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Exposure Misclassification in the Danish Mobile Phone Subscriber Cohort and its Influence on International Radiofrequency (RF) Radiation Cancer Risk Assessments

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Abstract

The Danish mobile phone subscriber cohort, updated in 2011, is one of the most frequently cited epidemiological studies concluding that mobile phone use is not associated with increased risk of brain tumors. Regulatory bodies routinely rely on this cohort as part of the evidence for null associations. However, the Danish cohort exhibits structural exposure misclassification and control group contamination that limit its ability to give information on health risks. The objective of this study was to critically examine methodological features, evaluate how they constrain inference regarding brain tumor risk, and document how the study was assessed in several international risk assessments. Methodological aspects, data on numbers of subscribers, minutes of mobile phone use over the cohort study period and incidence statistics of central nervous system (CNS) tumours were examined. We analyzed how the cohort's findings have been evaluated, critically analyzed and incorporated into major international risk assessments from the WHO, the EU and national expert groups.

Several structural limitations were identified: exposure classification restricted to pre-1996 private subscribers; misclassification of 200 507 corporate subscribers and all post-1995 users classified as "unexposed" leading to severe contamination of the unexposed group with exposed individuals; absence of individual usage data; DECT phone users classified as unexposed; insufficient window for slow-growing tumors. These factors bias the risks toward unity. Data from NORDCAN show increasing CNS tumour incidence in Denmark, which contradicts the findings in the cohort. Several expert evaluations have assessed the cohort as high quality evidence of absence of risk. The WHO commissioned review published in 2024 appears to be the assessment in which the cohort contributed most substantially to the overall results. Due to structural exposure misclassification and control group contamination, the Danish cohort cannot test associations between mobile phone use and brain tumor risk. The continued use of the study in international risk assessments bias overall results towards null. The study is scientifically flawed and is uninformative on health risks from mobile phone use.

Keywords: Radiofrequency electromagnetic fields; Brain tumours; Epidemiology; Exposure misclassification; Mobile phones

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Background

The Danish study on mobile phones and cancer is a cohort comparing cancer incidence among early mobile phone private subscribers in Denmark with the rest of the Danish population. First results of the cohort were published in 2001 [1], then in a second publication in 2006 [2] and the third last update was published in 2011 [3].

The Danish cohort study began as a collaboration between US and Danish scientists from the International Epidemiology Institute (IEI), Rockville, MD, USA, and the Danish Cancer Society. John D. Boice Jr. and Joseph K. Laughlin from IEI, were coauthors of the two first publications of the cohort, see [4,5]. The Danish Cancer Society was represented by Christoffer Johansen and Jørgen H. Olsen, with some additional authors in the second publication [2], among them Joachim Schüz, today Head of the International Agency for Research on Cancer (IARC) Department of Environment and Lifestyle Epidemiology including radiofrequency (RF) radiation. The cohort was established by grants from two Danish telecom companies (TeleDenmark Mobil and Sonafon), from IEI, and from the Danish Cancer Society [1]. IEI was an industry consulting firm that until October 15, 2000, listed "Corporate Counseling" and "Litigation Support" among its services (https://web.archive.org/web/20130325094914/http://www.cspinet.org/integrity/nonprofits/international_epidemiology_institute.html). Further, funding to IEI from Dow Corning had previously been documented for research on health issues related to Dow Corning's products [5].

The latest update of the Danish cohort, published in 2011 by Frei et al. [3], is frequently cited as the largest and methodologically strongest investigation of mobile phone use and is presented as evidence of no brain tumor risk. According to the journal's website it is in the top 5% of all research outputs in the journal, it has high attention score compared to outputs of the same age (99th percentile), and has been cited in 179 publications (Altmetric – Use of mobile phones and risk of brain tumours: update of Danish cohort study).

Aim of this study

A critical review of the Danish cohort study [6] was previously published. The aim of this study was to make an updated critical review of the 2011 cohort article [3], and an evaluation of the assessments of the Danish cohort made by various expert group's statements on cancer risks associated with exposure to RF radiation made between 2012 and 2025.

Methods

This article evaluates the methodological foundations by Frei et al. [3], including data on numbers of subscribers and minutes of mobile phone use over the cohort study period. Further, central nervous system (CNS) tumours incidence data for the Nordic countries was assessed from NORDCAN, a database of cancer statistics for the Nordic countries. We also document how the cohort's findings have been evaluated, critically analyzed, and incorporated into major international risk assessments made by the WHO, the EU and several national expert groups.

Design of the Danish cohort

According to the authors the entire Danish adult population was divided into mobile phone subscribers and non-subscribers. The exposed group in the cohort comprised Danish individuals who subscribed to private mobile phone services between 1982 and 1995. For the Frei et al 2011 version [3], subscribers from 1987 to 1995 were included. Subscriber lists were obtained from the two Danish telecom operators; 723 421 subscribers during 1982 and the end of 1995 were initially identified. However, many subscribers during that time period were excluded, in particular 200 507 corporate users who most likely were the heaviest users of mobile phones.

