, in the subgroup meta-analysis of all studies reporting cumulative call times greater than 1000 h, cellular phone use with cumulative call time greater than 1000 h (about 17 min per day over a 10 year period) increased the risk of tumors by 60%. Perhaps due to methodological deficiencies, cellular phone use appeared to reduce tumor risk in the INTERPHONE studies. These studies were partly funded by the mobile industry, had poor methodological quality, showed larger differences in response rates between the case and control groups, and did not use blinding at interview.

A substantial research literature documents potential mechanisms for the effects of cellular phone use on tumor risk. Although heating is the only biological effect of non-ionizing radiation (NIR) (including microwave radiation from cellular phones) recognized by most health agencies, numerous in vitro studies and animal studies demonstrated other possible mechanisms including increasing oxidative DNA damage and altering protein structure and expression

[59]. In addition to a human endothelial cell line study, a human volunteer study reported a local exposure of human skin to RF-EMF caused changes in protein expression [60].

Based on the findings from pre-clinical studies, previous observational epidemiological studies, mainly case-control studies have reported inconsistent findings on the associations between cellular phone use and tumor risk. In 2009, we first reported evidence linking mobile phone use to increased tumor risk in a meta-analysis of low-biased case-control studies, especially among mobile phone users of 10 years or longer [5]. Two years later, the WHO/IARC classified RF-EMF due to cellular phone use as Group 2B, or “possibly carcinogenic to humans.” [7] Since then, subsequent case-control studies have reported inconsistent findings regarding the association between cellular phone use (use vs. never or rarely use) and tumor risk, similar to our previous findings. Since we published our meta-analysis in 2009, six meta-analyses [61,62,63,64,65,66] have reported the associations between cellular phone use and risk of brain tumors or head and neck tumors, mainly glioma and salivary gland tumors. Among them, four meta-analyses concluded that there was a statistically significant increased risk of glioma among heavy or long-term (over 10 years) mobile phone users in meta-analyses of 10 to 12 case-control studies [61,64,65,66]. In addition, one [62] of the remaining meta-analyses demonstrated a statistically significantly higher risk of all types of intracranial tumors in long-term mobile phone users (over 10 years) in a meta-analysis of 24 case-control studies, and the other [63] reported a statistically significantly increased risk of parotid gland tumors in a meta-analysis of three case-control studies.

Although the above mentioned four recent meta-analyses of case-control studies reported a significant increased risk of glioma in heavy or long-term (over 10 years) mobile phone users with an odds ratio of 1.35 in Wang et al. [61], 1.44 in Yang et al. [64], 1.33 in Wang et al. [65], and 1.33 in Prasad et al. [66], our study found a non-significantly increased risk with an OR of 1.66. This difference is due to the following reasons: Wang et al.'s meta-analysis in 2016 [61] reported that a significant association was found between mobile phone use of more than 5 years and glioma risk (OR = 1.35; 95% CI, 1.09 to 1.62;  $p < 0.05$ ). However, when we reviewed the main results and [Figure 1](#) in their article, the OR with 95% CI for mobile phone use of more than 5 years was 1.64 with 1.12 to 2.15. More importantly, when we performed a random-effects meta-analysis using the same data used in their analysis, there was no significant association between long-term use (>5 years) of mobile phones (the correct OR with 95% CI was 1.12 with 0.80 to 1.56). Yang et al.'s meta-analysis in 2017 [64] used seven studies comprising a Hardell study, a study by another group, and five INTERPHONE studies for long-term mobile phone use of 10 years or longer. The five INTERPHONE studies [26,27,29,30,34] were four publications [26,27,29,30] from individual countries (Denmark, Sweden, UK, and Germany) and one publication [34] of a collaborative analysis from five countries (Denmark, Finland, Norway, Sweden, and UK) within the same study years (2000–2004). Thus, Yang et al. used identical populations in three countries (Denmark, Sweden, and UK) in duplicates and used a smaller dataset from five countries instead of collaborative data [40] on glioma for the INTERPHONE studies from 13 countries published in 2010. When we performed a meta-analysis

using the 2010's collaborative data [40] instead of the five studies used in Yang et al.'s analysis, which were partly duplicated and smaller in sample size and number of countries than the 2010 collaborative analysis of the INTERPHONE group, there was no significant association between long-term mobile use and the risk of glioma (OR, 1.49; 95% CI, 0.80 to 2.78;  $n = 3$ ;  $I^2 = 91.5\%$ ), which is closer to our finding. Wang et al.'s meta-analysis in 2018 [65] included two cohort studies as well as case-control studies. More importantly, they included four ORs of >10–15 years, >15–20 years, >20–25 years, and >25 years from Hardell's 2015 study [67]. If each OR is calculated from independent data (not overlapping), they can be combined. However, each reference used for the calculation of each OR was overlapping. When we conducted a meta-analysis using only an OR of 1.40 for 10–15 years of wireless phone use in Hardell's 2015 study based on the Wang et al. analysis, there was no significant association between long-term use and the risk of glioma (OR, 1.08; 95% CI, 0.90 to 1.30;  $n = 6$ ;  $I^2 = 49.2\%$ ).