Table 1 shows numbers of included and excluded subscribers from the cohort published in 2001 [1], and 2011 [3]. See also Figure 1 displaying the included and excluded subjects in the 2011 cohort. Of the private subscribers in the initial cohort only 0.9 % were subscribers the first three years, 1982-1984, while 69.1 % became subscribers during the last two years of the inclusion period, 1994-1995. Thus there was limited time period in the cohort for brain tumour induction.

Table 1: Number of included and excluded subscribers in the Danish cohorts published in 2001 [1] and 2011 [3].

	2001	2011
Total number	723421	723421
Excluded		
-Corporate users	200507	200507
-Errors in name or address	59535	59535
-No residential address	11687	11687
-Duplicates	10679	10679
-Subscritption after 1995	17921	17921
-Under age 18	2550	2550
-Residency in Greenland/Faroe Islands	394	394
-Refusal	53	53
-Other problems in data identified later		9
-Exclusion eligibility criteria		54350
-Excluded cancer cases		3117
-Censored before subscription		4216
Total excluded	303326	365018
Remaining	420095	358403
	58.07%	49.54%

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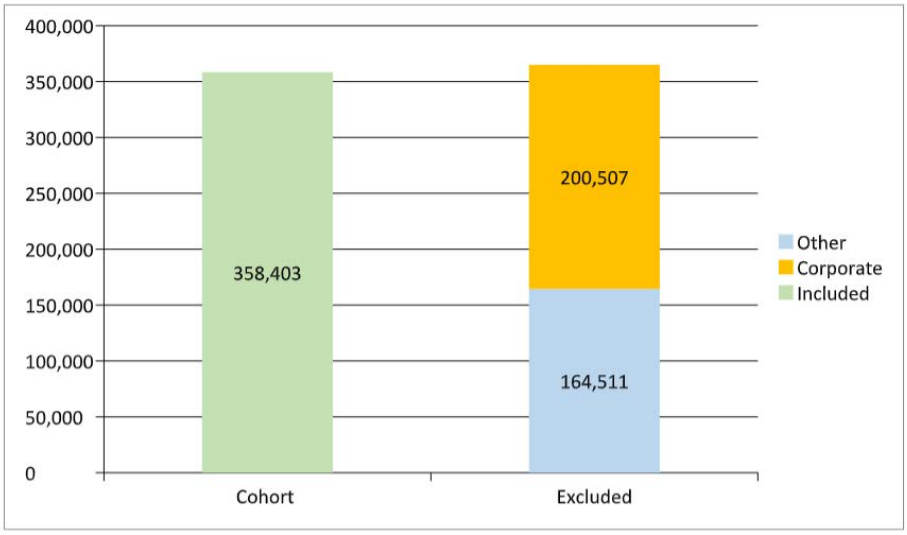

Figure 1: Numbers of included and excluded persons in the subscription records between 1982 and 1995 in the Danish cohort study 2011 [3].

The included individuals in the cohort were linked to a national register of the Danish population. Cancers among the included persons were obtained from the Danish Cancer registry based on the personal identification numbers. Their incidence rates of cancer were investigated through 1996 in the 2001 publication [1], through 2002 [2] in the 2006 publication, and through 2007 in the 2011 publication [3]. For the 2011 version of the cohort the included private subscribers´ incidence rates of cancer were compared with a population cohort, CANULI that included 3.21 million Danes aged 30 years or older.

Systematic errors

The Danish cohort [3] has severe and obvious systematic errors due to substantial misclassification of exposure and lack of information on real exposure. Table 2 describes the main problems:

- Exposure was defined for the included individuals as years from first subscription to a private mobile phone plan between 1987 and 1995 in Frei et al. [3]. Thus, first subscription was used as proxy for exposure. No information was collected on how many years the individuals actually held the subscription.

Table 2: Methodological aspects on the Danish cohort study on mobile phones and brain tumour risk in [3].

Design feature	Methodological issue	Mechanism of bias	Likely direction of bias
Exposure defined as years from first subscription to a private mobile phone during 1987 and 1995 [3]. Follow-up 1990-2007 for cancer.	Dichotomous exposure definition based on first subscription at one time before 1996 only. Rapid increase of subscribers and minutes of use among the population after 1995 reaching 100.4 subscriptions/100 people in 2005.	Individuals who initiated mobile phone use after 1995 are classified as unexposed despite subsequent increasing exposure. Reference group increasingly contaminated by subscribers of mobile phones.	Substantial non-differential misclassification leading to attenuation of incidence rate ratios towards the null.
Exclusion of large number of heaviest users (corporate subscriptions; n=200 507), and parts of private subscribers until 1995 (see Table 1).	Misclassification of users as unexposed.	Half of exposed individuals (n=365 018; 50.5 %, including heaviest users) are included among “unexposed”.	Substantial non-differential misclassification of exposure, bias risk estimates towards null.
Use of years since first private subscription as proxy for exposure.	No data on usage patterns, years of use, hours of use per week, cumulative hours of use, or the real user of the phone, no assessment of hands-free device, or use in a car with external antenna. Only years since first subscription analyzed.	Large heterogeneity in RF exposure within exposure category. True high-dose users not separable from low-dose users. The real user of the phone is unknown. No data on individual usage.	Reduced opportunity to detect the true risk. Biased risk towards null and limited statistical power to analyze dose response relationships. Years since first subscription was used as surrogate for latency.

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DECT phone users considered to be unexposed.	Misclassification of unknown number of exposed as unexposed.	The "unexposed" group includes DECT phone users exposed to RF radiation.	Non-differential misclassification of exposure. Risk estimates biased towards null.
No information on body localization of use (e.g., side of head).	Inability to assess site-specific dose, i.e. ipsilateral *vs* contralateral use including anatomical part of the brain during use of the mobile phone.	Localized RF exposure in the brain not assessed.	No ability to detect risk in most exposed part of head.
Limited latency window.	Insufficient induction time for long-latency malignancies [3].	For glioma only 117 men and 10 women with subscription ≥ 10 years, for meningioma only 21 men and 8 women with subscription ≥ 10 years in [3].	Underestimation of long-term risk.

- All subscribers after 1995, including heavy users, were included in the control group and were treated as unexposed. After 1995 the number of subscriptions increased rapidly in Denmark. By 2005 there were 100.4 subscriptions per 100 people in Denmark. (Source: Tele Year book 2006, IT- og Telestyrelsen, Denmark). Among the individuals who started using mobile phones after 1995 many could have been exposed up to 11 years but they were included in the unexposed group. This severe lack of sound methodological methods is illustrated in Tables 2,3 and Figure 2. In addition, exposure time increased rapidly after 1995, also contributing to increasing exposure in the control group. Table 3 and Figure 3 show outgoing minutes per year (in 1000) between 1987 and 2006. This is substantial misclassification of exposure and drives the results towards null.

Table 3: Outgoing mobile phone minutes (in 1000) per year, number of subscriptions per year, and subscription minutes per week during 1987-2006 in Denmark. Source: Tele Year book 2002 and 2006. IT-og Telestyrelsen, Denmark.

Year	Total outgoing minutes in 1000	Total number of subscriptions	Minutes per subscription per week
1987	81810	795230	22
1988	127730	1019030	27
1989	153310	1237920	26
1990	180216	1482200	25
1991	222464	1759430	26
1992	264120	2110630	26
1993	309164	3575890	21
1994	441971	5035000	20
1995	564189	8222640	16
1996	978601	13165920	18
1997	1301430	14440160	18
1998	1571919	19311010	18
1999	2104369	26285850	18
2000	2599586	33635520	17
2001	2884680	39601650	15
2002	3482066	44777520	16
2003	4163673	47671000	17
2004	5152448	51669120	19
2005	6477986	54492060	23
2006	7566317	58304790	25

- Exclusion of the supposedly most exposed group during 1987-1995, consisting of 200 507 corporate subscribers of mobile phones, represents misclassification of exposure. Instead, they were treated as unexposed and included in the control group. Corporate users during the study period on average used mobile phones considerably more than private subscribers due to high prices for mobile phone use. Data from the Swedish Telecommunication Agency (PTS), as an example, show that in 1999 corporate subscribers used the mobile phone for outgoing calls on average 188 minutes per month while a private subscriber used it 31 minutes per month. During the following years, 2000 – 2005, corporate subscribers also used the mobile phone substantially more on average than private subscribers, see Table 4. Data on corporate subscriber use compared with private subscriber use in Denmark for the period relative to the cohort study period is not available. It is reasonable to assume that differences between corporate and private users similar to those observed in Sweden also existed in Denmark. The corporate users would therefore constitute the most interesting user group to study for cancer risks. In addition 164 511 private subscribers were excluded for other reasons, see Table 1. This is substantial misclassification of exposure that drives the results toward no association.
- No investigation was made of how much the phone was used per day or per week, nor cumulative total time of exposure (only years since start of first subscription without information on the actual use or the user of the mobile phone). No separation was made between people who used the phone only occasionally and those who

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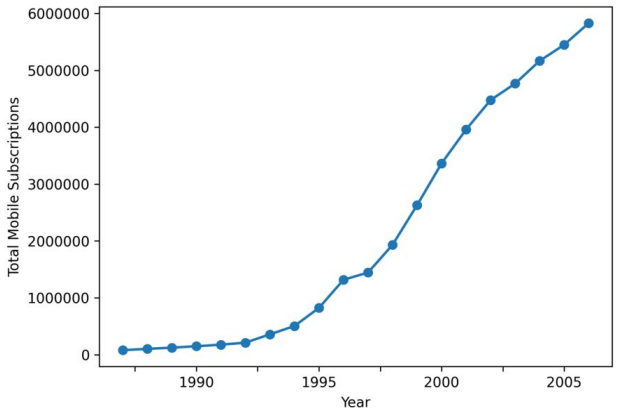

Figure 2: Number of mobile phone subscriptions per year in Denmark 1987-2006. Source: Tele Year book 2002 and 2006. IT- og Telestyrelsen, Denmark.