Compared to previous meta-analyses, the current meta-analysis has several strengths. First, the current meta-analysis is the most comprehensive study conducted to date, as it included 46 case-control studies with various types of tumors other than brain tumors. Second, we performed critical subgroup meta-analyses by factors that could affect individual results, such as the difference in response rates between cases and controls and funding sources, as well as use of blinding at interview for ascertainment of exposure and methodological quality. From these crucial subgroup meta-analyses, we confirmed that the opposite findings between the Hardell studies (increased tumor risk among cellular phone users) and the

INTERPHONE studies (decreased tumor risk among cellular phone users) were closely associated with these factors. The INTERPHONE studies had differential response rates in case and control groups, did not use blinding at interview, had low methodological quality scores, and were partly funded by the cellular phone industry. In contrast, the Hardell studies had comparable response rates in case and control groups, used blinding at interview, had high methodological quality, and had no industry funding. Although there was no statistical significance, similar findings were observed in the subgroup meta-analysis by the above mentioned factors in the studies by other groups. In the current main analysis of 36 case-control studies, nine out of 10 Hardell studies showed smaller differences in response rates between case and control groups and had high response rates of about 80–90% in both groups. In contrast, all of the INTERPHONE studies showed larger differences in response rates between both groups; most had lower response rates in the control group than in the case group, and most had low response rates of about 40–70%. Over the past decades, participation rates (response rates in this study) have decreased in case-control studies, particularly in controls, which could lead to non-representative selection of controls, reducing the validity of the effect estimates, and casting doubt on the veracity of study findings [68]. Thus, the decreased risks of tumors observed in the INTERPHONE studies might be due to selection bias from participation of cellular phone users in the control group [69]. We also found that studies partly funded by the cellular phone industry showed a statistically significantly decreased risk of tumors by cellular phone use, all of which were INTERPHONE studies. It remains unclear whether

cellular phone industry funding affected the study planning and conduct or data analysis and interpretation because the authors reported that the provision of funds to the study investigators via the UICC was governed by agreements that guaranteed INTERPHONE's complete scientific independence. Nonetheless, many of these investigators rely upon industry for future research funding so they may have "hidden conflicts" of interest despite such agreements [70].

Our meta-analysis is based upon case-control studies which potentially suffer from recall bias and selection bias. Although prospective cohort studies typically enable stronger inferences to be drawn regarding causality, these studies are difficult to conduct when the outcome is a rare chronic disease that requires long-term exposure and subjects are exposed to multiple potential toxins. So far, two prospective cohort studies have been published [71,72]. Both employed inadequate measures of cell phone use, and one misclassified many cell phone users as non-users [71]. A large, international prospective cohort study is ongoing but will not yield results on tumor risk for 20 or more years [73].

There are several limitations in the current study. Although cordless phones often have a much higher power output than cellular phones, and the users of analogue phones have used longer than those of digital phones, we excluded the impact of those phones in this analysis. This might lead to a bias that underestimates the effect of mobile phones on the risk of cancer. In addition, we did not consider ipsilateral and contralateral use of the cellular phones, which is beyond the scope of our study. Lastly, although we reported exposure-response relationships between the cellular phone use and

the cancer risk, it would be ideal to investigate those associations based on the actual time spent on cellular phones provided by the mobile telecommunication companies. However, most studies did not use those data. Further studies using the exact data on the time spent on cellular phones are warranted to confirm our findings.



## **5. Conclusions**

In sum, the updated comprehensive meta-analysis of case-control studies found significant evidence linking cellular phone use to increased tumor risk, especially among cell phone users with cumulative cell phone use of 1000 or more hours in their lifetime (which corresponds to about 17 min per day over 10 years), and especially among studies that employed high quality methods. Further quality prospective studies providing higher level of evidence than case-control studies are warranted to confirm our findings.

# Supplementary Materials

The following are available online at <https://www.mdpi.com/1660-4601/17/21/8079/s1>, Table S1: Methodological quality of case-control studies based on the Newcastle-Ottawa Scale (n = 46), Table S2: Methodological quality of case-control studies based on the National Heart, Lung, and Blood Institute quality assessment tool of case-control studies (n = 46), Table S3: Cellular phone use and risk of tumors in subgroup meta-analysis by type of tumor.

# Author Contributions

Conceptualization, S.-K.M. and Y.-C.H.; data curation, Y.-J.C., S.-K.M. and Y.-R.L.; formal analysis, Y.-J.C. and S.-K.M.; investigation, S.-K.M.; methodology, S.-K.M.; project administration, S.-K.M.; supervision, Y.-C.H.; validation, Y.-J.C. and S.-K.M.; visualization, Y.-J.C.; writing—original draft, Y.-J.C.; writing—review and editing, J.M.M., S.-K.M., Y.-R.L. and Y.-C.H. All authors have read and agreed to the published version of the manuscript.

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# **Conflicts of Interest**

The authors declare no conflict of interest.

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