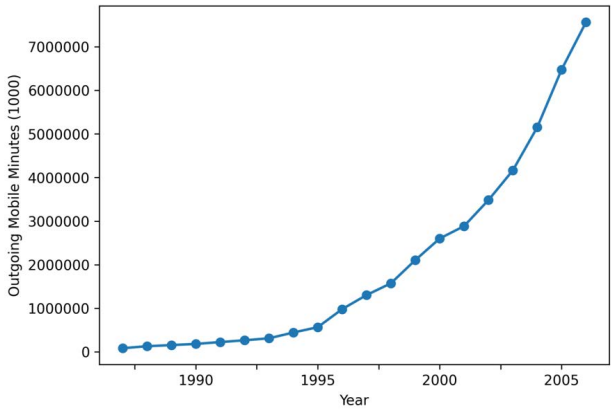

Figure 3: Outgoing mobile phone minutes (in 1000) per year in Denmark 1987-2006. Source: Tele Year book 2002 and 2006. IT- og Telestyrelsen, Denmark.

might have been heavy users. This contributes further to the cohort's reduced ability to detect real risks. The use of mobile phones per subscriber during 1987 to 1995 was low in outgoing minutes per subscriber, see Table 3. Also the included private subscribers can be assumed to have used the phone even less, since the average time per subscription according to the Tele Year Book (It- og Telestyrelsen Denmark), includes corporate subscribers that likely used the mobile phone substantially more than private subscribers. This aspect is important given that large case-control studies with individual exposure assessment have reported highest increased risk in the heaviest user group, i.e. totaling over 896 to 1640 cumulative hours of use, see Table 2 in [5].

- All use of cordless (DECT) phones was disregarded, although they also give exposure to similar RF radiation as from mobile phones. The Hardell group has shown that also use of cordless phones is associated with increased risk for glioma and acoustic neuroma [7,8]. This neglect contaminates the control group further with exposed individuals contributing to bias the results downward.

Table 4: Average mobile phone outgoing minutes for private and corporate subscribers per month, Sweden 1999-2005. Source: Svensk Telemarknad 2005, Post- och Telestyrelsen, PTS, Sweden.

Year	Minutes/month corporate	Minutes/month private
1999	188	31
2000	197	40
2001	187	39
2002	193	41
2003	199	39
2004	189	42
2005	198	67

- No analysis of laterality (the side where the phone is hold in relation to the localization of the brain tumor) was performed, thereby giving no ability to detect increased risk related to highest exposed part of the head.
- The latency (tumour induction time) in the cohort was limited. The time interval between exposure and tumour detection is crucial. For solid tumours long latency times, even decades, have been observed. Thus, for glioma and use of wireless phones highest risk was seen in the group with longest latency time, more than 20 years, see [7]. In Frei et al. [3] no subject had time since first subscription >20 years; further, data on real use (exposure) was unknown.

These errors entail that the authors of the article [3] did not compare cancer risks in mobile phone users versus non mobile phone users but rather a group of 358 403 mobile phone early subscribers likely to be on average light users but with unknown exposure, versus a mixed group of subscribers and non-subscribers with unknown exposure. The comparison group included the 200 507 heaviest early subscribers together with over time a rapidly increasing number of subscribers. The "unexposed" group actually included, to a large extent, exposed subjects leading to collapsed exposure contrast between the groups. These facts drive incidence rate ratios toward unity and make valid short term or long term risk detection methodologically impossible.

The results

The results of the 2011 updated Danish Cohort [3] were the following for tumours of the central nervous system as presented by the authors. The incidence rate ratios (IRR) were close to 1.0:

- Risk of tumours of the central nervous system for subscribers: IRR = 1.02, 95% confidence interval (CI)

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= 0.94-1.10 (men), IRR=1.02, 95 % CI = 0.86-1.22 (women).

- Longest time of subscription ≥13 years: IRR = 1.03, 95 % CI = 0.83 -1.27 (men), IRR = 0.91, 95 % CI = 0.41 -2.04 (women).
- For glioma ≥10 years subscription IRR = 1.04, 95 % CI = 0.85 – 1.26 (men), IRR = 1.04, 95 % CI = 0.56 – 1.95 (women).
- For meningioma ≥10 years subscription IRR = 0.90, 95 % CI = 0.57-1.42 (men), IRR = 0.93, 95 % CI = 0.46-1.87 (women).
- No indication of dose-response relation by years since first subscription

The incidence rate trends

The authors argue that "incidence rates for glioma after the introduction of mobile phones rule out mobile phones as a strong independent risk factor" [3] referring to four articles: two on incidence trends of brain tumours in Nordic countries covering periods only between 1974-2003 and 1969-1998, one study on incidence in Switzerland 1969-2002 and one on incidence 1992-2006 in USA [9-12].

However, data available in Nordcan (www.nordcan.iarc.fr) contradicts the results of the Danish Cohort study [3]. When studying the incidence rates of tumours in the brain and the central nervous system from 1995 to 2023 a clear increasing incidence trend in Denmark is observed, both among men and women, see Figures 4 and 5. It should be noted that data on increasing CNS tumour incidence in Denmark until 2008 was reported in the Danish Cancer Registry report published in December 2009. CNS tumours increased by 14% between 1999 and 2008 and by 23 % between 2003 and 2008 in men, and by 33% between 1999 and 2008 and by 39% between 2003 and 2008 among women, see table 1 in: (https://cdn1.gopublic.dk/sundhedsdatastyrelsen/media/16542/Kraefttilfaelde%202008.pdf). Data on increasing incidence in Denmark was clearly available by the time that the Frei et al. 2011 article [3] was submitted for publication, accepted 12 September 2011.

Data in Figure 5 from Nordcan also illustrates the considerable variation between the incidences in the Nordic countries. The combined Nordic incidence trends are biased downwards by the Swedish Cancer Registry with deficient registration of brain tumor cases shown by comparison with the hospital register data [13,14]. It is also to be noted that the Norwegian incidence curve indicates e.g., a shift of reporting routines. The scientific correct comparison would have been between the Danish cohort results and the Danish Cancer Registry incidence data.

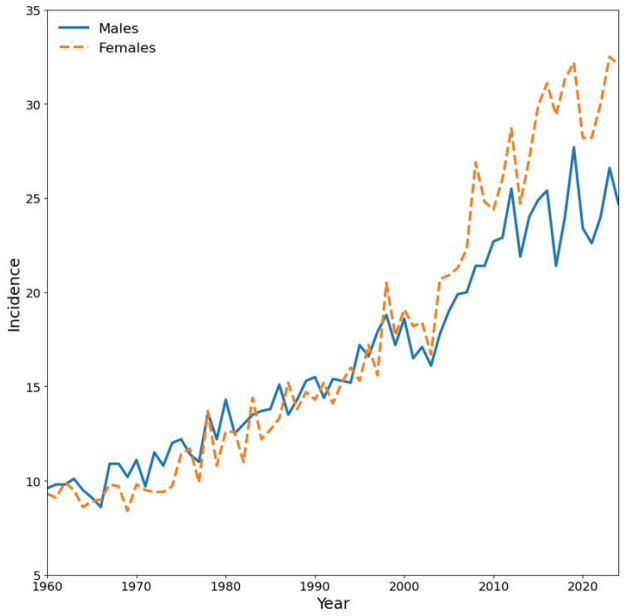

Figure 4: Incidence of central nervous system tumours per year and per 100 000 inhabitants, males and females in Denmark 1960-2023. Age standardized to Nordic 2000 data.

Source: nordcan.iarc.fr.

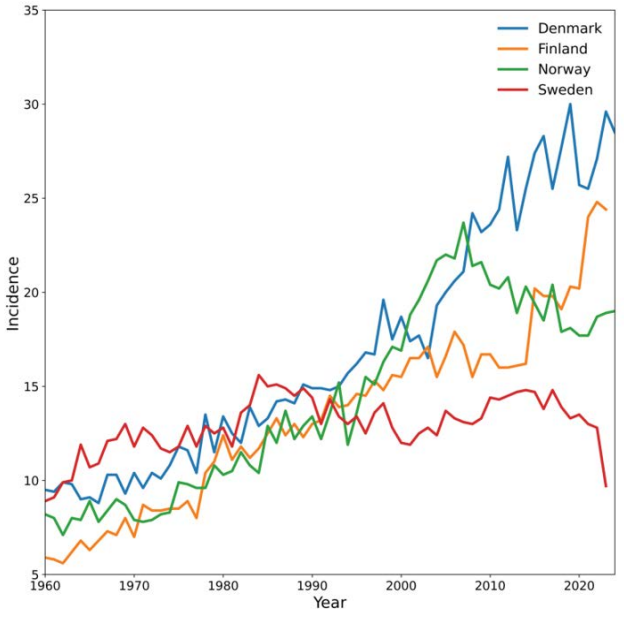

Figure 5: Incidence of central nervous system tumours per year and per 100 000 inhabitants, both sexes, in Denmark, Finland, Norway, Sweden, 1960-2023. Age standardized to Nordic 2000 data. Source: nordcan.iarc.fr.

Study assessment in expert reports

The Danish cohort study published in 2011 has been incorporated into assessments by different groups. We analyze in the following the overall assessments, and the conclusions. The reports analyzed are: the UK AGNIR 2012 report [15],

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the Swedish Radiation Safety Authority's Expert (SSM) report 2013 [16], the EU Commission's SCENIHR opinion report 2015 [17], The Health Council of the Netherlands reports 2013 and 2016 [18,19], the WHO commissioned report by Karipidis et al. 2024 [20], and the French ANSES report 2025 [21].

UK AGNIR 2012 [15]

Overall assessment of the Danish cohort: The AGNIR notes that the use of only private subscribers may lead to misclassification of exposure and that the subscriber may not be the user. This leads "to a dilution of the risk estimates should a true risk exist, but is not expected to lead to spurious increased or decreased risk estimates", see page 8 in (RCE-20_Health_Effects_RF_Electromagnetic_fields.pdf).

The exclusion of the corporate users is mentioned but not that they were the likely heaviest users. The authors argue that it "will affect the risk estimates only marginally" and that this misclassification would not explain the results of the study. It is also noted that the control group was contaminated by mobile phone users after 1995.

AGNIR concluded that the results on long-term mobile phone users are "informative" but not the results on short-term users due to the fact that a "considerable proportion of the comparison population will also be short-term mobile phone users."

Conclusion in [15]:

Methodological problems occur in subscriber based cohort studies which contribute to uncertainty of results. Cohort studies and cancer incidence trends "give no indication" of increased cancer risks from mobile phone use. "In conclusion, despite methodological shortcomings, the available data do not suggest a causal association between mobile phone use and fast-growing tumours such as malignant glioma in adults."

Swedish Radiation Safety Authority (SSM) 2013 [16]

In the overall assessment of the Danish cohort SSM argues that the Frei et al [3] results are "informative" regarding exposure duration but not as informative for the cumulative use of mobile phones "since non-subscribers may have caught up in exposure in the meanwhile." It is proposed that the misclassification of a substantial part of the initial cohort as unexposed would lead to only marginal effect on the result in terms of a "small underestimation" of potential risks, by referring to an article by Ahlbom et al. [22]. SSM also referred to Söderqvist et al. 2012 [6] critique of the cohort, among others the lack of data on amount of use.

Further, the authors of the 2013 SSM report argue that "most importantly, the subscriber group is not diluted by non-subscribers, and therefore, the hypothetical increased cancer rate in this group is estimated in an unbiased way", see [16].

According to this report the cohort makes "an important contribution to the total assessment in the field" and "added value to overall evidence by using objective exposure data that is not biased". Further, that the cohort has a "long period of follow-up which allows addressing long term exposure effects"

Conclusion in [16]:

No indication of effect of mobile phone use on tumour risk in particular in view of the cancer incidence data.

SCENIHR 2015 [17]

Overall assessment of the cohort: It is noted that "misclassification of exposure is of concern" since only private subscribers identified by name were included and no information is available on amount of use. Therefore risks with intensive use were not possible to assess which may lead to underestimation of risks from heavy use. Further, cordless phone use was disregarded.

The report stresses that the incidence rates of brain tumours do not increase which would provide evidence that normal mobile phone use is "unlikely" related to brain tumour increased risks. Further, the authors argue that incidence rates are "confirmed by the Danish cohort study that rules out risks that would affect large segments of the population."

Conclusion in [17]:

Epidemiological studies are claimed to not show an increased risk of brain tumours or an indication of increased risk for other cancers in head or neck region. "The results of cohort and incidence time trend studies do not support an increased risk for glioma while the possibility of an association with acoustic neuroma remains open."

Note:

The section on mobile phone use and brain tumor risks was drafted by one of the authors of the Frei et al. [3] article, Joachim Schuz.

Health Council of the Netherlands 2013, 2016 [18,19]

Overall assessment of the cohort: The study was given high quality score (7.9), among the highest in the evaluation. The Interphone [23] large case control study on brain tumours was given 6.6, as a comparison.

The cohort is presented as "The most important cohort study" but the authors note that the corporate users, potentially heavy users, were included in the unexposed group. Further, it

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is noted that no information on actual exposure was assessed and that the unexposed comparison group in the Frei et al. article [3] is "clearly not unexposed anymore as an estimated 100% of the Danish population currently uses mobile phones and many have been doing so for over 10 years since subjects included in the control group might have started their subscription as early as 1996". However the report argues that the effect of the misclassification of the results is minimal due to the misclassification being limited to the unexposed comparison group.

Conclusion in [18,19]:

Epidemiological results show "some weak indications" for increased risks related to intensive prolonged use of mobile phones and an association cannot be excluded. "The Committee considers it unlikely that exposure to radiofrequency fields, which is associated with the use of mobile telephones, causes cancer."

WHO-commissioned review 2024 [20]

Overall assessment of the cohort: Results from the Danish cohort study were included as evidence of no risk regarding risk of glioma from ever or regular mobile phone use, time since first use, or risk in long term users.

The evaluated studies were classified in three groups based on risk of bias. Tier-1 comprised studies with definitely or probably low risk of bias for all key items and most of other items; tier-3 included studies with definitely or probably high risk of bias for all key items and most of other items; and studies not meeting the above criteria were classified as tier-2. This ranking was used to assess the overall potential for bias in the body of evidence at the stage of quality of evidence assessment.

Table 5 is an extract from Table 7 in Karipidis et al [20] on assessment of risk of bias in Frei et al. [3] and Hardell, Carlberg [7].

It is unclear why attrition/missing data and exposure characterization in the Danish cohort study were not assessed by Karipidis et al. [20]. An objective evaluation would have been "probably high" risk of bias.

Frei et al [3] was given an overall relatively high, 20.48%, weight in the pooled result on glioma risk for ever/regular user, MA5 (main meta-analyses for glioma, meningioma, and acoustic neuroma) weight. This was much higher than for case-control studies, e.g. Interphone [23] 12.95%, and Hardell, Carlberg 2015 [7] 11.51%, see Figure 2 in Karipidis et al [20]. For glioma risk related to mobile phone use 10+ years, Frei et al [3] was given high weight, 7.55%, compared with case-control studies, 1.66% to 5.76%, see Figure 3 in [20].

Conclusion in [20]:

Karipidis et al. [20] concluded: "For near field RF-EMF exposure to the head from mobile phone use, there was moderate certainty evidence that it likely does not increase the risk of glioma, meningioma, acoustic neuroma, pituitary tumours, and salivary gland tumours in adults, or of paediatric brain tumours."

ANSES 2025 [21]

Overall assessment of the cohort: The cohort is argued to have a "solid" methodology and to be particularly informative on the risks related to duration of use. However, it is noted that the study does not permit to separate heavy users from light users and that the results based on years may be too short observation time if there are long term risks. The cohort studies are argued to contribute substantially to the level of evidence.

Conclusion in [21]:

Cohort studies do not report an excess risk of glioma but the evidence is equivocal: "the available evidence (derived

Table 5: Karipidis et al [20] assessment of risk of bias in Frei et al [3] and Hardell, Carlberg [7].

Risk of bias assessment	Results	
	Frei et al 2011	Hardell, Carlberg 2015
Selection	Definitely low (++)	Probably high (-)
Attrition/missing data	N.A*	Probably high (-)
Exposure characterization	N.A.*	Probably high (-)
Outcome	Definitely low (++)	Definitely low (++)
Confounding	Probably low (+)	Probably low (+)
Selective reporting	Definitely low (++)	Definitely low (++)
Statistical methods	Definitely low (++)	Definitely low (++)
Summary bias tier	1	2

*N.A. = not assessed

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from good-quality data or data with minor methodological limitations) does not allow one to conclude either that radiofrequencies have an effect or that they have no effect on the risk of glioma."

Discussion

The Danish cohort is structurally incapable of providing information on risks for brain tumours from mobile phone use due to:

- misclassification of many potentially high-exposure individuals that were included into the "unexposed" category
- rapid increasing contamination of the "unexposed" group over time due to inclusion of people starting the use of mobile phones after 1995
- inability to measure actual exposure
- first subscription used as proxy for exposure
- inability to separate high exposure individuals from low exposure individuals in the exposed group
- insufficient latency (tumour induction time)
- no analysis of the risk in the part of the brain with highest RF radiation exposure
- no assessment of use of cordless phones (DECT)

Despite wide citation, the Danish cohort could not by its design, investigate actual RF exposure levels, nor differentiate users from non-users, and high exposure individuals from non-exposed individuals. The exposure classification used only time since first private subscription instead of actual mobile phone use. In spite of the unknown exposure among the included persons in the cohort, the authors repeatedly use the term "exposure" throughout the article, which is misleading.

The control group was from the start contaminated by corporate users, cordless phone users, and increasingly by new mobile phone users after 1995. These features raise questions about the study's validity as evidence addressing RF carcinogenicity. It is particularly non-informative regarding potential risks with the amount of use that has become prevalent today, when mobile phones are used for conversations which may amount to several hours per day.

The authors of the Frei et al [3] report have not analyzed the impact on the study's result of the excluded corporate users incorporated into the control group and the increasing number of mobile phone users in the "unexposed" group. It is not unlikely that data on average mobile phone use by private subscribers and corporate subscribers could have been obtained from the two companies that provided the data for the cohort to the investigators. The authors only note that corporate users were misclassified as unexposed and that users that got subscription after 1995 were classified as non-users.

Rather the authors [3] chose to refer to Danish statistics on average use between 1987 and 2002 as an argument that the cohort had included heavier users than the subscribers excluded after 1995: "Interestingly, we found indications that early subscription holders before 1995 were in fact heavier users (based on outgoing calls) compared with all subscription holders in the years 1996-2002. The weekly average length of outgoing calls was 23 minutes for subscribers in 1987-95 and 17 minutes in 1996-2002."

The same source, as they referred to, provided data on rapidly increasing numbers of subscribers after 1995 and outgoing total mobile phone minutes, see Table 3 and Figures 2 and 3, as well as subscriptions per 100 inhabitants. In a paper on Nordic glioma incidence trends [24] by some coauthors of the Frei et al 2011 [3] article, i.e., J. Schuz, and C. Johansen, it is noted that in 2005 the Nordic countries had more than one subscription per inhabitant. In Denmark there were 100.4 subscriptions per 100 persons in 2005, but the authors did not highlight this increasing contamination of the control group in the Frei et al article [3].

Further, it is likely that the excluded corporate subscribers represented most of the average mobile phone outgoing minutes referred to between1987-1995. According to Swedish data, private subscribers used the phone for outgoing mobile phone calls ranging from 31 minutes per month in 1999 to 67 minutes per month in 2005. The corresponding data for corporate subscribers were 188 minutes and 198 minutes, respectively. Under the assumption that the Swedish ratio between private and corporate outgoing mobile phone minutes was applicable to the cohort, the average outgoing minutes among the included private subscribers during the inclusion period would be limited for Denmark, see Table 3.

Also noteworthy is that the authors of the cohort have not referred to the Danish statistics on CNS tumours incidence data, but the combined Nordic data (Denmark, Norway, Sweden and Finland). As shown in Figure 5 there are large differences between the countries. Clearly the incidence is highest in Denmark with highest increasing trend, see Figure 4.

Some of the authors of the Frei et al article concluded in 2022 [25] that "This study confirms and reinforces the conclusions that no changes in glioma incidence in the Nordic countries have occurred that are consistent with a substantial risk attributable to mobile phone use" and that "Our analyses of mobile phone use patterns and incidence trends of glioma in the Nordic countries during 1997–2016 among men aged 40–59 years indicate that the population rates of glioma were not compatible with increased risks from mobile phone use'

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and further that 'no increased glioma risk was reported in the Danish early mobile phone subscribers cohort". Deltour et al [25] based these general conclusions for the whole population on a limited study on men in the age group 40-69 years.

The reviews

None of the expert group reports have analyzed the amount of use by the corporate subscribers compared with the private subscribers. Several of the reports did highlight the misclassification of exposure in terms of increasing subscribers as well as corporate users and others that were included in the control group.

The Swedish SSM [16] referred to an article by Ahlbom et al. [22] and argued that the relative risk would be only 'marginally biased' by the misclassification. The misclassified group included 200 507 subscribers in the Danish cohort, likely the heaviest users. The "unexposed" comparison group increasingly contained many users during 1996–2007 (high penetration). Exposure was fixed at first subscription despite changing real world use. These points all give substantial attenuation of the risk toward the null.

SSM also refers to an accompanying editorial to the Frei et al, 2011 article [3] signed by Ahlbom and Feychting [26]. In their article Ahlbom and Feychting made most remarkable statements: …"more case-control or other studies with built in selection and recall bias are not needed".. and 'The search for an association between mobile telephone use and cancer risk …did not originate from a particular biophysical hypothesis or results of a seminal study but from a concern that some aspect of the interaction between radiofrequency fields and human physiology has been overlooked or misunderstood'. Initiated by a case report on brain tumours among mobile phone customers [27], our research group made a case-control study. It was to our knowledge the first in the world and indicated an increased risk for brain tumours associated with ipsilateral use of the mobile phone (same side as the tumour). It was published in 1999, that is more than two decades ago [28]. Further, research during the 1990's showed increased DNA-damage from RF-radiation as well as increased lymphoma risk in mice, which contributed to research projects being launched to investigate cancer risks from RF-exposure [29,30].

Most astonishing is the WHO commissioned analysis of the cohort by Karipidis et al. [20] that gave the cohort a high weight in the overall assessment and considered it to have definitely low or probably low risk of bias on most evaluated methodological aspects. As discussed previously there is no scientific basis to conclude that there was no selection bias in the Danish cohort study. Moreover, Karipidis et al [20] did not evaluate the risk of bias for "exposure". An objective assessment would give it "definitely high" since no assessment of individual exposure was made, leading to substantial misclassification of exposure. No individual, or "exposed" versus "non-exposed" exposure data exist in the Danish cohort study.

Most reviews underline that the cancer incidence trends do not show increased incidence trends. However, while some countries do not show increased incidence trends others do, for instance Denmark and Finland, see Figure 5. Data from UK show increasing incidence of glioblastoma [31]. Underreporting of brain tumours to the Swedish Cancer Registry was reported while increasing rates were observed based on the Swedish National Inpatient Register and the Causes of Death Registry [13,14]. It should be noted that these studies from UK and Sweden indicating increasing incidence of glioma were omitted by Karipidis et al [20].

Certainly as, discussed above, the high weight given to the Danish cohort study by Karipidis et al. [20] is not scientifically correct or defensible due to major epidemiological limitations and shortcomings in the study design and interpretation of the findings. Furthermore, it is remarkable that several other scientific bodies, in spite of acknowledge of the problems with exposure misclassification and unknown real exposure in both the "exposed" and the control group, have given the cohort a positive evaluation and incorporated the cohort into their overall assessments.

The Danish cohort is structurally incapable of detecting potential increased risks for brain tumours from mobile phone use. Therefore a null result cannot be interpreted as evidence of absence of risk. Its continued predominance in risk evaluations has contributed to the questions raised against the results of increased brain tumour risk seen in case–control studies.

This raises broader concerns: if a methodologically weak cohort is used as the defining evidence for safety, regulatory decisions may be grounded on biased or even false information.

Conclusions

Despite wide citation, the Danish cohort study [3] was not designed to distinguish actual RF exposure levels or to differentiate users from non-users. The exposure classification used time since first private subscription rather than mobile phone use and it excluded the heaviest users and an increasing number of new subscribers, which were included in the control group. These features raise questions about the study's validity to evaluate RF radiation carcinogenicity.

Danish brain tumour incidence data showing increasing trends are not compatible with the Danish cohort's results of no brain tumour risks associated with use of mobile phones.

The cohort has substantial and obvious systematic errors that undermine the possibility to evaluate associations

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between RF radiation exposure and brain tumors. Its frequent use in international risk assessments is therefore not methodologically justified. It provides no scientific correct and valid information on health risks associated with use of wireless phones.

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Availability of data and materials

The information generated and analyzed during the current study is available from the corresponding author on reasonable request.

Authors' contributions

Both authors participated in the conception, design and writing of the manuscript, and have read and approved the final version

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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